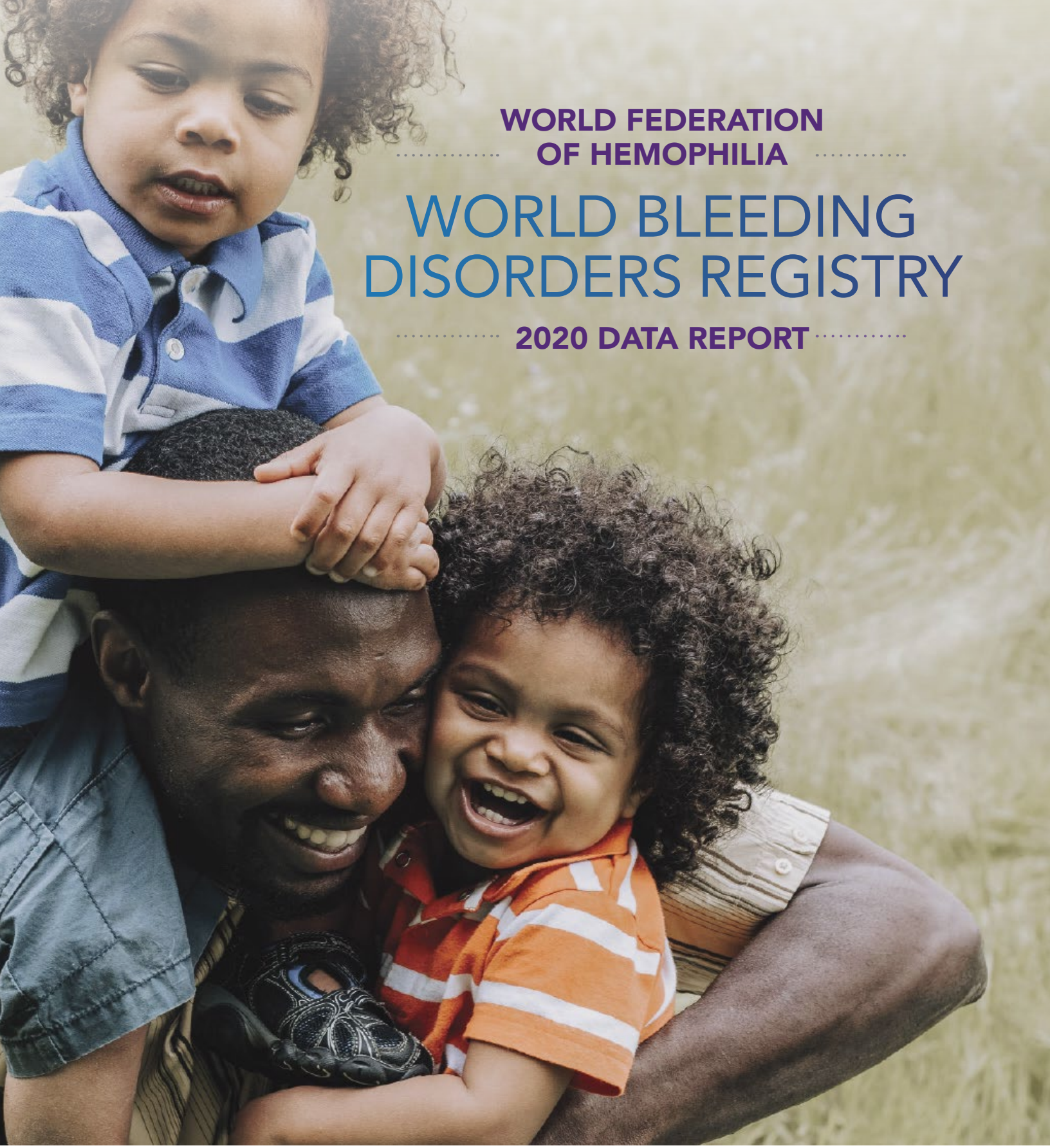


WORLD FEDERATION OF HEMOPHILIA

WORLD BLEEDING DISORDERS REGISTRY

2020 DATA REPORT

WBDR
WFH World Bleeding Disorders Registry

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

TABLE OF CONTENTS

ABOUT THE WFH

For over 55 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 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.

SOURCE OF DATA

The data presented in the WBDR 2020 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).

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

July 2021

Dear members of the bleeding disorders community,

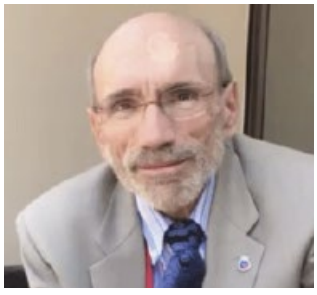
It is our pleasure to share the World Bleeding Disorders Registry (WBDR) 2020 Data Report with you. This report represents the third year of a worldwide effort to prospectively capture the real-world clinical experience of people with hemophilia (PWH) from around the globe. It is our hope that these 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, 2020, over 7,000 PWH from 86 hemophilia treatment centres (HTC) and 33 countries around the world have joined our efforts in achieving the World Federation of Hemophilia's (WFH) vision, *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 extended data set reported. For the second year in a row, we have successfully linked the Czech Republic national data directly with the WBDR. Our data integration program will be expanded to other countries in the upcoming year.

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 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 2021 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, 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 HEMEPHILIA 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 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 informed 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 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. In 2019, the first data linkage process was successfully completed with the Czech Republic, followed by another in 2020. The 2018 and 2019 data from the Czech Republic national registry are included in this report.

Please see page 35 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 33 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 2020 DATA REPORT

The data in the third edition of the WBDR Data Report includes patient data collected between the launch date of January 26, 2018 and December 31, 2020. These data stem from 86 participating HTCs (Appendix 2), representing 33 countries, who received institutional review board approval and enrolled at least one PWH into the WBDR as of December 31, 2020. At the time of publication of this Data Report (July 2021), an additional 6 HTCs are participating in the WBDR, for a total of 90 HTCs from 34 countries.

Please note, that at the time of data cut-off for this report (December 31, 2020), 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 2020 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, 2020

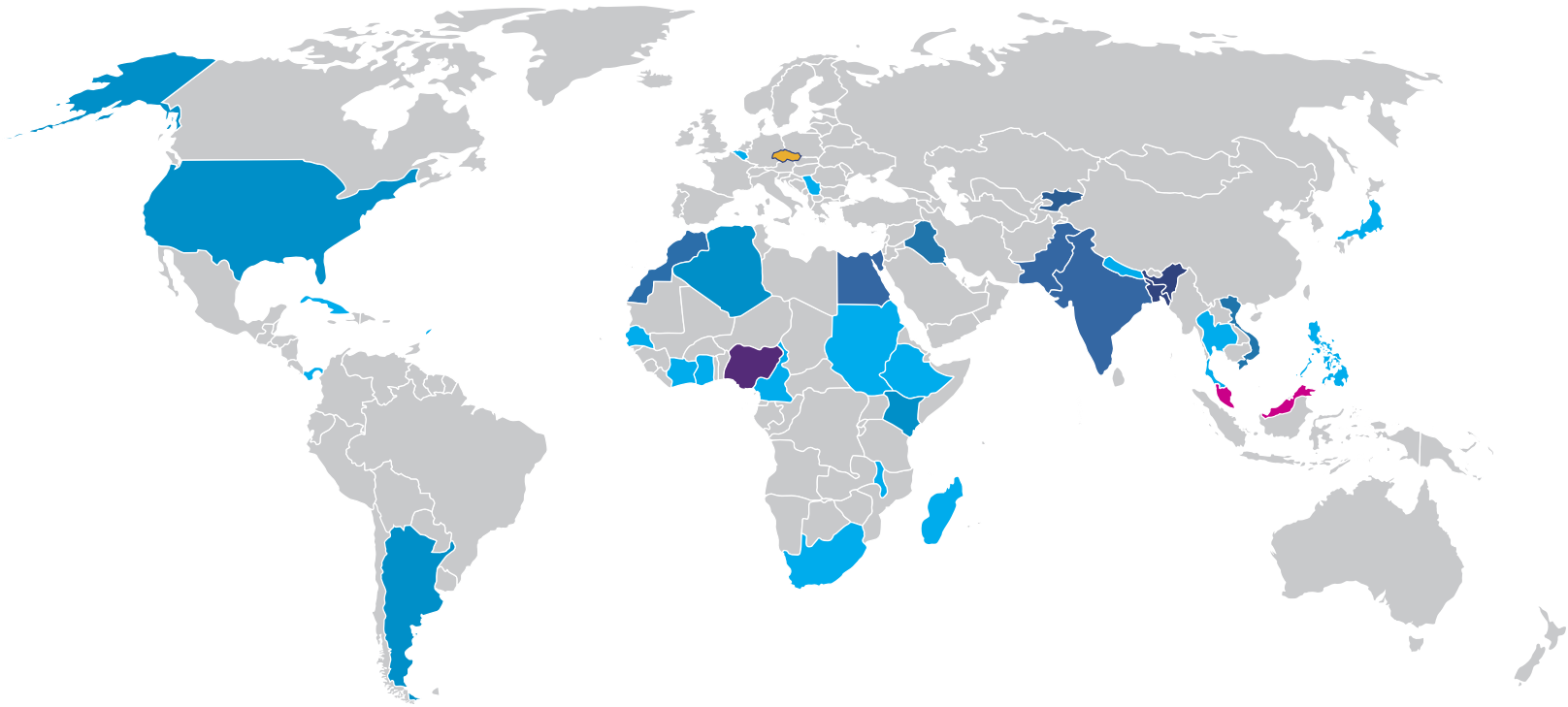


Figure 1
COUNTRIES AND HTCS PARTICIPATING IN THE WBDR

1 → 10 Number of HTCs per country

Data Linkage (Czech Republic)

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

DATA INCLUDED IN THE WBDR 2020 DATA REPORT

PARTICIPATION

From January 2018 up to December 31, 2020, 7,208 PWH were enrolled in the WBDR, representing 6 regions, 33 countries and 86 HTCs (Figures 1 and 2).

