



Dutch Hemophilia Registry

Annual Report 2020



HemoNED Foundation
April 2021

<https://hemoned.nl/en>

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Introduction

This annual report describes data from the Dutch Hemophilia Registry and the VastePrik digital infusion log for home treatment available on 31 December 2020.

HemoNED foundation

The HemoNED Registry & VastePrik are managed by the HemoNED foundation. The aim of the HemoNED foundation is described as follows:

“The Foundation aims to set up a nationwide registry of people with hemophilia and related disorders including data about their disease, treatment and complications, to perform scientific research, to publish reports and to provide education to contribute to an improvement of the quality of care.”

The board of the Foundation has set up a Steering Committee that is responsible for assessing and approving the annual reports and data applications. In a Governance document the Steering Committee has described which parties are involved in the HemoNED project, their responsibilities and rights and how the management and access of the registry data is regulated.

Dutch Hemophilia Registry

The Dutch Hemophilia Registry (HemoNED Registry) was established in 2017 as a joint initiative from the Dutch Hemophilia Treaters Society (NVHB), the Dutch Hemophilia Patient Society (NVHP) and the Dutch Hemophilia Nurses Society (NVHV). For rare diseases like hemophilia, for which there is an effective but expensive treatment, a national hemophilia registry is an important tool for monitoring treatment and improving quality of care. The anonymized registry data are used for overview reports, scientific research and efficacy and safety studies of drugs. Health care providers manually complete the registry with relevant medical information. The registry database has built-in validation checks to ensure quality of data.

VastePrik

The digital infusion log VastePrik was launched in April 2018 both as an app for smartphones and an online personal web page. Participants can register their home treatment and bleeds that occur. VastePrik is mainly used by participants on prophylaxis. Both the participant and his/her treater have access to the logged infusions and bleeds through a secured online web page. This way, during a consultation they can evaluate and adjust home treatment if necessary. In October 2020 a new version of VastePrik was introduced. This new version makes it possible to manage personal medication stock, add medication by scanning a QR code and record mild side effects of new medication. Because of security regulations it is necessary to log in with two-factor authentication. Since this change did not go smoothly for some of the VastePrik users, there was a small decrease in VastePrik users at the end of 2020.

Inclusion

All national certified Hemophilia Treatment Centers (HTCs) routinely invite possible participants for the Dutch Hemophilia Registry:

- Amsterdam UMC location AMC
- Erasmus MC Rotterdam
- LUMC Leiden & HagaZiekenhuis The Hague
- Radboudumc Nijmegen & MUMC Maastricht & MMC Veldhoven/Eindhoven
- UMC Groningen
- UMC Utrecht (Van Creveld Clinic)

People with one of the following diagnoses will be eligible to participate in the HemoNED registry:

- Hemophilia A or B
- Carriers with hemophilia A or B, coagulation factor levels $\leq 50\%$
- Von Willebrand disease, VWFact and/or VWFrct and /or FVIII levels $\leq 30\%$, and/or dependent on clotting factor concentrates

- Rare factor deficiencies and platelet disorders, prophylactic treatment and/or dependent on clotting factor concentrates at surgery/trauma
- Acquired hemophilia

Adverse events

For many years now, the NVHB is listing adverse events for people with bleeding disorders. Since January 2020 all HTC's enter the adverse events in the HemoNED registry. This report includes for the first time an overview of the reported adverse events. The adverse events data concern all the people treated in a HTC. Quarterly, HemoNED provides an overview of reported events to the NVHB, the HTC's, the European Haemophilia Safety Surveillance (EUHASS) and the Netherlands Pharmacovigilance centre Lareb (only inhibitors).

Data analysis

The HemoNED project office analyzed the data on behalf of the Steering Committee. The statistical software SPSS was used to perform describing statistical analyses (crosstabs, bar charts etc.) to analyze and describe the data. The HemoNED foundation ensures that all information provided for research and publication is fully anonymized. To further prevent indirect traceability this annual report presents, wherever possible, cells with values lower than 10 as '<10' or values have been aggregated with other (sub)categories.

