1 PRINCIPLES OF CARE

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Introduction

- These principles of care aim to provide globally relevant guidance based on current science and best practices in hemophilia diagnosis and treatment, as identified by the guidelines panel of the World Federation of Hemophilia (WFH). They include core concepts, requirements, and priorities in the delivery and management of hemophilia care, which together constitute a framework for implementing and advancing hemophilia treatment programs.
- The principles build on the original tenets set out by the WFH and the World Health Organization (WHO) in 1990[1] and the updated guidelines and recommendations developed collaboratively by the WFH, WHO, and International Society on Thrombosis and Haemostasis (ISTH) in 2002.[2]
- The principles integrate core components of principled integrated care[3] and primary health care, including: meeting people's lifetime health needs through comprehensive preventive, curative, and rehabilitative services as well as palliative care; addressing the broader determinants of health through multisectoral policy and action that engages relevant stakeholders and enables local communities to strengthen primary health care; and empowering individuals, families, and communities to take charge of their own health.[4]
- In addition, they align with the chronic care model's emphasis on the need to shift from acute, episodic, and reactive care towards care that embraces longitudinal, preventive, community-based, and integrated approaches.[5]
- In addition to guiding clinical practice, principles of care can also serve as a common foundation of understanding for patient organizations, healthcare providers, healthcare administrators, and policymakers; this in turn enables better discussion and collaboration on decisions surrounding allocation of resources for hemophilia programs, and priorities for achieving the best standards possible within the available resources.
- Principles of care aim for ideal hemophilia management to ensure that patients have access to appropriate, sustained, and high-quality medical services and comprehensive care; however, it should also be recognized that the priorities and capabilities in each country determine what is practical at any point in time.

1.1 Principle 1: National coordination and delivery of hemophilia care

- A coordinated hemophilia care program, administered through a designated agency and integrated within the existing healthcare system, improves outcomes for people with hemophilia.[2,6-8]
- Optimal hemophilia care within such a program requires the following key components[2]:
  - comprehensive hemophilia care provided by a multidisciplinary team of specialists;
  - a national or regional network of hemophilia treatment centres (HTCs);
  - a national registry of patients with hemophilia;
  - robust processes for the procurement and distribution of safe and effective therapies, particularly clotting factor concentrates (CFCs) and other types of hemostasis products used in hemophilia treatment;

- equitable access to these services and therapeutic products[9]; and
- recognition of the socioeconomic and cultural diversities within any given community, region, or country.

Comprehensive hemophilia care

- Treatment centres based on the multidisciplinary comprehensive care model should be established to ensure that people with hemophilia have access to the full range of clinical specialties and appropriate laboratory services.[6]
- See Principle 7: Multidisciplinary care for hemophilia and Chapter 2: Comprehensive Care of Hemophilia.

Network of hemophilia treatment centres

- Hemophilia care is best provided through designated diagnostic and treatment centres with clearly defined treatment protocols, standards of care, and quality and audit activities.[2]
- Hospitals providing clinical care for people with hemophilia and related disorders are strongly encouraged to seek formal designation as a hemophilia treatment centre (HTC) or hemophilia comprehensive care centre (HCCC), as applicable, by the local health authorities[6,9] (see Table 1-1).
- Such centres can also serve the needs of patients with other congenital bleeding disorders.

National patient registry

- Each country should have a national registry of patients with hemophilia, with standardized data collection by all hemophilia centres and centralized administration by a nationally mandated authority, or participate in a multinational or international registry.[10-13]
- The WFH's World Bleeding Disorders Registry (WBDR) provides an online platform for a network of HTCs around the world to collect uniform and standardized data to track treatment and management of patients, monitor patient outcomes, and guide clinical practice.[13] The WBDR can be used as a patient registry for some or all HTCs within a country.
- Patient registries are used to collect accurate data on people with hemophilia in terms of their treatment and outcomes including disease severity, type of treatment, bleeding episodes, adverse events, joint status, inhibitor status, comorbidities, and quality of life.
- Registry data allow analysis of standards of care and can be used as a tool for auditing clinical and laboratory services; this in turn can support the development of better quality of care and facilitate resource planning and allocation.[6]
- Patient registries can help to advance understanding of the variations in hemophilia treatment; describe care patterns, including appropriateness and disparities in the delivery and quality of care; indicate factors that influence prognosis and quality of life; and provide evidence on resource utilization.[14]
- Adequate provision must be made for data privacy, confidentiality, and respect for human rights[10] in compliance with national regulations and best ethical practices.[6]
- It is important to ensure that the patient and/or the parent or legal guardian (in the case of minors) understands a registry's purpose and uses and provides informed written consent for the collection and sharing of data related to the patient's care.[10,15]
- See Chapter 2: Comprehensive Care of Hemophilia and Chapter 11: Outcome Assessment.

