11 OUTCOME ASSESSMENT

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

11.1 | Introduction

- In order to optimize treatment and make economically sound clinical decisions, objective evidence of both short- and long-term outcomes of treatment regimens is required.[1]
- Outcome refers to the condition of a patient that results from a disease or medical intervention. It is assessed by clinical evaluation including the use of generic and disease-specific health-related quality of life (HRQoL) assessment instruments, measures of patient-reported outcomes (PROs), and laboratory tests including imaging studies.[2-7] These instruments measure a variety of parameters including activities and participation, body structure and function, burden of disease, and subjective health status, as described later in this chapter.
- Both generic and hemophilia-specific assessment instruments make it possible to evaluate the nature of the physical impairments and functional limitations and their impacts on the lives of people with hemophilia and their families.[1]
- The increasing use of these instruments will standardize assessment and permit comparison of data between individuals and cohorts.[8-10]

Purposes of outcome assessment

- Outcome assessment may be used to follow an individual's disease course, obtain information to guide routine clinical care, measure response to therapy, and determine whether there is a need to modify therapy. Outcome assessment may also be used to quantify the health of a group of patients, measure quality of care, and advocate for resources.
- In addition, outcome assessment may be used for research purposes such as to document the natural history of the disease, test new therapies, or compare different therapies.
- Health outcome research may be used to inform decisions regarding expenditures on treatment.

11.2 | Outcome assessment in hemophilia

- Outcome assessment in hemophilia should cover two aspects: disease-related and therapy-related outcomes.
- Disease-related outcomes pertain to the effectiveness of hemostatic therapy and are reflected in outcomes such as:
  - frequency of bleeding; and
  - impact of bleeding on the musculoskeletal system and other systems in the short and long term, including the psychosocial impact of hemophilia.
- Therapy-related outcomes need to be monitored using a prospective and systematic plan and should include screening and testing of people with hemophilia treated with clotting factor concentrates (CFCs) for inhibitor development. (See Chapter 8: Inhibitors to Clotting Factor.)
- Other less common complications of CFC replacement therapy include thrombosis and allergic/anaphylactic reactions. (See Chapter 9: Specific Management Issues.)

Frequency of bleeding

- Frequency of bleeding (particularly joint and muscle bleeds) and response to treatment have been the most important indicators of the effectiveness of hemostatic therapy and the best surrogate predictors of long-term musculoskeletal outcomes.
- All bleeds must be documented by patients/caregivers in real time as they occur using manual or electronic diaries or other reporting systems, and analyzed periodically (at least once a year) by their hemophilia treater using a standard protocol. (See Chapter 2: Comprehensive Care of Hemophilia – Home therapy – Self-management.)
- In particular, bleeding into the central nervous system (CNS) requires documentation because of its potential impact on neurological and musculoskeletal functions.
- Given the potential difficulties in clinical determination of joint and muscle bleeding and to bring consistency into documenting this important parameter, criteria defined by the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis should be followed.[11]
- A joint bleed is defined as an unusual sensation "aura" in the joint, in combination with any of the following[11]:
  - increasing swelling or warmth of the skin over the joint;
  - increasing pain; or
  - progressive loss of range of motion or difficulty in using the limb as compared with baseline.
- A muscle bleed is defined as an episode of bleeding into a muscle, determined clinically and/or by imaging studies, generally associated with pain and/or swelling and loss of movement over baseline.[11]
- In infants and young children, reluctance to use the limb alone may be indicative of a joint or muscle bleed.[11]
- Definitions for effectiveness of hemostatic therapy for joint and muscle bleeds have been developed and should be used when documenting treatment outcomes. (See Chapter 7: Treatment of Specific Hemorrhages – Table 7-1.)

