Overview of clinical practice guidelines

AUTHOR: Paul Shekelle, MD
SECTION EDITOR: Mark D Aronson, MD
DEPUTY EDITOR: Jane Givens, MD, MSCE

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Dec 2023.**
This topic last updated: **Mar 04, 2022.**

INTRODUCTION

Clinical practice guidelines are recommendations for clinicians about the care of patients with specific conditions. They should be based upon the best available research evidence and practice experience. This topic will provide an overview of practice guidelines.

OVERVIEW

The Institute of Medicine (IOM) defines clinical practice guidelines as "statements that include 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" [1].

Based on this definition, guidelines have two parts:

- The foundation is a systematic review of the research evidence bearing on a clinical question, focused on the strength of the evidence on which clinical decision-making for that condition is based.
- A set of recommendations, involving both the evidence and value judgments regarding benefits and harms of alternative care options, addressing how patients with that condition should be managed, everything else being equal.

As an example, the US Preventive Services Task Force (USPSTF) recommendations for colorectal cancer screening [2] were published with two separate background papers: an evidence report and systematic review [3] and a modeling study [4].

Formal advice on how clinicians should manage patients is not new. Local opinion leaders or the authors of widely circulated review articles have had a powerful influence on practice decisions. What has changed about modern clinical practice guidelines is that they are based on systematic reviews of the evidence, are often endorsed by national organizations, undergo intensive review, and are circulated across international boundaries and specialties.

Guidelines have largely focused on the effectiveness of interventions. Over time, however, they have paid more attention to the size of the effect and the balance between effects on the one hand and harms and costs on the other as well as on the feasibility of following guidelines. Another emerging development is the concept of individualized guidelines, whereby risk factors specific to the individual patient, rather than population-based risk factors, are incorporated into tools weighing risks and benefits to guide treatment decisions [5]. While such individualized guidelines have the potential to improve quality of care and lower health care costs, limitations to their practice application at this time include the availability of patient-specific data, validated disease models and risk calculators, and the potential impact on workflow. Guidelines developed in the United Kingdom by the National Institute for Health and Care Excellence (NICE) involve patients and caregivers in the development process and explicitly include patient choice and cost-effectiveness as factors in determining recommendations [6].

USE AND USERS

Guidelines are suggestions for care, not rules. There will always be individual patients who should be managed differently. Reasons for this include biologic differences in drug metabolism, immune response, or genetic endowment; the presence of comorbid conditions; available resources determined by the social and economic environment of medicine at the local level; and patient preferences [7]. However, most patients do fit the recommendations in most guidelines.

Guidelines are intended to help clinicians take better care of patients. However, others may use guidelines in different ways. For example, health plans and administrators may use them to measure quality and effect payment for care, and they may be used in malpractice cases. As an example of use by health plans, guideline recommendations may be translated into performance measures that are then used to assess the delivery of care. These performance measures may be used in "pay for performance" or similar programs that link clinician payment to quality of care as measured by guideline-derived parameters of clinical care. This use is an effort to deal with rising costs and the need for quality improvement. The concept is popular, but the evidence about the effects is mixed [8].

RECOGNIZING CREDIBLE GUIDELINES

Numerous guidelines have been published. They vary in quality.

The most trustworthy guidelines can be recognized by adherence to best practices for guideline development identified by the Institute of Medicine (IOM) (table 1) [9]. Such guidelines:

- Have an explicit description of development and funding processes that is publicly accessible
- Follow a transparent process that minimizes bias, distortion, and conflicts of interest
- Are developed by a multidisciplinary panel comprising clinicians, methodological experts, and representatives, including a patient or consumer, of populations expected to be affected by the guideline
- Use rigorous systematic evidence review and considers quality, quantity, and consistency of the aggregate of available evidence
- Summarize evidence (and evidentiary gaps) about potential benefits and harms relevant to each recommendation
- Explain the parts that values, opinion, theory, and clinical experience play in deriving recommendations
- Provide a rating of the level of confidence in the evidence underpinning each recommendation and a rating of the strength of each recommendation
- Undergo extensive external review that includes an open period for public comment
- Have a mechanism for revision when new evidence becomes available

Many guideline developers revised their processes on the basis of these IOM recommendations. The IOM noted that all of these criteria should be met for a guideline to be judged trustworthy [10]. Questions have been raised about the feasibility of implementing all of the IOM's criteria in settings where resources may be constrained.

Measuring the "trustworthiness" of guidelines based on how closely they adhere to the IOM or other standards was proposed. The National Guideline Clearinghouse (NGC) in the United States evaluated the IOM report and implemented the NGC Extent Adherence to Trustworthy Standards (NEATS) Assessments for all guidelines it had posted from March 2017 until its July 2018 closure [11]. After the closure of the NGC, the Emergency Care Research Institute (ECRI), who had been the contractor for the NGC, launched their own searchable database of guidelines [12], but access is no longer free. Guideline Central also has a searchable database of guidelines [13], which has both free content and summaries as well as other content requiring payment.

