ADVANCES VIEWPOINT

blood advances

Distinguishing ASH clinical practice guidelines from other forms of ASH clinical advice

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The American Society of Hematology (ASH) develops a variety of resources that provide guidance to clinicians on the diagnosis and management of blood diseases. These resources include clinical practice guidelines (CPGs) and other forms of clinical advice. Although both ASH CPGs and other forms of clinical advice provide recommendations, they differ with respect to the methods underpinning their development, the principal type of recommendations they offer, their transparency and concordance with published evidence, and the time and resources required for their development. It is crucial that end users be aware of the differences between CPGs and other forms of clinical advice and that producers and publishers of these resources use clear and unambiguous terminology to facilitate their distinction. The objective of this article is to highlight the similarities and differences between ASH CPGs and other forms of ASH clinical advice and discuss the implications of these differences for end users.

Introduction

The American Society of Hematology (ASH) produces a wide range of resources that provide guidance to clinicians on the diagnosis and management of blood diseases. These resources include clinical practice guidelines (CPGs) and CPG-derived products (eg, pocket guides, patient versions of guidelines, and teaching slide sets) as well as other forms of clinical advice (eg, How I Treat articles, webinars, frequently asked questions [FAQs], ASH annual meeting education sessions, the ASH Self-Assessment Program, and the Hematology Review Series).

It may not be clear to all users how these resources differ, particularly with respect to the methods underpinning their development and the recommendations they provide. The purpose of this article is to highlight the similarities and differences between ASH CPGs and other forms of ASH clinical advice and discuss the implications of these differences for end users.

Submitted 21 December 2023; accepted 1 March 2024; prepublished online on *Blood Advances* First Edition 9 April 2024; final version published online 11 June 2024. https://doi.org/10.1182/bloodadvances.2023011102.

Methodology

Methods for the development of ASH CPGs adhere to international standards[1-3] and have been detailed elsewhere.[4,5] Key elements include panel formation with diverse stakeholder representation including patients, explicit and transparent conflict of interest (COI) management, identification and prioritization of patient, intervention, comparison, outcome questions, systematic reviews of the evidence, development of recommendations using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework,[6,7] public review and commentary, organizational review, and peer review. These attributes distinguish ASH CPGs as methodologically rigorous, transparent, and trustworthy, as defined by standards established by organizations including the National Academy of Medicine (formerly the Institute of Medicine).[2]

Other forms of ASH clinical advice may not incorporate some or all of these elements. For example, How I Treat articles, webinars, FAQs, ASH annual meeting education sessions, the ASH Self-Assessment Program, and the Hematology Review Series are usually based on personal opinion and informal rather than systematic reviews of the evidence; usually include 1 or only a small number of authors who are not necessarily representative of diverse stakeholder interests; usually do not develop recommendations through GRADE or another structured framework; and usually do not seek public feedback before publication or presentation. Although many other forms of ASH clinical advice include disclosure of COI, they may not formalize a mitigation strategy when COIs exist; for example, they may not limit participation or require recusal based on COI as ASH CPGs do.

Recommendations

The usable end products of both ASH CPGs and other forms of ASH clinical advice are recommendations. Recommendations are actionable statements intended to guide decision-making about alternative health care options in a specific patient population. Several different types of recommendations are recognized.[8] ASH CPGs and other forms of ASH clinical advice differ with respect to the types of recommendations they include.

The backbone of ASH CPGs are formal recommendations. Formal recommendations are actionable statements based on systematic reviews of the evidence that name an explicit intervention and comparison and a specific population. Such recommendations include a direction and strength; the former advises an action, whereas the latter is related to the balance of desirable and undesirable consequences and the quality of evidence that informs the recommendation.[8] In addition to formal recommendations, ASH CPGs may include remarks, good practice statements, research-only recommendations, and implementation considerations (defined in Lofti et al[8]).

In contrast to ASH CPGs, other forms of ASH clinical advice do not include formal recommendations. Instead, they consist mainly of informal recommendations. Similar to formal recommendations, informal recommendations are actionable and explicitly list a target population and intervention. They may or may not include a comparison, direction, or strength. Unlike formal recommendations, informal recommendations are not based on a systematic review of the evidence, and they do not include rating of the quality of the evidence.[8] Examples of formal and informal recommendations are shown in Table 1.

Table 1. Examples of formal and informal recommendations

Type of recommendation	Example
Formal recommendation	For patients with uncomplicated DVT, the (ASH) guideline panel suggests offering home treatment over hospital treatment (conditional recommendation based on low certainty in the evidence of effects).[9]
Informal recommendation	We suggest that most patients with DVT can be managed as outpatients.[10]

Formal recommendations are actionable statements based on systematic reviews of the evidence that list a specific patient population, intervention, and comparison and include a direction and strength as well as a rating of the quality of the evidence. In the example formal recommendation in the table, the patient population is patients with uncomplicated DVT, the intervention is home treatment, the comparison is hospital treatment, the direction of the recommendation is in favor of home treatment, the strength of the recommendation is conditional or weak, and the quality of the evidence is low. Informal recommendations are also actionable statements that list a specific patient population and intervention, but they may not include a comparison, direction, or strength, and they do not include rating of the quality of evidence nor are they based on a systematic review of the evidence. In the example informal recommendation, the patient population is patients with DVT, and the intervention is home or outpatient treatment. The comparison is not stated but is implied to be inpatient treatment. The direction of the recommendation is in favor of outpatient treatment, but the strength of the recommendation and quality of the evidence are not given.

DVT, deep vein thrombosis.

