Recommendations for the development of Clinical Practice Guidelines

Recomendações para o desenvolvimento de Diretrizes de Prática Clínica

Patrick Alexander Wachholz<sup>a</sup> <sup>✉</sup>, Airton Tetelbom Stein<sup>b,c</sup> <sup>✉</sup>, Daniela Oliveira de Melo<sup>d</sup> <sup>✉</sup>, Renato Gorga Bandeira de Mello<sup>e</sup> <sup>✉</sup>, Ivan D. Florez<sup>f,g</sup> <sup>✉</sup>

Abstract
Clinical practice guidelines are statements that include recommendations intended to optimize patient care, are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options, and ensure that the best available clinical knowledge is used to provide effective and quality care. They can reduce inappropriate care and variability in clinical practice and can support the translation of new research knowledge into clinical practice. Recommendations from clinical practice guidelines can support health professionals by facilitating the decision-making process, empowering them to make more informed health care choices, clarifying which interventions should be priorities based on a favorable trade-off, and discouraging the use of those that have proven ineffective, dangerous, or wasteful. This review aims to summarize the key components of high-quality and trustworthy guidelines. Articles were retrieved from various libraries, databases, and search engines using free-text term searches adapted for different databases, and selected according to author discretion. Clinical practice guidelines in geriatrics can have a major impact on prevention, diagnosis, treatment, rehabilitation, health care, and the management of diseases and conditions, but they should only be implemented when they have high-quality, rigorous, and unbiased methodologies that consider older adult priorities and provide valid recommendations.

Keywords: clinical practice guideline; aging; aged; guideline.

Resumo
As diretrizes de prática clínica são declarações que incluem recomendações destinadas a otimizar o atendimento ao paciente, informadas por uma revisão sistemática de evidências e uma avaliação dos benefícios e malefícios de opções alternativas de atendimento, garantindo que o melhor conhecimento clínico disponível seja usado para fornecer atendimento eficaz e de qualidade. Elas contribuem reduzindo os cuidados inadequados e a variabilidade na prática clínica e podem apoiar a tradução de novos conhecimentos de pesquisa. As recomendações dessas diretrizes podem apoiar os profissionais de saúde, facilitando o processo de tomada de decisão, capacitando-os a fazer escolhas de cuidados de saúde mais informadas, esclarecendo quais intervenções devem ser prioritárias com base em um trade-off favorável e desencorajando o uso daquelas comprovadamente ineficazes, perigosas ou que consistam em desperdício. Esta revisão visa resumir os principais componentes de diretrizes confiáveis e de alta qualidade. Os artigos foram recuperados de várias bibliotecas, bancos de dados e mecanismos de busca por meio de buscas de termos de texto livre adaptados para diferentes bancos de dados e selecionados de acordo com o critério do autor. As diretrizes de prática clínica em geriatria podem ter grande impacto na prevenção, diagnóstico, tratamento, reabilitação, assistência à saúde e manejo de doenças e condições, mas só devem ser implementadas quando tiverem metodologias de alta qualidade, rigorosas e imparciais, que considerem as prioridades da pessoa idosa e fornecem recomendações válidas.

Palavras-chave: diretriz de prática clínica; envelhecimento; idoso; diretriz.
INTRODUCTION

Most health care systems worldwide are facing an increased demand for care, including that of aging populations, which is concurrent with rising health care costs and more expensive technologies. Variation in service delivery among providers in different settings is prone to ageism, misuse, over- or underuse of services, and the intrinsic desire of patients and professionals to receive and offer those services, respectively. There is evidence that health professionals must address these health inequities, especially in vulnerable populations.

Inequities and disparities in access to health care systems often reflect accumulated disadvantages and ageist attitudes and practices, whose causes are dynamic and multidimensional. For instance, economic circumstances can determine whether an individual can afford quality health care and proper nutrition from early life through old age. Social environmental factors, such as residential segregation, discrimination, immigration, social mobility, work, retirement, education, income, and wealth, can also seriously impact health and well-being. The oldest old have been systematically underrepresented in studies on which clinical guidelines are based. Most guidelines have not modified or discussed the applicability of their recommendations for older patients with multiple comorbidities or end-of-life conditions, and they are often limited by explicit or implicit age-based criteria.