The Guidelines International Network (G-I-N), an international network representing 103 organizations in 47 countries, works to establish minimal standards for guideline development [14-16]. G-I-N has also provided further guidance on how to operationalize disclosure of interests and management of conflicts [17].

Although some of the aspects of how best to implement guidelines development differ between IOM and G-I-N, generally the two bodies agree on the basic elements essential to develop high-quality guidelines, including:

- Utilizing a systematic literature review
- Establishing transparency and disclosing the methods used for all development steps
- A multidisciplinary development group
- Disclosure and management of both financial and non-financial conflicts of interests
- Clear and unambiguous guideline recommendations
- Using a specific grading systems to rate the strength evidence and recommendations
- External peer review
- Updating (or expiring) guidelines

The biggest issue about the proposed standards has been the complexity and practicality of implementing them.

Expertise — Guidelines prepared by panels representing the full range of expertise bearing on the clinical question are more likely to avoid the biases and potential singular perspectives of members who are all from a given specialty [18]. These panels should represent a wide range of expertise and may include, in addition to primary and subspecialty clinicians, representatives from allied health sciences, public health specialists, decision analysts, economists, consumers, and ethicists. Expertise in interpreting research evidence is a necessary component of the panel. It can be contributed by members who also have other expertise, or a methods expert can be included.

The US Preventive Services Task Force (USPSTF) makes special effort to balance the interests of its guidelines panels and that its guidelines are carefully prepared [19]. In the United Kingdom, evidence-based guidelines developed by the National Clinical Guideline Centre for implementation in the National Health Service are also rigorously developed over a period of about 2.5 years from inception to release and incorporate decisions based upon clinical and cost-effectiveness [20]. Guidelines prepared by specialty and subspecialty societies usually involve a narrower spectrum of interest limited to members in the society [21].

Incorporating patient perspectives — Since the focus of clinical guidelines is on patient outcomes, and the importance of achieving or avoiding specific outcomes may differ among patients, including the perspectives of patients in guideline development is important [22]. Almost all interventions influence multiple positive and negative outcomes; thus, specific benefits and specific harms need to be considered to determine the impact of an intervention on improving positive outcomes and generating negative outcomes (eg, side effects, adverse events, costs).

For some health care decisions, the values most patients place on these positive and negative outcomes can be inferred with confidence, such as the mortality benefit from the use of beta blockers following a myocardial infarction compared with the potential for side effects (eg, lethargy and sexual dysfunction) of beta blockers. These decisions often involve recommendations for which there is strong evidence of benefit for the intervention.

However, many health care decisions involve positive and negative outcomes for which the relative importance is not so clear cut and for which the evidence of benefit is weaker. In such circumstances (eg, the decision to treat lower urinary tract symptoms in men with a transurethral resection of the prostate or the decision to screen for breast cancer in women aged 40 to 49 years), patient values related to the importance of different outcomes are more likely to vary. Individual patients may differ in their priorities to diminish bothersome urinary symptoms or avoid sexual dysfunction or their desire to minimize risk of a delayed cancer diagnosis versus the desire to avoid biopsy. Priorities can vary sufficiently between two patients with identical clinical circumstances such that each might best maximize their individual health outcomes by choosing exactly opposite courses of care.

Guideline developers should consider patient preferences in formulating recommendations and explicitly identify assumptions made regarding patient preferences for various outcomes. For some conditions, there is strong literature regarding patient

values about competing outcomes (such as prolonged life versus sexual function in the treatment of prostate cancer). For many other conditions, the literature related to patient values is less robust and there is no agreement on how best to identify patient preference. Directly soliciting patient input as part of the guideline development process may be a reasonable solution.

Evidence based — Credible guidelines are based on a systematic review of published research that is likely to include reports of all scientifically credible studies that bear on the question at hand. The systematic review should follow explicit ground rules for identifying all relevant studies and judging their scientific strength and should make transparent the rationale for their decisions [23]. Expert opinion and usual practice not supported by research evidence may be included but should be labeled as such and not take precedence over stronger evidence [24]. The process of developing guidelines can be used as an impetus to encourage clinical research when evidence is not available [25,26].

High-quality evidence is often not available. In a review of guidelines from the Infectious Diseases Society of America, for example, only 14 percent of the 4000 recommendations were supported by the highest-level evidence [27]. A study of American Heart Association/American College of Cardiology (AHA/ACC) guidelines found that nearly half of recommendations were based on the lowest level of evidence [28].

Even when data from well-designed and well-implemented randomized controlled trials are available, they often are not directly applicable to the populations, interventions, or outcomes addressed by the guideline being developed [29].

The aim of practice guidelines to optimize patient management may be even more relevant in circumstances where evidence is equivocal and the clinician is less certain about the choice of strategy. In such circumstances, the synthesis of carefully weighed opinions of experts may be particularly helpful, considered in the context of individual patient factors and adapted as needed. Transparency is essential so that it is clear to readers what the quality or strength is of the evidence supporting the guideline recommendation.

