



Enhancing Quality of Life in Hemophilia

Rungrote Natesirinilkul, MD
Division of Hematology and Oncology,
Department of Pediatrics,
Faculty of Medicine, Chiang Mai University

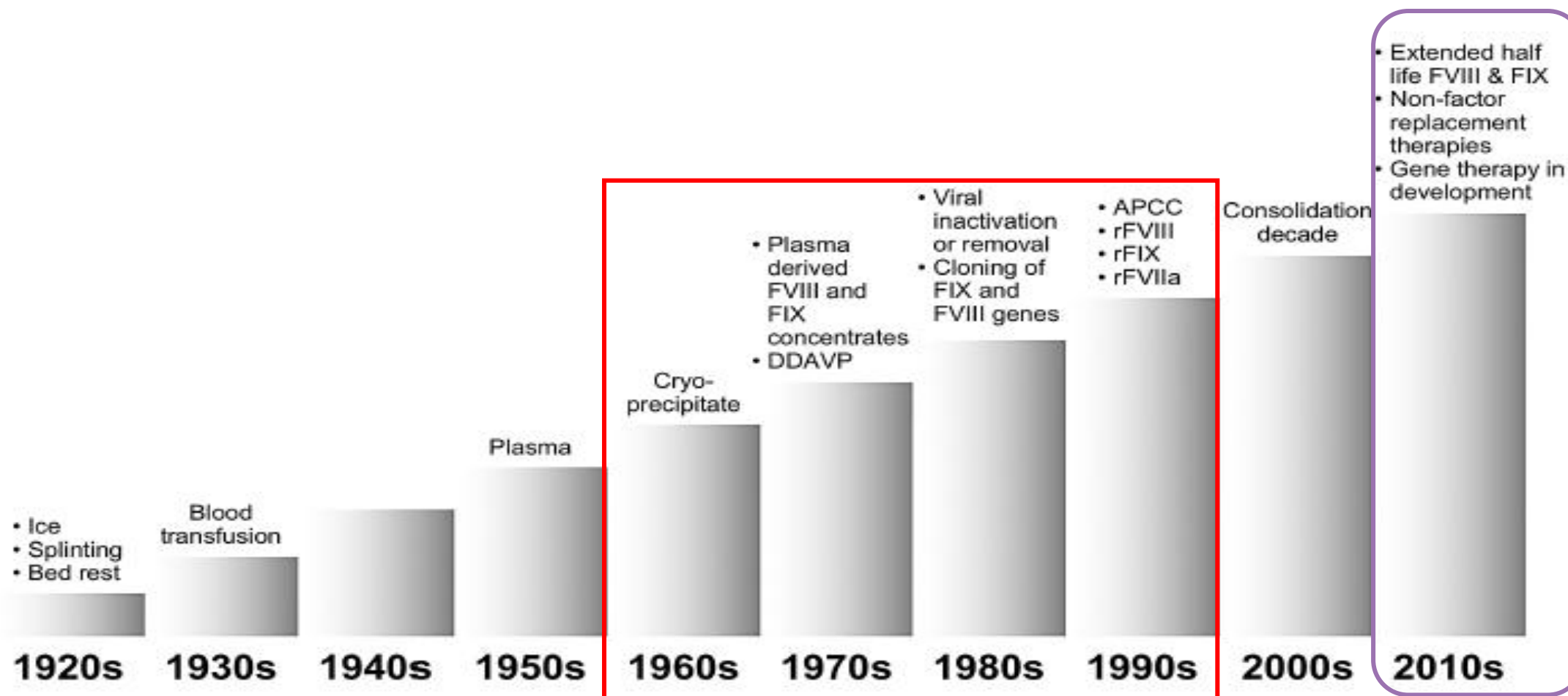
Scope of Talk

- Why do we need to monitor quality of life (QoL) in hemophilia?
- How to monitor QoL in hemophilia?
- Evidences of QoL in hemophilia in resource-limited countries

Scope of Talk

- Why do we need to monitor quality of life (QoL) in hemophilia?
- How to monitor QoL in hemophilia?
- Evidences of QoL in hemophilia in resource-limited countries