RECOMMENDATION 11.2.1:

- **For providers of care for people with hemophilia, the WFH recommends ensuring that the frequency of all bleeds is documented in real time by patients/caregivers and reviewed together at least annually, with particular reference to intra-articular, intramuscular, and central nervous system bleeds, including their recovery status. Standard criteria defined by the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis should be used.** CB

Pain assessment in hemophilia

- Pain in hemophilia can be either acute (as in an acute bleed) or chronic (as a result of arthropathy), or both may occur concurrently.
- Hemophilia-related pain can be assessed using single-dimensional numerical or visual rating scales[12] such as the Wong-Baker FACES Scale,[13,14] or multi-dimensional pain questionnaires like the generic McGill Pain Questionnaire[15] or the Brief Pain Inventory (BPI),[16,17] or disease-specific instruments like the Multidimensional Haemophilia Pain Questionnaire (MHPQ).
- Pain can also be scored through subscales within quality-of-life questionnaires—both generic[18] and disease-specific[19] questionnaires—and also within specific joint assessment instruments such as the Gilbert Score[20] and the Hemophilia Joint Health Score (HJHS).[21]
- Pain is best assessed and addressed in the context of a comprehensive care setting.[16]

Domains to assess the impact of bleeding on the musculoskeletal and other systems

- In conditions like hemophilia, it is recommended that outcomes be assessed according to the domains in the International Classification of Functioning, Disability and Health (ICF) model of the World Health Organization (WHO).[22,23]
- According to the ICF, evaluation of disability and health[4,24] should focus on the impact of the disease on body structures and functions, activities, and participation.
- These domains can be affected by individual contextual factors, which represent a person's circumstances and background, and include both environmental and personal factors.
- Environmental factors comprise the physical, social, and attitudinal environments in which an individual lives and conducts day-to-day activities.
- Personal factors include aspects that are not necessarily part of an individual's health condition or health status, such as age, sex, and indigenous status.
- See Figure 11-1 for an overview of the ICF model and outcome assessment instruments by domain.
- The concept of quality of life (QoL) is complex and encompasses many characteristics of an individual's social, cultural, economic, and physical environments as well as physical and mental health state.[4,22]
- Health-related quality of life (HRQoL) is a synonym for self-reported health state; HRQoL measurements generally include several aspects of the ICF model.[25] To be

