Evidence-based guidelines support integrated disease management as the optimal model of hemophilia care

S. W. Pipe[1] and C. M. Kessler[2]

1 Departments of Pediatrics and Pathology, University of Michigan, Ann Arbor, MI USA

2 Lombardi Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC, USA

The series of papers in this supplement of *Haemophilia* provide important evidence supporting the use of an integrated disease management model to deliver care to persons with hemophilia. The lead manuscript by Pai and co-authors reports the "National Hemophilia Foundation (NHF)-McMaster Guideline on Care Models for Haemophilia Management"[1]. Using direct evidence from published literature and the hemophilia community, as well as indirect evidence from other chronic diseases, the Guideline Panel has created evidence-based recommendations. The Guideline methodology utilized the suggested principles for developing transparent, evidence-based guidelines promoted by the Institute of Medicine, the National Guideline Clearinghouse, and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.

The conclusion that this systemic evidence review supports is that the integrated care model, as is utilized within the US federally funded network of Hemophilia Treatment Centers (HTCs), should be advocated for optimal care of persons with hemophilia. These guidelines will provide a catalyst to promote harmonization of care delivery and reduce practice variations within the US HTC network. This Guideline will inform the HTC network how best to prioritize additional "high-value" research to fill data gaps or strengthen the evidence base as outlined in the manuscript. The network is now prepared to support agreed upon evidence-based performance benchmarks that would allow for both internal and external evaluation of adherence to best practices and to benchmark available services within an HTC, potentially leading to the establishment of a US HTC self-audit or accreditation system as has been developed in other

countries. These guidelines will provide the ideal starting point for defining the best practices in an evidence-based manner and build a foundation for the development of key metrics that can be tracked within the network, supporting research studies, advocacy at state and federal levels, and highlighting the benefits of the implementation of those best practices by the HTC integrated care models[2].

To provide a historical perspective, NHF established the Medical and Scientific Advisory Council (MASAC) in 1954 to bring together physician experts in the field of coagulation to advance care for patients with hemophilia and develop recommendations for their treatment. The vision was to connect physicians and researchers to discuss challenges in care and research for this rare but severe bleeding disorder. MASAC has served a crucial role in disseminating information, serving as an intermediary between scientific and medical organizations and patients, the end-users of blood products. Recommendations from MASAC have detailed advances in therapy and communicated how to use them effectively, fostering communication to the broader clinical community and accelerating progress for patients. Its membership now includes not only physicians, scientists and patients from the bleeding disorder community, but also representatives from the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), the Health Resources and Services Administration/Maternal and Child Health Bureau (HRSA/MCHB), World Federation of Hemophilia (WFH) and the American Thrombosis and Hemostasis Network (ATHN).

In 2012, at the urging of the NHF MASAC Chair, NHF held a strategic summit to develop a plan for hemophilia care within the changing US healthcare landscape largely due to the changes occurring following the enactment of the Affordable Care Act, the major health care reform legislation[3]. The major tenets of the healthcare reform include: health insurance coverage not tied to employment, portability of that coverage with minimal exclusions, affordability, choice, quality, prevention and sustainability – all of these being highly relevant for how hemophilia care is provided within the US. To address the challenges of the shifting healthcare landscape, the Summit identified the need to strengthen the evidence-base for hemophilia care and promotion of the integrated care model. It was determined that generating and maintaining evidence-based guidelines would require a complete comprehensive assessment of existing

guidelines and resolutions, identifying gaps and prioritizing the standards that would need updating, and implementing a systematic process for updating and dissemination.

Following a scoping process by a Working Group of the current and former MASAC leaders and others, nine priority guideline topics were identified. The phase 1 priority as determined by the findings of the Summit and the Scoping Working Group would focus on models of hemophilia care with future guidelines following the framework established by this first guideline with a focus on more specific aspects of care and patient populations. This guideline is a foundational one upon which more specific guidelines addressing other aspects of care may be developed and will inform future areas of needed research.

The focus on models of hemophilia care is timely. Since 1974, Congress authorized and has funded hemophilia programs within the HRSA/MCHB and in the 1980's and 90's CDC surveillance and blood safety programs were established. These programs recognized that individuals with bleeding disorders had difficulty obtaining quality care due to the rarity and complexity of their disease. This funding led to the development of centers of excellence, designated as hemophilia treatment centers, which focused on the provision of individualized treatment plans, preventative care and education. They espoused the common goal of maximizing coordination, effectiveness, and efficiency in care delivery. The core HTC team has traditionally included a hematologist, specialized hemophilia nurse, physical therapist, and social worker. This guideline also identifies access to a specialized coagulation laboratory to be a critical element to support the integrated care team. However, beyond this core group, other care providers (e.g., dental professionals, genetic counselors, orthopedists, infectious disease specialists, etc.) are either available on-site or via established partnerships. Additional clinical practice guidelines would accomplish many important goals:

- specify the coordinated set of diagnostic, therapeutic, and certain auxiliary and supplemental services that are most important for haemophilia patients across the U.S.
- identify the range of clinical and non-clinical members of a haemophilia comprehensive care team
- identify best-practices and evidence-based standards of comprehensive/coordinated

care for haemophilia treatment centers (HTCs) and individual clinical practices.

