

Regional Perspective: Inherited Bleeding Disorders

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1 October 2021

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AGENDA

CONTEXT

- WFH in the Eastern Mediterranean Region

INDICATORS OF CARE

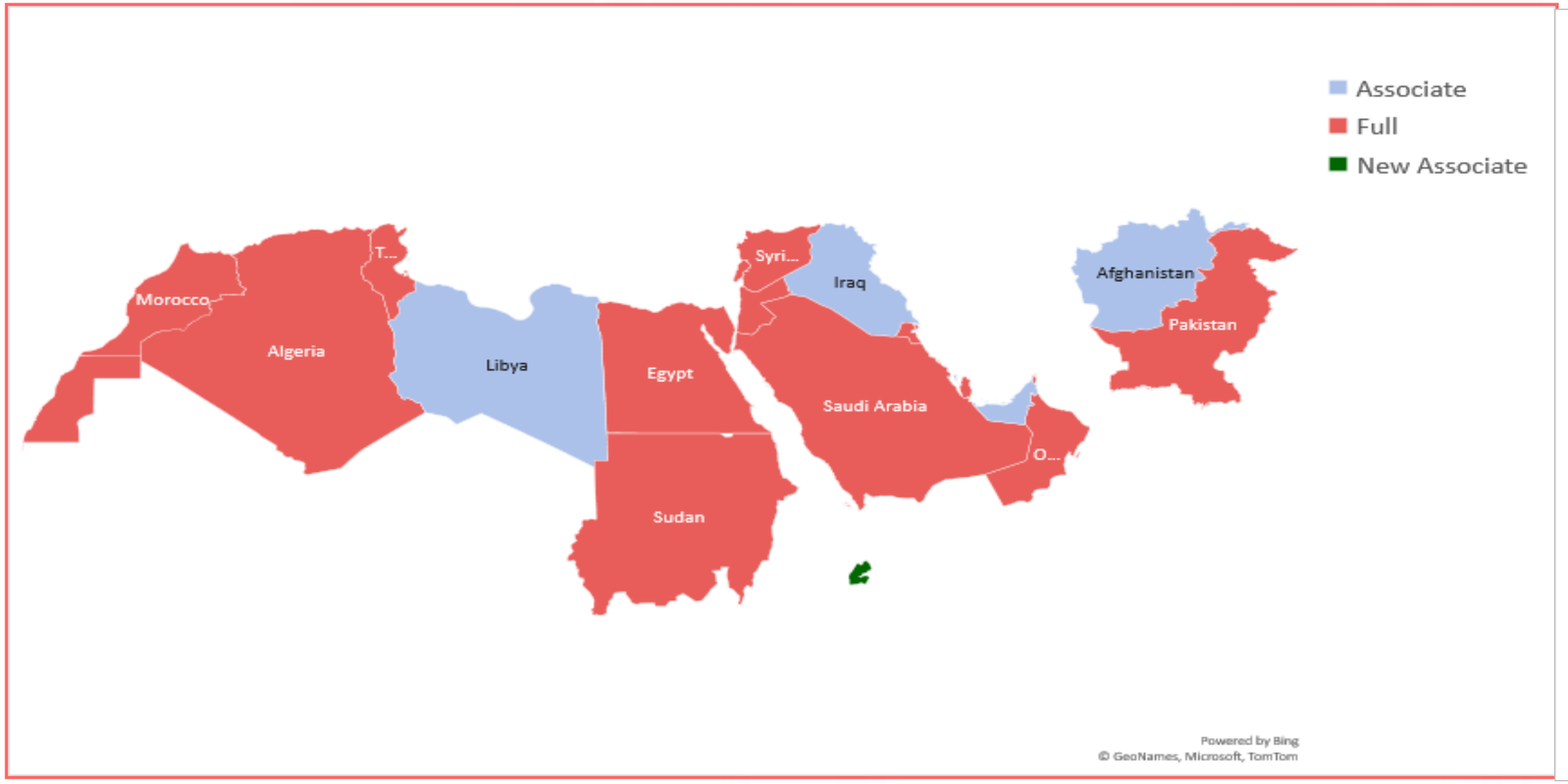
- Prevalence vs Identification of Hemophilia
- Access to Treatment
- Age at Diagnosis
- Annual Bleed Rates

CONCLUSIONS:KEY MESSAGES

- WFH Treatment Guidelines
- Regional Collaboration

CONTEXT

WFH EASTERN MEDITERRANEAN REGION



Received: 23 March 2020 | Revised: 26 March 2020 | Accepted: 26 March 2020

DOI: 10.1111/hae.14001

EDITORIAL

Haemophilia WILEY

The COVID-19 pandemic: New global challenges for the haemophilia community

Over the past few decades, several blood-borne viruses have targeted haemophilia patients requiring treatment with clotting factors derived from human plasma.[1] Even today, many haemophilia patients and their families still retain painful and indelible memories of HIV and hepatitis C infections or are confronted with the progressive health consequences of these infections.

Long considered true enemies of haemophilia patients, viruses, at least some of them, have now become partners in the cure of haemophilia as demonstrated by the successes of gene therapy clinical

pharmacies, hospitals or home delivery programs could be impacted. Haemophilia treatment centres are working hard to avoid such problems. The situation is totally different for the many countries whose only supply relies on the WFH humanitarian aid program.[9] The current paralysis of air transport may slow or impede the transport of replacement products and access to treatment for an undefined period of time.

The production of recombinant DNA produced replacement products (ie FVIII, FIX, FVIIa, emicizumab) is not expected to be af-

INDICATORS OF CARE



WFH DATA SOURCES FOR ADVOCACY

	Annual Global Survey	World Bleeding Disorders Registry	Gene Therapy Registry
Type of data	Country level data	Individual patient data	Individual patient data on PWH who receive gene therapy
Data source	NMO	HTC	HTC
Objectives	Global overview of # of patients identified and access to care	Patient level data; demographics and clinical outcomes	Patient level data; demographics and clinical outcomes
Value	Country level data; Benchmarking your country against other countries; Useful for Advocacy	Patient level data; Benchmarking your patient outcomes against other patients; Useful for clinical care and advocacy	Patient level data; Assessing long-term safety and efficacy of gene therapy

Stonebraker JS, Bolton-Maggs PHB, Brooker M, Evatt B, Iorio A, Makris M, O'Mahony B, Skinner MW, Coffin D, Pierce GF, Tootoonchian E. The World Federation of Hemophilia Annual Global Survey 1999-2018. Haemophilia. 2020 Jul;26(4):591-600. doi: 10.1111/hae.14012.
Konkle BA, Coffin D, Pierce GF, Clark C, George L, Iorio A, Mahlangu J, Naccache M, O'Mahony B, Peyvandi F, Pipe S, Quartel A, Sawyer EK, Skinner MW, Tortella B, Watson C, Winburn I; Members of the WFH Gene Therapy Registery Steering Committee. World Federation of Hemophilia Gene Therapy Registry. Haemophilia. 2020 Jul;26(4):563-564. doi: 10.1111/hae.14015.
Coffin D, Herr C, O'Hara J, Diop S, Hollingsworth R, Srivastava A, Lillicrap D, van den Berg HM, Iorio A, Pierce GF. World bleeding disorders registry: The pilot study. Haemophilia. 2018 May;24(3):e113-e116. doi: 10.1111/hae.13431.

