WBDR
WFH WORLD BLEEDING DISORDERS REGISTRY

WORLD BLEEDING DISORDERS REGISTRY

2021 DATA REPORT

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

TABLE OF CONTENTS

ABOUT THE WFH

For nearly 60 years, the WFH – an international not-for-profit organization – has worked to improve the lives of people with hemophilia, von Willebrand disease and other inherited bleeding disorders. Established in 1963, it is a global network of patient organizations in 147 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.

ACKNOWLEDGEMENTS

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

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

PRESIDENT & VP MEDICAL'S MESSAGE

May 2022

Dear members of the bleeding disorders community,

It is our pleasure to share the World Bleeding Disorders Registry (WBDR) 2021 Data Report with you. This report represents the fourth 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 support research and advocacy initiatives and serve as a tool to guide clinical decisions and improve care for people with hemophilia around the world.

We are very close to reaching our 5-year goal of 10,000 patients. As of December 31, 2021, over 9,000 PWH from 104 hemophilia treatment centres (HTCs) and 37 countries around the world have joined our efforts in collecting these valuable data. In this report you will find the aggregated summary of data for all PWH enrolled in the WBDR, including 2021 clinical data.

In the past year, continuous effort was made towards expanding the collection of data through the WBDR. Along with the data from Czech Republic, our International Data Integration Program was applied to include the data from 7 HTCs in Thailand. Furthermore, a patient mobile application was developed allowing PWH to track their bleeds and treatments, and monitor changes in their health status. The capturing of patient-reported data will not only permit patients to manage their care but also be used as a tool for healthcare providers to monitor their patients' health outcomes. Moving forward, in 2022 the WBDR platform will be available in French, Spanish and Russian, making it more accessible to users around the world. The platform will also be enhanced to allow the collection of data on people with von Willebrand Disease, to inform research, policies, and advocacy for this population.

On behalf of the WFH, we would like to warmly thank all of the dedicated health care providers and PWH who are part of this important initiative, and we look forward to more collaborations with HTCs interested in participating in the WBDR as WFH pushes towards its mission of *Treatment for All*.

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, Grifols, Novo Nordisk, Pfizer & Sanofi Genzyme.

Sincerely,

Cesar Garrido
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 WHO ARE PATIENTS 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 Institutional Review Board 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 people with hemophilia A and B 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 informed consent.

REPORT DATA SOURCE

The data presented in the WBDR 2021 Data Report 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).

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 contact 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.

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

WBDR 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 are 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.

INTERNATIONAL DATA INTEGRATION PROGRAM

The WBDR includes an international data integration component, whereby existing hemophilia registries can import their data directly into the WBDR and become part of this international registry.

Please see page 34 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 32 for more information on the WBDR data quality program.

HTC SUPPORT AND TRAINING PROGRAMS

The WBDR support and training program is available to all participating HTCs, including the Research Support Program and the HTC Funding Program. These programs were developed to ensure long-term success in the WBDR. In-person and webinar trainings are available on:

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

DATA ACCESS AND GOVERNANCE

Each HTC has access only to the data they enter into the WBDR, and they cannot view data that are entered from any other HTC. Every year, aggregate data from all enrolling HTCs are 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 are de-identified and confidential. Data policy guidelines of Health Solutions adhere to the CE-mark (Conformité Européenne) and the U.K. standard IG Soc (Information Governance Statement of Compliance) and are compliant with the General Data Protection Regulation. Please see the WBDR Data Privacy & Security document for more information.

ABOUT THE WBDR 2021 DATA REPORT

The data in the fourth edition of the WBDR Data Report includes patient data collected between the launch date of January 26, 2018, and December 31, 2021. These data stem from 104 participating HTCs (Appendix 2), representing 37 countries, who received institutional review board approval and enrolled at least one PWH into the WBDR as of December 31, 2021.

At the time of publication of this Data Report (May 2022), an additional 6 HTCs are participating in the WBDR, for a total of 110 HTCs from 39 countries.

Please note, that at the time of data cut-off for this report (December 31, 2021), it is possible that not all eligible PWH at participating HTCs had been enrolled into 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 2021 WBDR data are 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:

- Alfonso Iorio, MD, PhD, Co-Chair
- Catherine Lambert, MD, PhD, Co-Chair
- Barbara Konkle, MD
- Saliou Diop, MD
- Cedric Hermans, MD, PhD
- Declan Noone, MSc
- Jamie O'Hara, MSc
- Glenn Pierce, MD, PhD, VP Medical WFH
- Cesar Garrido, President WFH

GLOBAL REPRESENTATION IN THE WBDR, 2021

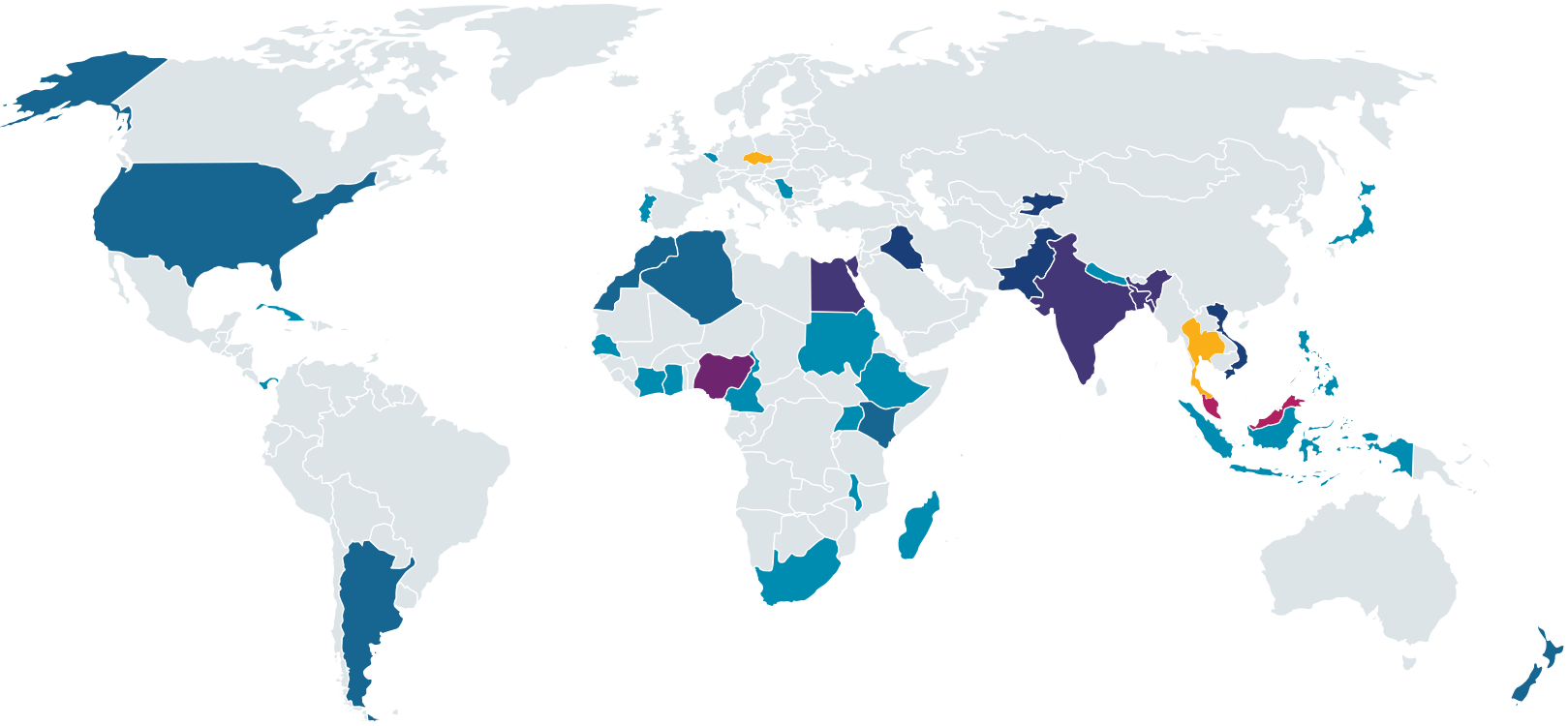


Figure 1
COUNTRIES AND HTCS PARTICIPATING IN THE WBDR

Number of HTCs per country

1 — 13

Data Linkage

For a complete list of HTCs, please refer to Appendix 2

Algeria	2
Argentina	2
Bangladesh	5
Barbados	1
Belgium	1
Cameroon	1
Côte d'Ivoire	1
Cuba	1
Czech Republic	17
Egypt	4
Ethiopia	1
Ghana	1
India	5
Indonesia	1
Iraq	3
Japan	1
Kenya	2
Kyrgyzstan	4
Madagascar	1
Malawi	1
Malaysia	13
Morocco	2
Nepal	1
New Zealand	2
Nigeria	7
Pakistan	3
Panama	1
Philippines	1
Portugal	1
Senegal	1
Serbia	1
South Africa	1
Sudan	1
Thailand	8
Uganda	1
USA	2
Vietnam	3

DATA INCLUDED IN THE WBDR 2021 DATA REPORT

PARTICIPATION

From January 2018 up to December 31, 2021, 9,414 PWH were enrolled in the WBDR, representing 6 regions, 37 countries and 104 HTCs (Figures 1 and 2).

