This guideline was developed to identify evidence-based best practices in haemophilia care delivery, and discuss the range of care providers and services that are most important to optimize outcomes for persons with haemophilia (PWH) across the United States. The guideline was developed following specific methods described in detail in this supplement and based on the GRADE (Grading of Recommendations, Assessment, Development and Evaluation approach). Direct evidence from published literature and the haemophilia community, as well as indirect evidence from other chronic diseases, were reviewed, synthesized and applied to create evidence-based recommendations. The Guideline panel suggests that the integrated care model be used over non-integrated care models for PWH (conditional recommendation, moderate certainty in the evidence). For PWH with inhibitors and those at high risk for inhibitor development, the same recommendation was graded as strong, with moderate certainty in the evidence. The panel suggests that a haematologist, a specialized haemophilia nurse, a physical therapist, a social worker and round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, over an integrated care team that does not include all of these components (conditional recommendation, very low certainty in the evidence). Based on available evidence, the integrated model of care in its current structure, is suggested for optimal care of PWH. There is a need for further appropriately designed studies that address unanswered questions about specific outcomes and the optimal structure of the integrated care delivery model in haemophilia.

Keywords: care model, delivery of health care, guideline, haemophilia, health care team, integrated care
The goal of these CPGs is to support patient-centred clinical decision-making and optimize haemophilia care for each patient.

For its first guideline, NHF has chosen the topic of Care Models for Haemophilia Management, and has partnered with McMaster University to provide expertise and support (Core Methods Group: MP, NS, CHTY, AI, and HJS) in CPG development. A number of guidance documents, including the 2013 World Federation of Haemophilia Guidelines for the Management of Haemophilia, the 2008 European Principles of Haemophilia Care, and a 1995 statement from the Association of Haemophilia Clinic Directors of Canada, have advocated for comprehensive care as the optimal model of care in individuals with haemophilia [2–4]. However, the effects of integrated care on patient-important outcomes in this complex disease have not been systematically synthesized and compared to alternative models, and questions about the ideal composition of services and providers for optimal haemophilia care remain unanswered.

**Care models for haemophilia management in the United States**

There are a variety of models used to deliver care to persons with haemophilia (PWH) in the US, three of which appear to operate currently [5]:

1. The integrated care model, also known as the ‘Comprehensive Care’ model or the ‘Hemophilia Treatment Center (HTC)’ model. This term refers to the continuous supervision of all medical and psychosocial aspects affecting the haemophilia patient and family, including supervision of home-based treatment (either prophylaxis or on-demand) [5–7]. It generally demands that all modalities of care – access to care providers, as well as diagnostic and therapeutic facilities – are available and delivered in a single specialized centre, by a team of health care providers. The composition of the integrated care team varies, but generally adheres to key components recommended by the World Federation of Haemophilia, including a medical director, a nurse coordinator, a physical therapist, a psychosocial expert (e.g. social worker) and a specialized coagulation laboratory [2]. Some integrated care centres also participate in outreach clinics or telehealth programmes. HTCs in the US that deliver integrated care are organized into regional and national networks that set standards of care, organize professional education and training, and engage in data collection and analysis [8].

2. The specialist based care model, where a haematologist (who may or may not have specific training in the management of haemophilia) provides care in a non-specialized centre, such as a hospital or medical office.

3. Care delivered by a non-specialist in a non-specialist setting. This may take the form of a family physician delivering care in private practice, or an emergency room (ER) physician delivering care in an ER setting.

Often operating in conjunction with one of the models listed above, and thus constituting a component of the care model rather than an alternative model, is pharmacy-based care. Private specialty pharmacies (typically, national or regional for-profit corporations) or HTC-affiliated pharmacies provide factor concentrates and ancillary services related to the provision of treatments directly to patients in their homes, as per a physician’s medical prescription.

We believe that the ‘No Care’ model, theoretically indicating complete absence of care, does not currently operate in the US. Yet, this is likely the de facto model of care for many individuals with haemophilia who do not have access to care due to profound resource constraints, particularly in developing countries or underserved minorities [9,10].