33
COUNTRIES

86
HEMOPHILIA TREATMENT CENTRES

7,208
PEOPLE WITH HEMOPHILIA

TABLE 1
Participation Summary

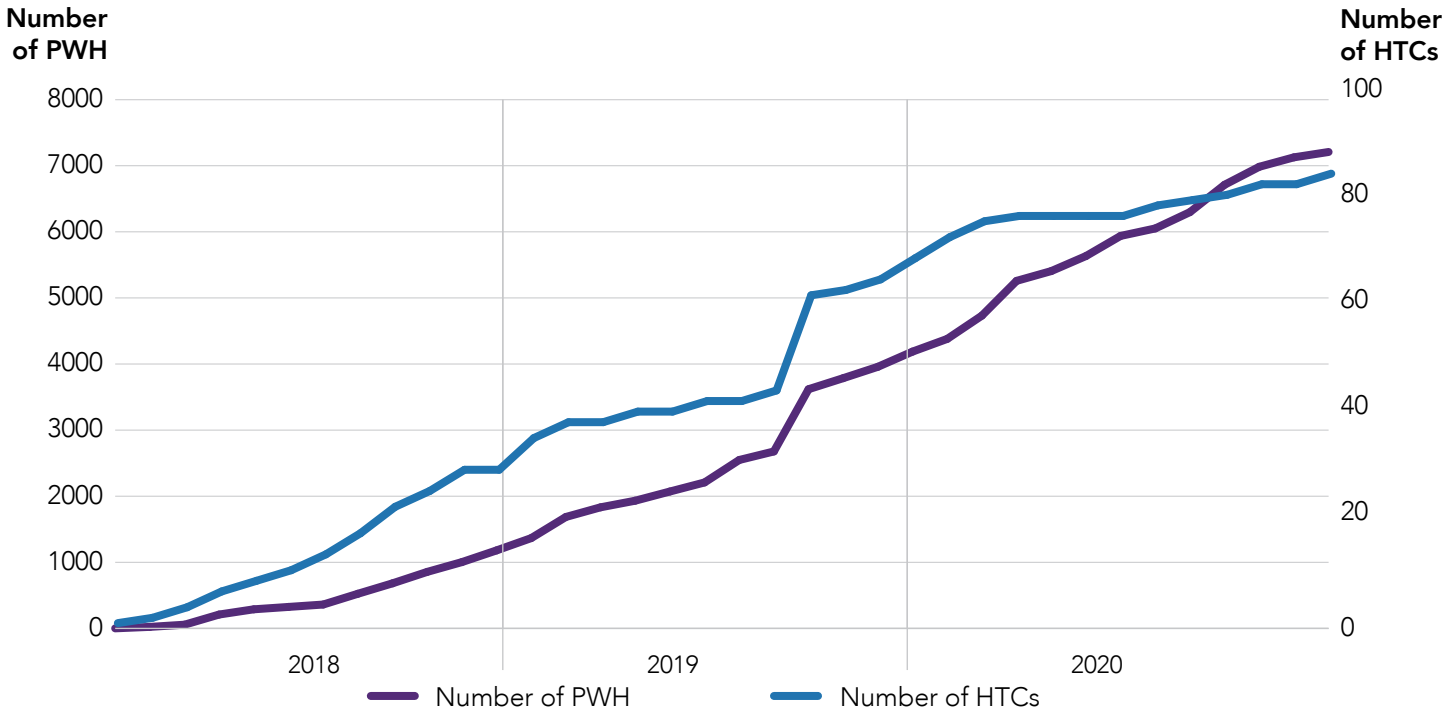
	All PWH	Severe PWH*
Countries, n	33	
Hemophilia treatment centres**, n	86	
People with hemophilia, n	7,208	3,812 (53%)
Distribution of PWH by region†, n (%)		
Africa	812	404 (50%)
Americas	311	228 (73%)
Eastern Mediterranean	1,539	889 (58%)
Europe	990	383 (39%)
South-East Asia	2,094	933 (45%)
Western Pacific	1,462	975 (67%)
Distribution of PWH by GNI§, n (%)		
High income	1,087	478 (44%)
Upper-middle income	1,289	870 (67%)
Low and lower-middle income	4,832	2,464 (51%)

* 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 enrolled by December 31, 2020
† Regions based on WHO regional groupings[1]
§ GNI = Gross National Income; Gross National Income categories based on The World Bank Group 2019 rankings for "Gross national income (GNI) per capita, Atlas method (current US$)"[2] . Low (n=168) and lower-middle (n=4,664) 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 2020

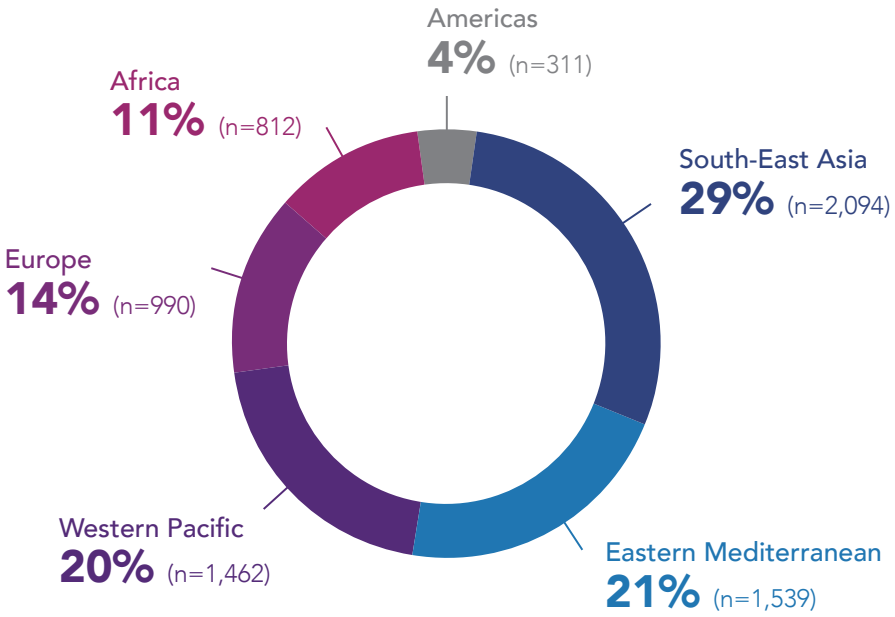


DISTRIBUTION OF PWH

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 (Bangladesh, India, Nepal, Thailand) and the Eastern Mediterranean (Algeria, Egypt, Iraq, Morocco, Pakistan, Sudan), representing 29% and 21% of PWH respectively (Figure 3).

Figure 3

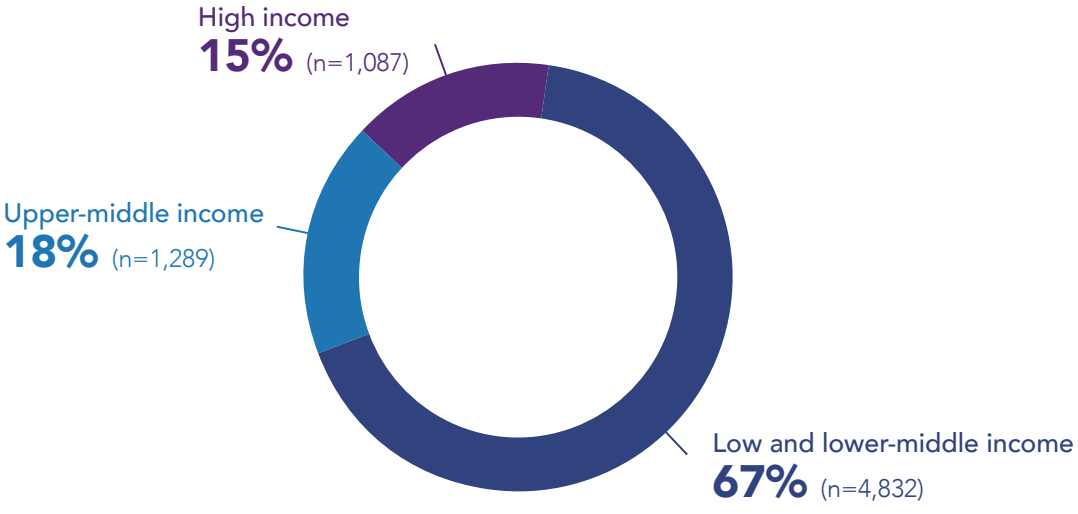
Distribution of PWH by Region



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 (67%), followed by upper middle and high income representing 18% and 15% respectively (Figure 4).

Figure 4

Distribution of PWH by Gross National Income



DEMOGRAPHICS

TABLE 2
Demographics summary

	All PWH (n=7,208)	Severe (n=3,812)
Type of hemophilia*, n (%)		
Hemophilia A	6,088 (84%)	3,315 (87%)
Hemophilia B	1,085 (15%)	491 (13%)
Sex, n (%)		
Male	7,181 (99%)	3,804 (99%)
Female	27 (<1%)	8 (<1%)
Age of PWH**		
Age, years, median (IQR)	20 (11-33)	20 (11-33)
Pediatrics (<18 years), n (%)	3,151 (44%)	1,692 (44%)
Adults (≥18 years), n (%)	4,057 (56%)	2,120 (56%)

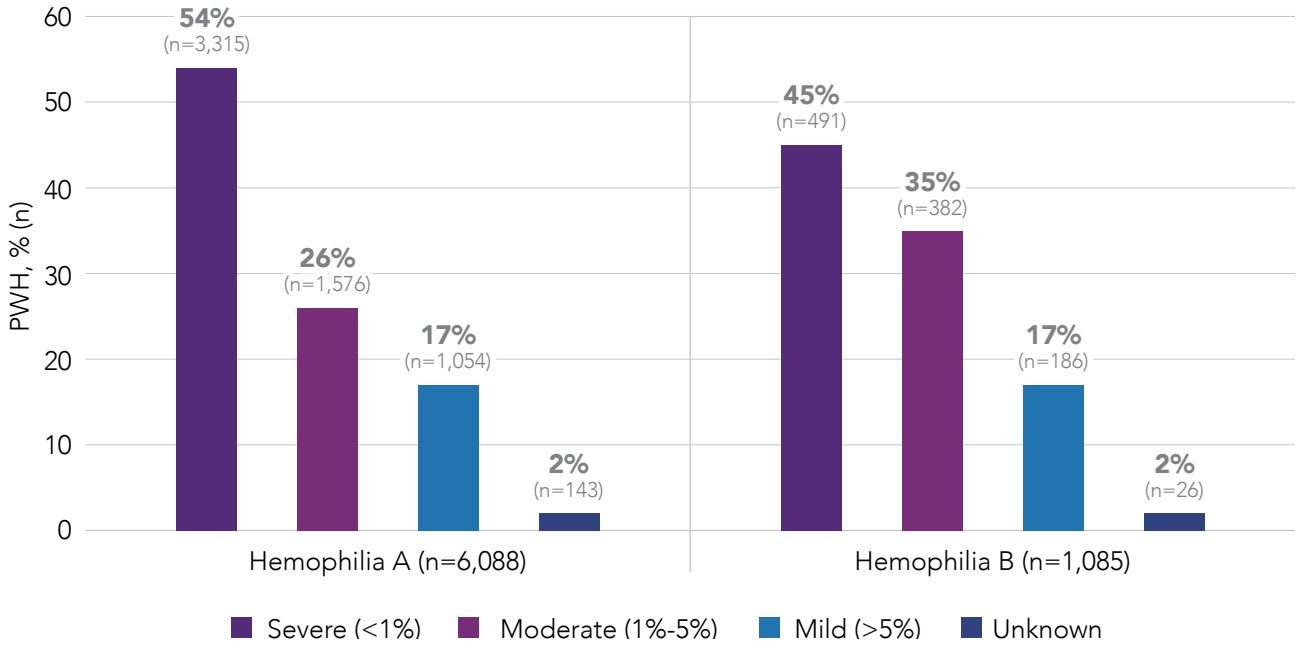
IQR=interquartile range
* 35 PWH had unknown hemophilia type and were excluded
**Age of PWH was calculated as of December 31, 2020

HEMOPHILIA TYPE AND SEVERITY

Overall, 99% (n=7,181) of participants were male, 84% (n=6,088) had hemophilia A and 15% (n=1,085) had hemophilia B (Table 2). The most frequent severity category among both hemophilia A and hemophilia B patients was severe at 54% and 45% respectively (Figure 5).

