Appendix B. Data extraction of methodological handbooks

Table B1 ACP Update of Methods

Guideline identification	
Organisation	American College of Physicians (ACP)
Year	2019
Country	USA
URL	10.7326/M18-3290 / https://doi.org/10.7326/M18-3290
Title of the publication	The development of clinical guidelines and guidance statements by the Clinical Guidelines Committee of the American College of Physicians: Update of Methods.
Summary/Overview	This peer-reviewed article outlines at a high level the policies, methods, and presentation format of the American College of Physicians' (ACP) clinical guidelines and guidance statements. It covers the process for selecting topics, developing key questions, and appraising evidence to formulate recommendations. It also discusses the ACP Clinical Guidelines Committee's (CGC) approach to managing conflicts of interest, incorporating patient values and preferences, and adopting GRADE methods. Considerations relating to resource implications, such as cost-effectiveness and budget impact analysis, planning and implementation, and monitoring and evaluating implementation are not covered. ACP do not conduct systematic reviews, instead relying on external sources, such as the Agency for Healthcare Research and Quality Evidence-based Practice Center or a Cochrane Centre.
RQ1: Description of core elements of clinical practice guidance	
What core elements have been stated in the document?	**Disclosure of interests and management of potential conflicts** ▪ The policy emphasises full disclosure of all healthcare-related interests for CGC members; CGC Public Panel members; relevant ACP staff; and any other persons involved in development of clinical guidelines, guidance statements, or evidence reviews. ▪ Participants disclose all financial and intellectual interests from the past three years, and an oversight panel consisting of ACP staff and the CGC chair and vice chair reviews the disclosures for conflicts of interest and determines management. ▪ The panel grades potential conflicts of interest as high, moderate, or low, and members are restricted from participation according to the conflict grade (restrictions may include recusal from authorship, voting, or discussion pertaining to recommendations). ▪ An author of a recent and relevant evidence review, regardless of whether it directly supports the guideline under consideration, cannot author the guideline or vote on recommendations. Participant disclosures and conflict management summaries for each CGC meeting are posted publicly online and linked to in CGC publications. **ACP produced clinical guidelines and guidance statements** ▪ ACP clinical guidelines and guidance statements address prevention, screening, diagnosis, and treatment of various diseases relevant to internal medicine. ▪ Guidance statements differ from clinical guidelines in several respects: o ACP clinical guidelines are developed through a de novo systematic evidence review that is specifically done for or used by ACP. o Guidance statements are developed on topics where several conflicting clinical guidelines are available. Guidance statements aim to reconcile existing clinical guidelines to help clinicians provide evidence-based care for their patients by rigorously reviewing the available guidelines and their

	evidence base and developing subsequent guidance statements based on an assessment of the reported benefits, harms, costs, and patient preferences and values from the existing guidelines and their evidence. o Unlike recommendations in clinical guidelines, the guidance in guidance statements is not derived from a de novo systematic evidence review that was specifically conducted for or used by ACP (that is, ACP is not directly involved with the topic development, key question or PICO refinement, or outcome rating), and hence the CGC does not use GRADE to assess the certainty of evidence or strength of recommendations. o As such, guidance statements are typically not suitable for the development of performance measures. **Selection and scope of topics and target audience for clinical guidelines and guidance statements** ▪ Topic ideas come from ACP members, CGC members, and other ACP committees and governance. ▪ In selecting a topic, the CGC considers the following characteristics of a condition: o its effect on morbidity and mortality, its prevalence and impact, o whether effective healthcare alternatives are available, o areas of clinical uncertainty, o evidence that current performance does not meet best practices, o cost and resource implications, o available management options, o the likelihood that evidence is available to develop recommendations, and o relevance to internal medicine and its subspecialties. ▪ For guidance statements, it is also necessary to ensure the availability of guidelines produced by other organisations. **Development and approval process for guidance statements** ▪ The guidance is based on an evaluation of the recommendations and evidence included in the selected and most highly-rated clinical guidelines (according to the AGREE II instrument). ▪ In developing the guidance, the CGC does not simply adopt recommendations from the guidelines with the highest AGREE II scores. Rather, it assesses the evidence base informing these recommendations and independently assesses benefits, harms, costs, and patient values and preferences. ▪ The CGC public members help to inform patient values and preferences by participating in the discussion during meetings, and the Public Panel provides further input by reviewing and commenting on the guidance statement. ▪ The final result is adoption or adaptation of the existing high-quality clinical guidelines. **Development and approval process for clinical guidelines** Key questions and scope ▪ The CGC and Clinical Policy staff assess the nature, quality, and quantity of evidence before commissioning an evidence review to support a new guideline. ▪ When proceeding with a new guideline, the assigned CGC topic subgroup, with input from a technical expert panel, drafts or revises the initial key questions and determines the PICO of interest, which are presented to the full CGC for feedback and approval.

	Evidence reviews ▪ All ACP clinical guidelines are based on systematic reviews of evidence, which are derived from several sources. ▪ The CGC may: o commission an evidence review directly from an external evidence review group, such as an Agency for Healthcare Research and Quality Evidence-based Practice Center or a Cochrane Center; o nominate a topic to the Agency's Effective Health Care Program for an evidence review conducted through the Evidence-based Practice Center Program or use an existing review; or o use an evidence review done by the Veterans Affairs Evidence Synthesis Program. ▪ A technical expert panel is convened to inform the evidence review and assist in refining the scope and PICO, as well as to provide clinical guidance for the review via e-mail and conference calls. Rating outcomes ▪ The CGC and CGC Public Panel independently rate outcomes according to criteria from the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) working group to consider in the evidence reviews and clinical guidelines via online surveys. ▪ Outcomes are categorised as critical, important, or not important for decision making. Those rated as critical are considered the most crucial for making recommendations and carry more weight in decision making than those rated as important. Determining certainty of evidence (Quality of Evidence) ▪ The evidence review team and the CGC use GRADE to rate the certainty of evidence for each critical and important outcome and for the overall body of evidence. ▪ The overall findings are summarised in standardised GRADE evidence summaries (evidence profiles or summary-of-findings tables), which report both relative and absolute effects. When possible, evidence reviews also address whether the effect met an established clinically meaningful threshold for the outcomes of interest. ▪ The CGC does not have a “very low” category for certainty of evidence and instead considers such evidence to be insufficient, a minor difference from the GRADE framework. Developing and finalising recommendations ▪ Evidence-to-decision tables o Following the GRADE framework, the CGC uses evidence-to-decision (EtD) tables, which serve as the roadmap for documenting decisions and the evidence used while drafting, deliberating, and finalising recommendations. o The EtD tables summarise the PICO, assessment of desirable versus undesirable effects of the intervention, certainty of evidence, patient values and preferences, costs and resources, and judgments to support the recommendation. o The EtD tables containing the final recommendations are published as an appendix to each guideline and ensure transparency about judgments in the development of recommendations from the available evidence. ▪ Determining the strength of recommendations

	○ The CGC rigorously considers an intervention's clinical benefits and harms, as well as variation in patient values and preferences, in deliberations about recommendations for each guideline. It also considers costs and burden of care when assessing healthcare value and developing recommendations. However, the CGC has to date not conducted cost-effectiveness analyses or incorporated information from such analyses into its recommendations. More rigorously assessing and incorporating cost into guideline recommendations is an ongoing initiative within the CGC. ○ The Public Panel helps to inform patient values and preferences via outcome rating, participation in various stages of guideline development, and thorough review of the guideline. ○ The CGC grades the strength of each recommendation as strong or conditional on the basis of the overall balance of benefits and harms, the certainty (or quality) of the evidence on treatment effects, patient preferences and values, and considerations about cost or resource allocation. ○ Strong recommendations usually support actions in which benefits clearly outweigh harms, or vice versa, and for which patient values and preferences would have little variation. Strong recommendations are generally based on high or moderate certainty in evidence. In rare and extenuating circumstances, a strong recommendation may be based on low-certainty evidence—for example, when the evidence indicates a substantial net benefit in a life threatening situation. ○ Conditional recommendations are often based on evidence that is of low certainty, shows benefits closely balanced with harms, or shows variability in patient preferences. They apply to many but not most patients and are not directly suited to translation into performance measures. Their implementation is often determined by variation in individual clinical situations, including disease factors, patient preferences and characteristics, and resource use, and usually involves a shared decision-making situation. **Addressing insufficient evidence in CGC clinical guidelines and guidance statements** ▪ When evidence is deemed inadequate to accurately assess the net benefit of an intervention overall or in particular patient or intervention subgroups, the CGC addresses this in a section of the guideline or guidance statement dedicated to inconclusive areas of evidence and does not issue recommendations. ▪ Areas often addressed include patients with multiple comorbid conditions, differences by sex or race, patients at higher or lower risk for the condition, variation in patient preferences or treatment burden, and the importance of cost and healthcare value in treatment considerations. **CGC clinical guideline and guidance statement presentation format** ▪ All clinical guidelines and guidance statements from the CGC follow a standard format that includes an introduction briefly outlining the condition, its prevalence, interventions of interest, and the intended purpose and target population. ▪ The CGC outlines the methods and data sources for both clinical guidelines and guidance statements, including the literature search dates. ▪ Systematic evidence reviews always accompany CGC clinical guidelines. ▪ For clinical guidelines, the CGC states the strength of each recommendation and the certainty of its evidence. The text below the recommendations or guidance statements highlights the evidence of benefits, harms, and costs, as well as other relevant information.

	▪ For guidance statements, the CGC describes, evaluates, summarises, and attempts to reconcile and explain commonalities and differences identified in the guideline group recommendations included in the selected existing guidelines. ▪ The CGC also describes the methods and evidence contained in the selected guidelines to further inform readers about factors that may have led to specific recommendation statements. ▪ The CGC includes a rationale for the final guidance statements. ▪ Clinical guidelines and guidance statements typically have five or fewer concise recommendations, which are also listed in the abstract in italics to enhance visibility. When possible, the CGC also includes information on patients with comorbid conditions, performance measurement implications, and future research needs. ▪ All papers include a summary figure with key information; clinical considerations; and, in many cases, talking points for patients. **Review and approval of clinical guidelines and guidance statements** ▪ **CGC review** o The CGC reviews and discusses all clinical guidelines and guidance statements at in-person meetings. o The topic subgroup introduces the clinical guideline or guidance statement with a brief presentation summarising the evidence and proposed recommendations. o For clinical guidelines, the CGC reviews and appraises the evidence reports, accompanying literature contained in those reports, and EtD tables to ensure an explicit link between evidence and recommendations. o For guidance statements, a similar process is followed with regard to assessment of the existing guidelines and their accompanying evidence. o Although no formal consensus method is used, members discuss recommendations and guidance statements and revise accordingly until they achieve a general consensus on the final version. ▪ **CGC Voting Policy** o Only CGC members can participate in voting. o Votes are taken for each recommendation or guidance statement individually. o A 75% agreement among eligible voters is required to approve a recommendation or guidance statement. This threshold is the same for both conditional and strong recommendations in clinical guidelines. o If the threshold is not met, the recommendation or guidance statement can be discussed further, revised, and voted on again, or removed from the paper. o Votes cast during CGC meetings are blinded during the meeting to avoid bias, and a record of voting results is kept and recorded in the meeting minutes (unblinded). o The CGC does not publicly disclose the voting records of individual members. ▪ **CGC public panel review** o The CGC Public Panel reviews and provides feedback on CGC clinical guidelines and guidance statements at various stages of development, including key questions, outcome rating (guidelines only), and the CGC approved guidelines or guidance statements.

	○ When papers include talking points with patients, the CGC Public Panel reviews this section carefully. The CGC reviews the comments and takes them into consideration in its decision making and in the final manuscript. ▪ **Peer review process** ○ ACP clinical guidelines and guidance statements are posted for review and comments by the ACP Board of Governors, which represents ACP members from all 50 states and territories, other countries, and various subspecialties. ○ The Board of Regents, ACP's highest governing body, provides comments and final approval of the guideline or guidance statement as ACP policy. ○ The Board of Regents votes to approve CGC papers with a simple yes-or-no vote and cannot make changes to the recommendations or guidance statements. ○ ACP may send out guidelines for external peer review and feedback by clinical experts before approval by the Board of Regents or for endorsement from other medical societies once the guideline is complete and approved. ○ Clinical guidelines and guidance statements also undergo a thorough peer review on submission to a journal for publication consideration. **Publication and dissemination** ▪ All ACP clinical guidelines, guidance statements, and evidence reviews are submitted for publication in a high-impact journal wherein each manuscript is independently peer reviewed. ▪ All ACP clinical recommendations and guidance statements are considered public documents and are available for free. **Expiration and updating of ACP clinical recommendations** ▪ All ACP clinical guidelines and guidance statements are considered automatically withdrawn or invalid five years after publication or once an update has been issued. ▪ Expired documents are available in an inactive clinical guidance section on the ACP website, as well as in the app. ▪ The CGC is working toward creating living systematic reviews and clinical guidelines and a core set of topics to ensure that certain topics do not expire. **Financial support** ▪ Financial support for the development of ACP clinical guidelines and guidance statements and for evidence reviews commissioned by ACP comes exclusively from the ACP operating budget. ▪ Financial support for external reviews not commissioned by ACP is described in the published reviews and frequently derives from public monies (for example, the Agency for Healthcare Research and Quality or Department of Veterans Affairs). ▪ ACP staff who author the clinical guidelines or guidance statements receive no additional compensation for the development of the papers beyond their salary, which comes out of the ACP operating budget. ▪ No industry funding is accepted for any stage of development of clinical guidelines or guidance statements.
RQ2: Description of quality measures/criteria for clinical practice guidance development	

What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	Living systematic reviews and clinical guidelines (currently in development).
What are the core elements of the key innovation?	N/R
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/R
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	RQ1: All components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review & evaluation process).
Associated peer-reviewed article(s)	Qaseem A, Wilt TJ; Clinical Guidelines Committee of the American College of Physicians. Disclosure of interests and management of conflicts of interest in clinical guidelines: methods from the American College of Physicians. Ann Intern Med. 2019. [Forthcoming].

Key: ACP - American College of Physicians, AGREE - Appraisal of Guidelines for REsearch & Evaluation; CGC- Clinical Guidelines Committee; EtD – Evidence to Decision; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; N/A – not applicable; N/R – not reported; PICO - Patient/population, Intervention, Comparison and Outcome.

Table B2 EHIF handbook for guidelines development

Guideline identification	
Organisation	Estonian Health Insurance Fund (EHIF)
Year	2020
Country	Estonia
URL	https://tervis.ut.ee/sites/default/files/inline-files/estonian_handbook_for_guidelines_development_2020.pdf
Title of the publication	Estonian handbook for guidelines development.
Summary/Overview	The Estonian handbook was first developed in 2011. Based on a stakeholder analysis conducted in advance of this updated handbook, experts from World Health Organization (WHO) made suggestions on how to create a more rigorous structure, applying the universal principles for the development of guidelines. As a result this updated handbook was prepared with the cooperation of WHO. The result is a comprehensive guideline, which follows the Appraisal of Guidelines for REsearch & Evaluation (AGREE) ll methodology and includes all core elements.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Composition of the Guideline Advisory Board (GAB) Guideline Unit and Panel** ▪ The GAB consists of representatives of various educational and research institutions, professional associations and other organisations, as well as individuals representing patients or lay people. The members of the GAB are expected to have experience in developing guidelines but, in the absence of such experience, any new member of the GAB should undergo training and participate in the preparation of at least one guideline. ▪ The Guideline Unit supports the GAB and the teams developing the guidelines (both the Panel and the Secretariat). The Panel and the Guideline Unit collaborate to ensure the trustworthiness of a guideline's content, consistent with the principles of evidence-based healthcare and the methodology agreed on in the handbook. ▪ Panels include the following members: health professionals with content knowledge, patients or patient representatives (or other lay people), methodology experts, and individuals with relevant expertise (e.g. in economics). The Panel must represent a balance of the various healthcare levels (primary care, hospital care, nursing care) according to the topic. ▪ The Panel formulates the guideline scope and recommendations, presents the interim progress report to the GAB, approves the final guideline, and submits it to the GAB for approval. The Panel then introduces the guideline and contributes to its implementation (also developing, if needed, the patients' version of the guideline and other derivative materials). **Roles and responsibilities** ▪ The majority of the work involved in developing guidelines is carried out by the Guideline Secretariat, which searches for and synthesises the evidence, and prepares preliminary answers to health questions, along with guidance for formulating recommendations. ▪ The main task of the Guideline Panel is to assess the applicability of the collected evidence and its relevance to the situation in Estonia. On the basis of the evidence, the Panel formulates recommendations and determines their strength. ▪ The Guideline Unit through the Secretariat supports the work of the Panel, arranges meetings, and provides methodological advice and support in the search for and synthesis of evidence-based scientific literature, the formulation of recommendations, and the writing of the guidelines.

	▪ The Guideline Unit works with specific Panel members on ensuring the completion of the Evidence to Decision (EtD) frameworks for each recommendation. The Guideline Unit should identify the requisite Panel members along with the Chair and the Secretariat. **Disclosure of interests, resolution of any conflict of interest and confidentiality** ▪ Each Panel member, including the Chair, the nominated Guideline Unit member, and consultant (if involved), should complete and submit a disclosure of interests (DOI) to the GAB (see Annex 5). The GAB then decides whether the declaration contains any conflicts that should result in the exclusion of a proposed Panel member. ▪ At the first Panel meeting, and at all subsequent meetings, each Panel member should verbally report any potential conflict of interest (COI). All Panel members and any individuals who have direct input into the guideline (e.g. consultants) should update their DOI form before each Panel meeting. Any changes to a Panel member's DOI should be recorded in the minutes of the meeting. The Panel Chair is responsible for ensuring this is done. If a member has a (new) COI, several possibilities exist. First, the member may be invited to participate, but only if their conflict is publicly disclosed. Second, the member may be asked not to participate in a particular portion of the meeting, discussion, or work that is directly related to their conflict. Or, third, the member may be asked to withdraw from the Panel entirely. ▪ Additionally, Secretariat members (including the head of the Secretariat and the nominated Guideline Unit member) are each required to complete and submit a DOI. The same rules about any DOI or COI apply to them as to the Panel members. ▪ The DOI will be updated if any new interests emerge, on an ongoing basis during the guideline development process. Any COI must be reflected in the guideline development documentation, with an explanation of what each conflict constituted and how it was managed. **Topic proposals and preparation of the scope** ▪ Proposing a topic for the guideline o The GAB can declare nationally important topics for guideline development, for which topic proposals can then be presented. They can also be submitted by specialist associations; professional associations of healthcare workers; healthcare providers; and educational facilities and other interested parties. Owing to a significant COI, proposals made by companies that manufacture or represent medicinal products or medical devices are not accepted. o The topic is proposed, together with an initial description of the scope, and submitted to the GAB using the relevant forms. o The submitted document must contain statistical data justifying the choice of topic, which requires the initiator to actively engage with applicable parties (including the Guideline Unit) for input and methodological guidance on developing the topic proposal. ▪ Selecting topics for guideline development o The members of the GAB evaluate the topics based on the information provided in the initial scope, according to their relevance and the expected benefits. In addition, the potential impact of the implementation of the guideline on resource use and healthcare management is taken into account. o The needs of interested parties should also be taken into account, along with existing evidence-based guidelines that can be adapted or used to prepare a new guideline.