The Evolution of Hemophilia Treatment



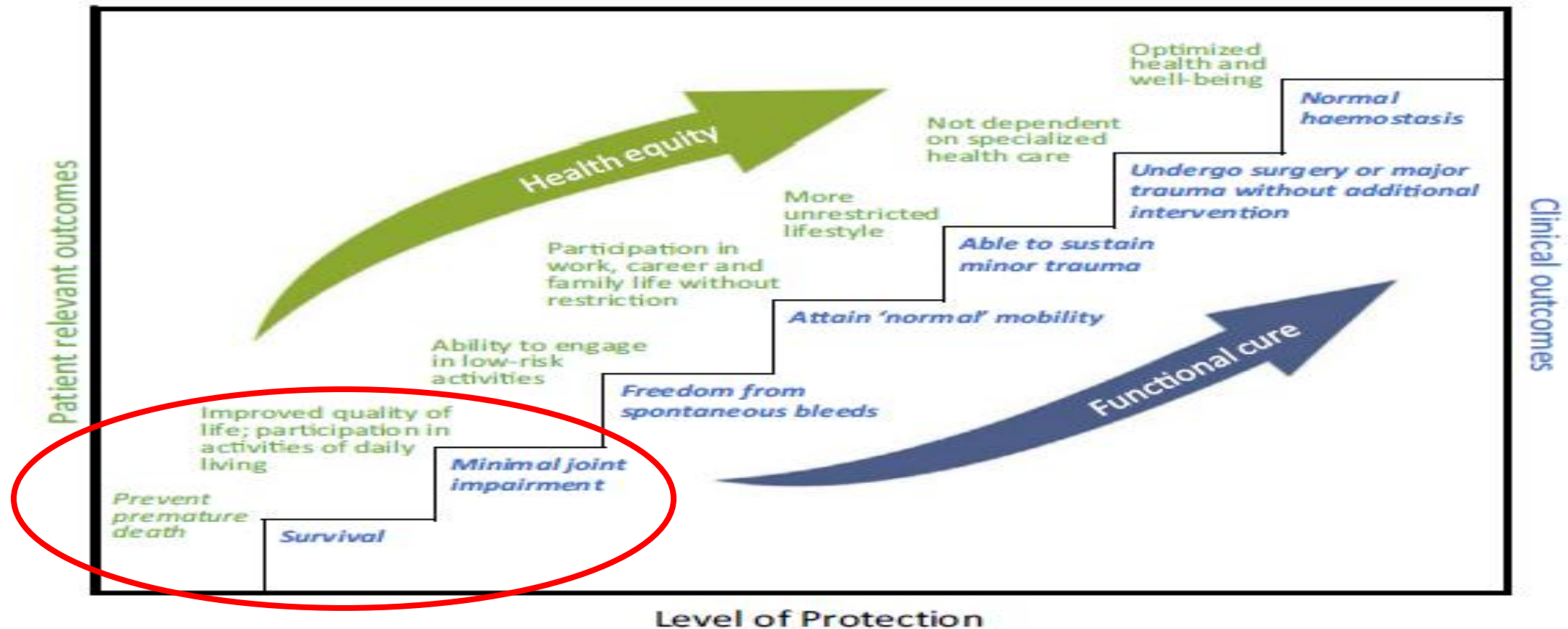
Bleeding Symptoms in Hemophilia

- **Hemarthrosis (70-80%)** and **muscle/soft tissue bleeding** (10-20%) are *hallmarks of hemophilia*
- Life-threatening bleeding (5-10%)
 - CNS bleeding (< 5%)
 - GI bleeding
 - Iliopsoas bleeding
 - Neck/throat bleeding

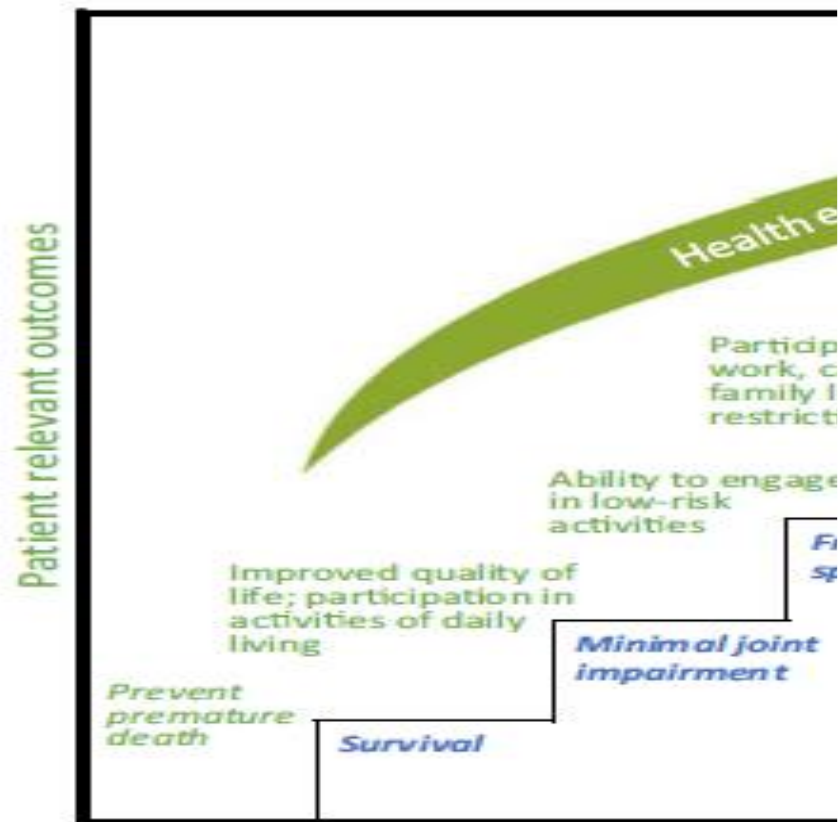
Current Aim for Hemophilia Care – HCPs' View

- **Prophylaxis** in hemophilia **consists of regular administration of therapeutic products** aimed at maintaining hemostasis **to prevent bleeding**, especially **joint hemorrhages**, which would lead to **arthropathy and disability**.

Current Aim for Hemophilia Care – Patients' View



How Can We Evaluate The Treatment?



Outcomes	Measures
Survival	Mortality rate
Joint impairment	• Annual bleeding rate (ABR) • Annual joint bleeding rate (AJBR) • Annual spontaneous joint bleeding rate • Number of target joints