Figure 5

Hemophilia type* and severity, % (n)



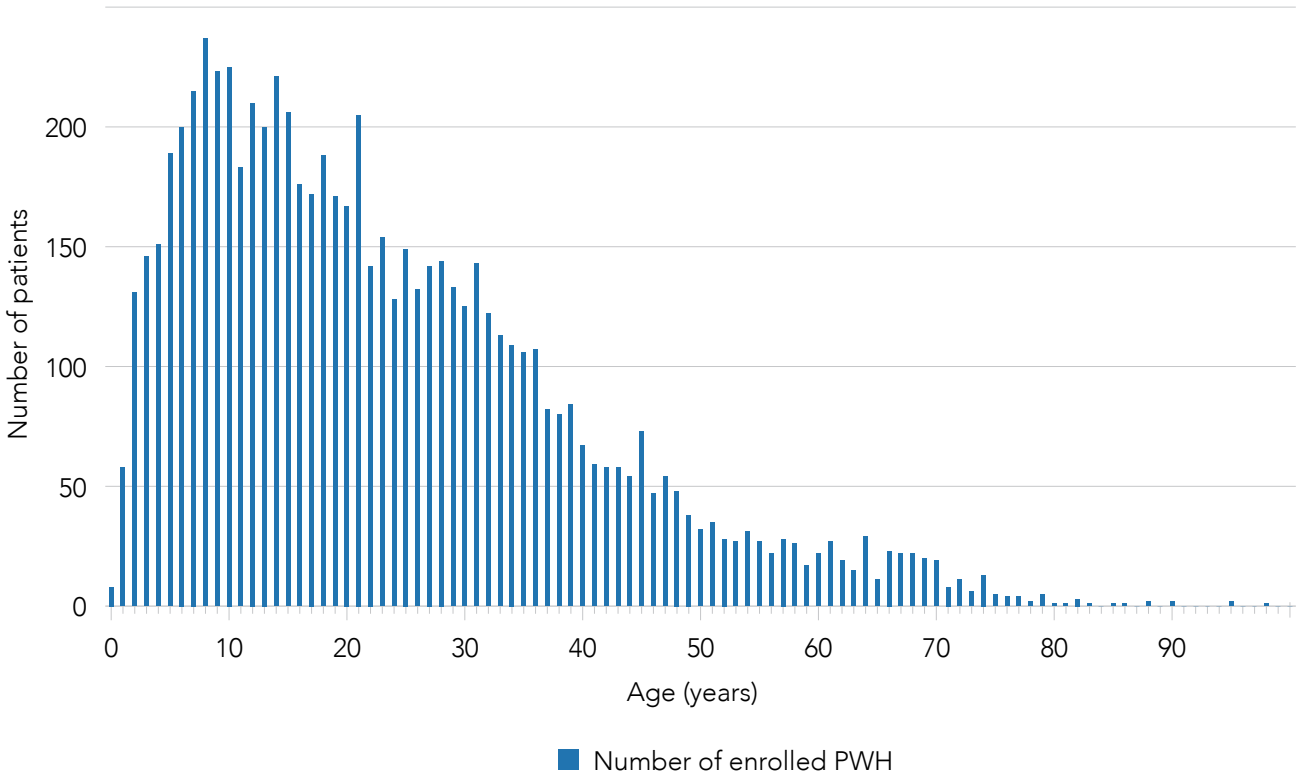
* 35 PWH had unknown hemophilia type and were excluded from this figure

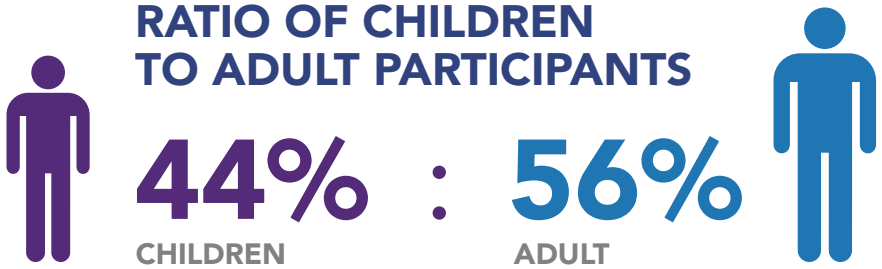
AGE OF PWH IN THE WBDR

The median age of participants was 20 years, ranging from 1 month to 98 years (Figure 6). Adults (≥18) comprised 56% (n=4,057) and children (< 18) comprised 44% (n=3,151) 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=7,208)	Severe (n=3,812)
Age at diagnosis, months, median (IQR)	36 (10-120)	19 (7-81)
Age at diagnosis by age category, n (%)		
0–11 months	2,062 (29%)	1,444 (38%)
1–4 years	2,180 (30%)	1,170 (31%)
5–17 years	1,796 (25%)	746 (20%)
18–44 years	871 (12%)	356 (9%)
45+ years	157 (2%)	35 (1%)
Age unknown	142 (2%)	61 (2%)

TABLE 3b

Newly diagnosed PWH in 2020, n (%)	136 (2%)	45 (33%)
Age at first bleed*, months, median (IQR)	12 (6-36)	9 (6-20)
Age at first joint bleed, months, median (IQR)**	24 (12-60)	24 (12-48)

* Based on 6,074 PWH with data on first bleed.
** Based on 5,230 PWH with data on first joint bleed.

AGE AT DIAGNOSIS

The median (IQR) age at diagnosis was 36 months (10 - 120) for all PWH, and 19 months (7-81) for severe PWH (Table 3a). For all PWH, median age at diagnosis by region ranged from 7 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 49 months and lowest was again the Americas at 8 months (Figure 7). Age at diagnosis decreased as GNI increased, from 46 months in low and lower middle income countries, to 23 months in high income countries for all PWH, with a similar pattern among PWH with severe disease at 30 months and 11 months (Figure 8).

There were 136 PWH newly diagnosed in 2020, with a median age of diagnosis of 77 months, ranging from 1 to 846 months (70 years).

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

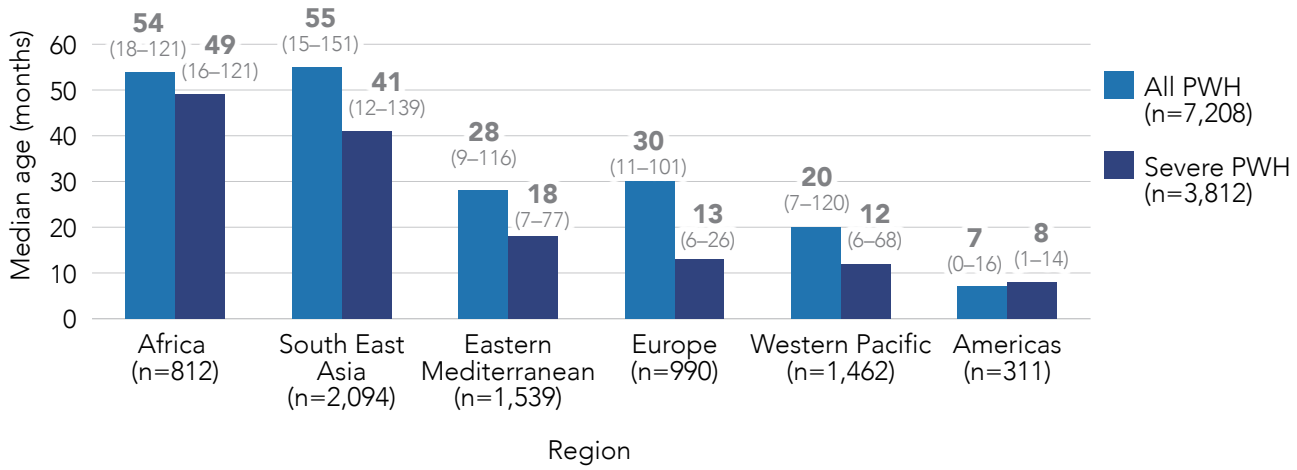
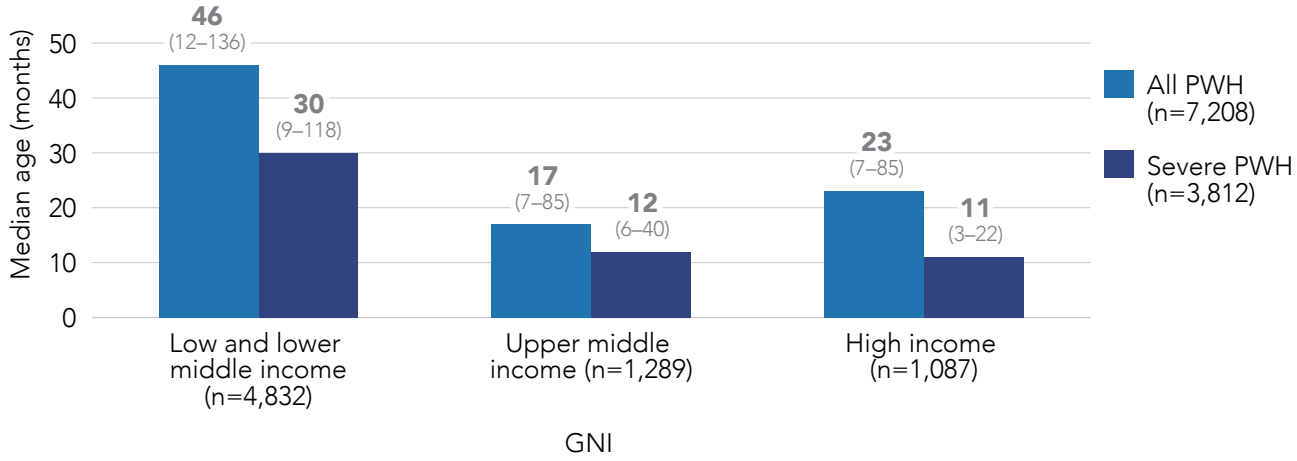