Publications

HemoNED presented a poster at the annual congress of the European Association for Haemophilia and Allied Disorders (The Hague, 5-7 February 2020) entitled "Validation of patient reported bleeds". On 18 June, an oral presentation entitled "The Dutch Hemophilia Registry HemoNED – Building an Ecosystem" was held at the worldwide World Federation of Hemophilia (WFH) congress (virtual) (<https://hemoned.nl/publicaties/publicaties-detail/>). Furthermore, in 2020 HemoNED provided numbers for the Annual Global Survey 2019 of the WFH in collaboration with the Dutch Hemophilia Patient Society.

Organisation

Board members HemoNED Foundation in 2020:

- **Chair: Dr. F.J.M. (Felix) van der Meer**, Internist LUMC
- **Secretary: Dr. M.H.E. (Mariëtte) Driessens**, Delegate Netherlands Hemophilia Patient Society (NVHP)
- **Treasurer: Dr. K. (Kathelijn) Fischer**, Pediatric hematologist Van Creveld Clinic UMC Utrecht

The following representatives were part of the HemoNED Steering Committee in 2020:

- **Dr. F.J.M. (Felix) van der Meer**, chair Steering Committee Expertise center for hemophilia and related disorders LUMC - HagaZiekenhuis
- **Dr. K. (Kathelijn) Fischer**, Van Creveld Clinic UMC Utrecht
- **Prof. Dr. C.J. (Karin) Fijnvandraat**, Amsterdam UMC location AMC Hemophilia Treatment Center
- **Dr. M.J.H.A. (Marieke) Kruip**, Erasmus MC Rotterdam Hemophilia Treatment Center
- **Dr. B.A.P. (Britta) Laros-van Gorkom**, Hemophilia Treatment Center Radboudumc Nijmegen, MUMC+ Maastricht & MMC Eindhoven/Veldhoven
- **Dr. M.A. (Marjet) Stein-Wit**, UMC Groningen Hemophilia Treatment Center
- **Mr. S.L.A. (Stephan) Meijer**, NVHP
- **Mrs. N. (Nanda) Uitslager**, Dutch Hemophilia Nurses Society (NVHV)

HemoNED Project Office in 2020:

- Dr. G. (Geertje) Goedhart**, Project coordinator HemoNED, LUMC
- Mrs. E.M. (Liesbeth) Taal**, Data manager HemoNED, LUMC

Results Dutch Hemophilia Registry

General

Figure 1a Number of unique participants in the HemoNED registry by gender



Total participants

Total completed **2223** (100%)



Gender

Man **1741** (78%)

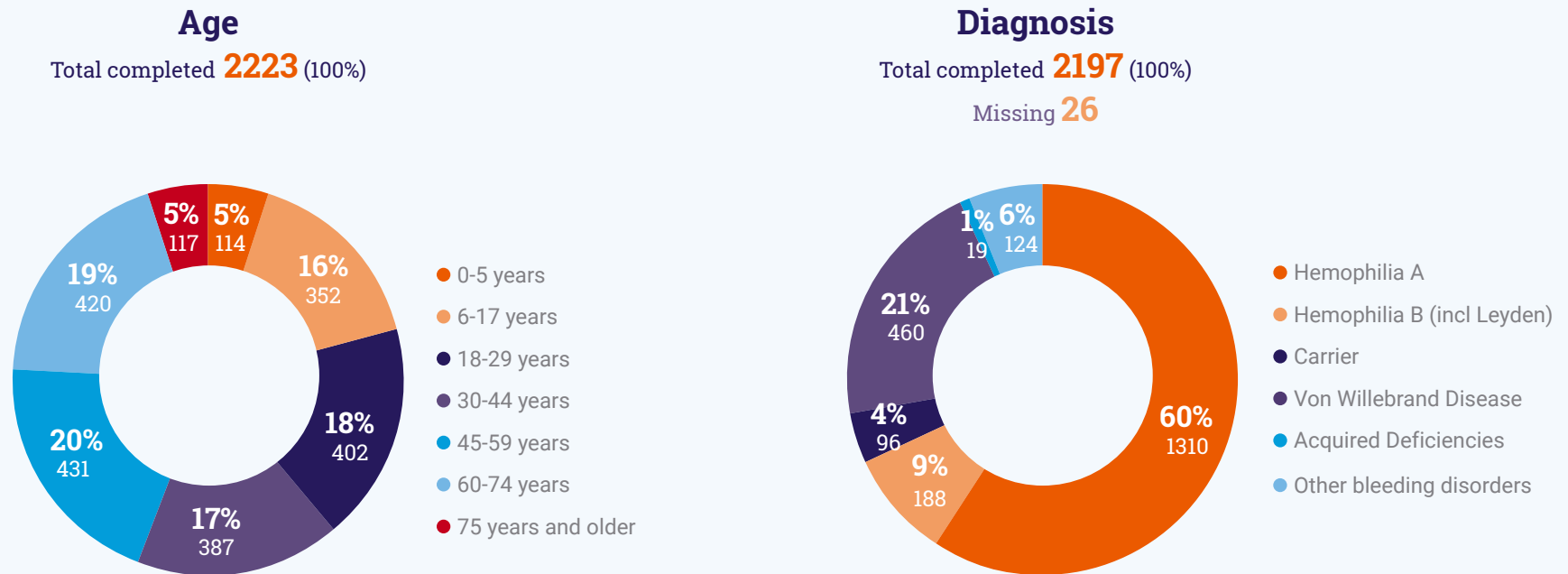
Woman **479** (22%)