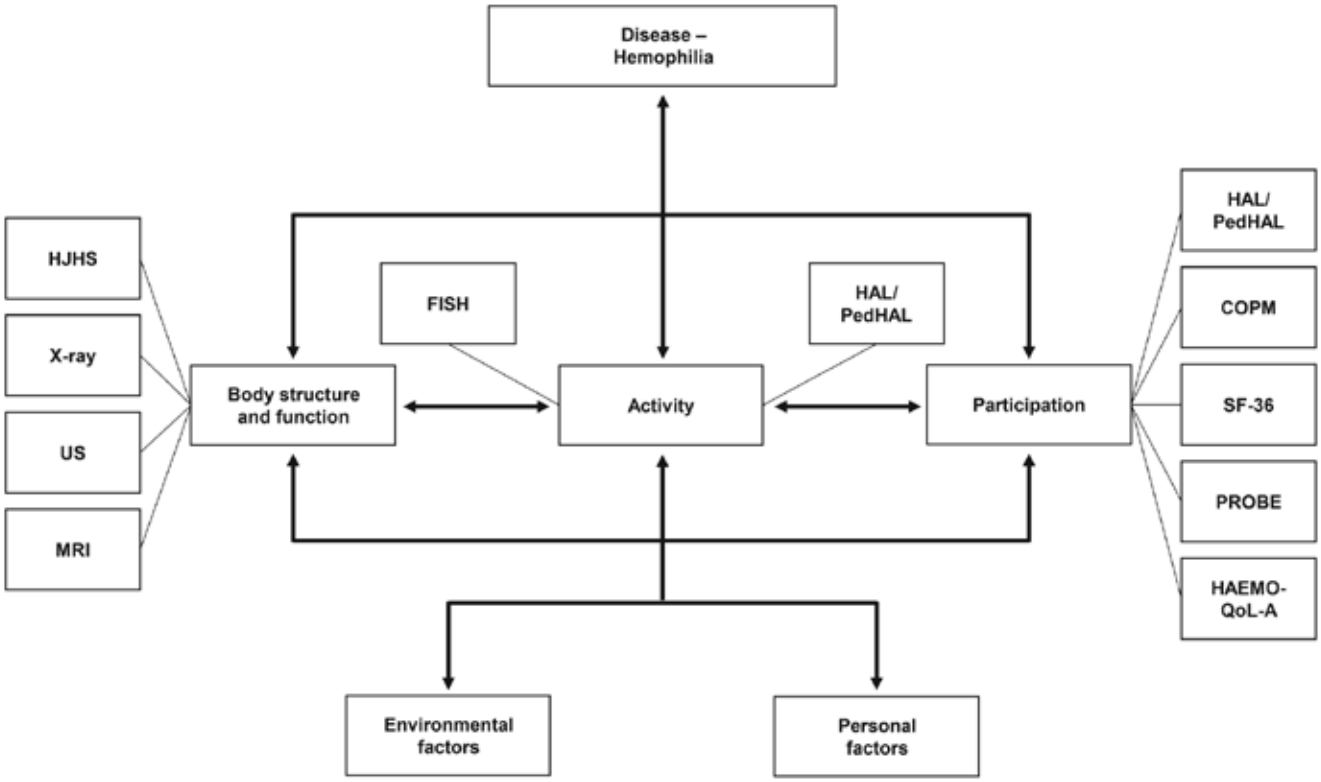

FIGURE 11-1 International Classification of Functioning and Health (ICF) model, with domain-related outcome assessment instruments. COPM, Canadian Occupational Performance Measure; FISH, Functional Independence Score in Hemophilia; HAEMO-QoL-A, hemophilia-specific quality-of-life questionnaire for adults; HAL, Haemophilia Activities List; HJHS, Hemophilia Joint Health Score; MRI, magnetic resonance imaging; PaedHAL, Haemophilia Activities List for children; PROBE, Patient-Reported Outcomes, Burdens and Experiences; SF-36, 36-Item Short Form Survey Instrument; US, ultrasound

meaningful, this is best not used in isolation but in addition to assessment of body structure, function, and activities.

- While most outcome assessment instruments have been validated for older children, there is a paucity of validated disease-specific instruments to assess outcomes in very young children with severe hemophilia (i.e., younger than 4 years of age) during the period when they are typically started on long-term prophylaxis and the chances of inhibitor development are at their highest.
- The ability of the instruments to detect subtle changes following treatment interventions in children with good joint status and low bleeding frequency is limited and needs further attention.[26]

11.3 | Body structure and function

- Body structure refers to anatomical structures and bodily parts, such as organs, limbs, and their components.[22,24]
- Body function refers to the physiologic functions of these systems, such as range of motion, strength, and joint stability.
- In hemophilia, this refers to, for example, the status of joints and specific muscle groups, assessed both clinically and radiologically.

Recommended measures of body structure and function in hemophilia

- The Hemophilia Joint Health Score (HJHS) is the best studied of the physical examination instruments in both children and adults.[21,27,28] (See Figure 11-2.)

Subject ID #:_____ **Name of Physiotherapist:**_____

Assessment #: _____ **Date:** _____
yyyy / mm / dd

Time: _____

Hemophilia Joint Health Score 2.1 - Summary Score Sheet

	Left Elbow		Right Elbow		Left Knee		Right Knee		Left Ankle		Right Ankle	
Swelling		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Duration (swelling)		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Muscle Atrophy		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Crepitus on motion		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Flexion Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Extension Loss		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Pain		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Strength		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE		☐ NE
Joint Total												

Sum of Joint Totals + [ ]

Global Gait Score [ ]

(☐ NE included in Gait items)

HJHS Total Score = [ ]

NE = Non-Evaluable

Swelling
0 = No swelling
1 = Mild
2 = Moderate
3 = Severe

Duration
0 = No swelling or < 6 months
1 = ≥ 6 months

Muscle Atrophy
0 = None
1 = Mild
2 = Severe

Crepitus on Motion
0 = None
1 = Mild
2 = Severe

Flexion Loss

	Contralateral:	Normative Tables:
0	= < 5°	0= within range
1	= 5° - 10°	1 = 1° - 4°
2	= 11° - 20°	2 = 5° - 10°
3	= > 20°	3 = > 10°

Extension loss (from hyperextension)