Figure 8

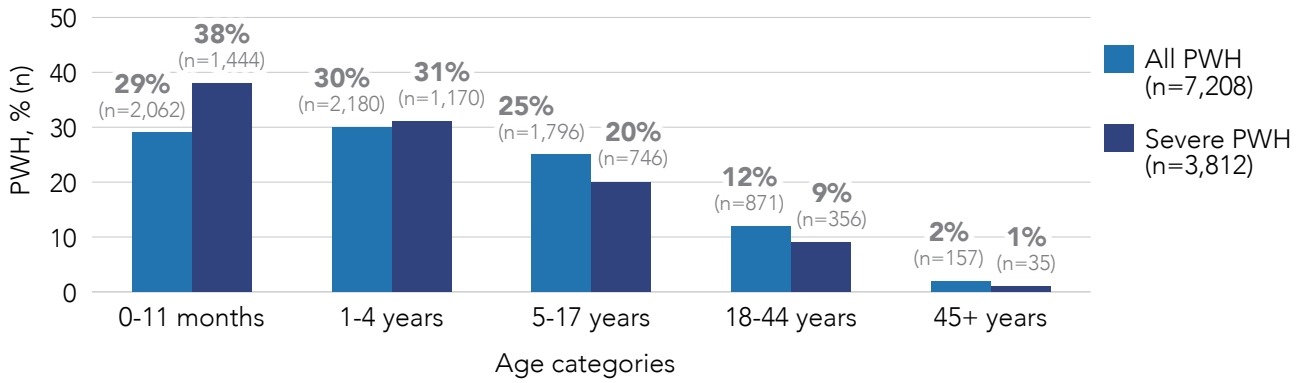
Age at diagnosis by Gross National Income



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

Figure 9

Age distribution of PWH at diagnosis, % (n)



AGE AT FIRST BLEED AND FIRST JOINT BLEED

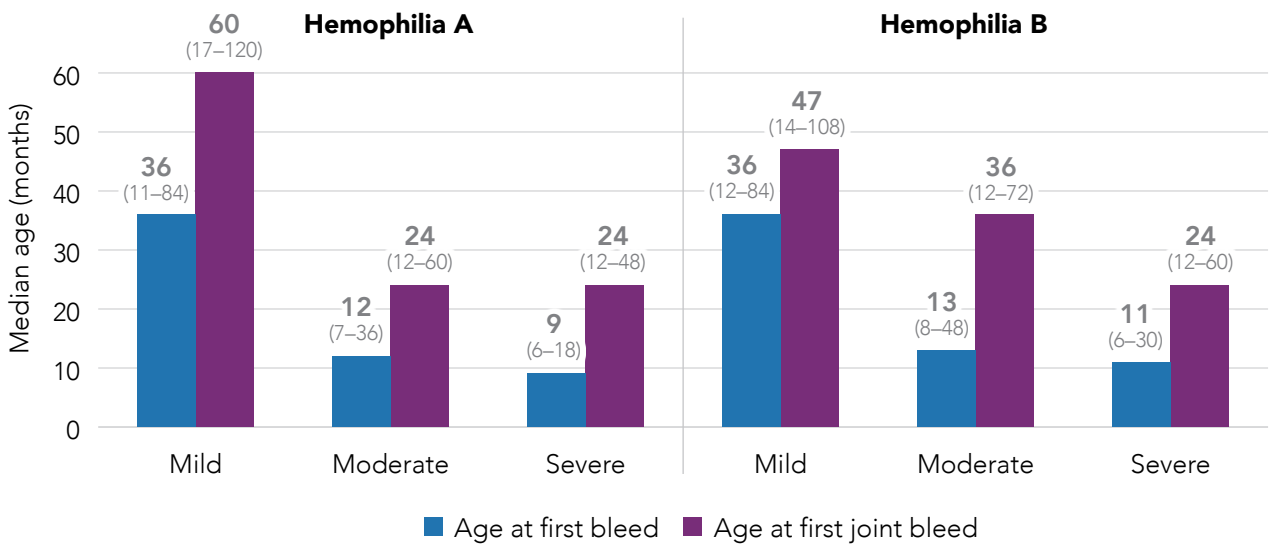
The median age at first bleed and first joint bleed were 12 and 24 months, respectively, for all PWH (Table 3b, Figure 10).

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 11 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)



* 135 patients with unknown severity not included

COMORBIDITIES

The data collected on comorbidities are not mandatory data fields. It was reported that 2,863 PWH were tested for HIV. Of those tested, 34 (1%) had positive results and of these, 32 (94%) were people with severe hemophilia (Table 4). For Hepatitis C Virus (HCV), 2,660 PWH were reported to have been tested. Of those tested, 325 (12%) had an active infection.

TABLE 4
HIV Status

	All PWH (n=7,208)	Severe (n=3,812)
Patients tested*, n (%)	2,863	1,729
Positive, n (%)	34 (1%)	32 (2%)
Negative, n (%)	2,829 (99%)	1,697 (98%)

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

TABLE 5
HCV Status

	All PWH (n=7,208)	Severe (n=3,812)
Patients tested*, n (%)	2,660	1,817
Active infection, n (%)	325 (12%)	229 (13%)
Infection resolved spontaneously, n (%)	21 (<1%)	47 (<1%)
Infection resolved with treatment, n (%)	57 (2%)	47 (3%)
No infection, n (%)	2,258 (85%)	1,527 (84%)

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

EMPLOYMENT AND EDUCATION

Of the 4,570 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 & Education

	All PWH (n=4,570)	Severe (n=2,584)
Employment status reported		
Employed full-time or part-time	1,072 (23%)	579 (22%)
Employed part-time due to hemophilia	244 (5%)	149 (6%)
Long term sick leave due to hemophilia	34 (<1%)	19 (<1%)
Not employed due to hemophilia	224 (5%)	152 (6%)
Retired due to hemophilia	32 (<1%)	16 (<1%)
Student	2,216 (49%)	1,196 (46%)
Other	748 (16%)	473 (18%)
Years of education completed*, median (IQR)	10 (5-14)	10 (5-14)

* Based on 3,804 PWH with data on education

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

CLINICAL DATA

THE CLINICAL DATA REPRESENT CLINICAL EVENTS WHICH OCCURRED IN 2020.

TABLE 7

Bleeding events summary, 2020

	All PWH* (n=6,393)	Severe (n=3,514)
Bleeds per patient, mean (SD)	5.6 (10.3)	6.7 (11.9)
Patients with 0 bleeds in 2020, n (%)	883 (14%)	503 (13%)
Target joints, n (%)**		
≥1	1,601 (25%)	1,114 (32%)
Total bleeding events, n	22,246	16,014
Location of bleed, n (%)		
Joint	17,223 (77%)	12,686 (79%)
Muscle	2,831 (13%)	1,776 (11%)
Central nervous system	52 (<1%)	29 (<1%)
Other location	2,186 (10%)	1,563 (10%)

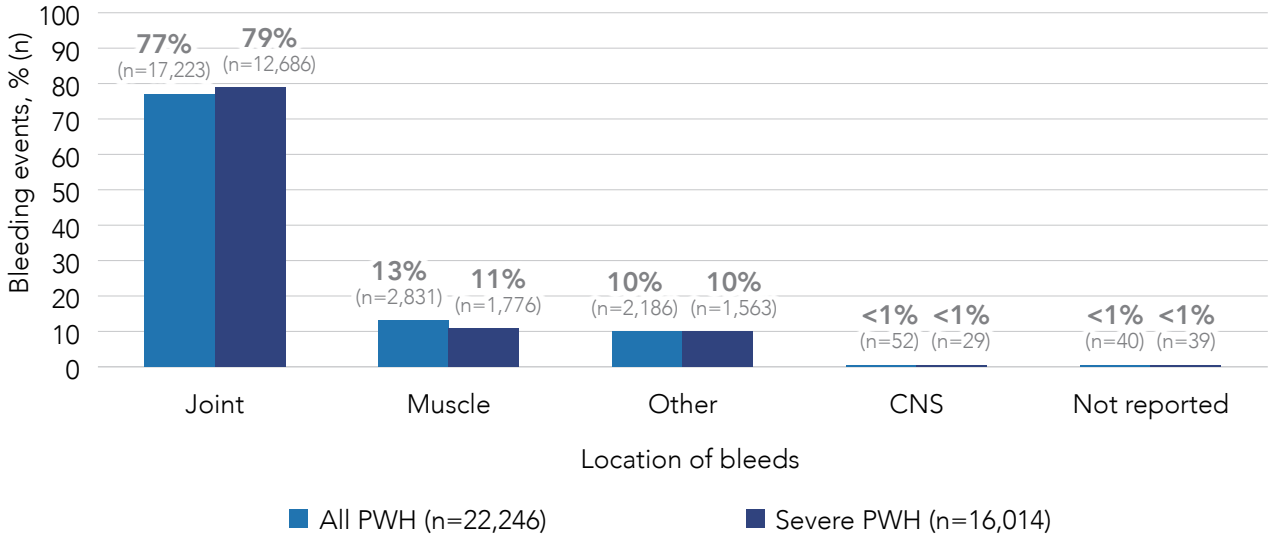
* 2020 Data for 815 PWH from the Czech Republic were not available at the time of publication
** Includes PWHs who reported at least one target joint in 2020; Target joints are defined as '3 or more spontaneous bleeds into a single joint within a consecutive 6 month period. Where there have been ≤ 2 bleeds into the joint within a consecutive 12 month period the joint is no longer considered a target joint';[3]

