






Overview of clinical practice guideline development, application to pharmacy practice, and roles for pharmacists

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Abstract

All health care professionals have a responsibility to integrate current evidence-based medicine into their clinical practice to ensure the best possible patient care. Clinical practice guidelines (CPGs) play a major role in helping clinicians identify when and how to implement evidence into routine clinical practice to improve patient outcomes. The primary intent of CPGs is to benefit patients by improving the quality of care; however, CPGs also improve efficiency and effectiveness within the health care system. The process used to develop CPGs is important to ensure the recommendations are trustworthy, based on the highest-quality evidence, and free of significant conflicts of interest. The National Academy of Medicine (NAM) published guidance on best practices for developing CPGs in 1990 and again in 2011. Additional guidance is provided by various reporting checklists for CPGs, such as the Appraisal of Guidelines for Research & Evaluation (AGREE) II and Reporting Items for Practice Guidelines in Healthcare (RIGHT) instruments. However, analyses of published CPGs show inconsistent application of these best practices. This paper discusses the benefits of CPGs, reviews the guideline development process, discusses limitations in this process and in applying CPGs to patient care, identifies opportunities for improvement, provides considerations for educating learners and other health care professionals about CPGs, and examines the role of pharmacists in CPG development, dissemination, and implementation.

KEYWORDS

clinical pharmacists, clinical practice guidelines, evidence-based medicine

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1 | BACKGROUND

Integrating evidence-based medicine into clinical practice is an essential component of improving the quality of health care and optimizing clinical and public health outcomes.¹ However, the frequency at which new evidence is published challenges clinicians' ability to remain up to date with the literature; as a result, patients may not receive the best care according to current scientific evidence.² In addition, it may take up to 17 years before new research is fully integrated into clinical practice.³ Barriers to incorporating new research into practice include inadequate knowledge management, lack of financial incentives, local standards out of line with desired level of practice, clinician attitudes toward change, and poor communication between clinicians and patients.⁴

Clinical practice guidelines (CPGs) can build a consensus around the available evidence, help support clinical decisions at the point of care, and improve clinicians' ability to discuss the benefits and risks of different treatments with patients. This paper discusses the benefits of CPGs, reviews the guideline development process, discusses limitations in the guideline development process and in applying CPGs to patient care, identifies opportunities for improvement, provides considerations for educating learners and health care professionals about CPGs, and examines the role of pharmacists in CPG development, dissemination, and implementation.

2 | ORIGIN AND HISTORY OF CLINICAL PRACTICE GUIDELINES

In 1989, the Agency for Healthcare Research and Quality (AHRQ), formerly the Agency for Health Care Policy and Research, was created to promote effective health care-related research through the development, dissemination, and evaluation of CPGs.⁵ This was a major shift from the traditional reliance on professional judgment with limited oversight. The impetus for this change was the culmination of both private and public concerns regarding the escalating costs of health care, inconsistency in medical practice, and evidence that not all health care services provided value. In 1990, the AHRQ contracted with the Institute of Medicine (IOM)—now the National Academy of Medicine (NAM)—to issue a report titled “Clinical Practice Guidelines: Directions for a New Program.”⁶ In 1992, the IOM subsequently formed a dedicated committee to assess guideline development processes and implementation of CPGs into clinical practice and published *Guidelines for Clinical Practice: From Development to Use*.⁷ This publication improved on the 1990 report and emphasized the impact of both CPG contents and their development processes on final guideline effectiveness.

2.1 | Terminology

Although several types of publications aim to translate research findings into recommendations for improving patient care, not all are considered CPGs.^{8,9} NAM defines CPGs as “statements that include

TABLE 1 Terminology

Term	Definition
Clinical practice guideline	A statement that includes recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefit-harm of alternative care options
Consensus statement	A statement developed by experts when guidance on a topic is desired, but evidence is limited to support a more definite statement, such as a clinical practice guideline
Protocol	Orders or instructions on how to implement a particular process in an explicit way without error
Care pathway	A sequence of evidence-based steps in managing patient care; this can involve a multidisciplinary team at various care levels
Practice standard	Rules or minimum requirements for clinical practice, which are only modified under unusual circumstances
Clinical practice recommendation	Documents that are systematically developed that represent best practices for specific clinical areas
Position statement	Documents that provide comprehensive explanations, justifications, and recommendations for solving a clinical issue or problem

recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.”⁵ Clinical practice guidelines are developed by experts in the field and provide diagnostic and treatment recommendations according to the available evidence, which is evaluated on the basis of quality.¹⁰ In contrast, consensus statements are developed by experts when guidance is needed on a topic for which evidence that might otherwise allow for a more definitive statement is insufficient.^{8,9} Table 1 summarizes descriptions of the documents used to guide clinical decision-making.