	Contralateral:	Normative tables:
0	= < 5°	0= within range
1	= 5° - 10°	1 = 1° - 4°
2	= 11°- 20°	2 = 5° - 10°
3	= > 20°	3 = > 10°

Joint Pain
0 = No pain through active range of motion
1 = No pain through active range; only pain on gentle overpressure or palpation
2 = Pain through active range

Strength (Using The Daniels & Worthingham's scale)
Within available ROM
0 = Holds test position against gravity with maximum resistance (gr.5)
1 = Holds test position against gravity with moderate resistance (but breaks with maximal resistance) (gr.4)
2 = Holds test position with minimal resistance (gr. 3+), or holds test position against gravity (gr.3)
3 = Able to partially complete ROM against gravity (gr.3-/2+), or able to move through ROM gravity eliminated (gr.2), or through partial ROM gravity eliminated (gr.2-)
4 = Trace (gr.1) or no muscle contraction (gr.0)
NE = Non-evaluable

Global Gait (walking, stairs, running, hopping on 1 leg)
0 = All skills are within normal limits
1 = One skill is not within normal limits
2 = Two skills are not within normal limits
3 = Three skills are not within normal limits
4 = No skills are within normal limits
NE = Non-evaluable

NOTE: There is an accompanying instruction manual and worksheets that are required when administering the HJHS

General Comments:

_____
_____
_____
_____

FIGURE 11-2 Hemophilia Joint Health Score 2.1 – Summary Score Sheet.[42] Available at: http://www1.wfh.org/docs/en/Publications/Assessment_Tools/HJHS_Summary_Score.pdf

- The radiological Pettersson score[29] is the most widely used imaging measure of joint structure. This score is not sensitive to early changes; therefore, more sensitive instruments have been developed to assess arthropathy. (See Table 11-1.)
- Magnetic resonance imaging (MRI) is likely the most sensitive measure of joint structure. There are a number of scales that can be used to quantify arthropathy on MRI[30,31]; however, this modality is expensive, time consuming, and difficult to perform in small children. (See Table 11-2.)
- Ultrasound (US) scoring systems to assess hemophilic arthropathy are now available[32-35] and can detect joint effusion,[36] early joint disease,[37] and subclinical joint disease,[38] and promote medication adherence.[39] (See Table 11-3.)
- US scoring algorithms can be relatively subjective, but their reliability can be improved if the assessment is performed by a hemophilia provider trained in musculoskeletal US.[35]
- There is emerging evidence that suggests musculoskeletal ultrasound (MSKUS) may be useful in the clinical assessment and management of painful hemophilic arthropathy as it can differentiate between joint bleeds and joint inflammation and between muscle bleeds and other regional pain syndromes.[40,41] Nonetheless, in any circumstance, if a patient or clinician suspects an acute joint or muscle bleed or has difficulty assessing whether a bleed is in progress, hemostatic treatment is advised immediately before performing confirmatory investigations or awaiting such results.

TABLE 11-1 Radiological Pettersson score[29]

Radiologic change	Finding	Score[a] (points)
Osteoporosis	Absent	0
	Present	1
Enlargement of epiphysis	Absent	0
	Present	1
Irregularity of subchondral surface	Absent	0
	Slight	1
	Pronounced	2
Narrowing of joint space	Absent	0
	<50%	1
	>50%	2
Subchondral cyst formation	Absent	0
	1 cyst	1
	>1 cyst	2
Erosions at joint margin	Absent	0
	Present	1
Incongruence between joint surfaces	Absent	0
	Slight	1
	Pronounced	2
Deformity (angulation and/or displacement of articulating bones)	Absent	0
	Slight	1
	Pronounced	2

[a] Possible joint score: 0- 13 points for each joint (total possible score, 6 × 13 = 78).