WBDR PARTICIPATION

EASTERN MEDITERRANEAN

COUNTRY	NO OF HTCs	TOTAL PWH
Pakistan	3	1,350
Iraq	3	680
Morocco	2	83
Egypt	4	70
Algeria	2	65

14 HTCS

Total PWH

2,248

Male 2,238

Female 10

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IMPORTANT DATA-DRIVEN INDICATORS OF CARE

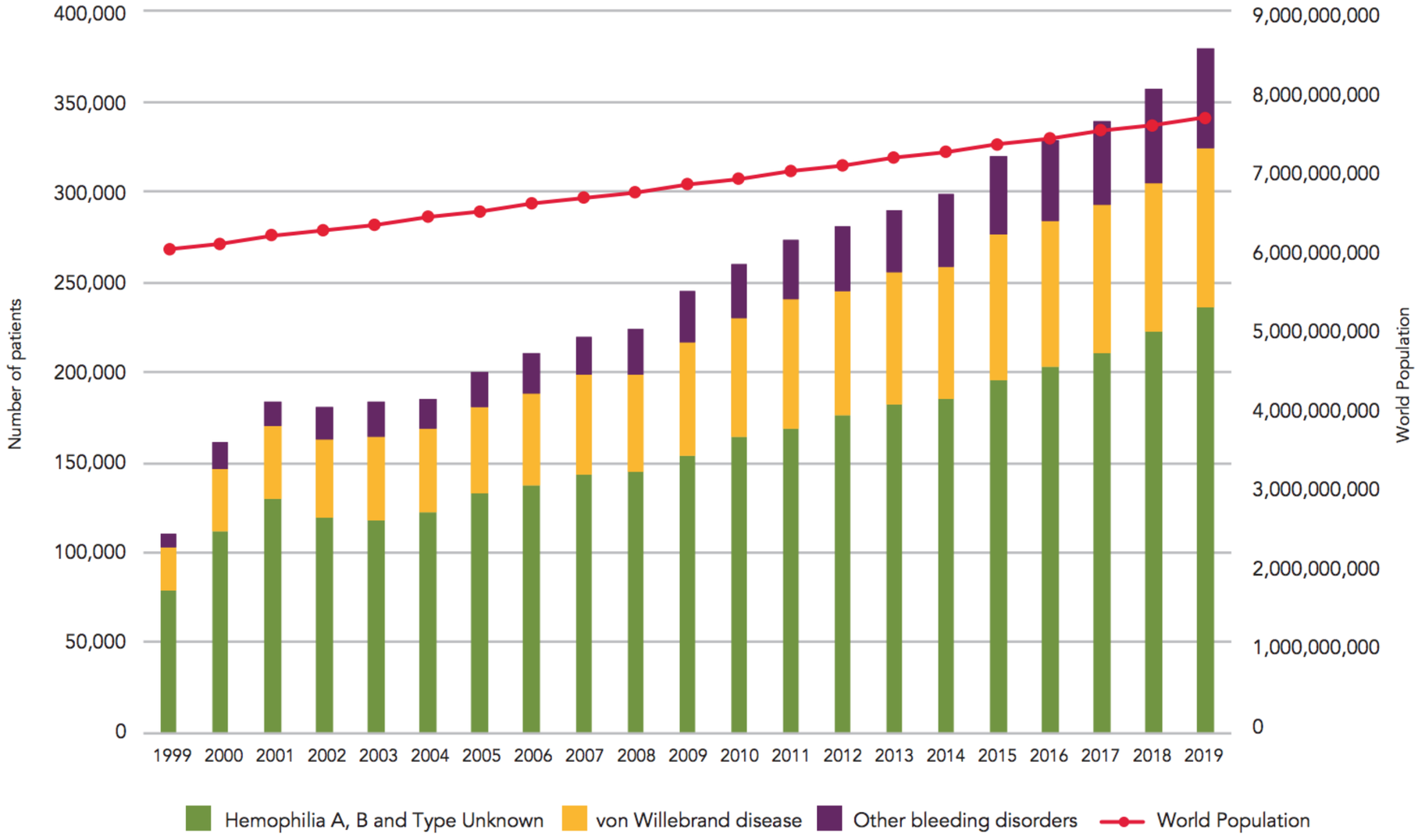
- PWH identification rate*
- Treatment use and availability in country*
- Age at Diagnosis**
- Annual Bleed Rate**

*data comes from WFH AGS
** data comes from WFH WBDR

IMPORTANT DATA-DRIVEN INDICATORS OF CARE

- PWH identification rate (% PWH diagnosed)
- Treatment use and availability in country
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Identified patients over time – all bleeding disorders



This graph was created using aggregate numbers to demonstrate the increase in patients identified over time. This graph contains historical data from the Annual Global Survey. That is, if a country reported data one year and not the next, the older data were used under the assumption that the number of patients did not change substantially from one year to the next.

Reference: WFH Report on the Annual Global Survey, 2019

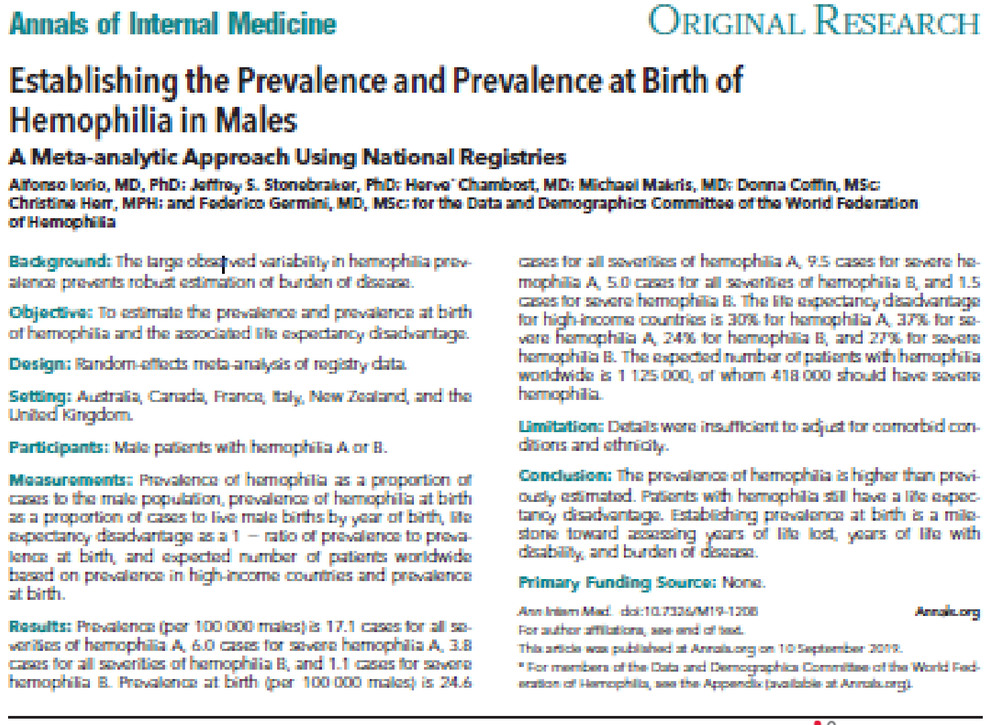
PREVALENCE VS IDENTIFICATION

HEMOPHILIA

Prevalence: 21 per 100,000 males OR 1/5000 males

Prevalence per 100,000 males		
	1998	**2019**
Prevalence	13.4	**21***
· Hem A	10.5	17
· Hem B	2.9	4
· Hem A Severe	-	6
· Hem B Severe	-	1
Prevalence	-	1/5000 males

**Per 100,000 males, 21 will have hemophilia, of which 7 will be severe; this is 57% higher than previously thought.*



Annals of Internal Medicine ORIGINAL RESEARCH

Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males

A Meta-analytic Approach Using National Registries

Alfonso Iorio, MD, PhD; Jeffrey S. Stonebraker, PhD; Hervé Chambost, MD; Michael Makris, MD; Donna Coffin, MSc; Christine Herr, MPH; and Federico Germini, MD, MSc; for the Data and Demographics Committee of the World Federation of Hemophilia

Background: The large observed variability in hemophilia prevalence prevents robust estimation of burden of disease.

Objective: To estimate the prevalence and prevalence at birth of hemophilia and the associated life expectancy disadvantage.

Design: Random-effects meta-analysis of registry data.

Setting: Australia, Canada, France, Italy, New Zealand, and the United Kingdom.

Participants: Male patients with hemophilia A or B.