3 | RATIONALE FOR CLINICAL PRACTICE GUIDELINES

3.1 | Benefits to patients

The primary benefit of CPGs is improving the quality of patient care and health outcomes.¹¹ Adherence to CPGs lowers the risk of hospitalizations and improves all-cause mortality.¹² However, data are conflicting regarding the extent of CPG impact on other patient outcomes. Although previous systematic reviews have reported significant improvements, the degree of improvement varies across studies. This may be related to the wide variety of outcomes measured across individual studies, methodological heterogeneity, and differences in the patient populations being evaluated.^{13,14}

FIGURE 1 Pathway to clinical practice guideline development

STEP 1. IDENTIFY

Identify guideline objectives and scope

- Identify target population and the specific outcomes to be addressed
- Create list of specific clinical questions to be answered.

STEP 2. CONVENE

Convene subject matter experts and stakeholders

- Representatives may include clinicians, researchers, patients, caregivers, and other community members

STEP 3. ASSESS

Assess body of published evidence by predetermined methodology

STEP 4. TRANSLATE

Translate evidence into recommendation

- Provide rubric for grading level of evidence, strength of recommendation, and detailed rationale for recommendation

STEP 5. REVIEW

Review of guideline by an internal and external review process

STEP 6. DISSEMINATE

Disseminate guideline to end users

Clinical practice guidelines can serve as a bridge between the available evidence and its implementation into clinical practice, providing guidance on diagnostic and treatment options on the basis of efficacy, safety, and cost; this in turn increases the likelihood that patients will receive a consistent level of care, regardless of geographic location, clinician type, or medical specialty.^{11,15,16} In addition, CPGs that are accompanied by educational tools for patients or caregivers and that are widely disseminated can empower patients to make more informed health care decisions and promote shared decision-making between patients and their providers.^{11,15}

3.2 | Benefits to the health care system

Implementation of CPGs can improve efficiency and effectiveness within the health care system.¹⁵ The summary of evidence and recommendations provided by CPGs can support formulary decisions and lead to the development of clinical pathways to ensure consistency and minimize practice variation within an organization. Guideline implementation and adherence can reduce hospital admissions, result in earlier discharge, and reduce inappropriate medication use, resulting in decreased health care costs.^{2,11} Clinical practice guidelines can also

drive quality improvement initiatives, with their evidence-based recommendations used to identify standards of care.^{11,15} Clinical practice guidelines can also aid health care systems and national, state, and community groups in developing or standardizing quality metrics and meeting accreditation, regulatory, and payment performance measures.

4 | OVERVIEW OF THE CLINICAL PRACTICE GUIDELINE DEVELOPMENT PROCESS

In 2011, NAM published a playbook describing the process for developing trustworthy CPGs (Figure 1).⁵ The purpose of CPGs should be clearly defined by the guideline development panel. The selection process of the guideline development panel varies across organizations and disciplines; however, the goal is to organize a panel of multidisciplinary experts to represent a diverse set of interests and expertise. A methodologist may also be included to help provide oversight of guideline development and navigate the systematic review of a large body of published evidence. Another important factor in the selection process is considering a panel member's possible conflicts of interest and how best to manage any that are relevant.

TABLE 2 Levels of evidence and strength of recommendation of commonly used grading systems

		ACC/AHA (2019)	GRADE (2016)	NICE (2020)	USPSTF (2012)
Levels of evidence	Levels	A, ^a B-R (randomized trial) or B-NR (nonrandomized trial), C-LD (limited data) or C-EO (expert opinion)	High Moderate Low Very low	High Moderate Low Very low	Good Fair Poor
	Considerations	Study design, number of studies, consistency with indirect evidence	Risk of bias, inconsistency, imprecision, indirectness, publication bias, magnitude of effect, dose-response relationship, opposing residual confounding	Risk of bias, inconsistency, imprecision, indirectness, publication bias	Risk of bias, applicability, inconsistency, number of studies/participants
Strength of recommendation	Use the intervention	Class I (strong) Class IIa (moderate)	Strong for	Must offer/refer/ advise	A, B
	May use, depending on circumstances	Class IIb (weak)	Conditional/weak for, conditional/weak against	Consider	C
	Do not use the intervention	Class III (no benefit) Class III (strong)	Strong against	Do not offer/do not refer/do not advise; must not	D

Note: Adapted from: Brignardello-Petersen R, Carrasco-Labra A, Guyatt GH. How to interpret and use a clinical practice guideline or recommendation: users' guides to the medical literature. *JAMA* 2021;326:1516.