BLEEDING EVENTS

In 2020, a total of 22,246 bleeds were reported by PWH. Of these, 17,223 (77%) were joint bleeds, 2,831 (13%) were muscle bleeds and 52 (<1%) were central nervous system (CNS) bleeds. There were 2,186 (10%) bleeds reported as 'other' locations, and the location of 40 (<1%) of bleeds was not reported (Figure 11). A total of 16,014 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 2020, 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 2020 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 2020, respectively. Patients with 0 bleeds in 2020 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

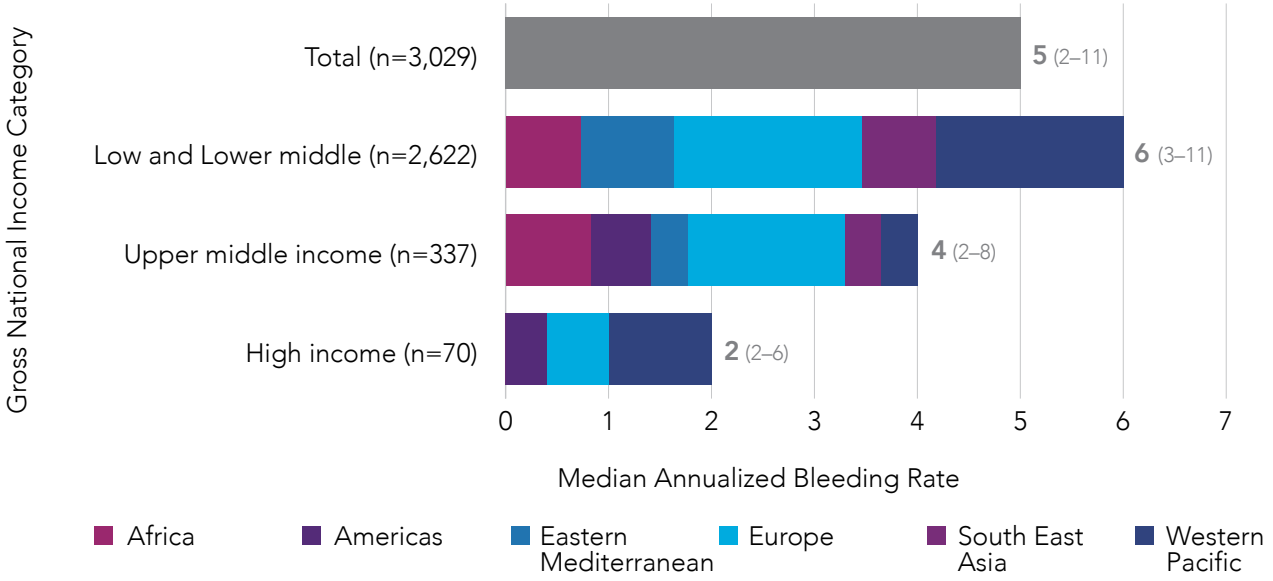
The median (IQR) ABR was 5 (2-11) for all PWH, and 6 (4-13) for severe PWH, varying by GNI and region (Figure 12). Figure 12 demonstrates that high income countries have the lowest ABR 2 (2-6) while those in low and lower middle income countries had the highest ABR 6 (3-11) (Figure 12).

AJBR

The median (IQR) AJBR was 4 (2-9) for all PWH, and 5 (2-11) for severe PWH, varying by GNI and region (Figure 13). The AJBR observed in low and lower middle countries was 4 (2-10) and 2 (2-6) for high income countries.

Figure 12

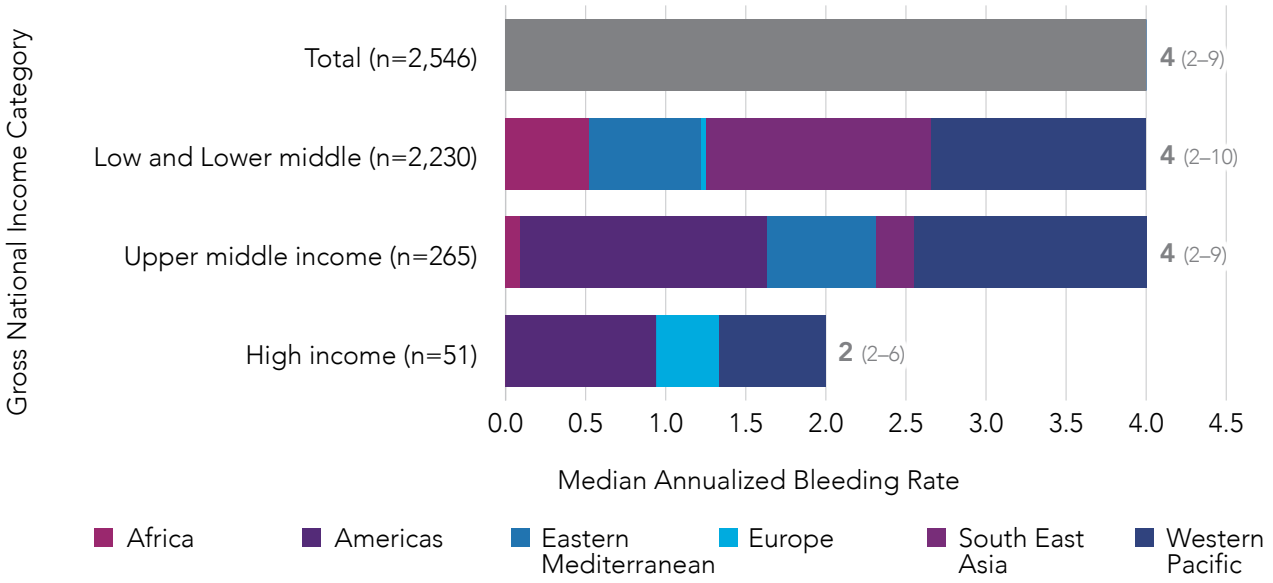
Median ABR by GNI and region



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 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

Forty-one percent of all PWH, and 47% of severe PWH, reported having at least 1 target joint in 2020. The percent of PWH reporting a target joint varied by region, ranging from 32% to 9% (Figure 14).

Figure 14

PWH with at least 1 target joint by Region

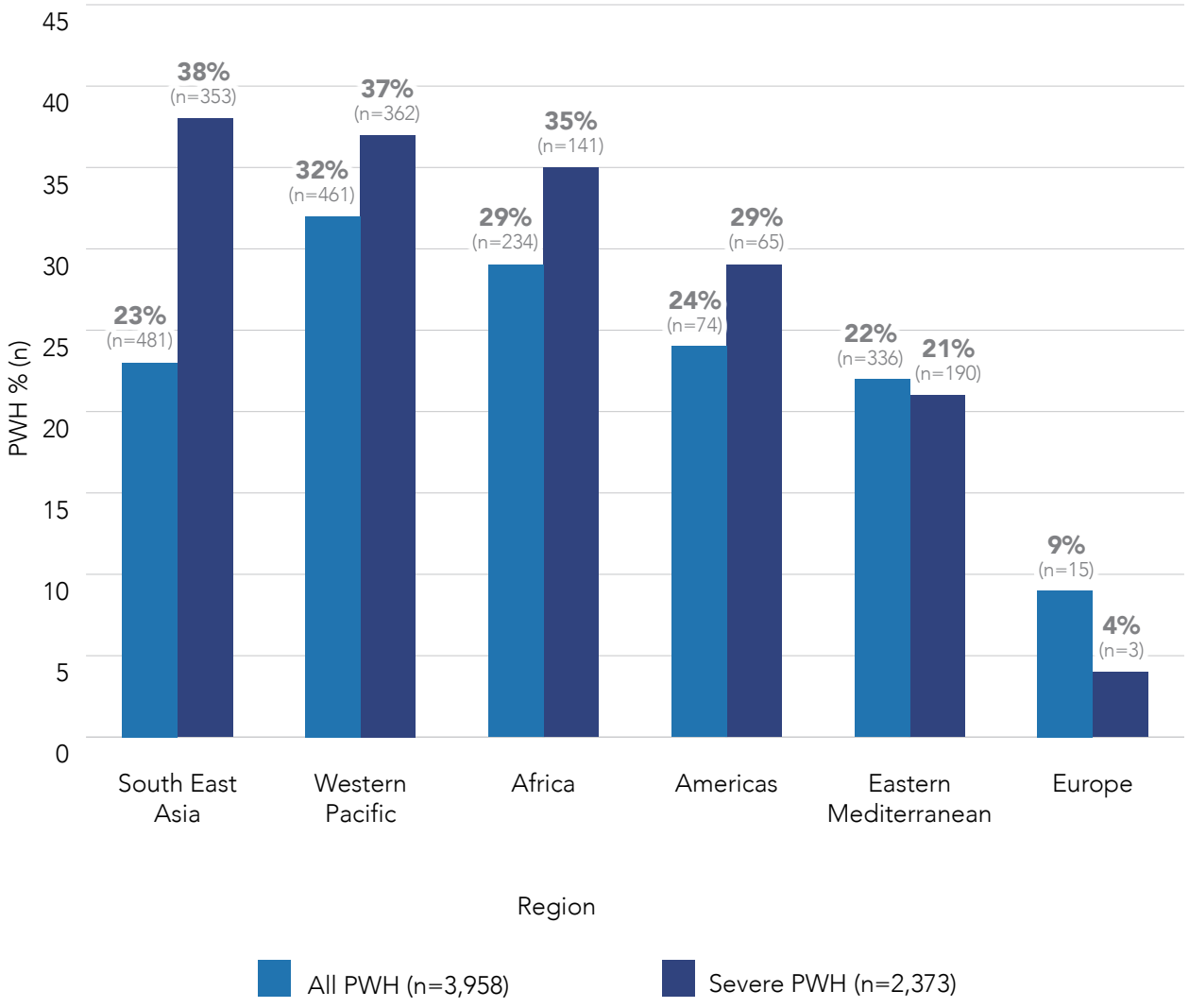


TABLE 8
Inhibitors summary, 2020

	All PWH (n=6,393)*	Severe PWH (n=3,514)*
Patients with a history of an inhibitor**, n (%)	393 (6%)	313 (9%)
Inhibitor testing in 2020		
Tested†, n (%)	438 (7%)	345 (10%)
Newly diagnosed with an inhibitor††, n (%)	54 (<1%)	42 (12%)
Patients with suspected inhibitor, but no testing available$, n(%)	30 (<1%)	2 (<1%)

* 2020 Data for 815 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 2020.
† Unique number of patients who had an inhibitor test in 2020. PWH who have never received factor treatment were removed from this analysis. Testing methods include Bethesda, Nijmegen-Bethesda, and mixing study (aPTT);
†† Unique number of patients who never had an inhibitor in the past and tested positive in 2020. PWH who never received treatment were removed from this analysis.
$ Includes all PWH with a baseline visit in 2020, PWH who never received factor treatment were removed from this analysis.