37
COUNTRIES

104
HEMOPHILIA TREATMENT CENTRES

9,414
PEOPLE WITH HEMOPHILIA

TABLE 1
Participation Summary

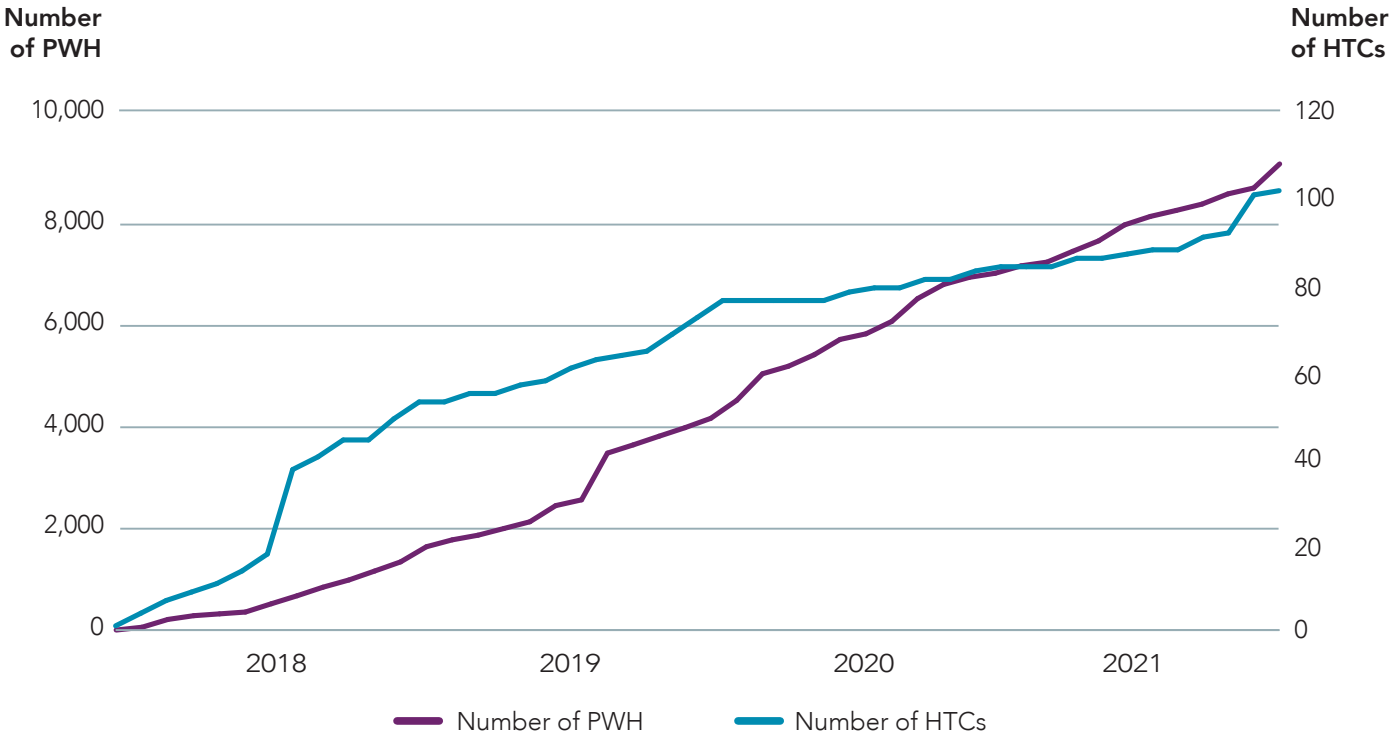
	All PWH	Severe PWH*
Countries, n	37	37
Hemophilia treatment centres**, n	104	104
People with hemophilia, n	9,414	4,686 (50%)
Distribution of PWH by region†, n (%)		
Africa	1,027	487 (47%)
Americas	354	249 (70%)
Eastern Mediterranean	2,418	1,291 (53%)
Europe	1,074	426 (40%)
South-East Asia	2,828	1,141 (40%)
Western Pacific	1,713	1,092 (64%)
Distribution of PWH by GNI§, n (%)		
High income	1,190	530 (45%)
Upper-middle income	1,731	1,131 (65%)
Low and lower-middle income	6,493	3,025 (47%)

* Severe PWH are defined by a factor level < 1%.
** HTCs included are those with Institutional Board Review approval and have enrolled at least 1 PWH by December 31, 2021
† Regions based on WHO regional groupings[1]
§ GNI = Gross National Income; Gross National Income categories based on The World Bank Group 2020 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)"[2]. Low (n=295) and lower-middle (n=6,918) income categories were combined due to the low number of patients in low-income countries.

Figure 2

PWH and HTC enrollment in the WBDR

January 2018 – December 2021

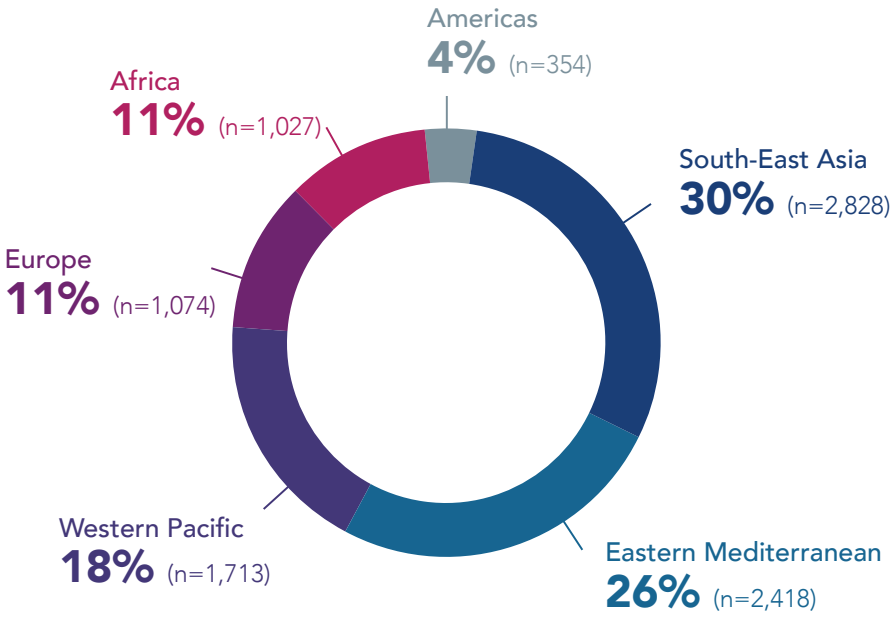


DISTRIBUTION OF PWH

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 (India, Bangladesh, Nepal, Thailand, Indonesia) and the Eastern Mediterranean (Pakistan, Iraq, Sudan, Morocco, Egypt, Algeria), representing 30% and 26% of PWH respectively (Figure 3).

Figure 3

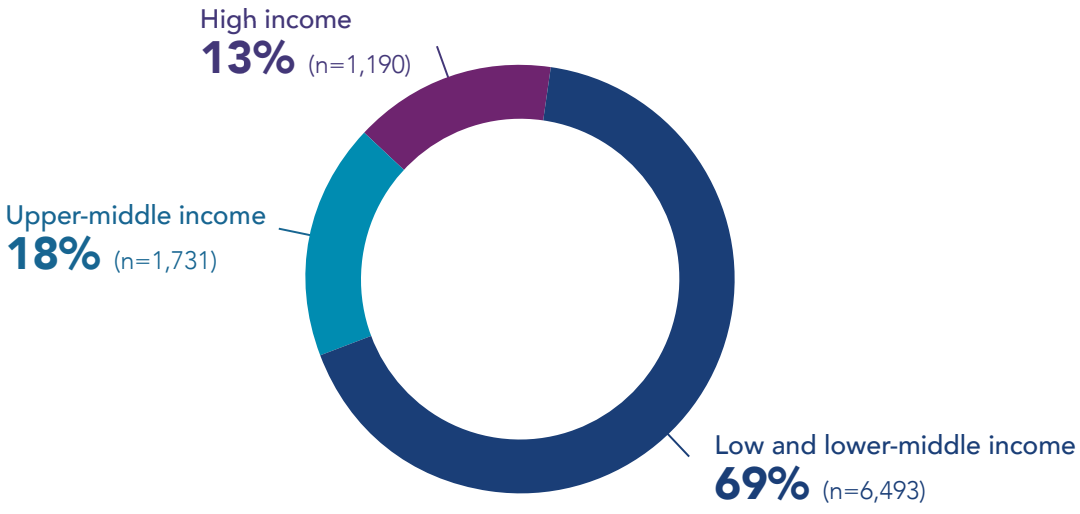
Distribution of PWH by region



The distribution of participants by Gross National Income (GNI) per capita[2], demonstrates that the majority of the participant PWH are from low and lower-middle income countries (69%), followed by upper-middle and high income representing 18% and 13% respectively (Figure 4).

Figure 4

Distribution of PWH by Gross National Income



DEMOGRAPHICS

TABLE 2
Demographics summary

	All PWH (n=9,414)	Severe (n=4,686)
Type of hemophilia*, n (%)		
Hemophilia A	7,943 (84%)	4,079 (87%)
Hemophilia B	1,428 (15%)	603 (13%)
Sex, n (%)		
Male	9,353 (99%)	4,671 (99%)
Female	60 (<1%)	15 (<1%)
Age of PWH**		
Age, years, median (IQR)	21 (11-33)	20 (11-33)
Pediatrics (<18 years), n (%)	4,061 (43%)	2,072 (44%)
Adults (≥18 years), n (%)	5,353 (57%)	2,614 (56%)

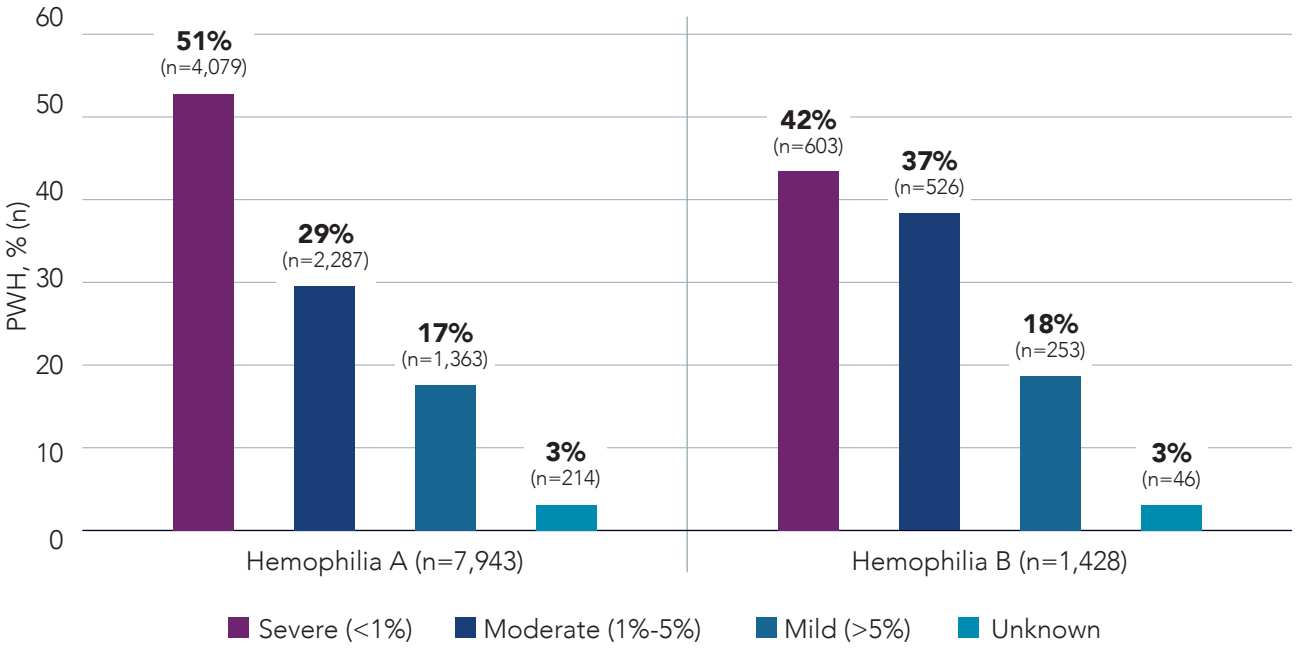
IQR=interquartile range
* 43 PWH had unknown hemophilia type and were excluded.
**Age of PWH was calculated as of December 31, 2021.

HEMOPHILIA TYPE AND SEVERITY

Overall, 99% (n=9,353) of participants were male, 84% (n=7,943) had hemophilia A and 15% (n=1,428) had hemophilia B (Table 2). The most frequent severity category among both hemophilia A and hemophilia B patients was severe at 51% and 42% respectively (Figure 5).

