COMMENTARY

blood advances

TO THE EDITOR:

ASH Clinical Practice Guidelines: strategies to stay up-to-date

Matthew C. Cheung,[1] Rob Kunkle,[2] Rob Plovnick,[2] Richard Lottenberg,[3] Suely M. Rezende,[4] Roy Silverstein,[5] Menaka Pai,[6] Matthew Seftel,[7] and Adam Cuker[8]

[1]Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada; [2]American Society of Hematology, Washington, DC; [3]Division of Hematology and Oncology, University of Florida, Gainesville, FL; [4]Department of Internal Medicine, Faculty of Medicine, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; [5]Medical College of Wisconsin and Versiti Blood Research Institute, Milwaukee, WI; [6]Department of Medicine, McMaster University, Hamilton, ON, Canada; [7]University of British Columbia and Canadian Blood Services, Vancouver, BC, Canada; and [8]Hematology, University of Pennsylvania, Philadelphia, PA

To remain trustworthy and relevant, clinical practice guidelines (CPGs) should be informed by recent systematic reviews of evidence and should reflect current clinicians' experiences and patients' values.[1] In 2015, the American Society of Hematology (ASH) began developing CPGs using formal methods.[2] In recent years, review and revision of the initial guidelines developed using these methods have become an ASH organizational priority. Two recent strategic approaches to monitor and revise ASH CPGs have now been piloted: (1) a living guideline approach and (2) an annual monitoring strategy.

The first approach, a living guideline approach, was used for the ASH Guidelines on use of anticoagulation in patients with COVID-19. Over several years during the pandemic, a research team continually and systematically searched for new evidence and then updated estimates of baseline risks of thrombosis and effects of anticoagulation. When prespecified criteria were met (ie, estimates met prespecified thresholds for change in direction or magnitude), the guideline panel revisited recommendations.[3] This living guideline approach addressed an unprecedented clinical need for timely recommendations about COVID-19–related thrombosis, as well as the challenge of synthesizing a rapidly changing, voluminous, and difficult-to-interpret body of evidence. However, the living approach was resource intensive, requiring both extensive time commitments from volunteers and ASH staff at significant cost, and is unlikely to be warranted or feasible for most ASH guidelines.

The second strategy, informed by a review of approaches by other international guideline developers[4] and piloted in 2021, enlists a small working group of experts and a librarian to review new evidence and decide when a revision is required (Figure 1). The librarian initially refreshes the original literature search, limited to new systematic reviews and randomized controlled trials (RCTs). Literature searches are also conducted to find studies of relevant new interventions. The expert working group, composed of members of the original guideline panel, subsequently reviews the search results and advises the ASH Committee on Quality on whether the guidelines should be revised, retired, or continue to be monitored. For all guidelines, the monitoring process begins 2 years after the initial publication and is repeated annually until there is a decision to revise or retire. Revisions may be broad or focused and urgent or not. Retirement would be warranted when a guideline is no longer valid or clinically relevant.

To date, ASH has completed this monitoring pilot process for 9 of its guidelines. Guideline panelists have been generous in volunteering their time and skills for this process and providing constructive feedback to improve the process. For example, early in the piloting of this approach, the ASH Guideline Oversight Subcommittee (GOS) attempted to define triggers or thresholds for ASH decisions to revise guidelines. Initially, the subcommittee informed guideline panels that a revision would generally be warranted if there were new RCTs relevant to at least half of a guideline's existing recommendations, including RCTs of new interventions compared with recommended ones. This guidance was later abandoned because it proved overly simple and potentially restrictive. Currently, guideline expert panels are asked to advise for or against revision based on the importance of new evidence and the potential

Submitted 19 August 2023; accepted 10 September 2023; prepublished online on *Blood Advances* First Edition 22 September 2023; final version published online 2 November 2023. https://doi.org/10.1182/bloodadvances.2023011481.