	▪ The problem statement and the purpose of the guideline
	  ○ Considerations must include the link between the topic and national healthcare priorities, and/or the relevance of the guideline.
	  ○ Information on the following should be provided:
	  ▪ Burden of disease in Estonia
	  ▪ Differences in practice and/or health outcomes and/or costs
	  ▪ Expected impacts on patient health indicators and/or use of resources
	▪ Evaluation by the GAB
	  ○ The GAB is not obliged to choose topics from among those that are proposed, particularly if they are not suitable for the development of a guideline.
	  ○ It is important to note that issues around the feasibility of creating a guideline may dictate the choice.
	  ○ The GAB documents the reasons for choosing or dismissing each topic and will respond to the topic initiator with a decision, including possible suggestions for improvement.
	  ○ If a topic is chosen, the GAB discusses the composition of the Panel and the Secretariat and selects the possible Chair(s) once they have been nominated.
	▪ The scope of a guideline
	  ○ The initial scope is prepared by the topic initiator and the final scope is developed by the Panel, together with the Secretariat and Guideline Unit.
	  ○ Based on the topic proposal, the Panel, together with the Secretariat, finalises the scope, which:
	  ▪ provides an overview of what the guideline contains and what it does not, as well as defining the population groups that are included and those that are excluded;
	  ▪ formulates the title of the guideline and identifies the key questions in patient/population, intervention, comparison and outcome (PICO) format;
	  ▪ sets clear boundaries for the guideline development process so that the work focuses on agreed outcomes, and chooses and evaluates outcomes for this purpose;
	  ▪ ensures that the guideline is of a reasonable size and is prepared within the prescribed time frame;
	  ▪ helps to establish whether guidelines exist on the same topic in Estonia or if there is any other up-to-date, relevant evidence.
	  ○ Panels should consider publication and dissemination plans early in the process, as this may help to refine the areas covered.
	Formulating questions for the scope
	▪ The choice of questions to be addressed in a guideline should be based on clinical and policy needs, and on the information provided by experts.
	▪ Contributions of the target group, patients and/or patient associations may also be helpful.
	▪ Definition and background questions
	  ○ Background information helps to describe the context of the problem and provides information about the factors that will formulate the PICO question.
	▪ Foreground questions

	○ The guideline questions are PICO-format clinical effectiveness questions about different interventions (including tests and complex interventions) for a specific population. ▪ Questions related to the organisation of healthcare ○ Organisational questions are commonly addressed in guidelines and lend themselves to systematic reviews. The interventions are often complex; that is, consisting of multiple separate interventions that require joint consideration and may or may not depend on other components of the intervention. ○ Healthcare questions address health outcomes but, in thinking about the scope, those proposing the guideline should also consider which of the other desirable and undesirable consequences in the EtD are relevant to the question. ▪ Selecting and rating outcomes for healthcare questions ○ When formulating questions to address health issues, the key outcomes that need to be considered should be identified. ○ Typically, up to seven outcomes can be assigned to one question, but instead of being the result of the evidence, they must pertain to the relevant clinical or public health practice(s) for the patient, focusing on what is critical for decision-making and for creating recommendations. ○ It is important to focus on the outcomes that are significant to the patient, rather than choosing without critical judgement those that are easy to measure or often reported, unless they really are relevant. As such, it can be useful to have an early hearing of the important stakeholders (i.e. patients) regarding critical outcomes. ▪ Identifying healthcare questions and outcomes ○ Step 1 is to create an initial, comprehensive list of possibly relevant outcomes for each question, including both desirable health effects and undesirable ones from the interventions that will be considered in the recommendations. ○ Step 2 involves each member of the Panel evaluating the outcomes one by one on a scale of 1–9, considering its importance to the patient. ○ Step 3 requires ratings to be tabulated by calculating the average score for each outcome. The results are submitted to the Panel, which decides which outcomes will be taken into consideration when assessing evidence and making recommendations. Generally, only important and critical outcomes are taken into account. ▪ Confirming and amending the scope ○ The final scope, approved by the Panel, together with the rated outcomes, are presented to the GAB for approval by the Chair of the Panel. **Evidence retrieval for guideline development** ▪ General considerations for prioritising guideline development in Estonia ○ To make the process efficient, existing guidelines and systematic reviews should be used as much as possible. A well-established process is called 'adolopment', for the adoption, adaptation and de novo creation of guideline recommendations. ○ A summary of all relevant research evidence is essential when developing a recommendation and, ideally, the summary should be based on systematic review(s). ▪ Approach for efficient guideline development in Estonia

	○ In order to ensure that the local context has been taken into account in developing the recommendations, the adolopment process should to be followed. ○ One or more existing guidelines can be used as a basis for developing Estonian guidelines. These can be used as a model for formulating health questions, and where original/initial references to published evidence can be found. ○ The Guideline Unit should establish contact with the original guideline developers; many are willing to share, or the information is already available publicly. For some organisations, asking for permission to use material (including paying fees) will be required, depending on the indicated copyright on the source material. ○ Guidelines in Estonia will therefore be established based on: ▪ recommendations developed from published health guidelines that were created by independent national and international authorities (e.g. the National Institute for Health and Clinical Excellence (NICE), World Health Organization (WHO), and other international professional organisations that follow evidence-based approaches to guideline development) and that meet specified criteria; ▪ recommendations developed from published clinical guidelines that were created by specialty societies that are not commercially funded, and that follow standardised criteria for guidelines (e.g. that provide evidence summaries and adequate descriptions of the processes used to manage any conflict of interest); ▪ recommendations developed from existing systematic reviews. ○ All guidelines that are used as sources should be assessed in terms of their quality using the Appraisal of Guidelines for Research & Evaluation (AGREE) II tool. ○ Systematic reviews can be assessed for quality using the latest version of the ROBIS checklist. When adopting recommendations, the Panel compares its judgements to those of the original Guideline Panel and determines if any changes to recommendations are required. ▪ Retrieving and assessing existing guidelines ○ It is strongly recommended that the search for evidence be carried out in consultation with an expert in information retrieval (e.g. a librarian, or medical research assistant) to ensure a sound search strategy is used. ○ The following sources, in addition to PubMed, should be searched: National Guideline Clearinghouse, the Guidelines International Network (GIN) database, the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) Working group database, websites of specialist medical societies relevant to the topic and the scope of the proposed guidelines. Websites of guideline producing agencies can also be searched, including: NICE, Canadian Agency for Drugs and Technologies in Health (CADTH), Agency for Healthcare Research and Quality (AHRQ), database of WHO guidelines, BiGG international database of GRADE guidelines. ○ The search strategy used should be documented and should specify: ▪ the details of the databases (including websites) searched, and the search strategy planned for each database; ▪ the details of each strategy, as actually performed, specifying the date on which the search was conducted and/or updated (this description must be included in the final guideline).

	○ The citation list resulting from the search strategy should then be screened to exclude obviously irrelevant guidelines. Potentially relevant citations should be retrieved as abstracts, if possible, and then further screening should be undertaken to identify possible guideline documents. These should then be retrieved in full text. ○ Relevant guidelines should then be assessed for the following aspects. ▪ Are the guidelines based on explicit use of evidence? ▪ Who funded the guideline development and what processes were used to manage any COI? ▪ What is the credibility of the guideline, based on the AGREE II rating instrument (questions 7–11 and 22–23 only)? ○ This assessment process should lead to the identification of a list of guidelines that may be used for developing local recommendations or as a source of evidence. The recommendations in these guidelines should be mapped in detail to the questions in the scope along with the summary of evidence used in each guideline. The process involves deciding to accept or modify whole guidelines or their specific recommendations by considering whether they are credible, up to date, acceptable and applicable, given the cultural and organisational context. ○ The next critical step after identifying potentially matching recommendations includes completing or using GRADE EtD frameworks for recommendations for either a matched recommendation or a new recommendation. ○ Depending on agreement with the information presented in the existing guidelines or requirements for new evidence, recommendations are adopted or adapted. If no information or recommendation is available, a new recommendation is developed. ▪ Retrieving and assessing systematic reviews and meta-analyses ○ If systematic reviews are to be used in guideline development, they should be assessed for how well they have been carried out; that is, how credible they are. ○ The search strategy for systematic reviews needs to be broad initially, and not limited by language or year. The Panel should be asked for advice on any limits by date of publication. The search strategy used should be documented. ○ Once the reviews are retrieved, they should be checked for: pre-specified criteria for including studies, potential commercial sources of funding, relevance to the questions to be addressed in the recommendations, timeliness and quality. **Evidence preparation, certainty of evidence and consideration of costs** ▪ The GRADE approach is used to assess the evidence and develop recommendations and make decisions. ▪ In addition to the evidence, the costs and resource use of preventive, diagnostic, and management strategies have to be taken into account by the Guideline Panel as they develop guideline recommendations The Panel must also consider the capacity of the existing health system and the feasibility of implementing the recommendations. This implies assessing the need for additional resources, the need for and availability of the labour force, as well as preventive and diagnostic interventions and administrative costs. It is important to record in the EtD whether research evidence was sought, or if it is a judgement of the Panel based on evidence provided by an expert.

	▪ The Panel needs to evaluate the budget impact of potential changes in current practice standards that may result from the recommendation. ▪ After defining the final scope of the guideline, the Panel has to decide which health questions are most likely to require consideration of costs and resource use in detail, including those for which a formal economic evaluation – as well as the budget impact analysis – may be required. ▪ The Secretariat provides an overview of the expected budget impact of the initial recommendations, compared to current or comparative practices. This analysis consists of three steps: o identifying what type of resource use is associated with the recommendation; o measuring how much would be used if the recommendation were to be implemented; o determining the monetary value (that is, how much it costs) ▪ A description of resource use and costs should be prepared from the point of view of the healthcare system, describing the main resources needed to implement the recommendations. ▪ If a significant change in treatment practices in Estonia is implicated, it may be necessary to carry out a focused budget impact analysis in cooperation with the EHIF, using its databases of healthcare service claims and reimbursed pharmaceuticals. ▪ At least one week before the meeting, the Panel should receive an initial GRADE EtD for each question, containing the GRADE evidence profile tables with a preliminary assessment of the impact of the recommendation on resources, applicability, values, equity, as well as feasibility and acceptability. ▪ The members of the Panel should assess whether the EtD summary lacks any significant aspect that is necessary for the formulation of the recommendation, before the meeting. This should be in collaboration with the member of the Panel assigned to the question, who will either present the information to the Panel or support the presentation. **Development of recommendations** ▪ **From evidence to recommendation** o The guideline recommendations are formulated by the Guideline Panel on the basis of an EtD and the draft recommendation provided by the Guideline Secretariat, which prepared the question(s). o The recommendations should be clearly and precisely worded and describe the action unambiguously. o For all recommendations, the direction of the recommendation (for/against), its strength (strong/conditional), and a summary of the quality of the evidence used to formulate it (high/moderate/low/very low) should be determined. o To explain the answer to each health question, the Secretariat prepares explanatory summaries within an EtD table, explaining the background of the recommendation. o The recommendation for each health question takes into account: the evidence relating to the question and its quality; the possible harm–benefit ratio; the values and preferences of patients; the applicability of the activities related to the recommendation; and equality of access to the service. o If no evidence exists in order to draw up a recommendation on a health-related question, the Panel must document, in the EtD format, the judgements established for the recommendation, justifying the decision made. o The process to achieve consensus is guided by the Panel co-Chairs. o Suggested process for the development of recommendations:

	▪ The question should be clearly introduced. ▪ The evidence is reviewed and discussed by the panel, considering the balance of evidence for benefits and harms. ▪ The panel considers costs, as presented by health economists from among the Secretariat, including resource and use costs, budget impact (as well as possibly cost–effectiveness), along with values and preferences. ▪ The draft recommendations are presented by the Secretariat, with justification and reference to the relevant evidence in the GRADE EtDs. ▪ If necessary, the first recommendation is modified. ▪ Final agreement on the recommendation is reached. ▪ **Involvement of panel members with and without COI** o All members will be involved in: ▪ preparing and reviewing research evidence; ▪ important additional considerations during the review of the research evidence; ▪ all stages up to the final step of making judgements and decisions on strength and direction of the recommendation (these are only to be made by non-conflicted members); ▪ meetings in person (conflicted members will be asked to remain silent and speak only when asked); ▪ the end of the process, at which point discussion is open to all. o Only non-conflicted members will be involved in: ▪ judgements on criteria; • (when online) only these members will be invited to make judgements; ▪ agreement on conclusions and recommendations. ▪ **Grading the strength of the recommendations** o The Panel must consider all known factors and justify the reasons for its decisions in detail, in order to maintain the recommendation's credibility. A definite recommendation is only made if the intervention or medicine meets the (capacity) requirements of the Estonian healthcare system. o Each recommendation – or the wording of the recommendation, provided as a bullet-point list – must contain only one primary activity. The recommendations should use the same style and terminology throughout and should take into account the linguistic and cultural context in which readers will understand them. o Formulation of recommendations should be based on the approach outlined here: ▪ The focus should be on what to do or what to use. ▪ Simple language should be used (in Estonian), avoiding ambiguity. ▪ Only the information necessary for the reader should be used. ▪ The strength of the recommendation should be included in the wording (in parenthesis following the recommendation, together with the certainty of evidence). ▪ The words person or patient should be used instead of the words individual, case, or subject. If possible, it is preferable to use the word person, rather than the word patient for people with mental health problems or long-term illnesses. In the case of people with mental health

problems, the term service recipient may also be used, instead of the word patient. The word patient should not be used for people who do not have a disease or condition (e.g. a pregnant healthy woman).

- Good practice statements
  - Good practice statements represent recommendations that guideline panels feel are important but that are not appropriate for formal ratings of quality of evidence.
  - To issue a good practice statement, the Panel should ensure five key criteria are met:
    - Is the statement clear and actionable?
    - Is the message really necessary in regard to actual healthcare practice?
    - After consideration of all relevant outcomes and potential downstream consequences, will implementing the good practice statement result in large net positive consequences?
    - Is collecting and summarizing the evidence a poor use of a Guideline Panel's limited time and energy (e.g. opportunity cost is large)?
    - Is there a well-documented clear and explicit rationale connecting the indirect evidence?

Interim report, review and approval of guidelines

- **Interim report**
  - In order to monitor the compliance of the guideline development process with the approved scope and timetable, the Panel submits an interim report on the development of the guideline to the GAB, no later than six months after the approval of the scope.
  - The interim report should describe the progress on the formulation of evidence-based recommendations and, if necessary, make reasoned proposals for modifying or complementing clinical issues in the final scope.
  - If necessary, the Chair of the Panel will submit suggestions for changes in the composition of the Panel and/or the Secretariat; for example, if an additional expert needs to be involved.
- **Review**
  - When the guideline is close to being finalised, the GAB initiates a review by three reviewers (ideally a general practitioner, a content expert and one GAB member).
  - The Chair of the Panel submits the final draft (approved by the Panel) to the Guideline Unit, who forwards it to the approved reviewers, as well as for consultation by other relevant parties.
  - A Panel member reviews the received feedback and comments, together with the Guideline Unit, and suggests any required changes to the guideline to be made by the Secretariat.
- **Approval by the GAB**
  - In order for the GAB to approve the guideline, including its implementation plan and other relevant material, it has to evaluate whether the guideline has been developed according to the principles and methodology set out in the handbook, and whether the necessary processes have been followed and documented.
  - The key questions that would signal to the GAB the quality, clarity and consistency of a guideline include:

	▪ Did the Panel and the Secretariat report using the Reporting Items for practice Guidelines in HealThcare (RIGHT) and, if an adaptation, RIGHT adopted, adapted, or developed de novo (RIGHT AD@PT) reporting checklist(s)? ▪ Did the recommendations appropriately describe the population, intervention and comparator (if necessary) and include the rating of the strength and quality/ certainty of the evidence? ▪ Is there a link between the evidence and the recommendations? - Are the reasons for the EtD judgements clear? ▪ Did the guideline working group only make strong recommendations when justified? (The rationale for all strong recommendations should be checked.) ▪ Was COI appropriately managed and addressed? (The meeting minutes should be checked.) ▪ Are the results of the public consultation available? - How does the guideline score on the AGREE items? **Dissemination of the guideline recommendations** ▪ All topic proposals and scopes approved by the GAB, along with the minutes of the meetings of the GAB are publicly available on the website. Recommendations that have been completed and approved by the Panel during the guideline development process are also published (in small informative recommendation units format) on the guidelines' website. ▪ During the guideline development process, implementation plans are prepared for the dissemination and use of the information contained in the guidelines by the various target groups. The evaluation metrics for implementing the guidelines are also provided. Once the guideline development process reaches the final stage, all assessments, comments, and reviews of interested parties are made publicly available, in addition to the working copy of the guideline, the summaries of the evidence gathered by the team, the protocols of the Panel meetings, and an overview of any DOI. ▪ Guidance material based on the guideline: ○ **Algorithms and other instructional materials**: The algorithm is developed by the Secretariat, which submits it to the Panel for supplementation and agreement. In the near future, GRADEpro will allow these pathways or algorithms to be developed within the tool. The algorithm is based on the guideline recommendations, informed by scientific sources and the organisation of the Estonian healthcare system. If the algorithm presents different solutions compared to the current division of labour (in terms of the sequence of the provision of health services or the assignment of tasks) the Panel must justify the feasibility of and approach to the evidence underpinning the proposed changes. The algorithm is presented, together with the guidelines, for approval by the GAB. ○ **Evidence based instruments**: For the successful implementation of the guideline, it may be necessary to translate into Estonian and validate the evidence-based instruments (scales and reflective tests) used to assess the patient's condition, its severity and/or the effectiveness of treatment. Developing or translating evidence-based instruments is considered a part of the implementation process. The relevant instruments must be ready for use and publicly available as appendices to the guideline. ○ **Guideline materials for patients and lay people**: If recommendations are to be included in the guidelines that help patients to better cope with their health condition and its management, simple language versions of the recommendations are developed. In addition to simple language

	recommendations, the Panel may decide that other information from the guideline should be provided to patients in order to ensure better implementation. In such cases, special information materials can be developed for independent use by the patient. Such materials, for instance in the format of an information leaflet will help the patient to better understand and follow certain recommendations in the guideline. In the interest of diversity of feedback when identifying any potential issues in the recommendations and material(s), people with a history of the illness/condition addressed in the guideline (or their representatives) should be included, ensuring people of varying ages and with different social and educational backgrounds are consulted. **Implementation of the guidelines** ▪ **Implementation plan** o The implementation plan is prepared by the Guideline Secretariat and approved by the Panel. It is added to the guideline after extensive discussion of all the responsibilities and needs (including scheduling) with the parties implementing the guidelines. o To prepare the implementation plan, certain steps should be carried out: ▪ Aims and target groups of the implementation activities should be determined, considering the challenges of the current practice, new recommendations and target groups along with their characteristics/specifications. ▪ Possible barriers to implementation should be identified and a plan prepared of measures for overcoming them. The criteria for success should be defined, along with the indicators that describe them. ▪ The need for resources should be assessed. The resources required should be clearly indicated in the operational plan, including funding, staffing and time requirements. ▪ Notification needs must be assessed and planned. It should be considered how vital information reaches interested parties, and the relevant spokespeople should be identified to disseminate information about the guideline. ▪ Training should be identified and the necessary activities outlined, such as regular training sessions and online training. ▪ Existing structures and networks should be used for implementation. If possible, the implementation of the guideline should be included in the performance management system. ▪ The reference data of the indicators should be measured, ensuring that the data collected adequately reflect the current situation and provide a starting point for tracking further changes. ▪ The implementation process should be monitored by setting up a system for regular evaluation. Feedback should be given and a report submitted to the GAB within the agreed time frame. ▪ Clear roles and responsibilities should be defined for each activity. ▪ Milestones and a schedule should be set out for each implementation activity. ▪ **Indicators for assessing guideline implementation** o In order to assess the implementation of guidelines, indicators are selected and added to the implementation plan. The indicators may be process indicators, outcomes or clinical cases. Processes or events that can be measured on the basis of health statistics or data received by the Estonian Health

	Insurance Fund, along with audits or applied research in cooperation with universities or healthcare institutions can also be used as indicators. ○ Upon the final selection of the indicators, the key stakeholders involved in the implementation of the guidelines should be consulted. ○ The Panel confirms the indicators – in particular, for the final recommendations evaluated as being "strong" – to monitor the implementation of the health guideline and assess its impact. From among the indicators prepared by the Guideline Secretariat, the Panel selects those that are considered relevant in implementing the recommendations. ○ Clinical indicators are confirmed within the implementation plan by the GAB. The Estonian Health Insurance Fund compiles and monitors the results of the actual implementation of guidelines in medical practice. **Updating guidelines** ▪ Review of the prepared guidelines is arranged by the Guideline Unit by requesting – at the latest during the fourth year after a guideline's approval – an expert opinion from the Chair and/or the members of the Panel that prepared the existing guideline. ▪ The expert opinion distinguishes between the guideline's health questions that would require the evidence to be updated, and other questions that have arisen in the meantime and which require further response. ▪ The Guideline Unit, on the basis of expert opinions, provides the GAB annually with an overview of approved guidelines that need to be updated, together with proposals for the content and volume of the updates. ▪ In addition, the GAB considers the need to update the guidelines on the basis of the results of relevant statistics, audits or applied research, or based on feedback from interested parties (all attached to the proposal of the Guideline Unit). ▪ The process of updating guidelines is based on the same principles and methodology as preparing a new guideline and should similarly be based on existing EtD frameworks.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	The entire process of guideline development and management – as well as implementation – are carried out using the GRADEpro Guideline Development Tool. Additional software is used to facilitate online collaborative working: email responses to invitations from Doodle (scheduling), Skype (attending meetings), GRADEpro and PanelVoice (input and voting on recommendations), and OneDrive (file sharing).
What are the core components of the key innovation?	Knowledge management.
What is the rationale behind the methodology? **OR**	Rationale: It is a purpose built ecosystem for developing and implementing guidelines created by researchers involved in developing methodology for guideline development.

What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	Criteria: It is standard practice.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	RQ1: All components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review & evaluation process).
Associated peer-reviewed article(s)	EHIF, University of Tartu Medical Faculty. Estonian handbook for guidelines development. Geneva: World Health Organization; 2011 (http://apps.who.int/iris/bitstream/10665/44734/1/9789241502429_eng.pdf, accessed 3 January 2018). Schünemann HJ, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa RA, Manja V, et al. GRADE evidence to decision (EtD) frameworks for adoption, adaptation and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017; 81:101–110 (https://doi.org/10.1016/j.jclinepi.2016.09.009, accessed 3 January 2018).

Key: AGREE - Appraisal of Guidelines for Research & Evaluation; AHRQ - Agency for Healthcare Research and Quality; BiGG – International Database of Grade Guidelines (translated from Spanish); CADTH - Canadian Agency for Drugs and Technologies in Health; CoI – conflict of interest; EHIF - Estonian Health Insurance Fund; GAB - Guideline Advisory Board; GIN – Guidelines International Network; EtD – Evidence to decision; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; N/A – not applicable; NICE - National Institute for Health and Clinical Excellence; N/R – not reported; PICO - Patient/population, Intervention, Comparison and Outcome; RIGHT - Reporting Items for practice Guidelines in HealThcare; RIGHT-AD@PT - Reporting Items for practice Guidelines in HealThcare - adopted, adapted, or developed de novo. WHO – World Health Organization.

Table B3 GPAC How our "Made in BC" clinical practice guidelines and protocols are developed

Guideline identification	
Organisation	Guidelines and Protocols Advisory Committee (GPAC), British Columbia (BC)
Year	2017
Country	British Columbia
URL	https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/gpac-handbook/gpachandbook2017.pdf
Title of the publication	How our "Made in BC" Clinical Practice Guidelines and Protocols are developed
Summary/Overview	Brief guidance that provides an overview of the guideline development process, publication and promotion, collaboration policy and quality assurance process. It lacks considerations relating to resource implications and planning and implementation. In terms of an evidence-based approach, systematic reviews of the evidence are not conducted by the working group. Instead, existing reviews are utilised.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	Development process for British Columbia guidelines ▪ Topic selection ○ Criteria considered by Guidelines and Protocols Advisory Committee (GPAC) in selecting and prioritising topics for guideline or protocol development: ▪ areas of clinical uncertainty, as evidenced by wide variation in practice or outcomes; ▪ conditions where there is good evidence for effective treatment and where mortality/morbidity can be reduced; ▪ procedures and tests that have a high per unit cost and high volume; ▪ priority areas for the achievement of specific healthcare goals in BC; ▪ input from practitioners and stakeholders based on compelling evidence; and existing guidelines that need to be renewed (or retired) three to five years from their previous review date. ▪ Working group selection ○ In general, each working group consists of a chair, general practitioners, a cross-section of relevant specialists, and Medical Services Commission medical consultants. ○ Each working group is facilitated by a project lead/research officer. ○ Each working group member must be free of conflict of interest and be knowledgeable and interested in the subject matter (but not necessarily a subject matter expert). If relevant, other healthcare professionals are included in the working group (e.g., a pharmacist from the Ministry PharmaCare team). ○ At times, working groups may invite additional health professionals or subject matter experts to consult on the development of the guideline. ○ A complete list of working group members are submitted to the GPAC Executive for approval. ▪ Guideline development process ○ Once a topic has been approved for development by GPAC, a working group is formed, and with the support of research officers from the Health Services and Policy Division, develops a draft version of the guideline.