Measurements: Prevalence of hemophilia as a proportion of cases to the male population, prevalence of hemophilia at birth as a proportion of cases to live male births by year of birth, life expectancy disadvantage as a 1 − ratio of prevalence to prevalence at birth, and expected number of patients worldwide based on prevalence in high-income countries and prevalence at birth.

Results: Prevalence (per 100 000 males) is 17.1 cases for all severities of hemophilia A, 6.0 cases for severe hemophilia A, 3.8 cases for all severities of hemophilia B, and 1.1 cases for severe hemophilia B. Prevalence at birth (per 100 000 males) is 24.6 cases for all severities of hemophilia A, 9.5 cases for severe hemophilia A, 5.0 cases for all severities of hemophilia B, and 1.5 cases for severe hemophilia B. The life expectancy disadvantage for high-income countries is 30% for hemophilia A, 37% for severe hemophilia A, 24% for hemophilia B, and 27% for severe hemophilia B. The expected number of patients with hemophilia worldwide is 1 125 000, of whom 418 000 should have severe hemophilia.

Limitation: Details were insufficient to adjust for comorbid conditions and ethnicity.

Conclusion: The prevalence of hemophilia is higher than previously estimated. Patients with hemophilia still have a life expectancy disadvantage. Establishing prevalence at birth is a milestone toward assessing years of life lost, years of life with disability, and burden of disease.

Primary Funding Source: None.

Ann Intern Med. doi:10.7326/M19-1208 Annals.org

For author affiliations, see end of text.

This article was published at Annals.org on 10 September 2019.

* For members of the Data and Demographics Committee of the World Federation of Hemophilia, see the Appendix (available at Annals.org).

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PWH IDENTIFICATION RATE

Identified # PWH = **29,117**

Expected # of PWH = **72,584**

Not identified # of PWH = **43,467**

40% of PWH in Eastern Med have been identified

60% remain undiagnosed

Reference: WFH Report on the Annual Global Survey, 2019

NO DIAGNOSIS= NO TREATMENT

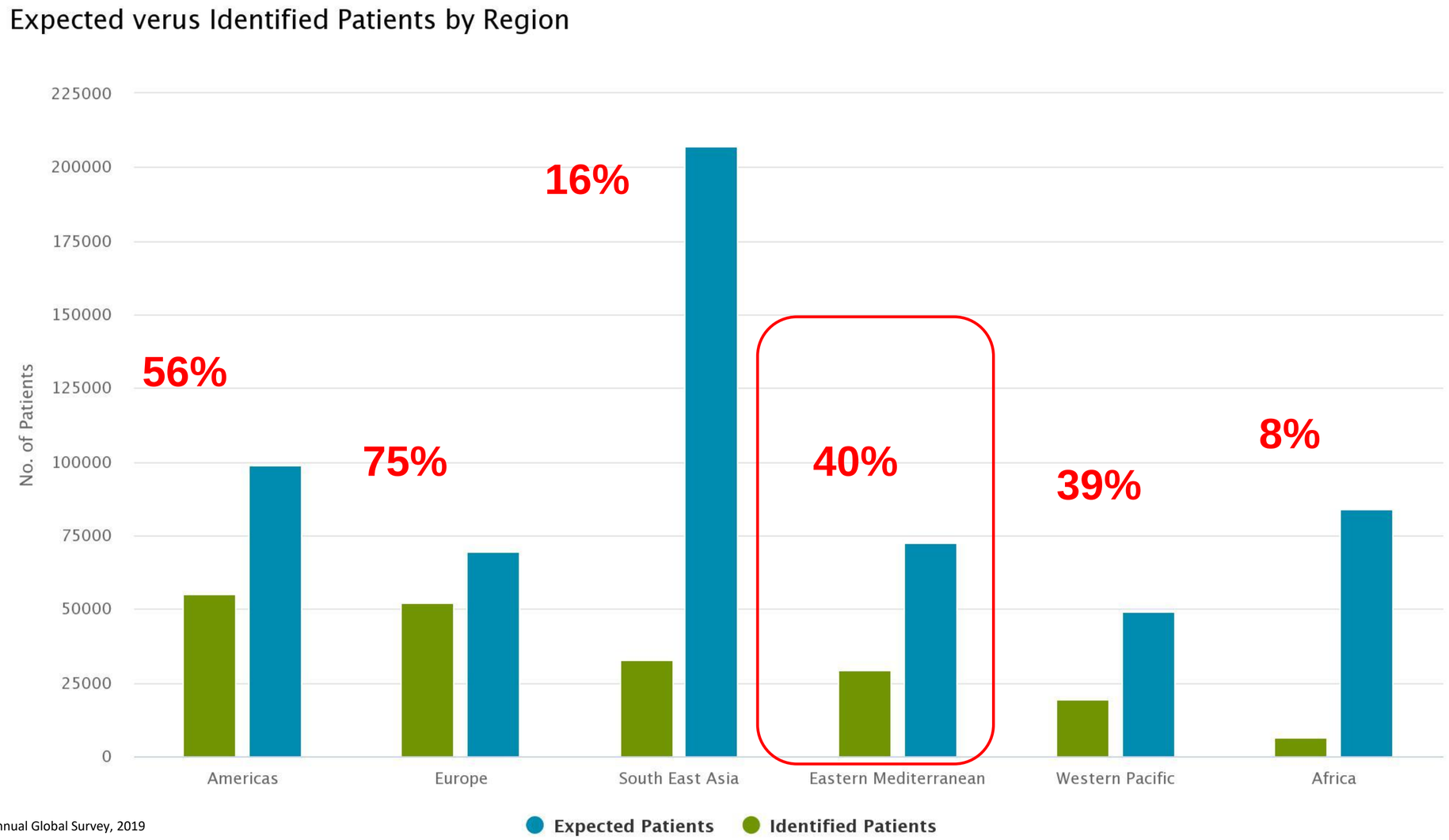
43,467 people with hemophilia are **undiagnosed** in Eastern Mediterranean

43,467 people with hemophilia are **not getting the care** they need in Eastern Mediterranean