Different models of care delivery have different implications for reimbursement and funding [11,12]. They may be more or less feasible to implement in a given setting, depending on local health care resources, culture, and patient values and preferences. These different models may have a differential impact on health outcomes in haemophilia [13–15].

**Purpose of this guideline**

The purpose of this guideline is to identify best practices in haemophilia care delivery, and discuss the range of care providers and services that are most important for PWH across the US.

This guideline was developed foremost for persons living with haemophilia, and for providers of haemophilia care. In addition, the guideline is meant to be a resource for hospitals and health care systems, Federal and State programmes and policy makers, private and public insurers, and other professionals in the health sector who are responsible for developing and implementing strategies to care for individuals with haemophilia and other bleeding disorders at the national, regional and state levels.

**Methods**

The methods used to develop these guidelines adhered to suggested principles for developing transparent, evidence-based guidelines promoted by the Institute of Medicine, the National Guideline Clearinghouse and the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) Working Group [16–20]. A brief summary of the methods
followed and further details are provided in a companion methods paper [21].

**Guideline panel composition**

The Guideline panel was composed of US and non-US health care providers (including physicians, nurses, physical therapists, and a genetic counsellor) with expertise in haemophilia care, individuals with experience in health policy, health care financing, and research related to haemophilia, PWH, parents of PWH, persons with other rare diseases, and methodologists. (See section on Guideline panel.)

**Guideline timeline and process**

Two Guideline panel meetings were held, with support from and direct involvement of the Core Methods Group: June 2014 in Milwaukee, WI and May 2015 in Chicago, IL. The goals of the first face-to-face panel meeting were to educate panel members on the guideline development methods, and finalize and manage declarations of conflicts of interest (COI). A draft set of questions and outcomes was also generated, started by discussing the results of large surveys of patient and provider groups previously administered by the Core Methods Group to identify potentially relevant questions and outcomes. Between the two meetings, the Guideline panel was engaged to perform a number of tasks, including: prioritizing the questions and outcomes of relevance; reviewing the evidence profiles (EP) and draft evidence to decision (EtD) tables generated by the Core Methods Group; providing structured experiential data for areas of scarce evidence; and judging the indirectness of evidence from diseases other than haemophilia. The goals of the second face-to-face panel meeting were to review, appraise, modify as needed and approve the versions of the EP prepared by the Core Methods Group by summarizing the body of evidence, panelist comments and providing explicit consideration of the quality of evidence; and to review, integrated and approve the EtD (inclusive of benefits and harms, patients’ values and preferences, acceptability, feasibility, equity and resource use) prepared by the Core Methods Group, and finally, formulating the guideline’s recommendations.

The panel graded recommendations as ‘strong’ or ‘weak’ for or against a specific intervention, as recommended by the GRADE working group [22,23]. The implications of strong recommendation for policy makers is that it can be adapted as a policy in most situations. For clinicians, most patients should receive the recommended course of action. For patients, a strong recommendation indicates a course of action that most patients would adopt and only a small proportion would not. On the other hand, a weak (also called conditional) recommendation indicates that policy making will require a more substantial debate and involvement of many stakeholders. For clinicians, different choices will be appropriate for different patients. For patients, weak recommendations suggest a course of action that many patients, but not all, would adopt. Agreement on the wording of the recommendations was also reached during the panel meeting by consensus of voting members.

After final review of the unabridged Guideline report by the panel members and consultants, the guidelines were presented to the Medical and Scientific Advisory Council (MASAC) at the NHF’s Annual Meeting in August 2015, Dallas, TX. All stakeholders (including members of the public) were invited to this meeting, after which the Guideline Report was posted on a dedicated webpage, and public comments were invited during a subsequent 6-week period.

