

# 2 COMPREHENSIVE CARE OF HEMOPHILIA

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**All statements identified as recommendations are consensus based, as denoted by **CB**.**

## 2.1 | Introduction

- Hemophilia is a rare X-linked congenital bleeding disorder characterized by a deficiency of coagulation factor VIII (FVIII), called hemophilia A, or factor IX (FIX), called hemophilia B. The factor deficiencies are the result of pathogenic variants in the *F8* and *F9* clotting factor genes.
- The best estimates of the prevalence of hemophilia, based on the most reliable national patient registry data available and recent World Federation of Hemophilia (WFH) annual global surveys, indicate that the expected number of males with hemophilia worldwide is 1,125,000, the majority of whom are undiagnosed, including an estimated 418,000 males with severe hemophilia.<sup>1</sup>

### Hemophilia A and B

- Hemophilia A is much more common than hemophilia B. Hemophilia A is estimated to account for 80%-85% of all hemophilia cases; hemophilia B is estimated to account for 15%-20% of all hemophilia cases. Estimated prevalence is 17.1 cases per 100 000 males for all severities of hemophilia A (6.0 cases for severe hemophilia A) and 3.8 cases per 100 000 males for all severities of hemophilia B (1.1 cases for

severe hemophilia B).<sup>1</sup> Estimated prevalence at birth is 24.6 cases per 100 000 males for all severities of hemophilia A (9.5 cases for severe hemophilia A) and 5.0 cases per 100 000 males for all severities of hemophilia B (1.5 cases for severe hemophilia B).<sup>1</sup>

- Hemophilia is usually inherited through an X chromosome with an *F8* or *F9* gene mutation. However, both the *F8* and *F9* genes are prone to new mutations, and about 30% of all cases result from spontaneous genetic variants. Prospective studies report that over 50% of people newly diagnosed with severe hemophilia have no prior family history of hemophilia.<sup>2,3</sup>
- Hemophilia usually affects only males who inherit an affected maternal X chromosome. Females with hemophilia (FVIII or FIX <40 IU/dL) are rare; in such cases, both X chromosomes are affected or one is affected and the other is inactive. A female with one affected X chromosome is called a carrier of hemophilia.<sup>4</sup>
- Hemorrhages, musculoskeletal complications, and other sequelae of hemophilia typically occur in males with hemophilia but may also occur in a proportion of female carriers. Since the baseline factor levels in carriers may be normal or variably reduced, the symptoms and complications of hemophilia are less common in females and are often overlooked and underdiagnosed; joint bleeds in carriers often remain unrecognized, leading to poorer joint outcomes due to undiagnosed joint problems. Better diagnosis and

management of bleeding problems in carriers are needed. (See Chapter 9: Specific Management Issues – Carriers.)

### Clinical diagnosis

- Hemophilia should be suspected in individuals presenting with a history of any of these symptoms:
  - easy bruising;
  - “spontaneous” bleeding (i.e., bleeding for no apparent/known reason), particularly into the joints, muscles, and soft tissues;
  - excessive bleeding following trauma or surgery.
- Early symptoms of joint bleeds in children at a very young age are a key indicator of severe hemophilia.<sup>5</sup> (See also “Bleeding manifestations” below.)
- If hemophilia is suspected, the clinician should obtain the patient’s bleeding history and family history of abnormal or unexplained bleeding experienced by any siblings or maternal male relatives (i.e., maternal cousin, uncle, or grandfather) to assess patterns of inheritance and assist with diagnosis.
- Accurate diagnosis of hemophilia is essential to inform appropriate management. A definitive hemophilia diagnosis is based on a factor assay to demonstrate deficiency of FVIII or FIX.
- See Chapter 3: Laboratory Diagnosis and Monitoring and Chapter 4: Genetic Assessment.

### Bleeding manifestations

- The characteristic phenotype in hemophilia is the bleeding tendency. The severity of bleeding manifestations in hemophilia generally correlates with the degree of the clotting factor deficiency (see Table 2-1).
- People with mild hemophilia may not necessarily have abnormal or prolonged bleeding problems until they experience serious trauma or undergo surgery.
- People with severe hemophilia most commonly experience bleeds into the joints, muscles, and internal organs (see Tables 2-2 and 2-3).

- In newborns and children with severe hemophilia less than 2 years of age, common types of bleeding include<sup>6,7</sup>:
  - soft tissue and intramuscular bleeding;
  - bleeding associated with a medical procedure (e.g., venipuncture, central line placement, circumcision, neonatal heel prick);
  - mucocutaneous bleeding (e.g., oral, nasal);
  - extracranial bleeding.
- Some types of bleeds can be life-threatening and require immediate treatment and medical attention.
- See Table 2-2 and Chapter 7: Treatment of Specific Hemorrhages.

### Patient/caregiver education

- People with hemophilia and family/primary caregivers must receive comprehensive education on hemophilia care, particularly on the prevention and treatment of bleeds and management of musculoskeletal complications, and training on essential skills for self-management, including bleed recognition, self-treatment, record-keeping, dental care, and risk management.<sup>10,11</sup> (See 2.5 Home therapy – Self-management, below.)

## 2.2 | Comprehensive care

- Comprehensive hemophilia care involves multidisciplinary medical services necessary for the diagnosis, treatment, and management of the condition and its complications. These services are typically delivered by a hemophilia treatment centre or hemophilia comprehensive care centre, as described in Chapter 1: Principles of Care – Principle 1: National coordination and delivery of hemophilia care. Comprehensive care promotes physical health, psychosocial well-being, and quality of life for people with hemophilia and reduces morbidity and mortality.<sup>11-13</sup> It should encompass family-centred care, particularly diagnosis and management of carriers.<sup>11,14</sup>

**TABLE 2-1** Relationship of bleeding severity to clotting factor level<sup>8</sup>

Severity	Clotting factor level	Bleeding episodes
<b>Severe</b>	<1 IU/dL (<0.01 IU/mL) or <1% of normal	Spontaneous bleeding into joints or muscles, predominantly in the absence of identifiable hemostatic challenge
<b>Moderate</b>	1-5 IU/dL (0.01-0.05 IU/mL) or 1-5% of normal	Occasional spontaneous bleeding; prolonged bleeding with minor trauma or surgery
<b>Mild</b>	5-40 IU/dL (0.05-0.40 IU/mL) or 5-<40% of normal	Severe bleeding with major trauma or surgery; rare spontaneous bleeding

### Key components of comprehensive care

- Hemophilia is a rare inherited disorder that is complex to diagnose and to manage. Optimal care, especially for people with severe forms of the disorder, requires more than treatment of acute bleeding.
- Priorities in hemophilia treatment and care include<sup>10,11</sup>:
  - prevention of bleeding and joint damage;
  - prompt management of bleeding episodes including physical therapy and rehabilitation after joint bleeds;
  - pain management;
  - management of musculoskeletal complications;
  - prevention and management of inhibitors;
  - management of comorbidities;
  - dental care;
  - quality-of-life assessments and psychosocial support;
  - genetic counselling and diagnosis;
  - ongoing patient/family caregiver education and support.
- Emergency care should be available at all times, with the following essential services and resources<sup>10,11</sup>:
  - coagulation laboratory services with the capacity to perform accurate and precise clotting factor assays and inhibitor testing;
  - provision of clotting factor concentrates (CFCs), either virus-inactivated plasma-derived or recombinant, as well as other hemostatic agents such as desmopressin (DDAVP) and antifibrinolytic agents (tranexamic acid or epsilon aminocaproic acid [EACA]) where available;
  - provision of safe blood components such as fresh frozen plasma (FFP) and cryoprecipitate if adequately screened, tested, and/or virus-inactivated where CFCs are not available;
  - casting and/or splinting and mobility/support aids, as needed.
- See Chapter 5: Hemostatic Agents.