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 2020. In 2020, 438 PWH were tested for inhibitors, 54 (12%) were newly diagnosed with an inhibitor (no history of inhibitors and no prior positive test reported) (Figure 15).

Figure 15
PWH with inhibitor test (n=438)

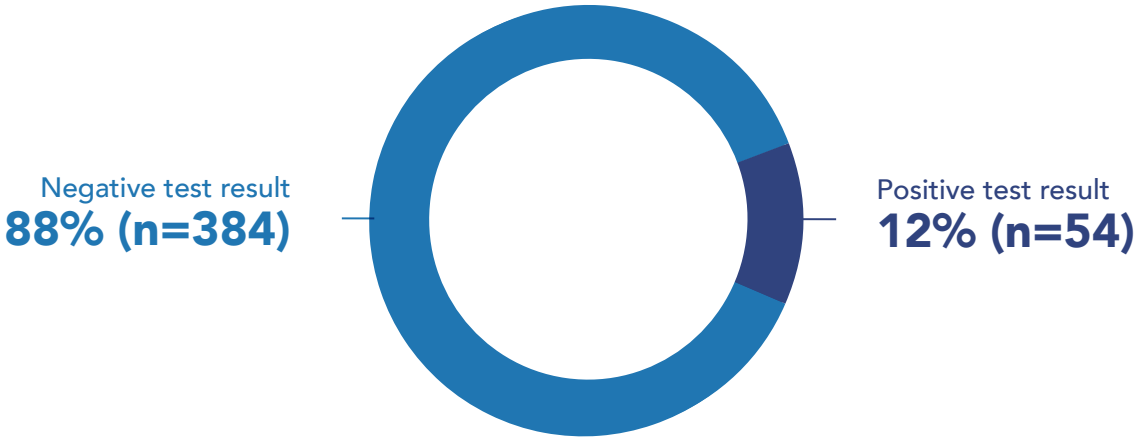


TABLE 9a

Hemophilia related hospitalizations summary, 2020

	All PWH (n=6,393)*	Severe PWH (n=3,514)*
Patients hospitalized**, n (%)	914 (14%)	595 (17%)
Total hospitalizations†, n	3,552	2,655
Days per hospitalization, median (IQR)	11 (5-25)	14 (6-30)
Number of hospitalizations per patient, median (IQR)	2 (1-5)	3 (1-6)

TABLE 9b

	All PWH (n=6,393)*	Severe PWH (n=3,514)*
Reason for hospitalizations, n (%)		
Joint bleeding	2,544 (40%)	1,943 (55%)
Surgery	27 (<1%)	12 (<1%)
Soft tissue bleeding	84 (1%)	55 (2%)
Other bleeding	466 (7%)	324 (9%)
Other muscle bleeding	473 (7%)	362 (10%)
Intracranial bleeding	32 (<1%)	22 (<1%)
Psoas muscle bleeding	35 (<1%)	21 (<1%)
Thromboembolic event	0 (0%)	0 (0%)
Other	59 (<1%)	43 (1%)

* 2020 Data for 815 PWH from Czech Republic were not available at the time of publication
** Number of unique PWH hospitalized.
† Hospitalization is defined as having at least 1 overnight stay in the hospital.

In 2020, 914 PWH experienced a total of 3,552 hemophilia related hospitalizations, with a median (IQR) stay of 11 days (5-25). The most common reason for hospitalization was joint bleed for both hemophilia A and B patients (70% and 60% respectively) (Figures 16 and 17). In total, 32 hospitalizations were for an intracranial bleed; 29 (1%) which were among hemophilia A patients and 3 (<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=3,101)

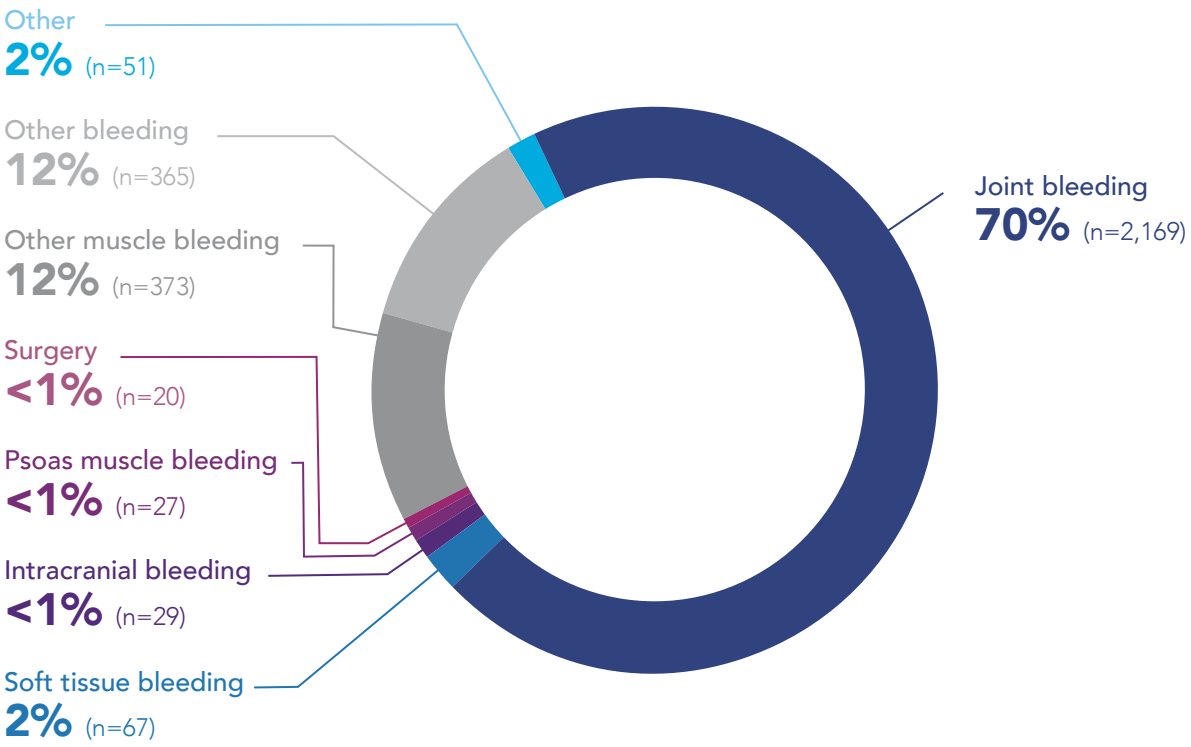
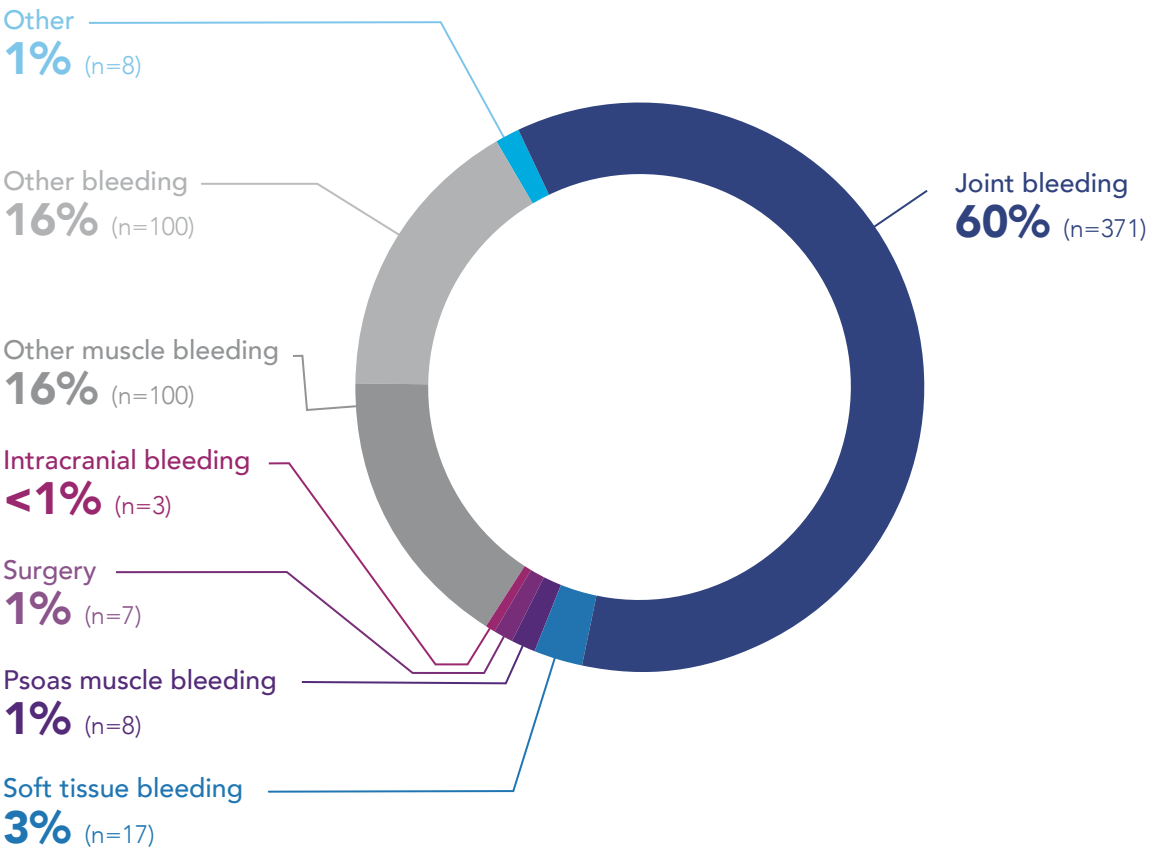


Figure 17

REASON FOR HOSPITALIZATION IN HEMOPHILIA B PATIENTS (N=614)



TREATMENT

TABLE 10

Treatment summary, 2020*

	All PWH (n=6,393)*	Severe (n=3,514)*
Received at least 1 prophylaxis treatment in 2020, n (%)**	1,295 (20%)	1,061 (30%)
Hemophilia A	1,106 (85%)	928 (87%)
Hemophilia B	186 (14%)	133 (13%)
Patients with no access to treatment at the time of a bleed, n (%)†	69 (<1%)	31 (<1%)
Hemophilia A	59 (86%)	26 (79%)
Hemophilia B	6 (9%)	4 (13%)