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association Clinical Practice Guideline Recommendation Classification System; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; NICE, National Institute for Health and Care Excellence; USPSTF, U.S. Preventive Services Task Force.

^aAn A level of evidence requires high-level evidence from more than one randomized controlled trial or meta-analysis of high-quality randomized controlled trials.

Guideline panels may follow several methods to define the guideline's analytic framework, including whether the guideline will integrate value and economic considerations into the recommendations.¹⁷ Each recommendation includes a comprehensive rationale of the benefit-harm of the recommendation, any gaps in the available evidence, and details regarding the role of expert opinion in influencing the final recommendation. Rating systems are used to assign both a level of evidence (LOE) and a strength of recommendation (SOR) in CPG development.¹⁸ Many rating systems are available; those most commonly used include the American College of Cardiology/American Heart Association (ACC/AHA) Clinical Practice Guideline Recommendation Classification System; the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system; the National Institute for Health and Care Excellence system; and the U.S. Preventive Services Task Force system.

4.1 | Level of evidence

Considerations for determining the LOE supporting a recommendation and how it is reported differ among the rating systems (Table 2).¹⁹ For example, the GRADE system would classify a randomized controlled trial (RCT) without serious limitations, inconsistency,

indirectness, imprecision, or bias as having the highest LOE.¹⁸ The LOE rating would decrease to moderate, low, or very low using the same system if issues were identified. Alternatively, the ACC/AHA rates the highest LOE as grade A, which requires high-quality evidence from more than one RCT, meta-analyses of high-quality RCTs, or one or more RCTs confirmed by registry studies. Lesser-quantity and/or quality evidence is rated as B-R (randomized) or B-NR (nonrandomized) and low or no evidence as C-LD (limited data) or C-EO (expert opinion).²⁰ There are also grading systems that only include the LOE and do not provide a SOR, such as those developed by the American Diabetes Association (ADA).²¹ Adoption of a single-evidence grading system would provide consistency across guidelines and might improve the level of agreement.

4.2 | Strength of recommendation

Strength of recommendation is also classified to determine how an intervention is to be used. Benefit and harm are assessed to determine whether the SOR is strong and should be recommended, is weak and should conditionally be recommended depending on circumstances, or has no benefit and should not be used. When the potential for harm exceeds the potential benefit, recommendations may also be

made against an intervention. Each of the rating systems uses different terminology when classifying the SOR (see Table 2).¹⁹ In general, a recommendation is considered strong if most informed decision-makers would agree with the recommended treatment. A conditional recommendation exists when many informed decision-makers would support the decision, but a few would not. When conditional or weak recommendations exist, the reason for the rating should be evaluated to determine how it might affect decision-making. Algorithms and diagrams for use as point-of-care resources are helpful to the practicing clinician, though these do not always include the LOE or SOR. Overlooking the SOR in CPGs may cause confusion between evidence-based information and information based on expert opinion.

4.3 | Peer review and dissemination

Finally, there is an external review process that often involves key stakeholders, especially if multiple professional societies are involved, to ensure the recommendations align with their respective mission and interests. This process often mimics the peer review process used for publication in a peer-reviewed journal. The draft may also be made available for public comment before the final draft is released for publication. The primary method of CPG dissemination is publication in a peer-reviewed journal, often one associated with the developing organization. These publications are usually, but not always, open access and available without a subscription. Some CPG developers use dedicated websites and mobile applications to assist with dissemination and access.²²

5 | LIMITATIONS IN THE GUIDELINE DEVELOPMENT PROCESS AND OPPORTUNITIES TO IMPROVE

Despite the established benefits of CPGs and the available guidance on the best practices for developing them, they have limitations. They are often complex, long, and cumbersome to use. Although it is rational for clinicians to want a simple and straightforward CPG with a handful of clear and concise recommendations,²³ clinicians also need guidance on how best to treat a patient when high-quality evidence is not available. Rather than oversimplifying CPGs, other strategies can effectively improve the CPG development process so that CPGs are most useful for clinicians. Of importance, clinicians should acknowledge these limitations when applying CPGs to patients (Table 3).