Missing **3**

Results Dutch Hemophilia Registry

General

Figure 1b Number of unique participants in the HemoNED registry by age and diagnosis



Mortality

2018-2019: 10 participants died. The data of these participants are excluded.
2020: 9 participants died. The data of these participants are included in this report.

Refusals

2018-2020: 116 people who were asked to participate in the HemoNED registry by a health care provider refused to give written informed consent. These are 72 people with hemophilia (32 severe hemophilia) and 44 people with other bleeding disorders.

General

Figure 2a Timeline: number of participants included in the HemoNED registry

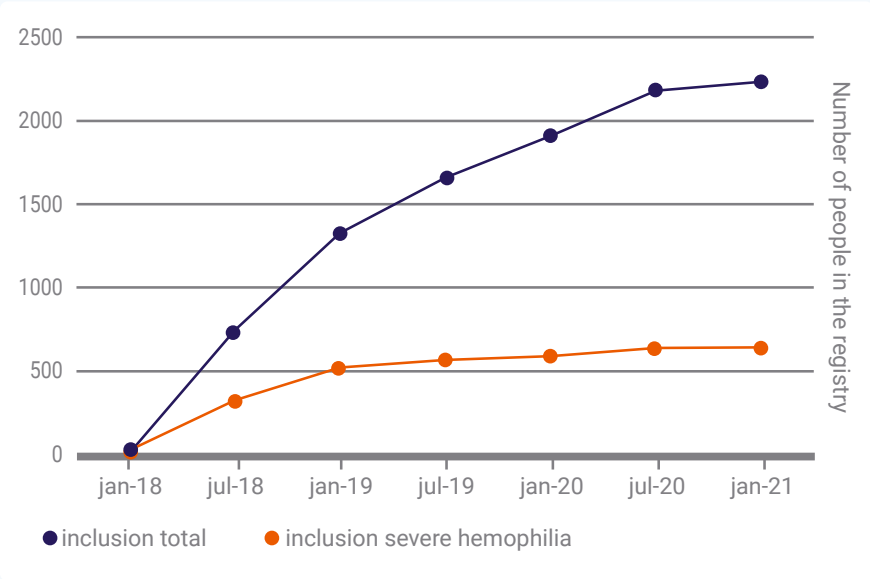
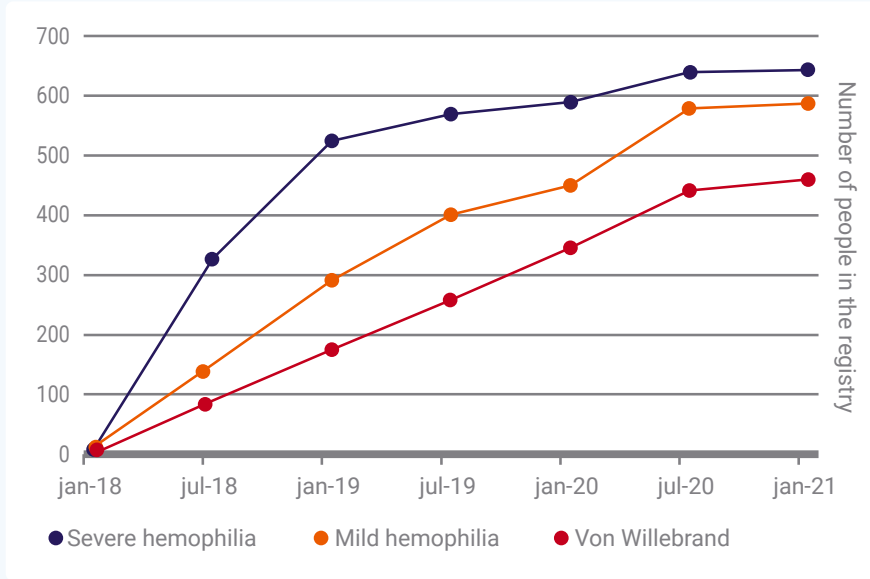