Figure 5

Hemophilia type* and severity, % (n)



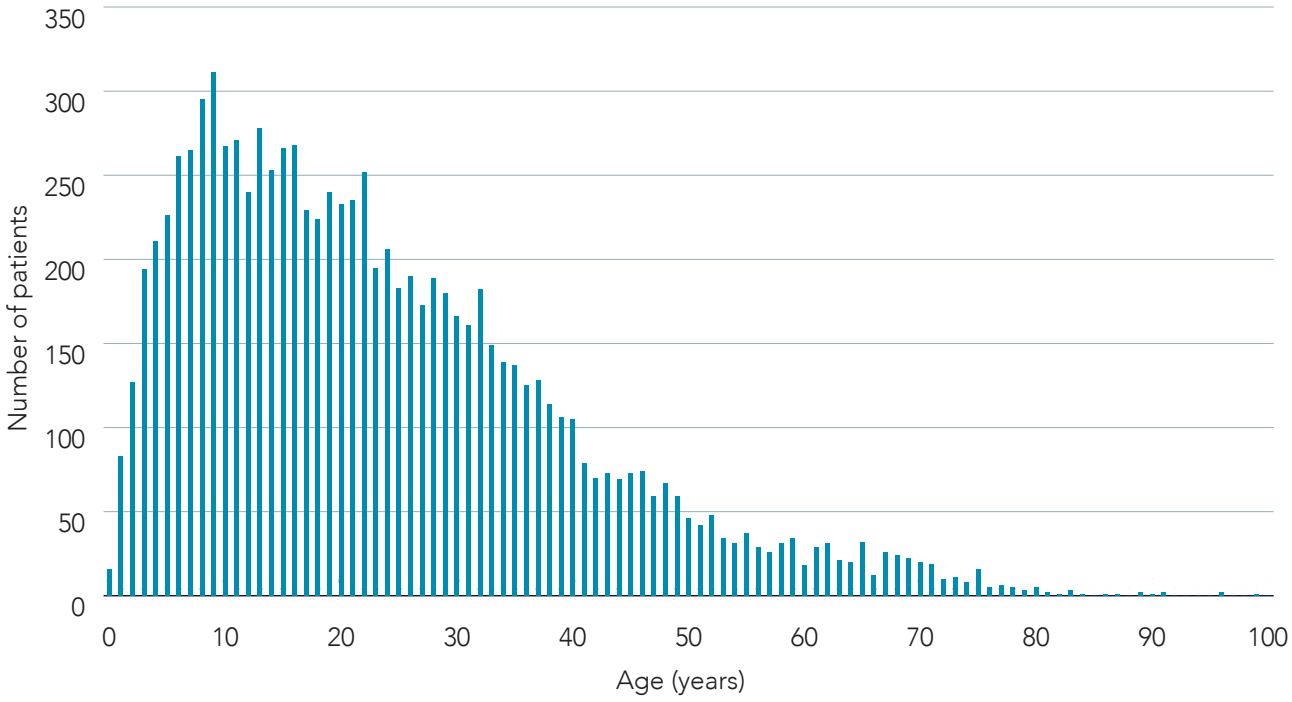
* 43 PWH had unknown hemophilia type and were excluded from this figure.

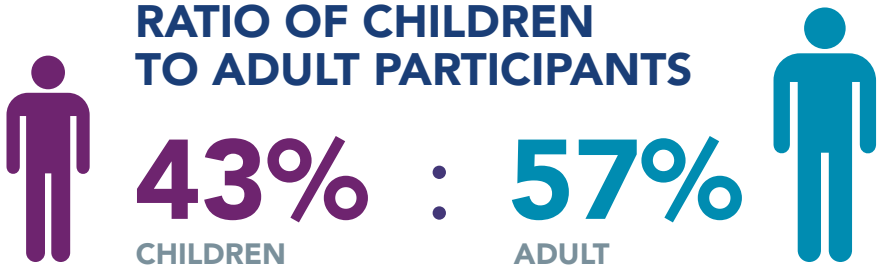
AGE OF PWH IN THE WBDR

The median age of participants was 20 years, ranging from 1 month to 99 years (Figure 6). Adults (≥18) comprised 57% (n=5,353) and children (< 18) comprised 43% (n=4,061) of all participants.

Figure 6

Age distribution of PWH in the WBDR





DIAGNOSIS AND CLINICAL HISTORY

TABLE 3a

Diagnosis and clinical history summary

	All PWH (n=9,414)	Severe (n=4,686)
Age at diagnosis, months, median (IQR)	36 (10-125)	19 (7-82)
Age at diagnosis by age category, n (%)		
0–11 months	2,685 (29%)	1,785 (38%)
1–4 years	2,834 (30%)	1,443 (31%)
5–17 years	2,350 (25%)	913 (19%)
18–44 years	1,199 (13%)	438 (9%)
45+ years	197 (2%)	41 (1%)
Age unknown	149 (2%)	66 (1%)

TABLE 3b

Newly diagnosed PWH in 2021, n (%)	270 (3%)	79 (2%)
Age at first bleed*, months, median (IQR)	12 (6-36)	9 (6-24)
Age at first joint bleed, months, median (IQR)**	24 (12-60)	24 (12-48)

* Based on 7,849 PWH with data on first bleed.
** Based on 6,425 PWH with data on first joint bleed.

AGE AT DIAGNOSIS

The median (IQR) age at diagnosis was 36 months (10-125) for all PWH, and 19 months (7-82) for severe PWH (Table 3a). For all PWH, median age at diagnosis by region ranged from 8 months in the Americas to 55 months in South-East Asia (Figure 7). In severe PWH, the highest age at diagnosis was in Africa at 47 months and lowest was again the Americas at 8 months (Figure 7). Age at diagnosis decreased as GNI increased, from 48 months in low and lower-middle income countries, to 22 months in high income countries for all PWH, with a similar pattern among PWH with severe disease at 30 months and 10 months (Figure 8).

There were 270 PWH newly diagnosed in 2021, 79 of which were severe PWH.

Twenty-nine percent of all PWH, and 38% of severe PWH, were diagnosed before 12 months. Fifty-nine percent of all PWH and 69% of all severe PWH were diagnosed before the age of 5 years (Table 3a, Figure 9).

36
MONTHS
MEDIAN AGE AT DIAGNOSIS

19
MONTHS
MEDIAN AGE AT DIAGNOSIS
FOR SEVERE PWH

Figure 7

Age at diagnosis by region

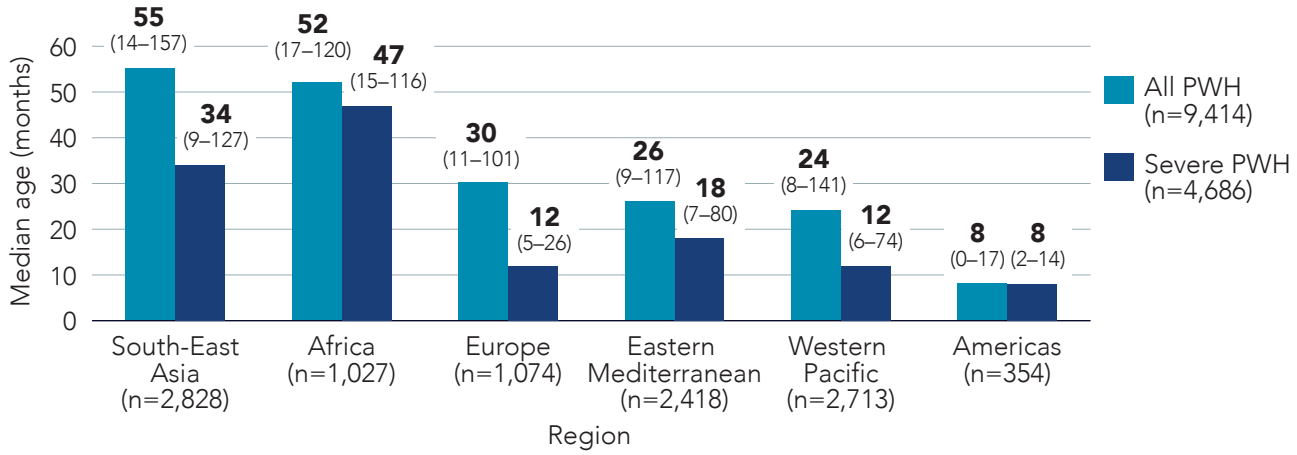
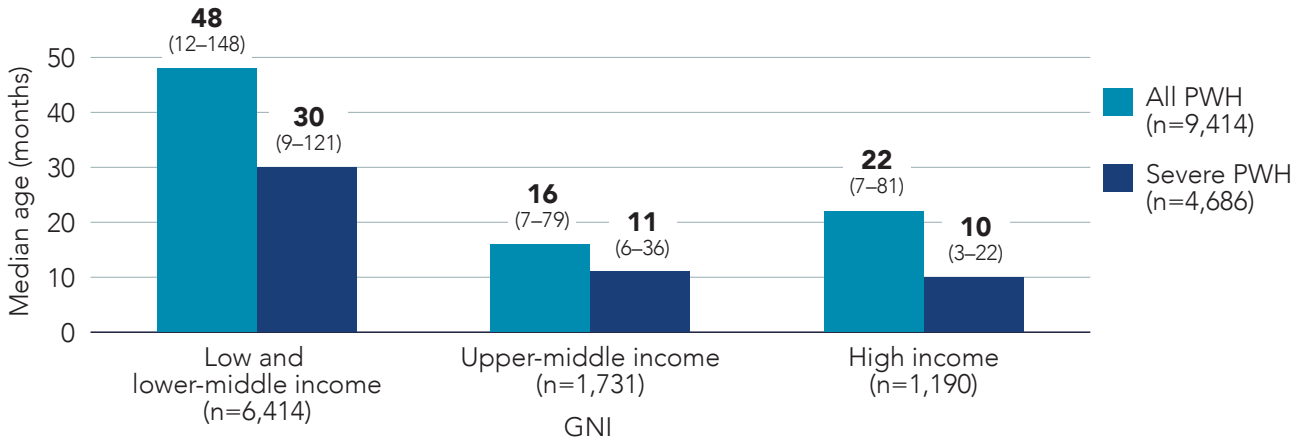


Figure 8

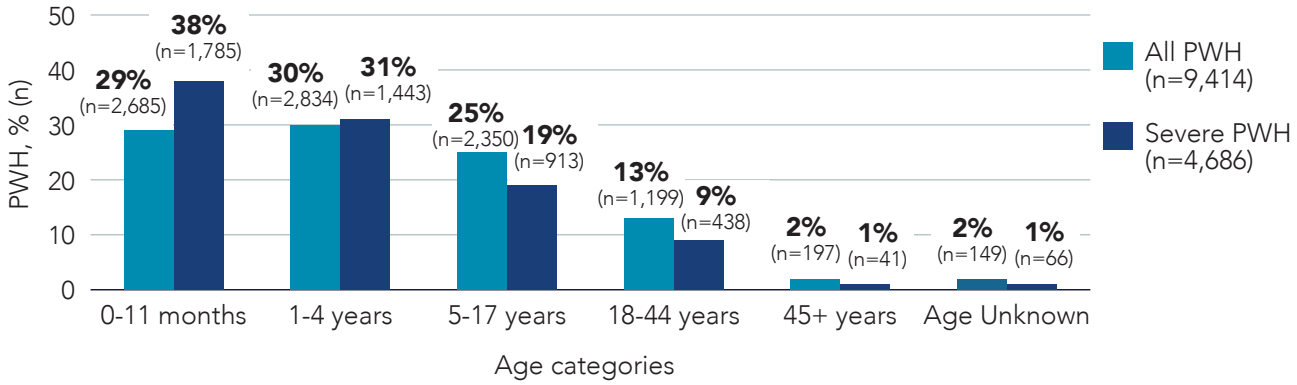
Age at diagnosis by Gross National Income



Note: Low (n=295) and lower-middle (n=6,918) income categories were combined due to the low number of patients in low-income countries.