Use of an established framework by CPG developers can help ensure CPGs are high quality, timely, and consistent. Currently, there is no independent body that oversees CPG development in the United States. Moreover, even when handbooks, clearinghouses, or methodological directions for guidelines do exist, there may still be gaps in development to be addressed. An analysis of 35 handbooks or frameworks for guideline development by various international organizations showed that less than one-third provided any guidance on

TABLE 3 Clinical practice guideline limitations and opportunities to improve

Limitation	Opportunities to improve
Lack of an established framework or process for development	Use the AGREE II or RIGHT reporting checklist
Inability to evolve rapidly with changing evidence	Provide more focused, brief updates Transition to digital “living” documents Use of point-of-care mobile applications
Limited applicability to underrepresented groups	Encourage increased enrollment of underrepresented groups in clinical trials Ensure the guideline panel represents the population the guideline is intended to serve
Many available guidelines	Add guidelines to centralized registries, such as the Guidelines International Network
Variability in interpretation of the available evidence	Adopt a single evidence rating system for consistency across guidelines
Conflicting recommendations between guidelines from different organizations	Execute local discussions regarding which guideline to follow to ensure practice consistency
Focus on single disease state without consideration of drug–drug and drug–disease interactions	Encourage collaboration between organizations with guidelines that overlap with other conditions (e.g., diabetes and hypertension)
Limited information regarding precision medicine and pharmacogenomics	Include recommendations for therapies with a high level of evidence
Limited mention of patients and their role in the process	Include a layperson on the writing committee Address patient-related factors that may influence treatment decisions
Real-world evidence is often not considered or included as part of the evidence base for a recommendation	Incorporate high-quality real-world studies to complement RCT data
Conflict of interest of authors and guideline developers	Establish a clearly defined and public process for how conflicts of interest are managed and reported

Abbreviations: AGREE, Appraisal of Guidelines for Research and Evaluation; RCT, randomized controlled trial; RIGHT, Reporting Items for Practice Guidelines in Healthcare.

how to assess the need for a process to update these documents, highlighting that these organizations should provide oversight as well as a comprehensive framework on all aspects of the process, including the frequency at which documents are updated.²⁴

Reporting checklists for CPGs can assist in guideline development and reporting. The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument was first developed in 2003 and consists of 23 appraisal criteria items used to validate CPG reliability on the basis of quality and recommendation for use.²⁵ In 2010, the instrument was revised (AGREE II) with additional minor updates in 2013 and 2017. In 2017, another reporting tool was developed by the international RIGHT (Reporting Items for Practice Guidelines in Healthcare) Working Group.²⁶ The RIGHT instrument has 22 items, with around half overlapping with those of the AGREE II instrument. According to a comparative analysis of AGREE II and RIGHT, either instrument can be used, but CPG developers should consider incorporating items unique to the instrument not used as part of a comprehensive approach into guideline development and reporting.²⁷ Both instruments are subjective, depending on a user's conclusions about the assessment criteria; however, they still provide a process guideline that developers can use to ensure better consistency across CPGs.

Even if the best CPG development process is followed, the rapid evolution of clinical scientific knowledge remains a challenge. Most CPGs are updated about every 5–10 years.²⁸ As new evidence is published, the potential for portions or even entire CPGs to become quickly outdated is a major limitation of their use. It has been suggested that CPGs should be reassessed every 3–5 years,²⁸ but a more recent retrospective descriptive analysis of CPG recommendations suggests a more aggressive timeline. In this analysis, 113 recommendations from four published CPGs determined that 1 in 5 recommendations were considered outdated after 3 years.²⁹ Most of these recommendations were graded B for strength or considered an expert opinion and were associated with a high degree of turnover in the references cited. These results suggest that rapidly evolving clinical areas need updating before 3 years. This point was confirmed in a textual analysis for 11 ACC/AHA guidelines published between 1998 and 2007 and then revised between 2006 and 2013.³⁰ In this analysis, after accounting for guideline-level factors, recommendations based on expert opinion, a single RCT, or observational studies were three times more likely to be downgraded, reversed, or omitted than recommendations supported by higher-quality studies. As such, it is recommended that CPG developers create processes allowing for routine surveillance of newly published research in dynamically changing areas and have a system in place to revise recommendations in a timely manner. Strategies to accomplish this include using more focused (or brief) guideline updates, transitioning to digital “living” documents in addition to publishing in traditional peer-reviewed journals, and expanding the use of point-of-care applications (e.g., mobile applications).²²

Guidelines are commonly used to improve patient care but may not apply to all patients.³¹ The lack of inclusion of underrepresented populations is a limitation of CPG development. In addition, lack of diversity among the CPG development panel, clinicians, and policy-makers may increase the risk of bias, depending on varying interpretations and views of management options and the magnitude of effect on the outcomes of interest.³² Given the growing body of evidence showing significant disparities in care across certain groups for various

medical conditions, it is imperative that clinical investigators implement strategies to improve enrollment of underrepresented minorities, women, and older adults and that CPG writing committees be as diverse as the population being served.