	○ Before the first working group meeting, the project lead will do the background research and create a first draft or an outline of the guideline with support from the medical consultants and the working group chair. ○ The chair and the project lead will then facilitate working group meetings in which the guideline is discussed and revised. Once a complete first draft is created, it is presented to GPAC for approval for external review. ▪ Keeping guidelines up to date ○ Guidelines are subject to review three to five years after the original effective date. ○ The guideline's effective date is typically within six to eight weeks from the date the guideline was approved by the Medical Services Commission (MSC). ○ Existing guidelines that undergo a substantive change to the content will be reissued with a new effective date; current guidelines that are subject to simple editorial changes or where only minor updates to the content are made will have a revised date added but will retain the original effective date. ▪ Evidence selection ○ The evidence review process used in the development of GPAC guidelines is conducted with reference to the Oxford Centre for Evidence-Based Medicine Levels of Evidence (March 2011 - www.cebm.net). ○ Levels of evidence are not explicitly stated within the GPAC guidelines but recommendations are given and referenced. ○ Working groups review available systematic reviews and base recommendations on these studies. In cases where systematic reviews are not available, recommendations are based on primary evidence searches including individual randomised controlled trials reviewed by the working group. A full systematic review may not be conducted. ▪ External review ○ GPAC uses two distinct external review methodologies: ▪ First, GPAC uses a randomised approach where an approved draft is mailed to a random sample of general practitioners (typically numbering between 500 and 800 individuals), relevant specialties (10-50% sample per speciality), University of British Columbia medical school, nurse practitioners and key stakeholders. Additional appropriate reviewers may be chosen for specific guidelines in consultation with the Medical Services Commission medical consultants and research officers. ▪ Second, GPAC sends every guideline to a selected and consistent group of key stakeholders through email (known as the "always list"). This list is made up of key contacts in the areas of pharmacy (e.g. Pharmaceuticals Services Division, Therapeutics Initiative), laboratory procedures (BC's Agency for Pathology and Laboratory Medicine, BC Association of Laboratory Physicians, LifeLabs Medical Laboratory Services), health authorities, Medical Service Plan billing, public health, and health professional colleges and associations. ○ The new or revised guideline is also reviewed with Ministry employees involved in developing standard laboratory or diagnostic requisition forms, billing rules and fee codes.

	○ Physicians who act as external reviewers for BC Guidelines may be eligible to receive credit towards continuing professional development or continuing medical education. ▪ Final version approved ○ Once GPAC approves the guideline, the research officer will prepare a Request for Decision (RFD) document that outlines all of the potential impacts of the guideline. ○ The Request for Decision focuses on improved patient outcomes (what recommendations will lead to better management of patients), utilisation (what are the financial impacts on Medical Service Plan, PharmaCare, other stakeholders, etc.). Projections of impact are generally a part of this document. The guideline package (includes guideline, RFD and the Minute of the Medical Services Commission) is then submitted to the MSC for approval. ▪ Deployment ○ Implementing and facilitating ▪ Once the Medical Services Commission approves a guideline, the research officers begin the publication process, which includes: ○ posting the full guideline on BCGuidelines.ca; ○ uploading the guideline to the BCGuideline mobile app; ○ ensuring the latest version of the guideline is included in the Canadian Medical Association Clinical Practice Guideline Database; ○ embedding guideline recommendations or resources into order sets or electronic medical records; ○ integrating guideline recommendations into lab reports; ○ linking General Practice Services Committee incentive payment or MSP billing rules to BC Guidelines; and ○ inviting physicians, nurse practitioners and University of British Columbia Medical School family practice residents to participate in the external review process; and collaborating with University of British Columbia Medical School family practice residents by creating opportunities for their second year research projects. ○ Promotion and awareness ▪ Guideline promotion and awareness activities include: ○ Promoting the guidelines and providing information to target audiences at conferences and professional development sessions; ○ Distributing USB flash drives containing copies of all BC Guidelines and Partner Guidelines, as well as print versions of select guidelines, at conferences and other promotional events; ○ Writing excerpts for journals and newsletters; ○ Including information on new and revised guidelines in broadcast messages sent by the Ministry of Health and other stakeholder organisations; and Promoting guidelines through social media platforms.
RQ2: Description of quality measures/criteria for clinical practice guidance development	

What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	N/R
What are the core components of the key innovation?	N/A
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/A
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/A
How is the innovation used in practice?	N/A
Notes	
Reviewer notes	RQ1: All core components (Service user and stakeholder involvement; Governance model; Audit, monitoring, review and evaluation process; Evidence-based; Knowledge management (Accessibility/sharing of best practice); Planning and Implementation).
Associated peer-reviewed article(s)	

Key: BC - British Columbia; GPAC -Guidelines and Protocols Advisory Committee; N/A – not applicable; N/R – not reported; RFD - Request for Decision; USB – universal serial bus.

Table B4 HAS Development of good practice guidelines

Guideline identification	
Organisation	Haute Autorité de Santé (HAS)
Year	2010, updated in 2016 and 2020
Country	France
URL	https://www.has-sante.fr/upload/docs/application/pdf/2018-02/good_practice_guidelines_cpg_method.pdf
Title of the publication	Development of good practice guidelines: "Clinical practice guidelines" method.
Summary/Overview	The HAS handbook (official English language version) provides a high level overview of the general procedure for developing a good practice guideline, as well as the specific steps involved in the systematic review and synthesis of literature, drafting, reading, and finalisation phases. The guide also includes information on forming a working group, analysing stakeholder responses, validating and distributing the guidelines, and updating them as necessary. Considerations relating to resource implications, planning and implementation are lacking. However, these considerations may be present in the French language version.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Clinical practice guidelines method** ▪ The methods for development of good practice guidelines described by HAS are: ○ the "Clinical practice guidelines" (CPG) method; ○ the "Formalised consensus guidelines" (FCG) method. ▪ The choice between these two methods is determined during the good practice guidelines (GPGs) outline phase. ▪ The CPG method is the preferred method for creating GPGs. However, the "Formalised consensus guidelines" method must be discussed if at least two of the following conditions are met: ○ absence or insufficiency of literature with a high level of evidence, specifically addressing the questions raised; ○ possibility of breaking down the topic into easily identifiable clinical situations (lists of indications, of criteria, etc.); ○ controversy, with the need for an independent group to identify and select among several alternatives the situations in which a practice is deemed appropriate. ▪ The CPG method is a rigorous method for GPG creation, which is based on: ○ the participation of professionals and representatives of patients and users affected by the topic of the GPG; ○ transparency, with provision of: ▪ critical analysis of the literature; ▪ essential points from debates and decisions made by members of the working group; ▪ ratings and comments of members of the reading group (version A) or comments of stakeholders (version B); ▪ the list of all participants of the various groups. ○ independent creation: ▪ independence related to the status of HAS, as an independent public scientific authority;

	▪ independence of the groups amongst each other; the working and reading groups each have a specific role that they accomplish independently of each other; ▪ financial independence; public financing in the context of HAS GPGs; ○ management of the interests declared by the experts of the working group, according to the procedure described in the HAS "Guide on the declaration of interests and management of conflicts of interest." **Development of a good practice guideline according to the CPG method** ▪ Outlining phase ○ HAS selects the topic ○ HAS specifies the objective and the list of questions ○ HAS specifies the professionals concerned ○ HAS specifies the population affected ○ HAS coordinates the project and resources ○ HAS specifies the composition of the working and reading groups ○ HAS selects the work method (CPG) ○ HAS appoints one or more project leaders. ▪ Procedure for the CPG method ○ Systematic literature review phase ▪ Drafting the evidence report (with levels of evidence). ○ Drafting phase ▪ Discussion of the evidence report ▪ Drafting the initial version of the guidelines (with grades). ○ Reading phase (consultation) ▪ Reading Group (version A): Ratings-comments via electronic questionnaire, or ▪ Stakeholders (version B): Comments via electronic questionnaire. ○ Finalisation phase ▪ Analysis of responses from the reading group or stakeholders ▪ Discussion of comments ▪ Finalisation of the text of the guidelines ▪ Validation distribution. **Conflicts of interest** ▪ the interests declared by the members of the group (and updated, if applicable); reiterate the commitment to confidentiality and the obligation for each participant to inform the public of any links with companies and establishments producing or distributing healthcare products, or advisory bodies when they speak about such products in the context of a public event or in print or broadcast media. **Document search** ▪ The document search must be systematic, hierarchical and structured. ▪ It is carried out over a period suitable for the topic. ▪ The languages retained will be at minimum English and French.

	▪ It cannot be limited to articles published and indexed in databases. Grey literature is found by consulting relevant sources. This search makes it possible to initially identify the French and international guidelines and evidence reports created by governmental agencies, independent evaluation agencies and learned societies. ▪ This search is updated until publication of the memo GPG. ▪ It is supplemented by the bibliographic contribution of the experts of the working group and reading groups, and the references cited in the documents analysed. ▪ The document search strategy must appear in the final document. **Grading of recommendations** ▪ Grade A o Level 1 ▪ High-power randomised comparative studies ▪ Meta-analysis of randomised comparative studies ▪ Decision analysis based on well-conducted studies. ▪ Grade B: Scientific presumption o Level 2: ▪ Low-power randomised comparative studies ▪ Well-conducted non-randomised comparative studies ▪ Cohort studies. ▪ Grade C: Low level of evidence o Level 3: ▪ Case control studies. o Level 4: ▪ Comparative studies with major biases ▪ Retrospective studies ▪ Case series. **Drafting of the initial version of the guidelines** ▪ The proposals for recommendations graded and written based on the critical analysis of the literature by the project leader(s) are sent to the members of the working group at least 15 days before the first meeting. ▪ The members of the working group meet twice, or more if necessary, to create, based on the evidence report and proposals for recommendations written by the project leader(s), the initial version of the guidelines that will be submitted to the reading group. ▪ During the meetings of the working group, the evidence report and the proposals for graded recommendations are discussed based on the data and existing practices. The levels of evidence and the grades assigned will be discussed based on any new data from the literature provided by the members of the working group. ▪ In the absence of scientific evidence, a proposal for a recommendation will appear in the guidelines text subject to the opinion of the reading group if it is approved by at least 80% of the members of the working group. Ideally, this approval will be obtained using an electronic voting system (failing this, by show of hands) and will constitute an “expert agreement”. If all of the members of the working group approve a proposal for a recommendation without the need to conduct a vote, this will be stated in the evidence report.

	Reading phase (consultation) ▪ Two methods are proposed for the reading phase: o version A: consultation of a reading group (field professionals); o version B: consultation of stakeholders (professional organisations, patient or user associations, institutions, etc. affected by the topic). ▪ The choice between version A and version B depends on the topic and the nature of the comments expected: experience of field professionals on medical management for version A, more global opinion with a professional component for version B. ▪ Consultation of stakeholders is preferred (version B) for a topic with an organisational component, while that of a reading group is more suitable for topics with a strong geographical disparity of practices (version A). The choice of the version selected will be noted and explained in the project outline. ▪ In version A, the reading group gives a formalised opinion on the form and substance of the initial version of the guidelines, in particular on its acceptability, its applicability and its readability. ▪ In version B, an open questionnaire on the guidelines text and the evidence report is sent to each stakeholder. The response sent by each stakeholder represents the official opinion of the organisation, association or institution asked about the topic. The responses of the stakeholders are compiled in the evidence report. **Distribution** ▪ At the end of the process, HAS puts the summary sheet(s), the guidelines and the entirety of the evidence report online on its website (www.has-sante.fr), and sends them to the requesting party. ▪ The distribution may be supplemented by scientific publications and presentations at conferences in which members of the working group may participate. ▪ The guidelines and evidence report distributed at the end of the process must indicate: o the requesting party, any other sponsors and the stakeholders called upon; o the list of names and capacities of all parties involved (work leader(s), working group, reading group, persons interviewed by the working group or during the outlining phase); o the number and names of participants who are not in agreement with the final report; o the funding sources of the project (including distribution). ▪ A summary sheet with a list of guidelines, supplemented when possible with decision trees or diagrams that may be useful, is the main objective of the distribution. ▪ Preference should be given to electronic formats that take into account modern technological options. Access should be direct to the list and decision trees, with links for access to the reports and other documents. Compatibility with software used by professionals should be sought. **Updating** ▪ Updating the guidelines must be considered depending on the data published in the scientific literature or significant practice modifications occurring since publication of the guidelines.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R

What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	N/R
What are the core components of the key innovation?	N/A
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/A
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/A
How is the innovation used in practice?	N/A
Notes	
Reviewer notes	RQ1: Core components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management).
Associated peer-reviewed article(s)	N/R

Key: CPG - clinical practice guidelines; FCG - formalised consensus guidelines; GPG – good practice guidelines; HAS - Haute Autorité de Santé; N/A – not applicable; N/R – not reported.

Table B5 KCE Process Book

Guideline identification	
Organisation	KCE (Belgian Health Care Knowledge Centre)
Year	2021
Country	Belgium
URL	https://processbook.kce.be/ https://kce.fgov.be/en/about-us/our-methods-and-procedures
Title of the publication	KCE Process Book
Summary/Overview	The KCE process book outlines how evidence is searched for and included in clinical guidelines. As such it is limited to evidence synthesis methodology while details relating to governance, resource implications, implementation and communication are lacking. However, in the process book KCE strongly recommend the use of the AGREE II instrument as a checklist during all phase of the guideline development.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Methodological approaches** ▪ **Search for evidence** ○ A search strategy consists of several aspects. The research question (in a structured format) should be used as a guide to direct the search strategy. For electronic searches, it is important to list the databases in which studies will be sought. Other sources can be consulted in order to identify all relevant studies. These include reference lists from relevant primary and review articles, journals, grey literature and conference proceedings, research registers, researchers and manufacturers, and the internet. ○ In practice, it is uncommon for a single search to cover all the questions being addressed within a review. Different questions may be best answered by different databases, or may rely on different study types. Authors are encouraged to take an iterative approach to the search, carrying out a search for high-level evidence first. After evaluating the results of this first search, the questions may need to be redefined and subsequent searches may need to be focused on more appropriate sources and study types. ○ In some cases, directly relevant good-quality evidence syntheses (secondary sources), such as good-quality systematic reviews or Health Technology Assessments (HTA), will be available on some of the issues that fall within the remit of the review. In these circumstances reference will be made to the existing evidence rather than repeating work that already has been done. All HTA reports or systematic reviews that are identified must be evaluated on their quality and must be shown to have followed an acceptable methodology before they can be considered for use in this way. ○ In other cases existing evidence may not be directly relevant or may be found to have methodological weaknesses. In these cases, existing evidence cannot be used in the review. Nevertheless, excluded systematic reviews or HTA reports still can be a useful source of references that might be used later on in the review. **1. Building a search question** ○ Break down the review question into facets ○ Some generic templates exist, e.g. PICOS (Population, Intervention, Comparator, Outcome and Study design), PIRT (Population, Index test, Reference test, Target disorder), SPICE, ECLIPSE, SPIDER, etc.

	○ The final search strategy will be developed by an iterative process in which groups of terms are used, perhaps in several permutations, to identify the combination of terms that seems most sensitive in identifying relevant studies. This requires skilled adaptation of search strategies based on knowledge of the subject area, the subject headings and the combination of 'facets' which best capture the topic. **2. Searching electronic sources** ○ The decision on which source to use depends on the research question. The three electronic bibliographic databases generally considered being the richest sources of primary studies - MEDLINE, EMBASE, and CENTRAL - are essential in any literature review for the KCE. ○ Systematic reviews can be found in the Cochrane Database for Systematic Reviews, in Database of Abstracts of Reviews of Effects (DARE) or in Medline. HTA reports can be found in the HTA database of International Network of Agencies for Health Technology Assessment or at individual agencies sites. ○ Specifically for drugs and technology reviews, data from the US Federal Drug Administration or European Medical Agency can be helpful. ○ Documenting a search strategy: The search strategy for electronic databases should be described in sufficient detail to allow that the process could be replicated. An explanation could be provided regarding any study not included in the final report (identified by electronic sources search or not). **3. Searching supplementary sources** ○ Checking references list ○ Using related citation tools ○ Other supplementary sources: websites, hand searching of journals, experts in the field. **4. Searching for evidence on adverse effects** ○ The first sources to investigate for information on adverse effects are reports from trials or other studies included in the systematic review. Excluded reports might also provide some useful information. **5. Selecting studies** **5.1 Inclusion and exclusion criteria:** ○ The final inclusion/exclusion decisions should be made after retrieving the full texts of all potentially relevant citations. Reviewers should assess the information contained in these reports to see whether the criteria have been met or not. Many of the citations initially included may be excluded at this stage. The criteria used to select studies for inclusion in the review must be clearly stated: ▪ Types of participants: The diseases or conditions of interest should be described here, including any restrictions on diagnoses, age groups and settings. Subgroup analyses should not be listed here. ▪ Type of interventions: Experimental and control interventions should be defined here, making it clear which comparisons are of interest. Restrictions on dose, frequency, intensity or duration should be stated. Subgroup analyses should not be listed here. ▪ Types of outcome measures: Outcome measures of interest should be listed in this section whether or not they form part of the inclusion criteria. ▪ Types of studies: Eligible study designs should be stated here, along with any thresholds for inclusion based on the conduct or quality of the studies. ○ It is worthwhile pilot testing the inclusion criteria.

	○ The use of at least two reviewers has an important effect on reducing the possibility that relevant reports will be discarded. Agreement between assessors may be formally assessed mathematically using Cohen's Kappa and any disagreements and their resolution should be recorded. ○ The influence of uncertainty about study selection may be investigated in a sensitivity analysis. ○ It is useful to construct a list of excluded studies at this point, detailing the reason for each exclusion. This list may be included in the report of the review as an appendix. The final report of the review should also include a flow chart or a table detailing the studies included and excluded from the review. In the appendix a flow chart is provided for documenting study selection. If resources and time allow, the lists of included and excluded studies may be discussed with the expert panel. It may be useful to have a mixture of subject experts and methodological experts assessing inclusion. **5.2 Selection process** ○ Before any papers are acquired for evaluation, sifting of the search output is carried out to eliminate irrelevant material. The number of people assessing the relevance of each report should be stated in the Methods section of the review ▪ Papers that are clearly not relevant to the key questions are eliminated based on their title. ▪ Abstracts of remaining papers are then examined and any that are clearly not appropriate study designs, or that fail to meet specific methodological criteria, will be also eliminated at this stage. ▪ All reports of studies that are identified as potentially eligible must then be assessed in full text to see whether they meet the inclusion criteria for the review. **6. Quality assessment of studies** ○ The process of critical appraisal consists of an evaluation by two independent reviewers who confront their results and discuss them with a third reviewer in case of disagreement. However, because of feasibility it could be acceptable that one reviewer does the quality appraisal and that a second reviewer checks the other's work. ○ KCE recommends the use of the following tools for critical appraisal of different studies: ▪ Systematic reviews: AMSTAR 2 (alternative is the ROBINS-tool) ▪ Randomised controlled trials: Cochrane Collaboration's Risk of Bias Tool ▪ Diagnostic accuracy studies: QUADAS 2 tool ▪ Observational studies: The KCE elaborated two new checklists for cohort studies and case-control studies based on the checklist of SIGN and NICE. For the evaluation of prospective, non-randomised, controlled trials, the Cochrane Collaboration's Risk of Bias Tool can be used. GRADE also offers a number of criteria that can be used to judge the methodological quality of observational studies. ▪ Guidelines: AGREE II. **7. Data extraction** ○ In order to allow an efficient data extraction, the process should be detailed in the protocol before the literature search is started. Key components of the data extraction include: ▪ information about study reference(s) and author(s); ▪ verification of study eligibility; ▪ study characteristics:

	▪ study methods ▪ participants ▪ interventions ▪ outcomes measures and result. **7.1 Evidence tables** o All validated studies identified from the systematic literature review relating to each key search question are summarised into evidence tables. The content of the evidence tables is determined by the entire project group. Completion for all retained articles is done by one member of the project group and checked by another member. **7.2 GRADE evidence profiles** o To provide an overview of the body of evidence for each comparison relevant to the research question, GRADE evidence profiles are created and added to the appendix of the report. These evidence profiles can serve as a basis for the content discussions during the expert meetings. To create these evidence profiles it is highly recommended to use the GRADEpro software. When a meta-analysis is possible, it is recommended to extract the necessary information to Review Manager (RevMan) first, and subsequently to import this information from RevMan into GRADEpro. **8. Analysing and interpreting results** o Once the eligible studies are selected and quality appraised, the magnitude of the intervention effect should be estimated. The best way to do this is by performing a meta-analysis (i.e. the statistical combination of results from two or more separate studies), although this is not always feasible. o The starting point of the analysis and interpretation of the study results involves the identification of the data type for the outcome measurements. Five different types of outcome data can be considered: ▪ dichotomous data: two possible categorical responses ▪ continuous data ▪ ordinal data: several ordered categories; ▪ counts and rates calculated from counting the numbers of events that each individual experiences; ▪ time-to-event data. **9. Reporting the literature review** o A literature search should be reproducible and therefore explicitly documented. The report of a literature search should contain the following items: 1. Description of the search methodology: o Search protocol ▪ Search question ▪ Searched databases ▪ Search terms, their combinations and the restrictions used (e.g. language, date) ▪ Inclusion and exclusion criteria for the selection of the studies. o Quality appraisal methodology. o Data extraction methodology. 2. Description of the search results:

	○ Number of retrieved articles, included and excluded studies, and reasons for exclusion; use of flow chart ○ Results of quality appraisal. ○ Evidence tables for each search question. ▪ **Literature review and international comparisons** ○ Rationales for international comparisons in health services research: does an international comparison serve your problem? ○ Adapt the "set-up2 of the international comparison to the problem you want to address. ▪ **Data collection and analysis** ○ Qualitative data. ○ Health services research. ○ Websurvey. ▪ **Economic evaluation and budget impact analysis** ○ KCE has developed guidelines for economic evaluation and budget impact analysis for Belgium. For economic evaluation, there are guidelines for ▪ the literature review, ▪ the perspective of the evaluation, ▪ the target population, ▪ the comparators, ▪ the analytic technique, ▪ the study design, ▪ the calculation of costs, ▪ the estimation and valuation of outcomes, ▪ the time horizon, ▪ modelling, ▪ handling uncertainty and testing the robustness of the results, ▪ the discount rate. ○ The guidelines for budget impact analysis encompass specificities with respect to the target population and the comparator and refers to guidelines for economic evaluation which should also be respected in the budget impact analysis. ▪ **Formulation of clinical recommendations** ○ Formulating a recommendation (even if the level of evidence is low) should always be the aim. The other options (not to formulate a recommendation, formulate an "only in research recommendation" or formulate a recommendation without grading should be exceptions. ▪ **Recommendation with grading** ○ The panellists should not be afraid with the formulation of recommendations even if evidence is poor. Absence of a statistically significant effect is not proof that an intervention does not work. It is only proven that an intervention does not work if the confidence interval around the effect estimation excludes a minimally important difference or decision threshold. Even when the confidence in an effect estimate is low and/or desirable and undesirable consequences are closely balanced, GRADE

	encourages to make recommendations (inevitably weak) to avoid clinicians' frustration with the lack of guidance. ▪ **No recommendation** o It could be proposed not to formulate a recommendation: ▪ When the confidence in effect estimates is so low that the panellists feel a recommendation is too speculative ▪ When there is moderate or high confidence in effect estimates but the trade-offs are very closely balanced, and the values and preferences and resource implications are not known or too variable, and the panel has great difficulty in deciding on the direction of the recommendation. o Choosing not to make a recommendation might be an exception. And if the panel chooses to make no recommendation, the reason (low confidence in effect estimate or close balance between harm and benefit) should be specified. ▪ **"Only in research" recommendation** o "Only in research" recommendation will be appropriate when 3 conditions are met: ▪ There is insufficient evidence supporting an intervention for a panel to recommend its use. ▪ Further research has a large potential for reducing uncertainty about the effects of the intervention. ▪ Further research is deemed good value for the anticipated costs. ▪ **Recommendation without grading** o In some cases, grading a recommendation can be superfluous, but the eligibility criteria to choose this option still have to be determined by the KCE and are currently under discussion. ▪ **Guideline development: Principles** o The clinical practice guidelines developed at KCE follow the AGREE principles. Hence, it is strongly recommended to use the AGREE II instrument as a checklist during all phases of the guideline development. ▪ **ADAPTE** o KCE suggest that ADAPTE should only be used when high-quality, recent guidelines are available that are in line with the defined PICO. This implies that a clinical practice guideline project always starts with a search for guidelines. The following criteria will need to be taken into account when assessing the relevance of a guideline: o All identified guidelines will need an assessment with the AGREE II instrument by two independent reviewers. Although the domain scores of AGREE II are useful for comparing guidelines and will inform whether a guideline should be recommended for use, the AGREE Consortium has not set minimum domain scores or patterns of scores across domains to differentiate between high-quality and poor-quality guidelines. These decisions should be made in consensus by the reviewers and guided by the context in which AGREE II is being used. Quantified cut-offs, while easy to use and enhancing reproducibility, are not recommended, because they have serious validity problems. The most important domain to be taken into account is 'Rigour of development'. o A criterion that could be taken into account as well is the degree of detail provided by the guideline on the evidence that was used for developing the recommendations. In order to apply GRADE correctly a

	lot of detail is needed: in case it is necessary to retrieve all the primary studies, the gain of adapting a guideline becomes limited. ○ Updating a guideline with a search date that is too old may not be efficient, although it is difficult to recommend a general rule. Two years could be used as a rule of thumb, although this is very context- and topic-specific. ▪ Each research team can decide to use or not to use ADAPTE based on written arguments. This decision should be made when the research protocol is written. In case of subcontracting, the choice of method will have to be discussed with the subcontractor. Transparent and documented judgement is key here, not the blind application of a set of rules. ▪ If it is decided to use ADAPTE, the ADAPTE Manual and Resource Toolkit should be carefully read. The protocol should contain a clear description of how ADAPTE will be used (e.g. only used for some research questions, update of source guidelines with new evidence, etc.). ▪ **GRADE system** ○ GRADE includes the following steps: ▪ Ask a specific healthcare question to be answered by a recommendation; ▪ Identify all important outcomes for this healthcare question; ▪ Judge the relative importance of outcomes; ▪ Summarise all relevant evidence; ▪ Grade the quality of evidence for each outcome and for each comparison; ▪ Decide on the overall quality of evidence across outcomes; ▪ Include judgments about the underlying values and preferences related to the management options and outcomes; ▪ Decide on the balance of desirable and undesirable effects; ▪ Decide on the balance of net benefits and cost; ▪ Grade the strength of recommendation; ▪ Formulate a recommendation; ▪ Implement and evaluate. ▪ **Patient involvement** ▪ **Standards for patient involvement in KCE research (adapted from NIHR INVOLVE, 2019)** ▪ Inclusive opportunities ○ patients are involved at an early stage ○ barriers for patients to getting involved in research are identified and addressed ○ information about opportunities for patient involvement in research are made available using different methods so that relevant and interested people are reached ○ processes for patient involvement in research are fair and transparent ○ choice and flexibility in ways to get involved in research are offered. ▪ Working together ○ the purpose of the patient involvement activity is jointly defined ○ patient involvement plans and activities are developed together

	○ there is shared understanding of roles, responsibilities and expectations, which may evolve over time ○ individual ideas and contributions are recognised and decisions are upheld together. ▪ Support and learning ○ resources to ensure and support effective patient involvement are designated and monitored ○ support is offered to researchers and patients to address identified needs ○ there is an identified point of contact for information and support ○ the team builds on what was learned in other projects. ▪ Communications ○ inclusive and flexible communication methods are used to meet the needs of different people ○ feedback is gathered, offered, shared and acted upon. ▪ Impact ○ patients are involved in the assessment of patient involvement in research ○ the purpose for patient involvement and its intended outcomes are agreed upon ○ information that will help assess the impact of patient involvement in research is collected ○ the extent to which the intended purpose and predicted outcomes are met are reflected upon, learnt from and reported. **Relevant information identified on the KCE website** ▪ Patient involvement ○ patient voices are heard, valued and included in decision making ○ patient involvement strategies and/or plans are in place and regularly monitored, reviewed and reported upon ○ responsibility for patient involvement is visible and accountable throughout the management structure ○ money and other resources are allocated for public involvement. ▪ Stakeholders ○ In each of its studies, KCE systematically invites interested stakeholders to participate to gather their opinions on the subject. These meetings tend to improve and professionalise the interface between the scientific world and the decision-makers in the field of healthcare. ▪ External validation of reports ○ All KCE reports are submitted to three external validators, at least one of which is international. These validators are chosen among recognised experts from the field. They are expected to validate the methodology, the data and the scientific conclusions of the work, but the policy recommendations are not their responsibility. ▪ Conflicts of interest ○ Researchers may not conduct any professional activities outside KCE that may lead to a conflict of interest. All external partners participating in a KCE project as subcontractor, external expert, or validator are requested to sign a declaration of conflicts of interest, and conflicts of interest (if any) are listed in the relevant report. ▪ Presentation and language of reports

	○ Each KCE report is published on the KCE website within one month of approval by the Board of Directors. For each report, a separate, specific page is created. Depending on the level of interest, the reader can choose between different options: The scientific report with the full description of the research, the methodological details and the results. This report is always written in English because it is the language of the scientific world (Belgian and international). ▪ Copyright ○ Unless explicitly mentioned otherwise, KCE documents are published under a "by/nc/nd" Creative Commons Licence 2.0. This licence allows reproduction (1), distribution and communication of the work to the general public under the following rules: "by" = Attribution. ▪ Governance ○ KCE's board of directors consists of representatives of public bodies active in healthcare, patient associations and health insurance. The composition is balanced and it plays a key role in scrutinising KCE's neutrality and safeguarding their independence. At each Board meeting new reports are presented. The scientific content is in principle not subject to modification, except on the basis of quantifiable methodological arguments. The political recommendations, based upon the scientific work, are discussed, sometimes nuanced, and approved by a simple majority, when voting turns out to be necessary. KCE is legally obliged to publish all of its results within one month of their approval by the Board, which is an additional guarantee for transparency.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	Rapid review
What are the core components of the key innovation?	Dimensions of standard systematic review that may be altered in a rapid review and whether this is an option for KCE guideline ▪ Scope ○ Limit the type of questions (e.g. efficacy only, new technology only, single technology only): Yes ○ Limit number of questions: Yes ○ Limit the number of studies that can be included: Yes ▪ Comprehensiveness ○ Limit search strategy (e.g. number of databases, grey literature, date, setting, language): Yes ○ Limit study types included (e.g. existing systematic reviews only, randomised controlled trials only): Yes ○ Limit textual analysis (e.g. no full-text review, limit number of extracted items): Limit number of items ▪ Rigour/quality control

	○ Eliminate dual study selection: Yes (done systematically at KCE) ○ Eliminate dual data extraction: Yes (done systematically at KCE) ○ Limit or eliminate internal or external review of final product (e.g. peer review): Limit to internal ▪ Synthesis ○ Limit or eliminate risk of bias/quality assessment of individual studies: No ○ Limit or eliminate either quantitative or qualitative analysis: No ○ Limit or eliminate strength/quality of evidence assessments (e.g.: using GRADE): No ▪ Conclusions ○ Simplify or eliminate any conclusive statements about the direction of the evidence: No
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	Increasingly, healthcare decision makers demand high-quality evidence in a short timeframe to support urgent and emergent decisions related to procurement, clinical practice, and policy. One consistently identified barrier to implementing results from evidence syntheses is an incongruence between the time required to produce a full systematic review and the time within which policy and other decision makers must render decisions. The concern regarding a timely decision on healthcare and policies is thus the driving force for rapid reviews.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	**RQ1: Core components:** Evidence based, Knowledge management, Service user/stakeholder involvement. **RQ3: Innovation:** Rapid review.
Associated peer-reviewed article(s)	National Institute for Health Research. National Standards for Public Involvement in Research. 2018 Available at https://www.nihr.ac.uk/news/nihr-announces-new-standards-for-public-involvement-in-research/23830

Key: AGREE - Appraisal of Guidelines for REsearch & Evaluation; RevMan – Review Manager; AMSTAR 2 – Assessing the Methodological Quality of Systematic Reviews; DARE – Database of Abstracts of Reviews of Effects; GRADE - Grading of Recommendations Assessment, Development and Evaluation; HTA - health technology assessments; KCE – Belgian Health Care Knowledge Centre (translation); N/A – not applicable; NICE - National Institute for Health and Care Excellence; N/R – not reported; PICOS – Population, Intervention, Comparison, Outcome; PIRT – Population, Index test, Reference test, Target disorder; SIGN - Scottish Intercollegiate Guidelines Network; QUADAS 2 - Quality Assessment of Diagnostic Accuracy Studies, 2nd edition; ROBINS-tool - Risk Of Bias In Non-randomized Studies - of Interventions - tool.

Table B6 KNGF guideline methodology: Development and implementation of KNGF guidelines

Guideline identification	
Organisation	Koninklijk Nederlands Genootschap voor Fysiotherapie (KNGF) [Royal Dutch Society for Physical Therapy]
Year	2019
Country	The Netherlands
URL	https://www.kngf.nl/binaries/content/assets/kennisplatform/onbeveiligd/guidelines/kngf-guideline-methodology-2019.pdf
Title of the publication	KNGF guideline methodology: Development and implementation of KNGF guidelines.
Summary/Overview	This guideline development manual is aimed at physical therapists and the methodology is based on the Appraisal of Guidelines for REsearch & Evaluation (AGREE) II instrument and the Guidelines International Network (GIN)-McMaster Guideline Development Checklist. It has a major emphasis on stakeholder engagement and implementation, includes a wide range of supporting templates but does not appear to require considerations around resource implications such as conducting a budget impact assessment. However, it does mention the potential need to include cost-effectiveness literature as part of the systematic searches for evidence and it also required a barrier analysis to be conducted during research question formulation.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	Phases of the KNGF guideline methodology and their components 1. Preliminary phase o Needs assessment and formulation of a recommendation to the Board o Inclusion of the guideline policy in the KNGF annual plan. 2. Preparation phase o Hiring of the subject-matter expert scientist by contracting a knowledge institute ▪ Approach subject-matter expert scientists and the knowledge institute where the scientists are employed, document the agreements made with the knowledge institute. o Setup of the guideline panel and review panel ▪ Approach members for the guideline panel and review panel and document agreements that were made. o Collection and prioritisation of barriers o Perform a barrier analysis. o Determination of the clinical questions ▪ Formulate and determine the clinical questions ▪ Formulate the search strategy. Existing evidence-based guidelines, systematic reviews and/or meta-analyses are then used in the first instance. If this strategy ultimately yields insufficient literature, then randomised controlled studies are searched for in the second instance and observational studies in the third instance. o Execution of orienting review* ▪ Execute orienting review as preparation for the guideline process. 3. Development phase o Formulation of the clinical questions ▪ Conduct systematic review

	▪ Discuss literature results and considerations using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach. ▪ Determine concept recommendations or description using evidence to decision making framework ○ Finalisation of the module ▪ Approve concept modules ▪ Finalise the modules. ○ Delivery of a concept guideline ○ Combine final modules into chapters ○ Combine chapters into a concept guideline. ○ Delivery of a summary of the guideline ▪ Summarise the KNGF guideline. ○ Start development of indicators and implementation products ▪ Develop concept quality indicators. 4. Review phase ○ Collection of internal reviews ▪ Collect reviews from the professional field ▪ Collect reviews from the WCF ▪ Collect reviews from the KNGF and VvOCM Boards. ○ Collection of external reviews ▪ Collect reviews from external involved stakeholders ▪ Collect reviews from the review panel. ○ Summarisation of the collected reviews ▪ Summarise all the collected reviews. ○ Discussion of the collected reviews ▪ Present and discuss the summary of the collected reviews ▪ Come to a consensus about the changes that need to be made. ○ Processing of the review ▪ Implement the desired changes into the guideline ▪ Resubmit the guideline to the guideline panel. ○ Finalisation of the guideline ▪ Give final approval of the guideline. 5. Editing phase ○ Editing of the final draft. 6. Authorisation phase ○ Authorisation of the final draft ▪ Submit the final draft to the KNGF Board and VvOCM Board ▪ Submit the final draft to the involved external stakeholders. 7. Dissemination and implementation phase ○ Publication of the guideline on the KNGF knowledge platform

	○ Communicating about the guideline ○ Submission of the guideline for inclusion in the Dutch Guideline Database of the Healthcare Institute of the Netherlands ○ Development of supplemental guideline (implementation) products and appendices. 8. Maintenance phase ○ Continuous collection of feedback from the professional field ○ Annual monitoring of publications and developments ○ Modification or complete revision of the guideline ○ Execution of a needs assessment and desk research ○ Continuous monitoring by the knowledge institute. Criteria for developing a new guideline: ▪ the needs of the professional field; ▪ the prevalence of the health problem in daily practice; ▪ the scope of the health problem, whereby it can be assumed that physical therapy will result in health benefits; ▪ the degree of scientific evidence; ▪ the degree of variation in physical therapy activities; ▪ the possibility of limiting the topic; ▪ whether it is realistic to expect the relevant stakeholders to reach a consensus; ▪ whether the guideline can be included in the short term or can be affiliated with an external guideline or healthcare standard; ▪ the importance of the guideline for the position of the physical therapy. Additional criteria for full or modular revision: ▪ the age of the guideline or module; ▪ the degree of relevance of new insights and/or scientific evidence ▪ the degree to which the guideline is employed in daily practice; ▪ the severity of the barriers that are found when applying the guideline or module; ▪ a new external guideline about the topic has been published, due to which the (organisation of) physical therapy care must change.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	N/R
What are the core components of the key innovation?	N/A
What is the rationale behind the methodology?	N/A

OR **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/A
How is the innovation used in practice?	N/A
Notes	
Reviewer notes	RQ1: All components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review & evaluation process).
Associated peer-reviewed article(s)	N/R

Key: AGREE - Appraisal of Guidelines for REsearch & Evaluation; GIN – Guidelines International Network; KNGF - Koninklijk Nederlands Genootschap voor Fysiotherapie; VvOCM - Vereniging van Oefentherapeuten Cesar en Mensendieck [Association of Cesar and Mensendieck Exercise Therapists], WCF - Wetenschappelijk College Fysiotherapie [Scientific College of Physical Therapy]; N/A – not applicable; N/R – not reported.

* this has been interpreted by the authors of this review as similar to a scoping review

Table B7 NHMRC Standards for Guidelines

Guideline identification	
Organisation	Australian National Health and Medical Research Council (NHMRC)
Year	2016
Country	Australia
URL	https://www.nhmrc.gov.au/guidelinesforguidelines/standards
Title of the publication	2016 NHMRC Standards for Guidelines.
Summary/Overview	The NHMRC handbook is a comprehensive outline of the standards for guideline development and additionally describes all of the necessary steps to fulfil these standards, which includes all the core components including the ADAPTE framework, Appraisal of Guidelines for Research & Evaluation (AGREE) II assessment tool, CAN-IMPLEMENT framework for assessing existing guidelines and the GRADE working group methodology. Initially, the standards were informed by the Institute of Medicine (2011) Clinical Practice Guidelines We Can Trust; since 2016, significant stakeholder engagement has informed their updating.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	Standard 1 - Be relevant and useful for decision making 1. To be relevant and useful for decision making, guidelines will: 1.1. Address a health issue of importance 1.2. Clearly state the purpose of the guideline and the context in which it will be applied 1.3. Be informed by public consultation 1.4. Be feasible to implement. Organisations and groups invest significant time, energy and resources into guidelines with the expectation that they will be used. To be relevant and useful, guidelines need to address issues that are important to their target audience. The relative importance of health issues depends on many factors such as prevalence, the burden of disease (the impact of living with illness and injury and dying prematurely) and cost. It is important for developers to clearly articulate the purpose of their guidelines. Not doing so could likely cause misinterpretation of key messages, unintended application of the recommendations, or create issues during implementation. This risks not just wasted resources but an increased risk of causing harm. Standard 2 - Be transparent 2. To be transparent, guidelines will make publicly available: 2.1. The details of all processes and procedures used to develop the guideline 2.2. The source evidence 2.3. The declarations of interest of members of the guideline development group and information on how any conflicts of interest were managed 2.4. All sources of funding for the guideline. Guideline transparency refers to the inclusion of information that enables the reader to understand how recommendations were developed and who developed them. It is necessary so that people using it can be confident about a guideline's trustworthiness. Thorough documentation of the process of identifying and assessing relevant evidence is an important step in doing this. Standard 3 – Be overseen by a guideline development group 3. The guideline development group will:

	3.1. Be composed of an appropriate mix of expertise and experience, including relevant end users 3.2. Have clearly defined, documented processes for reaching consensus The composition of the guideline development group should reflect the range of individuals and organisations whose activities, services or care will be covered by the guideline. Development groups must include a mix of expertise and experience and be representative of those most likely to be affected by the guideline, such as consumers, researchers, clinicians, policymakers and others expected to use or implement the guideline. It is important to get the membership and functioning of the development group right, since it is their judgement that influences the interpretation of evidence and the wording and strength of recommendations. Thorough documentation of the composition and decision making of the development group is also essential for a trustworthy guideline. For example, a guideline should state who the development group members were, how they were selected, their affiliations and disciplines, and any conflicts of interest that were identified and how they were managed. <u>Standard 4 - Identify and manage conflicts of interest</u> 4. To identify and manage conflicts of interest, guideline developers will: 4.1. Require all interests of all guideline development group members to be clarified 4.2. Establish a process for determining if a declared interest represents a conflict of interest, and how a conflict of interest will be managed. Credible and trustworthy guidelines are unbiased. When forming recommendations, guideline development groups will consider the available evidence and interpret how it should be applied in practice. Because there are often limitations in this evidence, considered judgement becomes an integral part of a guideline's development. To ensure a guideline's recommendations are objective and unbiased all members must declare their interests and careful steps must be taken to manage any conflicts. Policies on declaration and management of competing interests in guideline development are designed to protect the integrity of guidelines and the individuals involved in their development. <u>Standard 5 - Be focused on health and related outcomes</u> 5. To be focused on health and related outcomes, guidelines will: 5.1. Be developed around explicitly defined clinical or public health questions 5.2. Address outcomes that are relevant to the guideline's expected end users 5.3. Clearly define the outcomes considered to be important to the person/s who will be affected by the decision, and prioritise these outcomes. Focusing on the right outcomes ensures that guidelines will address the needs of the target population and those of other stakeholders and the general public. Chalmers and Glasziou *et al*, suggest that considerable research waste could be avoided by more effectively involving consumers in research planning and by addressing higher priority questions and outcomes. <u>Standard 6 - Be evidence informed</u> 6. To be evidence informed, guidelines will: 6.1. Be informed by well conducted systematic reviews 6.2 Consider the body of evidence for each outcome (including the quality of that evidence) and other factors that influence the process of making recommendations including benefits and harms, values and preferences, resource use and acceptability.

	6.3 Be subjected to appropriate peer review. The cornerstone of guideline development is that recommendations about practice and policy should be based on the best available evidence. Although this is an expectation held by health professionals and the public alike, a lot of health advice is developed with little or no evidence to support its claims. In some cases these claims may mislead people to reject policies or treatments that are proven to be effective in favour of non-evidence-based alternatives. <u>Standard 7 - Make actionable recommendations</u> 7. To make actionable recommendations, guidelines will: 7.1. Discuss the options for action 7.2 Clearly articulate what the recommended course of action is, and when it should be taken 7.3 Clearly articulate what the intervention is so it can be implemented 7.4 Clearly link each recommendation to the evidence that supports it 7.5 Grade the strength of each recommendation. For all the complexity of guideline development, the usability of guidelines comes down to the clarity of their recommendations. Recommendations must be concise and clearly worded but contain enough information to allow informed decisions about health. <u>Standard 8 - Be up-to-date</u> 8. To be up-to-date, guidelines will: 8.1. Ensure that the recommendation is based on an up-to-date body of evidence 8.2 Propose a date by which the evidence and the guideline should be updated. This may be specific to each recommendation. Guidelines can quickly become out of date, particularly in areas with an active research program. Keeping the evidence in guidelines up-to-date ensures that their recommendations are derived from current evidence, which is critical for their ongoing relevance and reliability. It is also one of the biggest challenges facing guideline developers in Australia. <u>Standard 9 - Be accessible</u> 9. To be accessible, guidelines will: 9.1. Be easy to find 9.2 Ideally be free of charge to the end user 9.3 Be clearly structured, easy to navigate and in plain English 9.2 Be available online. This is important because guidelines have to be easily located and accessible if they are to be used. Guideline developers write guidelines with the expectation that they will be used, but too often they publish them in ways that make them inaccessible to their intended users. For example, developers may set financial barriers by choosing to publish their guidelines in journals where they sit behind expensive paywalls, or on the websites of organisations which are only accessible to members, or by selling them directly to users. Guidelines can also be difficult to find, a problem which can be made worse by practices such as publishing guidelines without serial numbers and by allowing old and outdated versions to remain in circulation without rescindment. **Equity Considerations (new core component)** 1. Identify equity issues relevant to the guideline 2. Engage with communities affected by inequity 3. Ensure appropriate evidence is sought, identified and considered

	4. Understand the impact of guideline recommendations on disadvantaged populations 5. Identify areas where research is needed about equity and disadvantaged populations NHMRC Standards 5.1 and 6.2 apply to equity
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	Australia have implemented Living Reviews, but have yet to publish methodological guidance.
What are the core components of the key innovation?	N/R
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/R
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	Core components: clarity of scope and purpose; governance model; evidence-based; knowledge management; planning and implementation; stakeholder involvement.
Associated peer-reviewed article(s)	Armstrong, M. J. and J. A. Bloom (2017). "Patient involvement in guidelines is poor five years after institute of medicine standards: review of guideline methodologies." Research Involvement and Engagement 3(1):19. Chalmers, I. and P. Glasziou (2009). "Avoidable waste in the production and reporting of research evidence." Lancet 374(9683): 86-8.