**Guideline questions and outcomes**

The following clinical questions were selected by the panel, and are addressed in this guideline:

1. Should integrated care vs. non-integrated care be used for people with haemophilia?
2. For individuals with haemophilia, should a haematologist, a specialized haemophilia nurse, a physical therapist, a social worker or round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, vs. an integrated care team with a lesser complement?

The panel agreed on a number of subgroups of PWH to be specifically addressed in the guideline: disease severity (mild, moderate and severe haemophilia); inhibitor status; age (paediatric, defined as age 17 years or younger, and the older population, defined as age 65 years or older); and comorbidities (i.e. hepatitis C, HIV). The panel also agreed that when evidence could not be found for people with haemophilia, evidence from other chronic diseases, such as congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD) and asthma would be sought. These diseases were felt to share some features with haemophilia, including chronicity, high resource use, involvement over the life span (for asthma) and large use of delivery of care via multidisciplinary integrated models, on which a well-developed body of literature exists.

The outcomes identified as important to the decision-making process included mortality (or survival); missed days of school or work; number of ER visits; length of in-patient stay; quality of life; joint damage or disease; educational attainment; patient adherence; and patient knowledge. Many other outcomes, including bleeding and bleeding rate, were considered but not judged important enough to enter the final list of outcomes.
Results

Question 1: Should integrated care vs. non-integrated care be used for people with haemophilia?

The literature search for reports assessing models of care in haemophilia or other chronic diseases for the outcomes of interest retrieved the following: no randomized controlled trials comparing integrated care to non-integrated care for people with haemophilia; six systematic reviews of 52 randomized controlled trials comparing integrated care to non-integrated care for people with asthma or chronic obstructive pulmonary disease (four reviews), heart failure (one review) or multiple chronic conditions (one review); eight non-randomized studies that compared integrated care to non-integrated care for people with haemophilia; and 43 non-randomized studies that provided data from one group of people with haemophilia who received integrated care. Of the 43 non-randomized studies in haemophilia, 24 provided only descriptive (i.e. non-quantitative) information, and were thus excluded. The body of evidence provided by the retrieved studies was summarized in an EP (see Fig. 1, Appendix S1–S2).

The overall quality of evidence was judged as moderate. While there was very low quality evidence for two outcomes (knowledge and days of school or work lost), the direction of the effects was concordant (i.e. in favour of integrated care vs. other models of care) for all critical outcomes, several of which had moderate quality evidence. Therefore, the overall quality was not lowered. Although there was some debate about the magnitude of the benefits, the panel felt that there was a clear balance in favour of the integrated care option, given the complete absence of health harms.

Fig. 1. PRISMA flow diagram for care models in the management of haemophilia.
The panel felt that considerations on equity, feasibility and acceptability favoured integrated care if access to care and capacity were optimized, and implementation focused on making integrated care available to those PWH who are currently cared for in other models. It was acknowledged that integrated care may not be acceptable to some groups (e.g. health care practitioners who care for PWH outside of an integrated care model).

Resource use in different models of care was challenging to assess. Clotting factor concentrates account for 92% of total direct medical costs in PWH treated at HTCs [24]. The panel felt that, if the cost of clotting factor concentrates were assumed to be equal in all models of care, the additional costs that support the integrated care model (approximately, 8% of total direct medical costs in PWH treated at HTCs) would be worth the benefits seen.

A number of subgroups were considered by the panel. Disease severity was felt to be an important consideration. Individuals with mild and moderate haemophilia were thought to benefit from an initial visit to an integrated care centre for education, work-up and counselling. However, the frequency of further follow-up may then be lower than other subgroups. Special expertise is required to care for patients with mild haemophilia. For example, individuals with mild haemophilia and certain mutations are more likely to develop inhibitors in later life; inhibitor prevention in these individuals can lead to potential cost avoidance and better health outcomes [25,26]. The panel also underscored that not all PWH are male; female carriers can often fall into the category of ‘mild haemophilia,’ and their unique needs (e.g. obstetric/gynaecologic care, maternal care) may not fall within the capacity of all HTCs. Integrated care models should accommodate the needs of both male and female PWH.