* patients from Czech Republic were excluded from the table above
** 3 patients had unknown hemophilia type
† 4 patients had unknown hemophilia type

TABLE 11

Prophylaxis category*

	All PWH (n=6,393)	Severe (n=3,514)
Hemophilia A, n	1,106 (17%)	928 (26%)
Treatment category, n (%)		
FVIII, standard half-life	851 (77%)	735 (79%)
FVIII, extended half-life	210 (19%)	145 (16%)
Bypassing agent	10 (<1%)	9 (<1%)
Non-factor product	62 (6%)	55 (6%)
Other	38 (3%)	29 (3%)
Hemophilia B, n	186 (3%)	133 (4%)
Treatment category, n (%)		
FIX, standard half-life	96 (52%)	76 (57%)
FIX, extended half-life	80 (43%)	51 (38%)
Bypassing agent	1 (<1%)	1 (<1%)
Non-factor product**	1 (<1%)	1 (<1%)
Other	10 (5%)	5 (4%)

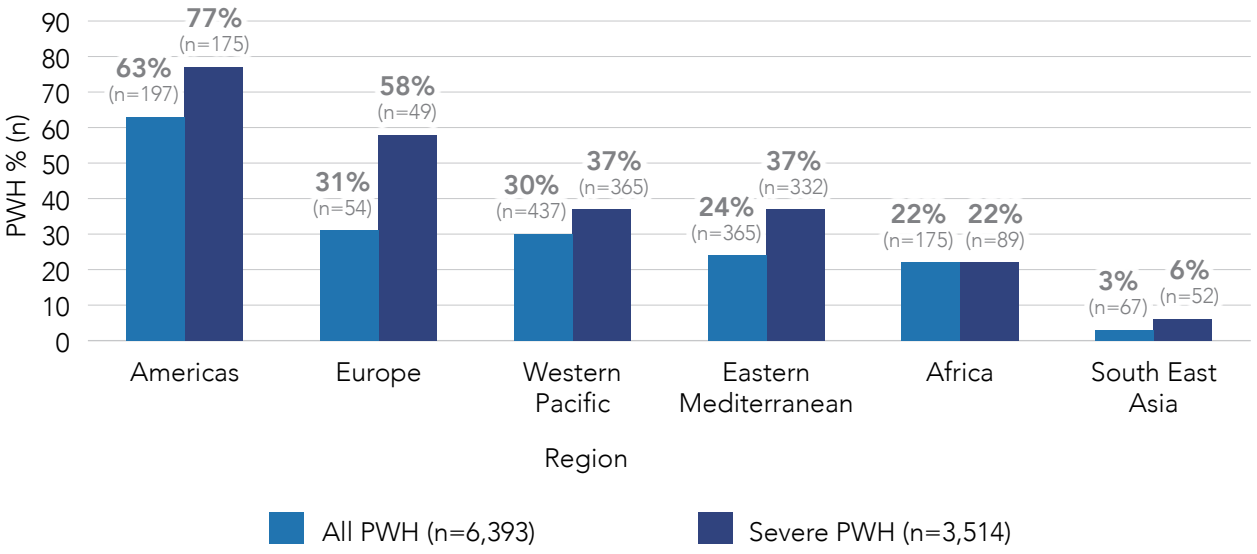
* Number of unique PWH who received prophylaxis treatment in 2020. This includes patients who started prophylaxis treatment or had an on-going treatment in 2020. Patients may be receiving treatments that fall under multiple categories.
** One hemophilia B patient using non-factor product via clinical trial

TREATMENT BY INDICATION

A total of 1,295 (20%) PWH received prophylaxis as treatment in 2020. Thirty percent of severe PWH received prophylaxis in 2020; 87% were PWH A and 13% were PWH B (Table 10, Figure 18). It is important to note that 18% of PWH in Africa had unknown severity and were not accounted for.

Figure 18

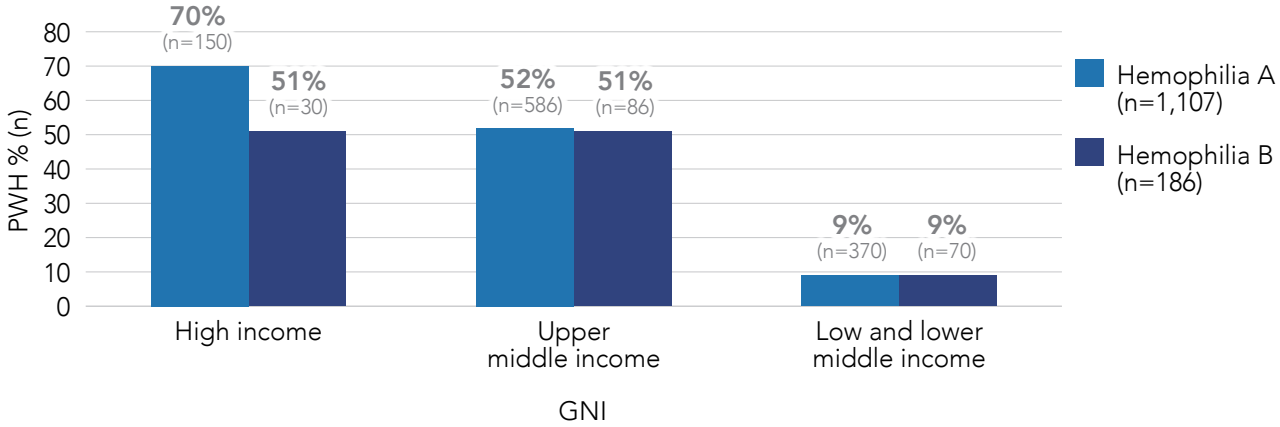
Percentage of PWH receiving prophylaxis in 2020 by region



* Data of PWH from Czech Republic excluded from total numbers

Figure 19

Percentage of PWH receiving prophylaxis in 2020 by GNI



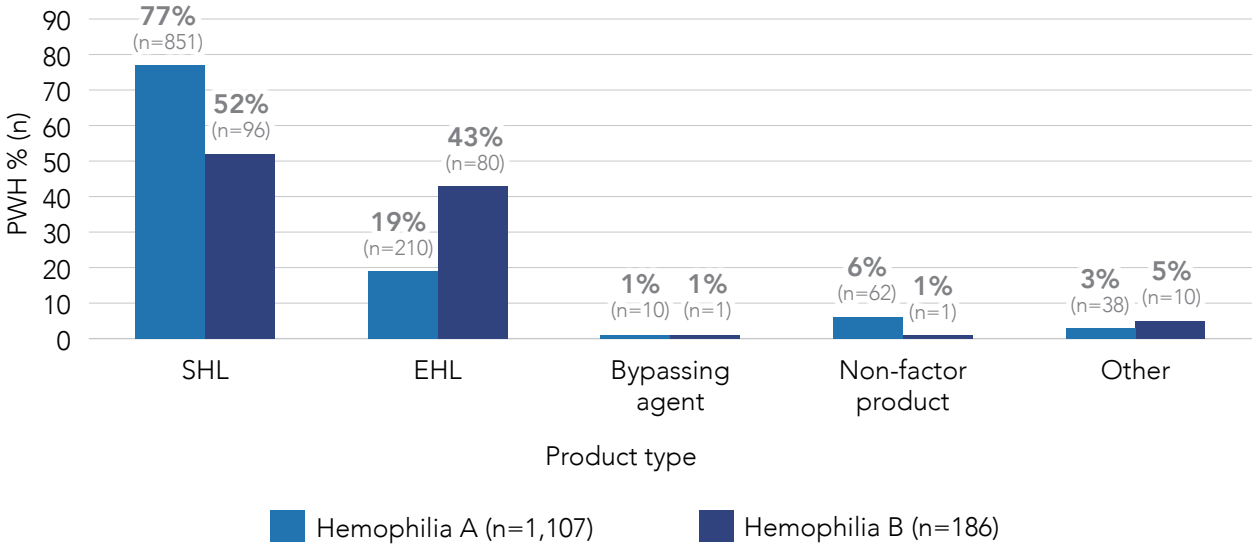
Note: Low and lower middle income categories were combined due to small number of patients in the low income category

TREATMENT BY PRODUCT CATEGORY

For PWH treated with prophylaxis, standard half-life (SHL) clotting factor concentrates were the most common type of treatment used in 2020 (77% of PWH A on prophylaxis, and 52% of PWH B on prophylaxis), followed by extended half-life (EHL) clotting factor concentrates, (19% of people with hemophilia A and 43% of people with hemophilia B) (Table 10, Figure 20).

Figure 20

Distribution of product type among PWH on prophylaxis treatment



Note: One hemophilia B patient using non-factor product via clinical trial

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).