National or regional procurement of hemophilia therapies

- Sustained availability of CFCs in sufficient quantities is strongly correlated with better outcomes for people with hemophilia.[16] To ensure that people with hemophilia have reliable access to safe and effective CFCs and other hemostasis products, countries must establish a rigorous national or regional system for the procurement and distribution of hemophilia therapies.[2]
- Hemophilia treatment relies on essential life-saving medicines that are relatively expensive compared to medications for other conditions.
- Setting up a national tender system or collaborating in a multinational system for the purchase of CFCs can help ensure that optimal products are selected at the best price.[17]
- The decision-making process for such tenders under the contracting authority (typically the Ministry of Health or other health authority) should include both well-informed hemophilia clinicians and patient representatives.[9]
- The WFH's *Guide to National Tenders for the Purchase of Clotting Factor Concentrates* describes tender and procurement systems around the world and explains how to set up a national procurement system and carry out tenders.[17]
- See Chapter 2: Comprehensive Care of Hemophilia and Chapter 5: Hemostatic Agents.

1.2 Principle 2: Access to safe CFCs, other hemostasis products, and curative therapies

Safe and effective CFCs

- People with hemophilia must have access to safe and effective treatment with optimal efficacy in the prevention of bleeding and treatment of any spontaneous, breakthrough, or trauma-related bleeding. For many, this involves treatment with specific CFCs or other hemostasis products.
- Both virus-inactivated plasma-derived and recombinant CFCs, as well as other hemostasis products when appropriate, can be used for treatment of bleeding and prophylaxis in people with hemophilia.[16]
- Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia, or for those with another congenital bleeding disorder that is associated with a severe bleeding phenotype and/or a high risk of spontaneous life-threatening bleeding.
- Episodic CFC replacement should not be considered a longterm option for the management of hemophilia as it does not alter its natural history of spontaneous bleeding and related complications.[18,19]
- The WFH's *Guide for the Assessment of Clotting Factor Concentrates* should be carefully reviewed in the context of the healthcare system in each country and incorporated into tender processes for procurement of hemophilia therapies.[16]
- The *WFH Online Registry of Clotting Factor Concentrates* lists all currently available plasma-derived and recombinant CFCs and their product details.[20]
- See Chapter 5: Hemostatic Agents and Chapter 6: Prophylaxis in Hemophilia.

Emerging therapies and potential cures

- Emerging therapies in development with alternative modes of delivery (e.g., subcutaneous injection) and novel targets may overcome the limitations of standard CFC replacement

TABLE 1-1 Roles of hemophilia comprehensive care centres and hemophilia treatment centres[6]

Hemophilia comprehensive care centre (HCCC)	Hemophilia treatment centre (HTC)
• Provide 24- hour service with experienced staff	• Provide 24- hour, appropriate hematological cover
• Provide inhibitor care and immune tolerance services	• Operate inhibitor care and immune tolerance services in cooperation with a HCCC
• Provide safe and effective CFCs and other hemostasis products	• Provide safe and effective CFCs and other hemostasis products
• Provide community liaison, including school and home visits	• Provide access to nursing staff, physical therapy services, social workers, and obstetric and gynecological services
• Offer laboratory services with 24- hour assay cover	• Provide preliminary genetic counselling followed by referral to a HCCC for full review
• Provide access to hospital- based nursing staff, physical therapy services, social workers, dental services, obstetric and gynecological services, and psychosocial support	• Provide access to HIV and hepatitis C care, through a HCCC, if necessary
• Provide HIV and hepatitis C care	• Offer regular follow- up and home treatment in cooperation with a HCCC
• Provide access to a genetics laboratory and genetic counselling	• Provide prophylaxis in cooperation with a HCCC
• Provide home treatment	• Keep reliable records
• Keep reliable records	• Undertake medical education
• Undertake medical education	• Collaborate with other HTCs in research and exchange of best practices
• Initiate and participate in research	