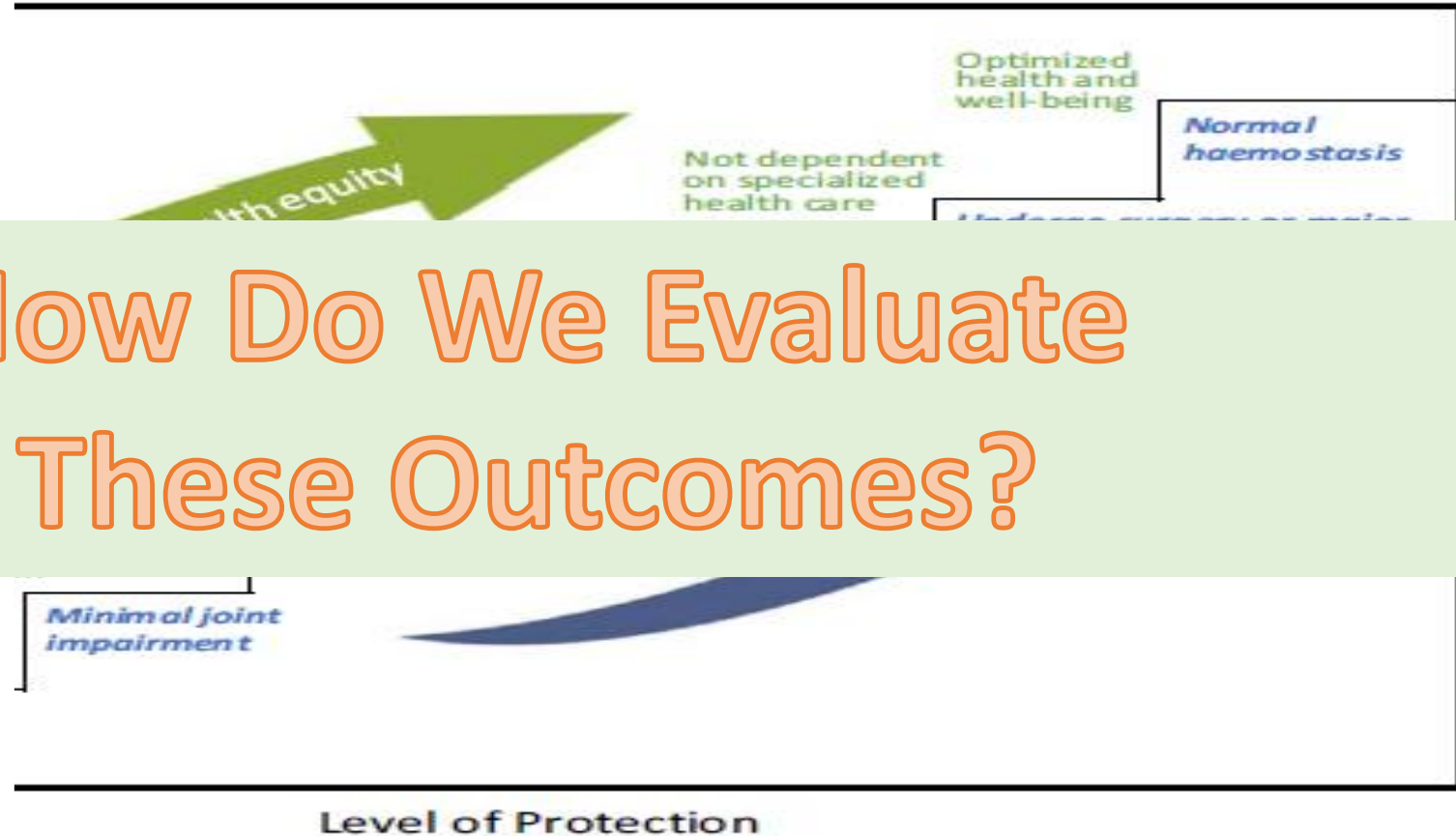
Decreased number = Better outcomes

Current Aim for Hemophilia Care – HCPs and Patients' View

- **Prophylaxis in hemophilia consists of regular administration of therapeutic products aimed at maintaining hemostasis to prevent bleeding, especially joint hemorrhages, which would lead to arthropathy and disability.**
- Prophylaxis should **enable people with hemophilia to lead healthy and active lives** including **participation in most** physical and social **activities** (at home, school, work, and in the community), **similar to the non-hemophilic population.**

Current Aim for Hemophilia Care – Patients' View

How Do We Evaluate
These Outcomes?



Scope of Talk

- Why do we need to monitor quality of life (QoL) in hemophilia?
- How to monitor QoL in hemophilia?
- Evidences of QoL in hemophilia in resource-limited countries

What Is Quality of Life?

- An individual's perception of their position in life in the context of
 - Culture and value systems in which they live
- In relation to their
 - Goals
 - Expectations
 - Standards
 - Concerns

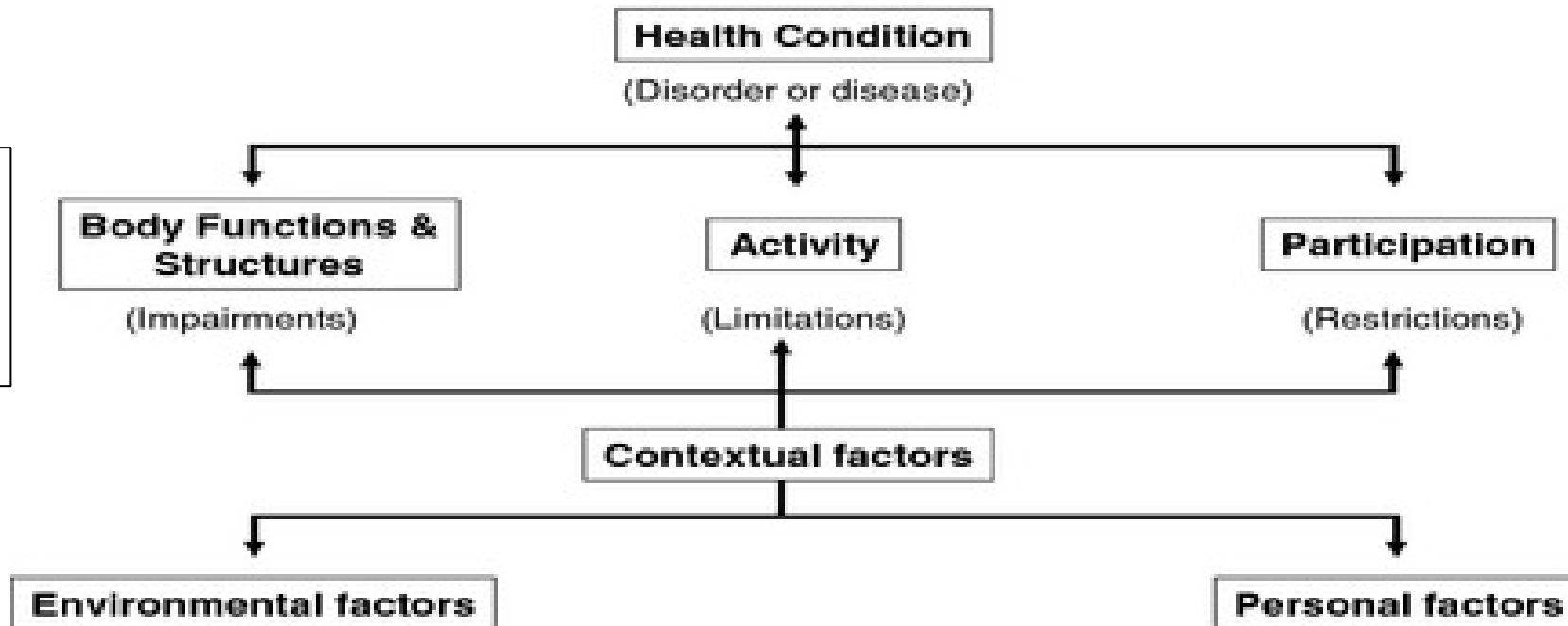
Model of Care in Chronic Diseases



World Health
Organization

International Classification of
Functioning, Disability and Health (ICF)

Health-
related
quality of life



Tools of Outcome Measures

- **Generic outcome measures (for any diseases)**

- Necessary to compare outcomes across different populations and interventions

- *Needed of validity, reliability, and responsiveness of generic and disease-specific measures in the same population and in minority and age-specific groups*

- **Disease-specific outcome measures**

- Special states and concerns of diagnostic groups
- May be more sensitive for the detection and quantification of small changes that are important to clinicians or patients.

Tools of Outcome Measures

- **Generic outcome measures (for any diseases)**

- EQ5D5L
- PedsQL
- SF36
- etc.

