WORLD FEDERATION OF HEMOPHILIA

WORLD BLEEDING DISORDERS REGISTRY

2019 DATA REPORT

WBDR
WFH WORLD BLEEDING DISORDERS REGISTRY

WFH
WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA

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ABOUT THE WFH

For over 50 years, the WFH – an international not-for-profit organization – has worked to improve the lives of PWH and other inherited bleeding disorders. Established in 1963, it is a global network of patient organizations in 140 countries and has official recognition from the World Health Organization (WHO).
To find out more about the WFH, visit www.wfh.org.

MISSION OF THE WORLD FEDERATION OF HEMOPHILIA

IMPROVE AND SUSTAIN CARE FOR PEOPLE WITH INHERITED BLEEDING DISORDERS AROUND THE WORLD.

SOURCE OF DATA

The data presented in the WBDR Data Report 2019 include aggregate and de-identified data from PWH who received care at a participating hemophilia treatment centre (HTC) and who consented to have their data entered into the World Bleeding Disorders Registry (WBDR).

ACKNOWLEDGEMENTS

To members of the WFH Research & Public Policy department who contributed to the creation of this report:

- Donna Coffin, MSc
- Mayss Naccache, MSc
- Ellia Tootoonchian, MPH
- Toong Youttananukorn, PhD
- Emily Ayoub, PhD

PRESIDENT & VP MEDICAL'S MESSAGE

April 2020

Dear members of the bleeding disorders community,

It is our pleasure to share the World Bleeding Disorders Registry (WBDR) Data Report 2019 with you. This report represents the second year of a worldwide effort to prospectively capture the real-world clinical experience of people with hemophilia (PWH) from around the globe. It is our hope that these data will serve as a robust tool, supporting research and advocacy initiatives, and pushing the boundaries of care for people with hemophilia for many years to come.

As of December 31, 2019, over 4,000 PWH from 53 hemophilia treatment centres (HTC) and 29 countries around the world have joined our efforts in achieving the World Federation of Hemophilia's (WFH) mission, *Treatment for All*, by participating in the WBDR. The aggregate data in this report are based on a minimal set of data, as well as the start of additional data fields, which make up the extended data set and are reported by the many dedicated health care providers and PWH who are part of this important initiative. We would like to recognize and thank the Czech Republic National Registry as a leader in the WBDR international data integration program. We have successfully completed the proof of concept study, linking the Czech Republic national data directly with the WBDR. Our data integration program will be expanded to other countries moving forward.

On behalf of the WFH, we would like to warmly thank all of our participating HTCs and PWH, who continue to recognize the value in data in our march towards *Treatment for All*. We welcome our new HTCs and look forward to working with all participating HTCs in 2020 and beyond. We would also like to recognize our visionary partners who have made it possible for us to develop this registry: Sobi and Takeda; as well as our collaborating partners: Bayer, CSL Behring, F. Hoffmann-La Roche Ltd, Grifols and Pfizer.

We would like to take a moment to thank all of our health care professionals for keeping our patients safe during the COVID-19 pandemic.

Sincerely,

Alain Weill
President

Glenn Pierce
VP Medical

ABOUT THE WBDR

Launched in January 2018, the WFH WBDR provides a platform for HTCs around the world to collect standardized data on PWH. The WBDR is a prospective, longitudinal, observational registry of patients diagnosed with hemophilia A and B. It is a privacy-protected online web-based data entry system, that allows for the collection of individual patient data, thus providing a clinical profile for each PWH.

THE WBDR IS OPEN TO
ALL PEOPLE WITH

HEMOPHILIA A OR B

ALL SEVERITIES, WHO ARE A PATIENT AT A PARTICIPATING HTC.

WBDR METHODOLOGY

Participating HTCs are at the forefront of recruiting PWH and entering the confidential and de-identified patient data into the WBDR database. The WFH works closely with all interested HTCs to guide and assist them through the required steps of participating in the program, including obtaining ethical approval, recruiting PWH, and managing their data.

The WBDR is open to all people with hemophilia A or B (all severities) who are a patient at a participating HTC. The HTCs are asked to invite all consecutive hemophilia A and B patients at their clinic to enroll in the WBDR in order to minimize the risk of selection bias. All PWH who agree to participate must provide consent.

IMPLEMENTATION

Implementation of the WBDR begins with the HTCs. Candidate HTCs are identified, with the help of our National Member Organizations (NMO), and invited to register with the WBDR, directly by the WBDR team. Interested HTCs can also express their interest in participating by completing the WBDR application form online or by emailing the WBDR team at wbdr@wfh.org. The WBDR team is available to assist HTCs in obtaining ethical approval from their local organization.

INSTITUTIONAL REVIEW BOARDS/ ETHICS COMMITTEE

Hemophilia treatment centres must obtain Institutional Research Board or Ethics Committee approval from their local institution prior to enrolling PWH into the WBDR. All WBDR documents required for ethics submission are provided to HTCs, and translated versions are available upon request.

CONSENT

People with hemophilia who are interested in participating in the WBDR must be a patient at participating HTC and must provide informed consent to have their confidential and de-identified data entered into the registry. If a PWH decides not to participate, they will continue to receive the same care as all other PWH at their HTC. For PWH who decide to participate in the WBDR, the treatment team of the HTC will record patient data after each clinic visit and enter it into the WBDR.

COLLECTION OF DATA AND FOLLOW-UP VISITS

Patient data are collected at the baseline visit (the visit PWH provide informed consent) and at all subsequent follow-up clinic visits. At the baseline visit, retrospective data based on the previous six months is collected. At each subsequent follow-up visit, data for the period since the previous clinic visit is collected. This method ensures that all data and events over the course of time are captured.

2019 DATA

At the time of the launch of the WBDR in 2018, a minimal data set was introduced. In February 2019, an extended data set (EDS) was developed and implemented. The data in this report is based on both minimal and extended data sets (Appendix 1).

UNIQUE PATIENT IDENTIFIER

Using a cryptographic hashing process, all PWH entered into the WBDR are provided a unique patient identifier (UPI). The UPI reduces the risk of duplicate patients being entered into the WBDR and will be useful for linking with other databases in the future. For more information on the UPI and the cryptographic process, please see the WBDR Data Privacy & Security document.

TRANSFER PATIENTS

Patients can be transferred between participating HTCs within the WBDR. This transfer function is useful in countries where PWH receive care at more than one HTC.

DATA LINKAGE

The WBDR includes a data integration component, whereby existing hemophilia registries can import their data directly into the WBDR and become part of this international registry. In 2019, the first data linkage process was successfully completed with the Czech Republic, and the 2018 data from the Czech Republic national registry is included in this report.

Please see page 36 for more information.

DATA QUALITY

The WBDR Data Quality Accreditation program is designed to enhance the completeness, accuracy and consistency of the data entered in the WBDR. The WBDR team works closely with all HTCs to ensure their data meets the WBDR data quality standards. Please see page 34 for more information on the WBDR data quality program.

DATA ACCESS AND GOVERNANCE

Each HTC has access to the data they enter into the WBDR, but they cannot view data that is entered from any other HTC and no other HTC can view their data. Every year, aggregate data from all enrolling HTCs will be published in the WBDR Data Report. Access to data for research and advocacy purposes will be available through the WBDR Research Governance Committee.

DATA PRIVACY

The WBDR database was developed through the collaborative efforts of the WFH, the Karolinska Institute, and Health Solutions—the latter two organizations based in Sweden. All patient information entered in the WBDR is de-identified and confidential. Data policy guidelines of Health Solutions adhere to the CE-mark (Conformité Européenne) and the U.K. standard IGSoc (Information Governance Statement of Compliance), and are compliant with the General Data Protection Regulation, which were enforced in the European Union as of May 25, 2018. Please see the WBDR Data Privacy & Security document for more information.

HTC SUPPORT AND TRAINING PROGRAM

The WBDR support and training program is available to all participating HTCs. It was developed to ensure long-term success in the WBDR. In-person and webinar trainings are available on:

- Ethics submission process
- Obtaining informed consent
- Data collection
- WBDR datasets
- Data quality management
- Using data effectively for research and advocacy purposes

ABOUT THE WBDR DATA REPORT 2019

The data in the second WBDR Data Report includes patient data collected between the launch date of January 26, 2018 and December 31, 2019. This data stems from 53 participating HTCs, representing 29 countries, who had ethical approval from their local organization and enrolled at least one PWH into the WBDR by December 31, 2019. At the time of publication of this Data Report (August 2020), an additional 29 HTCs are participating in the WBDR, for a total of 82 HTCs from 39 countries.

Please note, that at the time of data cut-off for this report (December 31, 2019), it is possible that not all eligible PWH at participating HTCs had been invited to join the WBDR. Therefore, the data in this report may not represent the entire patient population at each HTC, limiting generalizability. As the proportion of PWH enrolled in the WBDR at participating HTCs increases, the data will become more reflective of the patient population at each HTC.

The 2019 WBDR data is reported using frequency distributions and percentages for categorical data, and medians with quartiles 1 and 3, denoted as (Q1 - Q3), and/or range, for continuous variables.

WFH WBDR STEERING COMMITTEE

The WFH would like to thank the current WBDR Steering Committee for their dedication to the development and implementation of the WBDR:

- Barbara Konkle, MD, Co-Chair
- Alfonso Iorio, MD, Co-Chair
- Vanessa Byams, DrPH
- Saliou Diop, MD
- Cedric Hermans, MD
- Declan Noone, MSc
- Jamie O'Hara, MSc
- Glenn Pierce, MD, PhD, VP Medical WFH
- Alain Weill, President WFH

GLOBAL REPRESENTATION IN THE WBDR, 2019

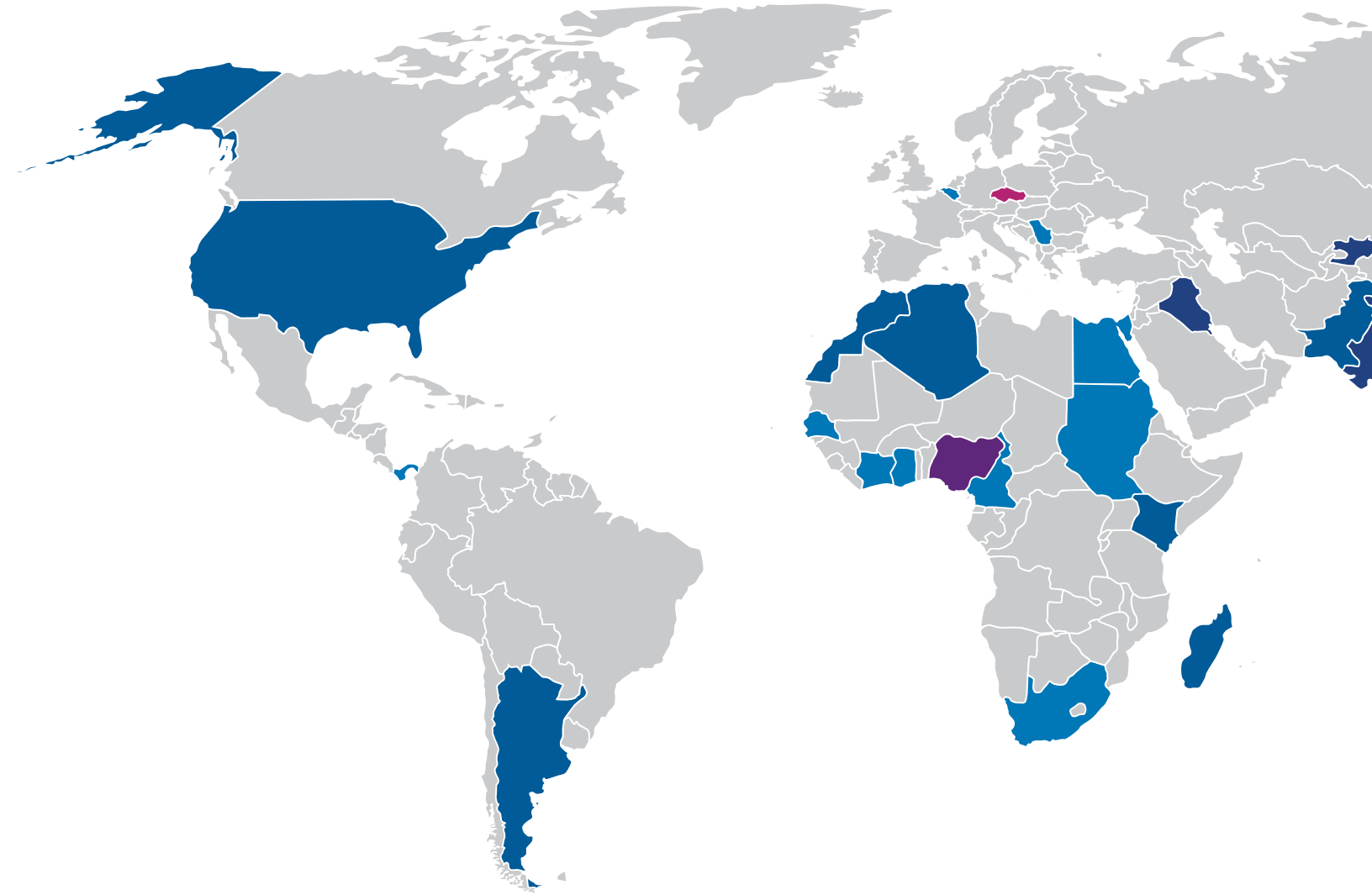
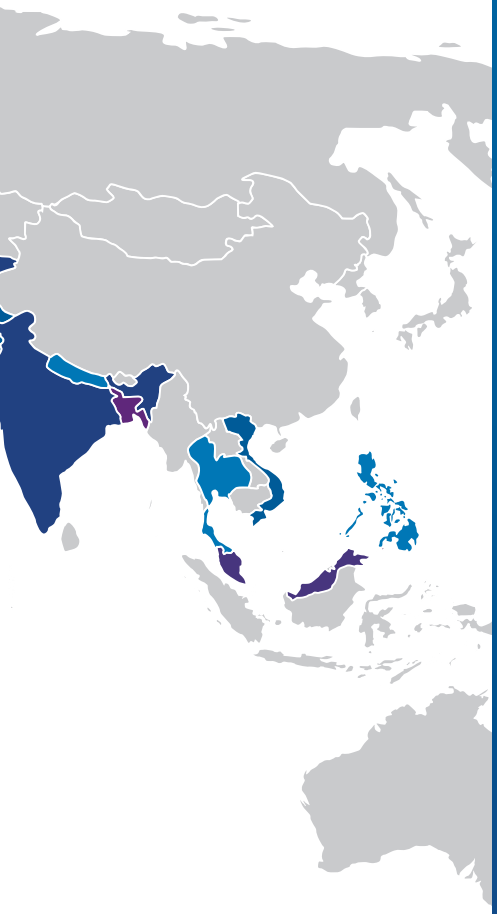