Figure 2b Timeline: number of participants with severe hemophilia, mild hemophilia and von Willebrand disease included in HemoNED



Hemophilia

Diagnosis and demographic data

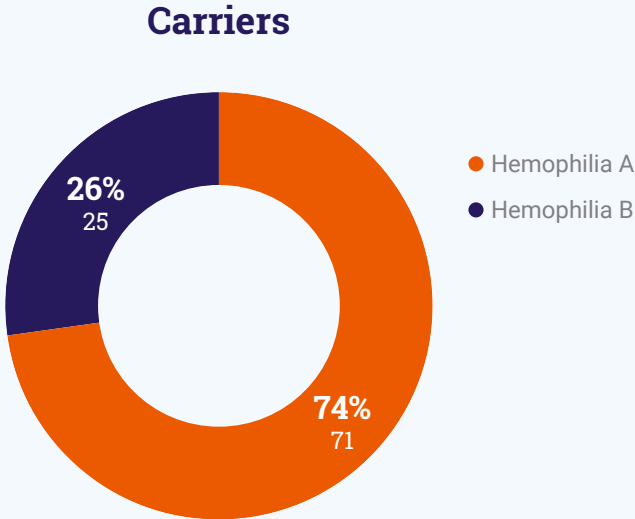
Table 1 Number of participants in the HemoNED registry with diagnosis Hemophilia

Diagnosis	Number	%
Hemophilia A	1310	100
Severe	565	43
Moderate	204	16
Mild	527	41
Severity unknown	14	

Diagnosis	Number	%
Hemophilia B	167	100
Severe	81	49
Moderate	31	19
Mild	53	32
Severity unknown	2	

Diagnosis	Number	%
Hemophilia B Leyden	21	

Figure 3 Carriers of Hemophilia A and B



Hemophilia

Figure 4a Participants with Hemophilia A by severity

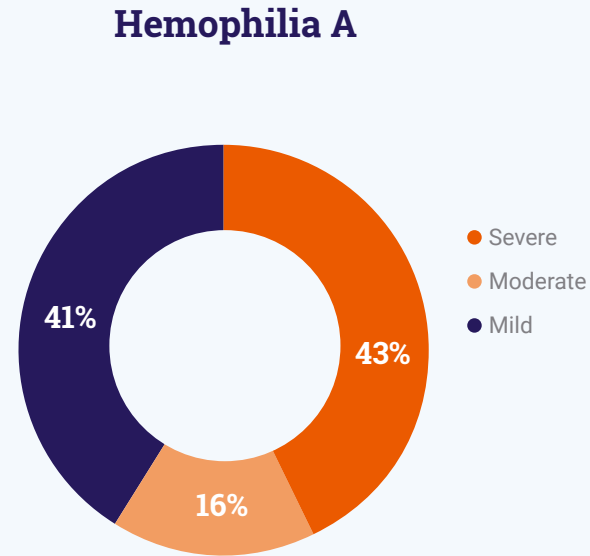
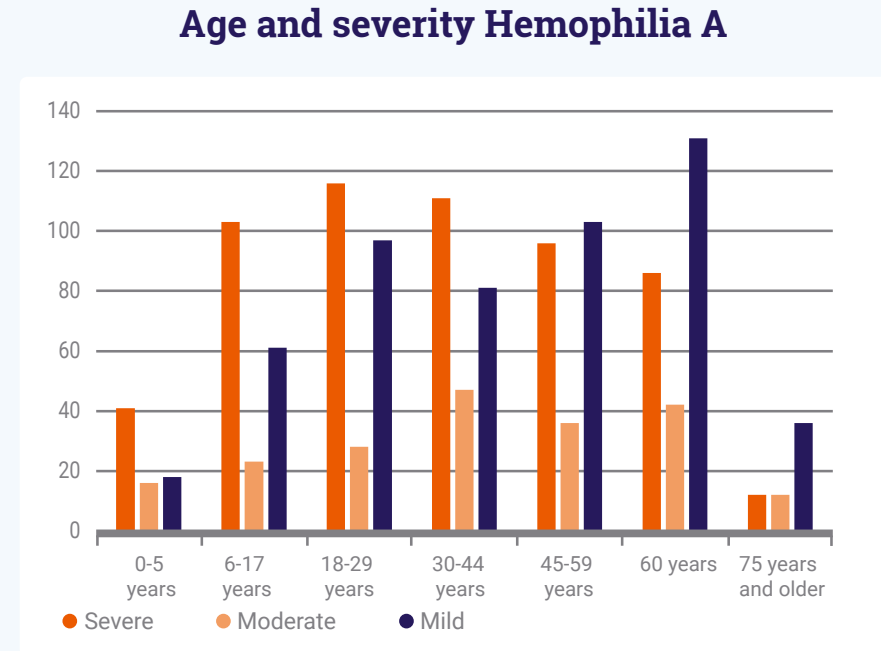