Measured by

- History taking and interviewing
- Physical examination
- Investigations (imaging)
- Observation
- Self-report

- **Disease-specific outcome measures**

- Gilbert score
- HJHS
- Imaging
- FISH
- HAL
- PedHAL
- COPM
- Haem-A-QoL
- etc.

EQ5D5L

- Euro Group Quality of Life (EQ)-5 Dimensions (5D)-5 Levels (5L)
 - 5D: mobility, self-care, usual activities, pain/discomfort and anxiety/depression
 - 5L: no problems (1), slight problems (2), moderate problems (3), severe problems (4) and extreme problems (5)
- Converted score
- -1 (worse than dead) – 0 (worst health) – 1 (best health)
- Adults and children aged 8-16 years

- Visual analog scale (VAS)

The best health you can imagine

We would like to know how good or bad your health is TODAY.

This scale is numbered from 0 to 100.

100 means the best health you can imagine.
0 means the worst health you can imagine.

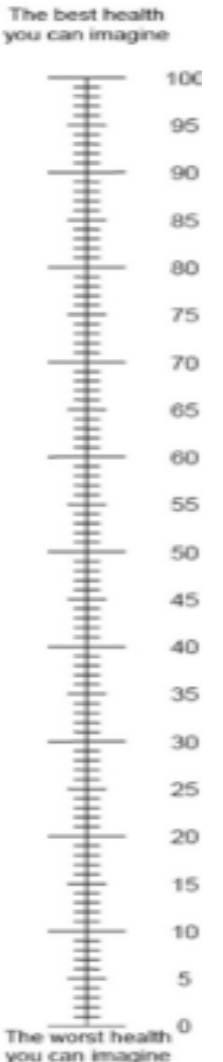
Mark an X on the scale to indicate how your health is TODAY.

Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =

Score: 0 (worst health) -100 (best health)

The worst health you can imagine



PedsQL

- 23 items in the PedsQL comprise four Generic Core Scales
 - Physical functioning (8 items)
 - Emotional functioning (5 items)
 - Social functioning (5 items)
 - School functioning (5 items)
- **Psychosocial Health Summary Score** and **Physical Health Summary Score** as well as a **Total Scale Score**
- Score 0 (worst health) – 100 (best health)
- Two types:
 - Parents (the proxy report)
 - **Aged 2-4, 5-7, 8-12, and 13-18 years**
 - Children (the self report)
 - Aged 5-7, 8-12, and 13-18 years
- 5 scales: 0 (“Never” = 100), 1 (“Almost Never” = 75), 2 (“Sometimes” = 50), 3 (“Often” = 25), 4 (“Almost Always” = 0)
- Condition-specific modules available e.g. cerebral palsy, cystic fibrosis

SF36

- 36-Item Short Form Survey
- RAND
- Score of each individual scale
- 0 (lowest health) – 100 (highest health)
- Adult aged > 18 years

Scale	Number of items	After recoding per Table 1, average the following items
Physical functioning	10	3 4 5 6 7 8 9 10 11 12
Role limitations due to physical health	4	13 14 15 16
Role limitations due to emotional problems	3	17 18 19
Energy/fatigue	4	23 27 29 31
Emotional well-being	5	24 25 26 28 30
Social functioning	2	20 32
Pain	2	21 22
General health	5	1 33 34 35 36

https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html
https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form/scoring.html

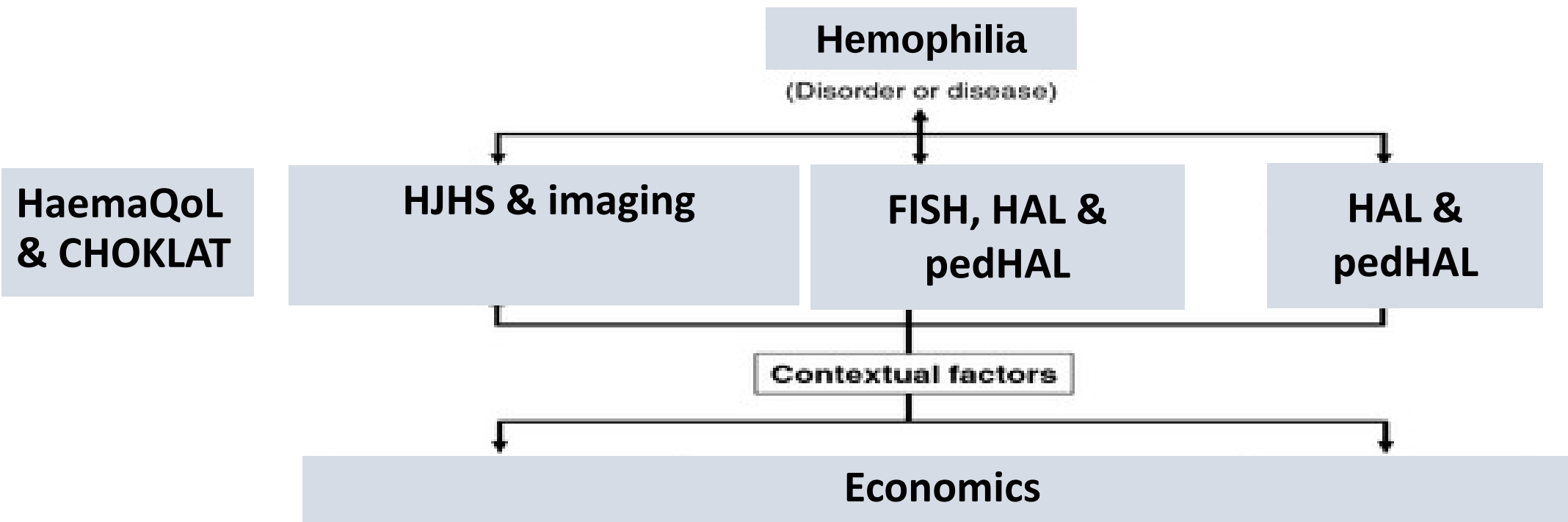
Item numbers	Change original response category *	To recoded value of:
1, 2, 20, 22, 34, 36	1 →	100
	2 →	75
	3 →	50
	4 →	25
	5 →	0
3, 4, 5, 6, 7, 8, 9, 10, 11, 12	1 →	0
	2 →	50
	3 →	100
13, 14, 15, 16, 17, 18, 19	1 →	0
	2 →	100
21, 23, 26, 27, 30	1 →	100
	2 →	80
	3 →	60
	4 →	40
	5 →	20
24, 25, 28, 29, 31	1 →	0
	2 →	20
	3 →	40
	4 →	60
	5 →	80
	6 →	100
32, 33, 35	1 →	0
	2 →	25
	3 →	50
	4 →	75
	5 →	100