Individuals with severe haemophilia represent the other side of the spectrum. Just as clinical consequences and burden of disease appear to be correlated with severity in haemophilia, the balance of benefits may also be correlated with severity. The panel felt that their recommendation for integrated care over other models of care is particularly applicable to individuals with higher burden of disease, and those with higher resource requirements (e.g. comorbidities, paediatric or older populations), but still important for patients with mild and moderate haemophilia.

Inhibitor status was also considered. The panel strongly recommended integrated care for inhibitor patients and those at higher risk for inhibitor development (e.g. genotype, family history, invasive procedures), as the overall balance of benefits and harms is more pronounced. Though relative benefits of the integrated care model are likely the same as the general haemophilia population, we would expect larger absolute benefits for individuals with inhibitors, as they are at highest risk of harms (and thus have the most potential for benefit).

Age was considered by the panel as well. There is a key opportunity for therapeutic intervention in the paediatric years (<18 years old) for PWH: prevention of inhibitor formation; disease-focused education and counselling; teaching around self-infusion; and laying the groundwork for future care. Paediatric PWH may thus benefit from more frequent visits to an integrated care centre. As the haemophilia population ages, and normal life expectancy becomes a realistic goal, models of care must also adapt to the older population. The panel felt that haemophilia care providers must determine whether they will provide holistic care for their older patients or develop relationships with other specialists and primary care providers outside of the integrated care centre who can manage comorbidities that may not be directly related to haemophilia.

Infectious comorbidities were the final subgroup characteristic considered. HIV and hepatitis inform burden of disease, and thus may be correlated with the balance of benefits. The recommendation for integrated care over other models of care is particularly applicable to these individuals, whose disease is more complicated to treat and often have higher resource requirement.

Recommendation: For persons with haemophilia, the Guideline Panel suggests that the integrated care model be used over non-integrated care models (conditional recommendation, moderate certainty in the evidence).

Recommendation: For persons with haemophilia with inhibitors, and those at high risk for inhibitor development, the Guideline Panel recommends that the integrated care model be used over non-integrated care models (strong recommendation, moderate certainty in the evidence).

**Question 2: For individuals with haemophilia, should a haematologist, a specialized haemophilia nurse, a physical therapist, a social worker or round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, vs. an integrated care team with a lesser complement?**

There were no randomized controlled trials or non-randomized studies comparing the impact of the presence or absence of different health care professionals as part of the integrated care team for people with haemophilia or any of the other chronic diseases. Therefore, a formal EP was not produced, and available evidence was presented in the EtD. (See
Appendix S4: Evidence to Decision Framework for Question 2.) In brief, two database originated by survey studies provided data on access to health care professionals within an HTC:

1. The Haemophilia Experiences, Results and Opportunities (HERO) study surveyed 189 PWH and 190 parents of children with haemophilia in the US [27]. It reported that 84% of PWH see a haematologist/haemophilia physician for management of haemophilia; 75% see a haemophilia nurse; 40% a physical therapist; 20% a general practitioner; and 43% see a social worker. US data from the HERO study also demonstrated that physical therapist involvement was more common in people with better quality of life scores (EQ-5D) and less pain. Social worker and nurse involvement were more common in people with increasing pain and disability [28].

2. International data from the HERO study reported information from 453 parents of children with haemophilia receiving care in HTCs globally. The nurse was involved in the care of ~70% of respondents, and a social worker was involved in care of ~30% of respondents. Social worker involvement was more common in parents reporting negative experiences with work, and with telling friends about their child’s haemophilia [27].

There is also indirect evidence from two systematic reviews in people with haemophilia:

1. Study of effects of exercise interventions [29] included two randomized studies of 56 PWH. Differences in pain, range of motion and strength favoured exercise over no exercise.