Figure 4b Participants with Hemophilia A by age and severity



Hemophilia

Figure 5a Participants with Hemophilia B by severity

Hemophilia B (Leyden)

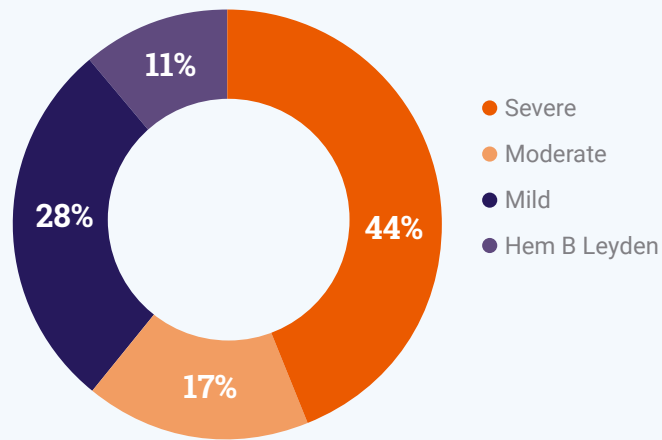
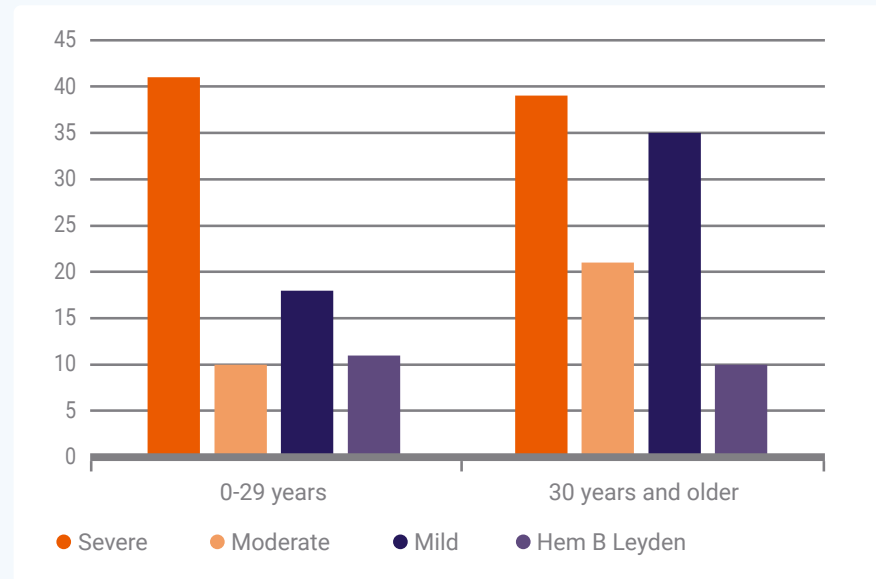


Figure 5b Participants with Hemophilia B (Leyden) by age and severity

Age and severity Hemophilia B



Hemophilia

Viral infections

Table 2 Number of participants born before 1992 with diagnosis Hemophilia that suffer(ed) from a viral infection

Viral infection	Number	%
Total completed*	505	100
Unknown	45	9
No	249	49
Yes**	211	42

Viral infection	Number	%
HIV infection	<10	

Viral infection	Number	%
Hepatitis B infection	62	

Viral infection	Number	%
Hepatitis C infection	186	100
Successfully treated	155	83
Spontaneously cleared	10	5
Still infected	14	8
Unknown	7	4

* Data available for 505 of 929 participants with hemophilia born <1992.