FIGURE 1

Countries and HTCs participating in the WBDR

1 → 6 Number of HTCs per country

Data Linkage (Czech Republic)



AFRICA

CAMEROON
CHU Yaoundé, Yaoundé

ETHIOPIA
Tikur Anbessa Hospital, Addis Ababa

GHANA
Komfo Anokye Teaching Hospital, Kumasi

IVORY COAST
CHU de Yopougon, Abidjan

KENYA
Kenyatta National Hospital, Nairobi

Moi Teaching and Referral Hospital, Eldoret

MADAGASCAR
CHU Joseph Ravoahangy Andrianavalona (HJRA), Antananarivo

NIGERIA
National Hospital, Abuja

University of Nigeria Teaching Hospital, Enugu State

Gombe State University, Gombe

Aminu Kano Teaching Hospital, Kano

Lagos University Teaching Hospital, Lagos

SENEGAL
Centre National de Transfusion Sanguine, Dakar

SOUTH AFRICA
University of the Free State, Bloemfontein

WESTERN PACIFIC

MALAYSIA
Terengganu Hospital, Terengganu

Sultanah Aminah Hospital, Johor Bahru

Hospital Ampang, Ampang

Sarawak General Hospital, Sarawak

PHILIPPINES
University of Santo Tomas Hospital, Manila

VIETNAM
National Institute of Hematology and Blood Transfusion, Hanoi

Blood Transfusion Hematology, Ho Chi Minh City

AMERICAS

ARGENTINA
Fundación de la Hemofilia and Instituto De Investigaciones Hematológicas "Dr. Mariano R. Castex", Buenos Aires

Centro Asist Reg de Hemoterapia, Bahía Blanca

PANAMA
Hospital del Niño, Panamá City

USA
University of Cincinnati Hemophilia Treatment Center, Cincinnati

Wake Forest Baptist Health, Winston-Salem

EUROPE

BELGIUM
Cliniques Universitaires Saint-Luc, Woluwe-Saint-Lambert

CZECH REPUBLIC
FN Brno – DN (Oddělení dětské hematologie), Brno

FN Brno – OKH, Brno

Nemocnice – Dětské oddělení, České Budějovice

Nemocnice – OKH, České Budějovice

FNHK – Dětská klinika, Hradec Králové

FNHK – IV. interní hematologická klinika, Hradec Králové

KN Liberec – OKH, Liberec

FN Olomouc – Dětská klinika, Olomouc

FN Olomouc – Hemato-onkologická klinika, Olomouc

FN Ostrava – Klinika dětského lékařství, Ostrava

FN Ostrava – Krevní centrum, Ostrava

FN Plzeň – Dětská klinika, Plzeň

FN Plzeň – ÚKBH, Plzeň

Městská poliklinika - Hemacentrum, Plzeň

FN Motol – Klinika dětské hematologie a onkologie, Praha

Masarykova nemocnice – Dětská klinika (hematologie), Ústí n.L.

Masarykova nemocnice – OKH, Ústí n.L.

KYRGYZSTAN
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National Center of Oncology and Hematology, Bishkek

Osh Interregional Joint Clinical Hospital, Osh

SERBIA
Mother and Child Health Care Institute of Serbia "Dr Vukan Cupic", Belgrade

EASTERN MEDITERRANEAN

ALGERIA
Service d'hématologie CHU Annaba, Annaba

Unité hémophilie et maladies hémorragiques héréditaires, Constantine

EGYPT
Shabrawishi Hospital, Giza

IRAQ
Hemophilia Center – Medical City, Baghdad

Mustansirya University, Baghdad

Basra Center for Hereditary Blood Diseases, Basra

MOROCCO
Centre de Référence de l'Hémophilie, Hôpital Ibn Sina, Rabat

Centre de Traitement de l'hémophilie de Rabat, Hôpital d'Enfants de Rabat, Rabat

PAKISTAN
Haemophilia Treatment Centre, Lahore

Haemophilia Treatment Centre, Rawalpindi

SUDAN
Haemophilia Center, Khartoum Teaching Hospital, Khartoum

SOUTH-EAST ASIA

BANGLADESH
Chittagong Medical College Hospital, Chittagong

Bangabandhu Sheikh Mujib Medical University, Dhaka

Dhaka Medical College, Dhaka

Lab One Foundation, Dhaka

Rajshahi Medical College & Hospital, Rajshahi

INDIA
Haemophilia Treatment Centre, District Hospital, Aluva

Christian Medical College, Ludhiana

Melaka Manipal Medical College, Hemophilia Society Manipal, Manipal

NEPAL
Civil Service Hospital, Kathmandu

THAILAND
Chiang Mai University Hospital, Chiang Mai

DATA INCLUDED IN THE WBDR 2019 DATA REPORT

PARTICIPATION

In 2018 and 2019, 4,166 PWH were enrolled in the WBDR, representing 6 regions, 29 countries and 53 HTCs (Figures 1 and 2).

29
COUNTRIES

53
HEMOPHILIA TREATMENT CENTRES

4,166
PEOPLE WITH HEMOPHILIA

TABLE 1
Participation Summary

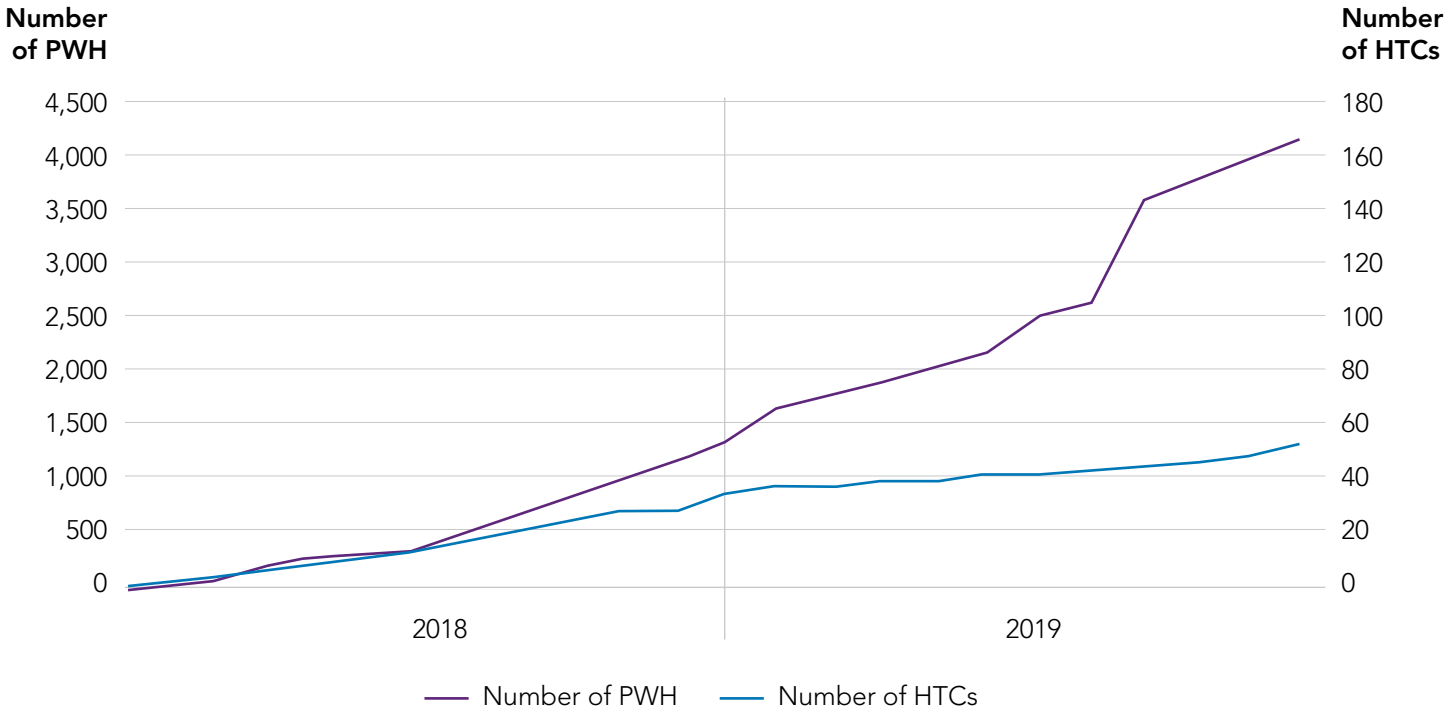
		Severity*		
	All PWH	Mild	Moderate	Severe
Countries, n	29			
Hemophilia treatment centres**, n	53			
People with hemophilia, n	4,166	874 (21%)	1,103 (26%)	2,064 (50%)
Distribution of PWH by region†, n (%)				
Africa	444	38 (9%)	84 (19%)	222 (50%)
Americas	268	32 (12%)	31 (12%)	205 (76%)
Eastern Mediterranean	888	125 (14%)	226 (25%)	535 (60%)
Europe	909	405 (45%)	133 (15%)	362 (40%)
South-East Asia	1,067	197 (18%)	471 (44%)	385 (36%)
Western Pacific	590	77 (13%)	158 (27%)	355 (60%)
Distribution of PWH by GNI§, n (%)				
Low income	400	53 (13%)	194 (49%)	146 (37%)
Lower-middle income	1,809	261 (14%)	626 (35%)	808 (45%)
Upper-middle income	1,054	147 (14%)	161 (15%)	744 (71%)
High income	903	413 (46%)	122 (14%)	366 (40%)

* Severity defined by factor level: mild > 0.05 IU; moderate = 0.01–0.05 IU; severe = < 0.01 IU. 125 PWH had unknown severity.
** HTCs included are those who had ethical approval and had enrolled at least 1 PWH
† Regions based on WHO regional groupings[1]
§ GNI = Gross National Income; Gross National Income categories based on The World Bank Group 2018 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)"[2]

Figure 2

PWH and HTC enrollment in the WBDR

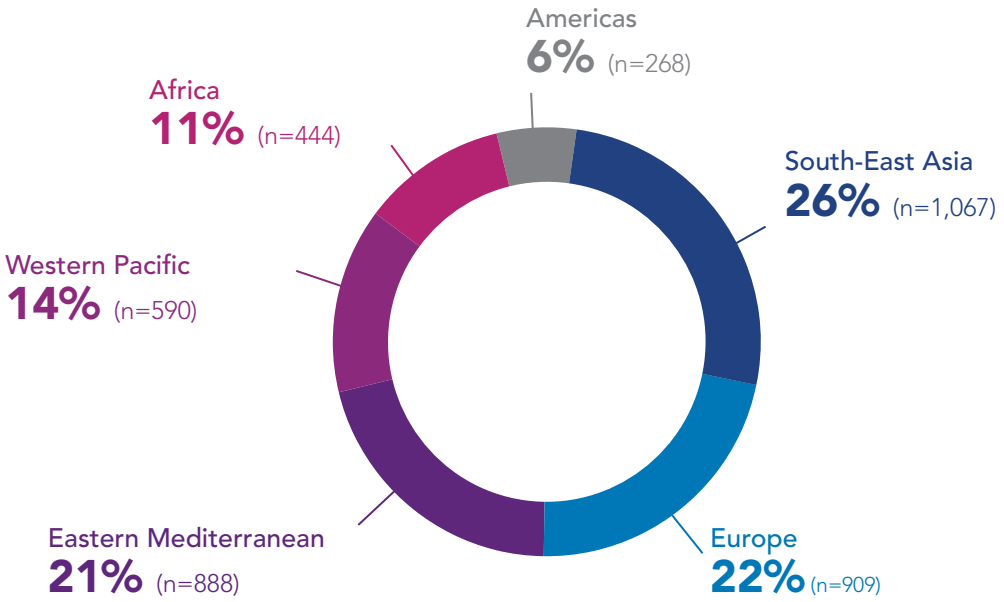
January 2018 – December 2019



The regional classification used in the WBDR is based on the WHO regional classification[1]. The majority of PWH are from the South-East Asia region (Bangladesh, Nepal, India, Thailand) and the Europe region (Czech Republic, Kyrgyzstan, Belgium, Serbia), representing 26% and 22% of PWH respectively (Figure 3).