Abbreviations: CFC, clotting factor concentrate; HCCC, hemophilia comprehensive care centre; HIV, human immunodeficiency virus; HTC, hemophilia treatment centre.

therapy (i.e., need for intravenous administration, short half-life, risk of inhibitor formation). These emerging therapies offer markedly improved pharmacokinetic (PK) profiles with a very low burden of administration (e.g., up to monthly dosing); therefore, they may help reduce treatment burden and increase compliance. These therapies are discussed in Chapter 5: Hemostatic Agents, Chapter 6: Prophylaxis in Hemophilia, and Chapter 8: Inhibitors to Clotting Factor.

- The development of gene therapies for hemophilia has advanced significantly, with product registration likely in the near future. Several clinical trials in both people with hemophilia A and B have demonstrated success with a favourable safety profile to date.[21,22]
- Gene therapy should make it possible for some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies. This will require evaluation through long-term follow-up as part of clinical trials and registries.
- Given the ongoing advances transforming the hemophilia treatment landscape, it is important to establish systems to constantly monitor developments in emerging and gene therapies for hemophilia and make them available as soon as possible following approval by regulatory authorities.
- See Chapter 5: Hemostatic Agents, Chapter 6: Prophylaxis in Hemophilia, and Chapter 8: Inhibitors to Clotting Factor.

1.3 Principle 3: Laboratory services and genetic diagnosis of hemophilia

Laboratory diagnosis and testing

- The diagnosis and treatment of hemophilia require access to laboratory facilities that are equipped with appropriate resources and expertise to accurately perform factor assays and other coagulation tests.
- Screening and testing for inhibitor development, now the most serious complication in hemophilia, is vital for any comprehensive hemophilia treatment program to be able to provide medical treatment and eradication of inhibitors[23]; however, most centres around the world do not have inhibitor testing capacities.
- In many resource-constrained countries, centres and hospitals lack the appropriate technologies and capabilities for diagnosing hemophilia. Therefore, developing or enhancing existing laboratories with the capacity to perform coagulation tests with assured quality is an important priority in these countries.[8]
- Coagulation laboratories must have well-trained laboratory staff and appropriate resources, including suitable and readily available reagents.
- Ideally, coagulation laboratories should be able to provide 24-hour services for coagulation tests and factor assays and be able to perform inhibitor assays in a timely manner.[6]
- It is essential to have good communication between the laboratory and the clinical team ordering the tests to ensure that the appropriate assays are carried out and that the results reported are correctly evaluated and well understood.[24]
- All coagulation laboratories should include quality assurance programs and be subject to external quality assessment.
- See Chapter 3: Laboratory Diagnosis and Monitoring – Quality assurance.

Genetic assessment of hemophilia

- Genetic assessment of hemophilia is important to define disease biology, establish diagnosis in difficult cases, predict risk of inhibitor development, and provide prenatal diagnosis if desired. Wherever possible, genotype analysis should be offered to all patients with hemophilia.[9] (See Chapter 2: Comprehensive Care of Hemophilia and Chapter 3: Laboratory Diagnosis and Monitoring.)
- Genetic testing will not always identify the underlying variant associated with the phenotype. Genetic counselling of the person with hemophilia referred for genetic testing should highlight this possibility.
- The opportunity for discussion of the genetic analysis results between the clinical and the laboratory teams involved is an essential aspect of the genetic diagnostic service.
- Advances in molecular genetic technologies are becoming routinely integrated into many genetic diagnostic laboratories. Full *F8* or *F9* gene screening is performed by polymerase chain reaction (PCR) and Sanger sequencing, or next-generation sequencing.[25-29] Use of these techniques is evolving and increasing internationally. The approach and use of a specific technique depend on the available technical expertise and resources. Genetic counselling must include comprehensive discussion about the possibility of incidental findings in genes other than *F8* or *F9,* depending on the methods being used for the assessment.
- See Chapter 2: Comprehensive Care of Hemophilia, Chapter 3: Laboratory Diagnosis and Monitoring, Chapter 4: Genetic Assessment, Chapter 8: Inhibitors to Clotting Factor, and Chapter 9: Specific Management Issues.