### Comprehensive care team

- The wide-ranging needs of people with hemophilia and their families are best met by a multidisciplinary team of healthcare professionals with expertise and experience in hemophilia, in accordance with accepted protocols and practices and national standards of care, if available.<sup>10,15,16</sup>

### Patient/healthcare provider partnership and decision-making

- People with hemophilia are regarded as distinct core members of the comprehensive care team who through day-to-day self-management become experts and partners in their own hemophilia care.

**TABLE 2-2** Sites of bleeding in hemophilia<sup>9</sup>

<b>Serious</b>	<ul style="list-style-type: none"> <li>• Joints (hemarthrosis)</li> <li>• Muscles, especially deep compartments (iliopsoas, calf, forearm)</li> <li>• Mucous membranes of the mouth, nose, and genitourinary tract</li> </ul>
<b>Life-threatening</b>	<ul style="list-style-type: none"> <li>• Intracranial</li> <li>• Neck/throat</li> <li>• Gastrointestinal</li> </ul>

**TABLE 2-3** Approximate frequency of bleeding at different sites

Site of bleeding	Approximate frequency
Joints	70-80%
<ul style="list-style-type: none"> <li>• More common in hinged joints: ankles, knees, elbows</li> <li>• Less common in multi-axial joints: shoulders, wrists, hips</li> </ul>	
Muscles	10-20%
Other sites (major bleeds)	5-10%
Central nervous system	<5%

- It is important to involve patients (and their parents/caregivers) in decision-making; incorporate their particular preferences, values, and personal experiences;<sup>17</sup> and obtain their concurrence with short- and long-term treatment and management plans. All parties should engage in truly shared decision-making through educated discussions about available healthcare options and anticipated outcomes, including evidence-informed guideline recommendations, benefits and risks of the various choices, and expressed concerns and values of the patient and care-givers.<sup>18</sup> They should work together on the development and periodic updating of individualized treatment guidelines that the patient/caregiver can consult at will and share with others involved in care.
- Increasingly, patients are not only active members of their own healthcare team; they are becoming full partners in the health-care team who are also involved in research, medical education, and student training in recognition of the value of their particular understanding and expertise.<sup>17</sup>

### Multidisciplinary team

- The core team typically consists of a medical director, nurse coordinator, physical therapist, laboratory specialist, and psychosocial counsellor; all of whom should be specifically trained in the field.
  - The medical director (normally a pediatric and/or adult hematologist or a physician with training and expertise in managing hemophilia and other bleeding disorders) oversees patient management including ordering diagnostic laboratory tests, prescribing treatment, and monitoring patient health and medical needs.
  - The nurse coordinator, who should have training in the management of patients with bleeding disorders, coordinates the provision of care by the multidisciplinary team, educates patients and their families, provides training for home therapy and other aspects of care, and assesses patients and institutes initial care where appropriate.
  - The physical therapist plays an important role in educating people with hemophilia and their caregivers on preventive measures, facilitating complete functional recovery after each bleed, and counselling individuals about preserving musculoskeletal health.<sup>19</sup> Other musculoskeletal specialists (i.e., occupational therapist, physiatrist, physical medicine/rehabilitation specialist, rheumatologist, orthopedist, orthopedic surgeon) provide treatment for specific musculoskeletal conditions.
  - The laboratory specialist performs specialized blood tests to establish the diagnosis and monitor therapy, including blood coagulation tests, factor assays, and inhibitor assays.
  - The psychosocial counsellor (preferably a social worker or psychologist) conducts psychosocial assessments and provides counselling and/or referrals to community resources.
- The roles assumed by core team members may differ at different centres, depending on the availability and expertise of trained staff and the organization of services within the centre.
- The comprehensive care team should also include or have access to dentists with hemophilia experience, and other specialists as needed to address specific medical and health-related issues that some people with hemophilia and carriers may encounter, including:
  - chronic pain specialist;
  - pharmacist;
  - geneticist;

- hepatologist;
- infectious disease specialist;
- immunologist;
- gynecologist/obstetrician;
- vocational counsellor.
- Other medical specialists may be needed to address comorbid conditions related to age, lifestyle, or other circumstances. (See Chapter 9: Specific Management Issues – Comorbidities.)
- Detailed clinical management protocols are essential to ensure continuity of care in the event of personnel changes within the comprehensive care team.<sup>10,15,16</sup>
- To foster the necessary expertise and experience in hemophilia, mentorships and fellowships can offer opportunities for recruiting medical professionals to the field and advancing clinical knowledge.

### RECOMMENDATION 2.2.1:

- **For people with hemophilia, the WFH recommends coordinated delivery of comprehensive care by a multidisciplinary team of healthcare professionals with expertise and experience in hemophilia.**
- **REMARK: The core members of the comprehensive care team should consist of a medical director, nurse coordinator, musculoskeletal specialists, medical laboratory specialist, psychosocial specialist, and the patient and family caregivers. The roles assumed by the core team members may differ at different centres depending on the availability and expertise of trained staff and the organization of services within the centre. CB**

### RECOMMENDATION 2.2.2:

- **For people with hemophilia, the WFH recommends availability of and access to:**
  - **appropriate emergency care at all times;**
  - **a coagulation laboratory capable of performing clotting factor assays and inhibitor testing;**
  - **appropriate clotting factor concentrates (CFCs), either plasma-derived or recombinant, as well as other hemostatic agents such as desmopressin (DDAVP), emicizumab, and antifibrinolytics;**
  - **safe blood components such as fresh frozen plasma (FFP) and cryoprecipitate that have been adequately screened, tested, and/or virus-inactivated if CFCs are not available;**
  - **casting and/or splinting for immobilization and mobility/support aids, as needed;**

- other specialists to address specific medical and health-related issues that some individuals may encounter, as needed. **CE**

### **RECOMMENDATION 2.2.3:**

- For all patients with hemophilia, the WFH suggests the preparation of written clinical management protocols to ensure continuity of care in the event of changes in clinic personnel. **CE**

### **Functions of a comprehensive care program**

- A comprehensive care program helps put into operation the key principles of comprehensive care for hemophilia. The core functions are described here.