Grading guidelines — Guidelines should provide an assessment of the strength of each individual recommendation. A common approach is to grade the strength of the evidence and the strength of the recommendation separately.

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system [30] is widely used [31-35]. In GRADE, grades have two components: a two-level representation of the strength of recommendation (strong or weak) and a four-level representation of the certainty of the evidence (high, moderate, low, and very low).

- **Strength of the recommendation** – A recommendation is a strong recommendation to do (or not do) something, where the benefits clearly outweigh the risks (or vice versa) for nearly all patients. UpToDate uses a number 1 to reflect a strong recommendation. A weak recommendation is made either when risks and benefits are more closely balanced or are more uncertain. UpToDate uses a number 2 to reflect a weak recommendation.

- **Certainty of evidence** – Assessment of evidence certainty in GRADE reflects confidence in the estimates of benefits, harms, and burdens. GRADE can be implemented with either four levels of evidence quality or with three levels such that the "low" and "very low" categories are combined. UpToDate uses three levels and uses a letter (A, B, or C) for high-, moderate-, or low-/very low-quality evidence. High-certainty evidence typically comes from well-performed randomized controlled trials or other overwhelming evidence (such as well-executed observational studies with very large effects). Moderate-certainty evidence typically comes from randomized trials with important limitations or from other study designs with special strength. Low-certainty evidence typically comes from observational studies or from controlled trials with very serious limitations. Very low-certainty evidence typically comes from nonsystematic observations, biologic reasoning, or observational studies with serious limitations. The UpToDate implementation of GRADE is shown in the table (table 2).

The USPSTF uses a rating system that is uniform across the multiple conditions it reviews [36]. The system rates the recommendations and provides suggestions for practice. Examples of USPSTF recommendations are included elsewhere. (See "Overview of preventive care in adults", section on 'Overview of USPSTF recommendations'.)

Consider outcomes and implementation — Guidelines should take into account not only whether an effect of an intervention is beyond chance but also other clinically relevant factors such as:

- The magnitude of effect
- Harms from the intervention
- Convenience and side effects
- The clinical skills necessary to carry out the intervention successfully
- Patient preferences
- Cost
- Cost-effectiveness
- The work force necessary to implement the recommendations

These factors, and others, are included in the GRADE Evidence to Decision framework, which may be useful for guideline developers to use when formulating a recommendation.

The role of and potential variation in patient preferences in particular is now recognized as being of great importance for many, if not most, health care decisions, and guidelines on most topics should explicitly state what are the assumptions about patient preferences that were used in reaching recommendations.

Recency — Guidelines may be produced only once or, as with the USPSTF or National Cholesterol Education Program, they may be updated at several-year intervals [37]. In fast-moving fields, such as treatment of human immunodeficiency virus (HIV) infection, these guidelines may be out of date in less than a year.

In a study of guidelines sponsored by the US Agency for Healthcare Research and Quality, more than three-fourths of guidelines needed updating [38]. A study of 100 quantitative systematic reviews found that new findings with impact on the review outcome occurred within two years of publication for 23 percent of the reviews [39]. The median time for "survival" of an analysis was 5.5 years. When it was active the NGC required evidence that a guideline has been developed, reviewed, or revised within five years for inclusion of the guideline in their listing [40]. It is reasonable that a guideline that has not undergone review (with updating if needed) within five years of publication, in the absence of strong justification, should not be considered current.

There is discussion in the guideline community about the prospect of future “living” guidelines that are continuously updated, supported by “living” systematic reviews [41]. Some examples have been produced during the COVID pandemic [42,43]. However, a number of challenges exist. For example, how often does the living guideline need to be revisited and possibly revised? (In a fast-moving field like COVID-19, situations have arisen where a newer version of the guideline is already being developed before the prior version has finished going through the editorial review process necessary before release and dissemination.) Further, cost is even more of a challenge when both systematic review and guideline processes need continual updating.

Sponsoring society — Statements formally endorsed by respected national bodies are subject to scrutiny by health professionals and sometimes by the public through coverage in the popular media. These organizations have a strong incentive to safeguard their reputation by having their guidelines stand up to scrutiny. However, the imprimatur of a sponsoring organization does not necessarily guarantee quality.

Review — It is preferable for guidelines to undergo careful review and endorsement by experts outside the organization, or at least by representatives of the sponsoring organization other than panel members.

Conflict of interest — The guideline should report conflicts of interest (COI), financial or others, bearing on the guideline for each member of the panel [18].

The IOM Committee on Standards for Developing Trustworthy Clinical Practice Guidelines recommends written disclosure of any commercial, noncommercial, intellectual, institutional, patient, or public activity pertinent to the guideline scope [1]. It also recognizes that, for some guidelines, a degree of COI might be unavoidable in panel participants (such as relevant clinical specialists whose income is related to providing services pertinent to the guideline) but that these members should be a minority of the panel and should not be chairs or co-chairs. In addition, the G-I-N recommends that COI should be publicly disclosed, updated regularly, and no one with relevant COIs should decide the direction or strength of a recommendation [17].