* WFH Annual Global Survey 2019

PERCENT OF IDENTIFIED PWH PER REGION



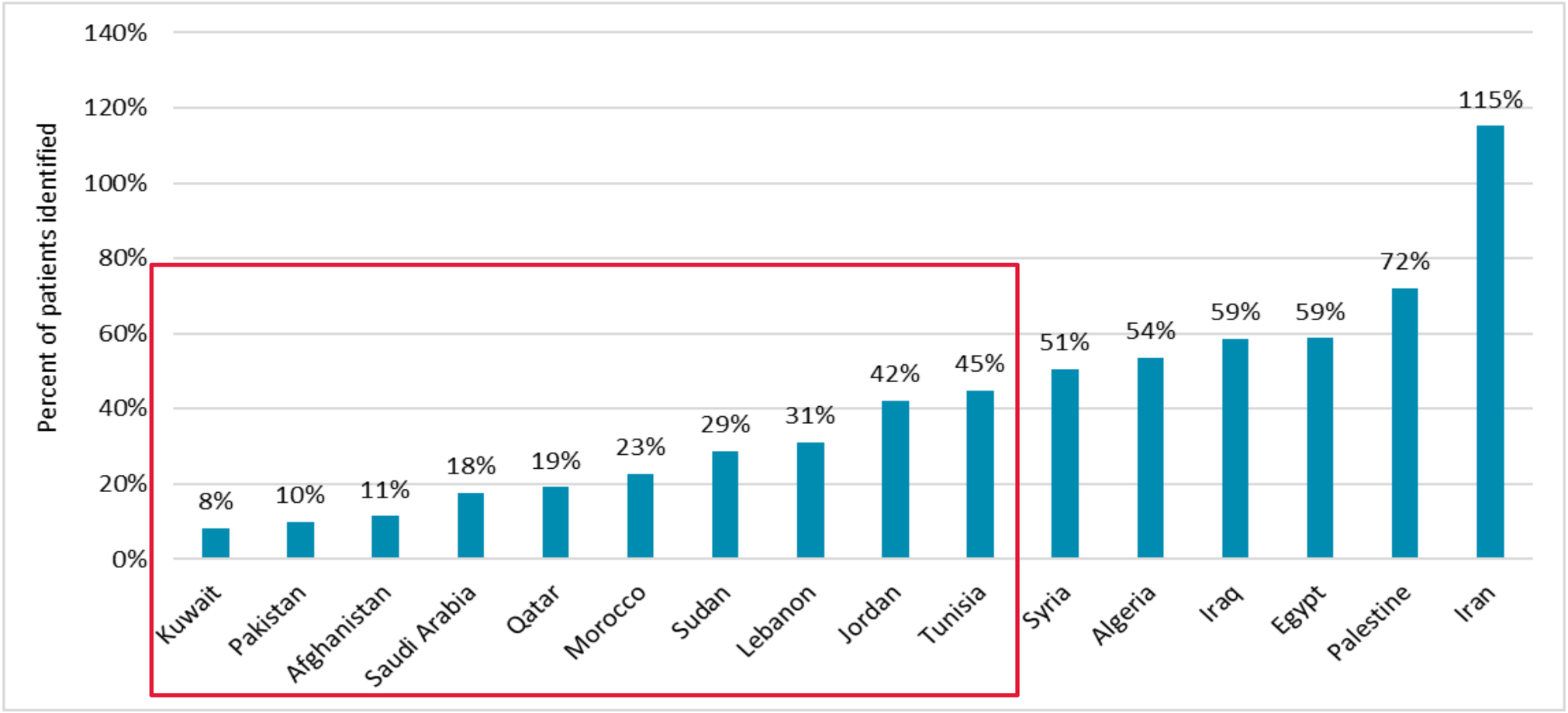
ANNUAL GLOBAL SURVEY

Reference: WFH Report on the Annual Global Survey, 2019

Data source: WFH Annual Global Survey

PREVALENCE VS IDENTIFICATION

Hemophilia: (AGS 2019)



ANNUAL GLOBAL SURVEY

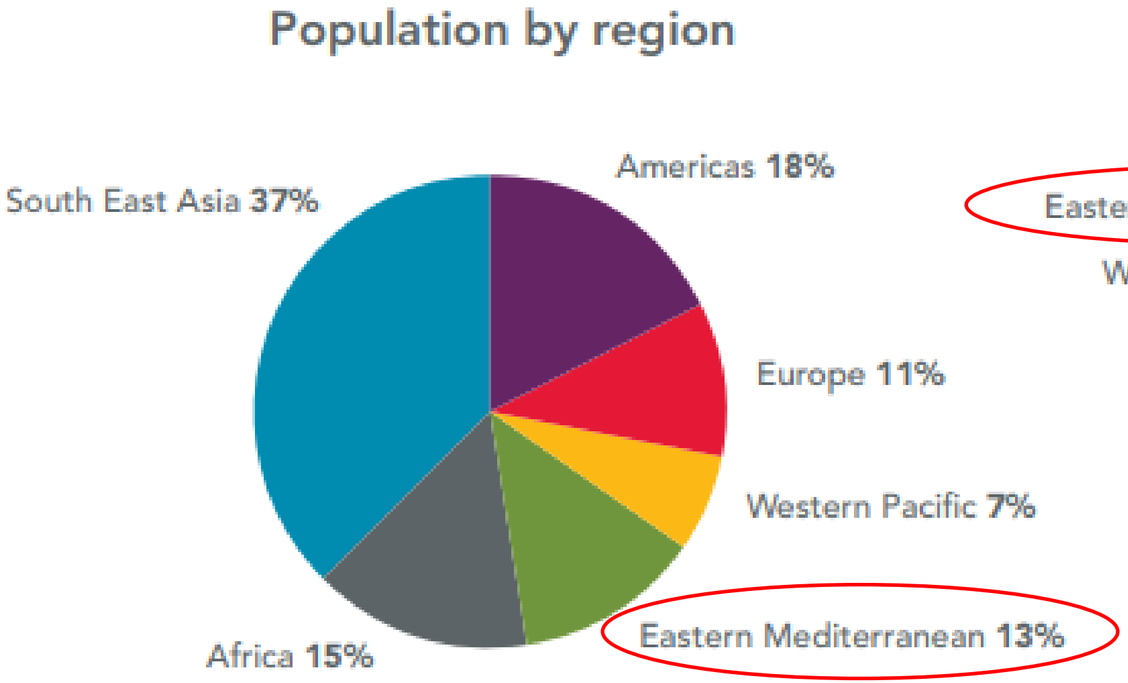
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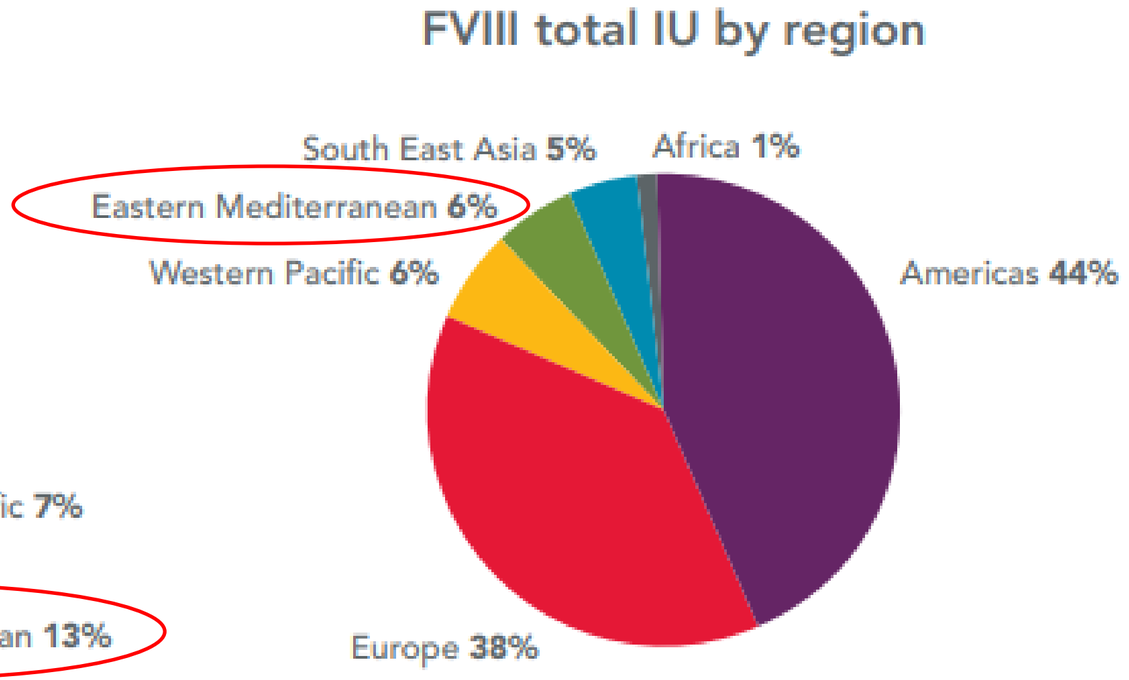
IMPORTANT DATA-DRIVEN INDICATORS OF CARE

- PWH identification rate (% PWH diagnosed)
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GLOBAL FACTOR USE
(BY REGION)