#### *Coordination and provision of care*

- A comprehensive care program enables centralized coordination of care from across multidisciplinary specialities, services, and facilities, and the provision of inpatient care (hospital stays) and outpatient care (checkups and other clinic visits) to patients and their families.
- People with hemophilia require periodic monitoring and assessment of their condition and circumstances. They should be evaluated at least once per year; those with mild or moderate hemophilia may require less frequent monitoring.<sup>20</sup>
- Referrals to other services (e.g., dentistry, surgery, obstetrics/ gynecology) including communication of the care management plan to all treaters and care facilities are arranged through the program, which helps ensure that patients receive optimal care from specialists with appropriate hemophilia expertise. Planning and coordination of procedures must involve patients/family caregivers in consultation with all specialists required (e.g., for surgery, the anesthesiologist, surgeon, and surgical staff including nurses).<sup>20-22</sup>
- Ongoing collaboration with patients and family caregivers to develop, audit, and refine the comprehensive care management plan is essential.

### **RECOMMENDATION 2.2.4:**

- For people with hemophilia, the WFH recommends a multidisciplinary checkup including hematologic, musculoskeletal, and quality-of-life assessments by the core comprehensive care team members at least yearly (every 6 months for children).
- **REMARK: Smaller centres and family physicians can provide primary care and management of some complications of hemophilia, in frequent consultation**

**with the hemophilia comprehensive care centre, especially for patients who live a long distance from the nearest hemophilia treatment centre. **CE****

#### *Patient registry and data collection*

- The comprehensive care program facilitates centralized patient data collection on sites of bleeds, types and doses of treatment administered, complications of treatment, and assessment of long-term musculoskeletal and other health outcomes and patient-reported outcomes (e.g., bleed-related activities, acute and chronic pain, days missed from school or work, impact of hemophilia on activities of daily living). The WFH's World Bleeding Disorders Registry (WBDR) is an online platform for use by hemophilia treatment centres around the world to collect such data to monitor patient outcomes and guide clinical practice.<sup>23</sup>
- Patient records should be maintained in accordance with confidentiality laws and other national regulations, ideally in a computerized patient registry that is updated regularly by designated clinic staff with direct or indirect patient input.
- Systematic data collection also serves to facilitate the auditing of services provided by the hemophilia treatment centre with the goal of improving care delivery and to help the patient better manage their health condition.
- See Chapter 9: Specific Management Issues, Chapter 10: Musculoskeletal Complications, and Chapter 11: Outcome Assessment.

### **RECOMMENDATION 2.2.5:**

- For all patients with hemophilia, the WFH recommends systematic data collection in patient registries, where possible, to inform allocation of resources, support improvement of care delivery services, and promote collaboration among centres in sharing data and conducting research. **CE**

#### *Clinical research*

- Basic and clinical hemophilia research should be conducted where possible. Since the number of patients with hemophilia at individual centres may be limited, clinical research is best conducted in collaboration with other hemophilia centres and national hemophilia patient groups such as national member organizations (NMOs) of the WFH.

### *Patient/caregiver education and support*

- Education and training on home therapy should be provided where available and should ideally include supervision of adherence to treatment.
- Ongoing support should be provided to families and caregivers including identifying resources and/or developing strategies to enable them to adapt to living with hemophilia.
- Potential challenges that patients and family members may encounter in everyday living, particularly those related to the management of bleeding, include:
  - changes associated with different stages of growth and development (especially adolescence and aging);
  - adherence to a complex medical regimen requiring frequent IV infusions in the midst of other competing family needs<sup>24</sup>;
  - issues with schooling and/or employment;
  - psychosocial and mental health issues;
  - bleeding problems and reproductive issues in carriers.
- In collaboration with hemophilia patient organizations, a comprehensive care program helps promote and/or facilitate hemophilia support groups, educational workshops, and recreational activities such as hemophilia camps.
- See 2.5 Home therapy and 2.8 Transition from pediatric to adult care, below, and Chapter 9: Specific Management Issues.

#### **RECOMMENDATION 2.2.6:**

- **The WFH recommends that adequate education be provided to people with hemophilia, their family members, and other caregivers to enable self-management and sufficient understanding of the disease for prevention of bleeds and related complications and for life planning. **CB****

#### **RECOMMENDATION 2.2.7:**

- **For people with hemophilia and their families, the WFH recommends promotion and/or facilitation of educational and recreational activities in collaboration with patient organizations, to provide them with opportunities to discover new interests and capabilities and build a support network with diverse members of the hemophilia community. **CB****

## **2.3 | Fitness and physical activity**

- Physical activity is important to promote normal neuromuscular development and physical fitness.<sup>19</sup>

- People with hemophilia may have an increased risk of low bone mineral density compared to the general population due to risk factors including hemophilia severity and hemophilic arthropathy and resulting immobility.<sup>25</sup> Ways to promote bone health include preventing hemarthrosis, regular exercise, and adequate vitamin D and calcium intake.<sup>26,27</sup>
- For those with significant musculoskeletal dysfunction, weight-bearing activities that promote development and maintenance of good bone density should be encouraged to the extent their joint health permits.<sup>26</sup>
- The choice of activities should reflect the individual's preferences/interests, physical condition and ability, local contexts, and available resources.
- Non-contact sports such as swimming, walking, jogging, golf, badminton, archery, cycling, rowing, sailing, and table tennis should be encouraged.
- High-contact and collision sports such as soccer, hockey, rugby, boxing, and wrestling, and high-velocity activities such as motocross racing and skiing are not advised due to the potential for life-threatening injuries, unless the individual is on adequate prophylaxis to cover such activities and is well educated on the potential risks.
- Custom-made dental mouthguards should be used by individuals with hemophilia for all contact sports to prevent trauma and injury to teeth and oral soft tissues.<sup>28</sup>
- Organized sports programs should be encouraged over unstructured sports activities where protective equipment and supervision may be lacking.
- Ideally, individuals with hemophilia (or their family caregivers) should consult a physical therapist before engaging in new sports and physical activities to discuss their appropriateness, required protective gear, prophylaxis (factor coverage and other measures), and required physical skills prior to beginning the activity. This is particularly important if the individual has any joint with recurrent bleeding (i.e., target joint).<sup>29</sup>
- Ongoing patient/caregiver education on the physical implications of a given activity in relation to hemophilia (i.e., joint flexion, joint or muscle trauma) is important so that they can make informed choices, adapt their self-management accordingly, and responsibly manage the way they participate in sports and physical activities.
- Target joints can be protected with braces or splints during physical activity, especially in the absence of factor coverage.<sup>30,31</sup>
- See Chapter 7: Treatment of Specific Hemorrhages and Chapter 10: Musculoskeletal Complications.