11.4 | Activities and participation

- Activity refers to the execution of a task or action by an individual.[4] In the context of hemophilia, activity generally refers to instrumental activities of daily living (e.g., walking, climbing steps, brushing teeth, toileting).
- Participation refers to involvement in life situations in the context of social interactions.
- It is often difficult to distinctly categorize items and outcome assessment instruments as belonging to only one of these two domains; therefore, the two domains are often combined in outcome assessment.
- In hemophilia, measurements of activities are defined as either self-reported or performance-based (i.e., observed).[22]

Recommended instruments for measuring activities and participation

- The Haemophilia Activities List (HAL)[15,44] is a disease-specific measurement instrument. It is the best-studied measure of self-reported activities for adults[45] and has been translated into many languages. The three subscores (upper extremity, basic lower extremity, and complex lower extremity) have been proven useful in the United States and the United Kingdom.[15,16,46] (See Table 11-4.)
- The Paediatric Haemophilia Activities List (PedHAL)[47] is derived from the HAL. It is a self-reported measure for children with hemophilia.[45] (See Table 11-5.)
- Both the HAL and PedHAL were developed by hemophilia treaters in the Netherlands; thus, they may not apply as well when used in other cultural settings.[48,49]

TABLE 11-2 IPSG MRI Scale to Assess Hemophilic Arthropathy[43]

Soft tissue changes	Effusion/hemarthrosis	Small	(1) ____
		Moderate	(2) ____
		Large	(3) ____
	Synovial hypertrophy	Small	(1) ____
		Moderate	(2) ____
		Large	(3) ____
	Hemosiderin	Small	(1) ____
		Moderate	(2) ____
		Large	(3) ____
Soft tissue changes subscore		Maximum 9 points	____
Osteochondral changes	Surface erosions involving subchondral cortex or joint margins	Any surface erosion	(1) ____
		Half or more of the articular surface eroded in at least one bone	(1) ____
	Subchondral cysts	At least one subchondral cyst	(1) ____
		Subchondral cysts in at least two bones, or cystic changes involving a third or more of the articular surface in at least one bone	
	Cartilage degradation	Any loss of joint cartilage height	(1) ____
		Loss of half or more of the total volume of joint cartilage in at least one bone	(1) ____
		Full-thickness loss of joint cartilage in at least some area in at least one bone	(1) ____
		Full-thickness loss of joint cartilage including at least one half of the joint surface in at least one bone	(1) ____
Osteochondral changes subscore		Maximum 8 points	____

Abbreviations: IPSG, International Prophylaxis Study Group; MRI, magnetic resonance imaging.

- The Functional Independence Score in Hemophilia (FISH)[48,50] is the best-studied observed performance measure for people with hemophilia,[45] with many reports of its use in different countries and age groups. (See Table 11-6.)
- The Patient-Reported Outcomes, Burdens and Experiences (PROBE) questionnaire also includes metrics that assess activities and participation, such as school/education, employment, family life, and impact on activities of daily living.[6,7] (See 11.8 Patient reported outcomes, below.)
- The Canadian Occupational Performance Measure (COPM)[51] and the McMaster Toronto Patient Disability Questionnaire (MACTAR)[52] are generic instruments that have been used for day-to-day assessment of a person's perception of changes in the domains of activities and participation. They can be used for goal attainment scaling.

11.5 | Environmental and personal factors

Environmental factors

- While environmental factors are part of the ICF model, they are not often considered "outcomes" *per se* but can be the major intervention in the rehabilitation process.[4]

TABLE 11-3 HEAD-US Scoring Method[32]

Disease activity (synovitis)	Scale
Hypertrophic synovium	
0. Absent/minimal	0
1. Mild/moderate	1
2. Severe	2
Disease damage (articular surfaces)	
Cartilage	
0. Normal	0
1. Echotexture abnormalities, focal partial-/full-thickness loss of the articular cartilage involving <25% of the target surface[a]	1
2. Partial-/full-thickness loss of the articular cartilage involving ≤50% of the target surface[a]	2
3. Partial-/full-thickness loss of the articular cartilage involving >50% of the target surface[a]	3
4. Complete cartilage destruction or absent visualization of the articular cartilage on the target bony surface[a]	4
Bone	
1. Normal	0
2. Mild irregularities of the subchondral bone with/without initial osteophytes around the joint	1
3. Deranged subchondral bone with/without erosions and presence of prominent osteophytes around the joint	2

Abbreviations: HEAD-US, Haemophilia Early Arthropathy Detection with Ultrasound.

[a]Elbow, anterior aspect of the distal humeral epiphysis; knee, femoral trochlea; ankle, anterior aspect of the talar dome.