Clinical practice guidelines (CPG), statements that include recommendations intended to optimize patient care, are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative care options, ensuring that the best available clinical knowledge is used to provide effective and quality care. CPG can reduce inappropriate care, variability in clinical practice, and support the translation of new research knowledge into clinical practice. CPG provide a list of recommendations based on the best available evidence, defining the most current practice according to the local context. Due to variations in practice, guidelines can help make decisions about appropriate and effective patient care.

CPG recommendations can support health professionals by facilitating the decision-making process, empowering them to make more informed health care choices, clarifying which interventions should be priorities based on a favorable trade-off (i.e., efficacy vs. the least significant adverse effects for high-frequency conditions in the community), discouraging those that have proven ineffective, dangerous, or wasteful. Finally, CPG can help organizations reduce the gap between research and practice based on the best available evidence.

CPG must define clinical questions, select relevant outcomes, synthesize relevant evidence, and rate the trustworthiness of effect estimates through a systematic approach. Finally, they must move from evidence to recommendation.

In addition to certainty of effect estimates, several other factors influence the strength of a recommendation. These factors include the magnitude of the potential benefits and harms of alternative courses of action, the value judgments and preferences of the individuals affected by the recommendation, the extent to which these value judgments and preferences are estimated to vary across population groups, and considerations about the use of resources. In the context of public health guidelines, additional factors, such as the burden of illness, an intervention's accessibility, feasibility and acceptability, the social context, the extent of current suboptimal practice, and the intervention's impact on health inequities, may be considered as well.

One essential requirement for trustworthy guidelines is being based on systematic reviews of the best available evidence. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) Working Group has provided guidelines for evaluating the certainty of evidence in several domains. However, for many clinical questions, published evidence may be limited, indirect, or simply nonexistent. Using an expert evidence approach provides a potential solution for critical clinical dilemmas in clinical practice guidelines when published evidence is limited or nonexistent. Likewise, the direct transposition of evidence from studies of more severely ill patients (or those treated in referral centers) to populations treated in primary care should be performed with caution. In such cases, transparency about how the document was prepared is even more relevant for engendering trust in the CPG's recommendations.

The attributes of a good CPG include validity, clinical applicability, documentation, transparency, reliability and reproducibility, clarity, clinical flexibility, and development through a multidisciplinary process that is free of competing interests. CPG should be distinguished from position papers and clinical consensus statements, which often provide expert advice on challenges in patient care, usually developed by consensus methods among members of an expert panel without the systematic approach of CPG.

In recent decades, the number of CPG has increased significantly. A broad range of organizations have published guidelines, some including contradictory findings of variable quality. For example, 87% of 431 guidelines published by specialty societies until 2000 did not report whether a systematic literature search was performed. A systematic review found that < 25% of the 421 CPG for common
noncommunicable diseases in primary care could be rated as high quality.24 Recommendations issued by the American College of Cardiology/American Heart Association are largely developed from lower levels of evidence or expert opinion, which highlights the need to improve the guideline writing process and expand the evidence base from which they are derived.26

Due to a lack of methodological expertise in planning and development, the proliferation of CPG without rigor or transparency is concerning. Due to this lack of rigor, several groups and organizations have proposed standards for guideline development, including the World Health Organization,27 the U.S. National Academy of Medicine (formerly known as the Institute of Medicine),21 the U.K. National Institute for Health and Clinical Excellence,28 the Australian National Health and Medical Research Council,29 the Guidelines International Network,11 etc. There is a trend to rely on guidelines that present evidence systematically and transparently, using methodologies such as GRADE to assess evidence quality.10,12,15,24

Considering the impact of population aging on the demands of social and health systems, the underrepresentation of older adults in clinical trials, and the need for more transparent recommendations for this group when preparing CPG, this narrative review aimed to summarize the key components of high-quality and trustworthy guidelines. Articles were retrieved from various libraries, databases, and search engines, including EMBASE, Google Scholar, PubMed, Science Direct, and Scopus. Using free-text term searches, the search syntax was adapted for different databases. Eligibility criteria included documents described as guidelines, methodology reports, or manuals, including the development process of care guidelines from local or global perspectives. The articles included in each section were selected according to author discretion by informal consensus. Specific details on the development and implementation of CPG in geriatrics will be discussed in a separate topic.

Forming a clinical practice guidelines development group
First of all, it must be determined whether an evidence-based CPG is necessary and if it should be aimed at health professionals or public health policymakers. When CPG represent the health system, they allow the entire population to be informed about the benefits, progress, and limitations of available health coverage.