Figure 3

Distribution of PWH by Region



The distribution of participants by Gross National Income (GNI) per capita[2], demonstrates that majority of the participant PWH are from lower middle income countries (43%), followed by upper middle income, low and high income countries, representing 25%, 22% and 10% respectively (Figure 4).

Figure 4

Distribution of PWH by Gross National Income

DEMOGRAPHICS

TABLE 2
Demographics summary

		Severity*		
Type of hemophilia, n (%)	**All PWH (n=4,166)**	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Hemophilia A	3,565 (86%)	763 (87%)	887 (80%)	1,809 (88%)
Hemophilia B	580 (14%)	108 (12%)	213 (19%)	250 (12%)
Unknown	21 (<1%)	3 (<1%)	3 (<1%)	5 (<1%)
Sex, n (%)				
Male	4,147 (99%)	871 (99%)	1,097 (99%)	2,054 (99%)
Female	19 (1%)	3 (1%)	6 (1%)	10 (1%)
Age of PWH**				
Age, years, median (IQR)	20 (11-33)	25 (13-42)	18 (10-28)	20 (11-32)
Pediatrics (<18 years), n (%)	1,878 (45%)	305 (35%)	556 (50%)	1,135 (55%)
Adults (≥18 years), n (%)	2,288 (55%)	569 (65%)	547 (50%)	929 (45%)

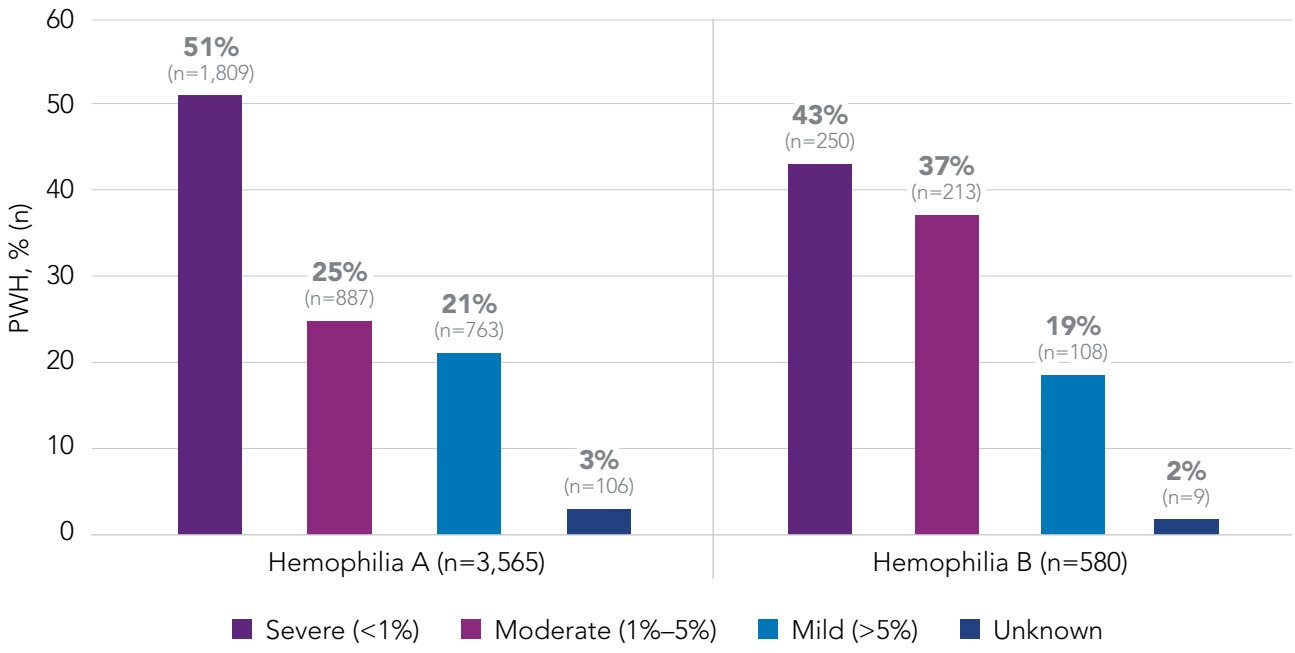
IQR=interquartile range
* 125 PWH had unknown severity
**Age of PWH was calculated as of December 31, 2019

HEMOPHILIA TYPE AND SEVERITY

Overall, 99% (n=4,147) of participants were male, 86% (n=3,565) had hemophilia A and 14% (n=580) had hemophilia B (Table 2). The most frequent severity category among both hemophilia A and hemophilia B patients was severe at 51% and 43% respectively (Figure 5).

Figure 5

Hemophilia type* and severity, % (n)



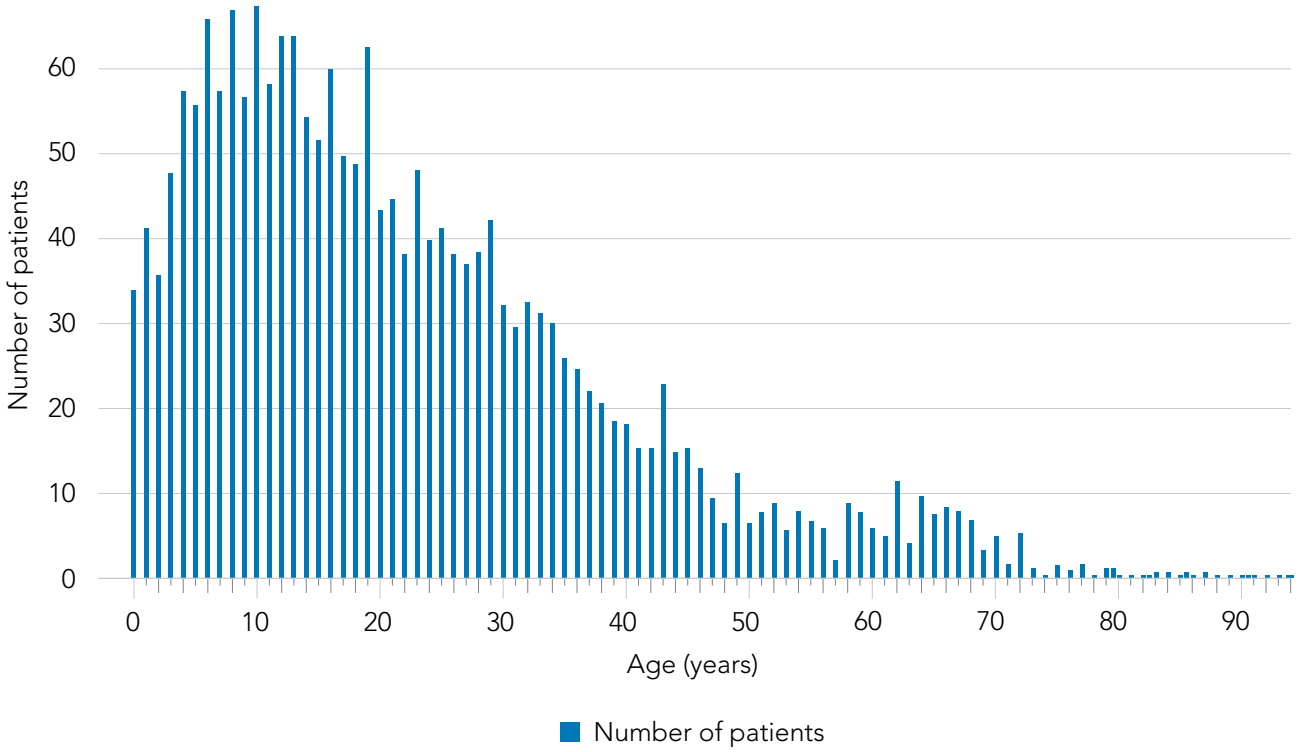
* 21 PWH had unknown hemophilia type and were excluded from this figure

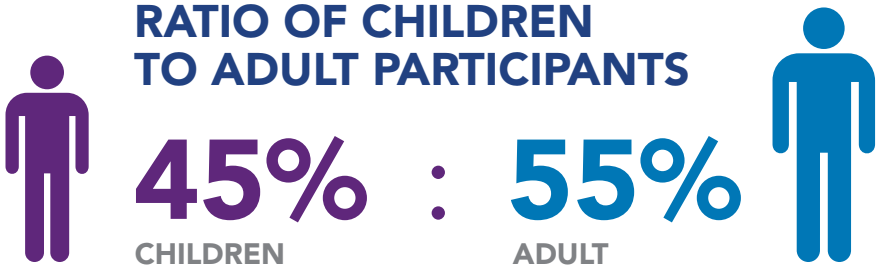
AGE OF PWH IN THE WBDR

The median age of participants was 20 years, ranging from 1 month to 98 years (Figure 6). Adults (≥18) comprised 55% (n=2,288) and children (<18) comprised 45% (n=1,878) of all participants.

Figure 6

Age distribution of PWH in the WBDR





DIAGNOSIS AND CLINICAL HISTORY

TABLE 3a

Diagnosis and clinical history summary

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Age at diagnosis, months, median (IQR)	27 (8-101)	76 (22-212)	36 (11-116)	15 (6–58)
By age category, n (%)				
0–12 months	1,321 (32%)	142 (16%)	290 (26%)	866 (42%)
1–4 years	1,260 (30%)	216 (25%)	351 (32%)	639 (31%)
5–17 years	965 (23%)	260 (30%)	309 (28%)	362 (18%)
18–44 years	414 (10%)	147 (17%)	126 (11%)	129 (6%)
45+ years	71 (2%)	53 (6%)	9 (1%)	8 (<1%)
Age unknown	135 (3%)	56 (6%)	18 (3%)	60 (3%)

TABLE 3b

Newly diagnosed PWH in 2019, n (%)	178	32 (18%)	67 (38%)	66 (37%)
Age at first bleed, months, median (IQR)**	10 (6-24)	24 (6-72)	11 (6-30)	8 (5-15)
Age at first joint bleed†, months, median (IQR)	24 (12-60)	59 (14-108)	24 (11-60)	19 (11-48)

* 125 PWH had unknown severity
** Based on 3,159 PWH with data on first bleed.
† Based on 2,765 PWH with data on first joint bleed.

AGE AT DIAGNOSIS

The median (IQR) age at diagnosis was 27 months (8 - 101) for all PWH, and 15 months (6 - 58) for severe PWH (Table 3a). For all PWH, median age at diagnosis by region ranged from 50 months in South-East Asia to 8 months in the Americas (Figure 7). In severe PWH, the highest age at diagnosis was in Africa at 38 months and lowest was again the Americas at 8 months (Figure 7). Age at diagnosis decreased as GNI increased, from 44 months in low-income countries, to 27 months in high income countries for all PWH, with a similar pattern among PWH with severe disease at 35 months and 11 months (Figure 8).

There were 178 PWH newly diagnosed in 2019, with a median age at diagnosis of 84 months, ranging from 0 to 946 months (79 years).

Thirty-two percent of all PWH, and 42% of severe PWH, were diagnosed before 12 months of age. Sixty-two percent of all PWH and 73% of severe PWH were diagnosed before the age 5 years (Table 3a, Figure 9).