Key: AGREE – Appraisal of Guidelines for Research & Evaluation; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; N/A – not applicable; NHMRC – Australian National Health and Medical Research Council; N/R – not reported.

Table B8 NICE Developing NICE guidelines: the manual

Guideline identification	
Organisation	National Institute for Health and Care Excellence (NICE)
Year	2022
Country	UK
URL	https://www.nice.org.uk/process/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869
Title of the publication	Developing NICE guidelines: the manual.
Summary/Overview	A comprehensive handbook that outlines all core components and provides detailed instructions on how to fulfil the NICE requirements. The guideline development process as outlined in the handbook is prescriptive in nature. The handbook is regularly updated with information readily available on what has changed. It has a major focus on resource implications and stakeholder engagement, in particular patient involvement is a key core component that is comprehensively detailed.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Main stages of guideline development** ▪ Topic referred to NICE or update commissioned by NICE ▪ Scoping ○ Developer drafts scope, including key issues and review questions ○ Stakeholders comment on draft scope ○ Final scope identified. ▪ Development ○ Structured review questions agreed ○ Literature searched ○ Call for evidence from stakeholders if needed ○ Evidence reviews and economic analysis prepared ○ Committee discusses evidence reviews and expert testimony and develops draft recommendations. ▪ Consultation ○ Stakeholders comment on draft guideline. ▪ Revision ○ Committee revise guideline in response to stakeholder comments. ▪ Quality assurance and sign off ○ Quality assurance by NICE staff ○ Guidance executive sign off guideline. ▪ Publication ○ Confidential advance copy released to stakeholders that commented on draft guideline ○ Resources to support implementation published. ▪ Updating ○ Regular checks to determine if an update is needed ○ Part or all of guideline updated according to usual process and methods. **Details on a section of core elements** ▪ **Decision-making committee**

	○ A decision-making committee (either a standing committee or a topic-specific committee) draws on its expertise to develop recommendations in the areas defined by the scope of the guideline. ○ All committee members, including the chair, and anyone who has direct input into the guideline (including the developer and expert witnesses) must declare any potential conflicts of interest in line with NICE's policy on declaring and managing interests for NICE advisory committees. ○ The committee needs to be multidisciplinary and include: ○ practitioners, professionals, providers, commissioners and researchers (specialists and generalists from the public, private or voluntary sectors, from other independent providers of care and support, or from services) ○ lay members (people using services, family members and carers, and members of the public and community or voluntary sector with relevant experience). ▪ **Identifying and meeting training needs of committee members** ○ All committee members, including topic expert members and co-opted members, receive an induction from NICE or the developer covering: ▪ key principles for developing NICE guidelines ▪ the process of developing NICE guidelines, including the importance of being familiar with relevant chapters of this manual ▪ how the elements of the guideline development process fit together, and the relationship to quality standards and products supporting implementation ▪ the role of the committee, including Terms of Reference and Standing Orders, and how lay members contribute ▪ the role of the developer and NICE teams ▪ formulating review questions ▪ reviewing evidence ▪ the basics of how economics methods are used in decision-making ▪ developing and wording recommendations ▪ how guidelines are presented on the NICE website ▪ information about resource impact and how this is considered alongside the economic evidence ▪ information about implementation ▪ NICE's principles and equality scheme ▪ declaration of interests. ▪ **Identifying the evidence: literature searching and evidence submission** ○ Literature searches should be systematic, transparent and reproducible to minimise 'dissemination biases'. These may affect the results of reviews and include publication bias and database bias. ○ NICE encourages the use of search methods that balance recall and precision. The aim is to identify the best available evidence to address a particular question without producing an unmanageable volume of results. If review questions are so broad that the information specialist has to restrict the searches to complete the review in the time available, this should be acknowledged as a limitation in the final review document.

	○ A flexible approach to the search for evidence should be adopted, guided by the subject of the question and type of evidence sought. When the guideline is an update, the approach can also be informed by searches for the existing guideline and subsequent surveillance review. Searching includes: ▪ tailoring the search approach to the eligibility or inclusion criteria of the review question, as specified in the review protocol ▪ selecting appropriate sources according to the eligibility or inclusion criteria of the review question, as specified in the review protocol ▪ using additional search techniques, such as citation searching, as appropriate ▪ continuous review of how best to find evidence and where. ▪ **Health inequalities and equality and diversity** ○ All searches should be inclusive, capturing evidence related to health inequalities or impacts on equality relevant to the guideline topic. ▪ **Assessing quality of evidence: critical appraisal, analysis and certainty in the findings** ○ Options for assessing the quality of the evidence should be considered by the developer. ○ The chosen approach should be discussed and agreed with NICE staff with responsibility for quality assurance, where the approach deviates from the standard (described in critical appraisal of individual studies). ○ The agreed approach should be documented in the review protocol together with the reasons for the choice. If additional information is needed to complete the data extraction or quality assessment, study investigators may be contacted. ○ Reporting reviews or using recommendations from previously published guidance from other organisations: ▪ If systematic reviews or qualitative evidence syntheses done as part of a published non-NICE guideline are used as evidence within a NICE guideline, those reviews should be assessed following the advice in the section above on reporting reviews based on a published systematic review or qualitative evidence synthesis. No assessment of other aspects of the guideline is needed, because only the evidence from the reviews is being used, not any other part of the non-NICE guideline. ▪ If parts of the non-NICE guideline other than evidence reviews are used (for example, if the recommendations made are themselves used as evidence, not just the underlying reviews) then the guideline should be assessed for quality using the Appraisal of Guidelines for REsearch & Evaluation (AGREE) II instrument. There is no cut-off point for accepting or rejecting a guideline, and each committee needs to set its own parameters. These should be documented in the methods of the guideline, and the full results of the assessment included in the evidence review document. ▪ **Critical appraisal of individual studies** ○ Every study should be appraised using a checklist appropriate for the study design. If a checklist other than those listed is needed, or the one recommended as the preferred option is not used, the planned approach should be discussed and agreed with NICE staff with responsibility for quality assurance and documented in the review protocol.

	▪ **Certainty or confidence in the findings by outcome** ○ Before starting an evidence review, the outcomes of interest that are important to people using services and the public for the purpose of decision-making should be identified. The reasons for prioritising outcomes should be documented in the evidence review. This should be done before starting the evidence review and clearly separated from discussion of the evidence, because there is potential to introduce bias if outcomes are selected when the results are known. ○ The committee discussion section should also explain how the importance of outcomes was considered when discussing the evidence. Alternatively, they may think that all prioritised outcomes are crucial for decision making. In this case, there will be no distinction between 'critical' or 'important' for all prioritised outcomes. ○ GRADE or GRADE-CERQual tables summarise the certainty in the evidence and data for each critical and each important outcome or theme and include a limited description of the certainty in the evidence. GRADE or GRADE-CERQual tables should be available (in an appendix) for each review questions. ▪ **Equality and diversity considerations** ○ NICE's equality and diversity duties are expressed in a single public sector equality duty. ○ The equality duty supports good decision making by encouraging public bodies to understand how different people will be affected by their activities. For NICE, much of whose work involves developing advice for others on what to do, this includes thinking about how people will be affected by its recommendations when these are implemented. ▪ **Health inequalities** ○ NICE considers that it should also take account of socioeconomic factors and the circumstances of certain groups of people (such as looked-after children and people who are homeless). If possible, NICE's guidance aims to reduce and not increase identified health inequalities. ○ Any equalities criteria specified in the review protocol should be included in the evidence tables. At the data extraction stage, reviewers should refer to the PROGRESS-Plus criteria (including age, sex, sexual orientation, disability, ethnicity, religion, place of residence, occupation, education, socioeconomic position and social capital) and any other relevant protected characteristics, and record these where reported, as specified in the review protocol. Review inclusion and exclusion criteria should also take the relevant groups into account, as specified in the review protocol. ○ Equalities should be considered during the drafting of the reviews. Equality considerations should be included in the data extraction process and should be recorded in the committee discussion section if they were important for decision making. ▪ **Incorporating economic evaluation** ○ Guideline recommendations should be based on the balance between the estimated costs of the interventions or services and their expected benefits compared with an alternative (that is, their 'cost effectiveness'). In general, the committee should be increasingly certain of the cost effectiveness of a recommendation as the cost of implementation increases. ○ The committee may require more robust evidence on the effectiveness and cost effectiveness of recommendations that are expected to have a substantial impact on resources. Economic analysis must be done when there is no robust evidence of cost effectiveness to support these recommendations.

	Any uncertainties must be offset by a compelling argument in favour of the recommendation. However, the cost impact or savings potential of a recommendation should not be the sole reason for the committee's decision. ▪ **Writing the guideline** o During development of the guideline, the developer and committee will write: ▪ the recommendations ▪ recommendations for research ▪ the rationale for the recommendations, and their likely impact on practice ▪ the context for the guideline – such as the need for the guideline, or the reason for updating an existing guideline ▪ summaries of evidence supporting shared decision making, if there are preference sensitive decision points in the guideline ▪ information about changes to published recommendations (if the guideline is an update) ▪ structured summaries of the committee's discussions ▪ summaries of the evidence – with details of analysis and any modelling ▪ the methods used for guideline development – highlighting the reasons for options taken, and any deviations from the methods and processes described in this manual. ▪ **Interpreting the evidence to make recommendations** o The committee must use its judgement to decide what the evidence means in the context of the guideline referral and decide what recommendations can be made to practitioners, commissioners of services and others. o The strength and quality of the evidence is assessed for both internal and external validity, but also requires interpretation. Evidence also needs to be assessed in light of any conceptual framework. o As soon as the committee has discussed the evidence, they should start drafting recommendations. They should decide what action to recommend and keep in mind which sectors (including which practitioners or commissioners within those sectors) should act on the recommendations. The record of the committee's discussion should explain clearly how they moved from the evidence to each recommendation, and document how any issues influenced their decision-making. o In line with the GRADE principles on 'evidence to decisions', summaries of the discussions should describe the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence, as well as other considerations o Findings from several evidence reviews may be integrated into a single summary of the committee's discussions if they relate to the same recommendation or group of recommendations. o For each group of recommendations, the committee should briefly explain their rationale for making the recommendations and record their views on any likely impact of the recommendations on practice or services. ▪ **The validation process for draft guidelines, and dealing with stakeholder comments** o Registered stakeholders are notified of the consultation dates in advance via the guideline page on the NICE website, and are reminded by email.

	○ Before the draft guideline is signed off for consultation, an equality impact assessment is completed by the developer and the committee chair to show which equality issues have been identified and considered during guideline development. The equality impact assessment is signed off by a member of NICE staff with responsibly for quality assurance, and published on the NICE website with the draft guideline. The assessment is updated by the developer and the committee chair after the consultation. ▪ **When a second consultation may be needed** ○ In exceptional circumstances, NICE may consider the need for a further stakeholder consultation after the first consultation. ○ NICE staff with responsibility for guideline quality assurance make the final decision on whether to hold a second consultation, and how long it should be. ▪ **Quality assurance of the guideline** ○ After changes agreed by the committee have been made to the guideline in response to consultation comments from registered stakeholders, the guideline is reviewed by NICE staff with responsibility for guideline quality assurance. ○ They check that the changes made to the guideline are appropriate and that the developer has responded appropriately to the registered stakeholders' comments. Further changes to the guideline may be needed; the developer continues to maintain an audit trail of all the changes. ○ Any supporting resources are amended in line with any changes to the guideline. ▪ **Equality impact assessment** ○ Before the guideline is signed off for publication, the equality impact assessment is updated by the developer and the committee chair to show whether any additional equality issues have been identified during consultation, and how these have been addressed. ○ The equality impact assessment also undergoes quality assurance and is signed off by NICE. ○ It is published on the NICE website with the final guideline. ▪ **Publication** ○ The guideline, including evidence reviews, methods, key messages for the public, equality impact assessment, responses to stakeholder comments, and most support tools are published on the NICE website at the same time. ▪ **Launching and promoting the guideline** ○ Members from the NICE media relations team discuss with the developer and the committee opportunities for promoting the guideline. Committee members may be asked to take part in such activities. ○ With help from the committee and the developer, they identify how to reach relevant audiences for the guideline, including people using services, carers, the public, practitioners and providers. ○ NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: ▪ notifying registered stakeholders of publication ▪ publicising the guideline through NICE's newsletter and alerts ▪ issuing a press release as appropriate, posting news articles and blogs on the NICE website, using social media channels, and promoting the guideline within NICE.

	○ NICE may also use other means of raising awareness of the guideline – for example, training programmes, conferences, implementation workshops, NICE field team support and other speaking engagements. ▪ **Resources to support putting the guideline into practice** ○ NICE teams work with committees to consider what can be done to address implementation challenges, for example, by producing tools to help people put the guideline into practice, in line with NICE's implementation strategy. ▪ **Ensuring that published guidelines are current and accurate** ○ A proactive approach (with an assessment of priority) is used to respond to events that may impact guideline recommendations at any time after guideline publication (for example a safety alert, or publication of a key study). ▪ **Proactive surveillance** ○ NICE takes a proactive approach to surveillance, and monitors key events (such as ongoing studies) that are judged to be relevant to the guideline. Events are identified through constant intelligence gathering. ○ This starts during initial guideline development, as the guideline committee and stakeholders can flag up future events that need to be monitored for impact. Ongoing studies are typically identified through discussions with the National Institute for Health Research. This approach means that NICE can quickly identify changes in the evidence base, and assess the impact on recommendations and the need for any changes. ▪ **Surveillance assessment process** ○ The NICE surveillance team considers how an event could affect a guideline. This involves checking how the event could affect the guideline recommendations, and taking feedback from topic experts in the area. The check may include intelligence gathering and literature searches, if needed. ○ Stakeholders are not normally consulted on the decision to update (or not update) a guideline in response to a surveillance check. ○ If the guideline needs updating, registered stakeholders are informed of the planned approach. ▪ **Scheduling updates** ○ When scheduling updates of guideline recommendations, NICE prioritises topic areas according to need for both new and updated guidelines. ▪ **Full updates of guidelines** ○ Sometimes an existing topic-specific committee is asked to update a guideline in their topic area. ○ Sometimes a new topic-specific committee is set up for the update. ○ The composition of the committee should be tailored to new requirements if a new scope has been developed. ○ The guideline is developed using the same methods and process as for a new guideline and the draft is subject to the normal 4- to 6-week consultation period. ○ The composition of the committee should be tailored to new requirements if a new scope has been developed. The guideline is developed using the same methods and process as for a new guideline and the draft is subject to the normal 4- to 6-week consultation period. ▪ **Updates of topic areas in guidelines**

	○ The scope is clear about exactly which sections of the guideline are being updated and which are not, including any sections that may be withdrawn (for example, if they are now covered in another guideline). Recommendations that are outside the scope of an update may be refreshed. ○ The update is developed using the same methods and process as for a new guideline. ○ Update of topic areas in a guideline are subject to the same level of scrutiny as full updates and new guidelines. ○ The draft is subject to a consultation period of up to 6 weeks, depending on length and complexity. ▪ **Refreshing the guideline recommendations** ○ All changes to recommendations made as part of the surveillance process should be agreed by the NICE surveillance team. ○ When it has been agreed which topic areas need updating, the publishing team also identifies recommendations that may need refreshing to feed into the scoping process. Occasionally during development of the update, additional recommendations that are not part of the update may be identified for refreshing by the committee or the publishing team. ○ Refreshing might involve: ▪ amending or adding cross references to other NICE guidance or hyperlinks to other NICE-endorsed tools or resources ▪ adding or amending a footnote to reflect changes to a medicine's marketing authorisation, to reflect changes in service configuration (for example, a change from primary care trusts to clinical commissioning groups) or a change to an organisation's name ▪ ensuring recommendations take into account the latest government policy or guidelines, for example, on alcohol consumption ▪ amending recommendations to reflect the current practice context, for example, removing references to tools or resources that no longer exist ▪ bringing recommendations in line with NICE's current policy on wording without affecting the intent. ▪ **Presenting updates** ○ When presenting updates of topic areas within guidelines, the aim is to ensure that there is a single set of publications that bring together the updated information and relevant information from all previous versions of the guideline. In this way, readers of the updated guideline will be able to easily identify what has changed. The rest of this section covers general principles to be used when part of a guideline has been updated. ▪ **Publication changes** ○ If an error or clarification meets the criteria for changing a published guideline recommendation, NICE's process for dealing with post-publication changes is followed. Routine maintenance changes may also be made after publication or update of a guideline. These include minor changes such as updating or fixing broken links or updating standard text in line with agreed template changes.
RQ2: Description of quality measures/criteria for clinical practice guidance development	

What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	Digital living guideline recommendations NICE plans to update some recommendations as soon as new evidence becomes available to provide useful and useable content to users. Interim principles for methods and processes that are used to develop NICE's digital living guideline recommendations have been published. It is a living document that is reviewed on a quarterly basis. After review, these interim principles will be updated and, following the usual consultation process for manual updates, they will become part of the main methods and processes in *Developing NICE guidelines: the manual*.
What are the core components of the key innovation?	Audit, monitoring, review & evaluation process.
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	Rationale: Digital health technologies, with the potential to transform healthcare, are constantly emerging. Evidence-based healthcare is evolving. The amount of health and care data has grown exponentially, and the healthcare system is facing unprecedented workforce and capacity pressures. Rationale: To help meet NICE's strategic aims, the NICE guidelines programme is transforming to a more flexible and proportionate approach to allow it focus on what matters most and to provide useful and useable advice. This flexible and proportionate approach will support the timely development or update of guideline recommendations, ensuring a sustainable living approach. NICE is testing this approach on selected topics within its guideline portfolio. Criteria: There are 4 key ways in which NICE is developing more proportionate, agile and responsive approaches to the development or updating of guideline recommendations. Decisions on updates are available on the NICE website. ▪ Prioritisation of key priority areas This includes categorising guidelines into guideline suites, independent guidelines, and foundational guidelines. The NICE guideline portfolio is undergoing a prioritisation process to identify KPAs where an update of recommendations is appropriate, initially in guideline suite content. This is an ongoing process that will include re-prioritisation to ensure a focus on what matters most. ▪ Multiple approaches to surveillance Moving from fixed, planned surveillance to more responsive approaches enables timely updating of recommendations. This includes evidence monitoring alongside the consideration of current health and care system priorities and contextual feedback. ▪ Use of the surveillance decision framework, followed by the multi-criteria decision framework to assess: o if new recommendations or an update of recommendations is needed, a proportionate approach to deciding methods for updating recommendations.

	Following a signal from the evidence or the health and care system, a topic area for possible update is assessed using the surveillance decision framework. This enables a clear and systematic assessment of key domains to decide whether recommendations in this topic area should be updated. ○ If the decision is to update recommendations, there is a further assessment, using the multi-criteria decision framework, of the possible methods and processes for updating guideline recommendations. ▪ Options for validation Validation of guideline recommendations and related outputs developed using the standard NICE guideline programme is by open stakeholder consultation. For digital living guideline recommendations, a proportionate approach to validation will be used. This will reflect the complexity of the update and a flexible range of approaches will be considered.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	During COVID-19, NICE rapidly created a suite of guidelines, which were continuously updated. The aim was to recreate this 'living guideline' approach across the topic portfolio. According to the NICE Strategy 2021 to 2026, NICE is exploring different tools for developing guidelines. For example, the managing COVID-19 guideline was authored using the Making GRADE the Irresistible Choice publishing platform (MAGICapp). In 2021, NICE signed a collaborative agreement with Cochrane to use Cochrane reviews to respond quickly when the evidence underpinning recommendations changes.
Notes	
Reviewer notes	Additional core component: equity/equality.
Associated peer-reviewed article(s)	Kirkham JJ, Gorst S, Altman DG et al. (2016) Core Outcome Set–STAndards for Reporting: The COS-STAR Statement. PLoS Medicine 13: e1002148 Kirkham JJ, Davis K, Altman DG et al. (2017) Core Outcome Set-STAndards for Development: The COS-STAD Recommendations. PLoS Medicine 14: e1002447 Cargo M, Harris J, Pantoja T et al. (2017) Cochrane Qualitative and Implementation Methods Group Guidance Series Paper 3: Methods for assessing evidence on intervention implementation. Journal of Clinical Epidemiology doi: 10.1016/j.jclinepi.2017.11.028. Flemming K, Booth A, Hannes K et al. (2018) Cochrane Qualitative and Implementation Methods Group Guidance Series Paper 6: Reporting guidelines for qualitative, implementation and process evaluation evidence syntheses. Journal of Clinical Epidemiology 97: 79–85 Harris JL, Booth A, Cargo M et al. (2018) Cochrane Qualitative and Implementation Methods Group Guidance Series Paper 2: Methods for question formulation, searching and protocol development for qualitative evidence synthesis. Journal of Clinical Epidemiology 97: 39–48 Cargo M, Harris J, Pantoja T et al. (2018) Cochrane Qualitative and Implementation Methods Group Guidance Series Paper 4: Methods for integrating qualitative and implementation evidence within intervention effectiveness reviews. Journal of Clinical Epidemiology 97: 59–69 Kneale D, Goldman R, Thomas J (2016) A scoping review characterising the activities and landscape around implementing NICE guidance [online; accessed 11 October 2018]

Key: AGREE - Appraisal of Guidelines for REsearch & Evaluation; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; GRADE-CERQual - Grading of Recommendations, Assessment, Development, and Evaluations-Confidence in the Evidence from Reviews of Qualitative Research;

MAGIC - Making GRADE the Irresistible Choice; N/A – not applicable; NICE – The National Institute for Health and Care Excellence; N/R – not reported; PROGRESS-Plus – Place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, social capital – personal characteristics associated with discrimination (e.g. age, disability), features of relationships (e.g. smoking parents, school exclusion), time-dependent relationships (e.g. respite care, leaving hospital).