2. Study of effects of haemophilia on psychosocial factors reported that quality of life was reduced in people with haemophilia; education was not affected but employment may be affected in men with severe haemophilia [30]. Life satisfaction, social support, self-esteem, anxiety, social desirability and depression may also be impacted.

Finally, structured experiential data were systematically gathered from individuals on the Panel and were incorporated in the EtD: a summary of the elicited evidence is presented in Box 1.

The overall certainty of the evidence was very low, as there were no available studies (randomized or non-randomized) comparing the impact of the presence or absence of different health care professionals as part of the integrated health team.

The marked paucity of data was noted by the panel. Although there was no evidence to support specific roles, the panel acknowledged that the integrated model as commonly implemented (physician, nurse, physical therapist, social worker, round the clock laboratory) produces a benefit and there is a clear balance in favour of the full complement of listed components as part of the integrated care team based on benefits and harms.

Equity, feasibility and acceptability were all felt to be enhanced by the full complement of listed components as part of the integrated care team. In particular, this option was judged to be acceptable to key stakeholders, and highly implementable based on the current existence of fully staffed HTCs in the US. In other words, the uncertainty about feasibility and acceptability of the intervention was greatly reduced by the widespread diffusion of the model across US and beyond.

**Box 1 Summary of results from the systematic observations completed by the panel members**

1. Haematologist: most indicated moderate to large benefit of this individual for all outcomes
2. Specialized haemophilia nurse: most indicated moderate to large benefit of this individual for all outcomes
3. Physical therapist: most indicated small benefit of this individual for most outcomes, but large to moderate benefit for joint damage/disease, and small to no effect for mortality or costs
4. Social worker: most indicated small benefit to no effect of this individual for most outcomes, but large to moderate benefit for quality of life
5. Specialized coagulation laboratory: most indicated that there was no effect of this component for most outcomes, but a large benefit for cost
6. One panel member reported that before the Universal Data Collection (UDC) project began, complete joint range of motion data for all 10 joints on about 1600 haemophilia patients receiving care from HTCs in six participating states could be found in the medical records of less than 1% (Personal communication, J. M. Soucie) Furthermore, data on joint range of motion were completely missing for 60% of patients in these HTCs. However, during the 13 years of UDC data collection which increased HTC access to trained physical therapists, range of motion data were available on all 10 joints on an average of 5000–6000 haemophilia patients receiving care in HTCs in nearly 90% of cases, whereas these data were completely missing for less than 5% of the patients. The Panel Member noted that most HTCs had to hire physical therapists to perform these measurements.

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There were no available data to assist the panel in estimating the resources required for the full complement of listed components as part of the integrated care team, nor was there certainty about whether the incremental costs were small relative to the net benefits.

For Recommendation 2, the panel had less confidence in the recommendation, as there was very low certainty in the evidence and the panel was unable to determine the relative impact of each component of the integrated care team. The haematologist, nurse, physical therapist, social worker and specialized coagulation laboratory were identified as components of interest by the panel, as they make up the current standard ‘core team’ for US HTCs. The final recommendation for question 2 focused on the synergistic effect of these core components, and supported the idea that changing or removing any one component may potentially impact the entire team.

Lack of data limited the panel’s ability to make statements about specific subgroups. However, just as the clinical consequences/burden of disease with haemophilia appear to be correlated with certain factors (severity, inhibitors, age, infectious comorbidities), the balance of benefits may also be correlated with these factors. Thus, the recommendation for the full complement of integrated care components may be particularly applicable to individuals with a higher burden of disease and those with higher resource requirements. The panel noted that the paediatric age group presents a key opportunity for therapeutic intervention, so a range of expert health care providers is likely necessary to provide these interventions. Similarly, as PWH age and develop additional comorbidities unrelated to their bleeding disorder, they may require access to different health care providers than those usually present in an integrated care centre (e.g. older population, cardiology). Integrated care centres must consider how to ensure that older PWH have access to this care.