27
MONTHS
MEDIAN AGE AT DIAGNOSIS

178
NEWLY DIAGNOSED PATIENTS IN 2019

Figure 7

Age at diagnosis by Region

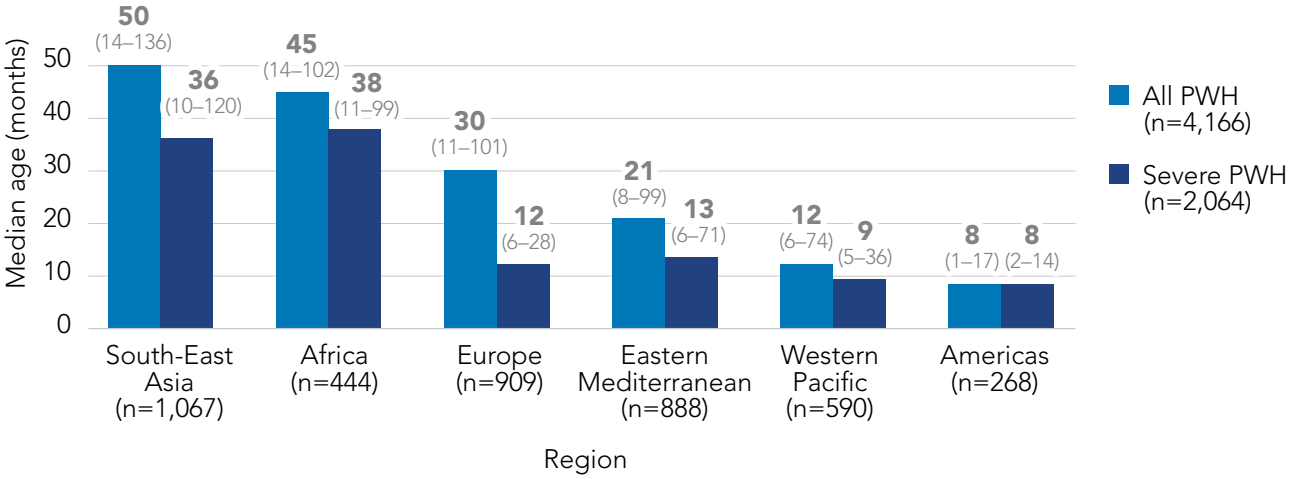


Figure 8

Age at diagnosis by Gross National Income

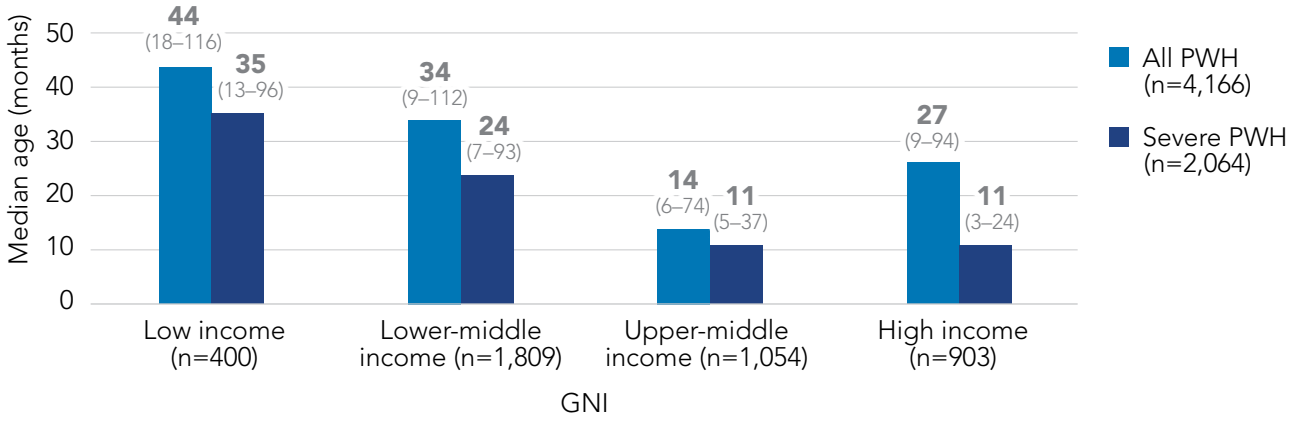
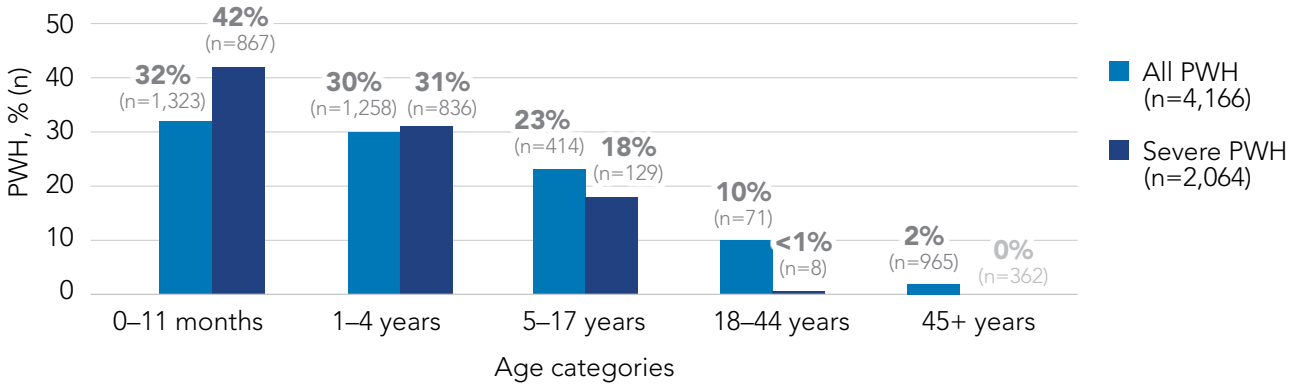


Figure 9

Age distribution of PWH at diagnosis, % (n)



AGE AT FIRST BLEED AND FIRST JOINT BLEED

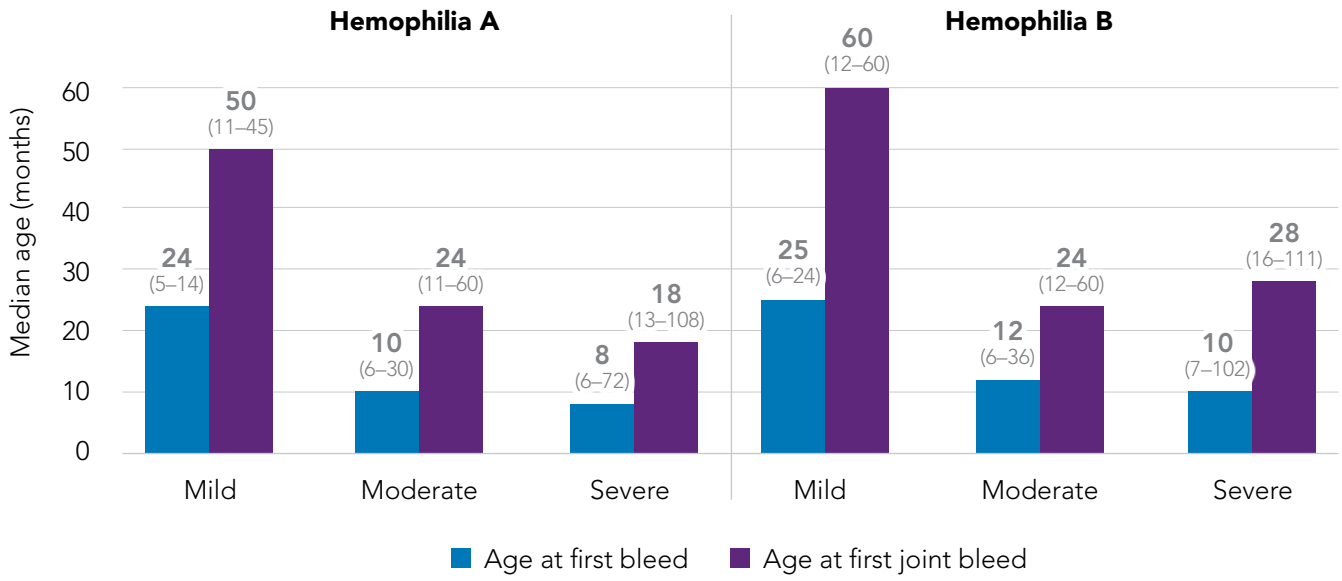
The median age at first bleed and first joint bleed were 10 and 24 months, respectively, for all PWH, both decreasing with more severe hemophilia, for the most part (Table 3b; Figure 10).

For hemophilia A patients, the median age at first bleed was 8 months for patients with severe hemophilia, increasing to 24 months for patients with mild hemophilia. The median age at first joint bleed was 18 months for patients with severe hemophilia, increasing to 50 months for mild patients (Figure 10; see Appendix 2, Table A).

For hemophilia B patients, the median age at first bleed was 10 months for patients with severe hemophilia and 25 months for mild hemophilia. Median age at first joint bleeds were 28, 24 and 60 months for severe, moderate and mild PWH, respectively (Figure 10; see Appendix 2, Table B).

Figure 10

Age in months at first bleed and first joint bleed by severity, Hemophilia A & B, months, median (IQR)



* 125 patients with unknown severity not included

COMORBIDITIES

The data collected on comorbidities are not mandatory data fields, however, of those that provided the information, 1,155 (28%) were tested for HIV. Of those who reported that they were tested, 12 (1%) had positive results and of these, 8 were people with severe hemophilia (Table 4). For Hepatitis C Virus (HCV), 1,300 PWH (31%) were reported to have been tested. Of those tested, 158 (12%) had an active infection. The rate of infection was similar among all severities (Table 5).

TABLE 4
HIV Status

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Testing reported	1,155 (28%)	91 (10%)	208 (19%)	837 (41%)
Positive, n (%)	12 (1%)	2 (2%)	2 (1%)	8 (1%)
Negative, n (%)	1,143 (99%)	89 (98%)	206 (99%)	829 (99%)

* 125 PWH had unknown severity

TABLE 5
HCV Status

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Testing reported	1,300 (31%)	118 (14%)	274 (25%)	891 (43%)
Active infection, n (%)	158 (12%)	13 (11%)	33 (12%)	112 (13%)
Infection resolved spontaneously, n (%)	19 (2%)	2 (2%)	1 (<1%)	16 (2%)
Infection resolved with treatment, n (%)	52 (4%)	7 (6%)	5 (2%)	40 (5%)
No infection, n (%)	1,071 (82%)	96 (81%)	235 (86%)	723 (81%)

* 125 PWH had unknown severity

EMPLOYMENT AND EDUCATION

Of those PWH that had their employment status reported, 42% were employed either part-time or full-Time. Hemophilia affected the employment status of 27% of PWH, forcing them into part-time employment, long-term sick leave, unemployment or retirement (Table 6; Figure 11).

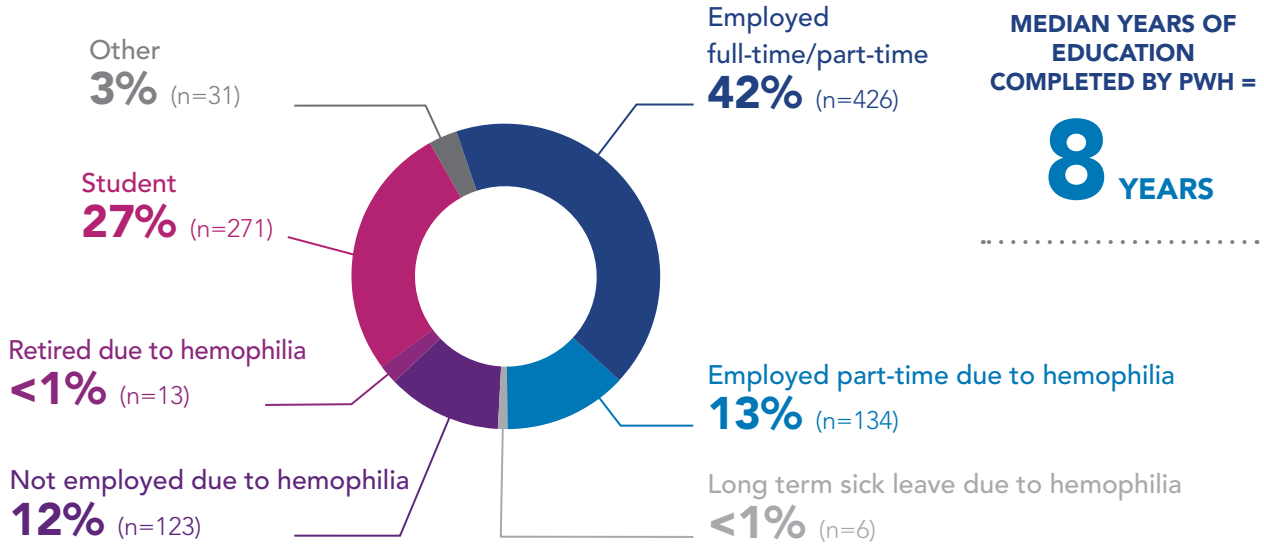
The median years of education completed by the PWH was 8. This includes years of study up to high school, plus vocational, professional, and advanced degrees.

TABLE 6
Employment & Education

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Employment status reported	1,004	150 (15%)	305 (30%)	524 (52%)
Employed full-time or part-time	426	77 (18%)	123 (29%)	217 (51%)
Employed part-time due to hemophilia	134	13 (10%)	38 (28%)	82 (61%)
Long term sick leave due to hemophilia	6	2 (33%)	2 (33%)	2 (33%)
Not employed due to hemophilia	123	9 (7%)	40 (33%)	70 (57%)
Retired due to hemophilia	13	3 (23%)	3 (23%)	7 (54%)
Student	271	40 (15%)	87 (32%)	133 (49%)
Other	31	6 (19%)	12 (39%)	13 (42%)
Years of education completed**, median (IQR)	8 (4–12)	9 (5–12)	8 (4–12)	8 (3–12)

* 125 PWH had unknown severity
** Based on 1,865 PWH with data on education

Figure 11
Employment Status of PWH



CLINICAL DATA

NOTE: The clinical data represent clinical events which occured and were reported in 2019. It is possible that patients did not have a follow up visit in 2019.