**Participants may (have) suffer(ed) from more than one infection.

Inhibitors

Table 3 Inhibitor status of participants with diagnosis Hemophilia A or B

Inhibitors and Hemophilia A	Number	%
Total completed	699	100
Never	595	85
Current or past inhibitor	91	13
Unknown	13	2

Inhibitors and Hemophilia B	Number	%
Total completed	99	100
Never	98	99
Current or past inhibitor	0	0
Unknown	1	1

Hemophilia

Treatment

Table 4 Number of participants with diagnosis moderate or severe Hemophilia A or B on prophylaxis

Prophylaxis	Number	%
Hemophilia A Severe		
Total completed	552	100
No	40	7
Yes	512	93
Hemophilia A Moderate		
Total completed	196	100
No	160	82
Yes	36	18
Hemophilia B Severe		
Total completed	80	100
No	5	6
Yes	75	94
Hemophilia B Moderate		
Total completed	31	100
No	22	71
Yes	9	29



Hemophilia

Table 5 Number of participants with diagnosis Hemophilia A or B by prescribed treatment product

Hemophilia A	Number	Hemophilia B	Number
Total completed	1588	Total completed	167 (for 162 participants)*
	(for 1266 participants)*		
Product A	519	Product A	104
Product B	198	Product B	49
Product C	196	Other products**	14
Product D	157		
Product E	124		
Product F	91		
Product G	76		
Product H	62		
Product I	48		
Product J	25		
Product K	25		
Product L	14		
Product M	12		
Product N	11		
Product O	11		
Other products**	19		

* For some of the participants more than one treatment product was prescribed.

**Number of prescriptions too small (<10).

Hemophilia

Table 6 Number of participants with diagnosis Hemophilia A or B by type of product*

Hemophilia A	Number	%	Number on prophylaxis	%
Total completed	1266	100	553	100
Standard Half Life	1030	81	378	68
Extended Half life	110	9	110	20
Non Replacement Therapy	62	5	62	11
Bypassing Agents	27	2	0	0
Plasma derived	16	1	<10	
Only Desmopressin	18	1	0	0
Other	<10		<10	

Hemophilia B	Number	%	Number on prophylaxis	%
Total completed	162	100	92	100
Standard Half Life	108	67	39	42
Extended Half life	53	33	52	57
Other	<10	<10	<10	<10

*Product prescribed in the treatment plan. Actual use of the products by the participants in the reporting year is uncertain. If more than one product was prescribed to a participant, the main product is shown.

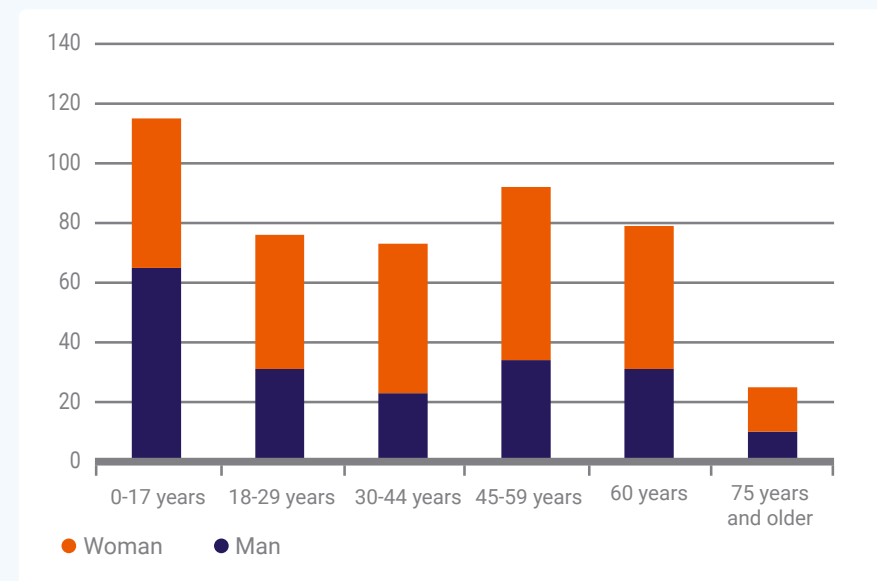
Von Willebrand Disease

Diagnosis and demographic data

Table 7 Number of participants in HemoNED registry with diagnosis von Willebrand disease