**RECOMMENDATION 2.3.1:**

- For people with hemophilia, the WFH recommends promotion of regular physical activity and fitness, with special attention on bone health maintenance, muscle strengthening, coordination, physical functioning, healthy body weight, and positive self-esteem. **CB**

**RECOMMENDATION 2.3.2:**

- For people with hemophilia, the WFH recommends promotion of non-contact sports. High-contact and collision sports and high-velocity activities should be avoided unless the individual is on a prophylactic regimen that is adequate to cover such activities and is properly educated on the potential risks and other required protective measures.
- **REMARK:** The choice of sports activities should take into consideration the individual's physical condition and ability, preferences and interests, local customs, and available resources. **CB**

**RECOMMENDATION 2.3.3:**

- For people with hemophilia, the WFH recommends consultation with a physical therapist or other musculoskeletal specialist before engaging in sports and physical activities to discuss their appropriateness specific to the individual's condition and their requirement for particular physical skills and/or protective gear. **CB**

**2.4 | Adjunctive management**

- Adjunctive therapies are important in the treatment of bleeds, particularly where coagulation therapies and hemostatic agents are limited (or unavailable), and may lessen the amount of treatment product required.
- First-aid measures are a key component of adjunctive management. In addition to CFCs to raise factor levels (or DDAVP in mild hemophilia A), the PRICE principles—protection, rest, ice, compression, and elevation—based on the conventional rest, ice, compression, and elevation (RICE) protocol for injuries, may be used for joint and muscle bleeds. Another approach, POLICE (protection, optimum loading, ice, compression, and elevation), replaces “rest” with “optimum loading” to focus attention on the need to balance rest with early mobilization and gradual weight-bearing to prevent complications associated with immobilization.<sup>32</sup> It is important to consider the appropriateness of each of these measures for the particular situation.

- In recent years, there has been debate on the application of ice, which is believed to help manage acute pain from joint bleeding and reduce blood flow to the injured tissue.<sup>33</sup> One study suggested that the cooling effect of ice may interfere with coagulation and slow the hemostasis process.<sup>34</sup> However, counter viewpoints note that many people with hemophilia appreciate ice for pain relief and that, for those without access to treatment products, ice for acute and chronic pain may be their only “treatment” option.<sup>35-37</sup>
- See Chapter 7: Treatment of Specific Hemorrhages – Joint hemorrhage – Adjunctive care.
- Physical therapy and rehabilitation are particularly important for functional improvement and recovery after musculoskeletal bleeds and for those with established hemophilic arthropathy.<sup>38,39</sup>
- See Chapter 7: Treatment of Specific Hemorrhages – Joint hemorrhage – Physical therapy and rehabilitation and Chapter 10: Musculoskeletal Complications – Hemophilic arthropathy and joint contractures – Physical therapy for hemophilic arthropathy.
- Antifibrinolytic drugs are effective as adjunctive treatment for mucosal bleeds and invasive dental procedures. (See 2.7 Dental care and management, below, and Chapter 5: Hemostatic Agents – Other pharmacological options.)
- Certain selective COX-2 inhibitors may be used for joint inflammation after an acute bleed and for chronic arthritis.<sup>40</sup> (See 2.6 Pain management, below.)
- Complementary techniques for pain management (e.g., meditation, distraction, mindfulness, or music therapy) may also be helpful for those with chronic hemophilic arthropathy. (See 2.6 Pain management, below.)

**RECOMMENDATION 2.4.1:**

- For people with hemophilia with a muscle or joint bleed, the WFH recommends following the PRICE principles (protection, rest, ice, compression, and elevation) in addition to increasing factor level. **CB**

**RECOMMENDATION 2.4.2:**

- For people with hemophilia recovering from a joint or muscle bleed, the WFH recommends gradual re-initiation of physical activities under the supervision of a physical therapist with experience in hemophilia to assess resumption of normal motor development and coordination.
- **REMARK:** For children with hemophilia recovering from a joint or muscle bleed, the physical therapist and family caregiver should remain in close contact

**to discuss and decide on the appropriate sports and activities for the child's progressive rehabilitation. **CB****

#### **RECOMMENDATION 2.4.3:**

- For people with hemophilia with established hemophilic arthropathy or after recovery from musculoskeletal bleeding, the WFH recommends physical therapy and rehabilitation activities. **CB**

#### **RECOMMENDATION 2.4.4:**

- For people with hemophilia, the WFH recommends the use of antifibrinolytic drugs (e.g., tranexamic acid, epsilon aminocaproic acid [EACA]) alone or as adjuvant treatment, particularly in controlling mucosal bleeds and for invasive dental procedures. **CB**

## **2.5 | Home therapy**

- Home therapy gives people with hemophilia immediate access to CFCs or other coagulation therapies and hemostatic agents (e.g., emicizumab, DDAVP, antifibrinolytics) and hence enables optimal early treatment, resulting in less pain, dysfunction, and long-term disability, and significantly reduced hospitalization rates for hemophilic bleeding complications, especially for those on prophylaxis compared to episodic therapy.<sup>41-43</sup>
- Home therapy also offers people with hemophilia substantially improved quality of life including less school/work absenteeism, the ability to safely participate in a larger variety of sports and physical activities, greater employment stability, and greater freedom to travel.<sup>44</sup>
- Home therapy must be supervised closely by the comprehensive care team and should only be initiated after comprehensive patient/caregiver education and training.<sup>41,42</sup>
- Education should focus on instilling essential knowledge of hemophilia and the basics of home therapy, including:
  - recognition of bleeds and common complications;
  - first-aid measures;
  - dosage calculation;
  - storage, preparation, and administration of CFCs and/or other treatment products;
  - aseptic techniques;
  - venipuncture (or access through a central venous catheter) and self-infusion/self-injection;
  - record-keeping;
  - proper storage and disposal of needles/sharps;
  - handling of blood spills.

- A patient/caregiver home therapy certification program is helpful for acknowledging and ensuring readiness to begin home therapy.
- Treatment adherence, level of education, and understanding of episodic and prophylactic treatment, infusion/injection techniques, and bleed records should be reviewed and evaluated with patients and family caregivers at clinic checkups.
- See also “Self-management” below.

### **Clotting factor replacement therapy**

- Home therapy with CFCs should ideally be achieved with products that are safe and are easily reconstituted. CFCs can be stored at room temperature or in a domestic refrigerator, depending on the product. People with hemophilia must be skilled in self-infusion to minimize time to treatment and improve their joint health outcomes.<sup>45</sup>
- Home therapy with CFCs can be started with young children with adequate venous access and motivated family caregivers who have undergone comprehensive training. Older children and teenagers can learn self-infusion with education and training from the hemophilia nurse coordinator (or home infusion nurse, where available) and family support.
- See “Self-management” below and Chapter 6: Prophylaxis in Hemophilia.