TABLE 7

Bleeding events summary, 2019

		Severity*		
	All PWH (n=4,166)**	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Average number of bleeds per patient, n	2.9	1.6	3.1	3.2
Number of patients with 0 bleeds in 2019, n (%)	500 (12%)	96 (11%)	81 (7%)	317 (15%)
Target joints§, n (%)				
≥1	1,182 (28%)	96 (11%)	289 (26%)	751 (36%)
Total bleeding events, n	11,950	1,429	3,450	6,671
Location of bleed, n (%)				
Joint	8,775 (74%)	951 (67%)	2,416 (70%)	5,077 (77%)
Muscle	1,928 (16%)	279 (20%)	729 (21%)	892 (13%)
Central nervous system	42 (<1%)	2 (<1%)	17 (<1%)	23 (<1%)
Other location	1,180 (10%)	197 (14%)	295 (9%)	647 (10%)
Not reported	25 (<1%)	0 (0%)	7 (<1%)	32 (<1%)

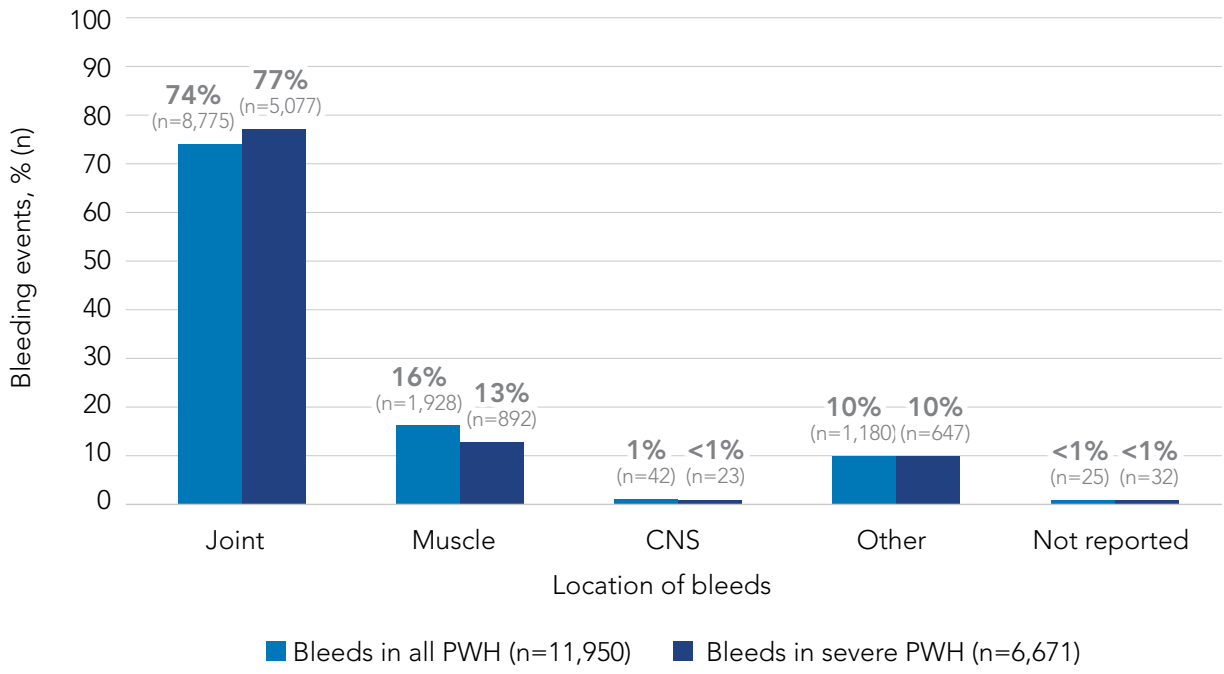
* 125 PWH had unknown severity
** 2019 Data for 771 Czech Republic patients were not available at the time of publication
§ Includes PWHs who reported at least one target joint in 2019; Target joints are defined as '3 or more spontaneous bleeds into a single joint within a consecutive 6-month period. Where there have been ≤ 2 bleeds into the joint within a consecutive 12-month period the joint is no longer considered a target joint';[3]

BLEEDING EVENTS

In 2019, a total of 11,950 bleeds were reported by PWH. Of these, 74% (n=8,775) were joint bleeds, 16% (n=1,928) were muscle bleeds and <1% (n=42) were central nervous system (CNS) bleeds (Table 7). There were 10% (n=1,180) of bleeds reported as 'other' locations, and the location of <1% (n=25) of bleeds was not reported (Figure 12). A total of 6,671 bleeds were reported for patients with severe hemophilia. The distribution by location was similar to that of all PWH (Figure 12).

Figure 12

Location of bleeding events, % (n)



ANNUALIZED BLEEDING RATE AND ANNUALIZED JOINT BLEEDING RATE

The annualized bleeding rate (ABR) and annualized joint bleeding rate (AJBR) were calculated by annualizing the number of bleeds, and number of joint bleeds respectively. ABR and AJBR were calculated based on the total number of bleeds reported at follow-up visits in 2019, divided by the observation period in days, and annualized, for ABR and AJBR separately. The calculation used is: (Number of bleeds / observation period in days) x 365.25. Only observation periods of greater than 30 days were used. In the event that a patient did not have an eligible follow up visit or observation period, the ABR and AJBR were annualized based on the baseline visit, which includes the number of bleeds reported for the 6 month period before entering the WBDR. The calculations of ABR and AJBR include only patients who experienced at least 1 bleed or joint bleed in 2019, respectively. Patients with 0 bleeds in 2019 were excluded from these calculations. It is assumed that patients with 0 bleeds in a year are receiving the treatment necessary to prevent bleeding. This allows for a more in-depth analysis of the need for care when observing ABR and AJBR by economic category or region.

ABR

The median (IQR) ABR was 7 (4-15) for all PWH, and 6 (4-14) for severe PWH, varying by GNI and region (Figure 13). An inverse relationship between ABR and GNI is demonstrated in Figure 13, with higher ABRs in low-income countries, and lower ABRs in high income countries. The highest ABR was observed in low-income countries at 24 (12-28). These countries were in Africa and South-East Asia. While, the lowest ABR was 4 (2-8) and 4 (2-7) in upper middle and high income countries respectively (Figure 13).

AJBR

The median (IQR) AJBR was 6 (4-14) for all PWH, and 6 (3-12) for severe PWH, varying by GNI and region (Figure 14). Similar to ABR, an inverse relationship between ABR and GNI is observed. The highest AJBR was observed in low-income countries at 16 (9-20) and the lowest was in upper-middle and high-income countries at 4 (2-8).

Figure 13

Median ABR by GNI and region

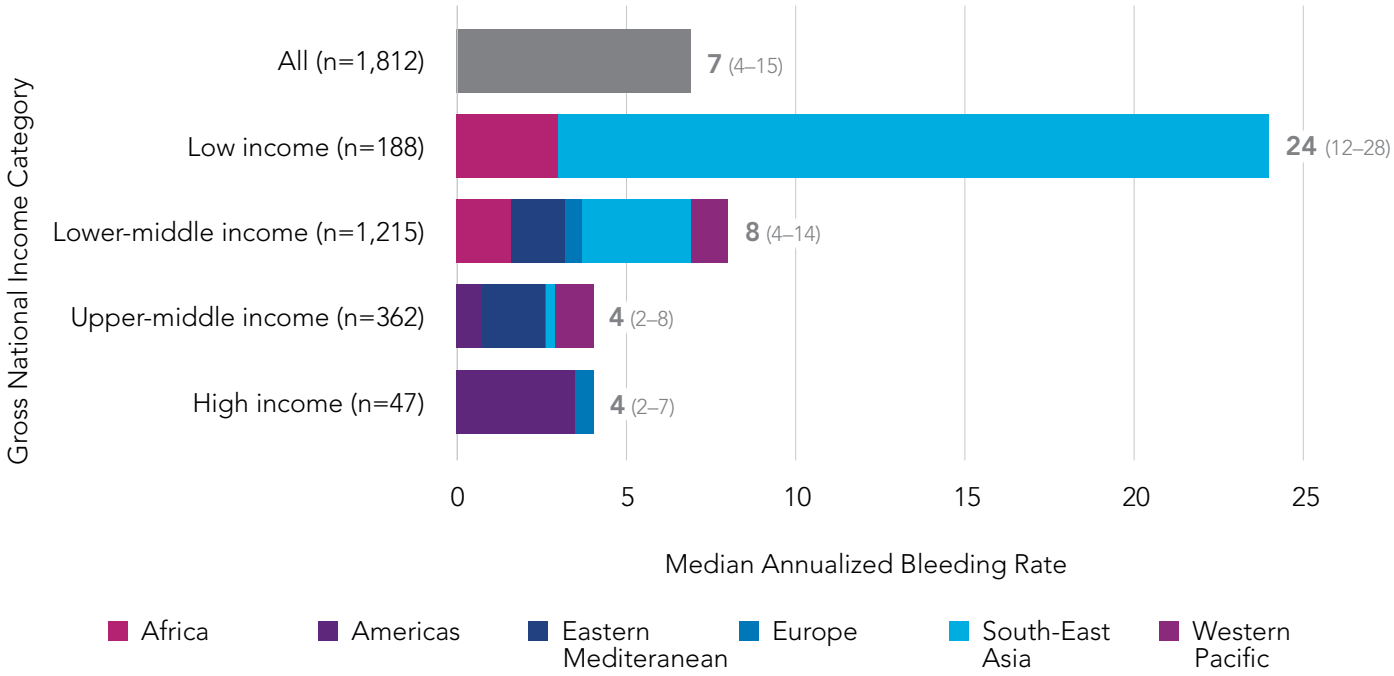
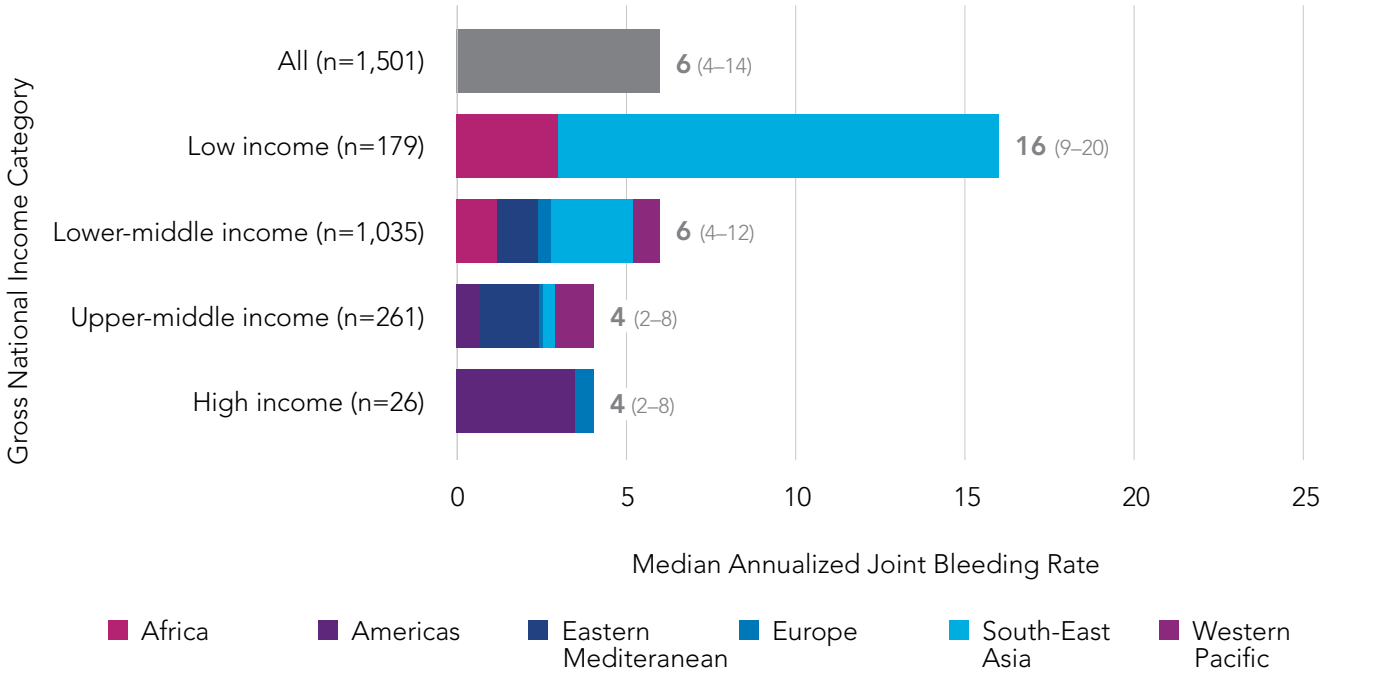


Figure 14

Median AJBR by GNI and region



TARGET JOINTS

Twenty-eight percent of all PWH, and 36% of severe PWH, reported having at least 1 target joint in 2019. The percent of PWH reporting a target joint varied by region, ranging from 63% to 41% (Figure 15).