TABLE 11-4 Haemophilia Activities List (HAL) 2005[15]

	Items (n)
HAL overall	42
HAL domains	
Lying/sitting/kneeling/standing	8
Functions of the legs	9
Functions of the arms	4
Use of transportation	3
Self-care	5
Household tasks	6
Leisure activities and sports	7
HAL components	
Upper extremity (HAL_{upper})	9
Basic lower extremity (HAL_{lowbas})	6
Complex lower extremity (HAL_{lowcom})	9

Note : Available in multiple languages at: http://elearning.wfh.org/resource/hemophilia-activities-list-hal/

TABLE 11-5 Haemophilia Activities List —Pediatric (PedHAL) v.11[47]

	Items (n)
PedHAL overall	53
PedHAL domains	
Lying/sitting/kneeling/standing	10
Functions of the legs	11
Functions of the arms	6
Use of transportation	3
Self-care	9
Household tasks	3
Leisure activities and sports	11

Note : Available at: http://elearning.wfh.org/resource/haemophilia-activities-list-pediatric-pedhal/

TABLE 11-6 Functional Independence Score in Hemophilia (FISH)[48]

List of activities tested		
Self-care	Transfers	Locomotion
Eating	Chair transferring	Walking
Grooming	Walking	Climbing stairs
Bathing		Running
Dressing		

Notes : Scores range from 1 to 4 for each activity depending on the degree of independence: 1, unable to perform; 2, requires the help of an assistant/aid; 3, able to perform the activity without an aid but not like a healthy subject; 4, able to perform the activity like other healthy subjects. Available at: https://elearning.wfh.org/resource/functional-independence-score-in-hemophilia-fish/

TABLE 11-7 Q-5D Instrument[68]

EQ-5D description system[a]	EQ-VAS
Mobility Self-care Usual activities Pain/discomfort Anxiety/depression	Records the respondent's self-rated health on a vertical, visual analogue scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state)

Abbreviations: EQ, EuroQoL; VAS, visual analogue scale.

[a] Three- item, five- item, and youth versions are available.

- Environmental factors that influence outcome include facilitators and barriers to treatment. These might include access to a comprehensive hemophilia care centre, availability of CFCs, medical understanding, medical insurance coverage,[53] and travel distance to a hemophilia treatment centre.[54]
- For children with hemophilia, family support and, if needed, additional psychosocial support and assessment provided by the hemophilia care team, may be an important facilitating factor.

Personal factors

- An individual's personal strengths and deficiencies may significantly influence treatment outcomes.
- Assessment of factors, such as the locus of control, and psychological characteristics, such as anger, depression, and optimism, can be used to guide and inform individual care or research.[55]
- Another important and measurable influence on treatment outcomes is patient/family treatment adherence.[56,57]

11.6 | Economic factors

- The costs and associated benefits of medical care can be quantified and used in research, program development, and advocacy.

Direct costs

- Direct costs include the cost of medical treatments, health services, and surgical and medical supplies.
- CFCs for patients with severe hemophilia usually account for more than 90% of treatment-related costs.[58]

Indirect costs

- Indirect costs arise from loss of work productivity of adult patients and of parents of pediatric patients due to the time they spend managing their child's hemophilia care.
- The costs that result from illness or seeking medical care are sometimes similar but often vary by country.[59]

11.7 | Health-related quality of life

- Health-related quality of life is a synonym for subjective (self- or family-reported) health status.[25]
- HRQoL measurements are usually questionnaires that aim to quantify a patient's health in a global way.
- Given their global nature, HRQoL measures are often more superficial in their scope than individual measures of the different domains listed above; therefore, they are best applied in combination with specific assessments of the ICF domains rather than in isolation.[60]
- An additional challenge in their use is that they must be validated in the language and social and cultural contexts of their application.