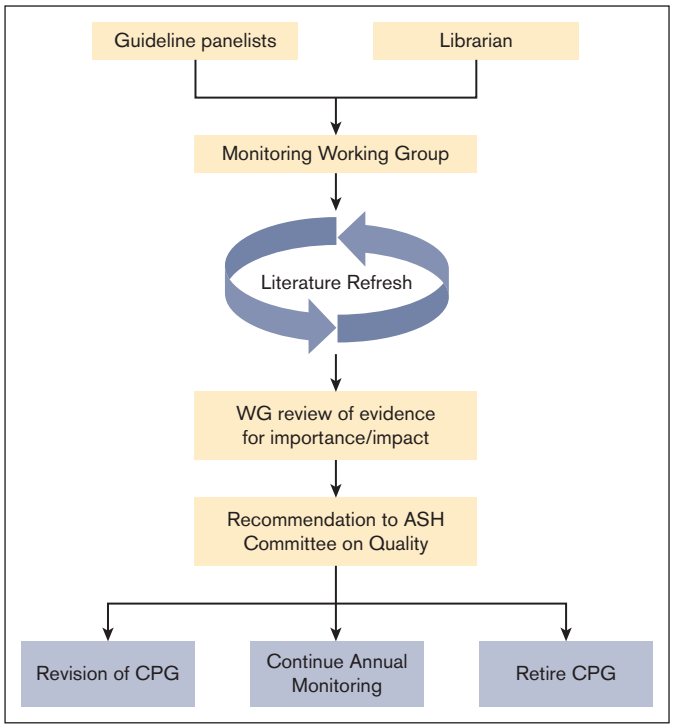

Figure 1. The current strategy to monitor and revise ASH CPGs. A monitoring working group (composed of guideline panelists and a librarian) will initiate the monitoring process 2 years after the initial CPG and annually thereafter. Based on the literature review of new evidence, the working group will decide on the importance and impact on the existing recommendations and make 1 of 3 recommendations to the ASH Committee on Quality: (1) revise the CPG, (2) continue to monitor annually, or (3) retire the CPG. CPG, clinical practice guideline; WG, working group.

impact of revisions, even if it relates to just 1 recommendation. When deciding whether a revision is needed, the Committee on Quality also takes into consideration available ASH resources to support a revision effort, current ASH priorities, and possible alternative projects.

During piloting, expert volunteers also noted that the focused literature search strategy was not comprehensive enough for topics in which the evidence base consists of few or no RCTs (eg, ASH 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia).[5] In contrast, a tremendous volume of new studies was found for other topics, with only a handful being relevant (eg, ASH 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients).[6] Thus, the literature search lacked sensitivity or specificity depending on the topic, illustrating the need for earlier expert involvement to contextualize and customize the search.

Advances in literature screening and systematic searches, including the use of machine learning algorithms and pragmatic literature searches,[7,8] respectively, are areas currently being explored by ASH. Future guidelines may be restructured into discrete sections, each capturing a specific area of knowledge (and generally encompassing a number of questions). It may be feasible to update individual sections as required by the evidence, without needing to update an entire guideline document. A forthcoming revision of the ASH 2019 guidelines for immune thrombocytopenia may serve as a pilot of this approach.[9] Based on new evidence identified during the literature search as well as clinical prioritization, the immune thrombocytopenia expert panel suggested a focused update of questions related to second-line therapy (allowing for multiple comparison among second-line options) while recommending continued monitoring of other topics within the guideline. A redeveloped cloud-based guideline architecture is another advance that would allow any update of the core guideline document to immediately update all associated derivative products, including teaching slides, point-of-care technologies (apps), patient-facing education documents, and decision support in electronic medical records.

The monitoring and updating process of ASH guidelines will continue to evolve as the evidence and available technologies allow; the commitment to provide valid and trustworthy recommendations will remain the guiding principle. Finally, to be transparent, ASH will convey these deliberations and the monitoring outcomes to the guideline audience broadly through notices within the published guidelines and commentaries submitted to *Blood Advances*.

Contribution: M.C.C., R.K., and A.C. designed the commentary and wrote the manuscript; and R.P., R.L., S.M.R., R.S., M.P., and M.S. wrote the manuscript.

Conflict-of-interest disclosure: The authors declare no competing financial interests.

ORCID profiles: S.M.R., 0000-0002-3083-7093; M.P., 0000-0002-6053-689X; A.C., 0000-0002-3595-5697.

Correspondence: Matthew C. Cheung, Sunnybrook Health Sciences Centre, University of Toronto, Odette Cancer Centre, Toronto, ON M4N3M5, Canada; email: matthew.cheung@sunnybrook.ca.

References

1. Institute of Medicine Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Clinical Practice Guidelines We Can Trust. National Academies Press (US); 2011.
2. Wiercioch W, Nieuwlaat R, Akl EA, et al. Methodology for the American Society of Hematology VTE guidelines: current best practice, innovations, and experiences. *Blood Adv*. 2020;4(10):2351-2365.
3. Cuker A, Tseng EK, Schunemann HJ, et al. American Society of Hematology living guidelines on the use of anticoagulation for thromboprophylaxis for patients with COVID-19: March 2022 update on the use of anticoagulation in critically ill patients. *Blood Adv*. 2022;6(17):4975-4982.
4. Vernooij RW, Sanabria AJ, Sola I, Alonso-Coello P, Martinez Garcia L. Guidance for updating clinical practice guidelines: a systematic review of methodological handbooks. *Implement Sci*. 2014;9:3.
5. Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Adv*. 2018;2(22):3360-3392.

6. Schunemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Adv*. 2018;2(22):3198-3225.

7. Martinez Garcia L, Sanabria AJ, Araya I, et al. Efficiency of pragmatic search strategies to update clinical guidelines recommendations. *BMC Med Res Methodol*. 2015;15:57.

8. van de Schoot R, de Bruin J, Schram R, et al. An open source machine learning framework for efficient and transparent systematic reviews. *Nat Mach Intell*. 2021;3(2):125-133.

9. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.