Figure 15

PWH with at least 1 target joint by Region

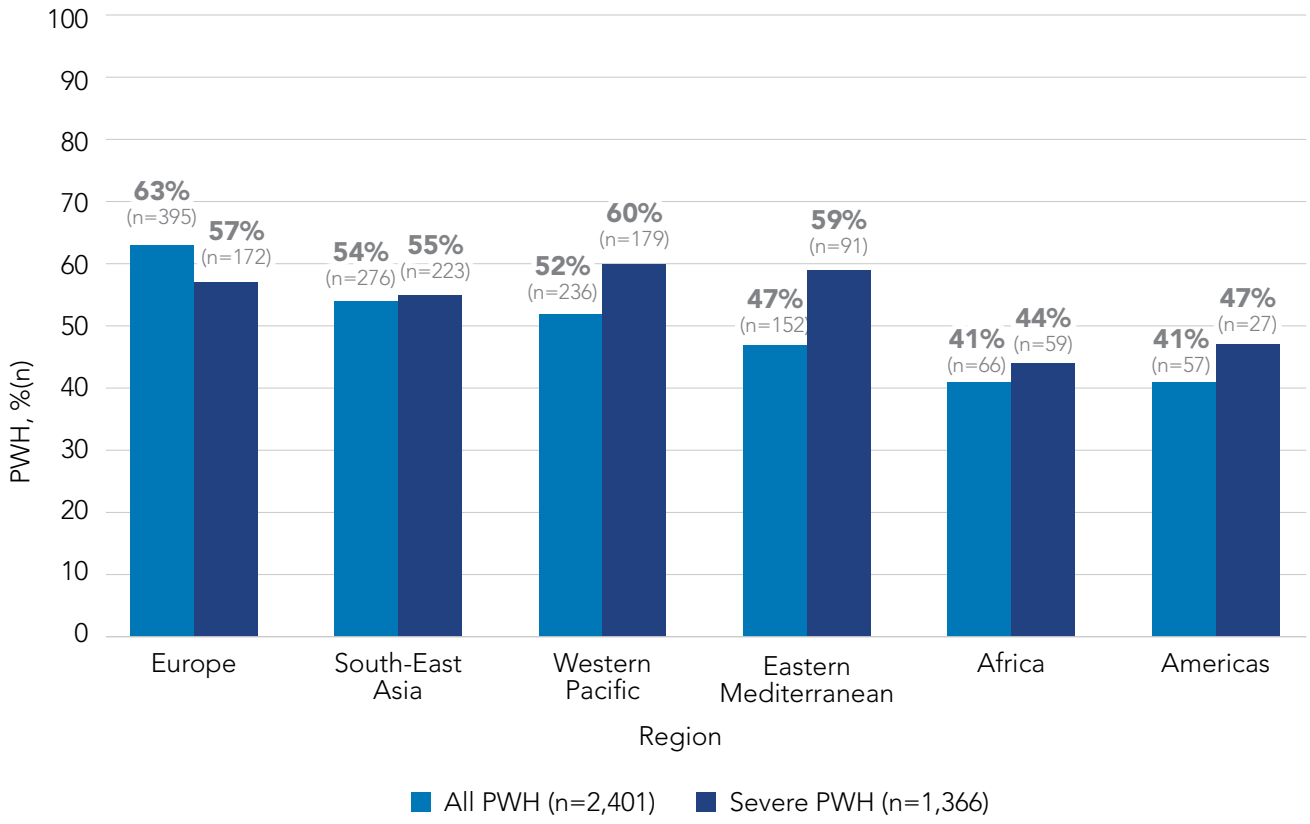


TABLE 8
Inhibitors summary, 2019

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe PWH (n=2,064)**
Patients with a history of an inhibitor**, n (%)	126	6 (5%)	24 (19%)	96 (76%)
Inhibitor testing in 2019				
Tested†, n (%)	439	17 (4%)	66 (15%)	356 (81%)
Newly diagnosed with an inhibitor††, n (%)	57	2 (4%)	6 (11%)	49 (86%)
Patients with no access to testing, n (%)	63	21 (33%)	38 (60%)	4 (6%)

* 125 PWH had unknown severity
** Unique number of patients who had an inhibitor prior to registration in the WBDR or had a positive test in 2018.
† Unique number of patients who had an inhibitor test in 2019. PWH who never received factor treatment were removed from this analysis. Testing methods include Bethesda, Nijmegen-Bethesda, and mixing study (aPTT); ‡ The cut- off value for the presence of inhibitors is defined as a titre ≥0.6 BU.
†† Unique number of patients who did not have a test in 2018 or tested negative, did not have inhibitors in the past and tested positive in 2019.

Data on inhibitor testing is collected at baseline visit (for 6 months prior) and at each follow-up visit thereafter. In this report, the number of PWH with a positive inhibitor test is defined as any PWH who has had at least 1 positive inhibitor test in 2019. In 2019, 439 PWH were tested for inhibitors, 57 (13%) were newly diagnosed with an inhibitor (that is, it was not indicated that the patient had an inhibitor in the past and they did not have a positive test in 2018) (Figure 16).

Figure 16
PWH with inhibitor test (n=439)

TABLE 9a

Hemophilia related hospitalizations summary, 2019

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Patients hospitalized**, n (%)	362	49 (14%)	113 (31%)	193 (53%)
Total hospitalizations‡, n	741	73 (10%)	214 (29%)	445 (60%)
Days per hospitalization, median (IQR)	4 (3-6)	4 (3-7)	4 (3-6)	4 (3-6)
Number of hospitalizations per patient, median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)	1 (1-3)

TABLE 9b

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Reason for hospitalizations, n (%)				
Joint bleeding	457 (62%)	30 (41%)	134 (63%)	290 (65%)
Surgery	15 (2%)	4 (6%)	4 (2%)	7 (2%)
Soft tissue bleeding	27 (4%)	8 (11%)	5 (2%)	11 (3%)
Other bleeding	105 (14%)	15 (21%)	29 (14%)	61 (14%)
Other muscle bleeding	71 (10%)	8 (11%)	25 (12%)	38 (9%)
Intracranial bleeding	20 (3%)	1 (1.4%)	7 (3%)	11 (3%)
Psoas muscle bleeding	20 (3%)	4 (6%)	7 (3%)	14 (3%)
Thromboembolic event	1 (<1%)	0 (0%)	1 (<1%)	0 (0%)
Other	41 (6%)	6 (8%)	8 (3%)	22 (5%)

* 125 PWH did not report severity
** Number of unique PWH hospitalized.
‡ Hospitalization is defined as spending at least 1 overnight in the hospital.

In 2019, 362 PWH experienced a total of 741 hemophilia related hospitalizations, with a median (IQR) stay of 4 days (3-6). The most common reason for hospitalization was joint bleed for both hemophilia A and B patients (62% and 51% respectively) (Figure 17, 18). In total, 20 hospitalizations were for an intracranial bleed; 18 (3%) which were among hemophilia A patients and 2 (2%) were among hemophilia B patients. One hemophilia B patient was hospitalized for a thromboembolic event. The distribution of reason for hospitalization was similar between PWH with hemophilia A and B (Figure 17 and 18).

Figure 17

Reason for hospitalization in hemophilia A patients (n=642)

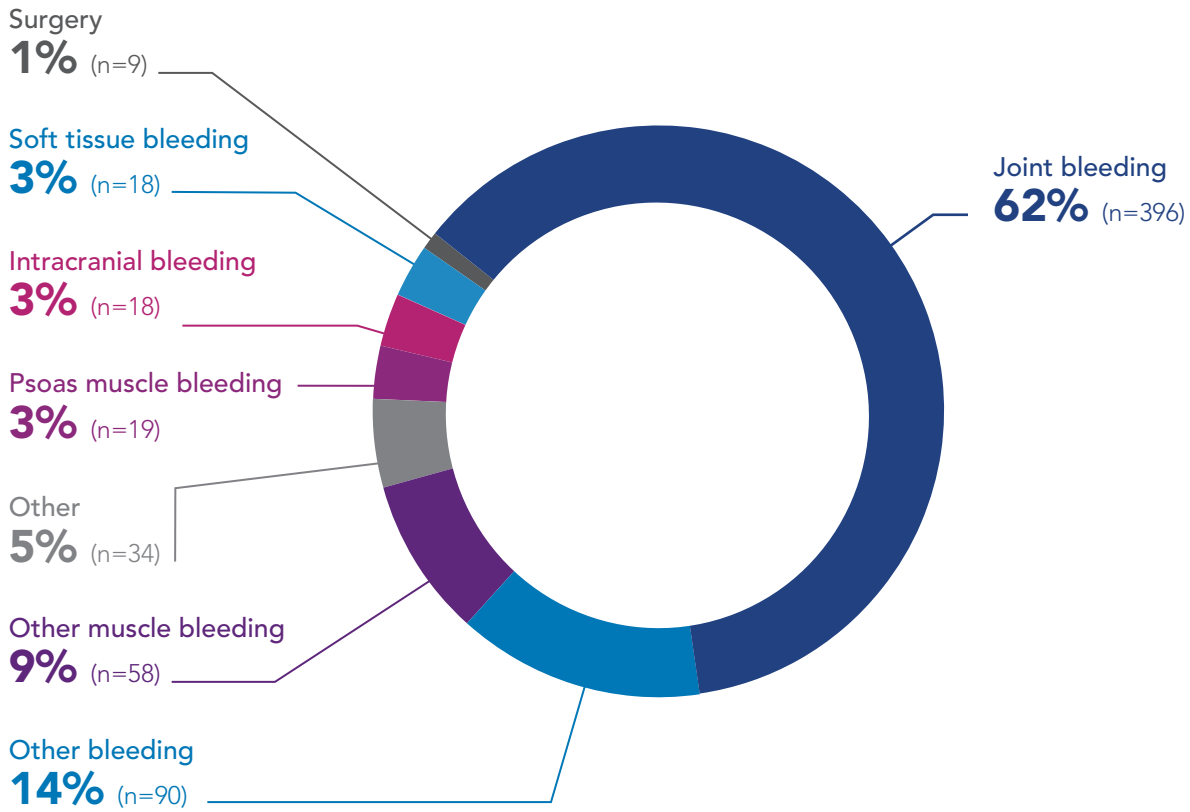
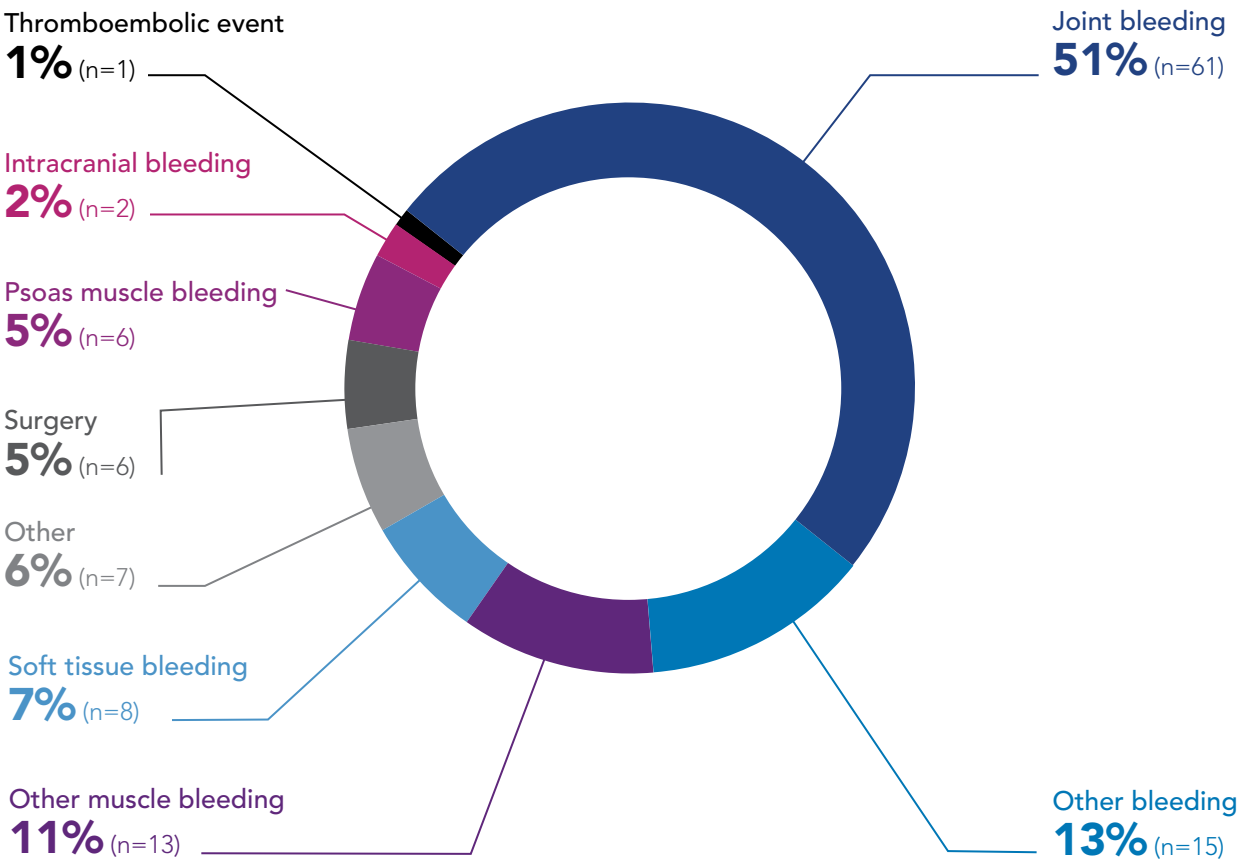


Figure 18

Reason for hospitalization in hemophilia B patients (n=119)



TREATMENT

TABLE 10

Treatment indication summary, 2019

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Hemophilia A, n	1,521	129	354	998
Indications**, n (%)				
On-demand	809 (53%)	107 (83%)	269 (76%)	404 (41%)
Prophylaxis	672 (44%)	14 (11%)	69 (20%)	580 (58%)
Surgery	13 (<1%)	3 (2%)	4 (1%)	6 (<1%)
Immune tolerance induction	15 (1%)	0 (0%)	0 (0%)	15 (2%)
Other	20 (1%)	3 (2%)	3 (<1%)	12 (1%)
Hemophilia B, n	252	27	81	142
Indications**, n (%)				
On-demand	145 (56%)	22 (82%)	62 (77%)	59 (42%)
Prophylaxis	102 (40%)	3 (11%)	17 (21%)	82 (58%)
Surgery	3 (1%)	1 (4%)	2 (3%)	4 (3%)
Other	2 (<1%)	0 (0%)	1 (1%)	1 (<1%)

* 125 PWH did not report severity
** Number of unique PWH in whom at least one treatment indication was reported in 2019. Total percentage can exceed 100% since a PWH may be counted in one more than one indication category; 5 PWH with hemophilia type unknown were excluded; If a patient was on prophylaxis, they were not counted in on-demand. Prophylaxis includes those patients with treatment for selective prevention of a bleed.