While it is recognized that transparency is essential when participants in the guidelines preparation process have conflicts of interest, it is less clear how best to adapt the process to avoid bias related to any COI [44]. Clinicians with notable expertise in an

area are both more likely to be sought out to participate in developing relevant guidelines and to participate in industry-sponsored activities such as speaker's bureaus or advisory panels. In various reports, the frequency of financial COIs among authors of clinical guidelines ranges from 35 to 87 percent [45-48].

Disagreement among guidelines — Guidelines on the same clinical question by different expert groups often provide different recommendations. Usually the differences are minor; with screening guidelines, for example, they might differ on the age at which screening should begin and end or the time interval between screening examinations. Uncommonly, recommendations are very different. For example, in 2008, two major guidelines for colorectal cancer screening were published within several months of each other [49,50]. The two guidelines included different sets of screening test options (three options for one, seven for the other) and preferences (in one, detection of adenomas in addition to cancers was preferred over detecting cancers only).

Sometimes guidelines result in voiced concern. For example, a previous guideline diverged from some professional society guidelines and did not recommend mammography screening for younger women. A review of eight guidelines on screening asymptomatic patients for peripheral arterial disease found conflicting recommendations from different organizations, with differing interpretations of the evidence base mostly related to the role of testing in symptomatic patients but not in asymptomatic people [51].

Disagreement may be a barrier to acceptance of guidelines. However, in one study of this question, the extent to which clinicians agreed with each other regarding intervals for cancer screening was not related to the extent to which guidelines agreed on recommended screening intervals [52].

Differing recommendations may occur for many reasons. A weak evidence base may lead to various conclusions. Guideline recommendations based upon subgroup analysis are particularly subject to limited sample size. Another reason that guidelines may disagree is because of the value system of the panel that developed them. One study showed that surgeons tended to favor more aggressive cancer screening intervals than family physicians and internists and that gynecologists favored more aggressive screening for cancers occurring in women [52]. The best possible care of patients may also vary according to availability of resources, health priorities, and social environment. As an example, screening guidelines tend to be less aggressive in Canada and the United Kingdom than they are in the United States. In some instances, there may be a financial COI or a lack of panel members with expertise in the interpretation of research evidence.

Pluralism — The United States has opted for guidelines prepared by a variety of organizations, mostly specialty societies or others in the private sector, and some by governmental organizations, rather than a single version prepared by the federal government. While the multiplicity of guidelines and their differences can be confusing, the absence of a single standard for practice allows for innovation and can be useful in the absence of strong evidence on the best practice.

Other countries have a single organization developing guidelines. Such organizations include the National Institute for Health and Care Excellence (NICE) in the United Kingdom, the Institute for Quality and Efficiency in Health Care in Germany, and the Dutch College of General Practitioners in the Netherlands.

FINDING GUIDELINES

Guidelines can be found at the websites of the sponsoring organizations (eg, major medical organizations and clinical specialty societies), or by entering "clinical practice guidelines" into a search engine. "Practice guideline" can also be set as a limit term for type of article when using PubMed to search the US National Library of Medicine.

OTHER TYPES OF PRACTICE GUIDANCE

Appropriate use criteria — Appropriate use criteria (AUC; sometimes referred to as "appropriateness criteria") are a variation on clinical practice guidelines but differ in several ways [53]:

- Appropriateness is tailored as much as possible to the specific characteristics of individual patients.

- AUC cover a broader array of specific conditions, sometimes hundreds for a given test or treatment decision, to encompass the majority of practice situations. Appropriateness may relate to individual patient demographic characteristics, clinical history, risk scores, and/or symptoms and signs.
- AUC are based upon scientific evidence where possible but, in part as a result of the breadth of specific clinical conditions addressed, rely more on expert opinion than do rigorous clinical practice guidelines.
- Panels that formulate AUC are typically comprised of representatives from the specialties that manage patients with the clinical question under consideration.
- A common approach is to rate specific clinical scenarios (or potential indications for an intervention) on a 1 to 9 scale by each panelist before and after a group face-to-face discussion, and the median of the panel ratings is then used to designate each clinical scenario as appropriate, uncertain, or inappropriate.
- AUC are intended not only to help clinicians make sound clinical decisions but also to educate patients and improve the effectiveness, efficiency, and equity of care.

Implementation of some AUC has been facilitated by the development of calculators or tables in which the clinician can input specific patient information. As with guidelines, AUC are not intended to replace clinical judgment.

The AUC approach was initially used primarily by subspecialty societies concerned with cardiovascular, rheumatologic, and pulmonary conditions, and associated imaging procedures. AUCs have also been developed for several surgical procedures [54].