Model of Care in Hemophilia



World Health
Organization

International Classification of
Functioning, Disability and Health (ICF)



Tools Available in Thai Language

- Hae-A-QoL
- Haemo-QoL
- CHO-KLAT
- PROBE

Health-related QoL

Domain	Tools	Clinical use	Research	Comments
Health-related QoL	HAEM-A-QoL (adults) and Haemo-QoL (pediatrics)	Optional/ recommended	Mandatory by each of these tools	- Translated and linguistic validated (77 languages), but partially validated in some languages (24 languages) - Short and full pediatric version for all three groups (4-7, 8-12 and 13-16 years)
	CHO-KLAT (only pediatrics)	Optional/ recommended		Validation was done in all available 8 languages (4-18 years) for children and parents
	H-FIT (family burden)	Optional/ recommended	Optional/ recommended	Validation in different languages is performing

HAEM-A-QoL

- 10 domains
- 46 items
- Adults aged ≥ 17 years
- 0 (lowest impaired QoL = best QoL) – 100 (highest impaired QoL = worst QoL)

Wyrwich KW, et al. Haemophilia 2015.

Table 1. Haem-A- QoL domains and an example item in each domain.

Haem-A-QoL domains	Example items
Physical health (5 items)	In the past month, it was painful for me to move
Feelings (4 items)	In the past month, I was worried because of my haemophilia
View of yourself (5 items)	In the past month, I felt different from others because of my haemophilia
Sports & leisure (5 items)	In the past month, I had to avoid sports that I like because of my haemophilia
Work & school (4 items)	In the past month, my everyday work/school activities were jeopardized by my haemophilia
Dealing with haemophilia (3 items)	In the past month, I was able to tell whether or not I was bleeding
Treatment (8 items)	In the past month, I had problems with how my treatment was administered
Future (5 items)	In the past month, I have been thinking that it will be difficult for me to lead a normal life
Family planning (4 items)	In the past month, I have been worrying about not being able to raise a family
Partnership & sexuality (3 items)	In the past month, I haven't been able to have a normal relationship because of my haemophilia

Haemo-QoL

- Children I: 8 subscales, 21 items, only 3 choices – conducted as an interview
- Children II: 9 subscales, 64 items, 5 choices – self-reported
- Adolescent III: 11 subscales, 77 items, 5 choices – self-reported
- Short version of Children II and Adolescents III 9 subscales, 35 items, 5 choices – self-reported
- Scoring: 0 (high QoL) to 100 (low QoL)

Canadian Hemophilia Outcomes–Kids’ Life Assessment Tool (CHO-KLAT) and Hemophilia Family Impact Tool (H-FIT)

- **CHO-KLAT (current version 3)**

- Parent-proxy report and self-report
- Boy aged 7-18 years
- 40 items, 7 domains
- 0 (worst QoL) – 100 (best QoL)

Domains for CHO-KLAT v3.0	
Domain	Number of items
Activities	5
Autonomy	7
Bleeding	4
Emotional health	4
Hemophilia Knowledge	3
Social Functioning	9
Treatment	8

H-FIT

- Parent-proxy report only
- 16 items, 4 domains
- 0 (most burden) – 100 (least burden)

H-FIT	
Number of items	16
Physical symptoms of stress	Not included
Cognitive functioning	Not included
Daily activities	Not included
Treatment administration/ burden of administration	Concept covered in 2 questions
Guilt/worry around functional limitations	Concept covered in 3 questions
Symptom-specific concerns (ie, bleeding)	Concept covered in 2 questions
Knowledge/confidence with hemophilia	Concept covered in 2 questions

Patient Reported Outcomes (PROs)

- PROBE (Patient Reported Outcomes Burdens and Experiences) questionnaire
- Four major sections (demographic data, general health problems, haemophilia-related health problems and health-related quality of life using EQ-5D-5L and EQ-VAS)
- The pilot study of the PROBE Project recruited 656 participants.
- 71% completed the questionnaire within 15 min, and all participants completed within 30 min.
- Over 30 languages available

Scope of Talk

- Why do we need to monitor quality of life (QoL) in hemophilia?
- How to monitor QoL in hemophilia?
- Evidences of QoL in hemophilia in resource-limited countries

How to Enhance QoL in Hemophilia

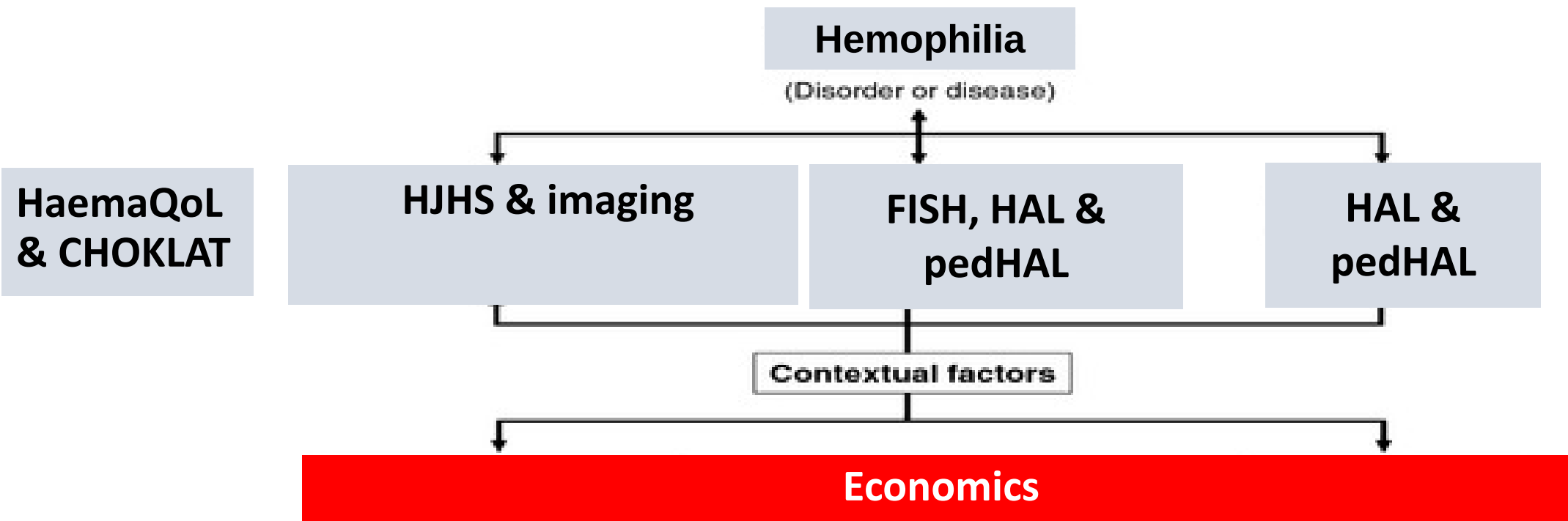
- Access to treatment
- Switch from episodic treatment to prophylaxis (even low dose prophylaxis)
- Establish multidisciplinary care
- Change to better hemostatic agents
- Cure