TABLE 11

Treatment product category summary, 2019

		Severity*		
	All PWH (n=4,166)	**Mild (n=874)**	**Moderate (n=1,103)**	**Severe (n=2,064)**
Hemophilia A, n	1,521	129	354	998
Treatment category**, n (%)				
FVIII, standard half-life	1,081 (71%)	69 (54%)	20 (6%)	783 (79%)
FVIII, extended half-life	343 (23%)	41 (32%)	123 (35%)	154 (15%)
Cryoprecipitate	35 (2%)	1 (<1%)	8 (2%)	26 (3%)
Bypassing Agent	51 (3%)	2 (2%)	2 (<1%)	47 (5%)
Plasma	70 (5%)	28 (22%)	37 (11%)	5 (<1%)
Other	89 (6%)	13 (10%)	25 (7%)	50 (5%)
Hemophilia B, n	252	27	81	142
Treatment category**, n (%)				
FIX, standard half-life	153 (61%)	12 (44%)	42 (52%)	99 (70%)
FIX, extended half-life	75 (30%)	5 (19%)	35 (43%)	33 (23%)
Plasma	19 (8%)	5 (19%)	12 (15%)	2 (1%)
Other	23 (9%)	6 (22%)	4 (5%)	13 (9%)

* 125 PWH did not report severity
** Number of unique PWH on whom at least one treatment type, were reported in 2019; A PWH may be counted in more than 1 treatment type

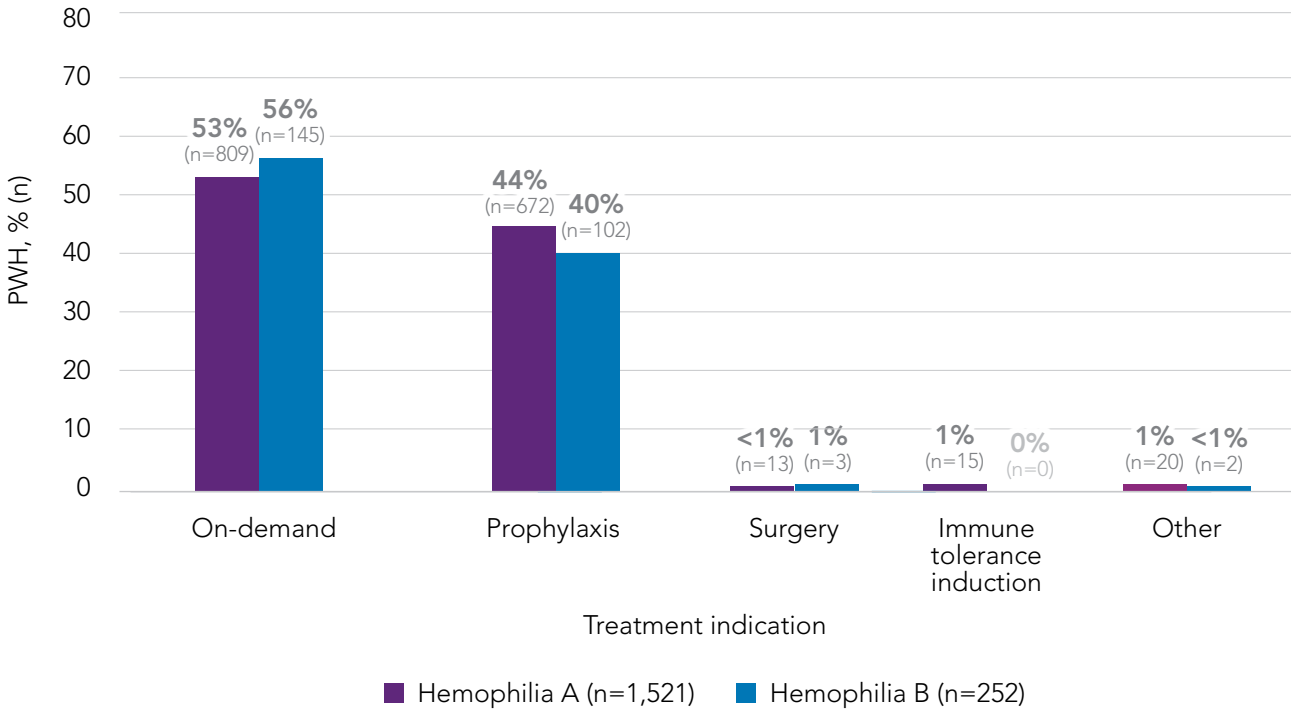
USED PROPHYLAXIS IN 2019

TREATMENT BY INDICATION

A total of 1,778 (43%) PWH received treatment in 2019. The most frequent indication reported for both hemophilia A and B patients was on demand; 53% of hemophilia A patients and 56% of hemophilia B patients. However, for severe PWH, prophylaxis was the most frequent indication; 58% for both hemophilia A and B patients (Table 10; Figure 19).

Figure 19

Treatment indication by hemophilia type, % (n)



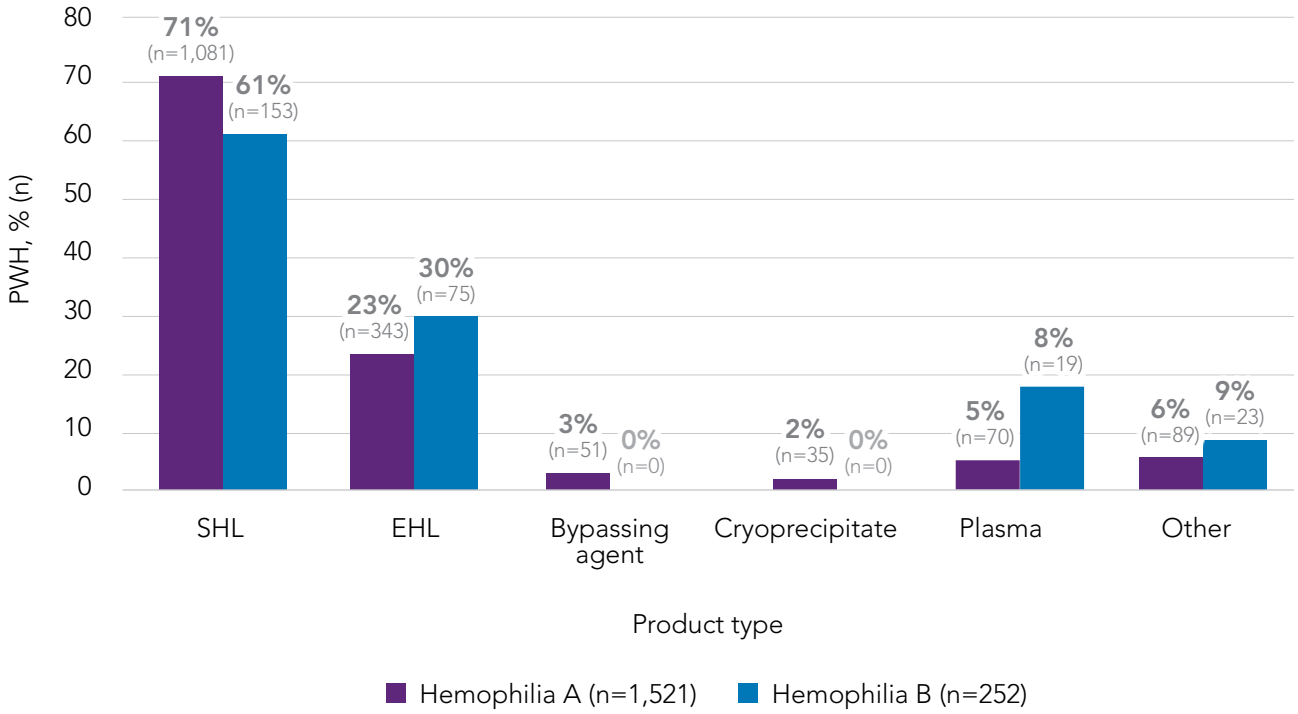
* Five PWH had unknown hemophilia type and were excluded from this graph

TREATMENT BY PRODUCT CATEGORY

Standard half-life (SHL) clotting factor concentrates were the most common type of treatment used in 2019 (71% of hemophilia A patients, and 61% of hemophilia B patients), followed by extended half-life (EHL) clotting factor concentrates, (23% of hemophilia A patients and 30% of hemophilia B patients). A total of 51 patients with hemophilia A (3%) used bypassing agents (Table 11; Figure 20).

Figure 20

Product category by hemophilia type



WBDR DATA QUALITY ACCREDITATION (DQA) PROGRAM

The objective of WBDR Data Quality Accreditation (DQA) Program is to standardize data collection procedures among HTCs, and to ensure that data entered in the WBDR are of high quality. A robust data cleaning and validation process is used to enhance data completeness, accuracy, and consistency. All data are evaluated on two data quality dimensions:

- Completeness: all data fields should be complete
- Accuracy: all data should be valid and consistent

The WFH data quality team works with all HTCs, providing training and feedback on the quality of all data. Incomplete and inconsistent data are communicated to HTCs via Data Clarification Forms, with requests to update data. Each HTC is evaluated on the overall level of data quality at their site, based on the WBDR Data Quality Rating classification levels (Figure 21).

43 (83%) OF THE 52 HTCs*

ACHIEVED THE HIGHEST LEVEL OF DATA QUALITY RATING, AND WERE **CLASSIFIED AS 'LEADERS'.**
(DATA QUALITY SCORE ≥95%)

In 2019, the WBDR data quality team continued to provide data quality feedback and training to both existing and new HTCs. Throughout the year, the team worked closely with 52 HTCs* (27 were from 2018). Forty-three (83%) of the 52 HTCs* achieved the highest level of data quality rating, and were classified as 'Leaders' (data quality score > 95%). All 'Leaders' from 2018 Data Report maintain their level of success. Out of 23 new HTCs in 2019, 18 (78%) of them were also classified as 'Leaders'. This was an improvement from 8 (35%) HTCs achieving this level prior to receiving data quality training and feedback. It is evident that the HTCs consider the importance of data quality and working hard towards that.

The data quality rating not only promotes a sense of ownership of quality data but also maintains the overall quality of the WBDR in the long run.

Figure 21

WBDR Data Quality Rating Scale

* Data imported through the Data Linkage Program is not verified under the WBDR's Data Quality Accreditation Program. Therefore, one HTC is excluded from the evaluation.

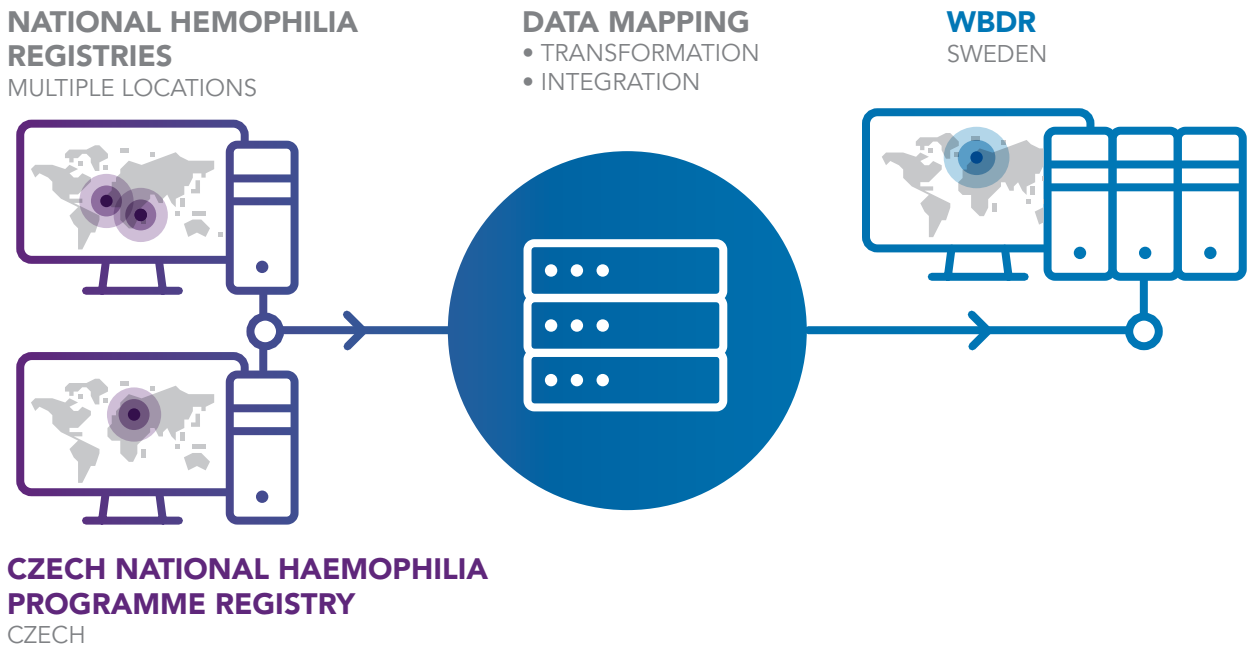
INTEGRATING EXISTING PATIENT REGISTRY DATA INTO THE WBDR

Registries, with international collaboration between countries, is the best way to pool sufficient data to increase the knowledge and evidence in rare disorders. In an effort to combine resources from existing hemophilia registries, and maximize the utility of data that currently exists, the development of the WBDR includes an international data integration component with the aim of facilitating data transfer from existing patient registries to the WBDR.