Once the scope and purpose of the CPG has been clearly defined, a multidisciplinary team must be gathered. CPG development groups should include diverse and relevant stakeholders, including content experts (ie, specialists and health care professionals involved in treating patients with the disorder or clinical scenario of interest), methodologists with evidence appraisal and synthesis skills, and, ideally, patient representatives and health economists.13,30 Information about the composition, disciplines, and relevant expertise of the CPG development group should be described in the document or in its appendices.30,31

The CPG development group should be led by a chairperson whose task is to facilitate discussion and consensus and avoid preconceived opinions and deliberations. Although there is no ideal size for such groups, small groups may lack relevant stakeholders, while larger groups may be challenging to manage.11 Recent evidence highlights the importance of patient and public involvement in CPG development, yet there is a lack of clear methodology for integrating their values and preferences and a need to identify the optimum stages for their involvement.32,33 Whenever possible, patients participating in CPG should have basic training in evidence-based medicine. The Guidelines International Network PUBLIC Toolkit34 describes how to include and conduct public and targeted consultations during CPG development.

The declaration and management of conflicts of interest (COI) are essential for developing impartial and credible recommendations.18 Member COI related to the interventions or diagnostic tests considered in the CPG may be harmful to the document’s content and reputation. COI can introduce bias into almost every step of the CPG development process, from developing key questions to formulating recommendations.35 All members should provide COI statements early in the development of the drafting group, expert panel, and external review group. When collecting this information, the institution must determine the amount and severity of potential COI of prospective group members and how to manage them.36

Some steps may help limit both actual and perceived bias in CPG development. Whenever possible, CPG members, chairpersons, and co-chairpersons should have no COI. The majority of the group should not have COI, and funders (whether profit or nonprofit) should have no role in the document’s development. COI may vary in terms of nature and extent. Some COI may be minor, such as being invited to a dinner by a company that produces an intervention included in the CPG, while others, such as receiving funds as a speaker or consultant or participating in a scientific or advisory board, are serious. Members with serious COI may be excluded from decision making, deliberations, producing recommendations on specific topics, or from the CPG group entirely. Varying the composition of the group’s members...
helps neutralize possible biases at the individual level and stimulates a sense of ownership in the final product, which can facilitate the document’s acceptance by different groups. Figure 137 describes the guideline development process.

The scope and development of questions
The CPG’s overall objectives, scope, and purpose should be defined *a priori* and be clearly stated in the document, including the key questions addressed. The scope should be described in detail and should include the diagnostic criteria, target population, health care setting/context, and intended users of the CPG. When relevant, characteristics of the clinical condition, severity/stage, and comorbidities should be declared, as well as excluded populations.

The initial proposal for a CPG’s scope is often prepared (or co-prepared) by the institution that requests it, and it is evaluated by external stakeholders, including experts, potential members of the drafting group, and organizations representing future users. Key questions may be drafted by incorporating best practice approaches. Since the answers to the action questions (those that guide the adoption or not of a conduct or intervention) will provide the supporting evidence for the recommendations, they should be formulated in such a way as to facilitate the search for evidence. They can cover one or more of the following areas: prevention, diagnosis, treatment, rehabilitation, and prognosis.

CPG seek to support the decision-making process in specific clinical circumstances at the local, regional, national, or international levels. The broader the scope and target audience, the more complex the decision-making process can be, since it encompasses more factors and scientific evidence when forming recommendations.

Questions are usually developed based on the most important clinical scenarios. Groups usually brainstorm and develop an initial list of questions that are discussed with the funders (e.g., with government-related organization or professional societies) and refined to prioritize the most important issues. Each question may then be transformed into the PICO framework. The PICO framework is a mnemonic device used in evidence-based practice for framing and answering clinical or healthcare-related questions. PICO stands for: P – patient, problem, or population;
I – intervention(s); C – comparison, control, or comparator(s); and O – outcome(s).

When developing questions to guide CPG, it is important to consider that recommendations for patients in areas with very high complication rates may not apply in more common contexts. The quality and availability of evidence for patients of different age groups, those with multiple comorbidities, or those with reduced survival expectations should also be considered. Some questions may require subdivision to cover these specific issues.

Methods and evidence synthesis

Transparency is a fundamental principle in the high-quality systematic reviews used to support CPG development. Therefore, a clear description of the development process is mandatory, if not within the CPG document itself or its appendix, in a referenced separate article.