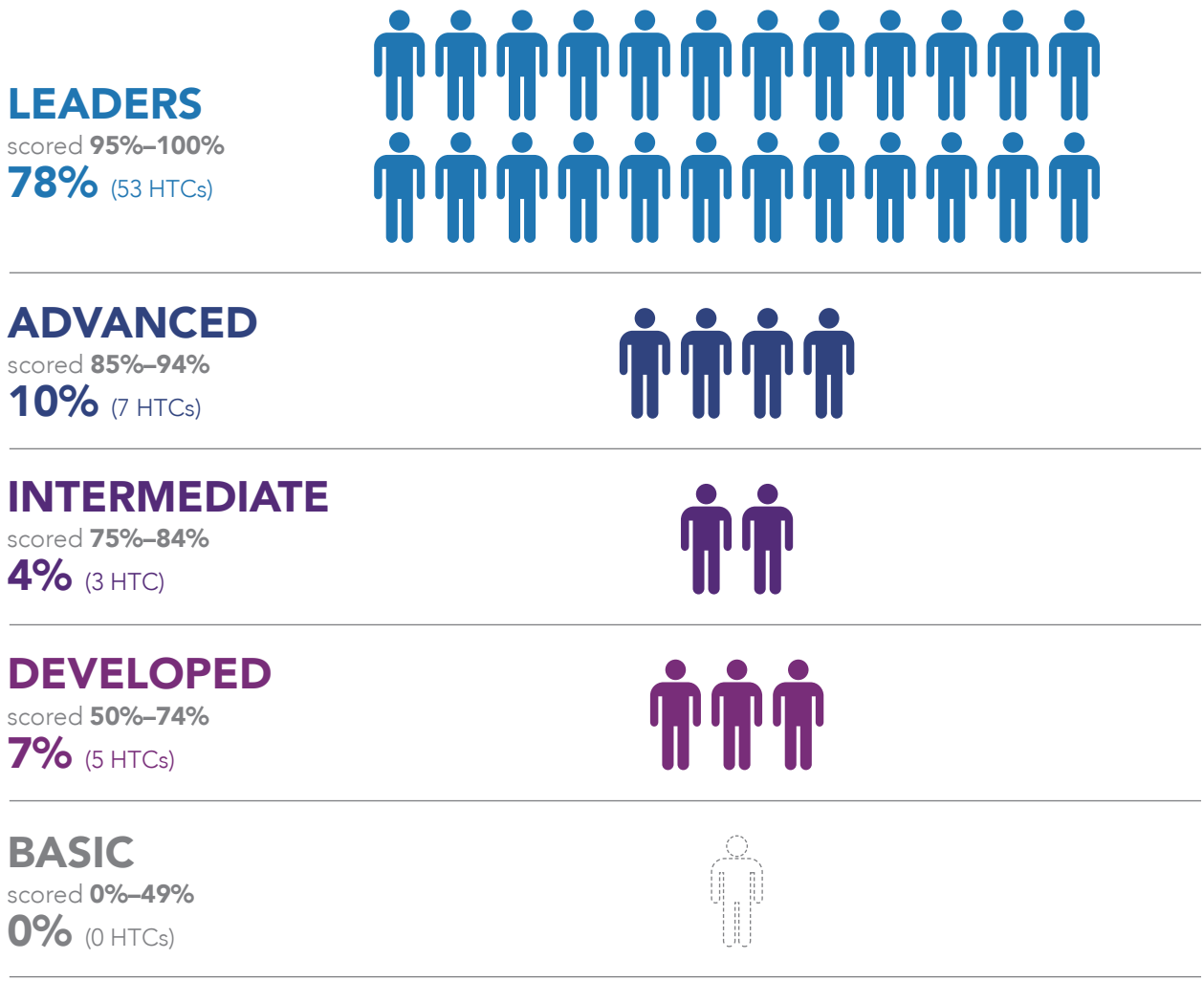
53 (78%) OF HTCs

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. All 'Leaders' from the 2019 Data Report have maintained their level of success, illustrating ownership in quality data. In 2020, the WBDR team worked directly with 68 HTCs. Fifty-three (78%) HTCs were classified as 'Leaders' (data quality score >95%), which is the highest level of data quality. All 53 'Leaders' will be presented with a *Certificate of Data Excellence* from the WBDR.

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.

> *On behalf of our centre / National Centre of Hematology/Mustansiriyah University, I would like to thank you all, for your continuous support and feedback, and because of that we achieved the highest degree under the WBDR Data Quality Accreditation Program for the second year. It is our pleasure to continue working with WFH to achieve better care for PWH in Iraq, and your advice is most welcome.*
>
> Iraq - Baghdad - National Center of Hematology - Al-Mustansirya University

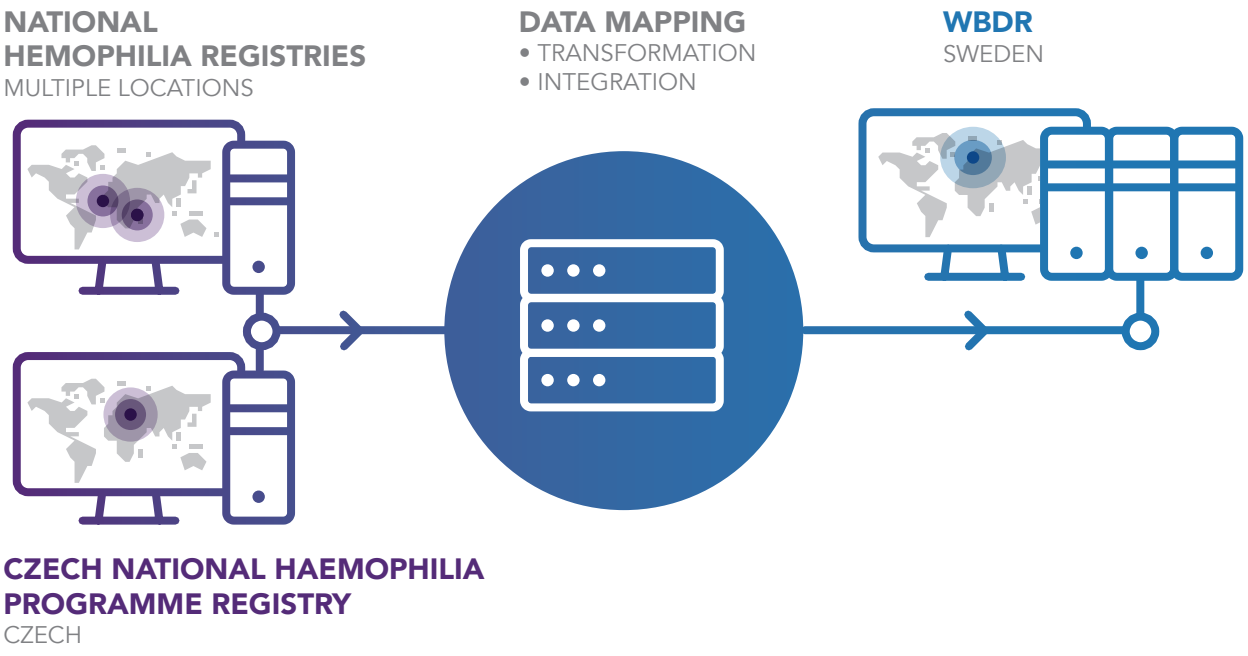
> *Many thanks to the World Federation of Hemophilia Team for such an important honor, it is for our Hospital and Center for the Treatment of Congenital Coagulopathies, a pride to receive this outstanding mention. We continue working day by day for our population of people with bleeding disorders*
>
> Argentina - Bahia Blanca - HTC Centro Asist Reg de Hemoterapia

INTERNATIONAL DATA INTEGRATION PROGRAM

Registries, with international collaboration between countries, are the best way 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 data collection 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, a de-identified minimal set of data from the 2018 Czech National Haemophilia Programme Registry (CNHPR) were imported into the WBDR. The CNHPR collects data from eight pediatric and eight adult hemophilia centres. Following the success of the first import, 2019 data were imported to update the minimal dataset and add an extended dataset. Total of 815 patients, including 45 new patients, and data on genetic testing, the Hemophilia Joint Health Score (HJHS), comorbidities, and hospitalizations on all patients were added as part of the latest import.

A protocol to import data from existing patient registries into the WBDR has been developed and tested. The 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 ten HTCs in 2020 who were awarded funding for their research project.

	2020	2019	2018	OVERALL
AMOUNT AWARDED (in USD)	$29,915	$35,682	$33,229	$100,000
RESEARCH PROJECTS FUNDED	7	8	8	23
COUNTRIES	5	7	8	14
HTC PARTICIPATED	10	8	8	24
RESEARCHERS INVOLVED	20	16	16	50 +
PUBLICATIONS	n/a	n/a	4 Abstracts and 2 featured articles (EAHAD, HWO, ISTH)	4 Abstracts and 2 featured articles (EAHAD, HWO, ISTH)

Note: Countries or HTCs can apply for the RSP each year. The overall numbers are unique counts.

WBDR HTC FUNDING PROGRAM

The WBDR HTC Funding Program (HFP) is a new WFH initiative 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.

For more information, please visit our webpage.

USD $16,000
AMOUNT AWARDED IN 2020

20
RECIPIENT HTCS

10
COUNTRIES

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-HTC
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 • Praha - ÚHKT • 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 • Zagazig - pediatrics department, Zagazig University
Ethiopia	• Addis Ababa - Tikur Anbessa Hospital
Ghana	• Kumasi - Komfo Anokye Teaching Hospital
India	• Aluva - Haemophilia Treatment Centre, District Hospital • Ludhiana - Christian Medical College • Manipal - Melaka Manipal Medical College, Hemophilia Society Manipal
Iraq	• Baghdad - Hemophilia Center - Medical City • Baghdad - National Center of Hematology - Al-Mustansirya University • Basra - Basra Center for heriditery Blood Diseases
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 Sultanah Aminah • Klang - Hospital Tengku Ampuan Rahimah • Kota Kinabalu - Hospital Queen Elizabeth • 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
Nigeria	• Abuja - National Hospital, Abuja • 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 - National Institute of Blood Disease & BMT • Lahore - Haemophilia Treatment Centre • Rawalpindi - Haemophilia Treatment Centre
Panama	• Panamá City - Hospital del Niño
Philippines	• Manila - University of Santo Tomas 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	• Chiang Mai - Chiang Mai University 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.

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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]

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NOTES

NOTES

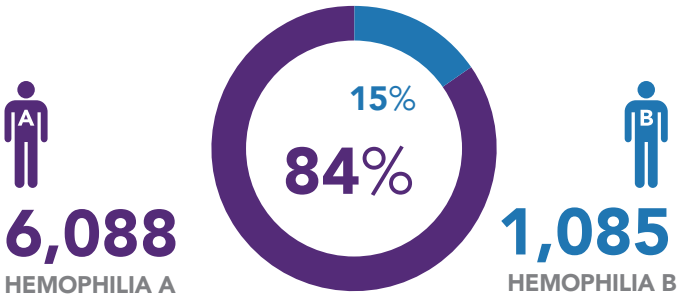
NOTES

WBDR 2020 HIGHLIGHTS

86
HTCs ENROLLED

33
COUNTRIES REPRESENTED

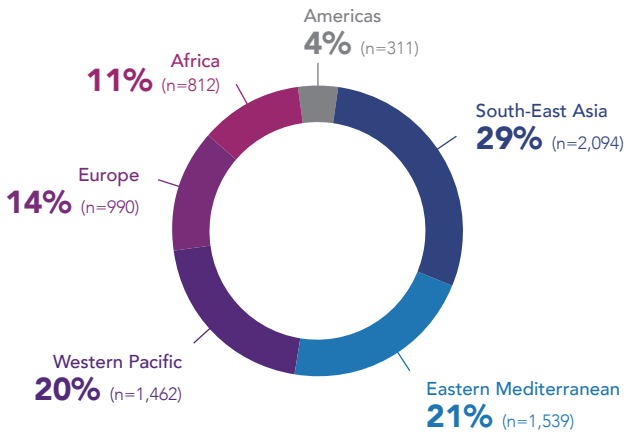
7,208
ENROLLED PATIENTS



6,088
HEMOPHILIA A

1,085
HEMOPHILIA B

Distribution of PWH by Region



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