Figure 9

Age distribution of PWH at diagnosis, % (n)



AGE AT FIRST BLEED AND FIRST JOINT BLEED

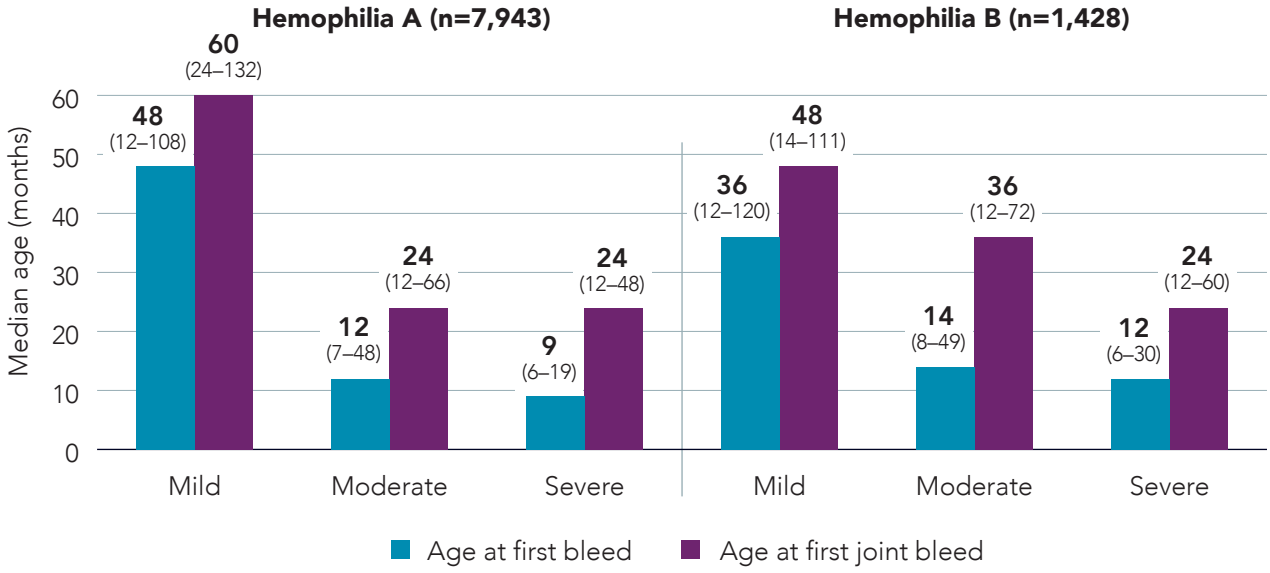
The median age at first bleed and first joint bleed were 12 and 24 months, respectively, for all PWH (Table 3b, Figure 10).

For people with severe hemophilia A, the median age at first bleed was 9 months and the median age at first joint bleed was 24 months (Figure 10).

For people with severe hemophilia B, the median age at first bleed was 12 months and the median age at first joint bleed was 24 months (Figure 10).

Figure 10

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



COMORBIDITIES

The data collected on comorbidities are not mandatory data fields. It was reported that 4,097 PWH were tested for HIV. Of those tested, 50 (<1%) had positive results and of these, 43 (2%) were people with severe hemophilia (Table 4). For Hepatitis C Virus (HCV), 4,800 PWH were reported to have been tested. Of those tested, 456 (10%) had an active infection.

TABLE 4
HIV Status

	All PWH (n=9,414)	Severe (n=4,686)
Patients tested*, n	4,097	2,470
Positive, n (%)	50 (<1%)	43 (2%)
Negative, n (%)	4,047 (99%)	2,427 (98%)

* Includes PWH who had at least 1 positive test reported.

TABLE 5
HCV Status

	All PWH (n=9,414)	Severe (n=4,686)
Patients tested*, n	4,800	2,741
Active infection, n (%)	456 (10%)	312 (11%)
Infection resolved spontaneously, n (%)	105 (2%)	81 (3%)
Infection resolved with treatment, n (%)	158 (3%)	123 (5%)
No infection, n (%)	4,081 (85%)	2,225 (81%)

* In the event that more than 1 test was performed in a year, the latest test result was considered in this summary.

EMPLOYMENT

Of the 6,012 PWH that had their employment status reported, 23% were employed either part-time or full-time. Hemophilia affected the employment status of 12% of PWH, forcing them into part-time employment, long-term sick leave, unemployment or retirement (Table 6).

TABLE 6
Employment

	All PWH (n=6,012)	Severe (n=3,113)
Employment status reported		
Employed full-time or part-time	1,397 (23%)	669 (21%)
Employed part-time due to hemophilia	292 (5%)	163 (5%)
Long term sick leave due to hemophilia	45 (1%)	26 (1%)
Not employed due to hemophilia	284 (5%)	185 (6%)
Retired due to hemophilia	37 (1%)	18 (1%)
Student	3,006 (50%)	1,534 (49%)
Other	951 (16%)	518 (17%)

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

CLINICAL DATA

THE CLINICAL DATA REPRESENT CLINICAL EVENTS WHICH OCCURRED IN 2021.

TABLE 7

Bleeding events summary, 2021

	All PWH* (n=8,578)	Severe (n=4,383)
Bleeds per patient, mean (SD)	5.4 (8.7)	6.4 (9.3)
Patients with 0 bleeds in 2021, n (%)	814 (9%)	401 (9%)
Target joints, n (%)**		
≥1	1,148 (13%)	636 (15%)
Total bleeding events$, n	19,366	12,170
Location of bleed, n (%)		
Joint	14,553 (75%)	9,258 (76%)
Muscle	2,769 (14%)	1,734 (14%)
Central nervous system	65 (<1%)	34 (<1%)
Other location	2,157 (11%)	1,307 (11%)

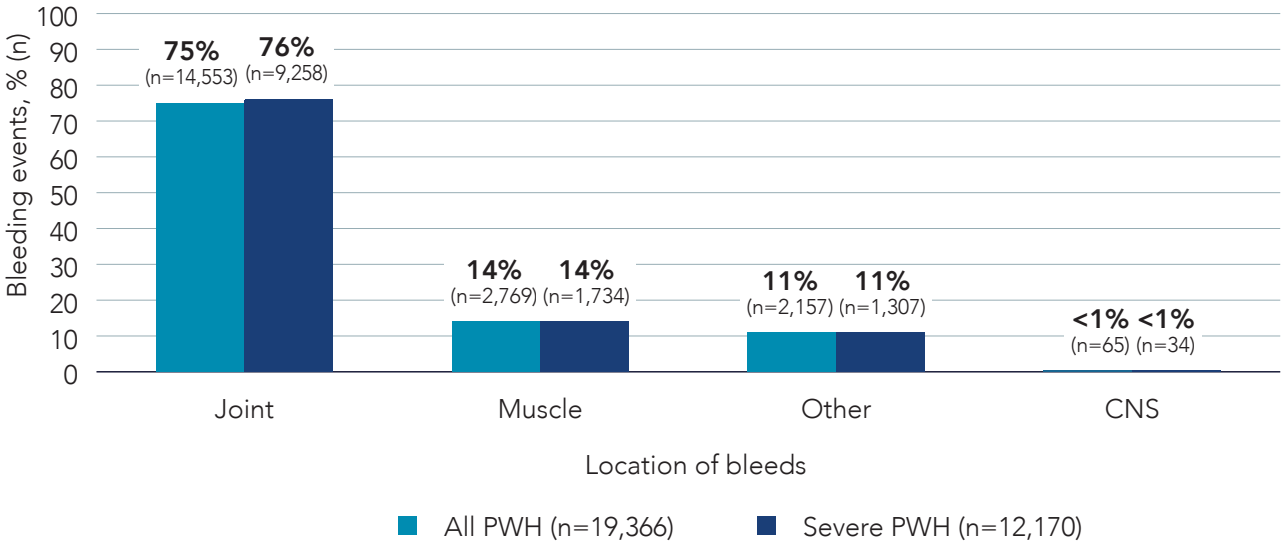
* 2021 Data for 836 PWH from the Czech Republic were not available at the time of publication.
** Includes PWHs who reported at least one target joint in 2021; Target joints are defined as '3 or more spontaneous bleeds into a single joint within a consecutive 6 month period. Where there have been ≤ 2 bleeds into the joint within a consecutive 12-month period the joint is no longer considered a target joint'[3].
$ It is possible that PWH had bleeds in more than one location.

BLEEDING EVENTS

In 2021, a total of 19,366 bleeds were reported by PWH. Of these, 14,553 (75%) were joint bleeds, 2,769 (14%) were muscle bleeds and 65 (<1%) were central nervous system (CNS) bleeds. There were 2,157 (11%) bleeds reported as 'other' locations (Figure 11). A total of 12,170 bleeds were reported for people with severe hemophilia. The distribution of bleeding events in people with severe hemophilia by location was similar to that of all PWH (Figure 11).

Figure 11

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 visits in 2021, 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 a visit in 2021 or an observation period less than 30 days, the ABR and AJBR were not calculated. The calculations of ABR and AJBR include only PWH who experienced at least 1 bleed or 1 joint bleed in 2021, respectively. Patients with 0 bleeds in 2021 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

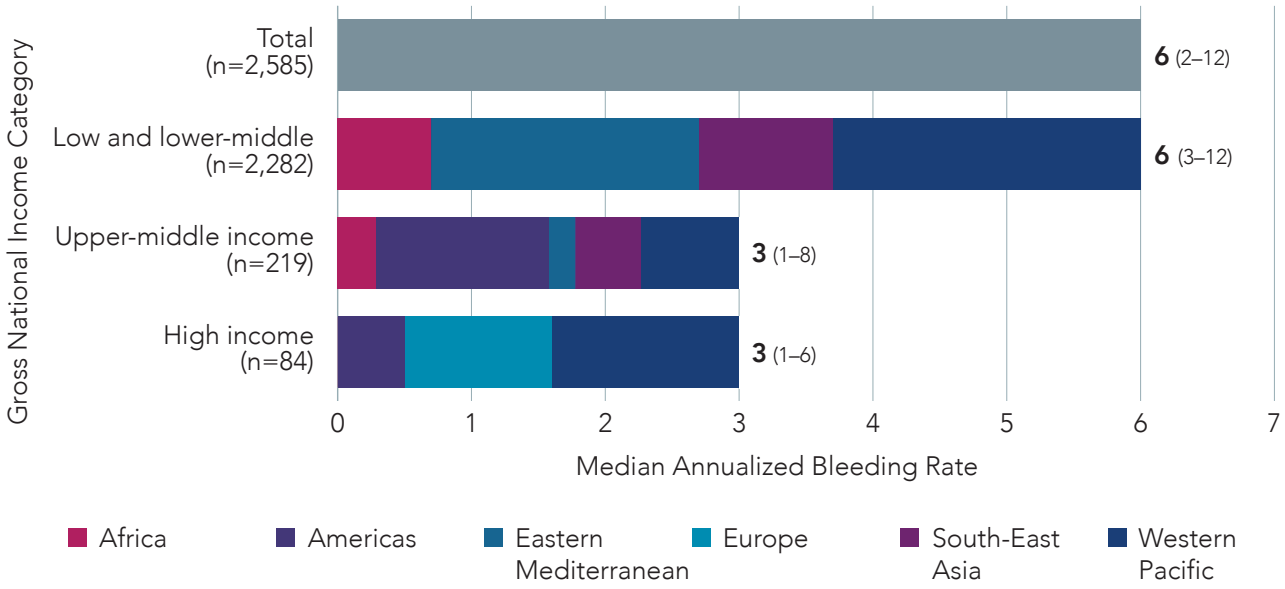
The median (IQR) ABR was 6 (2-12) for all PWH, varying by GNI and region (Figure 12). Figure 12 demonstrates that high income countries have the lowest ABR 3 (1-6) while those in low and lower-middle income countries had the highest ABR 6 (3-12) (Figure 12).