1.4 Principle 4: Education and training in hemophilia care

Recruitment of medical specialists

- As hemophilia is a rare disorder in which the availability of specialized care is a critical determinant of burden of disease,[30] recruitment and training of medical specialists in hemophilia management are key to establishing, maintaining, and advancing standards of care to reduce morbidity and mortality among people with hemophilia in well-resourced and resource-constrained countries alike.
- Recruitment of physicians, hematologists, and scientists in the area of thrombosis and hemostasis to the field of hemophilia is essential to ensure sustained, high-quality medical care, together with recruitment of medical laboratory specialists, nurses, physical therapists, occupational therapists, and other musculoskeletal specialists (e.g., orthopedic surgeons, rheumatologists, and physiatrists), dentists, and psychosocial counsellors. All are integral to multidisciplinary comprehensive care for hemophilia and require ongoing specialist education and development for practice in this field.
- Hemophilia education for allied specialists needed to help address specific medical and health-related issues that may arise in some patients is also important.
- Mentorship and fellowship opportunities are valuable and effective means to attract and retain new healthcare providers to the field of hemophilia.
- A coordinated approach to advancing clinical expertise in hemophilia (i.e., continued education, training, and fellowship programs) based on local, regional, and/or national needs and priorities will provide the foundation for sustaining and improving standards of care.
- Collaboration between hemophilia centres in resource-constrained and well-resourced countries and support from established expert bodies are effective avenues for advancing hemophilia knowledge, expertise, and standards of care.[8]
- The WFH works in many countries around the world to help develop and expand local, regional, and national capacities in laboratory diagnosis and treatment of hemophilia through its medical twinning program, humanitarian aid program,[31] and multidisciplinary education and training workshops for healthcare providers.[32]
- See Principle 7: Multidisciplinary care for hemophilia and Chapter 2: Comprehensive Care of Hemophilia.

1.5 Principle 5: Clinical and epidemiological research

- Evidence-based research in hemophilia is greatly needed, but it is hampered by significant challenges due to the small size of the patient population.
- As most aspects of clinical management of hemophilia are empirical and lack high-level evidence, well-designed studies to generate the necessary evidence to evaluate current practices are needed.[8] A mutual basic scheme, such as the WHO's International Classification of Functioning, Disability and Health (ICF), ensures that disciplines are connected by the same model.
- Given the differences in priorities in practice around the world, it is important to promote locally relevant clinical research.
- Standardization of outcome assessment will permit meaningful comparison across studies.[33]
- Priority areas for clinical research in hemophilia include optimization of clotting factor replacement therapy; better understanding and prevention of inhibitor formation; and clinical data collection on existing hemophilia therapies and clinical practices, newer therapies such as extended half-life CFCs and non-factor hemostasis products, and potential gene therapies.
- Patient registries, with national and international collaboration between centres and countries, are an effective way to pool data to achieve the required sample size to conduct clinical research on rare disorders such as hemophilia.
- The WFH's World Bleeding Disorders Registry allows researchers to address important questions around patient care, compare country-specific levels of care, and use the evidence to advocate for better hemophilia care.[13]
- See Chapter 5: Hemostatic Agents, Chapter 6: Prophylaxis in Hemophilia, Chapter 8: Inhibitors to Clotting Factor, and Chapter 11: Outcome Assessment.