### **New coagulation therapies**

- The use of new innovative therapies administered via different routes requires carefully planned patient/caregiver education, training, and supervision including specific training for those transitioning to another type of therapy (e.g., from intravenous factor replacement therapy to subcutaneous factor substitution therapy with emicizumab).
- Patients and their caregivers should understand the differences, benefits, and any risks associated with a particular treatment. Importantly, they should be taught how to monitor treatment and response, and under which circumstances they should contact their healthcare provider and/or hemophilia treatment centre (e.g., breakthrough bleeding, upcoming surgery).

#### **Emicizumab**

- People with hemophilia A on prophylaxis with emicizumab may begin home therapy after proper training in subcutaneous injection technique.<sup>46</sup>
- Emicizumab and those non-factor agents in development differ from conventional types of prophylaxis as they do not replace the missing coagulation factor, are administered



subcutaneously and, in some cases, can be administered as infrequently as once or twice monthly.<sup>47</sup> Additionally, these agents are not associated with the peak and trough curves of protection that are now seen with factor prophylaxis regimens.

- Efficizumab's subcutaneous route of administration is already making it easier to start pediatric patients on prophylaxis at very young ages and without the need for central venous access devices (CVADs). Efficizumab makes it feasible to initiate prophylaxis at birth to provide protection of newborns and infants newly diagnosed with severe hemophilia A; however, further research in infants less than 1 year of age is required.<sup>48</sup>
- Efficizumab is not intended to treat acute bleeding episodes. Breakthrough bleeding is treated with doses of CFCs (or bypassing agents in the case of patients with inhibitors) that are sufficient to achieve hemostasis. Caution is required when treating breakthrough bleeding episodes while on efficacyzumab as several patients have developed either venous thromboembolism or thrombotic microangiopathy with concomitant administration of activated prothrombin complex concentrate (aPCC).<sup>49</sup> Consult the individual product inserts for precautions and risk management guidance.
- See Chapter 5: Hemostatic Agents, Chapter 6: Prophylaxis in Hemophilia, and Chapter 8: Inhibitors to Clotting Factor.

### Self-management

- Self-management focuses on patient empowerment and refers to a patient's ability to acquire the necessary skills and knowledge to become competent in their own care and apply it in their daily activities to keep their condition under control and minimize its impacts on their physical and psychological health.<sup>45</sup> For people with hemophilia, self-management requires concrete knowledge of bleeding mechanisms and treatment strategies (when and how to treat and what dose to give).<sup>45</sup>
- The key self-management skills required for people with hemophilia include<sup>45</sup>:
  - bleed recognition;
  - self-infusion/self-treatment skills;
  - self-care (i.e., nutrition and physical fitness) and medicines management (i.e., record-keeping, treatment routines, maintenance of adequate treatment supply, skills in storage, reconstitution, and administration of treatment products);
  - pain management; and
  - risk management and conceptualizing preventive therapy.

- Knowledge of appropriate adjunctive therapies (e.g., antifibrinolytics, pain medications) and adjunctive management (e.g., the PRICE principles) are also important to self-management.
- See 2.3 Fitness and physical activity, 2.4 Adjunctive management, and 2.5 Home therapy, above, and 2.6 Pain management, below.

### Bleed recognition

- Bleed recognition, especially of joint and muscle bleeds, is an essential part of self-management so that prompt treatment can be initiated to minimize the short and long-term impacts of bleeds. In hemophilia, a wait-and-see approach for potential bleeds or missed doses may result in the onset and progression of bleeding symptoms that are not only painful but ultimately lead to joint damage.
- It is important for family members/caregivers to be able to recognize subtle signs of bleeds in young children with hemophilia; in infants and young children, reluctance to use a limb may be indicative of a joint/muscle bleed.<sup>50</sup> The signs and symptoms of common types of hemorrhage in hemophilia<sup>50</sup> are described in Chapter 7: Treatment of Specific Hemorrhages and Chapter 11: Outcome Assessment.
- For those on prophylaxis with new types of coagulation therapy, it is important to monitor and assess the ability of patients/caregivers to recognize breakthrough bleeds and initiate prompt episodic treatment with CFCs or appropriate hemostatic agents.

### Self-infusion/self-treatment

- In young children, injections or infusions are normally given by the parents and/or caregivers until the child is old enough to switch to self-treatment.<sup>51</sup>
- Children with hemophilia typically learn to self-infuse or self-inject in late childhood or early adolescence. Self-infusion requires skill and expertise developed through trial and error as well as education and support.<sup>45</sup> Becoming sufficient at self-infusion is complex as it requires a one-handed technique to perform all steps; however, most children self-infuse at least part of the time by 12 years of age.<sup>45</sup>
- Establishing routines, such as self-infusing at the same time every day, can help significantly with treatment adherence.<sup>45</sup>

### RECOMMENDATION 2.5.1:

- **Patients (or caregivers of children) with hemophilia should be taught how to manage their care at home**

**and be able to demonstrate understanding of how to recognize bleeds and the ability to infuse or self-infuse, with monitoring of venous access skills over the patient's lifetime. **CB****

### *Self-care and medicines management*

- Because people with hemophilia self-manage largely at home, healthcare providers have to depend on the patient/caregiver to inform them of their type of bleed episodes, bleeding frequency, and usage of treatment products.<sup>52</sup>
- Therefore, it is important for patients/caregivers to keep accurate bleed treatment records (paper or electronic) that include the date and site of bleeding, the dosage and lot number of the product used, any adverse effects, bleed-related activities, and other outcomes to be reported as required.
- Hemophilia treatment centres now have the option to use electronic diaries (e-diaries) in the form of smartphone applications, handheld wireless monitoring systems, and online platforms that allow real-time entries and direct data analysis. With these tools, healthcare providers no longer need to rely on patient visits to the hemophilia treatment centre to review paper diaries.<sup>53-56</sup>
- Studies on e-diaries have demonstrated that their use increases the amount of information provided as well as the completeness of data reporting.<sup>53</sup> Remote patient record management may also improve treatment compliance, increase patient quality of life, support healthcare providers in modifying treatment regimens, and improve communication with the healthcare team.<sup>54-56</sup>

### **RECOMMENDATION 2.5.2:**

- **For patients with hemophilia, a detailed record of all treatments administered (reason, batch number, number of units, etc.) should be documented and used to personalize treatment plans. **CB****

### *Risk management and conceptualizing preventative therapy*

- Risk management requires the ability to judge and balance chances and risks encountered in daily life, including controlling and navigating risks that arise and distinguishing between negative risk-taking and positive risk management.<sup>45</sup> In addition, it requires being able to self-advocate for appropriate hemophilia care with support from the hemophilia treatment centre such as emergency care, surgical management, or dental treatment. (See 2.3 Fitness and physical activity, above, 2.7 Dental care and management, below, and Chapter 9: Specific Management Issues.)