Advantages and disadvantages of ASH CPGs and other forms of ASH clinical advice

Use of rigorous and explicit methods serve to minimize bias and enhance the transparency of ASH CPGs. These methods result in recommendations that have a clear and predictable relationship to the best available supporting evidence. In contrast, informal recommendations are at risk of bias from selective use of evidence or from COI. For example, Yao et al[11] analyzed 81 CPGs from the American College of Cardiology/American Heart Association and the American Society of Clinical Oncology. Of the 908 recommendations based on low-quality evidence in these CPGs, 416 were formal recommendations based on systematic reviews of the evidence, and 492 were informal recommendations based on consensus. Recommendations were classified as discordant if they were strong recommendations with low-quality evidence and inappropriately discordant if they did not satisfy GRADE criteria for issuing a strong recommendation based on low-quality evidence. Informal consensus-based recommendations were more likely than formal evidence-based recommendations to be discordant (odds ratio, 1.9; 95% confidence interval, 1.4-2.7) and inappropriately discordant (odds ratio, 2.5; 95% confidence interval, 1.7-3.5).[11]

A major disadvantage of ASH CPGs is that they tend to be more time consuming to develop than other forms of ASH clinical advice. This vulnerability was particularly relevant early in the COVID-19 medical emergency, a time when there was an urgent need for clinical guidance. Despite the adoption of a rapid approach to guideline development, the first ASH CPG on COVID-19 and anticoagulation was not completed until December 2020 and was not published until February 2021,[12] some 9 to 11 months after COVID-19 was declared a pandemic by the World Health Organization. At the same time, ASH was able to stand up less rigorous forms of clinical advice such as online FAQs[13] within a matter of weeks. Although the development of CPGs may never be as rapid as some other forms of clinical advice, efforts are needed to further streamline CPG development without compromising methodologic rigor, transparency, or trustworthiness, particularly during medical emergencies.

Table 2. Comparison of ASH CPGs and other forms of ASH clinical advice

	Diverse stakeholder representation including patients	COI management	Identification and prioritization of PICO questions	Systematic reviews of the evidence	Development of recommendations using GRADE or another structured framework	Public review and commentary	Peer review	Main type of recommendation	Transparency and concordance with best available evidence	Time to develop	Cost to develop
ASH CPGs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Formal	High	Mo to y	High
Other forms of ASH clinical advice*	Usually not	Varies	Usually not	Usually not	Usually not	Usually not	Varies	Informal	Lower	Wk to mo	Low to moderate

PICO, patient, intervention, comparison, outcome.
*Includes but not limited to How I Treat articles, webinars, FAQs, ASH annual meeting education sessions, the ASH Self-Assessment Program, and the Hematology Review Series.

CPGs are also more expensive than other forms of clinical advice, often substantially so. Guideline development costs include administrative staff support, travel and meetings, and systematic evidence reviews. Although most organizations including ASH do not publicize their guideline development costs, systematic evidence reviews alone often cost in excess of $100 000.[14] Technological advances, including virtual meeting platforms and systematic reviews supported by machine learning and artificial intelligence, offer the potential to reduce labor and costs associated with CPG development.

A third disadvantage of CPGs is that they tend to be lengthy and complex.[15] In addition, they often consist of isolated recommendations that are not linked together via pathways or decision trees. Other forms of clinical advice may be more concise and better equipped to articulate a comprehensive diagnostic or management strategy to meet the needs of clinicians.[16] ASH produces CPG-derived products (eg, pocket guides, patient versions of guidelines, and teaching slide sets) to facilitate the implementation of its guidelines and is exploring the incorporation of decision trees in future CPG efforts.[17]

Terminology

In light of the substantial differences between CPGs and other forms of clinical advice, it is crucial that developers and publishers use clear language and labels to disambiguate these different types of guidance. For example, all ASH CPGs include "ASH guidelines" in the title and are grouped within the *Blood Advances* website under a CPG article type.

The label "guidelines" should not be used to describe other forms of clinical advice. Terms that hint at or could easily be confused with CPGs such as "guidance" or "consensus" should also ideally be avoided. Some organizations distinguish "evidence-based" guidelines from "expert-based" or "consensus-based" guidelines. ASH has avoided this nomenclature because it is misguided and misleading. All CPGs should be based on a systematic review of the evidence, even if the evidence is low quality, and all guidelines require expert opinion and consensus building to appraise and interpret such evidence.[18]

Currently, *Blood Advances* requires that CPG submissions be consistent with the criteria laid out by the Institute of Medicine.[2] *Blood* does not list specifications or formal criteria for CPG submissions. Neither journal imposes restrictions on the use of terms such as "guidance" and "consensus." We recommend that ASH consider standardizing nomenclature across its publication portfolio with the goal of clearly distinguishing CPGs from other forms of clinical advice.

Conclusion

ASH CPGs and other forms of ASH clinical advice both provide recommendations for the diagnosis and management of blood diseases but differ with respect to methodology, the primary type of recommendations they provide, their transparency and concordance with the best available evidence, and the time and resources they require (Table 2). It is important for clinicians and other users to distinguish CPGs from other forms of clinical advice and be aware of the differences between these tools when they are applied in clinical practice. Developers and publishers of these products, including ASH, have a responsibility to use clear and unambiguous labels to facilitate this distinction for end users.

Authorship

Contribution: A.C. and M.C.C. wrote the manuscript; and all other authors critically reviewed and revised the manuscript.

Conflict-of-interest disclosure: A.C. has served as a consultant for MingSight, New York Blood Center, Sanofi, and Synergy, and has received authorship royalties from UpToDate. R.K. is an employee of the American Society of Hematology. D.R.T. has served as a consultant for Sanofi. All authors except R.K. are members of the ASH Guideline Oversight Subcommittee. The remaining authors declare no competing financial interests.

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