Guidance statements — The American College of Physicians (ACP) has issued several "guidance statements" that are based on reviews of other guidelines and not a de novo systematic review of evidence. These address conditions such as breast cancer screening in women aged 40 to 49, prostate cancer screening, or colorectal cancer screening for which there is general agreement on all or most of the eligible trials but difference in how the evidence from those trials is interpreted. The ACP reviews existing guidelines on the topic and appraises them using criteria from the "Appraisal of Guidelines, Research, and Evaluation (AGREE II)" [55]. The ACP then formulates its own guidance based on a review of the literature, recommendations in existing high-quality guidelines, and considering the needs and values of its general internist membership and their patients.

ATTITUDES AND ACCEPTANCE

In general, clinicians are most likely to accept recommendations from their own specialty society, less likely to trust those prepared by government agencies, and least likely to believe in guidelines prepared by managed care organizations and insurance companies. In one study of internists' attitudes toward guidelines, 82 percent had confidence in guidelines prepared by the American College of Physicians (ACP) and only 6 percent in those prepared by Blue Cross and Blue Shield [56]. Attitudes related to who prepared guidelines appear to be independent of the scientific validity of the guidelines themselves, although this has not been specifically studied.

Clinicians disagree on whether clinical practice guidelines promote "cookbook medicine" with "not enough recipes in the cookbook" [57] or evidence-based medicine. In one study of a national sample of internists, the majority believed that guidelines are good educational tools, a convenient source of advice, and intended to improve the quality of care and decrease health care costs [56]. However, a majority also believed that guidelines are biased, oversimplified, and rigid, likely to decrease physician reimbursement, challenge physician autonomy, and decrease physician satisfaction.

Clinicians are more likely to trust guidelines if they have had a hand in them. However, it is neither practical nor necessary for local clinicians to build new guidelines from the ground up if guidelines by national groups already exist. Much of the work needed to assemble the evidence, which can take thousands of hours, has been done. Local review of guidelines, with modifications if necessary to take into account the conditions of practice, resources, and patient preferences, can foster local buy-in.

Potential benefits/problems of guidelines — Evidence-based, carefully developed, and updated guidelines provide many potential benefits:

- Synthesis of the literature by experts
- Clear recommendations for translating the evidence base into clinical application to foster best practice
- Opportunity to evaluate the outcomes of implementation in the "real world" setting

However, several aspects of guidelines and their implementation need to be recognized as potential problems:

- The challenge of keeping guidelines updated when the literature changes.
- The potential for inappropriate use of guidelines for other than clinical purposes
- Difficulty accessing guidelines at the point of care – Many are lengthy or specific components relevant to a patient are not readily searchable or retrievable
- Lack of coordination among guideline development groups, generating differing recommendations
- Potential for conflicts of interest
- Application of guidelines developed to address a specific condition to patients with multiple comorbidities [58,59]

EFFECTS OF GUIDELINES ON PRACTICE

Experts in guidelines and evidence-based medicine urge clinicians to use them as a guide rather than as a set of rules or cookbook and to tailor clinical decisions to individual patients. Guidelines often do not adequately account for severity of illness, patient preferences, or clinical judgment to be able to be used as quality measures [60].

Simply providing guidelines seems to improve practice, but the effects are small [61]. It is clear that there can be significant gaps between guidelines' recommendations and practice. As an example, in one study of practice in the United States, it was estimated that 68,000 deaths could be prevented if six recommendations from guidelines for the management of heart failure were closely followed [62]. There are many reasons why clinicians do not adhere to guidelines' recommendations. In one report using focus groups of general practitioners in the Netherlands to explore reasons why recommendations from 12 national guidelines were not followed, the most frequently perceived barriers to adoption were identified as disagreement with the recommendations, environmental factors based on organizational constraints, lack of knowledge of the recommendations, and unclear or ambiguous guidelines [63]. In other studies, recommendations were more likely to be followed when they were supported by clear evidence, were compatible with existing norms and values, did not require new skills or change in practice routine, were less controversial, and were stated in specific actionable terms [64,65].

Thus, the "actionability" of a guideline is an important attribute. While well-formulated guidelines can be an invaluable tool to guide best practice in medicine, they should not alone be considered a complete plan for quality improvement. Rather, they need to be delivered in the context of a program to engage patients and clinicians in appropriate decision-making, supported by implementation strategies involving systems enhancements, clinical reminders, other quality improvement and decision support tools, and outcomes measurement and feedback. However, even when such support is provided, it remains challenging to change clinician practice. In a randomized trial related to guidelines for the management of nonvariceal upper gastrointestinal bleeding, 43 hospitals were randomly assigned to an intervention (clinicians received published consensus guidelines, algorithms, and written reminders and participated in multidisciplinary guideline education groups and case-based workshops) or control (received guidelines and algorithms) [66]. At one year, guideline adherence was not significantly different between the intervention and control hospitals, with adherence below 10 percent in both groups.

Implementing practice guidelines — Increasing attention has been focused on how best to disseminate guidelines and foster adoption of their recommendations, once developed [67,68]. A framework for the study of guideline implementation ("implementation science") includes five principal domains: characteristics of the intervention, the outer setting, the inner setting, characteristics of the involved individuals, and the process of implementation [69].