- In addition, healthcare providers can educate and guide people with hemophilia in planning their daily lives to reduce bleeding risk. Strategies may include adapting the treatment regimen to fit within other priorities (e.g., school and sports), routines, activities, and events in their lives.<sup>45</sup>

### **Central venous access devices**

- An implanted central venous access device can enable stable, long-lasting venous access to make infusions easier and may be required for administering prophylaxis or immune tolerance induction (ITI) therapy in young children with problematic venous access.<sup>57,58</sup>
- The complications and risks associated with surgical implantation of CVADs (i.e., hospitalization, bleeding, catheter infection, thrombosis, breakage, and/or malfunction) need to be weighed against the advantages of early initiation of intensive prophylaxis.<sup>59-61</sup> Many pediatricians and hemophilia treaters are shifting from the use of CVADs to peripheral venous access for early initiation of prophylaxis, starting with once-weekly prophylaxis then gradually escalating infusion frequency,<sup>62</sup> together with more intensive caregiver training.
- Alternatively, the use of emicizumab obviates the need for CVADs, and it is increasingly among the treatment options for people with hemophilia A in many countries. (See Chapter 6: Prophylaxis in Hemophilia.)
- The protocol used for device care (using aseptic precautions), quality of patient/caregiver education, and user compliance may affect frequency of infections; therefore, careful guidelines and surveillance protocols are important to reduce the risk of complications.<sup>59</sup>
- Parents and caregivers must be taught to keep CVADs scrupulously clean and to flush out the catheter properly after each therapy administration to prevent CVAD infection and clot formation.<sup>59</sup> Fibrinolytic agents may be helpful for preventing clotting and infections.<sup>60</sup>
- It is essential to ensure that parents and caregivers have a thorough understanding of all aspects of home therapy and are prepared and able to handle the issues and challenges that commonly arise in children with hemophilia at each development stage. (See 2.8 Transition from pediatric to adult care, below.)
- For patients in whom venous access is problematic, non-factor replacement therapy that can be administered subcutaneously (i.e., emicizumab) should be considered. (See Chapter 6: Prophylaxis in Hemophilia – Non-factor replacement therapy.)

**RECOMMENDATION 2.5.3:**

- For children with hemophilia, central venous access devices could be considered to facilitate early access to bleed treatment and prophylaxis. **CE**

**2.6 | Pain management**

- Acute and chronic pain are common in people with hemophilia. Proper assessment of the cause of pain is essential.<sup>63</sup>
- See also Chapter 7: Treatment of Specific Hemorrhages.

**RECOMMENDATION 2.6.1:**

- For people with hemophilia with acute or chronic pain, the WFH recommends the use of age-appropriate pain assessment tools to determine the cause and guide appropriate management. **CE**

**Pain caused by venous access**

- In general, no pain medication is given. If required, application of a local anesthetic spray or cream at the site of venous access may be helpful.<sup>64-66</sup>

**RECOMMENDATION 2.6.2:**

- For people with hemophilia with venous access pain, discomfort or anxiety, the WFH recommends the application of a local anesthetic spray or cream at the site of venous access. **CE**

**Pain caused by joint or muscle bleeding**

- While hemostatic treatment should be administered as soon as possible to stop bleeding, additional medications are often needed for pain control (see Table 2-4).
- Other adjunctive measures may be required.<sup>40</sup>
- See also Chapter 10: Musculoskeletal Complications.

**RECOMMENDATION 2.6.3:**

- For people with hemophilia with acute pain due to a joint or muscle bleed, the WFH recommends immediate administration of clotting factor concentrates to stop bleeding, pain medication, and adjunctive measures such as immobilization, compression, and splinting to minimize pain, if appropriate. **CE**

**Postoperative pain**

- Intramuscular injection of analgesics should be avoided.
- Postoperative pain management should be coordinated with the anesthesiologist or pain specialist.

- Initially, narcotic analgesics can be given, followed by an oral opioid.
- When pain decreases, paracetamol/acetaminophen may be used.

**RECOMMENDATION 2.6.4:**

- For patients with hemophilia and postoperative pain, the WFH advises proportionate management of postoperative pain in coordination with the anesthesiologist or pain specialist. **CE**

**RECOMMENDATION 2.6.5:**

- For patients with hemophilia and postoperative pain, the WFH recommends analgesia similar to that used in patients without hemophilia including, as appropriate, the use of intravenous morphine or other narcotic analgesics, followed by an oral opioid (e.g., tramadol, codeine, hydrocodone, etc.) and paracetamol/acetaminophen as pain decreases.
- **REMARK:** With the exception of selective COX-2 inhibitors, NSAIDs should not be used in patients with hemophilia.
- **REMARK:** The intramuscular route for administration of analgesia is not advised. **CE**

**TABLE 2-4** Pain management strategies for people with hemophilia

Severity	
1	Paracetamol/acetaminophen <i>If not effective</i> ↓
2	COX-2 inhibitor <sup>a</sup> (e.g., celecoxib, meloxicam, nimesulide, and others) <i>or</i> paracetamol/acetaminophen plus codeine (3-4 times/day) <i>or</i> paracetamol/acetaminophen plus tramadol (3-4 times/day)
3	Morphine: Use a slow-release product with a rapid-release product as an escape analgesic. Increase use of the slow-release product if the rapid-release product is used more than 4 times/day.

Note: If for any reason medications have been stopped for a period of time, individuals who have been taking and tolerating high-dose narcotic drugs should restart the drug at a lower dose, or use a less powerful painkiller, under the supervision of a physician.

<sup>a</sup>COX-2 inhibitors should be used with caution by people with hemophilia with hypertension and renal dysfunction.

### Pain due to chronic hemophilic arthropathy

- Chronic hemophilic arthropathy develops in individuals who have not had adequate treatment and follow-up physical therapy and rehabilitation for joint and muscle bleeds.
- Pain management for chronic hemophilic arthropathy should include functional training and adaptation, and appropriate analgesics as detailed in Table 2-4.<sup>19,67-69</sup>
- Pain medications that may be used by people with hemophilia for chronic hemophilic arthropathy include paracetamol/acetaminophen, selective COX-2 inhibitors, tramadol, and opioid analgesics.<sup>70,71</sup> Other NSAIDs should be avoided in people with hemophilia.<sup>72</sup> Codeine should not be administered to children under 12 years of age.
- For individuals with disabling chronic pain due to hemophilic arthropathy, orthopedic surgery may be indicated.<sup>73</sup>
- See Chapter 10: Musculoskeletal Complications – Hemophilic arthropathy.