1.6 Principle 6: Acute and emergency care for bleeds

- In critical situations, people with hemophilia need immediate access to emergency medicines and treatment as well as to specialist care at hospital emergency departments.[6] Lack of experience and knowledge of hemophilia management among medical professionals, particularly in emergency departments, may lead to serious treatment-related complications.[8,34]

- Therefore, it is essential to establish systems that are accessible around the clock for the management of acute life- or limb-threatening complications of hemophilia.[8]
- Treatment centres should develop protocols for emergency care for people with hemophilia, including those with inhibitors, that include management of serious acute complications such as intracranial hemorrhage (ICH) and other types of major internal hemorrhage and trauma.[8] (See Principle 9: Management of patients with inhibitors.)
- People with hemophilia should not be kept waiting in emergency departments and should be assessed immediately, even for less serious complications which can deteriorate while waiting. Prompt intervention is mandatory.[8]
- Primary physicians and HTC staff must be prepared to attend to emergency situations and provide advice and specialist support without delay.[6]
- The use of national online databases or the WBDR to capture treatment and health-related patient data allows for better acute and long-term management of people with hemophilia, and the use of digital mobile devices allows patients to record their bleeds and transmit their information to their HTC in real time.[8]
- See Principle 7: Multidisciplinary care for hemophilia and Chapter 2: Comprehensive Care of Hemophilia.

1.7 Principle 7: Multidisciplinary care for hemophilia

- Optimal care of people with hemophilia, especially those with severe forms of the disorder, requires treatment and comprehensive care provided by a multidisciplinary team of specialists.
- Priorities in treatment and care to ensure the best health and quality-of-life outcomes for people with hemophilia include[6,8]:
  - prevention of bleeding and joint damage;
  - prompt management of bleeding episodes including follow-up physical therapy and rehabilitation;
  - appropriate emergency care;
  - appropriate pain management;
  - management of musculoskeletal complications and inhibitor development;
  - management of comorbidities;
  - regular psychosocial assessment and support as needed; and
  - ongoing education on treatment and self-care for people and families living with hemophilia.

Patient self-management and empowerment

- Self-management, i.e., the ability of patients to undertake daily management of their health and health care,[5] is essential in hemophilia. People with hemophilia must be competent in controlling bleeding symptoms to preserve their health, joint integrity, and functional independence.[2] Self-management allows them to minimize the short- and long-term consequences of the disorder and can help provide a sense of normalcy and control.[35]
- Key components of self-management in hemophilia include[35]:
  - bleed recognition;
  - record-keeping of bleeds and treatment;
  - self-administration of CFCs or other hemostasis products;
  - self-care (i.e., nutrition and physical fitness) and medicines management (i.e., record-keeping, treatment routines, maintenance of adequate treatment supply, proper storage, reconstitution, and administration of treatment products);
  - pain management;
  - risk management; and
  - participation in outcome reporting and documentation.
- Patient advocacy organizations have played an important role in advancing hemophilia care around the world. Such organizations should therefore be encouraged and supported to cover those aspects of care which are not covered by the healthcare system, including emphasis on patient empowerment and working with other agencies to advance care.
- See Chapter 2: Comprehensive Care of Hemophilia, Chapter 7: Treatment of Specific Hemorrhages, Chapter 8: Inhibitors to Clotting Factor, Chapter 9: Specific Management Issues, and Chapter 10: Musculoskeletal Complications.

Transition from pediatric to adult care

- The transition from pediatric to adult care, during which adolescents and young adults with hemophilia gradually assume responsibility for their own health and hemophilia management, can be a challenge for patients and their families.[36]
- Treatment adherence is a key challenge at two transition points: when young people with hemophilia switch to self-infusion, and again when they move away from home and assume the full responsibility of self-care.[37]
- Comprehensive hemophilia care should therefore include a conscientious approach to transition of care that starts in early adolescence[38] and supports the development of

young people's self-efficacy and self-management skills, including psychosocial coping.[37]
- Both pediatric and adult healthcare providers must be engaged in considering the individual needs of patients and families to ensure a smooth transition and to ensure the best care possible during this time.[36]
- Engagement of adolescents and their caregivers early in the transition process allows time for acceptance and better understanding of the transition from the pediatric to the adult model of care as well as the associated reallocation of health management and medical decision-making responsibilities.[39]
- See Chapter 2: Comprehensive Care of Hemophilia – Transition from pediatric to adult care and Chapter 9: Specific Management Issues – Psychosocial issues.