Recommendation: For individuals with haemophilia, the Panel suggests that a hematologist, a specialized haemophilia nurse, a physical therapist, a social worker, and round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, over an integrated care team, vs. a social worker, and round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, over an integrated care team that does not include all of these components (conditional recommendation, very low certainty in the evidence).

**Implementation considerations and monitoring**

**Question 1:** Should integrated care vs. non-integrated care be used for people with haemophilia?

**Question 2:** For individuals with haemophilia, should a haematologist, a specialized haemophilia nurse, a physical therapist, a social worker or round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, vs. an integrated care team with a lesser complement?

Standardization is needed to define the components of the integrated care model, and lay out performance metrics (that take into consideration the impact of care on patient outcomes). These are currently lacking. The panel advocates that integrated care models aim to standardize their different components of care to minimize practice variations. The standardization of these components, and their impact on patient-important outcomes, should be evaluated.
The panel has made a recommendation on the minimum team cohort for integrated care centres – a physician, a nurse, a physical therapist, a social worker and a specialized coagulation laboratory. However, as noted above, PWH have unique needs and characteristics, so there may be situations where there is a need for additional health care providers or components of care. Demographic studies have confirmed that the natural history of haemophilia is changing [31–33]. Moreover, the US health care system is also changing. Thus, it is important that integrated care centres respond to the needs of their patient population in a dynamic way, to ensure the long-term sustainability of these centres.

The panel’s recommendations around components of care refer to the current state of haemophilia care in the US; they acknowledge that the landscape of health care systems and insurance is changing rapidly. Integrated care centres and the larger haemophilia community must optimize their ability to train, recruit and retain specialized health care team members to meet the needs of PWH. This would ensure that all integrated care centres have a standardized team of expert health care providers.

Research priorities

Question 1: Should integrated care vs. non-integrated care be used for persons with haemophilia?

The panel noted gaps in data when it considered the population, the intervention, the outcomes and the certainty of the evidence. They indicated the need for research to address these gaps:

1. Populations that should be studied: older populations (≥65 years old), populations with poor access to care (in order to identify barriers to care and better integrate them into current models of care), PWH who access care outside of HTCs or integrated care models.

2. Interventions that should be studied: The impact of telemedicine, outreach clinics and other remote care delivery systems as an alternative/add-on to integrated care would be useful, and the panel noted that there is ongoing research taking place in these areas. Randomized trials may be possible to answer these questions.

3. Outcomes that should be studied: the cost and effectiveness of care outside of HTCs is not known. Further, data on factor utilization within and outside of HTCs is not available, and there are limited data on lost days of school/work, educational attainment or employment attainment within and outside HTCs. There is a potential for well-designed retrospective matched cohort studies or prospective data collection to address this gap.

4. Qualitative data may address barriers to care, particularly in non-HTC patients.

5. Studies identifying predictive factors for poor outcomes in different models of care would be valuable.

6. European guidelines have recommended that HTCs be active in data collection [34]. US HTCs must build further capacity to collect and analyze data, in order to power higher quality, comprehensive studies. There must also be continued efforts to address the dearth of data in the non-HTC population.

Question 2: For individuals with haemophilia, should a haematologist, a specialized haemophilia nurse, a physical therapist, a social worker or round-the-clock access to a specialized coagulation laboratory be part of the integrated care team, vs. an integrated care team with a lesser complement?

The panel noted significant gaps in data when it considered the population, the intervention, the outcomes and the quality of the evidence. They cited the need for research to address these gaps, and define the truly necessary and essential components of the integrated care team:

1. Populations that should be studied: older populations, populations with poor access to care (in order to identify barriers to care and better integrate them into current models of care).

2. Interventions that should be studied: it is unclear which aspects of the integrated care model add value, as current data reflect a very heterogeneous group of models. The haemophilia community must consider if randomized trials are possible to answer these questions or if research could be conducted in other (non-US) settings. The latter may offer opportunities to study teams with a smaller complement of health care providers. If financial resources limit the ability of US HTCs to offer the full complement of health care providers in all HTCs simultaneously, a staggered cluster randomized trial (with HTCs as the unit of randomization) to look at patient-important outcomes may be feasible.