#### RECOMMENDATION 2.6.6:

- For people with hemophilia and chronic hemophilic arthropathy in need of pain management, the WFH recommends functional training and adaptations alongside appropriate analgesics. **CB**

#### RECOMMENDATION 2.6.7:

- For people with hemophilia and chronic hemophilic arthropathy, the WFH recommends education on pain management including the use of complementary pain management techniques (e.g., meditation, distraction, mindfulness, or music therapy). **CB**

#### RECOMMENDATION 2.6.8:

- For children and adults with hemophilia with pain due to chronic hemophilic arthropathy, the WFH recommends the use of paracetamol/acetaminophen, selective COX-2 inhibitors, tramadol, or morphine, and avoidance of other NSAIDs. Codeine may be used for children over 12 years of age but is contraindicated in younger children.
- **REMARK:** Prolonged use of these medications may have risks of dependence or addiction, as well as organ damage, and must be carefully monitored.
- **REMARK:** People with persistent pain should be referred to a specialized pain management team. **CB**

#### RECOMMENDATION 2.6.9:

- For patients with hemophilia with disabling pain from chronic hemophilic arthropathy, the WFH recommends

referral to an orthopedic specialist for consideration of orthopedic surgery. **CB**

### Dental pain

- People with hemophilia experiencing dental pain should always be referred for a professional dental consultation. Proportionate pain management measures should be applied (see Table 2-4).

#### RECOMMENDATION 2.6.10:

- For children and adults with hemophilia, the WFH recommends interim management of dental or orofacial pain according to a proportionate approach for pain relief and referral to a dental care professional for assessment. **CB**

## 2.7 | Dental care and management

- Maintaining good oral health and preventing dental problems is of great importance in people with hemophilia to prevent oral diseases and conditions such as gingivitis, dental caries, and periodontal diseases which may cause serious gum bleeding, especially in those with severe/moderate hemophilia,<sup>74</sup> and to avoid the need for major dental surgery.<sup>75</sup>
- Since prolonged bleeding after dental treatment can cause severe or even life-threatening complications, people with hemophilia are a priority group for preventive dental and oral health care.<sup>74</sup>
- It is important to ensure that people with hemophilia have access to dental treatment and regular preventive dental care at a designated dental care centre with expertise in the management of people with hemophilia according to evidence-based dental protocols.<sup>75-77</sup>
- See also Chapter 7: Treatment of Specific Hemorrhages – Oral hemorrhage.

#### RECOMMENDATION 2.7.1:

- For children and adults with hemophilia, the WFH recommends provisions for access to regular preventive dental and oral health care as part of comprehensive hemophilia care. **CB**

#### RECOMMENDATION 2.7.2:

- For children with hemophilia, the WFH recommends referral to a designated dental care centre at the time of the first tooth eruption (around 6 months of age) or by age 1 in order to reduce the complications, morbidity,

costs, and health and psychosocial impacts associated with oral diseases in people with hemophilia. **CB**

#### **RECOMMENDATION 2.7.3:**

- For adults with hemophilia, the WFH recommends facilitating access to appropriate adult dental services and procedures, with regular dental assessments throughout their lives to monitor and safeguard oral health using evidence-based and personalized preventive dental protocols. **CB**

#### **RECOMMENDATION 2.7.4:**

- For people with hemophilia, the WFH recommends preventive dental and oral care as a priority to ensure optimal oral health and hygiene to prevent periodontal disease and dental caries, which predispose to gum bleeding, dental pain, tooth loss, chewing difficulties, and social impacts. **CB**

#### **Oral care**

- Optimal oral hygiene is essential to prevent periodontal disease and dental caries, which predispose to gum bleeding, dental pain, tooth loss, chewing difficulties, and social impacts (e.g., halitosis and low self-esteem).<sup>76,78</sup> This involves the use of oral hygiene products and toothbrushes which can be adapted based on individual needs.<sup>79</sup>
- Dental pain occurring spontaneously or with facial swelling usually indicates the presence of advanced stages of oral disease and/ or infection and should trigger a professional dental consultation. Short-term pain control should be achieved as described (see 2.6 Pain management, above), with paracetamol/acetaminophen as the drug of choice to manage toothache in children.<sup>77</sup>

#### **RECOMMENDATION 2.7.5:**

- For all people with hemophilia, the WFH recommends education on the importance of good oral hygiene to prevent dental problems and complications, including instructions for twice-daily brushing of the teeth using a soft- or medium-texture toothbrush and fluoridated toothpaste to remove plaque deposits; the toothpaste should not be rinsed away but rather retained (“spit, but don’t rinse”) after brushing to maximize fluoride benefit.
- **REMARK:** The use of dental floss or interdental brushes should be encouraged to ensure complete plaque removal.
- **REMARK:** Individuals with elbow or shoulder restrictions may benefit from modified or electric toothbrushes and flossing aids. **CB**

#### **RECOMMENDATION 2.7.6:**

- For children with hemophilia 6 years of age and younger, the WFH recommends parental/caregiver supervision of toothbrushing. **CB**

#### **Dental surgery and invasive procedures**

- Before any dental surgery or other invasive procedure within the oral cavity, hemostasis management should be individually planned under the advisement of a hematologist.<sup>80</sup>
- Systemic or topical antifibrinolytics (i.e., tranexamic acid or EACA) are effective as adjunct treatment in the management of dental interventions pre- and postoperatively and have the potential to reduce the need for factor replacement therapy.<sup>76,81,82</sup>
- Antibiotics should only be prescribed if clinically indicated for management of infection.
- Local hemostatic measures such as wound suture, topical antifibrinolytics, oxidized cellulose, and fibrin sealant should be used as appropriate whenever possible following a dental extraction.<sup>82,83</sup>
- Patients must be advised to immediately report any prolonged bleeding and/or difficulty speaking, swallowing, or breathing following dental surgery to the hematologist/dental surgeon as this can be life-threatening. Those who are not in hospital must report to the nearest emergency centre without delay.
- For many dental procedures, adequate local anesthesia is necessary, and most dental injections can be delivered safely.<sup>84,85</sup>
- Higher-risk intramuscular oral injections may require systemic hemostatic measures. These measures should be established preoperatively under advisement of a hematologist.<sup>80</sup>
- Alternative low-risk routes of delivery such as intraligamentary single-tooth anesthesia (STA) or buccal infiltration injections are effective alternatives to inferior alveolar nerve blocks (IDB).<sup>84,86</sup>
- Other nonsurgical dental procedures carry variable levels of bleeding risk. Most restorative dental procedures such as dental fillings are low risk and can be carried out without the need for factor replacement therapy.
- Minimally invasive buccal infiltration or intraligamentary injections and techniques to protect soft tissues should be used, and standard local measures to aid mucosal hemostasis should be applied as appropriate.
- Professional dental cleanings can be provided with the use of antifibrinolytic agents, if necessary.<sup>82</sup>

**RECOMMENDATION 2.7.7:**

- For patients with hemophilia, the WFH recommends that dental extraction or other invasive procedures within the oral cavity (e.g., dental implantation, periodontal surgery, or gum biopsy) be performed only with a personalized plan for hemostasis management in consultation with a hematologist. **CE**

**RECOMMENDATION 2.7.8:**

- For patients with hemophilia, the WFH recommends the use of systemic or topical tranexamic acid or epsilon aminocaproic acid (EACA) as adjunct treatment in the management of dental interventions pre- and postoperatively, to reduce the need for factor replacement therapy. **CE**