Key components to be described are the selection of group members and the chairperson, the methods used in the systematic literature review, the process for deliberating about the evidence and formulating recommendations, and the dissemination and implementation of the CPG.11,30 It is also desirable to formulate and describe a plan for updating the document.39

Regarding evidence selection, a detailed and comprehensive systematic review process is mandatory for reducing bias in literature selection and appraisal, which could lead to flawed recommendations. The objectives of the CPG should be clear, favoring a precise review strategy. The literature search must be sensitive enough to retrieve, if not all, most studies that address each of the target questions. Thus, at least two major biomedical databases (such as Medline, Embase, CENTRAL, etc.) should be searched. The search strategy should be fully described to allow replication, i.e., including search terms and their combinations, applied filters, databases searched, and the time frame of the literature.21,38

It is mandatory to apply a formal instrument or strategy for rating the certainty of evidence (also called evidence quality) and the strength of the recommendations. The GRADE approach is a pragmatic consensus that categorizes evidence according to its quality, implying a gradient of confidence in estimates and conclusions derived from individual clinical studies.16,40 GRADE rates evidence by evaluating the following criteria: study limitations, inconsistency, imprecision, indirectness, and publication bias.

Study limitations can be determined by evaluating the risk of bias in randomized and non-randomized studies, respectively.41 Inconsistency, imprecision, indirectness, and publication bias are the other GRADE criteria that should be assessed, but they are applicable to the body of the evidence, rather than individual studies. Finally, after all criteria have been applied, GRADE classifies the certainty of evidence into four categories (high, moderate, low, and very low quality), implying a gradient of confidence in the effect estimates obtained from the evidence.

From evidence to recommendations

An explicit link between recommendations and the supporting evidence should be described. CPG recommendations should be clear and actionable statements that provide users with specific information about how to deliver care.14,24 Even though the evidence is crucial, additional factors should be considered when formulating recommendations. Considerations should be made about the balance of benefits/harms, use of resources, cost-effectiveness, patient values and preferences, feasibility, and equity before the recommendations are considered definitive. Frameworks such as GRADE EtD42 and WHO-Integrate43 can assist panels in the process of deliberating about recommendations.

Because resources are limited, panelists and decision-makers must consider the implications of new/alternative interventions, in addition to their cost-effectiveness. When necessary, cost-effectiveness models may be employed to better inform the recommendations. However, de novo economic analyses may not always be feasible.42,44 Understanding an intervention’s impact on health system equity and public health options is essential because these decisions are usually made from a population perspective. Moreover, it is unhelpful to recommend impractical interventions, and concerns about a treatment option’s feasibility can affect decisions about whether to recommend it or not.42,44

Some interest in the publication and dissemination of CPG is due to the need for better allocation and rational use of resources, considering:

1. Increasing health care costs due to population aging and the availability of increasingly expensive technologies;
2. Findings that service delivery varies among providers, hospitals, and regions; and
3. The fact that health professionals want to offer, and patients to receive, the best possible care.1,45

The literature is not unanimous about whether CPG should consider intervention costs. In an effort to identify tests/procedures whose usefulness should be reevaluated (i.e.,
to reduce unnecessary expenses), medical societies have developed the “Choosing Wisely” initiative.46 On the other hand, a strict focus on costs may lead to intervention rationing and, consequently, the distrust of society. However, there is also fear that financial incentives for adopting CPG may also lead to inappropriate decisions.47-49 Several authors have shown that costs are not considered in all CPG, especially those developed by professional societies.50-52 Intervention costs can be a limiting factor in CPG implementation for both health systems and patients, especially among older adults due to potential income loss.

Thus, CPG development groups must decide whether or not to recommend certain interventions or diagnostic tests and should define the strength of their recommendations. According to Moberg et al.,42 the more uncertainty/variability there is about the effect of an intervention on the main outcomes (i.e., the lower the certainty of the evidence), the less likely a panel will strongly recommend it.