AJBR

The median (IQR) AJBR was 5 (2-10) for all PWH, varying by GNI and region (Figure 13). The AJBR observed in low and lower-middle countries was 5 (2-11) and 3 (1-7) for high income countries.

Figure 12

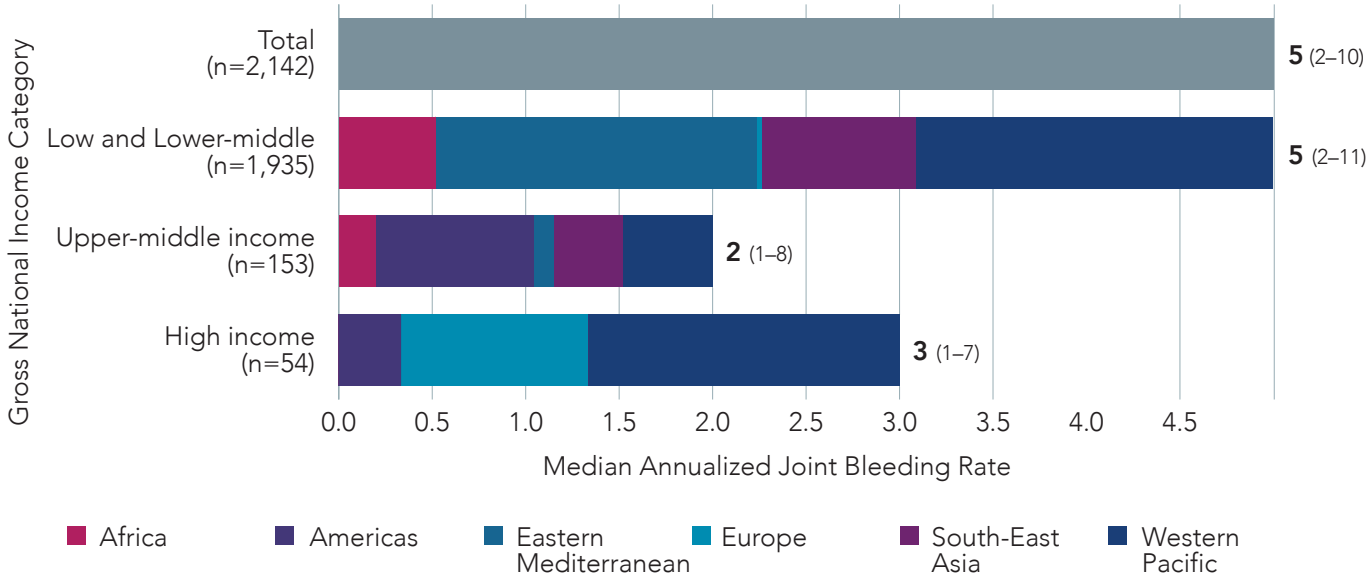
Median ABR for all PWH by GNI and region



Note: The low and lower-middle income categories were combined due to a small number of patients in the low income category.

Figure 13

Median AJBR for all PWH by GNI and region



Note: The low and lower-middle income categories were combined due to a small number of patients in the low income category.

TARGET JOINTS

Thirteen percent of all PWH, and 15% of severe PWH who had a clinic visit in 2021, reported having at least 1 target joint. The percent of PWH reporting a target joint varied by region, ranging from 48% to 19% (Figure 14).

Figure 14

PWH with at least 1 target joint by region

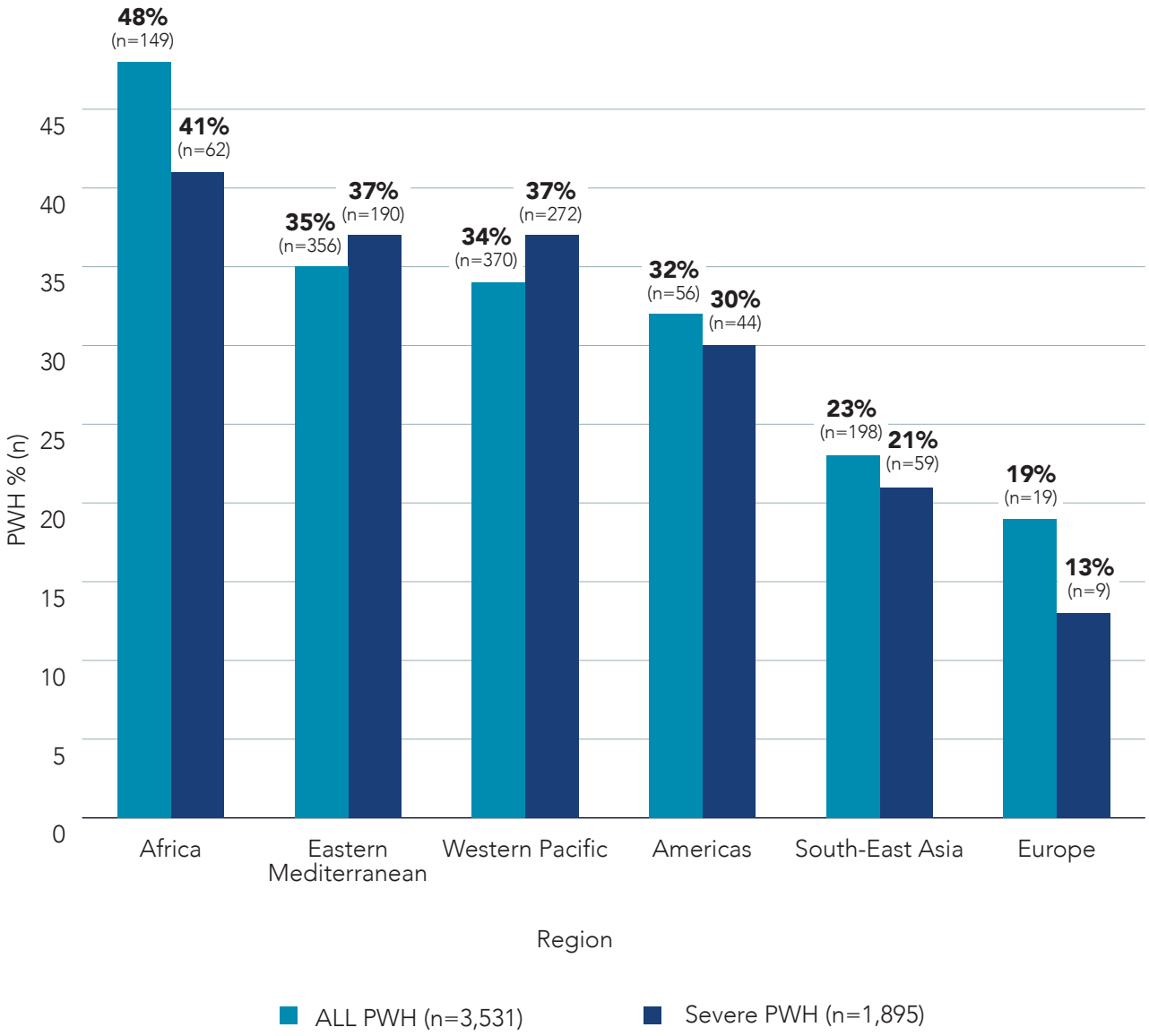


TABLE 8
Inhibitor summary, 2021

	All PWH (n=8,578)*	Severe PWH (n=4,383)*
Patients with a history of an inhibitor**, n (%)	411 (5%)	306 (7%)
Inhibitor testing in 2021		
Tested†, n (%)	424 (5%)	315 (7%)
Positive test results	106 (25%)	81 (2%)
Negative test results	318 (75%)	234 (98%)
Newly diagnosed with an inhibitor††, n (%)	48 (11%)	32 (10%)
Patients with suspected inhibitor, but no testing available$, n (%)	37 (<1%)	2 (<1%)

* 2021 Data for 836 PWH from Czech Republic were not available at the time of publication.
** Unique number of patients who had an inhibitor prior to registration in the WBDR or a positive test prior to 2021.
† Unique number of patients who had an inhibitor test in 2021. Testing methods include Bethesda, Nijmegen-Bethesda, and mixing study (aPTT).
†† Unique number of patients who never had an inhibitor in the past, were tested in 2021, and had a positive result.
$ Includes all PWH with a baseline visit in 2021.

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 2021. In 2021, 424 PWH were tested for inhibitors, 106 (25%) tested positive and 48 (11%) were newly diagnosed with an inhibitor (no history of inhibitors and no prior positive test reported) (Table 8 and Figure 15).

Figure 15
PWH with inhibitor test, 2021 (n=424)

TABLE 9a

Hemophilia related hospitalizations summary, 2021

	All PWH (n=8,578)*	Severe PWH (n=4,383)*
Patients hospitalized**, n (%)	881 (10%)	557 (13%)
Total hospitalizations†, n	3,248	2,292
Days per hospitalization, median (IQR)	11 (5-23)	13 (6-26)
Number of hospitalizations per patient$, median (IQR)	2 (1-5)	3 (1-5)

TABLE 9b

	All PWH (n=8,578)*	Severe PWH (n=4,383)*
Reason for hospitalizations, n (%)		
Joint bleeding	2,303 (27%)	1,649 (38%)
Other bleeding	421 (5%)	288 (7%)
Other muscle bleeding	386 (5%)	295 (7%)
Soft tissue bleeding	110 (1%)	61 (1%)
Other	72 (<1%)	47 (1%)
Surgery	36 (<1%)	19 (<1%)
Intracranial bleeding	27 (<1%)	12 (<1%)
Psoas muscle bleeding	13 (<1%)	11 (<1%)
Thromboembolic event	1 (<1%)	1 (<1%)

* 2021 Data for 836 PWH from Czech Republic were not available at the time of publication.
** Number of unique PWH hospitalized.
$ Based only on patients who were hospitalized.
† Hospitalization is defined as having at least 1 overnight stay in the hospital.

In 2021, 881 (10%) PWH experienced a total of 3,248 hemophilia related hospitalizations, with a median (IQR) stay of 11 days (5-23) (Table 9a). The most common reason for hospitalization was joint bleed for both hemophilia A and B patients (70% and 61% respectively) (Figures 16 and 17). In total, 27 hospitalizations were for an intracranial bleed; 24 (1%) were among hemophilia A patients and 1 (<1%) were among hemophilia B patients. PWH with hemophilia type unknown, who were hospitalized are not included in the graphs below (Figures 16 and 17).