The effectiveness of the HTC model has been well documented through studies conducted by both HRSA/MCHB and the CDC. From a 1985 analysis, HRSA/MCHB reported the outcome data from 31 centers through the first 10 years of the HTC network, demonstrating that the network increased the number of patients with hemophilia regularly receiving comprehensive care by 326%, while the number of patients with the ability to treat at home increased by 390% with a 73% reduction in missed school/work days during the same period[4]. Subsequently, the Hemophilia Surveillance Study was reported by the CDC in 1995, utilizing data sources from the HTCs, the CDC, and state health departments in 6 states that identified all patients within these states with hemophilia, including those treated outside of an HTC[5]. The study documented a 40% decrease in mortality among patients treated at HTCs, which was particularly notable given that HTCs provided care to a higher proportion of severely affected patients and patients with complications including inhibitors, liver disease, and HIV/AIDS as compared to hemophilia patients managed in non-HTC settings. Among the 2,950 patients followed over 3 years, the relative mortality rate increased by 70% and the relative hospitalization rate increased by 40% for patients who received care outside of the HTC network. Despite the impressive outcome results, these studies are now 20-30 years old, and there exists wide variation in the characteristics and capabilities of current HTCs in terms of funding, geography covered, affiliation (e.g., hospital/university, standalone, etc.), available provider specialties, and patient populations served. Within the shifting US healthcare landscape, all stakeholders are looking for evidence that the integrated care models that are in place within the HTCs are responding to the major tenets of healthcare reform and continuing to deliver with respect to the quality of care for hemophilia and other bleeding disorders. This guideline confirms and updates this prior research.

However, the guideline takes note of the paucity of data addressing some important patient outcomes and highlights the importance of unified data systems in US HTCs to facilitate research. The reality of the current healthcare environment requires the presence of a process to evaluate the successes and shortcomings of various models of care delivery and their impact on patient important outcomes. The HTC infrastructure provides a unique model to track, in a

longitudinal manner, the safety of new emerging therapies, as well as contribute valuable evidence to the development of cost-effective treatment paradigms that could serve as a role model for other chronic disease. HTCs must build further capacity to collect and analyze data as well, to power higher quality, comprehensive studies.

We commend the work of the NHF and investigators at McMaster University in developing this important guideline and extend our thanks to the guideline panel members for their efforts over the past two years. We believe the guideline is an important addition to the evidence base of hemophilia care and management. MASAC and NHF are prepared to continue our efforts to improve the evidence base. We are pleased to report the NHF-McMaster Guidelines on Models of Care for Hemophilia have been endorsed by the American Society of Hematology, the International Society for Thrombosis and Haemostasis, the World Federation of Hemophilia. We encourage others to collaborate and take advantage of this unique new resource for our community.

Disclosures: SWP is the current chair of the NHF Medical and Scientific Advisory Council (MSASC). CMK served as MASAC chair from 2008 to 2015. The authors stated that they had no interests which might be perceived as posing a conflict or bias.

References:

1. Pai et al., *to be added by publisher*

2. Skinner MW, Soucie JM, McLaughlin K. The National Haemophilia Program Standards, Evaluation and Oversight Systems in the United States of America. *Blood Transfus* 2014; **12** (Suppl 3): s542-8.

3.National Hemophilia Foundation: Strategic Summit Report. Retrieved from https://www.hemophilia.org/sites/default/files/article/documents/HemophiliaSummitFinalReportOct2012.pdf

4. Baker JR, Riske B, Drake JH, Forsberg AD, Atwood R, Voutsis M, and Shearer R. US Hemophilia Treatment Center population trends 1990-2010: patient diagnoses, demographics, health

services utilization. *Haemophilia* 2012; **19**:21-26.

5. Soucie JM, Nuss R, Evatt B, Abdelhak A, Cowan L, Hill H, et al. Mortality among males with hemophilia: relations with source of medical care. The Hemophilia Surveillance System Project Investigators. *Blood* 2000; **96**: 437–42.