The GRADE-EtD44 is a framework for helping groups provide two types of recommendations, conditional (formerly called, weak) and strong.16,40 A strong recommendation is when the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. A conditional recommendation is when the panel concludes that the desirable effects of adherence probably outweigh the undesirable effects, but they are not completely confident about it.53

The methods used to formulate the recommendations must also be clearly stated. For instance, the group’s final recommendations may have been ratified through a voting system or through informal or formal consensus techniques (e.g., Delphi, Glaser), which should be described in detail. Information on the conflict resolution process should also be provided.21,30

External review, updating, and funding statements
Before publication, it is helpful for external reviewers not involved in the CPG development group to appraise the document, including experts in methodology and in the field. Finally, procedures for updating the CPG should be provided, since keeping the CPG up to date is an important goal for good patient care.54 Financial support and sponsoring organizations should be disclosed, with an explicit description of their role in the development of the CPG and its final recommendations, including any honoraria or financial support provided to the authors.21,30

Tools for assessing clinical practice guidelines quality
Several tools have been developed for assessing the quality of CPG.10 In 1992, the U.S. National Academy of Medicine published a Provisional Instrument for Assessing Clinical Practice Guidelines,21 providing an explicit method for examining the soundness of CPG through seven attributes. In 2012, the Guidelines International Network also issued a set of key components for CPG development.11

In 1999, Chuteau et al.55 published an instrument that included a critical appraisal tool for assessing whether CPG developers minimized the biases inherent in creating guidelines and addressed effective dissemination and implementation requirements. That same year, Shaneyfelt et al.56 published a 25-item instrument to assess the methodological quality of CPG development and reporting. Most of the items evaluated principles of evidence-based medicine and implementation issues.

In 2001, a group of researchers from 13 countries developed the Appraisal of Guidelines for Research & Evaluation (AGREE) instrument to assess the quality of CPG and how well they are generated and reported. It consists of 23 items covering 6 domains; each domain is intended to capture a separate dimension of CPG quality. Each item is rated on a 4-point Likert scale ranging from 4 (strongly agree) to 1 (strongly disagree).

In 2010 the AGREE II, an update of the original tool, was published10 in an effort to improve its usability and methodological properties, namely validity and reliability. AGREE II contains the same six domains as the original, using a 7-point Likert scale ranging from 7 (strongly agree) to 1 (strongly disagree). It includes two final assessment items that require overall judgments of the CPG and ratings of the 23 items. The AGREE II is a generic instrument, and it can be applied to CPG for any disease and any stage of health care, including health promotion, public health, screening, diagnosis, treatment, and interventions. At present, AGREE II is not designed to assess the quality of guidelines for organizational health care issues, whose role in health technology assessment has not yet been formally determined.57

AGREE II, the most widely used instrument in CPG quality assessment studies, has been validated and translated into multiple languages. Despite a steady improvement in CPG quality over time, particularly after 2010, certain domains of CPG remain unsatisfactorily low according to this instrument.15,32

Using the AGREE II, Molino et al.24 reported that primary care professionals and policymakers should be aware that the quality of CPG regarding primary care varies widely: < 25% of CPG included in their review were rated as “high quality”. According to these authors, of 421 CPG with pharmacological recommendations for chronic non-communicable diseases published between 2011 and 2017, only 23% scored ≥ 60% in the AGREE II’s rigor of development domain.24 Table 1 describes the domains and items of the AGREE II instrument.
The AGREE collaboration (www.agreetrust.org) has provided additional tools to support CPG users and developers, such as CHECKUP (a checklist for updating CPG), the AGREE Checklist (checklist for guideline reporting), AGREE GRS (a tool for a rapid assessment of guideline quality) and the recently launched AGREE REX, which was developed to complement the AGREE II in assessing the quality and credibility of recommendations.

Finally, the international Reporting Items for practice Guidelines in Healthcare (RIGHT) checklist was produced to help developers with CPG reporting and support journal editors and peer reviewers when considering CPG reports.

Table 2 summarizes online resources for developing and appraising clinical practice guidelines.

### Methods for efficient clinical practice guidelines development

CPG adaptation is a systematic approach to endorsing and/or modifying a CPG produced in one cultural or organizational setting for application in a different one. Where high-quality CPG are already available, adaptation may be used as an alternative to de novo CPG development, customizing existing CPG to the needs of local users.