Model of Care in Hemophilia



World Health
Organization

International Classification of
Functioning, Disability and Health (ICF)



How to Enhance QoL in Hemophilia in Resource-constrained Countries

- **Access to treatment:** health care professionals with patient group collaborate with the government, humanitarian aids
- **Switch from episodic treatment to prophylaxis:** start with low dose prophylaxis
- **Establish multidisciplinary care:** still need less budget but require more advocacy
- **Change to better hemostatic agents:** may be possible with lower dose than clinical trials (e.g. low-dose extend half-life factor concentrate, low-dose emicizumab)
- **Cure:** only when clinical trials are available now

Hemophilia Data in Thailand (upper middle-income country, UMIC)



FIGURE G5a. Mean per capita factor VIII use in 2022 – regional and GNI comparisons of IU/total population: South-East Asia



FIGURE G5b. Mean per capita factor IX use in 2022 – regional and GNI comparisons of IU/total population: South-East Asia

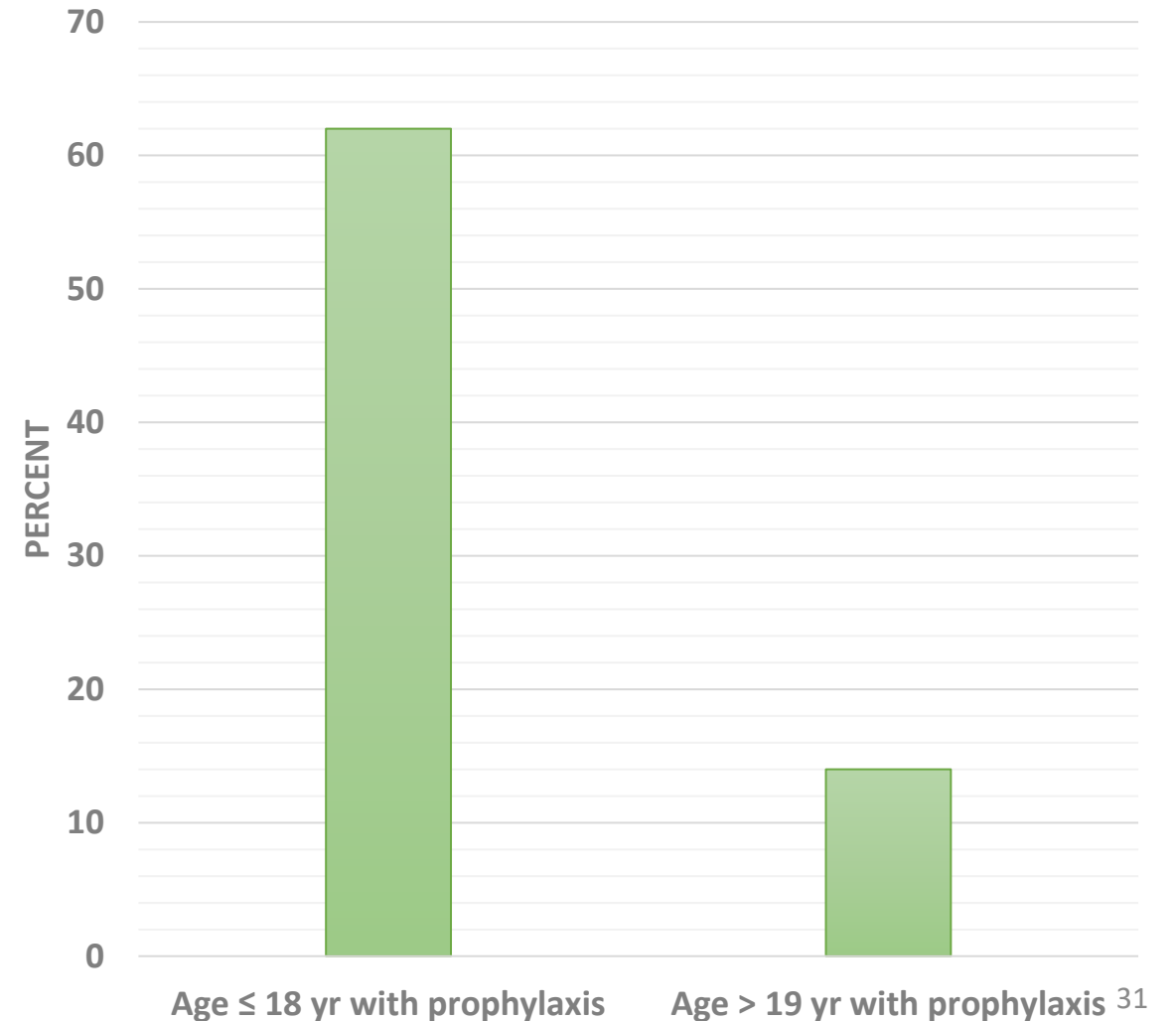
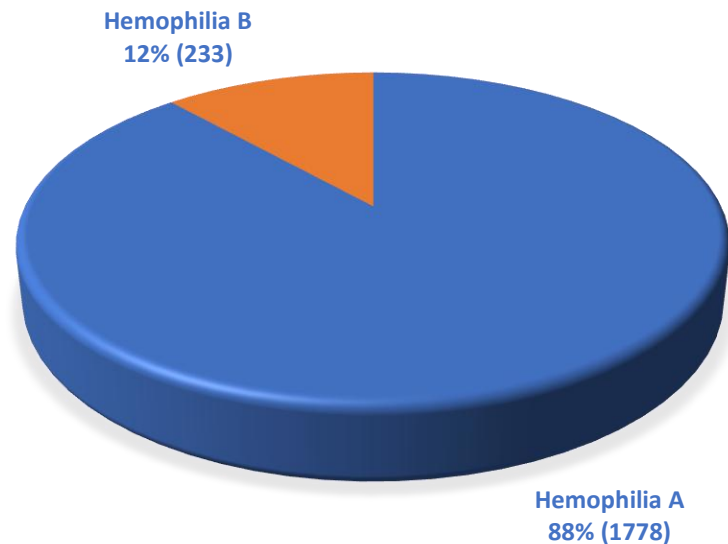


Annual global survey, WFH. 2022.