Instruments most used for measurement of health-related quality of life

- The EQ-5D[2,3] and SF-36[61,62] are widely used generic instruments for assessing QoL in hemophilia. (See Tables 11-7 and 11-8.)
- The PROBE questionnaire assesses QoL in addition to burden of disease in people with hemophilia.[6,63-65]
- For children with hemophilia, the Canadian Hemophilia Outcomes-Kids Life Assessment Tool (CHO-KLAT) has been extensively used.[4,66]
- For adults with hemophilia, the Hemophilia Well-Being Index[67] and the hemophilia-specific QoL questionnaire for adults (HAEMO-QoL-A) have been widely used.[4,5]

RECOMMENDATION 11.7.1:

- **The WFH recommends assessing and documenting the musculoskeletal and overall health of each patient at least annually. This should include an assessment of body structure and function, activity levels, participation and health-related quality of life as per the World Health Organization's International Classification of Functioning, Disability and Health (WHO ICF), as much as possible, in the right clinical context.**
- **REMARK: Standard definitions and validated tools should be used as much as possible, including the following:**
  - **For body structure and function, clinical assessment of joints is (most) commonly done using the Hemophilia Joint Health Score (HJHS) in both children and adolescents.**
  - **Under the same domain, early structural changes in joints are best assessed using ultrasound (US) or magnetic resonance imaging (MRI). Late osteochondral changes may be assessed on plain radiographs.**
  - **Functional activity levels should be assessed using the most appropriate option available for that individual, including the Haemophilia Activities List (HAL), the Haemophilia Activities List for children (PedHAL), or the Functional Independence Score in Hemophilia (FISH).**
  - **HRQoL is an important aspect of outcome measurement that may be assessed using either generic or disease-specific tools, but only in combination with the other domains of the WHO ICF.** CB

11.8 | Patient-reported outcomes

- Patient-reported outcomes (PROs) provide a report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else.[70]
- It encompasses both single-dimensional and multi-dimensional measures of symptoms, HRQoL, health status, adherence to treatment, satisfaction with treatment, and other measures.[71]
- PROs include generic instruments such as EQ-5D-5L, Brief Pain Inventory v2 (BPI), International Physical Activity Questionnaire (IPAQ), Short Form 36 Health Survey v2 (SF-36v2), Patient-Reported Outcomes Measurement Information System (PROMIS),[71,72] and disease-specific instruments such as the HAL,[73] HRQoL measures such as CHO-KLAT,[66] HAEMO-QoL-A,[5] and burden of disease questionnaires such as PROBE.[6]
- While data generated by a PRO instrument can provide evidence of a treatment benefit from the patient perspective, the choice of instrument should be tailored to the study design or clinical need for specific outcome assessment, rather than just psychometric properties of the instrument.[74]

11.9 | Core set of measures for use in the clinic or research setting

- In health care, the focus is increasingly shifting from the volume of services delivered to the value created for patients. In this context, value is defined as outcomes achieved relative to costs.[75]
- While many outcome assessment options have been described here, in practice, hemophilia treatment centres and clinicians may select the instruments most appropriate for their patients. Outcome assessment instruments may be classified as mandatory, recommended, and optional.[1]
- To extract the potential of value-based health care, standardized outcome measures must be encouraged.
- This will mean committing to measuring a minimum sufficient set of outcomes for every major medical condition, with well-defined methods for their collection, which will then need to be applied universally.

TABLE 11-8 36-Item Short Form Survey Instrument (SF-36)[69]

	Items (n)
SF-36 overall	36
SF-36 domains	
Physical functioning	10
Role limitations due to physical health problems	4
Role limitations due to personal or emotional problems	3
Energy/fatigue	4
Emotional well- being	5
Social functioning	2
Pain	2
General health	5

- The WFH World Bleeding Disorders Registry (WBDR) provides a platform for hemophilia treatment centres to collect uniform and standardized patient data and outcomes globally to guide clinical practice (http://www.wfh.org/en/our-work-research-data/world-bleeding-disorders-registry).[8,9]
- Defining a standardized core set of outcome measures for specific clinical settings within which hemophilia is managed worldwide is key to advancing the clinical care of people with hemophilia and conducting further studies on treatment options.[1] A selection of outcome assessment instruments can be accessed at the WFH Compendium of Assessment Tools webpage (http://elearning.wfh.org/resource/compendium-of-assessment-tools/).[10]

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SUPPORTING INFORMATION

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