### Table 2. Online resources for developing clinical practice guidelines

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<tr>
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<td>ECRI Guidelines Trust</td>
<td><a href="https://guidelines.ecri.org/">https://guidelines.ecri.org/</a></td>
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<tr>
<td>COVID-END (Portfolio of resources to support guideline developers, adapters and decision makers interested in guidelines)</td>
<td><a href="https://www.mcmasterforum.org/networks/covid-end/resources-for-researchers/supports-for-guidance-developers/">https://www.mcmasterforum.org/networks/covid-end/resources-for-researchers/supports-for-guidance-developers/</a></td>
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<tr>
<td>AGREE Collaboration website</td>
<td><a href="http://www.agreetrust.org">www.agreetrust.org</a></td>
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The tool can be used by different groups:

- Health care professionals who wish to assess a CPG before implementing its recommendations in their practice;
- CPG developers using a structured, rigorous development methodology to conduct an internal assessment to ensure their CPG is sound or are evaluating CPG from other groups with a view to adapting them to their context;
- Health policymakers and health care managers deciding which CPG could be recommended or implemented, or who wish to inform health policy decisions; and
- Educators improving critical appraisal skills and essential policy development skills in health professionals.

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Developing and updating high-quality CPG requires substantial time, expertise, and resources. Health organizations are increasingly confronted by the need to standardize health policies and practices to better manage finite resources and promote optimal, evidence-based patient care.

Under certain circumstances, CPG must be developed in a short period of time, which can be challenging. The World Health Organization has defined two types of CPG developed in response to urgent need: emergency (rapid response) CPG, which are produced within hours or days, and rapid advice guidelines. Using the Guideline International Network–McMaster Guideline Development Checklist, Morgan et al. published a list of principles to guide CPG developers who are responding to urgent situations, such as public health crises. Whenever feasible, urgent guideline development (e.g., in the context of the COVID-19 pandemic) should include rapid reviews and could refer to Interim Guidance from the Cochrane Rapid Reviews Methods Group. However, developing guidelines in an emergency context is a challenging task. CPG related to COVID-19 were found to have poor methodological quality in almost every case. Stamm et al. found that most of these CPG lacked appropriate systematic reviews, failed to assess evidence quality, and their editorial independence was unclear, among other methodological flaws. Potential solutions, according to Florez et al., can be summarized as:

1. Developing clear methodological guidance and templates for rapid guidance and systematic reviews;
2. Reducing duplication of efforts via encouraging adoption/adaptation when possible;
3. Enhancing CPG registration and collaboration;
4. Enhancing coordination with evidence synthesis teams;
5. Developing and maintaining appropriate evidence synthesis repositories; and
6. Strengthening the CPG editorial processes.

The following steps have been suggested for urgent CPG:

1. Assessing the level of urgency and feasibility;
2. Setting up the organizational logistics;
3. Specifying the question(s) the CPG will answer (ensuring its scope is reasonably narrow and prioritizes outcomes that are essential, whenever necessary relying on outcomes prioritized for a similar disease or prioritizing only one critical outcome);
4. Collecting the required information;
5. Assessing the adequacy of the identified information;
6. Developing the recommendations (using one of the four potential approaches: adopting existing recommendations, adapting existing recommendations, developing new recommendations based on existing systematic and/or rapid reviews, or developing new recommendations using evidence provided by panelists);
7. Considering a plan for updating the CPG.

The process of adapting a CPG demands as much methodological rigor and transparency as developing a new one. Several methods have been developed to guide CPG adaptation, among which we highlight ADAPTE (The Adapted ADAPTE, developed by the Alexandria Center for Evidence-Based Clinical Practice Guidelines), RADAPTE (for rapid guideline development) and GRADE-ADOLOPMENT. While the first is most frequently used for this purpose, the second is based on the GRADE approach, allowing for the inclusion of recommendations adapted, adopted, or developed de novo.

**Clinical practice guidelines implementation**

Implementing CPG is a complex task that involves numerous frameworks, facilitators, and barriers, which have been described in the literature. CPG implementation was previously described as the process of changing health care practice according to the best level of evidence available in the literature.

The key information needed to implement a recommendation includes a clear description of the population for whom it is appropriate, the baseline risk of this population, the quality of the evidence, and the strength of the recommendation. The strength of a recommendation is an essential factor for implementation from the perspective of policymakers. Implementation should focus on strong recommendations. Lower-grade (weak, discretionary, conditional) recommendations are not candidates for incorporation unless patient measurements have been included in relevant discussion and patients have been introduced to all available treatment options.