1.8 Principle 8: Regular replacement therapy (prophylaxis)

- The standard of care for all patients with severe hemophilia is regular replacement therapy (prophylaxis) with CFCs, or other hemostasis products to prevent bleeding, started early in life (before age 3) to prevent musculoskeletal complications from recurrent joint and muscle bleeds.[40]
- Episodic ("on demand") clotting factor replacement therapy should no longer be considered to be a long-term treatment option.
- Implementation of home-based prophylaxis programs increases compliance and allows people with hemophilia to live relatively normal lives. These programs should be accompanied by education of patients, families, and healthcare providers on the benefits of prophylaxis and the importance of adherence to treatment regimens.[35,37,41]
- Prophylaxis in young children may be the best way for a country to begin implementing universal prophylaxis for people with hemophilia.[8]
- See Chapter 6: Prophylaxis in Hemophilia and Chapter 10: Musculoskeletal Complications.

1.9 Principle 9: Management of patients with inhibitors

- Systematic surveillance for inhibitors and comprehensive management of inhibitors should be implemented for people with hemophilia A,[23] particularly when patients are at highest risk during their first 20 exposures to CFCs (with one exposure defined as all CFCs administered within a 24-hour period[8,42]), and thereafter up to 75 exposures.[43]
- Eradication of inhibitors is currently best achieved through immune tolerance induction (ITI) therapy.
- Patients who develop inhibitors should have access to ITI and to suitable hemostatic agents for control of bleeding as well as surgical interventions, if needed, at specialized centres with relevant experience.[9,23]
- Bypassing agents and other suitable treatment products should be available for patients who do not respond to enhanced factor dosages or ITI.[23,40,44]
- Given the costs and other limitations of current treatment modalities, research and innovation in the prevention and treatment of inhibitors are required.[8]
- See Chapter 5: Hemostatic Agents and Chapter 8: Inhibitors to Clotting Factor.

1.10 Principle 10: Management of musculoskeletal complications

- The prevention and treatment of musculoskeletal complications in people with hemophilia are important to their health, autonomy, and quality of life.
- In all cases of musculoskeletal bleeding, adequate treatment generally requires a combination of clotting factor replacement therapy and physical therapy with an experienced physical therapist to achieve complete functional recovery.[45]
- People with hemophilia should also have access to musculoskeletal specialists (i.e., physical therapist, occupational therapist, physiatrist, physical medicine/rehabilitation specialist, rheumatologist, orthopedist, orthopedic surgeon) with experience in hemophilia, with annual musculoskeletal assessments and longitudinal monitoring of their musculoskeletal outcomes and preventive or corrective measures as needed.
- Surgical interventions may become necessary for musculoskeletal complications if nonsurgical measures fail to provide satisfactory pain relief and improved function. Orthopedic surgeons should have specific training in surgical management of patients with hemophilia.
- See Chapter 2: Comprehensive Care of Hemophilia and Chapter 10: Musculoskeletal Complications.

1.11 Principle 11: Management of specific conditions and comorbidities

- Specific complications and management issues may affect people with hemophilia and their families at different life stages. Treatment and care for these conditions should be established as part of national hemophilia programs.

Carriers of hemophilia

- Some carriers of hemophilia experience bleeding problems, including joint hemorrhages, similar to males; in addition, they may experience problems that are specific to women, such as prolonged or heavy menstrual bleeding.[46-49] Symptomatic carriers are considered to have mild or moderate hemophilia. It is therefore important to include a gynecologist in the comprehensive care team for the management of carriers.
- Carriers may experience a significant impact on various aspects of their lives and thus require specialist care specific to reproductive issues, including genetic counselling, genetic testing, prenatal diagnosis and planning, newborn testing, and psychosocial counselling.
- See Chapter 9: Specific Management Issues – Carriers.