Figure 16

Reason for hospitalization in hemophilia A patients (n=2,772)

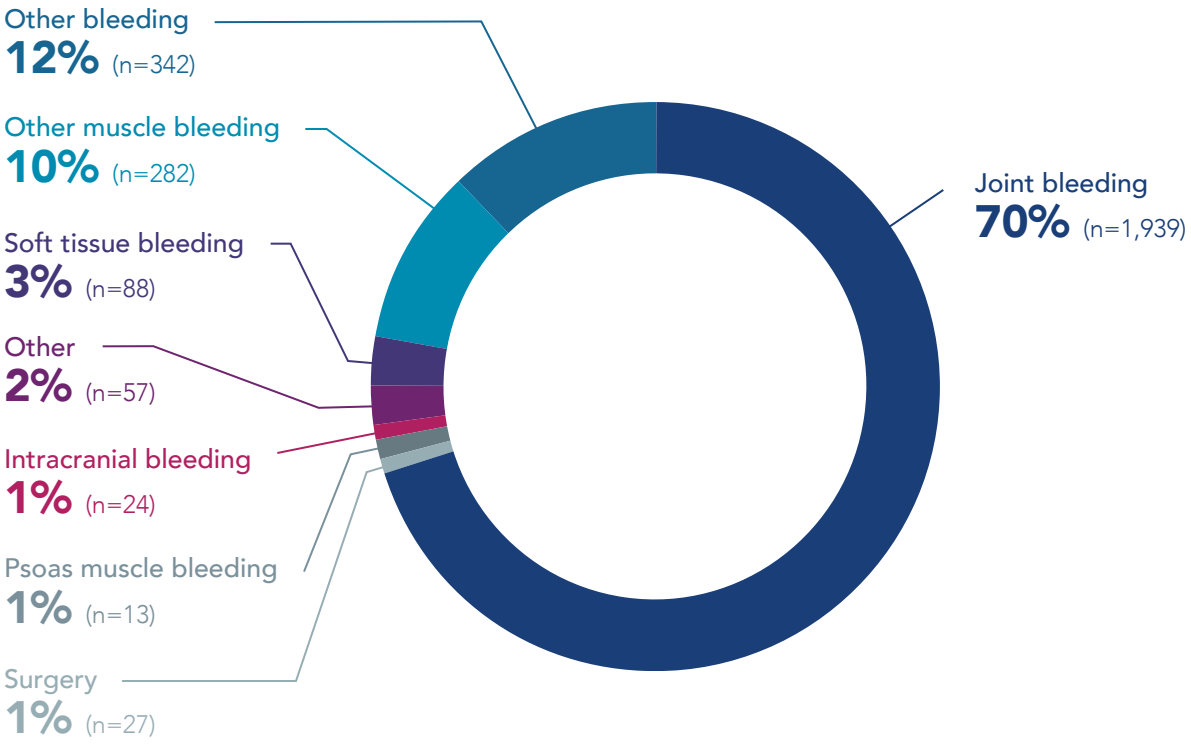
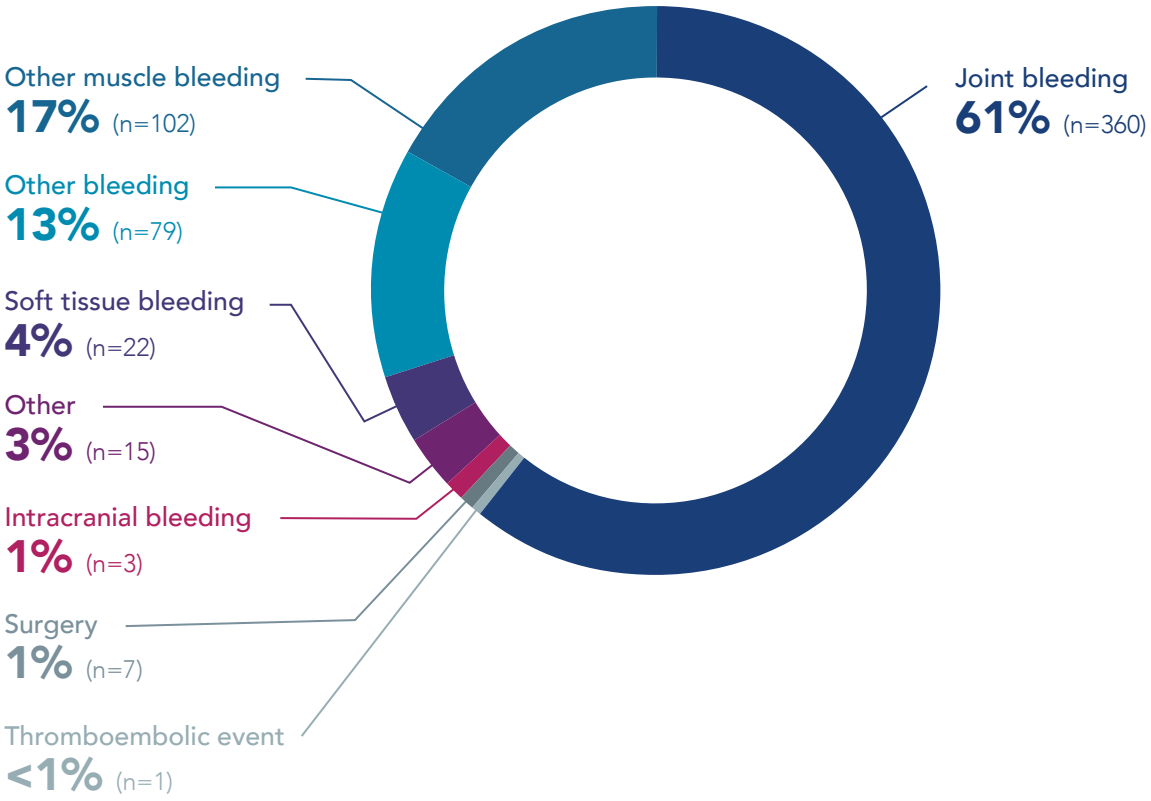


Figure 17

Reason for hospitalization in hemophilia B patients (n=589)



TREATMENT

TABLE 10

Treatment summary, 2021*

	All PWH (n=8,578)*	Severe (n=4,383)*
Received at least 1 prophylaxis treatment in 2021, n (%)**	1,625 (19%)	1,299 (30%)
Hemophilia A, n (%)	1,431 (17%)	1,159 (27%)
FVIII, standard half-life	900 (63%)	745 (64%)
FVIII, extended half-life	222 (16%)	170 (15%)
Bypassing agent	7 (<1%)	7 (<1%)
Non-factor product	325 (23%)	255 (22%)
Other	43 (3%)	32 (3%)
Hemophilia B, n (%)	190 (2%)	140 (3%)
FIX, standard half-life	100 (53%)	81 (58%)
FIX, extended half-life	78 (41%)	52 (37%)
Bypassing agent	1 (<1%)	1 (<1%)
Non-factor product	0 (0%)	0 (0%)
Other	18 (9%)	10 (7%)

* 2021 Data for 836 PWH from Czech Republic were not available at the time of publication.
** Number of unique PWH who received prophylaxis treatment in 2021. This includes patients who started prophylaxis treatment or had an on-going treatment in 2021. Patients may be receiving treatments that fall under multiple categories.

PROPHYLAXIS USE

A total of 1,625 (19%) PWH received prophylaxis as treatment in 2021. Thirty percent of severe PWH received prophylaxis in 2021; 90% of these were PWH A and 10% were PWH B (Table 10, Figure 18).

Figure 18

Percentage of PWH receiving prophylaxis in 2021 by region

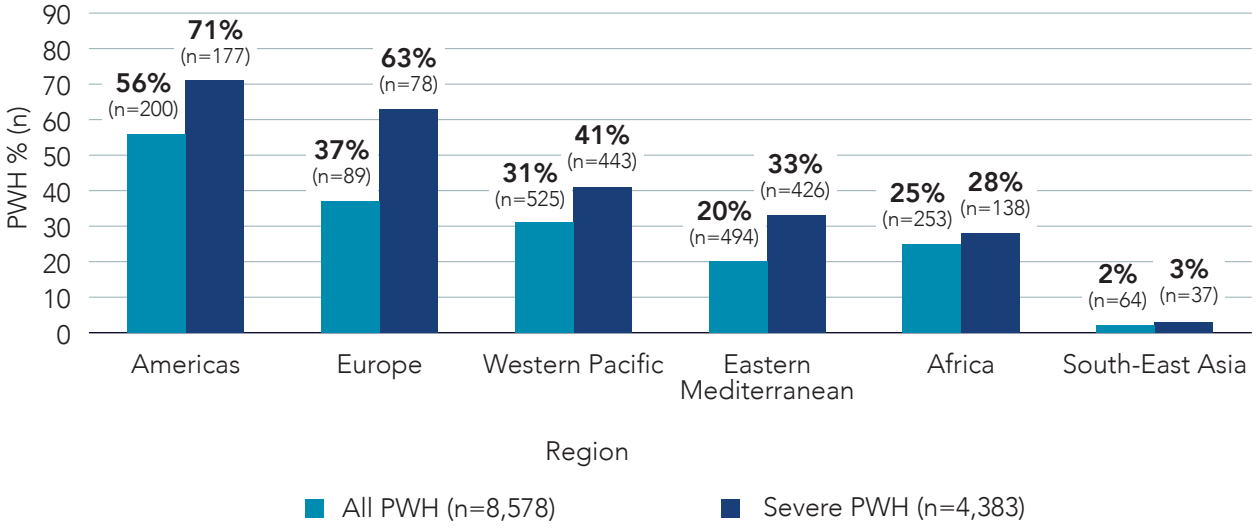
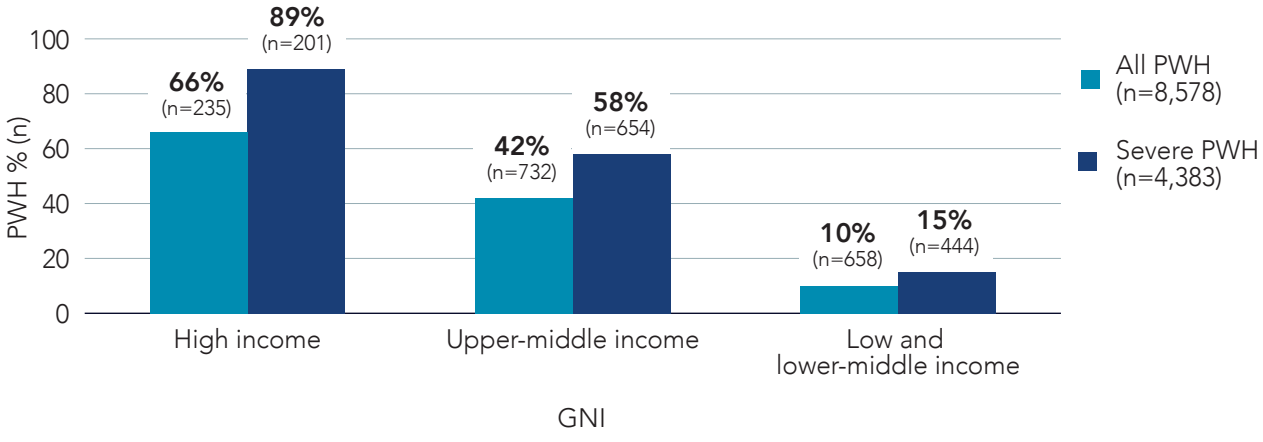