3. Outcomes that should be studied: though there are published data that look at the impact of integrated care on patient-important outcomes, they are scarce. Further, there are limited data that look at the impact of individual components of the integrated care team, or that consider the impact of the individual who delivers it (e.g. physical therapist), not of the intervention
4. Qualitative data may prove valuable in addressing equity, feasibility and acceptability issues.
5. As per this Guideline’s first recommendation, the panel again recommends that US HTCs build further capacity for data collection and analysis.

Conclusion

Using an evidence-based methodology, the NHF-McMaster Guideline on Care Models for Haemophilia Management suggests an integrated care model for people with haemophilia. Major strengths of this guideline are its development by a panel of relevant stakeholders, the rigorous process to minimize conflict of interest, the use of innovative evidence gathering strategies (i.e. formal assessment of indirectness, use of systematic observations) and its transparent, evidence-based development approach. Although there was a limited amount of direct, high-quality evidence pertaining to models of care delivery in haemophilia, and a paucity of data addressing some patient-important outcomes, resource use, and impact on equity, feasibility and acceptability, the panel considered all of these factors to make recommendations based on the best available evidence to date. For this reason, the panel has supplemented its recommendations with clear suggestions to guide NHF and the broader haemophilia community in setting research priorities to consolidate and expand the evidence base of these recommendations.

In conclusion, a qualified panel of non-conflicted, relevant stakeholders has issued, using a transparent and rigorous methodology, unanimous support of the provision of integrated care for people with haemophilia.

Guideline panel

Kari Atkinson is a PWH, or has a family member who is a PWH. She was a voting member of this panel.
Marianne Clancy is the Executive Director of the Hereditary Hemorrhagic Telangiectasia (HHT) Foundation. She was a voting member of this panel.
Randall Curtis is a PWH. He is a haemophilia researcher and was a non-voting member of this panel.
Sue Geraghty is a retired haemophilia nurse. She was a voting member of this panel.
Alfonso Iorio is the director of a Canadian HTC. He was a voting member of this panel.
Craig Kessler is a US haemophilia clinic director. He was a non-voting member of this panel.
Nigel Key is a US haemophilia clinic director. He was the Clinical Chair and a non-voting member of this panel.
Kristy Lee is a genetic counsellor. She was a voting member of this panel.
Jeanne Lusher was a former US haemophilia clinic director. She was a voting member of this panel.
Mike Makris is a UK haemophilia clinic director. He was a voting member of this panel.
Maria Martins-Lopes is a Chief Medical Officer, CDMI/Magellan, a public and private payer consulting group. She was a voting member of this panel.
Ruth Mulvany is a physical therapist at a US HTC. She was a non-voting member of this panel.
Holger Schünemann was the Panel Chair. He was a voting member of this Panel.
Michelle Sholzberg is a Canadian haemophilia physician. She was the American Society of Hematology Representative. She was a voting member of this panel.
Mark Skinner is a PWH, or has a family member who is a PWH. He was the World Federation of Hemophilia (WFH) and National Hemophilia Foundation (NHF) Past President. He was a voting member of this panel.
Mike Soucie is a haemophilia researcher working at the US Centers for Disease Control and Prevention (CDC). He was a voting member of this panel.
Doug Stratton is the Chairman and CEO for the Foundation for Complex Healthcare Systems and provided a payer perspective. He was a voting member of this panel.
Vicky Whittemore is the Epilepsy Program Director, at the National Institute of Neurological Disorders and Stroke (NINDS)/National Institutes of Health (NIH). She was a voting member of this panel.

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Disclosures

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References


Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Evidence profiles and characteristics of comparative studies for Question 1

Appendix S2 Evidence summaries and characteristics of non-comparative observational studies for Question 1

Appendix S3 Evidence to decision framework for Question 1

Appendix S4 Evidence to decision framework for Question 2