**Specific geriatric issues in clinical practice guidelines**

Older adults are more likely to experience drug-drug interactions, adverse drug reactions, more costly therapeutic regimens, lower rates of treatment compliance, and higher hospitalization rates due to polypharmacy complications. When exposed to multiple concurrent interventions, age-related physiological changes and comorbidities may predispose older adults to potential harm. Furthermore, medication costs and risk-benefit ratios change from patient to patient, particularly in distinct settings (hospital, community, and long-term care facilities).
Although some CPG have considered different age-related health care scenarios, most address single diseases and do not discuss the applicability of their recommendations to older patients with multiple comorbidities.\textsuperscript{78,79} Most do not incorporate or explain how and when pharmacological interventions should be reduced or stopped when no longer needed.\textsuperscript{78} These challenges are further compounded in frail older adults and in patients with life-limiting illnesses, where disease-specific CPG routinely advocate medication regimens of increasing complexity.

Several authors have questioned the applicability of disease-specific CPG for older patients with multiple comorbidities.\textsuperscript{78-80} Until recently, very few recommendations have been based on evidence from clinical trials targeted at older adults with comorbidities.\textsuperscript{90} Addressing care quality standards and pay-for-performance, Boyd et al. concluded that CPG were not designed for use in quality assessment and that “performance standards for the care of older patients with complex comorbidities could be problematic.”\textsuperscript{79} Finally, single-disease CPG should include explicit statements to help clinicians understand limitations that might impede their application in older patients with complex comorbid illnesses.

Despite focusing on conditions predominantly found in older adults (e.g. heart failure, COPD, acute peripheral arterial occlusion, hypertension), most disease-specific CPG do not consider geriatric syndrome, physical functional status, and multimorbidity in their recommendations.\textsuperscript{81} On the other hand, the International Diabetes Federation CPG for older people with type 2 diabetes\textsuperscript{82} is a unique and comprehensive document. When using this CPG, clinicians are presented with a range of aging phenotypes and distinct functional categories and are provided with a broad spectrum of risk assessment indications, diagnostic criteria, treatment approaches, and glycemic control targets according to each functional category.

CPG that address care for older adults usually focus on identifying and managing geriatric syndrome, as in the following examples: fall prevention,\textsuperscript{83} frailty,\textsuperscript{84} end-of-life care in frail patients,\textsuperscript{85} vaccinating older adults,\textsuperscript{86} dementia care,\textsuperscript{87} clinical nutrition and hydration in geriatrics,\textsuperscript{88} managing delirium in older adults,\textsuperscript{89} inappropriate medication use in older adults,\textsuperscript{90} multimorbidity and life-limiting illnesses in older adults,\textsuperscript{91} etc. Of note, most CPG geared towards geriatric populations are developed and published by geriatric associations, such as the American Geriatrics Society, the British Medical Society, and the Brazilian Geriatrics and Gerontology Society.

Several CPG have focused on disease-centered rather than patient-centered care. Patient-centered care is responsive to patient preferences, values, and needs. This clinical model is an important feature of the high-value based health care concept, which balances potential clinical benefits with harms, costs, and patient preferences to optimize net clinical benefit,\textsuperscript{92} a key objective of CPG.\textsuperscript{1}

Thus, to improve a CPG’s net clinical benefit, discussing the complexity of clinical care, rather than merely the best scientific evidence, is a major step toward high-value based health care and ease of implementation. Therefore, the implications of aging in clinical practice (multimorbidity, functional capacity, clinical and mental vulnerability, iatrogenic risk, and patient values and preferences) must be included during CPG planning and development, even for disease-specific guidelines.

Discussion about implementing recommendations in older patients are necessary to improve the net clinical benefit of CPG and promote high-value based health care. Furthermore, encouraging discussion of non-pharmacological interventions, systematic prescription review before recommending a new treatment, deprescribing unnecessary or potentially harmful medications, prognostication, and shared decision making may also improve CPG quality.

**CONCLUSION**

CPG can have a major impact on prevention, diagnosis, treatment, rehabilitation, health care, and the management of diseases and conditions, but only those identified as high-quality, rigorous, and with unbiased methodologies whose recommendations consider older adult priorities should be implemented.

**Conflicts of interest**

The authors declare no conflicts of interest

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**Authors’ contribution**

PAW: conceptualization, investigation, methodology, project administration, visualization, writing – original draft, writing – review & editing. ATS: conceptualization, investigation, methodology, visualization, writing – original draft, writing – review & editing. DOM: conceptualization, investigation, methodology, writing – original draft, writing – review & editing. RGBM: conceptualization, investigation, methodology, writing – original draft, writing – review & editing. IDF: conceptualization, investigation, methodology, project administration, supervision, visualization, writing – original draft, writing – review & editing.

REFERENCES


Recommendations for Clinical Practice Guidelines