Surgery and other invasive procedures

- Surgeries and other invasive procedures pose particular risks to patients with hemophilia; however, these procedures can be performed safely with the provision of adequate laboratory support, careful preoperative planning, appropriate hemostasis with sufficient quantities of CFCs and other hemostasis products during and after surgery, and optimal postoperative recovery and rehabilitation.
- Therefore, treatment centres and hospitals should establish protocols to ensure that people with hemophilia, with or without inhibitors, have ready access to these services, both in acute and elective surgery situations.
- See Chapter 9: Specific Management Issues – Surgery and invasive procedures.

Management of comorbidities

- Improved life expectancy in hemophilia has led to a greater interest in age-related disorders, with cardiovascular disease, hypertension, and other cardiovascular risk factors increasingly reported in adults with hemophilia.[50-54]
- The treatment of comorbidities, especially cardiovascular diseases, is one of the most important challenges.[50]
- Although most evidence suggests that hemophilia, at least the severe form, partially protects against myocardial infarction, stroke, and venous thromboembolism, typical cardiovascular risk factors may still be present and cause disease despite the clotting defect.[50,55]
- People with hemophilia are equally or even more prone to obesity, hypertension, and diabetes than the general population.[50]
- Preventive strategies are needed to identify people with hemophilia who are at higher risk of developing cardiovascular disease in adulthood.[56]
- See Chapter 9: Specific Management Issues – Comorbidities.

Medical issues with aging

- As they age, people with hemophilia require education and preventive strategies to reduce the risks and impacts of age-related morbidities.
- The hemophilia team should be closely involved in the planning and management of specialist care for people with hemophilia with comorbidities and any complications related to aging, to facilitate close consultation and agreement on treatment plans.
- Elderly patients with hemophilia should be managed in the same way as their peers in the general population, except for the necessary additional correction of impaired hemostasis with CFCs.[50]
- Specialist services should be well versed in bleed management and the specific treatment requirements of people with hemophilia.[8]
- See Chapter 9: Specific Management Issues – Medical issues with aging.

Management of transfusion-transmitted infections

- Transfusion-transmitted infections, particularly those with the human immunodeficiency and hepatitis C viruses, have been major complications in the treatment of hemophilia in the past.
- It is absolutely imperative to ensure that current replacement therapy products are well tested and virally inactivated to avoid any chance of such infections being transmitted.
- While the management of these conditions will not be covered further in these guidelines, given the effectiveness of current anti-viral therapies for both these conditions, it is important that relevant services be universally accessible to all patients with hemophilia who need them.[57]

1.12 | Principle 12: Outcome assessment

- In the management of hemophilia, outcome assessment refers to the use of specific tools designed to monitor an individual's disease course and to measure the consequences of the disease and its treatment (i.e., effectiveness of hemostatic therapy and associated complications).[33]
- To ensure that all consequences of the disorder are evaluated, outcome assessment should follow the WHO's ICF model.[58,59]
- Standardized, validated outcome assessment is necessary for the clinical management of individual patients, to assess the quality of care provided, and for research or advocacy purposes.[33]
- The most important indicator of the efficacy of hemostatic therapy is frequency of bleeding, particularly joint and muscle bleeds. Bleeding frequency is the primary parameter for treatment decisions and is also used as a predictor of long-term musculoskeletal outcomes.[6]
- In hemophilia care, the impact of bleeding on the musculoskeletal and other systems is measured across several domains, including body structure and function and activities and participation. All of these domains may be affected by contextual factors including environmental, personal, and economic factors.[33]
- Multiple clinical and radiological tools are used to assess the status of joints and specific muscle groups. Measurements of activities and participation are either self-reported or observed.[6,60]
- The ongoing development of hemophilia-specific measurement and assessment tools offers opportunities for clinicians and patients to better understand and evaluate the nature of the impairments and functional limitations associated with the condition.[8,60]
- Increasingly in recent years, health authorities, including health technology assessment bodies, are relying on patient-reported outcome data to evaluate the benefits of health interventions.[61]
- Despite the availability of numerous assessment options, a core set of measures for outcome assessment in hemophilia remains to be defined. Such a core set should ideally be applicable to the clinical and cultural realities of hemophilia management worldwide.[12,13]
- See Chapter 11: Outcome Assessment.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.