Strategies to facilitate implementation of practice guidelines have been proposed and include [70]:

- Guidelines should incorporate a checklist of prioritized specific interventions

- Identify barriers to adoption, and design supports to address specific barriers
- Integrate guidelines for common coexistent conditions
- Identify systems and technological solutions to promote adherence with recommendations
- Develop transdisciplinary teams (clinical epidemiology, implementation science, systems engineering) to study ways to foster best practices

The Institute of Medicine (IOM) recommends that guidelines that are based upon strong evidence should be worded so that it is possible to evaluate whether care followed recommendations [71]. The IOM suggests that guidelines be structured in format, vocabulary, and content to foster use of computer-aided decision supports by guidelines users.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. Specific guideline links topics can be found using the UpToDate search tool.

SUMMARY AND RECOMMENDATIONS

- Clinical practice guidelines are recommendations for clinicians about the care of patients with specific conditions. Guideline development should involve a systematic review of the research evidence related to decision-making for the targeted condition/question and recommendations about patient management based on the evidence and value judgments that should be explicitly identified as such. (See 'Overview' above.)

- Guidelines are suggestions for care, not rules. There will always be individual patients who should be managed differently for reasons including biologic differences (eg, rates of drug metabolism, strength of immune response, or genetics), comorbidities, availability of resources, cultural preferences, and patient preferences. For some health care decisions, differences in patient preferences for various health outcomes can mean that there is no one course of care that can be strongly recommended. (See 'Use and users' above.)

- Guidelines vary widely in quality. Credible guidelines involve development by a panel representing a full range of expertise; an unbiased systematic review of the evidence; grading the strength of the evidence and recommendation; incorporation of multiple relevant factors including feasibility, harms, costs, and patient preferences; and a process for ongoing review and updating (table 1). (See 'Recognizing credible guidelines' above.)

- While well-formulated guidelines can be an invaluable tool to guide best practice in medicine, they should not alone be considered a complete plan for quality improvement. Guidelines need to be delivered in the context of a program to engage patients and clinicians in appropriate decision-making, supported by implementation strategies involving systems enhancements, clinical reminders, other quality improvement and decision support tools, and outcomes measurement and feedback. (See 'Effects of guidelines on practice' above.)

ACKNOWLEDGMENT

The UpToDate editorial staff acknowledges Robert H Fletcher, MD, MSc, who contributed to an earlier version of this topic review.

REFERENCES

1. Consensus report, Institute of Medicine. Clinical practice guidelines we can trust. March 23, 2011. http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx (Accessed on January 13, 2012).

2. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. JAMA 2016; 315:2564.
3. Lin JS, Piper MA, Perdue LA, et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2016; 315:2576.
4. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies: Modeling Study for the US Preventive Services Task Force. JAMA 2016; 315:2595.
5. Eddy DM, Adler J, Patterson B, et al. Individualized guidelines: the potential for increasing quality and reducing costs. Ann Intern Med 2011; 154:627.
6. Peterson PN, Rumsfeld JS. The evolving story of guidelines and health care: does being NICE help? Ann Intern Med 2011; 155:269.
7. Wilson MC, Hayward RS, Tunis SR, et al. Users' guides to the Medical Literature. VIII. How to use clinical practice guidelines. B. what are the recommendations and will they help you in caring for your patients? The Evidence-Based Medicine Working Group. JAMA 1995; 274:1630.
8. Mendelson A, Kondo K, Damberg C, et al. The Effects of Pay-for-Performance Programs on Health, Health Care Use, and Processes of Care: A Systematic Review. Ann Intern Med 2017; 166:341.
9. Laine C, Taichman DB, Mulrow C. Trustworthy clinical guidelines. Ann Intern Med 2011; 154:774.
10. Ransohoff DF, Pignone M, Sox HC. How to decide whether a clinical practice guideline is trustworthy. JAMA 2013; 309:139.
11. Jue JJ, Cunningham S, Lohr K, et al. Developing and Testing the Agency for Healthcare Research and Quality's National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards (NEATS) Instrument. Ann Intern Med 2019; 170:480.
12. Emergency Care Research Institute. ECRI Guidelines Trust. Available at: https://guidelines.ecri.org/ (Accessed on March 03, 2022).
13. Guideline Central. Available at: https://www.guidelinecentral.com/ (Accessed on March 03, 2022).
14. Qaseem A, Forland F, Macbeth F, et al. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med 2012; 156:525.
15. Van der Wees P, Qaseem A, Kaila M, et al. Prospective systematic review registration: perspective from the Guidelines International Network (G-I-N). Syst Rev 2012; 1:3.
16. http://www.g-i-n.net/about-g-i-n/introduction (Accessed on November 21, 2017).
17. Schünemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. Ann Intern Med 2015; 163:548.
18. Sniderman AD, Furberg CD. Why guideline-making requires reform. JAMA 2009; 301:429.
19. AHRQ. The Guide to Clinical Preventive Services 2005. Available at: www.preventiveservices.ahrq.gov/#uspstf (Accessed on February 05, 2006).
20. Hill J, Bullock I, Alderson P. A summary of the methods that the National Clinical Guideline Centre uses to produce clinical guidelines for the National Institute for Health and Clinical Excellence. Ann Intern Med 2011; 154:752.
21. Brook RH. Practice guidelines: to be or not to be. Lancet 1996; 348:1005.
22. Montori VM, Brito JP, Murad MH. The optimal practice of evidence-based medicine: incorporating patient preferences in practice guidelines. JAMA 2013; 310:2503.
23. Institute of Medicine. Finding what works in health care: Standards for systematic reviews. http://www.iom.edu/Reports/2011/Finding-What-Works-in-Health-Care-Standards-for-systematic-Reviews.aspx (Accessed on July 31, 2013).
24. Fletcher RH. Building the Evidence. In: Implementing Clinical Practice Guidelines, Margolis CZ, Cretin S (Eds), AHA Press, Chicago 1998.
25. Deresinski S, File TM Jr. Improving clinical practice guidelines--the answer is more clinical research. Arch Intern Med 2011; 171:1402.