Hemophilia Data in Thailand

- Annual global survey reported by WFH 2022
- Total 2011 persons with hemophilia



Regimen	Advantages	Disadvantages
High dose/high frequency	• Ensures that, on average, patients with hemophilia will have at all times measurable FVIII/FIX levels; i.e., levels above 1 IU/dL (1%) • Ensures that virtually all individuals receive enough treatment to prevent virtually all bleeds • Achieves lowest AJBRs and best long-term joint outcomes • Offers benefits for very active individuals	• May be associated with adherence and convenience issues due to increased infusion demands on patients • Is associated with highest factor utilization and consequently highest cost • Results in high need for CVADs or AVFs • May overtreat some individuals who have a milder phenotype which may negatively impact adherence • Is not ideal for resource-constrained countries
Intermediate dose/intermediate frequency	• Reduces AJBRs by approximately 90% to <1 per year • Is less expensive than high-dose prophylaxis and consequently affordable in more countries • Provides quality of life and activity participation rates comparable to high-dose prophylaxis • Might be best for adolescents and adults	• Results in undertreatment of some patients • Leads to slightly worse long-term MSK outcomes
Low dose/low frequency	• Is the least expensive of the fixed regimens and consequently affordable in more countries • Reduces the incidence of bleeding by ~80% or more in comparison to episodic therapy and can achieve AJBRs of around <3 per year²⁰	• Has unknown long-term effect on MSK outcomes which are likely worse than those achieved with intermediate-/high-dose regimens

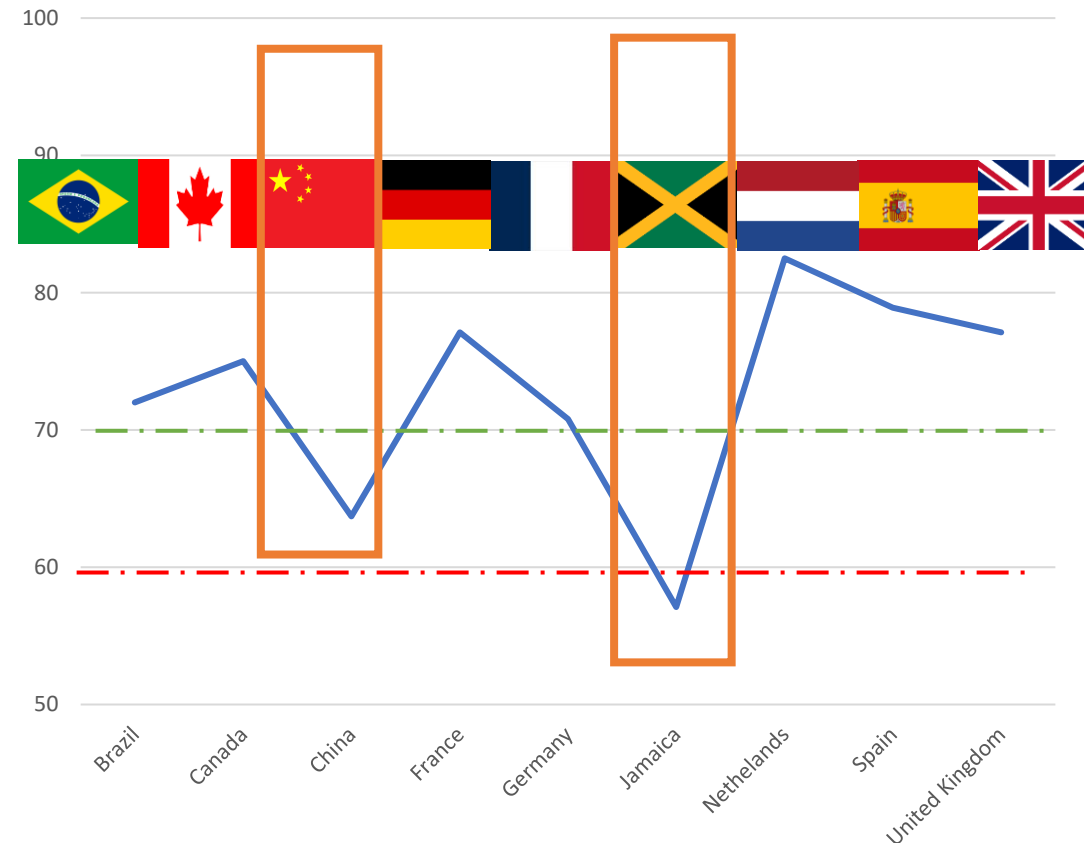
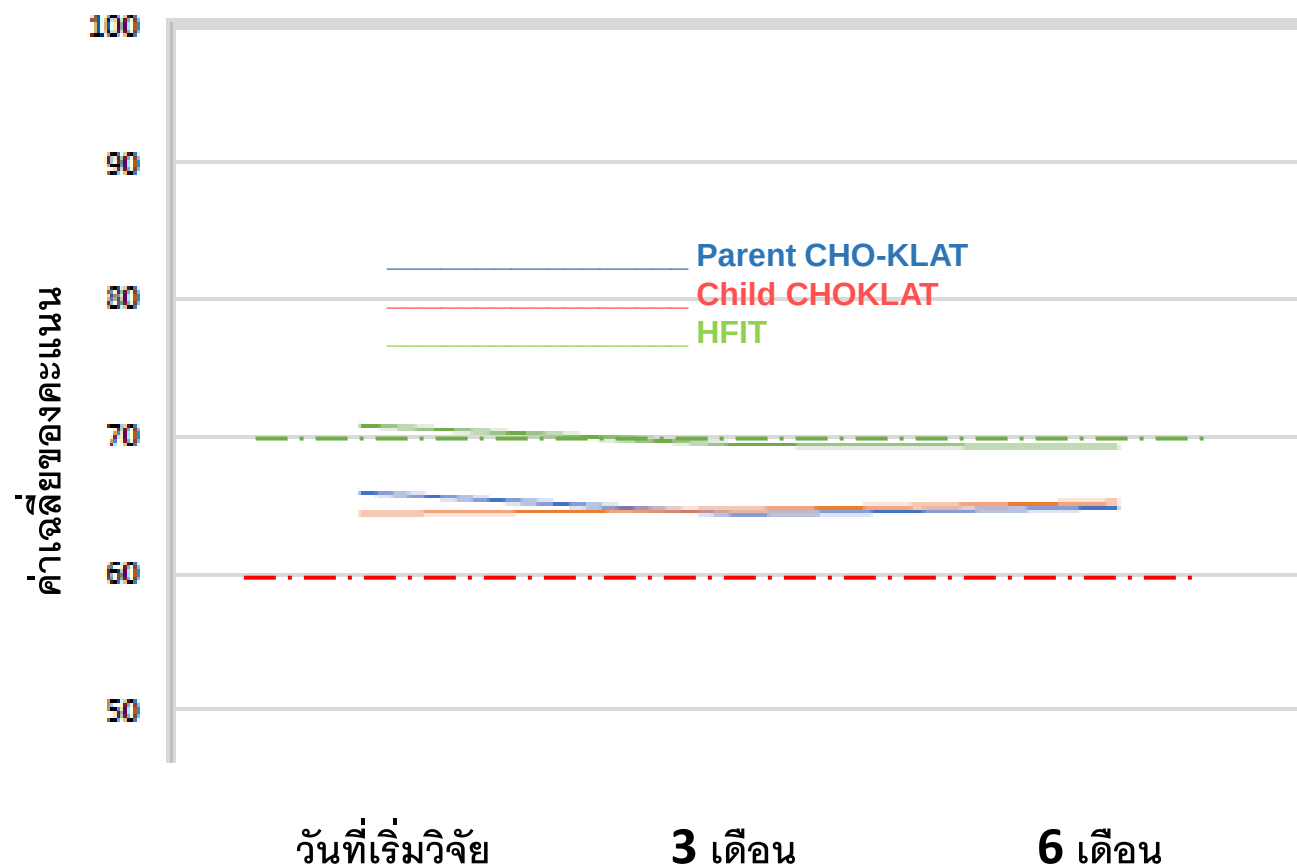
Evidences of QoL in Hemophilia in Thailand