As part of a proof of concept study, an export of de-identified data from the 2018 Czech National Haemophilia Programme Registry (CNHPR) was imported into the WBDR. This import was based on a minimal set of data common to both registries. The CNHPR is a national registry, which collects data from eight pediatric and eight adult hemophilia centres.

At the end of 2019, the WBDR team started collaborating with the Hemostasis Registry of the Thai Society of Hematology (TSH) to link the data from Thailand. The same concept of data linkage where a minimal set of data common to both the WBDR and the TSH has been applied. This collaboration will enable the WBDR to collect data from hemophilia centres from Thailand. At the time of publication of this Data Report (August 2020), the data fields from both registries have been mapped. It is expected that the data linkage from Thailand will be fully implemented by the end of 2020.

A protocol to import data from existing patient registries into the WBDR has been developed based on the proof of concept study. The program is available to interested countries who want to set up an import process to combine their national data with the WBDR. Interested individuals are encouraged to contact the WFH at wbdr@wfh.org.



WBDR RESEARCH SUPPORT PROGRAM

The WBDR is dedicated to improving the lives of people with hemophilia by collecting high quality data that can be used for research and advocacy, by the WBDR community of investigators and PWH.

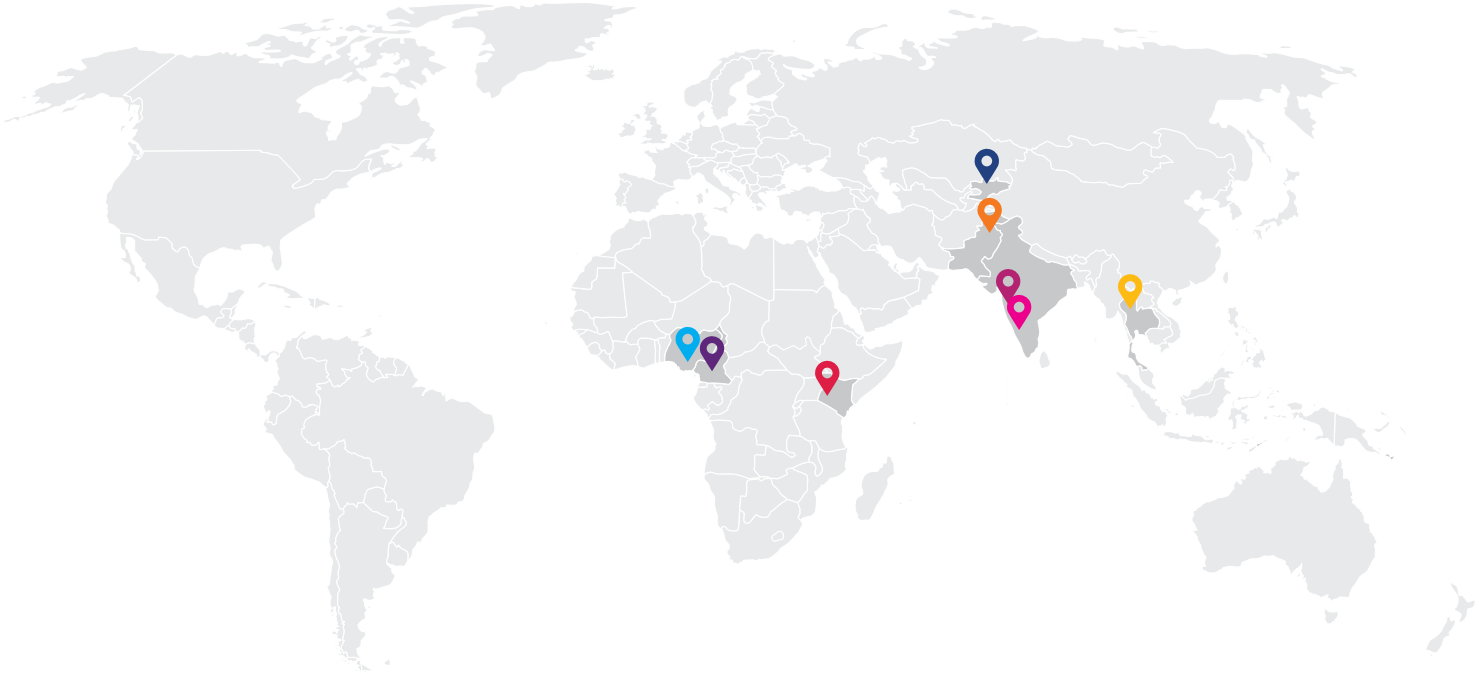
The **WBDR Research Support Program** is designed to provide small research funding to encourage the use of WBDR data. This program is open to all participating HTCs. In 2019, eight investigators were awarded funding for a period of one or two years.

Congratulations to the eight HTCs who were awarded funding for their research project:

WINNERS OF 2019 RESEARCH SUPPORT PROGRAM

8 AWARDS GRANTED

OVER $35,000



- CHU Yaoundé, Yaoundé, Cameroon
- Melaka Manipal Medical College, Hemophilia Society, Manipal, India
- Aluva Hemophilia Treatment Center, District Hospital, Aluva, India
- Moi Teaching and Referral Hospital, Eldoret, Kenya
- National Center of Oncology and Hematology, Bishkek, Kyrgyzstan
- South East Haemophilia Treatment Center, Enugu State, Nigeria
- Hemophilia Treatment Center, Rawalpindi, Pakistan
- Chiang Mai University, Chiang Mai, Thailand

APPENDIX 1 – DATA SETS

Minimal Data Set, Extended Data Set

Demographics	Diagnostics	Clinical
Date of birth	**Date of diagnosis**	**Bleeding events**
Gender	**Hemophilia type**	**Target joints**
Country of residence	**Hemophilia severity**	**Treatments**
Employment	**Hemophilia factor level**	**Inhibitor status**
Education	**Inhibitor history**	**Hospitalization**
Marital status	**Treatment history**	**Mortality**
	Bleeding history	Adverse events
	Genetic testing	Comorbidities
	Blood type	Functional scales*
	Family history	Quality of life scales†

Fields identified in bold represent the minimal data set.
* Functional scales include: Haemophilia Joint Health Score, Joint Disease, Range of Motion, WFH Gilbert Score, Functional Independence Score for Haemophilia
† Quality of life scale: EQ-5D-5L

APPENDIX 2 – SUPPLEMENTAL TABLES

Table A

Median age in months at first bleed and first joint bleed by severity, Hemophilia A

	Hemophilia A (n=3,565)	
Severity	**Age at first bleed, months** (median, IQR) n=1,568*	**Age at first joint bleed, months** (median, IQR) n=1,310**
Severe (<1%)	**7 (4-15)**	**6 (3-14)**
Moderate (1%–5%)	**8 (4-16)**	**8 (4-14)**
Mild (>5%)	**7 (2-16)**	**4 (4-13)**
Unknown	**6 (4-10)**	**6 (4-12)**

*Never had a bleed or not reported for 1,997 PWH
**Never had a bleed or not reported for 2,255 PWH

Table B

Median age in months at first bleed and first joint bleed by severity, Hemophilia B

	Hemophilia B (n=580)	
Severity	**Age at first bleed, months** (median, IQR) (n=228)*	**Age at first joint bleed, months** (median, IQR) (n=180)**
Severe (<1%)	**6 (4-12)**	**6 (3-12)**
Moderate (1%–5%)	**6 (4-16)**	**6 (4-12)**
Mild (>5%)	**4 (2-12)**	**4 (4-13)**
Unknown	**8 (7-24)**	**23 (15-32)**

*Never had a bleed or not reported for 352 PWH
**Never had a bleed or not reported for 400 PWH

THANK YOU TO PWH

To each PWH enrolled in the WBDR who has kindly agreed to share their data: thank you for helping improve the quality of care for people with hemophilia around the world!

THANK YOU TO HTCs

Thank you to all the dedicated staff at participating hemophilia treatment centres who work hard to ensure that their data meets WBDR data quality standards!

THANK YOU TO SPONSORS

The WFH thanks all of our sponsors for their generous financial support which is allowing us to continue to develop this important initiative.

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GLOSSARY

Cryoprecipitate: A fraction of human blood prepared from fresh plasma. Cryoprecipitate is rich in factor VIII, von Willebrand factor, and fibrinogen (factor I). It does not contain factor IX.

Factor concentrates: These are fractionated, freeze-dried preparations of individual clotting factors or groups of factors derived from donated blood.

Extended half-life factor concentrate: A new generation of recombinant factor concentrates, which extend their half-life. Half-life is the time it takes for infused factor to lose half of its potency. Traditional factor VIII has a half-life of 8 to 12 hours; an extended factor VIII half-life is defined as a ratio greater than 1.3-fold, of the traditional high-life.

Gross National Income: Gross National Income (GNI) per capita (current US$) calculated by The World Bank into four income groups using the Atlas method. The classification is updated each year on July 1st.

Hemophilia A: A condition resulting from factor VIII deficiency, also known as classical hemophilia.

Hemophilia B: A condition resulting from factor IX deficiency, also known as Christmas disease.

Hemophilia treatment centre: A specialized medical centre that provides diagnosis, treatment, and care for people with hemophilia and other inherited bleeding disorders.

HIV: Human immunodeficiency virus. The virus that causes AIDS.

Inhibitors: A PWH has inhibitors when their body's immune system acacks the molecules in factor concentrate, rendering it ineffective.

Mild hemophilia: Condition resulting from a level of factor VIII or factor IX clotting activity above 5% and below 40% of normal activity in the bloodstream. (National definitions differ on the upper limit for mild hemophilia, ranging from 24% to 50%.)

Moderate hemophilia: Condition resulting from a level of factor VIII or factor IX clotting activity between 1 to 5% of normal activity in the bloodstream.

Plasma-derived products: Factor concentrates that contain factor VIII or IX that have been fractionated from human blood.

PWH: Person with hemophilia.

Registry: A database or record of identified people with hemophilia or inherited bleeding disorders. A registry includes information on personal details, diagnosis, treatment and complications.

Severe hemophilia: Condition resulting from a level of factor VIII or factor IX clotting activity of less than 1% in the bloodstream.

Standard half-life factor concentrate: Traditional recombinant factor concentrates with a half-life of 8 to 12 hours.

Target joint: '3 or more spontaneous bleeds into a single joint within a consecutive 6-month period. Where there have been ≤ 2 bleeds into the joint within a consecutive 12-month period the joint is no longer considered a target joint[3].

REFERENCES

[1] World Health Organization. 2019. Definition of regional groupings. https://www.who.int/healthinfo/global_burden_disease/definition_regions/en/. Accessed on March 10, 2019.

[2] World Bank 2015. World Development Indicators 2015. http://documents.worldbank.org/curated/en/795941468338533334/World-development-indicators-2015. Accessed October 25, 2019.

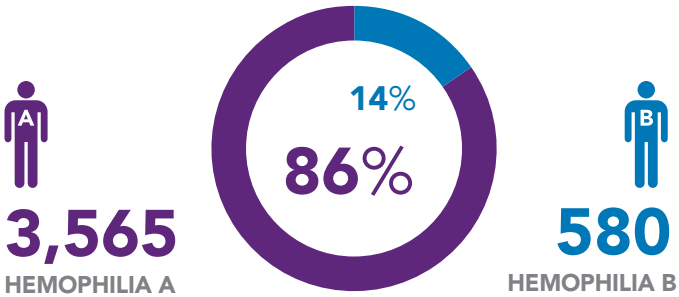
[3] Blanchette VS, Key NS, Ljung LR, Manco-Johnson MJ, van den Berg HM, Srivastava A; Subcommittee on Factor VIII, Factor IX and Rare Coagulation Disorders of the Scientific and Standardization Committee of the International Society on Thrombosis and Hemostasis. Definitions in hemophilia: communication from the SSC of the ISTH. J Thromb Haemost. 2014 Nov;12(11):1935-9.

WBDR 2019 HIGHLIGHTS

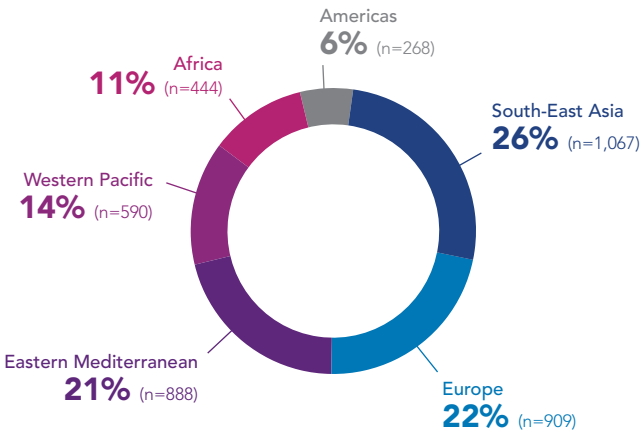
53
HTCs ENROLLED

29
COUNTRIES REPRESENTED

4,166
ENROLLED PATIENTS



Distribution of PWH by Region



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