26. Li T, Vedula SS, Scherer R, Dickersin K. What comparative effectiveness research is needed? A framework for using guidelines and systematic reviews to identify evidence gaps and research priorities. Ann Intern Med 2012; 156:367.
27. Lee DH, Vielemeyer O. Analysis of overall level of evidence behind Infectious Diseases Society of America practice guidelines. Arch Intern Med 2011; 171:18.
28. Tricoci P, Allen JM, Kramer JM, et al. Scientific evidence underlying the ACC/AHA clinical practice guidelines. JAMA 2009; 301:831.
29. McAlister FA, van Diepen S, Padwal RS, et al. How evidence-based are the recommendations in evidence-based guidelines? PLoS Med 2007; 4:e250.
30. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. BMJ 2004; 328:1490.
31. Guyatt G, Vist G, Falck-Ytter Y, et al. An emerging consensus on grading recommendations? ACP J Club 2006; 144:A8.
32. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force. Chest 2006; 129:174.
33. Guyatt GH, Oxman AD, Schünemann HJ, et al. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol 2011; 64:380.
34. Guyatt GH, Helfand M, Kunz R. Comparing the USPSTF and GRADE approaches to recommendations. Ann Intern Med 2009; 151:363; author reply 363.
35. Jaeschke R, Guyatt GH, Dellinger P, et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. BMJ 2008; 337:a744.
36. US Preventive Services Task Force Grade Definitions https://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions (Accessed on May 08, 2018).
37. Shekelle PG. Updating practice guidelines. JAMA 2014; 311:2072.
38. Shekelle PG, Ortiz E, Rhodes S, et al. Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated? JAMA 2001; 286:1461.
39. Shojania KG, Sampson M, Ansari MT, et al. How quickly do systematic reviews go out of date? A survival analysis. Ann Intern Med 2007; 147:224.
40. National Guideline Clearinghouse (NGC) Inclusion Criteria https://www.ahrq.gov/gam/summaries/inclusion-criteria/index.html (Accessed on August 27, 2018).
41. Akl EA, Meerpohl JJ, Elliott J, et al. Living systematic reviews: 4. Living guideline recommendations. J Clin Epidemiol 2017; 91:47.
42. Qaseem A, Yost J, Etxeandia-Ikobaltzeta I, et al. What Is the Antibody Response and Role in Conferring Natural Immunity After SARS-CoV-2 Infection? Rapid, Living Practice Points From the American College of Physicians (Version 1). Ann Intern Med 2021; 174:828.
43. Qaseem A, Yost J, Etxeandia-Ikobaltzeta I, et al. Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid, Living Practice Points From the American College of Physicians (Version 2). Ann Intern Med 2021; 174:673.
44. Jones DJ, Barkun AN, Lu Y, et al. Conflicts of interest ethics: silencing expertise in the development of international clinical practice guidelines. Ann Intern Med 2012; 156:809.
45. Taylor R, Giles J. Cash interests taint drug advice. Nature 2005; 437:1070.
46. Okike K, Kocher MS, Wei EX, et al. Accuracy of conflict-of-interest disclosures reported by physicians. N Engl J Med 2009; 361:1466.
47. Choudhry NK, Stelfox HT, Detsky AS. Relationships between authors of clinical practice guidelines and the pharmaceutical industry. JAMA 2002; 287:612.
48. Campsall P, Colizza K, Straus S, Stelfox HT. Financial Relationships between Organizations That Produce Clinical Practice Guidelines and the Biomedical Industry: A Cross-Sectional Study. PLoS Med 2016; 13:e1002029.