It has also been suggested that CPGs should primarily be developed by the end users, such as primary care clinicians developing guidelines for areas such as hyperlipidemia or diabetes, rather than specialists.²³ Although ACCP agrees with primary care representation on CPG panels, the primary authors should be experts in the field, who are often specialists.

6 | LIMITATIONS IN APPLYING CLINICAL PRACTICE GUIDELINES TO PATIENT CARE AND OPPORTUNITIES TO IMPROVE

6.1 | Challenges in implementing CPGs

A prominent limitation of implementing CPGs into clinical practice is the many guidelines available.³³ This can present challenges for generalist clinicians (e.g., primary care clinicians) in keeping abreast of the guideline recommendations for many different disease states. From 1999 through 2018, the AHRQ supported the National Guideline Clearinghouse, which provided standards for U.S.-based CPG developers and provided audiences with access to an online collection of available guidelines.³⁴ However, this service was shut down in 2018 because of a lack of federal funding. Currently, the Guidelines International Network, representing 111 organizations in 61 countries, has an online database with links to over 3000 guidelines where clinicians can search for published guidelines as well as those in development.^{35,36}

Inconsistent recommendations may also exist among CPGs from different organizations. In addition to evaluating benefit-harm, writing committees may place varying importance on quality-of-life outcomes, patient values, acceptability, practical application, cost, and fairness.¹⁹ Inconsistency among guidelines may also arise because of the evidence available at the time of a publication, the intended population, the potential bias of the guideline panel or developing organization, and the rating system used. It is important to be aware of the reason for inconsistency among guidelines and to carefully interpret the recommendations. One example of inconsistent guideline information pertains to when to add ezetimibe to maximally tolerated statin therapy in adults with diabetes and additional cardiovascular risk factors (Table 4).^{37–40} In these situations, a careful review of the rating system used, the evidence forming the recommendation, the year of publication and evidence cited, and the individual patient characteristics should be considered. Discussion at the local practice level may also be necessary to agree on which guideline recommendations to follow to help ensure consistent practice among clinicians on the health care team.

Guidelines themselves need to be assessed for feasibility of implementation, using the Guideline Implementability Appraisal.⁴¹ This 31-item, 10-dimension set of questions examines each guideline recommendation on the basis of decidability, executability, global applicability, presentation and formatting, measurable outcomes,

TABLE 4 Example of inconsistent clinical practice guideline recommendations

Guideline	Recommendation	Class	LOE
2018 AHA/ACC/Multisociety Guideline on the Management of Blood Cholesterol	In adults with diabetes and a 10-yr ASCVD risk \geq 20%, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL by \geq 50%	IIb	C-LD
2022 ADA Standards of Medical Care in Diabetes		N/A	C
2019 ESC/EAS Guidelines on Management of Dyslipidemias	If the goal is not reached, statin combination with ezetimibe should be considered	IIa	B
2020 VA/DoD Clinical Practice Guidelines on the Management of Dyslipidemia for Cardiovascular Risk Reduction	Insufficient evidence to recommend for or against using ezetimibe with or without statins	Neither for nor against	

Abbreviations: ACC, American College of Cardiology; ADA, American Diabetes Association; AHA, American Heart Association; ASCVD, atherosclerosis cardiovascular disease; DoD, Department of Defense; EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LOE, level of evidence; N/A, not applicable; VA, Veterans Affairs.

apparent validity, flexibility, effect on process of care, novelty/innovation, and ease of computerized implementation. These criteria were developed and validated and can prove useful in both guideline development by correcting guideline defects and guideline implementation by addressing barriers to implementation.

