

The value of clinical practice guidelines in hematology

This issue of *Blood Advances* marks the much-anticipated publication of the first in a series of clinical practice guidelines led by the American Society of Hematology (ASH), in collaboration with McMaster University, addressing critical issues in the care of patients with venous thromboembolism (VTE). Clinical practice guidelines are defined by the Institute of Medicine (IOM) as “recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and assessment of the benefits and harms of alternative care options.”^{1(p4)} Clinical practice guidelines are valuable, not only to clinicians at the bedside, but also to patients, families, payors, and policy makers.

ASH recognizes the complex, changing landscape of hematology practice worldwide, and the need for members to make informed decisions so that they can continue to deliver the highest quality care. With this in mind, several years ago, ASH committed to developing rigorous evidence-based guidelines for its members. Subsequently, ASH formed a Guideline Oversight Subcommittee, which reports to the ASH Committee on Quality. The Guideline Oversight Committee has developed standard operating procedures to address every step in the guideline development process, from handling conflicts of interest, to vetting potential new guideline topic areas in hematology.

The VTE Clinical Practice Guidelines mark the first guidelines completed using ASH's rigorous new infrastructure. Several other guidelines relevant to ASH members are currently in various phases of development, including guidelines focused on sickle cell disease, immune thrombocytopenia, acute myeloid leukemia in older adults, and von Willebrand disease.

Creating trustworthy guidelines with practical recommendations

In its 2011 publication, *Clinical Practice Guidelines We Can Trust*, the IOM laid out a number of standards for guideline developers and users.¹ These include ensuring that guideline panels have representation from methodologists, clinicians, and patients; ensuring that only a minority of panel members have material conflicts of interest; basing recommendations on a rigorous systematic review of the evidence; and many others. The IOM standards set high expectations for what constitutes trustworthy clinical practice guidelines. Meeting these standards undoubtedly benefits guideline users and, ultimately, patients.

The ASH VTE guideline panels used the Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach to rate the quality of evidence from systematic reviews transparently and to evaluate the strength of the guidelines' recommendations.² *Blood Advances* readers will find that these guidelines offer clear recommendations on the care of patients with VTE. In many areas, the evidence supporting the recommendations is plentiful and high quality, and it is clear that the benefits of the management strategies outweigh their undesirable effects. In these cases, the panels have made *strong* recommendations, suggesting that most patients should receive and would want the recommended course of action. Where evidence is less plentiful and of lower quality, and the risks and benefits are less clearly weighted, panels have made *conditional* recommendations. Conditional recommendations are still useful. They imply that a majority of patients would want the recommended course of action, though some would not. Clinicians should be more prepared to help patients make a decision that is consistent with their own values and preferences; researchers should consider the evidence base and aim to extend it with additional study and debate.

In addition to collecting and evaluating evidence transparently, and making clear recommendations, the ASH VTE guidelines are aligned with IOM recommendations on management of the conflicts of interest of the funder and of the guideline panel. No direct industry support for the development of these guidelines was accepted. Disclosure forms, included as supplements with the guidelines, describe all declared financial and nonfinancial interests of the guideline panelists as well as the researchers on the systematic review team, ASH judgments about which interests posed potential conflicts, and the management strategy for all conflicts. Also in alignment with the IOM standards, every guideline panel included 1 or 2 patient representatives. Although best practices around how to include patients in guideline development are still being explored, the inclusion of patients on the ASH panels represents

a significant advancement: a commitment to having the patient voice resonate throughout the guideline-development process. The end results are guidelines that are patient centered, transparent, and evidence based.

Maintaining clinical practice guidelines

After guidelines are developed, a critical component of the process is maintaining them. As new evidence is published, guideline recommendations can become outdated. Maintenance of guidelines can take many different forms and 3 main factors need to be considered: (1) when should the guidelines be updated; (2) what aspects of the guidelines should be updated; and (3) how should the guidelines be updated. The Guideline Oversight Subcommittee is currently working to determine the best process to keep ASH guidelines current, and acknowledges that a mix of strategies may be involved. For example, the “living guideline” strategy is based on a regularly updated systematic review that locates and incorporates new evidence.³ The living systematic review then directly informs the guideline, and recommendations are changed if new or different quality evidence is identified.

Supporting a living guideline process requires a significant commitment, including a team to locate new evidence and update the systematic review, a team to incorporate new evidence into the guideline, and a platform to disseminate updated recommendations (and link them to the original publication). Having a dynamic, online, open-access journal like *Blood Advances* facilitates living guidelines, and ensures that clinicians always have access to updated information.

Guideline dissemination and implementation

Once guidelines get published, promoting their dissemination and implementation is essential. Not surprisingly, bringing a clinical practice recommendation into broad, consistent use can take years. Multiple barriers to guideline implementation exist, including hesitancy to change routine, difficulty navigating recommendations, concern that guidelines promote “cookbook medicine,” and difficulty accessing guidelines at the point of care.⁴ To break down these barriers, ASH has already begun developing resources that will promote guideline uptake, including mobile apps and pocket guides to make guidelines readily accessible as well as decision aids to help clinicians tailor recommendations to unique patient situations and view guidelines in a user-friendly format. *Blood Advances*, which has led the charge in offering online multimedia resources to enhance its content, is able to link these resources to ASH's published guidelines.

The launch of the ASH-sponsored VTE guidelines in *Blood Advances* marks an exciting milestone for ASH. The Society's

rigorous, trustworthy clinical practice guidelines are expected to be an important high-quality resource for the hematology community. We thank the ASH Executive Committee for their commitment to this process, and the members of the VTE guideline panels for the time and care they have invested in this work.

Julie A. Panepinto
Associate Editor, Blood Advances

Menaka Pai
Appointed Member, ASH Publications Committee

Acknowledgment

Robert Kunkle (Deputy Director, Quality Improvement Programs, ASH) read the commentary for accuracy on the guideline process.

Authorship

Contribution: J.A.P. wrote the first draft of the commentary; M.P. revised and critiqued each subsequent draft of the article.

Conflict-of-interest disclosure: J.A.P. serves as the Chair of the ASH Guideline Oversight Committee, and has received research funding from the National Institutes of Health and Health Resources and Services Administration. M.P. serves as the Associate Chair of the ASH Guideline Oversight Committee and has received research support from the International Society on Thrombosis and Haemostasis, and speakers' honoraria from Bayer and Novartis (both <\$2000).

Correspondence: Julie A. Panepinto, 8701 Watertown Plank Rd, Milwaukee, WI 53226; e-mail: jpanepin@mcw.edu.

References

1. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. *Clinical Practice Guidelines We Can Trust*. Graham R, Mancher M, Wolman DM, et al, eds. Washington, DC: National Academies Press; 2011.
2. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction- GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383-394.
3. Akl EA, Meerpohl JJ, Elliott J, Kahale LA, Schünemann HJ; Living Systematic Review Network. Living systematic reviews: 4. Living guideline recommendations. *J Clin Epidemiol*. 2017;91:47-53.
4. Vander Schaaf EB, Seashore CJ, Randolph GD. Translating clinical guidelines into practice: challenges and opportunities in a dynamic health care environment. *N C Med J*. 2015;76(4):230-234.