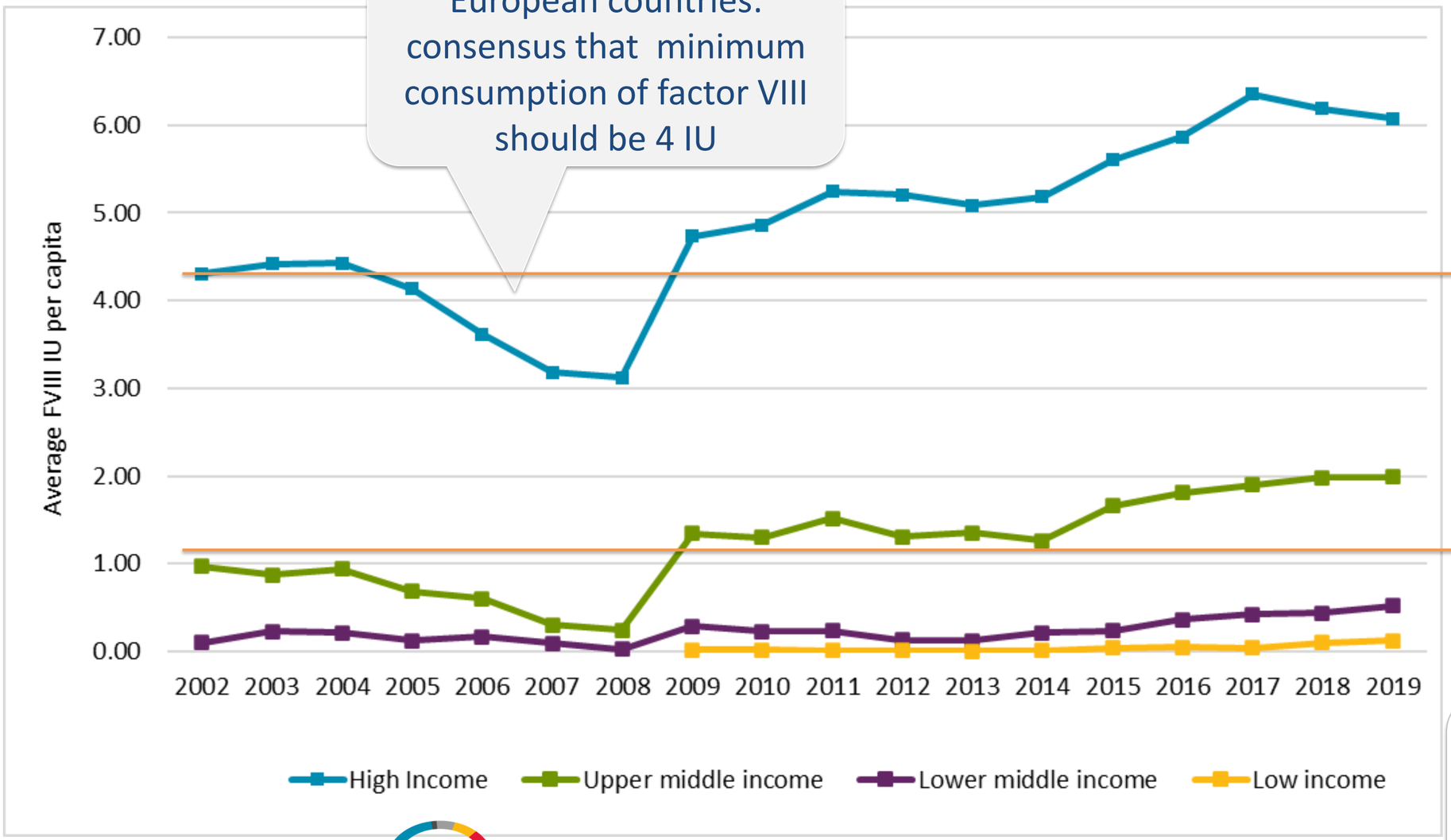
82% of the total FVIII IUs are used by 29% of the population (Americas and Europe)





Reference: WFH Report on the Annual Global Survey, 2019

GLOBAL FACTOR VIII USE
(OVER TIME – BY GNI)