6.2 | Considerations when applying recommendations to individual patients

Disease state CPGs are used as a starting point and guide for clinicians to provide evidence-based care to patients. Many CPGs primarily rely on RCTs to guide expert recommendations; however, limitations in the number and quality of RCTs available, as well as the lack of diversity in the populations included, often require CPGs to rely more heavily on lesser-quality evidence. A study examining the populations included in the ACC/AHA atrial fibrillation, acute coronary syndromes, and heart failure guidelines found that the included RCT populations were composed of less than 33% women and 27% non-White patients, and only 2% were 75 and older.⁴² A similar study conducted on stress urinary incontinence guidelines showed that most of the studies cited did not report the participants' race or ethnicity and that the studies that did only included non-White participants at a fraction of the rate compared with White participants.⁴³ These discrepancies and the underrepresentation of women, non-White individuals, and older adults raise concerns and weaken the generalizability of guidelines to a diverse population. This underrepresentation demonstrates the need for improved health equity in CPGs because these patients may not achieve the same outcomes represented in the studies driving guideline recommendations. The differences in outcomes can be the result of both population- and individual-level factors, such as the physical environment (e.g., limited access to health care) or other social determinants of health, lack of trust in the health care system, health literacy, and the policy environment (e.g., discrimination).^{44,45} To advance health equity and increase applicability, equitable representation of study subjects by race, ethnicity, and sex/gender and consideration of multiple comorbidities is necessary.⁵ Recently, NAM published a consensus report advocating research equity for women and underrepresented minorities.⁴⁶

Another limitation to interpreting CPGs is that considerations for comorbid conditions on guideline recommendations are often omitted. Patients seldom have a single medical condition, yet guidelines tend to focus on and guide clinicians through the lens of the disease state prioritized in the guideline. Patients often have multiple comorbidities and take several medications, and guidelines may not consider other drug–drug and drug–disease interactions. Furthermore, guidelines from different organizations may have different goals to achieve disease control. For example, blood pressure goals vary between guidelines for patients with chronic kidney disease. The Kidney Disease: Improving Global Outcomes guidelines recommend a systolic blood pressure goal of less than 120 mm Hg in patients with kidney disease, whereas the ACC/AHA/Multisociety guidelines recommend a goal of less than 130 mm Hg.^{47,48} This conflict can cause differences in how clinicians practice and leave patients confused. It is important for clinicians to examine the CPGs available for comorbid conditions that affect others to ensure alignment in optimizing drug therapy.

An emerging avenue in clinical practice seldom discussed in CPGs is the application of precision medicine and pharmacogenomics, which use an individual's genetics, environment, and lifestyle to guide disease treatment and prevention.⁴⁹ Pharmacogenomics is specific to how genes may influence an individual's response to medications.⁵⁰ Pharmacogenomics evidence-based guidelines have been developed by the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetics Working Group, the Canadian Pharmacogenomics Network for Drug Safety, and the French National Network of Pharmacogenetics.⁵¹ These guidelines can provide health care professionals with steps to take when genotype results are available, but not whether to perform a genotype on a patient. Moreover, an analysis of U.S. guidance sources (e.g., CPIC, FDA) found wide variability in the recommendations provided across various therapeutic areas.⁵² In a comparison of these guidelines, medications with the highest-level evidence for genetic testing and patient treatment are abacavir, clopidogrel, fluoropyrimidines, thiopurines, irinotecan, codeine, and cisplatin.⁵¹ An increasing number of medications contain pharmacogenomic guidance information in FDA labeling. Around 483 medications and pharmacogenomic biomarker pairs are currently listed in various sections of the FDA label.⁵³ Pharmacist-led pharmacogenomics programs implemented across various practice areas have

improved patient outcomes.⁵⁴ Pharmacists have also served on panels for developing pharmacogenomics guidelines. However, because this is still an emerging field, application of these principles is lacking in other CPGs. This can lead to discordant outcomes between the patients represented and described in the guidelines and other patients because of lack of implementation of genomics-driven medication therapy management.

Another consideration that CPGs seldom mention is the importance of involving the patient in the decision-making process and the use of decision aids. Shared decision-making and decision aids can be useful when implementing CPG recommendations into clinical practice to determine whether the recommendations align with patients' treatment goals, whether patients can afford the treatment, and whether they are willing to take the treatment. The NIH Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV have specific sections addressing important patient factors that may help providers more easily discuss lifelong therapy with patients.⁵⁵ Some have advocated for CPGs to wholly center on the use of shared decision-making principles²³; however, evidence to support the effect of shared decision-making on behavioral and health outcomes varies.^{56,57} Additional research is needed to demonstrate how best to implement shared decision-making and which decision aids are most effective.