**RECOMMENDATION 2.7.9:**

- For patients with hemophilia requiring dental extractions, the WFH recommends local hemostatic measures. Typical procedures include wound suture, topical use of antifibrinolytics, oxidized cellulose, and fibrin sealant, applied as appropriate.
- **REMARK:** Patients should be advised to maintain a soft diet and undertake careful brushing around the wound site for a minimum of 3-5 days postoperatively to avoid disturbing the clot and wound healing within the tooth socket. **CE**

**RECOMMENDATION 2.7.10:**

- For patients with hemophilia, the WFH recommends appropriate local anesthesia for dental treatments as an essential part of pain and anxiety management. Most dental injections pose a low risk for patients with hemophilia when delivered by a dental care professional using local anesthesia with a vasoconstrictor, and when the agent is delivered slowly with a single-use fine-gauge needle. **CE**

**RECOMMENDATION 2.7.11:**

- For patients with hemophilia requiring higher-risk intramuscular oral injections commonly associated with the provision of surgical dentistry (such as inferior alveolar dental block [IDB], superior alveolar nerve block, or injections in the floor of the mouth or vascular lingual tissues), the WFH recommends systemic hemostatic measures preoperatively to avoid the risk of hematoma. These measures should be established in consultation with the hematologist.

- **REMARK:** The availability and effectiveness of alternative low-risk routes of local anesthetic delivery (such as intraligamentary single-tooth anesthesia, or buccal infiltration injections with 4% articaine) are effective alternatives to IDB and permit dental procedures in primary and permanent mandibular molar teeth. **CE**

**RECOMMENDATION 2.7.12:**

- For patients with hemophilia, the WFH recommends the use of antifibrinolytic agents as effective adjunct treatment in the management of dental hygiene therapies that facilitates access to regular dental care delivered by a dental hygienist. **CE**

**RECOMMENDATION 2.7.13:**

- In patients with hemophilia, the WFH asserts that the presence of blood-borne infections does not affect the safety of dental treatment as stringent universal cross-infection procedures are now mandatory across all disciplines of dentistry and recommends the provision of full dental services regardless of infectivity or immunological status. **CE**

**2.8 | Transition from pediatric to adult care**

- At different life stages, people with hemophilia and their caregivers go through transitions that involve transfer of care beyond the family, such as when a young person with hemophilia starts school, a new sport or leisure activities, and adolescence, and when moving from pediatric to adult medical care, moving away from home, starting new relationships, and making career choices.<sup>51</sup>
- Parents and/or caregivers typically assume primary responsibility for the management of care for children and adolescents with hemophilia; in particular, for administering treatment and maintaining adherence to therapeutic regimens.<sup>51</sup>
- Two transition periods are particularly challenging for treatment adherence: when adolescents switch to self-treatment; and when young adults move away from home and assume full responsibility for self-care.<sup>51</sup> Many children and adolescents with hemophilia on prophylaxis who receive excellent comprehensive care do not experience the serious sequelae of their disorder, which may result in complacency in young adulthood.<sup>87</sup>
- Ideally, young people with hemophilia should obtain the necessary knowledge and skills for self-management before transitioning to adult care; however, many young

people still require parental assistance with hemophilia care even in their later teenage years.<sup>87</sup>

- Adherence to prophylaxis has been found to be suboptimal in many adolescents (13-17 years of age) and young adults (18-30 years of age) with hemophilia.<sup>51</sup>
- In general, the main barriers to adherence to prophylaxis include high perceived burden of treatment; no or low burden of bleeds and symptoms; venous access difficulties; and viewing prophylaxis as complicated and time-consuming.<sup>51</sup>
- In adolescents and young adults with hemophilia in particular, barriers to treatment adherence include<sup>51</sup>:
  - low symptom burden;
  - forgetfulness and lack of basic self-management skills such as treatment routines;
  - lack of knowledge about hemophilia, including low perceived benefit of prophylaxis;
  - inability to identify and act on bleeds;
  - disease denial;
  - the desire to be “normal”;
  - perceived negative impact on activities and social participation;
  - lack of transition planning;
  - difficulties with self-treatment; and
  - challenges communicating with a hemophilia treatment centre to receive optimal care.
- The transition to adulthood, with increased independence in living situations (e.g., living alone or away at college/university) and financial responsibilities, may be particularly challenging for young adults with hemophilia.<sup>88</sup>
- Hemophilia treatment centres and healthcare providers can play an important role in helping young people with hemophilia maintain treatment adherence as they make the transition to adulthood, by ensuring that patient education encompasses knowledge and technical skills and development of self-efficacy and self-management skills including psychosocial coping.<sup>51</sup>
- As no definitive systematic approach to transition from pediatric to adult care has yet been defined, the comprehensive care team should continuously assess and follow up on individual needs, preferences, and barriers to treatment adherence with age-appropriate, tailored support.<sup>51,89</sup>
- Key components of transition strategies include<sup>51</sup>:
  - development of a structured transition plan;
  - monitoring with systematic assessments of a patient’s readiness;
  - individualized support; and
  - added support when switching to self-treatment or moving away from home.

- In addition, readiness self-assessment tools, such as the *HEMO-Milestones* tool, may be useful for promoting a standardized approach to assess self-management competency.<sup>90</sup>
- Outcome indicators for assessing the effectiveness of transition from pediatric to adult hemophilia care include:
  - measurement of adherence;
  - any change in bleeding rate;
  - self-efficacy skills;
  - hemophilia knowledge;
  - patient and caregiver satisfaction;
  - time gap between last pediatric and first adult clinic visit; and
  - number of emergency room or hospital admissions.<sup>91</sup>
- Self-management programs available on the Internet may also help to support young people with hemophilia in their transition to adult care.<sup>87</sup>
- See Chapter 6: Prophylaxis in Hemophilia and Chapter 11: Outcome Assessment.

#### **RECOMMENDATION 2.8.1:**

- **Children and adolescents with hemophilia should be supported with ongoing education and skills development, including the ability to self-infuse and other self-efficacy skills, to gain necessary hemophilia knowledge for self-management of their condition before they make the transition from pediatric to adult care.**
- **REMARK: The comprehensive care team should support young patients and their families through the transition period. When possible, the first visit should be performed by both the pediatric and adult hematologists. CB**

#### **RECOMMENDATION 2.8.2:**

- **For adolescents with hemophilia on prophylaxis, the WFH recommends individual education and training, ideally from a hemophilia nurse coordinator, to ensure adequate knowledge of hemophilia, and to support prophylaxis adherence and self-care management. This should include understanding measurements of adherence, as well as factors and risks that can lead to changes in bleeding rates. CB**

#### **RECOMMENDATION 2.8.3:**

- **For adolescents 12-18 years of age with hemophilia, the WFH recommends age-specific hemophilia camps to foster peer group support and develop their self-infusion skills and understanding of the importance of adherence to treatment. CB**

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#### **SUPPORTING INFORMATION**

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