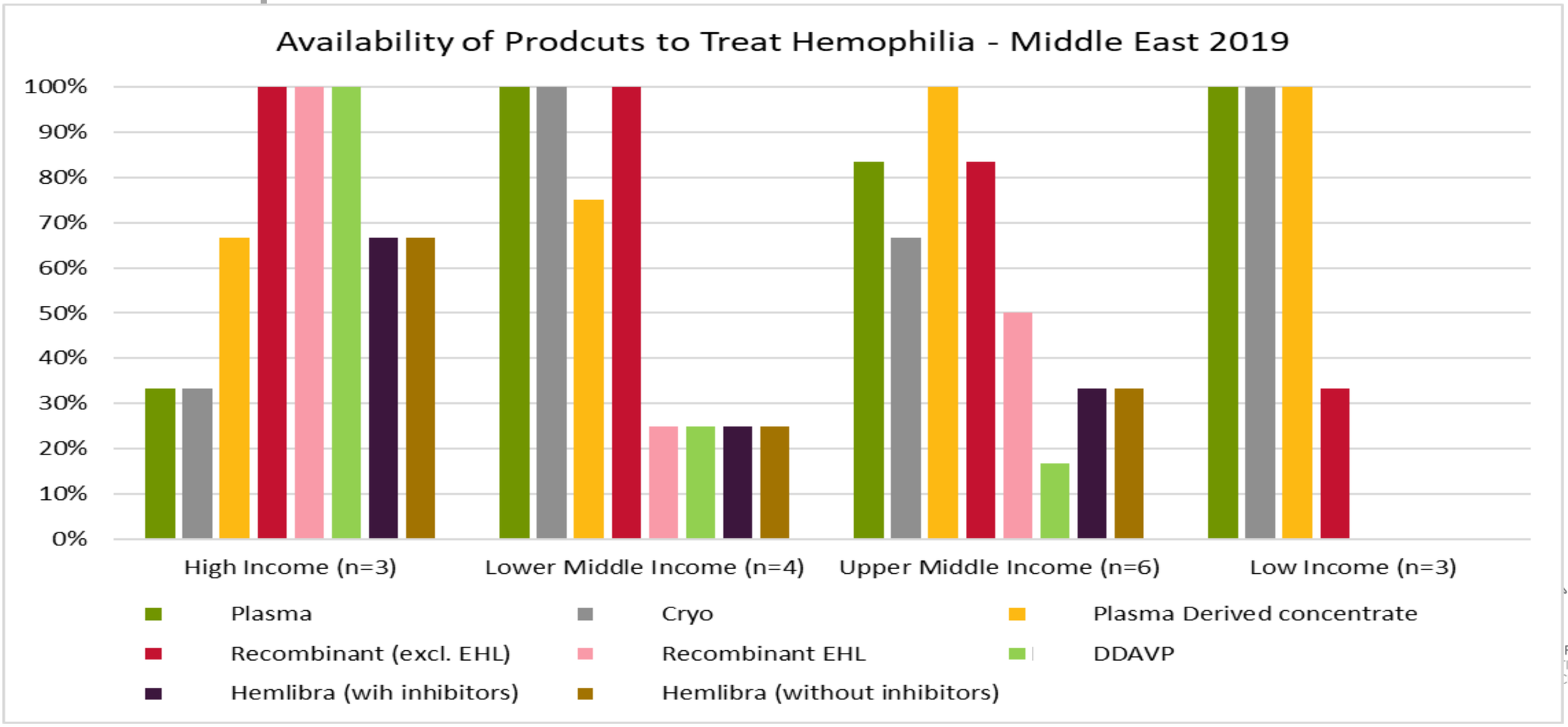


the target minimum to achieve survival for the hemophilia population

Reference: WFH Report on the Annual Global Survey, 2019

ACCESS TO TREATMENT – MIDDLE EAST

Hemophilia - AGS



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AGE AT DIAGNOSIS

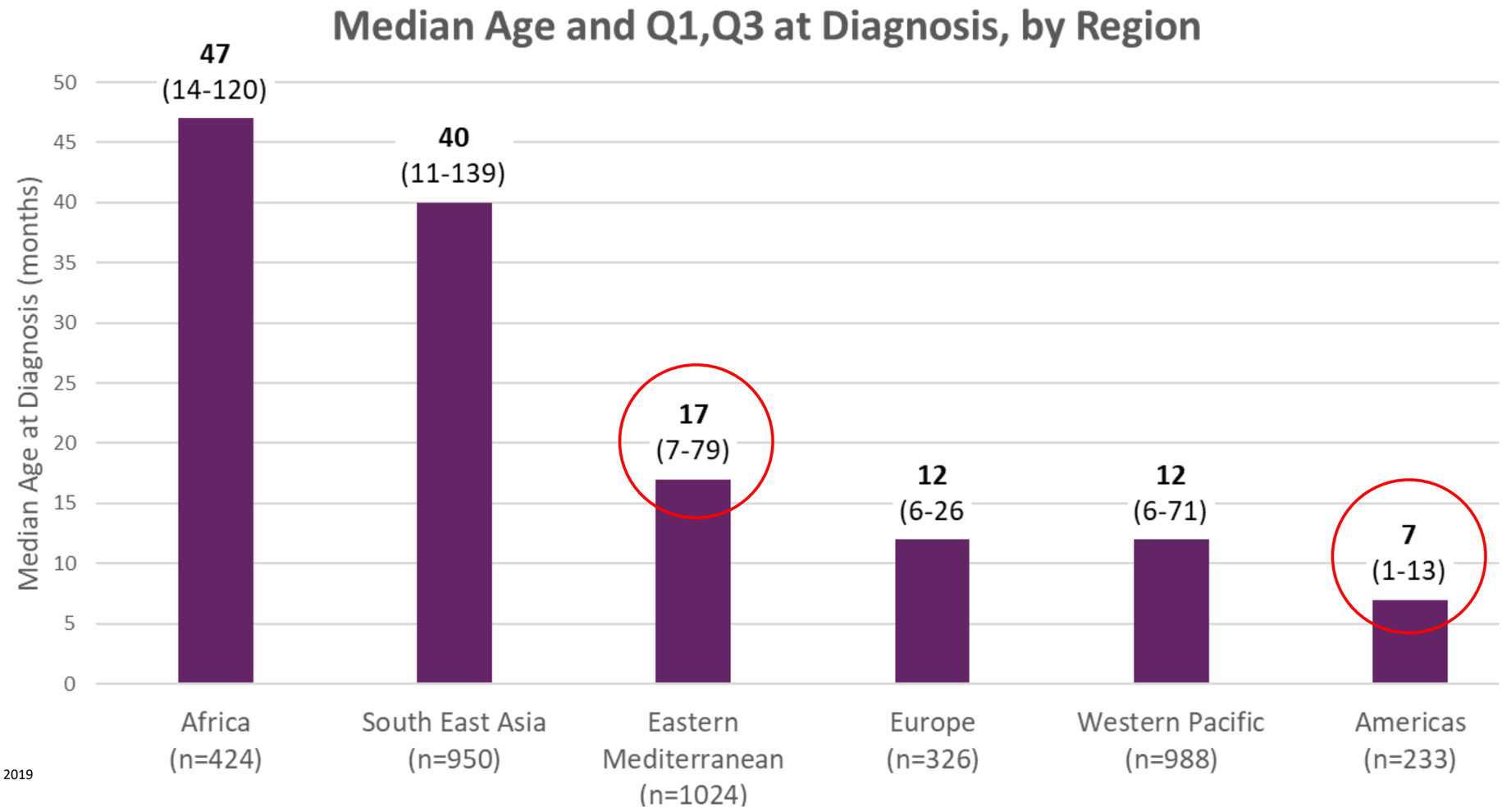
Age at Diagnosis is an important indicator of care.

Diagnosis early in life = best chance at getting early care and treatment

Early care and treatment = best chance at decreasing risk of long-term consequences of hemophilia, such as joint disease.

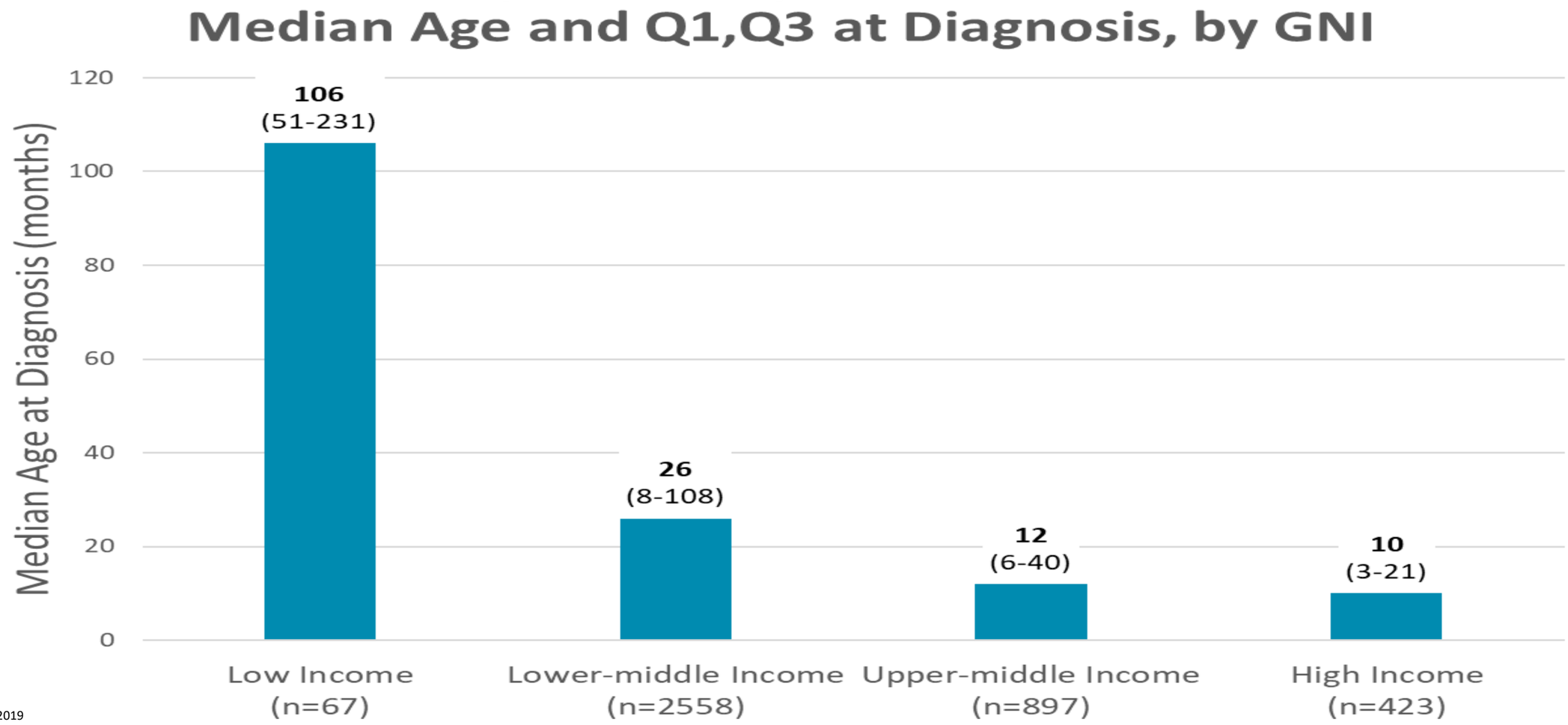
A late diagnosis = getting care and treatment later in life, which means more risk of long-term consequences of bleeding.

AGE AT DIAGNOSIS, SEVERE PWH (BY REGION)



Reference: WFH WBDR Data Report, 2019

AGE AT DIAGNOSIS, SEVERE PWH (BY GNI)



Reference: WFH WBDR Data Report, 2019

IMPORTANT DATA-DRIVEN INDICATORS OF CARE

- PWH identification rate (% PWH diagnosed)
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- Age at Diagnosis
- Annual Bleed Rate

ANNUAL BLEED RATE(ABR)

Annual Bleed Rate is the number of bleeds a PWH experiences in 1 year.