Many guidelines do not consider real-world evidence, despite its increasing importance in guiding health care decision-making.⁵⁸ Studies designed around real-world evidence have greater generalizability than RCTs, partly because they include a more diverse population. This is important for most clinicians because it is challenging to extrapolate results from RCTs to patients who may not fit into the inclusion/exclusion criteria.⁵⁹ Clinical trials (e.g., pragmatic clinical trials) that use real-world data while still using randomization act as the middle ground between RCTs and observational studies, such as case-controls and cohorts.⁶⁰ Real-world data may originate from a variety of sources but most often consist of information routinely collected in the delivery of health care. For example, real-world data can come from sources such as electronic medical records, claims and billing activities, mobile devices capturing health-related data, and in-home medical devices. The FDA has published a framework to guide clinicians wanting to engage in studies based on the real-world evidence program, but lack of time and support to conduct meaningful research remains a barrier.⁶¹

7 | CONSIDERATIONS WHEN EDUCATING LEARNERS AND THE HEALTH CARE TEAM ABOUT CLINICAL PRACTICE GUIDELINES

Use of CPGs by health care teams decreases variability in clinical decisions and increases the quality of patient care.⁶² However, implementation of CPGs can be delayed by limitations in dissemination, education and training, and marketing.⁶³ Education and training of students, trainees, and other clinicians are particularly important to improve the use of CPGs (Figure 2).

Health professional students' initial exposure to CPGs is often in the classroom setting; thus, faculty members are heavily relied on for up-to-date information. The WHO 2013 guideline on transforming health professional education recommended the implementation of continuous development programming for faculty members as a core part of relaying relevant information to students (quality moderate, strength conditional).⁶⁴ In addition to providing up-to-date information, educators who demonstrate a commitment to the profession serve as positive role models, which is a beneficial component to student development.⁶⁵

Learning in postgraduate training programs relies more heavily on self-investigation than on structural formats.^{64,66,67} Yet some programs that teach CPGs use didactic lectures, which have not been found to be an effective learning technique.^{67,68} Instead, active learning methods, such as a flipped training model, are both more effective and more efficient in improving knowledge and attitudes toward using CPGs in clinical practice.⁶⁶ If trainees start clinical practice unfamiliar with CPGs or how to locate them, they are more likely to ask point-of-care clinical questions of colleagues and search internet websites or general databases to find the answers than to use high-quality references.⁶⁹

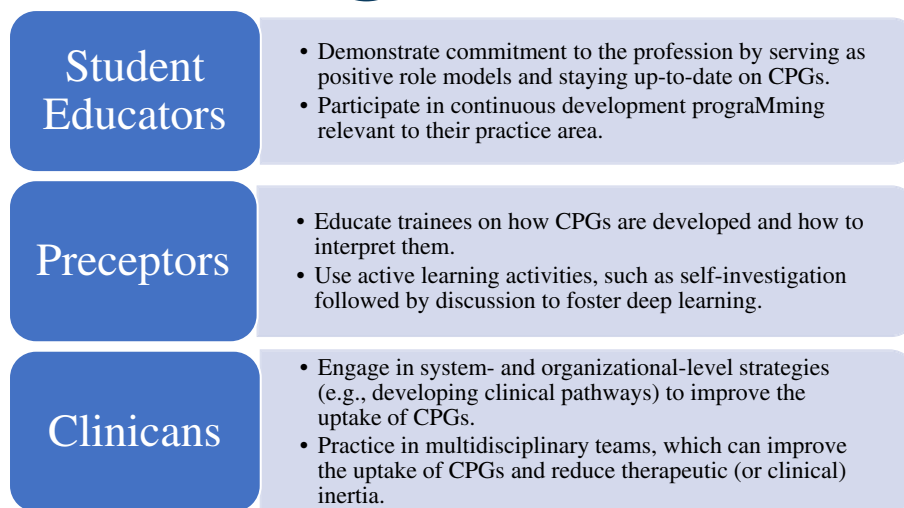
Lack of proper education on CPGs and how to use them appropriately is just one reason why CPG uptake may be low among practicing clinicians, with a recent study reporting estimated average times to CPG implementation of 8–18 months.⁷⁰ Factors that contribute to whether new CPGs are implemented include clinicians' personal beliefs regarding CPGs, need to tailor the recommendations to specific patient needs such as concomitant comorbid states, lack of an established teaching mission of implementation of new guidelines, and inadequate time away from day-to-day responsibilities to dedicate to CPG implementation.⁷¹

Clinician education on CPGs is also important in reducing clinical (or therapeutic) inertia in clinical practice.²² A systematic review of 38 studies that examined provider-, system-, and organization-level strategies to enhance clinician uptake and use of CPGs for the care of patients with heart failure found that creating a clinical pathway and using a multidisciplinary team were associated with increased uptake of new guidelines in the clinical setting and improved clinical outcomes.⁷² Because each health system is unique in resources and implementation priorities, a thorough review of potential barriers once structure changes are suggested is essential to successful implementation.⁷² In addition, employee buy-in is important in overcoming clinical inertia, in which institutional financial incentives and a strong leadership commitment can play a positive role.⁷² Overall, successful guideline implementation within practice settings requires a multifaceted approach combining provider-, system-, and organization-level strategies.