ผู้วิจัย (ปี ค.ศ. ที่ ทำการศึกษา)	กลุ่มประชากรที่ศึกษา	วิธีการป้องกันหรือรักษาโรคฮีโมฟีเลีย	เครื่องมือวัดคุณภาพชีวิตที่ใช้	ผลการศึกษา
นัทธี นาคบุญนำ และคณะ (2022)	ผู้ป่วยโรคฮีโมฟีเลีย เอ และ บี ที่มีอายุ 8-25 ปี และมีความรุนแรงปานกลางและมาก	การให้แฟกเตอร์เข้มข้น 5-10 ยูนิต/กก. 1-2 ครั้งต่อสัปดาห์ เทียบกับการรักษาเฉพาะเมื่อมีอาการเลือดออก	- Haemo-QoL สำหรับผู้ป่วยอายุ 8-16 ปี - Haem-A-QoL สำหรับผู้ป่วยอายุ 17-25 ปี	- ผู้ป่วยที่มีอายุ 8-16 ปีและความรุนแรงมากที่ได้รับแฟกเตอร์ป้องกันเลือดออกในขนาดต่ำมีคุณภาพชีวิตดีกว่ากลุ่มที่ได้รับการรักษาเวลาเมื่อมีอาการเลือดออก (p-value = 0.036) ในเรื่องร่างกาย ครอบครั้ว กีฬา/งานอดิเรก และการรักษา (p-value < 0.05)
อรุณทัย รักษมนธรรม และคณะ (2023)	ผู้ป่วยโรคฮีโมฟีเลีย เอ ที่มีอายุ 7-25 ปีและมีความรุนแรงปานกลางและมากและมีอาการเลือดออกรุนแรง	การให้แฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตมาตรฐาน (standard half-life) ตามน้ำหนักตัว เทียบกับการให้แฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตยาวตามเภสัชจลนศาสตร์ (pharmacokinetics)	- Haemo-QoL สำหรับผู้ป่วยอายุ 8-16 ปี - Haem-A-QoL สำหรับผู้ป่วยอายุ 17-25 ปี	- ผู้ป่วยกลุ่มที่ได้รับแฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตยาวตามเภสัชจลนศาสตร์ที่คุณภาพชีวิตที่ดีกว่ากลุ่มที่ได้รับแฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตมาตรฐาน
ชลธิศ ศรีชุมพวง และคณะ (2024)	ผู้ป่วยโรคฮีโมฟีเลีย เอ ที่มีอายุ 7-25 ปีและมีความรุนแรงปานกลางและมากและมีอาการเลือดออกรุนแรง	การให้แฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตยาวตามเภสัชจลนศาสตร์ร่วมกับการออกกำลังกายแบบเฉพาะบุคคล (individualized exercise protocol)	- Haemo-QoL สำหรับผู้ป่วยอายุ 8-16 ปี - Haem-A-QoL สำหรับผู้ป่วยอายุ 17-25 ปี	- ผู้ป่วยกลุ่มที่ได้รับแฟกเตอร์แปดเข้มข้นที่มีค่าครึ่งชีวิตยาวตามเภสัชจลนศาสตร์ที่คุณภาพชีวิตที่ดีขึ้นภายหลังได้รับการออกกำลังกายเฉพาะบุคคล

Health-related quality of life, and burden of caring for, Thai patients with hemophilia using the Canadian Hemophilia Outcomes–Kids’ Life Assessment Tool v3.0 and Hemophilia Family Impact Tool

แบบทดสอบคุณภาพชีวิตของโรคฮีโมฟีเลีย: คะแนน 0 (คุณภาพชีวิตไม่ดี) – 100 (คุณภาพชีวิตดี)



Summary

- Why do we need to monitor quality of life (QoL) in hemophilia? **As we try to turn the people with hemophilia to live normal life as much as possible.**
- How to monitor QoL in hemophilia? **By using validated generic or hemophilia-specific tool**
- Evidences of QoL in hemophilia in resource-limited countries:
Increased **access to treatment**, **start low-dose prophylaxis**, **establish multidisciplinary care within the possible budget**