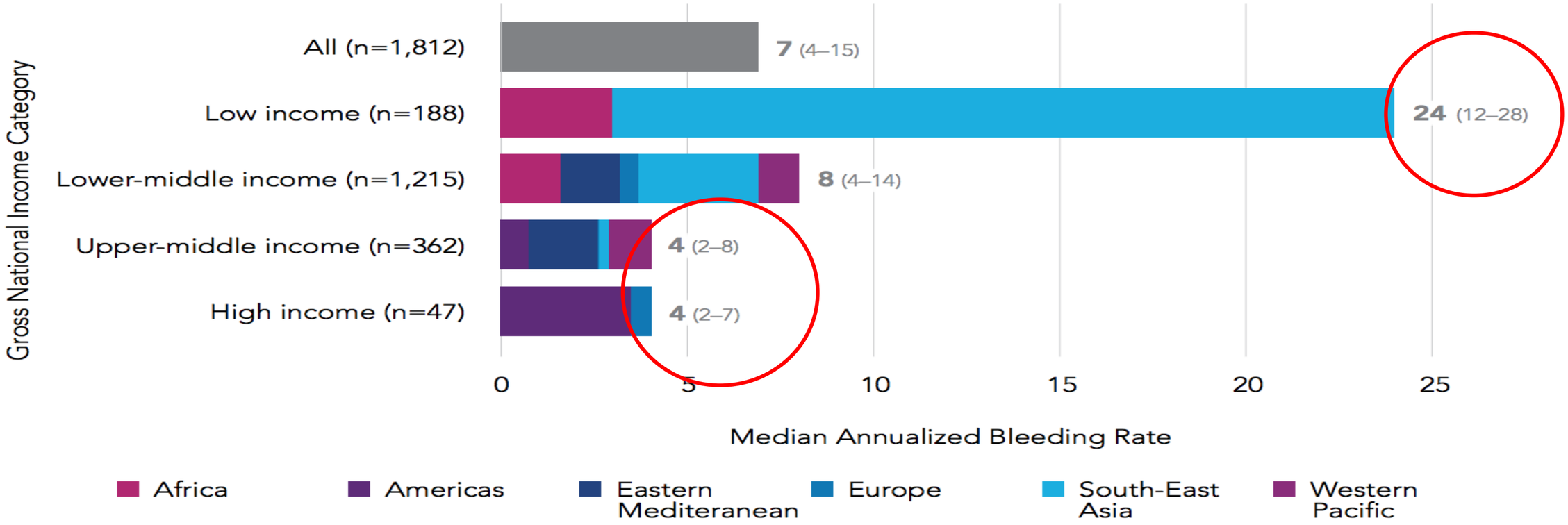
Treatment = lower ABR
Lower ABR = less symptoms and less long-term consequences of hemophilia

ABR, SEVERE PWH

(BY REGION AND GNI)

Figure 13

Median ABR by GNI and region



Reference: WFH WBDR Data Report, 2019

BURDEN OF BLEEDS: EMPLOYMENT AND EDUCATION

- Median years of education in PWH is ~10 years



12% OF PWH REPORT THEIR EMPLOYMENT STATUS IS NEGATIVELY* AFFECTED BY HEMOPHILIA

***Forced into part-time employment, long-term sick leave, unemployment, or retirement**

Data from the World Bleeding Disorders Registry 2020 Data Report

FUTURE PROSPECTS: KEY MESSAGES



1. **Diagnosis**
   Building Diagnostic Capacity

2. **Access to Treatment**
   - National Coordination and Care Delivery
   - Prophylaxis -

3. **Data Collection**
   Outcome Assessment and AGS/WBDR

4. **REGIONAL COLLABORATION**
   HEMNET

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EARLY DIAGNOSIS

Build Diagnostic Capacity to Identify PwBDs

CONSENSUS RECOMMENDATIONS

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Chapter 3: **Laboratory Diagnosis and Monitoring**

Steve Kitchen, Francisco de Paula Careta, Silmara A. de Lima Montalvão, Emna Gouider, Radoslaw Kaczmarek, Claude T. Tagny, Pierre Toulon, Glenn F. Pierce, Alok Srivastava

RECOMMENDATIONS

3.1 | Introduction

Recommendation 3.1.1

The WFH recommends that testing for diagnosis and monitoring of hemophilia must be carried out by staff with knowledge and experience in coagulation laboratory testing using equipment and reagents that have been validated for this specific purpose.

• REMARK: Details of laboratory tests for the diagnosis and monitoring of hemophilia are described in the WFH laboratory manual. CB



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INCREASE ACCESS TO TREATMENT (1)

Improve Delivery of Care

Principle 1: National coordination and delivery of hemophilia care

- A coordinated hemophilia care program, administered through a designated agency and integrated within the existing healthcare system, improves outcomes for people with hemophilia.[2,6-8]
- Optimal hemophilia care within such a program requires the following key components[2]:

✓ **comprehensive hemophilia care provided by a multidisciplinary team of specialists;**
✓ **a national or regional network of hemophilia treatment centres (HTCs);**
✓ **a national registry of patients with hemophilia;**
✓ **robust processes for the procurement and distribution of safe and effective therapies, particularly clotting factor concentrates (CFCs) and other types of hemostasis products used in hemophilia treatment;**
✓ **equitable access to these services and therapeutic products[9]**; and
✓ recognition of the socioeconomic and cultural diversities within any given community, region, or country



Chapter 1
PRINCIPLES OF CARE

Alok Srivastava, Gerard Dolan, Lisa Bagley, Margareth C. Ozelo, Emma Gouider, Debbie Hum, Steven W. Pipe, Bradley Rayner, Alison Street, Glenn F. Pierce

12 guiding principles of care that aim for ideal hemophilia management to ensure that people with hemophilia have access to appropriate, sustained, and high-quality medical services and comprehensive care

(it should be recognized that the priorities and capabilities in each country determine what is practical at any point in time)

Principle 1	National coordination and delivery of hemophilia care
Principle 2	Access to safe CFCs, hemostasis products, and curative therapies
Principle 3	Laboratory services and genetic diagnosis of hemophilia
Principle 4	Education and training in hemophilia care
Principle 5	Clinical and epidemiological research
Principle 6	Acute and emergency care for bleeds
Principle 7	Multidisciplinary care for hemophilia
Principle 8	Regular replacement therapy (prophylaxis)
Principle 9	Management of patients with inhibitors
Principle 10	Management of musculoskeletal complications
Principle 11	Management of specific conditions and comorbidities
Principle 12	Outcome assessment

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INCREASE ACCESS TO TREATMENT (2)

Prophylaxis

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Rectangular Snip



Chapter 6: **Prophylaxis in Hemophilia**

Manuel Carcao, H. Marijke van den Berg, Emna Gouider, Kate Khair, Manuel A. Baarslag, Lisa Bagley, Francisco de Paula Careta, Rolf C. R. Ljung, Margaret V. Ragni, Elena Santagostino, Glenn F. Pierce, Alok Srivastava

RECOMMENDATIONS

6.1 | Introduction

Recommendation 6.1.1

For patients with hemophilia A or B with a severe phenotype (note that this may include patients with moderate hemophilia with a severe phenotype), the WFH strongly recommends that such patients be on prophylaxis sufficient to prevent bleeds at all times, but that prophylaxis should be individualized, taking into consideration patient bleeding phenotype, joint status, individual pharmacokinetics, and patient self-assessment and preference.