Figure 19

Percentage of PWH receiving prophylaxis in 2021 by GNI

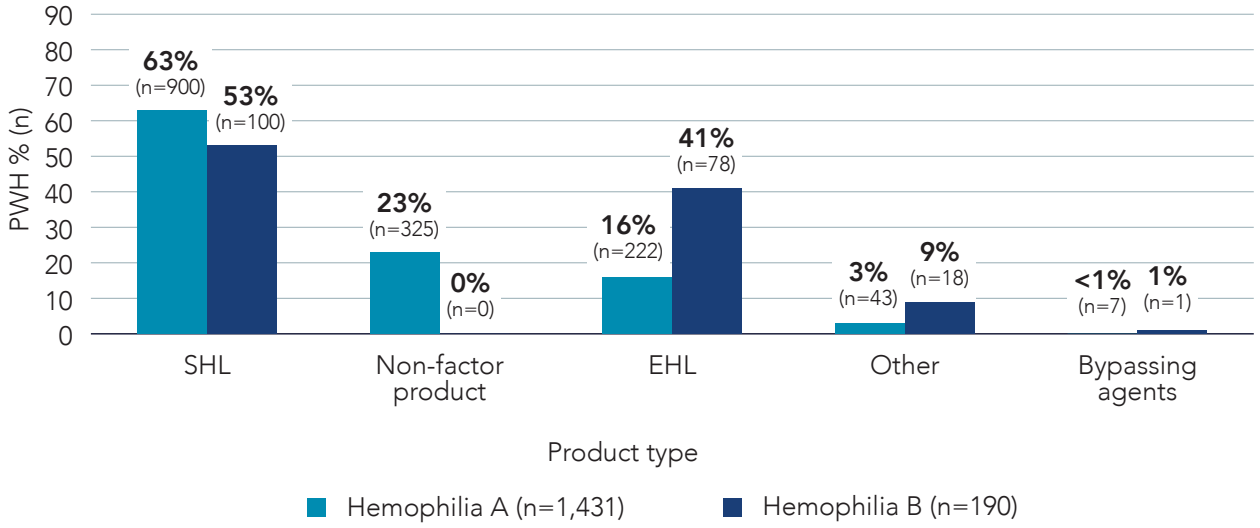


Note: Low and lower-middle income categories were combined due to small number of patients in the low income category.

For PWH treated with prophylaxis, standard half-life (SHL) clotting factor concentrates were the most common type of treatment used in 2021 (63% of PWH A on prophylaxis, and 53% of PWH B on prophylaxis), followed by extended half-life (EHL) clotting factor concentrates, (16% of people with hemophilia A and 41% of people with hemophilia B). Twenty three percent of people with hemophilia A received non-factor product treatments (Table 10, Figure 20).

Figure 20

Distribution of product type among PWH on prophylaxis treatment



WBDR DATA QUALITY ACCREDITATION 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 WBDR 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).

63 (80%) OF HTCs

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

Throughout the year, the WBDR team provided data quality feedback and training to both existing and new HTCs. In 2021, the WBDR team worked directly with 79 HTCs. Sixty-three (80%) HTCs were classified as 'Leaders' (data quality score ≥95%), which is the highest level of data quality.

Figure 21

WBDR Data Quality Rating Scale

Note: Data imported through the International Data Integration Program is not verified under the WBDR's Data Quality Accreditation Program.

INTERNATIONAL DATA INTEGRATION PROGRAM

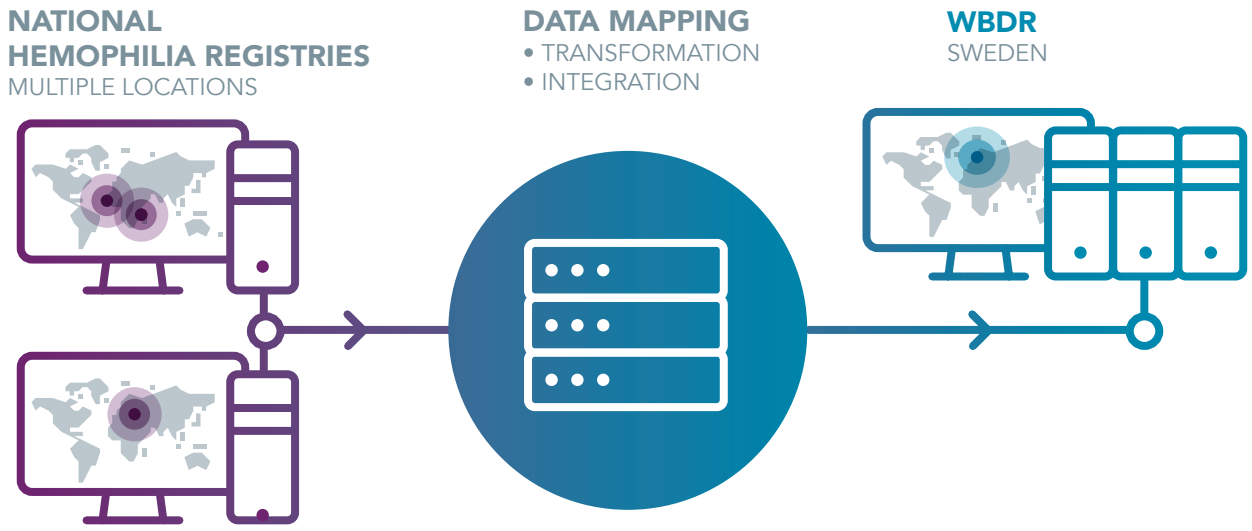
Registries, with international collaboration between countries, offer an opportunity to pool sufficient data to increase the knowledge and evidence in rare disorders across different regions and economies. In an effort to combine resources from existing hemophilia registries and maximize the utility of data that currently exist, the WBDR established the International Data Integration Program with the aim of facilitating data transfer from existing patient registries to the WBDR. A protocol to import data from established registries into the WBDR has been developed and tested.

In 2019, the WBDR started a data linkage collaboration with the Czech National Haemophilia Programme Registry (CNHPR). Since 2019, de-identified data from the CNHPR are annually imported into the WBDR. To date, 2018, 2019 and 2020 data on over 840 PWH have been collected and annually updated, with 21 newly enrolled PWH in 2021.

In 2021, the Hereditary Bleeding Disorders Registry (HBDR) of the Thai Society of Hematology (TSH) collaborated with the WBDR to integrate their 2020 and 2021 data in the global registry. Eight of 10 HTCs at the university hospitals took part in this collaboration. By the end of 2021, the minimum and extended data sets of 300 people with hemophilia A and B have been transferred to the WBDR. Besides successful data integration from the HBDR to the WBDR, partnership between the TSH and the WFH has yielded another output, which is an article in Haemophilia journal[4] explaining the process of data integration between the two registries.

At time of the publication of this report, the TSH and the WFH are evaluating the expansion of this project. In Phase 2 of the project, both organizations will study the possibility of directly transferring selected data from the HBDR to the WFH Annual Global Survey. Currently, the National Member Organization in Thailand compiled all required data from Thai HTCs and submit them to the WFH on a yearly basis. By directly transferring the data from the HBDR to the WFH Annual Global Survey, it is believed that the submitted data will be more reliable, accurate, and less time consuming.

The International Data Integration Program is available to interested countries who wish to join this global initiative by sharing their national data and having their PWH represented in the WBDR. Interested individuals are encouraged to contact the WFH at wbdr@wfh.org.



WBDR RESEARCH SUPPORT PROGRAM

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.

Congratulations to the seven HTCs in 2021 who were awarded funding for their research project. To date, we have provided funding to 30 research projects in 15 countries.

Since 2018:

COUNTRIES

15

RESEARCH PROJECTS

30

HTCs PARTICIPATED

26

AMOUNT AWARDED

>130,000

USD

PUBLICATIONS AT INTERNATIONAL CONFERENCES

(ABSTRACTS AND FEATURED ARTICLES)

7

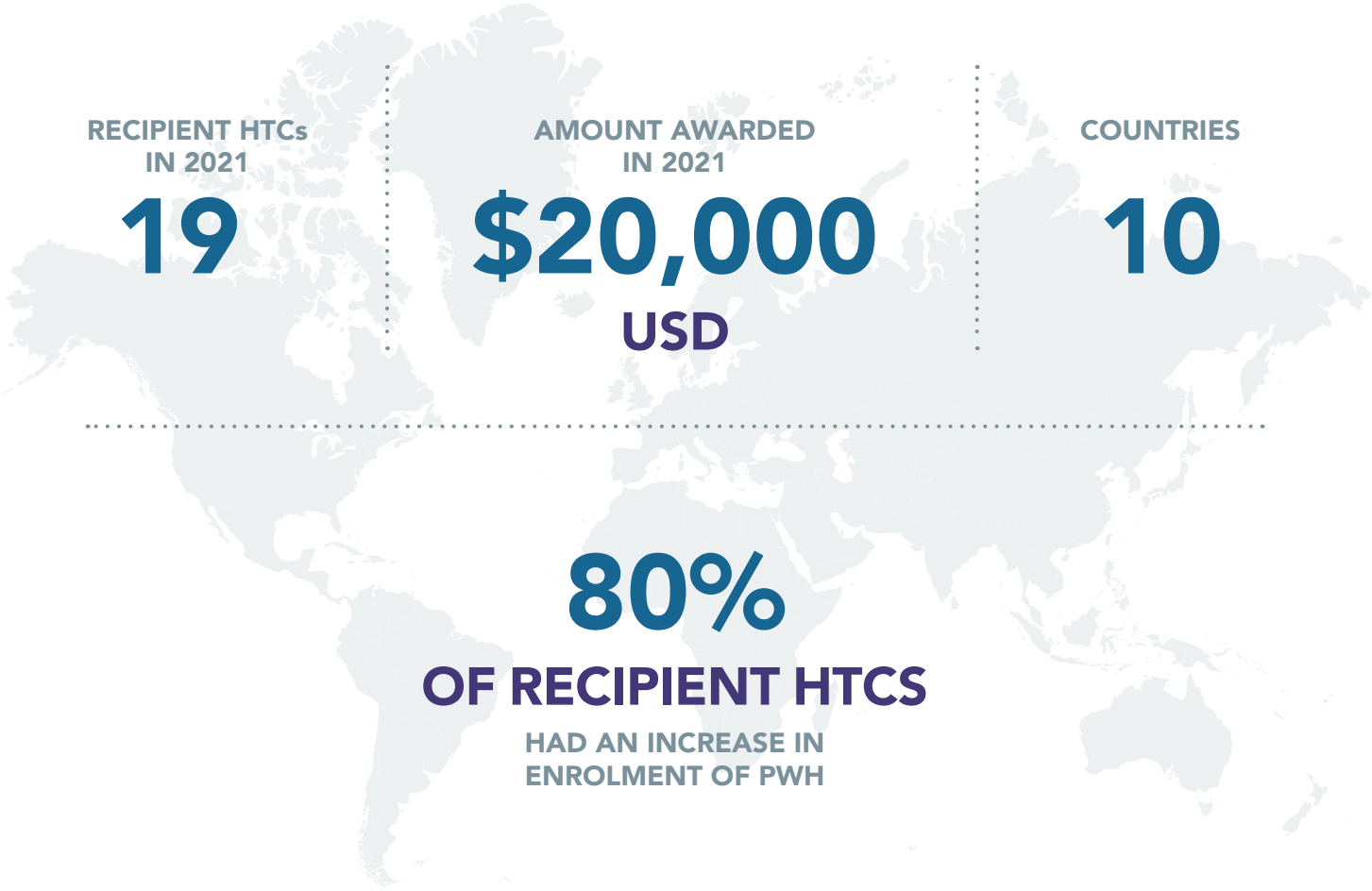
WBDR HTC FUNDING PROGRAM

The WBDR HTC Funding Program (HFP) is designed to provide funds to support data collection activities at participating WBDR HTCs in low and lower-middle income countries.