49. Whitlock EP, Lin JS, Liles E, et al. Screening for colorectal cancer: a targeted, updated systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2008; 149:638.
50. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin 2008; 58:130.
51. Ferket BS, Spronk S, Colkesen EB, Hunink MG. Systematic review of guidelines on peripheral artery disease screening. Am J Med 2012; 125:198.
52. Czaja R, McFall SL, Warnecke RB, et al. Preferences of community physicians for cancer screening guidelines. Ann Intern Med 1994; 120:602.
53. Patel MR, Spertus JA, Brindis RG, et al. ACCF proposed method for evaluating the appropriateness of cardiovascular imaging. J Am Coll Cardiol 2005; 46:1606.
54. Lawson EH, Gibbons MM, Ingraham AM, et al. Appropriateness criteria to assess variations in surgical procedure use in the United States. Arch Surg 2011; 146:1433.
55. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ 2010; 182:E839.
56. Tunis SR, Hayward RS, Wilson MC, et al. Internists' attitudes about clinical practice guidelines. Ann Intern Med 1994; 120:956.
57. Parmley WW. Clinical practice guidelines. Does the cookbook have enough recipes? JAMA 1994; 272:1374.
58. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. BMJ 2012; 345:e6341.
59. Lugtenberg M, Burgers JS, Clancy C, et al. Current guidelines have limited applicability to patients with comorbid conditions: a systematic analysis of evidence-based guidelines. PLoS One 2011; 6:e25987.
60. Sackett DL, Rosenberg WM, Gray JA, et al. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312:71.
61. Farmer AP, Légaré F, Turcot L, et al. Printed educational materials: effects on professional practice and health care outcomes. Cochrane Database Syst Rev 2008; :CD004398.
62. Fonarow GC, Yancy CW, Hernandez AF, et al. Potential impact of optimal implementation of evidence-based heart failure therapies on mortality. Am Heart J 2011; 161:1024.
63. Lugtenberg M, Zegers-van Schaick JM, Westert GP, Burgers JS. Why don't physicians adhere to guideline recommendations in practice? An analysis of barriers among Dutch general practitioners. Implement Sci 2009; 4:54.
64. Burgers JS, Grol RP, Zaat JO, et al. Characteristics of effective clinical guidelines for general practice. Br J Gen Pract 2003; 53:15.
65. Grol R, Dalhuijsen J, Thomas S, et al. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. BMJ 1998; 317:858.
66. Barkun AN, Bhat M, Armstrong D, et al. Effectiveness of disseminating consensus management recommendations for ulcer bleeding: a cluster randomized trial. CMAJ 2013; 185:E156.
67. Grol R. Successes and failures in the implementation of evidence-based guidelines for clinical practice. Med Care 2001; 39:II46.
68. Grimshaw JM, Thomas RE, MacLennan G, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. Health Technol Assess 2004; 8:iii.
69. Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci 2009; 4:50.
70. Pronovost PJ. Enhancing physicians' use of clinical guidelines. JAMA 2013; 310:2501.
71. Institute of Medicine. Standards for Developing Trustworthy Clinical Practice Guidelines. http://iom.edu/Activities/Quality/ClinicPracGuide.aspx (Accessed on July 05, 2011).

Topic 2767 Version 46.0

GRAPHICS

Criteria for trustworthy clinical practice guidelines

Standard	Comments
1. Transparency	Guidelines should include an explicit description of process and funding.
2. Conflict of interest	Conflicts of interest for the guidelines development group should be managed by reporting, exclusion, and divestments.
3. Members of the guidelines development group	The group should be multidisciplinary and balanced.
4. Review of the literature	The guideline should be based on systematic reviews of the literature.
5. Rating strength of evidence and recommendations	Each recommendation should be accompanied by the underlying reasoning, potential benefits and harms, the evidence and its quality, the contribution of values and experience, rating of the level of confidence in the evidence and the strength of the recommendation, and differences of opinion regarding recommendations.
6. Presentation of recommendations	The guideline should state precisely the recommended actions, when they should be performed, and how they could be measured for evaluation of compliance.
7. External review	The guidelines should be reviewed by the full spectrum of relevant stakeholders. The general public should have an opportunity to review the guidelines before they are final.
8. Updating	Guidelines should state date of publication and evidence review and be updated when new, clinically-important evidence is available.

Based on data from the consensus report: Clinical Practice Guidelines We Can Trust. Institute of Medicine of The National Academies. Report available at: http://nationalacademies.org/hmd/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx.

Graphic 68090 Version 4.0

GRADE for practice guidelines

Grade of recommendation*	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A Strong recommendation High quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendation, can apply to most patients in most circumstances without reservation
1B Strong recommendation Moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation, likely to apply to most patients
1C Strong recommendation Low quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Relatively strong recommendation; might change when higher quality evidence becomes available
2A Weak recommendation High quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values
2B Weak recommendation Moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
2C Weak recommendation Low quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable

* GRADE can be implemented with either three or four levels of quality of evidence. UpToDate implements three levels and uses numbers and letters to represent strength of recommendation and quality of evidence respectively.