Table B9 SIGN 50: A guideline developer's handbook

Organisation	Scottish Intercollegiate Guidelines Network (SIGN)
Year	2019
Country	Scotland
URL	https://www.sign.ac.uk/media/2038/sign50_2019.pdf
Title of the publication	SIGN50: A guideline developer's handbook.
Summary/Overview	A very comprehensive manual based on international best practices such as AGREE II guideline development methodology.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Composition of the guideline development group** ▪ At the outset of a new guideline development project the SIGN Executive, in discussion with all relevant bodies, aims to bring together a group that will fulfil the following parameters: o multidisciplinary, with all relevant clinical specialties represented alongside lay input o relevant to current care practice, with a balance between members actively involved in day-to-day delivery of healthcare with topic experts and academics where appropriate. Ideally, membership should represent the range of care or treatment settings related to the clinical condition (e.g. primary, secondary and tertiary care centres) o encompasses the range of skills and expertise required for the specific project. Specialists other than clinicians may be recruited when necessary, for example health economists, social workers o geographically representative, including participants from across Scotland both from urban centres and rural locations. ▪ SIGN guideline development groups vary in size depending on the scope of the topic under consideration, but generally comprise between 15 and 25 members. ▪ The approximate life span of each guideline development group varies depending on whether it is a new project (around 29 months), an update (around 15 months) or a minor revision (3–6 months). **Selection of new topics for SIGN guideline development** ▪ Any group or individual may propose a guideline topic to SIGN. ▪ Proposal form completed by groups or individuals interested in submitting a topic to SIGN. ▪ A topic proposal form designed for patients, carers, voluntary organisations and members of the public can be downloaded from the patient involvement section of the SIGN website. ▪ SIGN Senior Management Team (SMT) uses a screening tool to exclude proposals that are not appropriate for the SIGN process based on the following criteria: o Is this an appropriate clinical topic for a SIGN guideline? (considering whether the topic is clinical, its breadth and the need for the guideline as identified in the proposal) o Is there a suitable alternative product which would address this topic? (considering whether other Healthcare Improvement Scotland products could better address the topic) o Has this topic been considered before and rejected? (reasons for rejection would be reviewed and assessed for current applicability). ▪ Accepted proposals are worked up in more detail, to include: o Completing a scoping search

	○ Addressing public health issues ○ Obtaining information on morbidity/mortality. ▪ Proposals are considered and prioritised by the Guideline Programme Advisory Group (GPAG) using the suitability screen. The following criteria are considered in selecting and prioritising topics for guideline development: ○ clinical priority areas for NHS Scotland ○ areas of clinical uncertainty as evidenced by wide variation in practice or outcomes ○ conditions where effective treatment is proven and where mortality or morbidity can be reduced ○ iatrogenic diseases or interventions carrying significant risks ○ the perceived need for the guideline, as indicated by a network of relevant stakeholders. ▪ GPAG also considers guidelines that are deemed to be in need of update, either through: scheduled scoping three years after publication, or a request from a group or individual to make a change to a published guideline. ▪ GPAG decision ratified by SIGN Council. ▪ Topics are included on the SIGN programme. Topic proposals under consideration can be found on the SIGN website. **Systematic review** ▪ SIGN guidelines are produced using a considered judgement process informed by systematic reviews of evidence. ▪ The SIGN approach is to carry out a systematic review of the evidence for each key question (KQ) to be addressed in the guideline. Evidence tables are produced as supporting documents and the essential components of a systematic review are met in that the literature is: ○ identified according to an explicit search strategy ○ selected according to defined inclusion and exclusion criteria ○ evaluated against consistent methodological standards. ▪ All stages of the review process are thoroughly documented ▪ Addressing patient perspectives' in the literature search ○ In order to incorporate the patient's perspective, a specific search is conducted on patient issues in advance of the first meeting of the guideline development group. ○ This search is designed to cover both quantitative and qualitative evidence, and is not limited to specific study designs. ○ It is carried out over the same range of databases and sources as the main literature review, but will normally include both nursing and psychological literature. ▪ Using existing guidelines ○ As more good-quality guidelines are being produced by other agencies, SIGN is making use of the evidence base underlying guidelines produced elsewhere for use in NHS Scotland. Guidelines are evaluated using the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument and must be shown to have followed an acceptable methodology before they can be considered for use by SIGN guideline developers. ▪ Defining key questions

	○ SIGN guideline development groups break down the guideline remit into a series of structured key questions using the patient/population, intervention, comparator, outcome (PICO) format. ▪ Identifying and selecting the evidence ○ SIGN uses a set of standard search filters that identify systematic reviews (including meta-analyses), randomised controlled trials, observational studies, diagnostic studies, economic studies. ○ As a minimum, SIGN requires searches to cover the following sources: Cochrane library (including Cochrane Central Register of Controlled Trials (CENTRAL) for RCTs), Medline, Embase, Internet sites relevant to the topic (including patient organisations), WHO International Clinical Trials Registry Platform. Specialised databases such as CINAHL, ERIC or PsycINFO will only be searched for questions specific to their area of coverage. ▪ Evaluating the literature ○ Once studies have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The SIGN checklist for systematic reviews is based on the AMSTAR tool while that for RCTs is based on an internal project carried out in 1997. Checklists for observational studies are based on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. The checklist for diagnostic accuracy studies is based on the QUADAS programme. **Assessing the quality of evidence** ▪ Existing systematic review ○ For many questions systematic reviews will already exist, and in these cases the guideline development groups are provided with a complete systematic review plus an evidence table summarising more recent studies. Where there are multiple existing reviews, an evidence table summarising the findings of all existing reviews is provided. ○ Consideration of the evidence in relation to different outcomes is considerably simplified if a summary of findings table is available. Any summary of findings produced as part of a systematic review should be included in the material submitted to the guideline group. If they are not included in a systematic review, the authors may be contacted to see if summary of findings tables are available. ▪ Internally conducted reviews ○ A completed evidence table based on an internally conducted systematic review of the literature will be provided for all questions. These will either update existing reviews or provide a review of all relevant literature. ▪ Considering the quality of evidence ○ SIGN is committed to following the principles of the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) methodology. ○ The guideline development group agree on the overall quality of the evidence for all critical outcomes for the key questions being addressed. ▪ In the context of SIGN guideline development, heterogeneity calculations will normally only be available through published meta-analyses.

	▪ Studies carried out in the UK are likely to be directly applicable to the target population for a SIGN guideline. For studies carried out elsewhere, some thought has to be given to what factors, if any, might influence relevance of the results in the target population. ▪ Published reviews should include an assessment by the authors of the likelihood of publication bias. For internal reviews carried out by SIGN staff, it may be assumed that the literature searches coupled with the knowledge of the guideline development group members have covered the majority of the available literature. Some papers may have been missed, but there will not be any systematic bias in the search results. SIGN searches do not cover unpublished material, and it is a matter of judgment for the guideline development group to decide if there is likely to be a substantial body of unpublished literature that might influence the results. ▪ Trial results are commonly reported in terms of relative effect or relative risk. Wherever possible, estimates of absolute risk or benefit should also be used along with the appropriate confidence intervals. Precision around an effect estimate is usually presented as 95% confidence intervals. **Recommendations** ▪ The Evidence to Decision (EtD) tool is used to inform the development of recommendations. ▪ The following factors should be considered while developing recommendations: o Strong versus weak recommendation o Balancing benefits and harm o Whether or not the outcomes are sufficiently valued by the patients o Equity o Costs and benefits. ▪ Forms of recommendations and overall judgment of the guideline development group: o Strong recommendation against: Undesirable consequences clearly outweigh desirable consequences o Conditional recommendation against: Undesirable consequences probably outweigh desirable consequences o Recommendation for research and possibly conditional recommendation for use restricted to trials: Balance between desirable and undesirable consequences is closely balanced or uncertain o Conditional recommendation for: Desirable consequences probably outweigh undesirable consequences o Strong recommendation for: Desirable consequences clearly outweigh undesirable consequences ▪ The published guideline and supporting documentation should contain a justification for the recommendation highlighting the supporting evidence and the factors that have been taken into account when arriving at a conclusion. **Good practice points and consensus recommendations** ▪ Good Practice Points are intended to assist guideline users by providing short pieces of advice which may not have an evidence base, but which are seen as essential to good clinical practice. ▪ If the group feels strongly that they want to make a recommendation even though there is no significant evidence, this should be done as a weak recommendation based on very-low quality evidence. Note that there must be some evidence of opinion supporting the recommendation from outside the guideline group. If no such evidence exists, formal methods should be used to develop a consensus-based recommendation

	which will be clearly identified as such within the guideline by a statement accompanying the recommendation. **Key recommendations** ▪ The key recommendations are identified by the guideline development group as the recommendations that, in order to improve patient outcomes, should be prioritised for implementation. ▪ A consensus-based recommendation may be included as a key recommendation. **Consultation and peer review** ▪ SIGN seeks feedback on a draft version of a new guideline from the wider health and social care community through: o open consultation o a national open meeting o peer review. ▪ Consultation and peer review phases of guideline development o Systematic review and draft recommendations o Draft guideline o Available for comment on SIGN website for one month o Option for presentation and discussion at national open meeting o Targeted peer reviewers invited to comment o Feedback discussed by guideline development group and draft guideline revised o SIGN Editorial Group reviews guideline and consultation report o Publication. **Presentation and publication** ▪ Guidelines should be written in unambiguous language and should define all terms precisely. The most appropriate format for presenting guidelines will vary depending on the target group(s), the subject matter, and the intended use of the guideline. Ideally, end users should be consulted on methods of presentation. ▪ Content of the guideline o Introduction o Evidence and recommendations o Key recommendations o Information for patients o Implementation resources o Guideline development o Recommendations for research o Review and updating. ▪ Publishing the guideline o All SIGN guidelines are available free of charge on the SIGN website. Updates including any corrections are made to the electronic version of the guideline, which is the definitive version at all times. o The search strategy and register of interests declared by the guideline development group, and consultation report are published alongside the guideline. A report of any updates is also available. Other supporting material may include:

	▪ implementation resources, e.g. patient pathways, costing tools ▪ patient resources, e.g. booklets, sample leaflets ▪ learning resources, e.g. slide sets, online tutorials. ▪ Updating published guidelines o SIGN considers whether or not published guidelines need to be reviewed after a period of three years and all SIGN guidelines carry a statement indicating that they will be considered for review three years after publication. o The process for carrying out the update is largely the same as when developing a new guideline. The principal difference is that the update will focus on those sections of the original guideline that have been identified, through the scoping, as being in need of updating. o Requests for a change to a published guideline ▪ All comments received on published SIGN guidelines, or information on important new evidence in the field, or evidence of impacts on equality groups is considered, either for immediate response or for more detailed consideration on review of the guideline. ▪ Individuals commenting on published guidelines are invited to complete a small change proposal form, which can be downloaded from the SIGN website. Once received, small change proposals are processed alongside full proposals. o Making a small change to a guideline ▪ Guideline Programme Advisory Group, a subgroup of SIGN Council, considers proposals for small changes to published guidelines on a rolling basis and guidelines will be updated if a proposal meets the following criteria: o new evidence substantially changes a small number of recommendations in the guideline (corresponding to no more than two related key questions); OR o a specific issue such as a new drug therapy or national issue such as a new government policy will give rise to a new key question; AND o the nature of the update may not warrant assembling a multidisciplinary group. ▪ When the Guideline Programme Advisory Group decides that a guideline is in need of a small change, the process for this is largely the same as that described for updating a guideline, although the scope of the update is much narrower and the timescale shorter. The level of involvement of a guideline development group and extent of consultation will depend on the nature of the changes to the guideline. ▪ Living guidelines o As with an update to a guideline, the process for updating a living guideline is largely the same as that described elsewhere in this manual. The main difference is that a living guideline is developed on a rolling programme of regular updates. o The frequency of updating will depend on the rate at which new evidence is emerging, but will normally be annual or biennial. Each update focuses on those areas of the current guideline where new evidence has been identified.

	○ The same methodological principles apply and literature searches are based on a series of existing key questions. They seek to update and build on the evidence base used in the original guideline and subsequent updates. ○ The only new questions that may be addressed are any arising from the patient issues search, or that arise from new developments identified during the process of scoping the update. ▪ Implementation ○ Interventions that have a variable level of effectiveness: ▪ Audit and feedback ▪ Local consensus conferences ▪ Opinion leader ▪ Patient-mediated interventions. ○ Intervention that are largely effective: ▪ Reminders ▪ Educational outreach (for prescribing) ▪ Interactive educational workshops ▪ Multifaceted interventions. ○ Improving processes ▪ Robust dissemination: Dissemination of SIGN guidelines in NHS Scotland is organised within each NHS board by local distribution co-ordinators, who are responsible for disseminating guidelines across their board. The distribution co-ordinators are notified of all new guidelines and updates to published guidelines and given an opportunity to order Quick Reference Guides to distribute within their board. ▪ Notification of new guidelines is also sent to the Royal Colleges in Scotland, the chairs of NHS boards, the chief executives of NHS boards, the chief scientist's office, other guideline development organisations, postgraduate college deans and voluntary organisations listed in the guideline. ○ Awareness raising and education ▪ Awareness raising activities ▪ Local clinical champions ▪ Patients as champions for change ▪ Education and training modules. ○ Networking ▪ Linking with existing networks and projects: Building relationships with the various professional networks, Scottish Government, NHS Education for Scotland and others as part of a wider cohesive approach to improving patient care should facilitate implementation. ○ Implementation support resources which include: ▪ Algorithms, care pathways and integrated care pathways ▪ Resource implication tools ▪ Datasets ▪ Electronic decision support tools

	▪ Other tools, such as posters highlighting key recommendations, audit proforma, easily accessible and editable lists of the recommendations, slide sets and case studies may also be developed with each guideline and made available on the SIGN website. **Involving patients and their representatives** ▪ SIGN has developed a literature search strategy to identify both qualitative and quantitative studies that reflect patients' experiences and preferences in relation to the clinical topic. This search is performed at least three months prior to the first group meeting to ensure adequate time to obtain relevant articles and summarise their findings for presentation at the first guideline group meeting. ▪ SIGN writes to the organisations and charities that aim to represent and/or lobby for patients at least four months before the first meeting of the guideline development group, asking them to inform SIGN of the issues they think the guideline should address. ▪ SIGN also writes to members of the Patient and Public Involvement Network asking them which issues they think the guideline should address. ▪ Where published evidence is scarce and inadequate feedback from patient organisations has been received, patient and carer views may be sought through direct contact with users of the service. Engagement techniques used to date have included focus groups with patients in different regions of Scotland, attending patient support group meetings, and SIGN-organised meetings for patients and carers. ▪ The Public Involvement Advisor reviews the results of the patient literature search, and seeks to identify common themes that emerge from the literature. A theme is recorded for each literature paper and a subject bibliography is created. These themes are used alongside the findings that emerge from the other engagement approaches described and are presented at the first meeting of the guideline development group by the Public Involvement Advisor. The group is asked to take account of these issues when it drafts the key questions. Guideline groups are not obliged to take on board all the issues raised through the patient consultative process, but they are expected to give explicit reasons if they choose to omit particular topics that have arisen from this source. ▪ SIGN recruits a minimum of two patient representatives to guideline development groups by inviting nominations from the relevant 'umbrella', national and/or local patient-focused organisations in Scotland. Where organisations are unable to nominate, patient representatives are sought through other means, for example from consultation with Scottish Health Council staff. Where patients have been consulted directly (e.g. if a focus group has been held) this may also provide a source of possible future patient and carer representatives. ▪ Further patient and public participation in guideline development is achieved by involving patients, service users, carers and voluntary organisation representatives at the national open meeting, which is held to discuss each draft guideline. The meetings are advertised widely and are free of charge. ▪ Patients, service users, carers and voluntary organisation representatives are invited to take part in the peer review stage of each guideline and specific guidance for them has been produced. ▪ Members of the SIGN Patient and Public Involvement network are also invited to comment on draft documents such as patient versions of guidelines, patient sections of guidelines and other literature aimed at patients.

RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	**Living guidelines** Living guidelines are developed on a rolling programme of regular updates and the process for updating a living guideline is largely the same as for non-living guidelines. They seek to update and build on the evidence base used in the original guideline and subsequent updates.
What are the core components of the key innovation?	Audit, monitoring, review & evaluation process.
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	No rationale nor criteria provided.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	To date, SIGN has developed one living guideline: the British guideline on the management of asthma in collaboration with the British Thoracic Society. Updated drafts of this guideline were presented at one of the British Thoracic Society biannual meetings, as well as being published on the SIGN and British Thoracic Society websites for a fixed period, during which time comments were invited.
Notes	
Reviewer notes	RQ1: All core components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review & evaluation process).
Associated peer-reviewed article(s)	Fearns N, Graham K, Johnston G, Service D. Improving the user experience of patient versions of clinical guidelines: user testing of a Scottish Intercollegiate Guideline Network (SIGN) patient version. BMC Health Serv Res 2016;16:37. Fearns N, Kelly J, Callaghan M, Graham K, Loudon K, Harbour R, et al. What do patients and the public know about clinical practice guidelines and what do they want from them? A qualitative study. BMC Health Serv Res 2016;16:74. Armstrong MJ, Mullins CD, Gronseth GS, Gagliardi AR. Impact of patient involvement on clinical practice guideline development: a parallel group study. Implement Sci 2018;13(1):55. Boivin A, L'Esperance A, Gauvin FP, Dumez V, Macaulay AC, Lehoux P, et al. Patient and public engagement in research and health system decision making: A systematic review of evaluation tools. Health Expect 2018;21(6):1075-84.

Key: AGREE – Appraisal of Guidelines for REsearch & Evaluation; AMSTAR - Assessing the Methodological Quality of Systematic Reviews; EtD – Evidence to Decision; GPP – good practice points; MERGE – Method for Evaluating Research and Guideline Evidence; N/A – not applicable; N/R – not reported; RCTs-randomised controlled trials; SIGN - Scottish Intercollegiate Guidelines Network; SMT – Senior Management Team.

Table B10 SIGN Rapid guideline methodology

Guideline identification	
Organisation	Health Improvement Scotland, SIGN Evidence based clinical guidelines
Year	2021
Country	Scotland
URL	https://www.sign.ac.uk/media/1836/20210408-rapid-guideline-manual-10.pdf
Title of the publication	Rapid guideline methodology.
Summary/Overview	This handbook is a guide for guideline developers on how to create rapid guidelines. It details the processes that differ from the SIGN manual. It covers the core principles, topic selection process, and engagement strategies to ensure successful and efficient guideline development. The handbook aims to provide a reference tool that may be used to develop a guideline rapidly at times of urgent need.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	N/A
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/A
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	**Rapid guideline** World Health Organization (WHO) defines rapid guideline as "guidelines completed within a 1 to 3 month timeframe to provide guidance in response to an emergency, urgent need or new evidence."
What are the core components of the key innovation?	Guideline development process ▪ Topic scoping ○ Discussion is held with the topic proposers to identify the key issues to be addressed in the guideline. ○ The scope is focused on key issues that need to be addressed urgently. To ensure the guideline is clinically meaningful, the number of key questions will vary and depend on the topic. ▪ Multidisciplinary guideline development group ○ A multidisciplinary team of people with relevant clinical expertise is recruited to form a guideline development group (GDG). The number and range of members may be limited due to the scope of the guideline and time constraints. ○ Declarations of interests are submitted by all GDG members and any potential conflicts of interest are addressed. ▪ Patient/carer involvement ○ Patient or carer representatives, or representatives from patient organisations are invited to join the guideline development group.

	○ Patient and carer representatives are invited to peer review the consultation draft of the guideline. ▪ Defining key questions ○ Key question are set using the People; Intervention; Comparison; Outcome (PICO) format. However, there may be a lack of evidence for comparisons and/or relevant outcomes in novel situations. ▪ Literature searching ○ A systematic literature search is conducted for each key question, across relevant sources, but the date range may be shorter, the range of sources smaller and the inclusion/exclusion criteria more focused than for a full guideline. Searches are conducted by a Health Services Researcher and/or an Information Specialist. ▪ Study selection and critical appraisal ○ Studies are selected by a Health Services Researcher. Depending on the volume and/or the nature of evidence identified, studies are either critically appraised or a general observation is made about the robustness of the overall evidence base (e.g. if it includes preprints then a caveat is given that the quality of the evidence is undetermined). ▪ Developing evidence statements and recommendations ○ A Health Services Researcher produces a rapid review report of the evidence, including the results and strength of the evidence base and the balance of benefits over harms. The GDG meet to produce recommendations, based on the evidence review. Where evidence is lacking, a statement may be made that no recommendation can be made, or, if there is a need, a recommendation can be made using the informal consensus of the GDG. All recommendations should take into account: ▪ The strength of the evidence base, and how applicable it is to the Scottish setting. ▪ The balance of benefits over harms. ▪ The feasibility of implementation, including likely resource implications. ▪ Acceptability to patients. ▪ Consultation and peer review ○ Targeted peer reviewers (including patient and carer reviewers) are invited to provide feedback on the interpretation of the evidence and feasibility and appropriateness of the recommendations. ○ All feedback is addressed by the GDG and actions recorded in the consultation report. ▪ Editorial ○ The Editorial Group ensures that each point raised at consultation has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. ▪ Publication and dissemination ○ The guideline is published on the SIGN website and disseminated across NHS Scotland. ▪ Review and update ○ A flexible approach to updating is used to ensure rapidly emerging evidence can be incorporated. The frequency of update is agreed and stated at publication. The option to withdraw the guideline is considered. ○ Criteria for updating a rapid guideline includes new evidence, data or information: ▪ that would significantly change a recommendation; either strengthen, for example from conditional to strong recommendation, or reverse it

	▪ that would warrant a new key question to cover new interventions, for example add another treatment option ▪ about patient safety, for example side effects from real-time data ▪ about patient preferences or equity. ○ New research that adds to the body of evidence supporting a recommendation without changing it would not warrant an update. ○ Withdrawing a rapid guideline is based on the following reasons: ▪ contextual changes render the guideline unnecessary ▪ superseded by a more recent or more comprehensive guideline ▪ evidence that the guideline is complied with by NHS Scotland, and has become accepted practice ▪ emergence of new treatments or preventive measures that render the guideline irrelevant.
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	Rationale: Increased methodological expectations translate into increased guideline development time and costs. Full guideline development as set out in SIGN 50 requires active participation from a multidisciplinary group of healthcare professionals, who volunteer to be involved in the process. Criteria: Requests for rapid guidelines are considered as part of this process. If at the filter stage, in addition to the standard screening criteria, the topic meets the following additional criteria, it will be developed as a rapid guideline: Does the topic relate to: ▪ emergent and dangerous situations (e.g. epidemic of an infectious disease) ▪ new, urgent and recommendation-changing evidence about: ○ patient safety ○ efficacy that could change current knowledge or practice ○ cost-effectiveness.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	RQ3: Innovation.
Associated peer-reviewed article(s)	Morgan RL, Florez I, Falavigna M, Kowalski S, Akl EA, Thayer KA, et al. Development of rapid guidelines: 3. GIN-McMaster Guideline Development Checklist extension for rapid recommendations. Health Res Policy Syst. 2018;16(1):63. doi: 10.1186/s12961-018-0330-0. Browman GP, Somerfield MR, Lyman GH, Brouwers MC. When is good, good enough? Methodological pragmatism for sustainable guideline development. Implement Sci. 2015;10:28.(doi):10.1186/s13012-015-0222-4.