- REMARK: Individualizing prophylaxis means that if patients continue to experience bleeds, their prophylaxis regimen should be escalated (in dose/frequency or both) to prevent bleeding.
- REMARK: In countries with significant healthcare constraints, the WFH still advocates for the use of prophylaxis over episodic therapy but recognizes that less intensive prophylaxis may be used. CB

Recommendation 6.1.2

For pediatric patients with severe hemophilia A or B, the WFH recommends early initiation of prophylaxis with clotting factor concentrates (standard or extended half-life FVIII/FIX) or other hemostatic agent(s) prior to the onset of joint disease and ideally before age 3, in order to prevent spontaneous and breakthrough bleeding including hemarthroses which can lead to joint disease. CB

Recommendation 6.1.3

For adolescents and adults with hemophilia who show evidence of joint damage and have not as yet been on prophylaxis, the WFH recommends commencing tertiary prophylaxis in order to reduce the number of hemarthroses, spontaneous and breakthrough bleeding, and slow down the progression of hemophilic arthropathy. CB

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IMPROVE DATA COLLECTION

Outcome Assessment + AGS and WBDR

CONSENSUS RECOMMENDATIONS

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Chapter 11: **Outcome Assessment**

Pradeep M. Poonnoose, Brian M. Feldman, Piet de Kleijn, Manuel A. Baarslag, Radoslaw Kaczmarek, Johnny Mahlangu, Margaret V. Ragni, Glenn F. Pierce, Alok Srivastava

RECOMMENDATIONS

11.2 | Frequency of bleeding

Recommendation 11.2.1

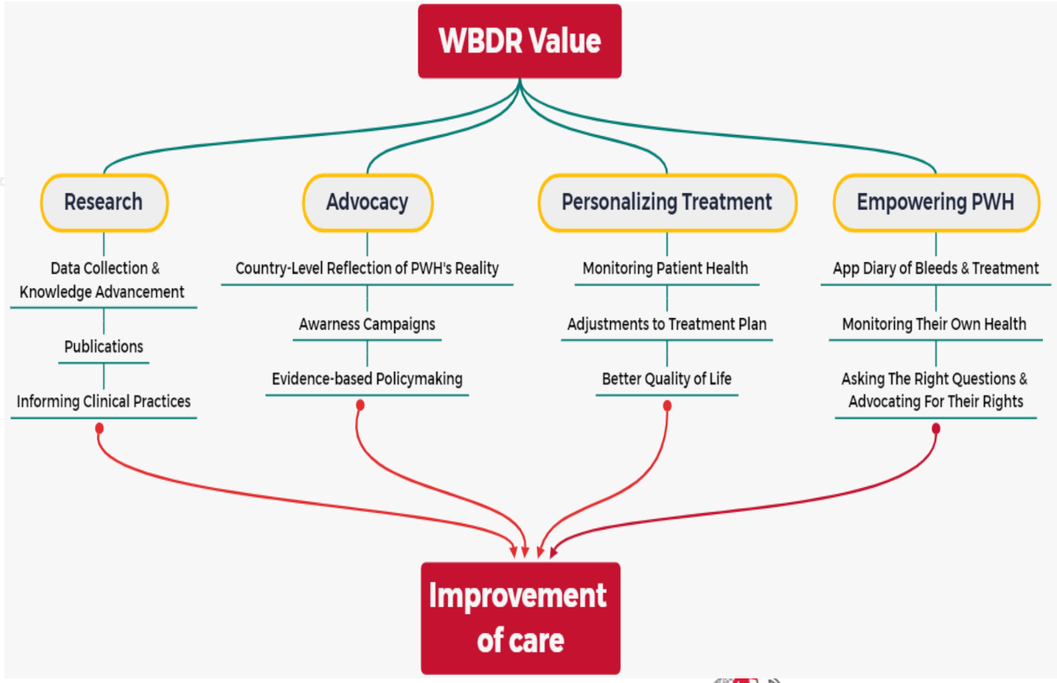
For providers of care for people with hemophilia, the WFH recommends ensuring that the frequency of all bleeds is documented in real time by patients/caregivers and reviewed together at least annually, with particular reference to intra-articular, intramuscular, and central nervous system bleeds, including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

11.7 | Health- related quality of life

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



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ENHANCE REGIONAL COLLABORATION

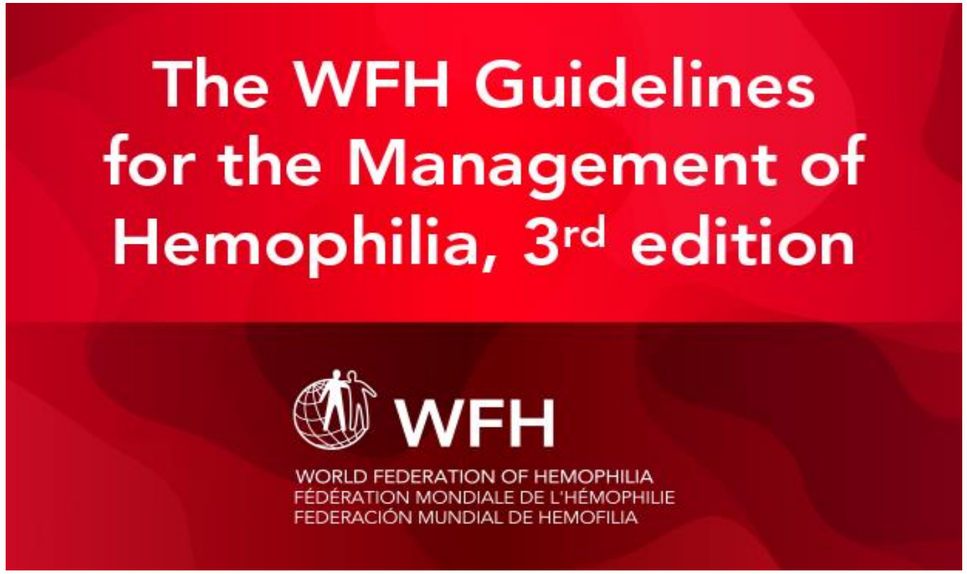
HEMNET





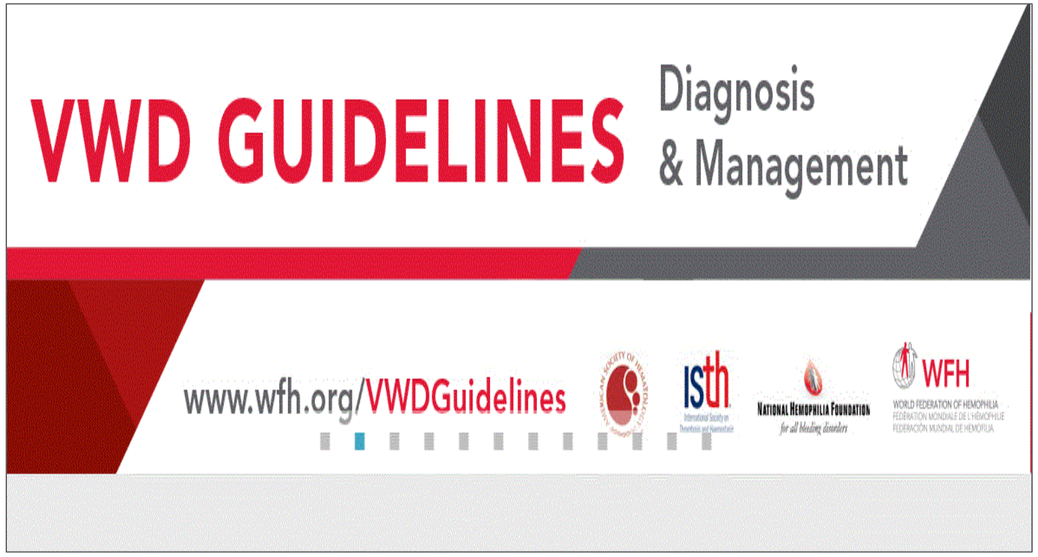
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WFH RESOURCES



12 Chapters; 337 practical recommendations

https://guidelines.wfh.org/



11 recommendations

https://ashpublications.org/bloodadvances/article/5/1/301/474884



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WFH RESOURCES: E-LEARNING CENTERS

ELEARNING CENTRES



INHERITED BLEEDING DISORDERS



INTRODUCTION TO HEMOPHILIA



NOVEL THERAPIES



CARRIERS AND WOMEN WITH HEMOPHILIA



INHIBITORS



PROPHYLAXIS



VON WILLEBRAND DISEASE



RARE CLOTTING FACTOR DEFICIENCIES

https://elearning.wfh.org/



THANK YOU
شكرا