The HFP aims to help HTCs improve patient enrolment, the recording of follow-up visits, functional scales, and quality of life measures. Eligible HTCs are compensated based on the number of active patients enrolled in the WBDR or the number of identified hemophilia patients being followed at the HTC at the time of the application. The funds are allocated for a period of one year.

Following the first year of funding, the impact of the HFP at recipient HTCs is demonstrated by the significant improvement in patient enrolment and overall data collection. HFP recipient HTCs have enrolled 1080 PWH during 2021.

For more information, please visit our webpage.



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**
		COVID-19

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 – PARTICIPATING HTCs

Country	City-Clinic
Algeria	• Annaba - Service d'hématologie CHU Annaba • Constantine - Unité hémophilie et maladies hémorragiques héréditaires
Argentina	• Bahía Blanca - CARDHE • Buenos Aires - Fundación de la Hemofilia and Instituto De Investigaciones Hematológicas "Dr. Mariano R. Castex"
Bangladesh	• Chittagong - Chittagong Medical College Hospital • Dhaka - Bangabandhu Sheikh Mujib Medical University • Dhaka - Dhaka Medical College • Dhaka - Lab One Foundation • Rajshahi - Rajshahi Medical College & Hospital
Barbados	• Bridgetown - Queen Elizabeth Hospital
Belgium	• Woluwe-Saint-Lambert - Cliniques Universitaires Saint-Luc
Cameroon	• Yaoundé - CHU Yaoundé
Côte d'Ivoire	• Abidjan - CHU de Yopougon
Cuba	• Havana - Instituto de Hematología e Inmunología
Czech Republic	• Brno: FN Brno - DN (Oddělení dětské hematologie) • Brno: FN Brno - OKH • České Budějovice: Nemocnice - Dětské oddělení • České Budějovice: Nemocnice - OKH • Hradec Králové: FNHK - Dětská klinika • Hradec Králové: FNHK - IV. interní hematologická klinika • Liberec: KN Liberec - OKH • Olomouc: FN Olomouc - Dětská klinika • Olomouc: FN Olomouc - Hemato-onkologická klinika • Ostrava: FN Ostrava - Klinika dětského lékařství • Ostrava: FN Ostrava - Krevní centrum • Plzeň: FN Plzeň - Dětská klinika • Plzeň: FN Plzeň - ÚKBH • Plzeň: Městská poliklinika - Hemacentrum • Praha: FN Motol - Klinika dětské hematologie a onkologie • Ústí n.L.: Masarykova nemocnice - Dětská klinika (hematologie) • Ústí n.L.: Masarykova nemocnice - OKH
Egypt	• Cairo - Pediatric Hemophilia Centre, Ain Shams University • Giza - Shabrawishi Hospital • Mansoura - Mansoura University Children Hospital • Zagazig - Pediatrics department, Zagazig University
Ethiopia	• Addis Ababa - Tikur Anbessa Hospital
Ghana	• Kumasi - Komfo Anokye Teaching Hospital
India	• Aluva - Haemophilia Treatment Centre, District Hospital • Bhopal - Gandhi Medical College • Ludhiana - Christian Medical College • Manipal - Melaka Manipal Medical College, Hemophilia Society Manipal • Tiruvalla - Believers Church Medical College Hospital
Indonesia	• Banjarmasin - Ulin General Hospital
Iraq	• Baghdad - Hemophilia Center - Medical City • Baghdad - National Center of Hematology - Al-Mustansirya University • Basra - Basra Center for heriditery Blood Diseases

Country	City-Clinic
Japan	• Tokyo - Ogikubo Hospital
Kenya	• Eldoret - Moi Teaching and Referral Hospital • Nairobi - Kenyatta National Hospital
Kyrgyzstan	• Bishkek - National Center for Maternity and Childhood • Bishkek - National Center of Oncology and Hematology • Osh - Adult Hematology - Osh Interregional Joint Clinical Hospital • Osh - Dept of Pediatric Hematology - Interregional Children's Clinical Hospital
Madagascar	• Antananarivo - CHU Joseph Ravoahangy Andrianavalona (HJRA)
Malawi	• Lilongwe - Kamuzu Central Hospital
Malaysia	• Alor Setar - Hospital Sultanah Bahiyah • Ampang - Hospital Ampang • George Town - Hospital Pulau Pinang • Johor Bahru - Hospital Sultan Ismail • Johor Bahru - Hospital Sultanah Aminah • Klang - Hospital Tengku Ampuan Rahimah • Kota Bharu - Hospital Raja Perempuan Zainab II • Kota Kinabalu - Hospital Queen Elizabeth • Kota Kinabalu - Hospital Wanita dan Kanak-Kanak Sabah • Kuala Terengganu - Hospital Sultanah Nur Zahirah • Kuching - Hospital Umum Sarawak • Seremban - Hospital Tuanku Ja'afar • Taiping - Hospital Taiping
Morocco	• Rabat - Adultes - Centre de Référence de l'Hémophilie, Hôpital Ibn Sina • Rabat - Enfants - Centre de Traitement de l'hémophilie de Rabat, Hôpital d'Enfants de Rabat
Nepal	• Kathmandu - Civil Service Hospital
New Zealand	• Christchurch - Christchurch Hospital • Palmerston North - Palmerston North hospital
Nigeria	• Abuja - National Hospital, Abuja • Benin - University of Benin Teaching Hospital • Enugu State - South East HTC, Department of Haematology, UNTH Ituku Ozalla Enugu • Gombe - Gombe State University • Ibadan - University of Ibadan • Kano - Aminu Kano Teaching Hospital • Lagos - Lagos University Teaching Hospital
Pakistan	• Karachi - Haemophilia Welfare Society, Karachi • Lahore - Haemophilia Treatment Centre • Rawalpindi - Haemophilia Treatment Centre
Panama	• Panamá City - Hospital del Niño
Philippines	• Manila - University of Santo Tomas Hospital
Portugal	• Lisbon - Comprehensive Care Centre of Congenital Coagulopathies, Santa Maria Hospital
Senegal	• Dakar - Centre National de Transfusion Sanguine
Serbia	• Belgrade - Mother and Child Health Care Institute of Serbia "Dr Vukan Cupic"
South Africa	• Bloemfontein - University of the Free State
Sudan	• Khartoum - Haemophilia Center, Khartoum Teaching Hospital
Thailand	• Bangkok - Department of medicine, Siriraj Hospital • Bangkok - Department of medicine, Thammasat University • Bangkok - Department of paediatrics, Chulalongkorn University • Bangkok - Department of paediatrics, Ramathibodi Hospital • Bangkok - Department of paediatrics, Thammasat University • Chiang Mai - Chiang Mai University Hospital • Nakohn Ratchasima - Department of paediatrics, Maharat Nakohn Ratchasima Hospital • Songkla - Department of paediatrics, Prince of Songkla University
Uganda	• Kampala - Mulago Hospital
USA	• Cincinnati - University of Cincinnati Hemophilia Treatment Center • Winston-Salem - Wake Forest Baptist Health
Vietnam	• Hanoi - National Children's Hospital • Hanoi - National Institute of Hematology and Blood Transfusion • Ho Chi Minh City - Blood Transfusion Hematology

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.

Support for the WBDR is provided by:

Visionary Partners

Takeda

sobi rare strength

Collaborating Partners

novo nordisk®

Pfizer

Roche

BAYER

CSL Behring Biotherapies for Life™

GRIFOLS

SANOFI GENZYME

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 attacks 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: Three 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. 2021. Definition of regional groupings. https://www.who.int/about/who-we-are/regional-offices. Accessed on March 10, 2021.

[2] World Bank 2015. World Development Indicators 2015. http://documents.worldbank.org/curated/en/795941468338533334/World-development-indicators-2015. Accessed October 25, 2018.

[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.

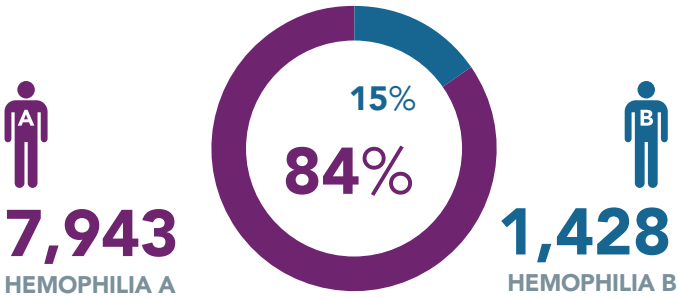
[4] Chuansumrit, A., Youttananukorn, W., Sirachainan, N., Natesirinilkul, R. and Ruchutrakool, T. (2022), Direct transfer of data of people with haemophilia from the Thai Haemophilia Treatment Centre Registry to the World Bleeding Disorders Registry of the World Federation of Hemophilia. https://doi.org/10.1111/hae.14496.

WBDR 2021 DATA REPORT HIGHLIGHTS

104
HTCs ENROLLED

37
COUNTRIES REPRESENTED

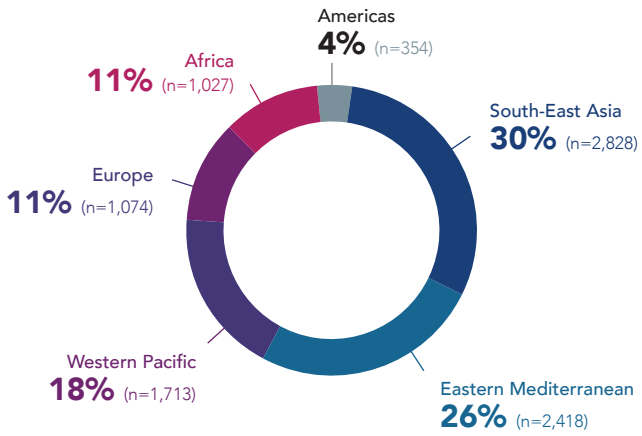
9,414
ENROLLED PATIENTS



7,943
HEMOPHILIA A

1,428
HEMOPHILIA B

Distribution of PWH by region



World Federation of Hemophilia

1425, boulevard René-Lévesque Ouest, Bureau 1200
Montréal (Québec) H3G 1T7, Canada

T +1 514.875.7944 **F** +1 514.875.8916
wfh@wfh.org

Charitable solicitations for the common purposes of WFH and WFH USA within the U.S. are conducted through WFH USA, a 501(c)3 affiliated entity.