Key: GDG – guideline development group; N/A – not applicable; N/R – not reported; PICO – Population, Intervention, Comparison, Outcome; SIGN – Scottish Intercollegiate Guidelines Network; WHO – World Health Organization.

Table B11 USPSTF Standards for guideline development

Guideline identification	
Organisation	U.S. Preventive Services Task Force
Year	May 2021
Country	USA
URL	https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/inline-files/standards-guideline-dev%20%281%29.pdf
Title of the publication	U.S Preventive Services Task Force Standards for guideline development.
Summary/Overview	Comprehensive guideline manual based on the Institute of Medicine (2011) guideline standards. All core components are covered. However, the core component relating to resource implications are not sufficiently addressed. For example, the search for and inclusion of cost-effectiveness studies is not required but may be included for contextual information regarding costs for use by providers. Considerations for potential resource implications are not outlined and there is no mention/requirement to conduct a budget impact assessment. There is a strong emphasis on governance and the use of an evidence-based approach to form recommendations.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	U.S Preventive Services Task Force Policy **1. Establishing transparency** 1.1 Independent of the federal government, U.S. Preventive Services Task Force (USPSTF) members are volunteer experts in evidence-based medicine and are not federal employees. The U.S. Congress mandates that the USPSTF receive administrative, scientific, and dissemination support from the Agency for Healthcare Research and Quality. 1.2 All USPSTF systematic evidence reviews, recommendation statements, and other materials are developed according to methods explained in detail in a publicly available procedure manual. Draft research plans, draft evidence reviews, and draft recommendation statements are available for public comment. **2. Management of conflict of interest** 2.1 Anyone being considered for appointment to the USPSTF must provide written disclosure of all interests and activities that may be a conflict of interest (COI) with USPSTF activities. These forms are updated prior to the start of each topic cycle. ○ Disclosure reflects all current and planned involvement in commercial (including services from which a clinician derives a substantial proportion of income), non-commercial, intellectual, institutional, and patient/public activities related to the potential scope of the recommendation. 2.2 Disclosure of COIs within the GDG ○ USPSTF members report and discuss all COIs prior to starting work on each topic and prior to each meeting. ○ Each member explains how his or her COI could influence specific recommendations. 2.3 Divestment ▪ The leadership of the USPSTF may ask members to divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by USPSTF recommendations.

	2.4 Exclusions ○ Whenever possible, USPSTF members do not have COI. ○ Members with a real or potential COI may be asked by the USPSTF leadership to either disclose the COI, not participate in a topic workgroup or as a lead member, or remove themselves from discussion of and voting on a topic. ○ Members with significant COIs do not participate in discussion of or voting on a topic. ○ The chair and vice chairs are subject to all COI policies. ○ The USPSTF makes its recommendations independent of the federal government. **3. Guideline development group composition** 3.1 The USPSTF makes recommendations for a broad range of prevention topics and populations seen in primary care settings. It comprises a multidisciplinary and balanced group of experts in primary care and clinical preventive services, including methodological experts and clinicians. The USPSTF seeks the input of disease specialists as expert consultants and reviewers and engages patient advocacy groups and consumer organisations for their opinions and input at various stages of the evidence review. 3.2 The USPSTF solicits patient, consumer, and public involvement during the draft research plan, draft evidence review, and draft recommendation stages. 3.3 The USPSTF engages patient and consumer representatives through regular conference calls and meetings with liaisons from its dissemination and implementation partners, including those representing patients and consumers. These calls and meetings often include discussions about the methodological issues related to evaluating evidence and making evidence-based recommendations. **4. Clinical practice guideline and systematic review intersection** 4.1 The USPSTF uses systematic reviews that are independently performed by Evidence-based Practice Centers, which are funded by the Agency for Healthcare Research and Quality. These systematic reviews meet the standards by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research. 4.2 The UPSTF and the systematic review team interact regularly regarding the scope, approach, and output of both processes. **5. Establishing evidence foundations for and rating the strength of recommendations** 5.1 Each USPSTF recommendation provides: An explanation of the reasoning underlying the recommendation, including: ○ A clear description of potential benefits and harms. ○ A summary of relevant available evidence and evidence gaps and a description of the quality, applicability, quantity, and consistency of all available evidence. ○ An explanation of any values, opinion, theory, and clinical experience that the USPSTF may have used in deriving the recommendation. ○ A rating of the level of confidence in (certainty regarding) the evidence informing the recommendation. ○ A rating of the strength of the recommendation in light of the preceding bullet points. ○ A statement that summarises and explains the range of opinions regarding the recommendation. **6. Articulation of recommendation**

	6.1 The USPSTF writes recommendations in a standardised format, detailing what the recommended action is and under what circumstances clinicians should perform it. 6.2 The USPSTF's "A" and "B" recommendations are worded so that compliance with the recommendation(s) can be evaluated. A recommendation with Grade A has a high certainty that the net benefit is substantial. Grade B has a high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. **7. External review** 7.1 External reviewers of USPSTF documents include relevant stakeholders, such as scientific and clinical experts, healthcare and specialty organisations, and federal health agencies. Public input is solicited from patients and representatives of the public. 7.2 Unless given permission, the identity of external reviewers is kept confidential. 7.3 The USPSTF considers all external reviewer and public comments and keeps a written record of the rationale for modifying or not modifying a recommendation statement in response to reviewers' comments. 7.4 A draft of the recommendation statement is made available to the general public for comment. Reasonable notice of impending upcoming publication is provided to interested public stakeholders. **8. Updating** 8.1 The recommendation statement and systematic evidence review publication dates are documented. The USPSTF aims to keep all recommendations current and review each topic every 5 years for either an update or reaffirmation. 8.2 Through a separate Scientific Resource Center funded by the Agency for Healthcare Research and Quality, the literature is monitored regularly to identify the release of new, potentially relevant evidence and to evaluate the continued validity of the recommendation statement. 8.3 The USPSTF updates its clinically important recommendations when new evidence shows the need for re-evaluation and modification. This could mean that a recommended intervention causes previously unknown harm, a new intervention is significantly superior to a previously recommended intervention, or a recommendation can be applied to a new population(s). **Topic Selection** ▪ Anyone—including individuals, organisations, Evidence-based Practice Centers, and USPSTF members—can nominate a new topic for USPSTF consideration or request an update of an existing topic through an online nomination form on the USPSTF website. ▪ Once a year, the USPSTF Topic Prioritization Workgroup drafts a prioritised list of topics, including new topics and updates, to be started during that year. ▪ This list is made according to the following criteria for prioritisation: o public health importance (burden of suffering and potential of preventive services to reduce the burden); o potential change to a prior recommendation (e.g., because new evidence has become available); and o potential for a USPSTF recommendation to affect clinical practice (based on existing controversy or the belief that a gap exists between evidence and practice). **Dissemination of USPSTF Recommendations and Processes** ▪ USPSTF recommendations are widely disseminated to professional audiences in professional peer-reviewed

	journals, in an electronic tool ('Prevention TaskForce') available online or as a mobile application, in print through the "Guide to Clinical Preventive Services," and as reprints in peer-reviewed journals, such as *American Family Physician*. ▪ Tools for clinicians, including 'Prevention TaskForce', are available on the USPSTF website. **Consideration for financial implications** ▪ The USPSTF does not consider the financial costs of providing a service in its assessment of the balance of benefits and harms, but may provide contextual information regarding costs for use by providers, including cost-effectiveness studies.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	N/R
What are the core components of the key innovation?	N/A
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/A
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/A
How is the innovation used in practice?	N/A
Notes	
Reviewer notes	RQ 1: Core components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review & evaluation process).
Associated peer-reviewed article(s)	Institute of Medicine. 2011. *Clinical Practice Guidelines We Can Trust*. Washington, DC: The National Academies Press. https://doi.org/10.17226/13058

Key: COI – conflict of interest; GDG – guideline development group; N/A – not applicable; N/R – not reported; USPSTF - U.S. Preventive Services Task Force.

Table B12 USPSTF An update on the US Preventive Services Task Force Methods for developing recommendations for preventive services

Guideline identification	
Organisation	US Preventive Services Task Force (USPSTF)
Year	2023
Country	USA
URL	https://www.annfammed.org/content/annalsfm/21/2/165.full.pdf
Title of the publication	Putting evidence into practice: An update on the US Preventive Services Task Force Methods for developing recommendations for preventive services.
Summary/Overview	This article provides an overview of the updated USPSTF methods for developing evidence-based recommendations for clinical preventive services such as screenings, counselling services, and preventive medications. It discusses how the USPSTF methods are evolving to address preventive health equity and identifies evidence gaps for future research. Additionally, it covers topic nomination, prioritisation, and updating, grading system, and efforts to address health equity and research gaps.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Steps in topic prioritisation** ▪ Identify all topics >3 years since last USPSTF recommendation ▪ Step 1: Topic prioritisation workgroup reviews brief background paper ▪ Step 2: Topic prioritisation workgroup assigns tentative category (active, inactive, refer) ▪ Step 3: Feedback requested from USPSTF and partner organisations on all active topics. ▪ Step 4: Topic Prioritisation Workgroup assigns tentative priority level (low, moderate, high) ▪ Step 5: Full USPSTF votes on category and priority level ○ Active topics placed into review queue based on priority level ○ Repeat yearly for topics not selected for review in preceding year ○ Evidence reviews initiated for prioritised topics. **Development of the research plan** ▪ In the draft research plan, the USPSTF describes steps to address equity and study heterogeneity in a new section titled *Approach to Assessing Health Equity and Variation in Evidence across Populations*. ▪ The plan is developed by an Evidence-Based Practice Center (EPC) in collaboration with the USPSTF and Agency for Healthcare Research and Quality (AHRQ). The analytic framework is a graphical representation of the evidence needed to connect the performance of a preventive service to a health outcome; it depicts the population under consideration, interventions, intermediate health outcomes, and final health outcomes, capturing both benefits and harms. ▪ Key questions articulate the chain of evidence needed to determine the net benefit of a preventive service. Contextual questions address other important considerations for the recommendation, such as barriers to accessing interventions. **Systematic evidence review** ▪ Systematic reviews addressing key questions are conducted by EPCs and follow the rigorous methods of the AHRQ EPC program in addition to those of the USPSTF. ▪ The USPSTF considers randomised controlled trials and well-conducted systematic reviews and meta-analyses as methodologically strongest.

	▪ Separate methods have been developed to conduct expedited reviews for topics suitable for reaffirmation. ▪ Because the USPSTF has many counselling topics, such as behavioural counselling interventions, recommendations include a table describing the key intervention characteristics, which allows the USPSTF to provide information to help facilitate implementation. ▪ Although the systematic reviews focus on randomised controlled trials, nonrandomised studies with unbiased comparator groups may be included to address limitations in the trial evidence on the effectiveness or harms of any given preventive service. ▪ Finally, the USPSTF recognises that improving the health of people nationwide necessitates improving the health of those who experience greater morbidity and mortality from a condition; therefore, the USPSTF continues to innovate methods to synthesise evidence for these populations and integrate this evidence into recommendations. **Use of simulation modelling** ▪ The USPSTF commissions modelling studies when empiric data are sufficient to recommend a preventive service but important questions remain. For screening, the questions are typically regarding intervals for screening, starting and stopping ages, and the screening tests used. ▪ The USPSTF does not make recommendations on the basis of modelling alone without supporting empiric evidence. The USPSTF usually considers multiple models simultaneously. Because these collaborative models are developed independently, they use different assumptions and structures. When collaborative models yield consistent findings, they provide a robust basis for answering remaining questions. **Recommendation development** ▪ **Assessing adequacy of evidence** o The adequacy of evidence at the key question and linkage level is categorised as convincing, adequate, or inadequate. o In assessing evidence adequacy, the following six questions are considered: ▪ Do the studies have the appropriate research designs? ▪ Are the studies of sufficient quality? ▪ Are the results of the studies generalisable to the primary care population? ▪ How many and how large are the studies? ▪ How consistent are study results? ▪ Are there additional factors that assist in drawing conclusions? ▪ **Assessing magnitudes of benefits and harms** o If the evidence is deemed convincing or adequate, the USPSTF then determines the magnitudes of benefits and harms of the preventive service. o The magnitude of benefit describes the change in health outcomes that would be expected from providing versus not providing the service for a population. o The estimate is based on effect sizes from studies as well as on the public health burden of the disease and the incidence, severity, and duration of outcomes. o When evidence is limited, conceptual upper or lower bounds may be established by extrapolating from studies of different baseline risk populations or in settings other than primary care. ▪ **Assessing coherence linkage**

	○ Whenever possible, the USPSTF looks for direct evidence of benefit. ○ Direct evidence is ideal for limiting bias, providing the greatest confidence. ○ The USPSTF also examines the indirect evidence pathway, which connects the target population to improved health outcomes by linking key questions (How accurate are screening tools? How well does treatment work? Can intermediate outcomes predict health outcomes? What are the harms of each step?). To make this linkage, the USPSTF looks at the coherence of the evidence, or how well the pieces fit together, and the applicability of the evidence to an asymptomatic primary care population. Compared to direct evidence, indirect evidence has a greater risk of bias. ▪ **Intermediate outcome** ○ Intermediate outcomes are pathologic, physiologic, social, or behavioural measures that a patient does not feel or experience. ○ A preventive service might affect an intermediate outcome without improving health outcomes. The USPSTF has developed methods for considering the linkage between intermediate and health outcomes. When assessing linkage, the USPSTF looks for evidence showing a consistent relationship between a change in an intermediate outcome and a change in health outcome. ▪ **Determining a recommendation grade** ○ To make a recommendation, the USPSTF judges the certainty and magnitude of the net benefit (benefits minus harms) of the preventive service at the population level. Certainty, categorised as high, moderate, or low, is based on the quality of the evidence. Assessing certainty requires a synthesis of evidence across the analytic framework to judge whether the results observed would be expected when the intervention is delivered for primary care populations and how likely future research would change that assessment. ○ The magnitude of net benefit is categorised as substantial, moderate, small, zero, or negative. **Communicating recommendations** ▪ In its statements, the USPSTF describes the chain of evidence used to arrive at the recommendation in the *Assessment of Magnitude of Net Benefit* section and the *Rationale Table*. ○ **Understanding Grades** ▪ Grade A: The USPSTF recommends the service. There is high certainty that the net benefit is substantial. Suggestion for practice: Offer or provide this service. ▪ Grade B: The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. Suggestion for practice: Offer or provide this service. ▪ Grade C: The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small. Suggestion for practice: Offer or provide this service for selected patients depending on individual circumstances. ▪ Grade D: The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits. Suggestion for practice: Discourage use of this service. ○ **Practice Considerations**

	▪ The *Practice Considerations* section provides clinicians a concise, streamlined summary of information needed to implement the recommendation. Companion materials may include infographics and office conversation guides. ○ **Research gaps** ▪ The USPSTF includes a *Research Needs and Gaps* section in its recommendations to communicate key research still needed. ▪ The USPSTF has become increasingly concerned about widespread inequities in preventive care, such as those based on sex, gender, race, and ethnicity. ▪ The USPSTF considers inequities in Black, Hispanic/Latino, Asian and Pacific Islander, and Indigenous populations that face systemic racism leading to greater risks of preventable diseases and a lower likelihood of receiving appropriate preventive services followed by diagnosis and treatment. ▪ The USPSTF continues to report research gaps addressing health inequities to the US Congress and research funders. **Stakeholder engagement** ▪ The USPSTF values input from the public, specialists, and other stakeholders at every stage of the recommendation process. Via the USPSTF website, anyone can nominate topics and provide feedback on draft research plans, recommendation statements, and evidence reports. ▪ Every comment is considered by USPSTF members before finalisation of documents. In addition, the USPSTF reaches out to stakeholder organisations directly and invites them to provide comments. ▪ All draft evidence reports are reviewed by experts in the field and USPSTF federal health partners; organisations with content expertise are also invited to nominate reviewers. ▪ The USPSTF continuously engages with federal and non-federal partners via regular meetings. This feedback makes recommendations more understandable to clinicians and stakeholders. **Approach to addressing inequities (new core component)** ▪ Potential approaches under consideration to address equity are the use of robust comparative cohort or interrupted time series studies with sufficient participant diversity to identify variations in net benefits by race, ethnicity, sex, gender, or social determinants of health. Additional analytic approaches, such as individual participant meta-analyses and modelling with race as an independent variable, may also be considered. Sex and gender of participants are not often clearly specified in studies of preventive services. The USPSTF is developing inclusive approaches to addressing sex and gender in recommendation development. Additional approaches include a taxonomy to categorise evidence gaps and inform future research addressing health inequities. As these changes crystalise, they will be reflected in updates to the USPSTF Procedure Manual. ▪ There is a need to assess whether these approaches decrease any influence of systemic racism or sources of bias and inequity at each step of recommendation formation; for example, whether recommendations might create implementation barriers that disproportionately affect some population groups. This process will also inform the development of a health equity framework that aligns with these approaches. As part of future evidence reviews and as outlined in prior articles, the USPSTF will continue to pilot test the inclusion of evidence on variation in benefits and harms as well as implementation barriers by population groups.

	▪ The USPSTF is dedicated to meeting the health needs of an increasingly diverse US population and recognises the impact of social determinants on the delivery of preventive services. Given that many important population groups, particularly groups bearing a disproportionate burden of disease, are often not included in trials, the USPSTF continues to refine its methods to develop evidentiary rules (for nonrandomised studies, epidemiologic data, and modelling) and criteria for extrapolation to better address racial, ethnic, and gender disparities in the use of preventive services and in health outcomes. ▪ The approach to addressing inequities is exemplified in the recent update of the USPSTF lung cancer screening recommendation. The updated recommendation was informed by new trial evidence and simulation modelling that allowed the USPSTF to identify the most efficient screening strategies, particularly among Black people, who have a greater burden of lung cancer. On the basis of simulation modelling, the 2021 recommendation, which decreased the starting age from 55 to 50 years and the smoking criterion from ≥30 to ≥20 pack-years, would increase the relative percentage of adults eligible for screening by 78% in non-Hispanic White persons, 107% in non-Hispanic Black persons, and 112% in Hispanic/Latino persons.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	N/R
What are the core components of the key innovation?	N/A
What is the rationale behind the methodology? OR What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?	N/A
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/A
How is the innovation used in practice?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
Reviewer notes	RQ 1: Core components (Clarity of scope and purpose; Governance model; Communications; Service user and stakeholder involvement; Evidence-based; Knowledge management; Resource implications; Planning and Implementation; Audit, monitoring, review and evaluation process).
Associated peer-reviewed article(s)	

Key: AHRQ - Agency for Healthcare Research and Quality; COI – conflict of interest; EPC – Evidence-based Practice Centre; GDG – guideline development group; N/A – not applicable; N/R – not reported; USPSTF - U.S. Preventive Services Task Force.

Table B13 USPSTF Procedure Manual

Guideline identification	
Organisation	U.S Preventive Services Task Force (USPSTF)
Year	2021
Country	USA
URL	https://www.uspreventiveservicestaskforce.org/uspstf/sites/default/files/inline-files/procedure-manual-2023.pdf
Title of the publication	Procedure Manual.
Summary/Overview	The USPSTF manual provides a comprehensive overview of the processes used by the USPSTF to identify, review, and synthesise evidence, as well as to develop and disseminate recommendations that align with the Institute of Medicine's guideline principles. There is a strong focus on the roles and responsibilities of the USPSTF members, staff, and external partners, and guidance on how to interpret and apply the recommendations. With limited focus on the core components that relate to resource implements and planning and implementation. The USPSTF does not consider the financial costs of providing a service in its assessment of the balance of benefits and harms, but guidelines may provide contextual information regarding costs for use by providers, including cost-effectiveness studies. Systematic reviews must meet the standards set by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research.
RQ1: Description of core components of clinical practice guidance	
What core components have been stated in the document?	**Stages of evidence review development** ▪ Determination of topic scope and review approach ▪ Literature searches ▪ Abstract review ▪ Full text article review ▪ Internal validity (quality) - assessment of individual studies ▪ External validity (applicability) - assessment of individual studies ▪ Data abstraction ▪ Data synthesis ▪ Evidence report **Workgroups of the USPSTF** ▪ Several standing and ad hoc workgroups are committed to ensuring that the USPSTF's methods and processes are up to date and implemented consistently and transparently. ○ The Methods Workgroup reviews and updates USPSTF methods and processes to follow best practices for guideline-setting bodies and incorporate methodological advances. This workgroup identifies issues that need further consideration, recommends the creation of new workgroups as needed to address these issues, and incorporates input from all other workgroups into USPSTF methods and processes. ○ The Topic Prioritization Workgroup develops procedures for prioritising the portfolio of USPSTF topics and reviews and prioritises nominations for new topics and suggestions for reconsidering or updating existing topics from the public. It also proposes a determination of the status of all topics (active, inactive, and referred to others) and prioritisation of the active queue of topics each year for consideration by the full USPSTF.