8 | ROLE OF PHARMACISTS IN DEVELOPING, DISSEMINATING, AND IMPLEMENTING CLINICAL TREATMENT GUIDELINES

Clinical pharmacy has an obligation to contribute to the generation of new knowledge that advances health and quality of life, and clinical

FIGURE 2 Recommended approaches to educating learners and clinicians on clinical practice guidelines. CPG, clinical practice guideline



CPG = clinical practice guideline.

pharmacists are well positioned to participate in developing inter-professional guidelines, as well as in disseminating and implementing evidence-based guidelines.⁷³ For many years, professional pharmacy organizations, including ACCP, have responded to requests for names of their members with therapeutic expertise to serve on interprofessional CPG writing panels. In recognition of the level and breadth of expertise among their members, the ACCP Board of Regents added an initiative to develop methods to further increase the number of ACCP members involved in this type of work as part of its 2020 Strategic Plan, resulting in new opportunities for collaboration.⁷⁰

All guidelines involving pharmacotherapy should include at least one clinical pharmacist on the writing panel or committee. The inclusion of clinical pharmacists in CPG development continues to increase, but there remains room for improvement. Clinical pharmacist representatives are on key national and international guidelines such as those issued by the ADA Standards of Medical Care in Diabetes,²¹ the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group,⁷⁴ the American Epilepsy Society,⁷⁵ the ACC/AHA,⁷⁶ the NIH,⁷⁷ the Society of Critical Care Medicine (SCCM),^{78,79} the Infectious Diseases Society of America,⁸⁰ and the SCCM/American Society for Parenteral and Enteral Nutrition.⁸¹ However, clinical pharmacists are lacking inclusion on other major guidelines involving pharmacotherapy, such as those from the Global Initiative for Asthma, the American College of Endocrinology, and the American Academy of Neurology.^{82,83}

Clinical pharmacists are encouraged to join and actively participate in medical associations that align with their subject matter expertise. Clinical pharmacists should share their knowledge and expertise at professional meetings and organizations beyond pharmacy through presentations, posters, and networking, to spread awareness of their expertise and the important role of pharmacists' contributions to both patient care and scientific discussion. These steps can increase recognition of pharmacists' expertise and provide subsequent opportunities for their involvement on guideline writing panels or committees.

Organizations like the ADA have an application process in which clinical pharmacists can directly apply to serve on guideline writing committees.⁸⁴

Dissemination and implementation of guidelines is critically important to ensure evidence-based recommendations serve their ultimate purpose, which is to improve patient care. Clinical pharmacists work in interprofessional clinical settings, have advanced knowledge of pharmacotherapy, and use evidence-based guidelines to inform patient care decisions, making them ideal opinion leaders to influence CPGs, especially regarding medication use recommendations. As educators of student pharmacists, pharmacy residents and fellows, and other health care professionals, clinical pharmacists can contribute to guideline education at multiple levels, leading to wider dissemination and more rapid implementation. Opportunities for clinical pharmacists to provide such education include presentation of guidelines within patient care settings and professional conferences, in didactic and experiential curricula, and in peer-reviewed publications (e.g., review articles). Clinical pharmacists can also incorporate medication-focused recommendations within clinical decision tools such as clinical pathways, algorithms, and best practice alerts that are embedded within the electronic health record. These activities align with the principles and application of interprofessional education and collaborative practice for which ACCP advocates.⁸⁵

9 | CONCLUSION

Clinical practice guidelines are important tools to ensure evidence-based medicine is incorporated into the decisions made in patient care to improve health outcomes. Clinical pharmacists should have a thorough understanding of how CPGs are developed, their limitations, and how to apply them in patient care and should take responsibility for educating students, trainees, colleagues, and other health care professionals. Although clinical pharmacists are increasingly involved in all

aspects of CPG development, dissemination, and implementation, ACCP must continue to advocate for the inclusion of clinical pharmacists on CPG writing committees and as reviewers for all CPGs involving medication use.

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