	○ The Subpopulation Workgroup assesses methods for using evidence from published studies on the differential effects of clinical preventive services within relevant population subgroups defined by race/ethnicity, sex, age, and other clinically relevant characteristics. It also suggests processes for incorporating this evidence into the USPSTF's deliberations and recommendations. ○ The Older Adults Workgroup helps the USPSTF assess the applicability of its recommendations to older adults by offering guidance on the benefits and harms of clinical preventive services at older ages. ○ The Child and Maternal Health Workgroup provides specialised knowledge to inform the work of the USPSTF and develop new methods and procedures for making recommendations for child and maternal health. Activities of the workgroup include publishing articles on USPSTF methods related to child and maternal health, addressing methodological issues such as the challenges of identifying meaningful health outcome measures for children and adolescents, and serving as consultants on relevant USPSTF projects and topics. ○ The Conflict of Interest Workgroup is an ad hoc committee that reviews and updates USPSTF policy on reporting and addressing USPSTF members' conflicts of interest in regard to USPSTF topics. ○ The Behavioural Counselling Intervention Workgroup makes recommendations related to the standards of evidence for behavioural counselling interventions, relevant measures and metrics, coordination with the Community Preventive Services Task Force, knowledge gaps, and other methodological issues related to behavioural counselling interventions. ○ The Modelling Workgroup identifies opportunities to further inform the recommendation process through the use of decision models as a complement to systematic evidence reviews. ○ The Dissemination and Implementation Workgroup helps the Task Force better communicate with clinicians and members of the public about its recommendations, and also writes the USPSTF's annual report to the United States Congress. ▪ The USPSTF also occasionally convenes groups of experts to advise on a particular topic. **Steps taken by the USPSTF to make a recommendation** ▪ Create research plan ○ Draft research plan: The USPSTF works with researchers from an Evidence-based Practice Center (EPC) and creates a draft research plan that guides the review process ○ Invite public comments: The draft research plan is posted on the USPSTF website for public comment. ○ Finalise research plan: The USPSTF and EPC review the comments and address them as appropriate, following which the USPSTF creates a final research plan. ▪ Develop evidence report and recommendation statement ○ Draft evidence report: Using the final research plan, the EPC independently gathers and reviews the available published evidence and creates a draft evidence report. ○ Draft recommendation statement based on an assessment using six critical appraisal questions: The USPSTF then discusses the draft evidence report and the effectiveness of the service. Based on the discussion, the USPSTF creates a draft recommendation statement. ○ Invite public comments: The draft evidence report and draft recommendation statement are posted on the USPSTF website for public comment.

	○ Finalise evidence report: The EPC reviews all comments on the draft evidence report, addresses them as appropriate, and creates a final evidence report. ○ Recommendation statement: The USPSTF discusses the final evidence report and any new evidence. The USPSTF then reviews all comments on the draft recommendation statement, addresses them as appropriate, and creates a final recommendation statement. ▪ Disseminate recommendation statement ○ The final recommendation statement and supporting materials, including the final evidence report, are posted on the USPSTF website. At the same time, the final Evidence Report and final Recommendation Statement are published together in a peer-reviewed journal. The final Recommendation Statement is also made available through electronic tools and a consumer guide. **Conflict of interest disclosure** ▪ The USPSTF requires each member to disclose all information regarding any financial and nonfinancial conflicts of interest related to any topic in the USPSTF's portfolio. Potential USPSTF members disclose potential conflicts prior to joining the USPSTF. Disclosures are also updated throughout members' tenures and for all in-progress topics to reflect changes in members' situations over time. ▪ All disclosures are reviewed by the USPSTF Chairs according to the criteria specified in the *USPSTF Procedure Manual* and determined to be either Level 1, 2, or 3: ○ Level 1 and Level 2 disclosures include nonfinancial disclosures that are not anticipated to affect the USPSTF member's judgment on a topic and smaller financial disclosures (under $1,000). These disclosures do not limit the USPSTF member's participation in the topic process. ○ Level 3 disclosures include relevant financial disclosures over $1,000 and significant nonfinancial disclosures that may affect the USPSTF member's view on the topic. Actions for Level 3 disclosures vary according to the nature of the conflict and may include preventing the member from serving as lead of a topic or on the workgroup of a topic, preventing the member from serving as a primary spokesperson for a topic, or preventing the member from taking part in all topic activities. ▪ For all Level 3 disclosures, the USPSTF Chairs determine the final action on the member's eligibility to participate on a specific topic based on the nature and significance of the potential conflict. Level 3 disclosures and related actions are displayed publicly on the USPSTF website to ensure transparency. This page provides up-to-date Level 3 disclosures of current USPSTF members for in-progress topics. Once the final recommendation for a topic is published, it is removed from this page and the disclosure information is added to the topic page under the *Conflict of Interest Disclosures* heading in the *Copyright and Source Information* section.
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/R
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	

What innovative methodologies have been used to develop and or implement clinical practice guidance?	Living guidelines are currently being considered. No further details were reported.
What are the core components of the key innovation?	N/R
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	N/R
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	N/R
Notes	
Reviewer notes	RQ1: Core components - Evidence based, Knowledge management, Governance model.
Associated peer-reviewed article(s)	

Key: EPC – Evidence-based Practice Centre; N/A – not applicable; N/R – not reported; USPSTF – U.S Preventive Services Task Force**.**

Table B14 WHO/Europe handbook for guideline contextualization

Guideline identification	
Organisation	World Health Organization (WHO) – Europe Region
Year	2023
Country	Denmark
URL	https://apps.who.int/iris/bitstream/handle/10665/372275/9789289060028-eng.pdf
Title of the publication	Strengthening countries' capacities to adopt and adapt evidence-based guidelines: a handbook for guideline contextualization.
Summary/Overview	This handbook provides an overview of main principles and approaches in guideline development and contextualisation. It also describes 15 steps on how to apply GRADE-ADOLOPMENT for developing contextualised recommendations based on source guidelines and local relevant evidence. Reference is also made to other useful resources and tools. In addition to the adolopment process, brief information is provided about implementation and dissemination as well as about required quality assurance steps.
RQ1: Description of core components of clinical practice guidance	
What core elements have been stated in the document?	N/A
RQ2: Description of quality measures/criteria for clinical practice guidance development	
What quality measure tools are there to examine the robustness of methodological process used to develop the various types of clinical practice guidance?	N/A
What criteria does the tool use to assess quality?	N/A
What are the strengths and limitations of the tool?	N/A
RQ3: Description of key innovations in the development and implementation of clinical practice guidance	
What innovative methodologies have been used to develop and or implement clinical practice guidance?	Contextualisation of guidelines using the "GRADE-ADOLOPMENT" approach Contextualisation of recommendations describes the process of: ▪ acknowledging the need for dialogue and formal consideration of local best available evidence and criteria for adopting, adapting or de novo creation of recommendations from an existing trustworthy source guideline to the national, local or other level; ▪ deciding whether the recommendations are right for that setting; and ▪ modifying or adding to the recommendations to optimise their implementation using structured and transparent processes. GRADE-ADOLOPMENT is an approach that describes an efficient way for guideline contextualisation allowing for local, national or regional input, as well as stakeholder involvement and ownership, which is critical in the uptake of recommendations. The approach allows a systematic and transparent approach to adoption, adaptation and or full development of recommendations to fit the context of interest, alongside and in accordance with the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) methodology.
What are the core components of the key innovation?	**Main principles of guideline development and contextualisation** ▪ The process of guideline development should be transparent, well planned and carried out in close cooperation

	with all relevant stakeholders, including the relevant health professionals, patients and the public. ▪ Considerations for organisation, planning and training encompass the entire guideline development project and steps such as documenting the methodology used and decisions made, as well as considering any conflict of interest occurring during the entire process. ▪ The guideline group comprises an oversight committee, a guideline panel and various working groups (which include support staff, technical and content experts, evidence synthesis and or systematic review groups, and observers, among others). ▪ The oversight committee is tasked to manage and supervise priority setting, such as for a ministry of health or professional society, and the selection of a guideline panel. ▪ The guideline panel is responsible for making recommendations that start with defining the guideline or recommendation question that should be answered through the use of summarised evidence from systematic reviews complemented by contextual evidence (e.g. costs, acceptability and feasibility) to formulate the new recommendations. This evidence should be appraised and assessed for the level of certainty of the underlying evidence. ▪ The panel will pay careful attention to the formulation of recommendations before they are peer reviewed through processes such as submission for public consultation or for publication in a journal. ▪ Every guideline should be accompanied by an implementation plan (including measurable outcomes, who is responsible for what in the implementation phase and when as well as how it is done) and be followed by monitoring and evaluation. ▪ Contextualisation is not only a prerequisite but is also part of implementation and, therefore, these two aspects should be considered as equally important. There is no implementation without contextualisation and there should be no contextualisation without implementation. **Adopted recommendation versus an adapted recommendation** ▪ An adopted recommendation is not of less value than one that has undergone context-specific changes (adapted). This is because if a recommendation is relevant for the context without changes, it is as important as one that required extensive contextualisation. **Guideline checklist** ▪ Generally, guideline developers should use the Guidelines International Network (GIN)-McMaster Guideline Development Checklist to plan and conduct the guideline effort (an extension specifically referring to adaptation is being developed) **Steps for the adolopment process** Step 1: Selection of guideline topic ▪ Identify guideline topics – This requires establishment of an oversight committee that can oversee the process. ▪ Carry out scoping exercise – To identify what guidelines exist on the topic of interest. ▪ Create the organisational aspects required – selecting a guideline group follows established guideline processes (see above), such as identifying a multidisciplinary guideline panel with relevant representation. Step 2: Prioritisation of questions ▪ The prioritisation process for questions does not differ significantly between original guideline development and guideline adaptation projects, with the exception that in GRADE-ADOLOPMENT, the selection of questions is driven by priorities of the local stakeholders.

	▪ On occasion, guideline panels may identify priorities not covered by the original guideline and, therefore, not available for adoption or adaptation. Such questions can follow a traditional de novo development process, within the same guideline development or as a follow-up update of the guideline. Step 3: identification of appropriate source guidelines or systematic reviews ▪ To ensure that all potential source guidelines are identified, a systematic search for existing guidelines needs to be conducted. ▪ Potential guidelines should be evaluated with the Appraisal of Guidelines for REsearch & Evaluation (AGREE) tool to identify if they address the priority questions and before they can be used, assessed to understand if it is relevant (i.e. addresses the topic of interest), credible (i.e. achieves high enough (>60%) AGREE II instrument scores on the key domains of editorial independence and rigour of development), recent (i.e. an update would be unreasonable or the guideline is up to date) and whether it is, ideally, based on GRADE. Ideally, a suitable guideline will include freely accessible Summary of Findings (SoFs) and Evidence to Decision (EtDs) tables, ideally in compatible electronic format. ▪ Systematic reviews that have been carried out to support a recommendation in a source guideline can be assessed for risk of bias using the risk of bias in systematic reviews (ROBIS) checklist or A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2 tool for methodological quality, which is sometimes required to complete the AGREE scoring of a source guideline. ▪ If no guideline is identified, groups conducting GRADE-ADOLOPMENT may decide to search for systematic reviews about the health effects of the interventions of interest. If lacking, teams can build the EtD framework by adding local evidence about costs, values and preferences, and equity, acceptability and feasibility considerations. ▪ If more than one systematic review is identified for a particular question, teams may decide to combine the data from the reviews by conducting their own meta-analysis. ▪ It is important to emphasise that no trustworthy formal recommendation can be produced if the original guideline is not based on a systematic review or there is no independent systematic review available; if that is the case teams may be better off starting their own development process. Step 4: matching source guideline recommendations to each prioritised question ▪ Recommendations matching the prioritised questions are searched for within one or more guidelines; that is, the process follows a single recommendation as the unit of work. ▪ To accomplish optimal adaptation, the patient/population, intervention, comparison, outcome (PICO) domains in the source guideline should be matched with the prioritised question. ▪ This approach maximises usefulness for the context and distinguishes GRADE-ADOLOPMENT from other adaptation approaches that suggest using existing recommendations in a guideline and their adaption, as opposed to focusing on the priorities of the new recommendation, which may be contained in several guidelines or not be covered at all. ▪ However, it is possible that a guideline developer will choose one guideline to be 'adoloped' based on an identified need. ▪ Therefore, the main difference between typical guideline adaptation and guideline adolopment is that adolopment focuses on the questions that are relevant or important for a stakeholder who wants to adapt and implement a guideline, whereas classic guideline adaptation focuses on a source guideline and how it can be applied in a particular new setting.

	▪ adolopment starts with identifying individual questions for which a recommendation is necessary and then moves on to look for source guidelines and evidence syntheses. Step 5: does a matching recommendation exist? ▪ If a matching recommendation exists, it needs to be decided whether new or updated systematic reviews are required. ▪ If a matching recommendation exists, the creators of the original guideline should be contacted with a request for adolopment of the source guideline, assuming that the AGREE scores and evaluation of the systematic reviews in the source guidelines are appropriate. ▪ If no matching recommendation exists and this is still the case after checking or considering whether the prioritised recommendation could be slightly modified, the new recommendation will require a de novo development, which can, however, be based on existing evidence syntheses, such as a Cochrane review, if available. Step 6: update systematic review(s) (as needed) ▪ An existing systematic review may require updating or a new systematic review or other evidence synthesis may be required, particularly considering local contextual evidence. ▪ Criteria for updating, expanding or conducting an evidence synthesis include: 1. the reviews available are outdated (e.g. it is evident that research evidence exists that informs a criterion on the EtD but has not been included in the source guideline); 2. the existing recommendation does not include all outcomes of interest for a prioritised question (e.g. the local guideline panel determines that quality of life is a critical outcome but the source guideline does not consider this outcome in its recommendation); or 3. there is no evidence synthesis that includes evidence about the context of interest for important EtD criteria such as values, benefits and harms, feasibility, acceptability, equity and resource use. ▪ Updated systematic reviews will require that SoFs and EtDs are updated. ▪ Contextualisation requires focusing on relevant contextual evidence, including context-specific baseline risks, feasibility, acceptability, resource use and equity. This information may or may not have been included in the source guideline, but even if included will also be local in nature. ▪ A search for evidence about how people with the condition of interest value the outcomes in the target setting may be needed, or a search for local cost information may be required. This can also include eliciting expert evidence to inform the context. Step 7: EtD from source guideline ▪ If the source guideline does not include a complete EtD framework, an EtD should be developed (step 8). If there is one, then the EtD will require a review of the judgements made in the source guideline (outlined in step 9) and integration of the contextual evidence. Step 8: develop an EtD ▪ If no EtD exists, one needs to be developed based on extracting information that explains the rationale for the recommendation in the source guideline (if a guideline is judged credible, this information should be available in the source guideline). ▪ However, if not all information that is required for an EtD is available in the source guideline, it will lead to an incomplete EtD. In that case, a search for evidence supporting judgements of the guideline group on the missing EtD criteria is required (as opposed to using the contextual evidence if it was included in an evidence review

	informing the source guideline). It may also be necessary to use expert evidence to complete an EtD. ▪ It should be recognised that local evidence must often be identified (possibly for updates) in order to contextualise and inform the recommendation. Contextualisation should be based on (local, regional, etc.) evidence and not on how things currently are being done; the latter is not contextualisation and would not allow for a new practice or policy to be accepted (i.e. the direction and strength of a recommendation should be based on evidence from existing circumstances that may modify an existing recommendation). Step 9: reassess EtD judgements ▪ The conduct of the meeting, such as conflict of interest (COI) management, documenting plans, necessary quorum, management of disagreements and voting, should be developed and agreed before the meeting. ▪ Reassessing EtD judgements can be carried out in one of three ways: 1. The original guideline panel judgements are left in place, and the local panel decides whether they agree or not – This saves time but may limit the discussion and may reduce ownership of the final recommendation - This takes more time but is probably the best option if significant changes are made to the EtD framework. 2. The original guideline panel judgements are hidden, and the local panel makes the judgements again – Some judgements may be left in place while others may be open for discussion. 3. A mixed approach combines options 1 and 2 – some judgements may be left in place while others may be open for discussion. ▪ Importantly, the selection has to be reported explicitly in the adapted guideline. Step 10: develop recommendations ▪ During the panel meeting, the evidence presented in the EtDs will be discussed, judged and recommendations agreed on by the panel. During the deliberations, the research gaps and implementation considerations as well as the considerations for monitoring and evaluation may be documented. Monitoring and evaluation aspects will inform the drafting of the implementation plan. A search for evidence about existing decision thresholds that help to balance health benefits and harms may be helpful. Step 11: adoloped recommendation similar to source ▪ If the recommendation is the same as the source recommendation and there are no changes to the judgements on the EtD, then the recommendation is an adopted recommendation (step 12). The recommendation is adapted (step 13) if the evidence differs because of an update, the recommendation is altered (a judgement is changed) or the recommendation is different (e.g. the population is narrower or broader). Step 12: adopted recommendation ▪ The recommendation is labelled as adopted from the source guideline (with reference) and left as is (it may be translated or may include the name of the organisation developing it rather than the name of the original organisation). Step 13: adapted recommendation ▪ The recommendation is labelled as adapted from the source guideline (with reference) and formulated to express the changes. Step 14: de novo development ▪ If step 5 determined that there is no source recommendation, a new recommendation is required (step 15) with a full recommendation development process to ensure the quality of the destination guideline. This can be based on an existing evidence synthesis from systematic reviews or guidelines. This includes developing an EtD for that

	recommendation if possible. Step 15: new recommendation ▪ By applying trustworthy recommendation development processes, a new recommendation can be developed. The process should be documented and reported appropriately, for example, by using the Reporting Items for practice Guidelines in HealThcare - adopted, adapted, or developed de novo (RIGHT-AD@PT) reporting tool. Five approaches are mentioned in the WHO handbook to facilitate quality assurance of the adoloped recommendations: ▪ check the 15 steps of GRADE adolopment for completion. ▪ report the guidelines using the RIGHT-AD@PT reporting checklist ▪ check the group process and use of evidence in the adolopment using the PANELVIEW instrument ▪ evaluate if it is possible to have an independent assessment of the credibility of the guidelines, and utilise external peer review.
What is the rationale behind the methodology? **OR** **What criteria were used to determine if an innovation was necessary and if it was necessary, the type of innovation indicated?**	Rationale: The process is robust, rapid, and inexpensive. In order for guidelines to be implemented, they need to be both easy to use and timely and must be relevant and responsive to the needs, values and preferences of the target populations or individuals affected by the recommendations and their individual risks for the outcomes of interest. In addition, guidelines also need to be suitable for the available resource and organisational contexts. Contextualisation is needed to achieve efficient implementation on different levels and to use existing guidelines developed by other organisations. This document describes an approach to adopt and adapt evidence-based guidelines from WHO and other agencies. Criteria: Not specified.
What changes have been made in governance procedures for tracking of guidance as it becomes available for updating?	N/R
How is the innovation used in practice?	▪ The WHO eTB guidelines platform is a digital platform to promote adolopment of WHO recommendations by guideline development groups. The process begins with the WHO source guideline, which can be obtained from the database of evidence-based recommendations. These recommendations are updated centrally, which facilitates data linkage to information at the country level to provide input on contextualisation implementation. ▪ WHO Member States or other entities adoloping recommendations would use the WHO source guideline and conduct a prioritisation process of questions that are relevant for the context. Recommendations that are relevant are selected and assessed and the corresponding EtD framework created using tools such as GRADEpro. The guideline development group would review the judgments and the evidence within, and would update systematic reviews as needed to include contextual data such as data on values from the country itself. ▪ The guideline development group either adapts or adopts a recommendation by assessing the EtD framework supporting a recommendation. A recommendation is adapted if judgments on the EtD change based on the context, or it could be altered if, for example, different judgments or a different population are considered. If the new guideline development group agrees with all the judgments made by the guideline development group for the source guideline, the new group would adopt the recommendation without modifications. ▪ This process also enhances implementation by engaging patients, people involved with the condition of interest and all other stakeholders relevant for a country setting in the guideline implementation process. This approach

	will make the process more efficient by avoiding repeating the evidence synthesis and by enhancing the use of contextualised data while creating appropriate ownership of the recommendations that are relevant for a country or similar setting.
Notes	
Reviewer notes	
Associated peer-reviewed article(s)	Chen Y, Yang K, Marusic A, Qaseem A, Meerpohl JJ, Flottorp S et al. A reporting tool for practice guidelines in health care: the RIGHT statement. Ann Intern Med. 2017;166(2):128–32. doi: 10.7326/M16-1565. Wiercioch W, Akl EA, Santesso N, Zhang Y, Morgan RL, Yepes-Nunez JJ et al. Assessing the process and outcome of the development of practice guidelines and recommendations: PANELVIEW instrument development. CMAJ. 2020;192(40):E1138–45. doi: 10.1503/cmaj.200193 Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M et al. GRADE evidence to decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. BMJ. 2016;353:i2089. doi: 10.1136/bmj.i2089 Schünemann HJ, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa RA, Manja V et al. GRADE evidence to decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017;81:101–10. doi: 10.1016/j.jclinepi.2016.09.009 Wiercioch W, Nieuwlaat R, Zhang Y, Alonso-Coello P, Dahm P, Iorio A et al. New methods facilitated the process of prioritizing questions and health outcomes in guideline development. J Clin Epidemiol. 2022;143:91–104. doi: 10.1016/j.jclinepi.2021.11.031 Checklist for guideline panel chairs. Hamilton: McMaster University;2020 (https://heigrade. mcmaster.ca/guideline-development/chair-checklist, accessed 11 January 2023).

Key: AGREE – Appraisal of Guidelines for REsearch & Evaluation; AMSTAR - A MeaSurement Tool to Assess systematic Reviews; COI –conflict of interest; GIN – Guidelines International Network; GRADE - Grading of Recommendations, Assessment, Development, and Evaluations; N/A – not applicable; N/R – not reported; PICO – Patient/population, Intervention, Comparison, Outcome; RIGHT - Reporting Items for practice Guidelines in HealThcare; RIGHT-Ad@pt - Reporting Items for practice Guidelines in HealThcare - adopted, adapted, or developed de novo; WHO – World Health Organization.