Diagnosis	Number	%
Von Willebrand	460	100
Type 1	251	55
Type 2A	78	17
Type 2B	48	10
Type 2M	31	7
Type 2N	11	2
Type 3	29	6
Other/unknown	12	3

Figure 6 Participants with von Willebrand disease by age and gender



Von Willebrand Disease

Inhibitors

Table 8 Inhibitor status of participants with diagnosis von Willebrand disease

Inhibitors and von Willebrand disease	Number	%
Total completed	221	100
Never	208	94
Current or past inhibitor	1	1
Unknown	12	5

Treatment

Table 9 All prescribed treatment products for participants with diagnosis Von Willebrand disease

Products and Von Willebrand	Number
Total completed	561 (for 424 participants)*
Product A	343
Product B	79
Product C	66
Product D	34
Product E	16
Other products**	23

* For some of the participants more than one treatment product was prescribed.

**Number of prescriptions too small (<10).

Table 10 Prescribed type of treatment products for participants with Von Willebrand disease on prophylaxis

Product types and Von Willebrand	Number
Total completed	22
Factor VIII	<10
Combination Factor VIII/VWF (1 or 2 products)	19
VWF	<10

Other bleeding disorders

Table 11 Number of participants in HemoNED registry with other bleeding disorders

Diagnosis	Number	%
Other bleeding disorder	143	100
Factor VII deficiency	21	15
Glanzmann's disease	16	11
Factor XI deficiency/Hemophilia C	15	11
Acquired hemophilia A	13	9
Factor XIII deficiency	12	8
Other bleeding disorders*	66	46
Various platelet disorders	30	
Rare factor deficiencies	28	
Other acquired bleeding disorders	<10	
Unknown	<10	

*Other bleeding disorders subcategories (<10 participants)

Other bleeding disorders in the HemoNED Registry:

- Afibrinogenemia
- Dysfibrinogenemia
- Hypofibrinogenemia
- Hypodysfibrinogenemia
- Factor II deficiency
- Factor V deficiency
- Combined Factor V and Factor VIII deficiency
- Factor X deficiency
- Gray platelet syndrome
- Hermansky Pudlak syndrome
- Storage Pool disease
- Alpha-2-antiplasmin deficiency
- Other factor deficiency
- Other platelets disorder

Adverse events

Table 12 Adverse events and complications reported in HemoNED registry

Adverse events and complications	Number
Reported in 2020*	38
Mortality	19
Cause:	
Liver disease	<10
Bleed	<10
Other	16
Malignancy	<10
Inhibitor	<10
Thrombosis	<10
Allergic or other acute event	<10
Severe bleeding	<10
Other	<10

*Reports from HemoNED participants and non-participants (these are reported anonymously).



Results VastePrik

Diagnosis and demographic data

Figure 7 Age distribution of the VastePrik users in 2020 (N=493, missing 31)

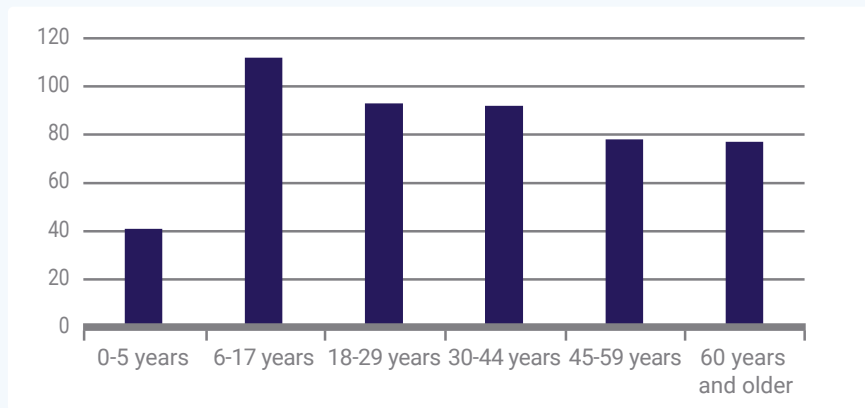


Figure 8 Timeline: Number of unique VastePrik users each month in 2020

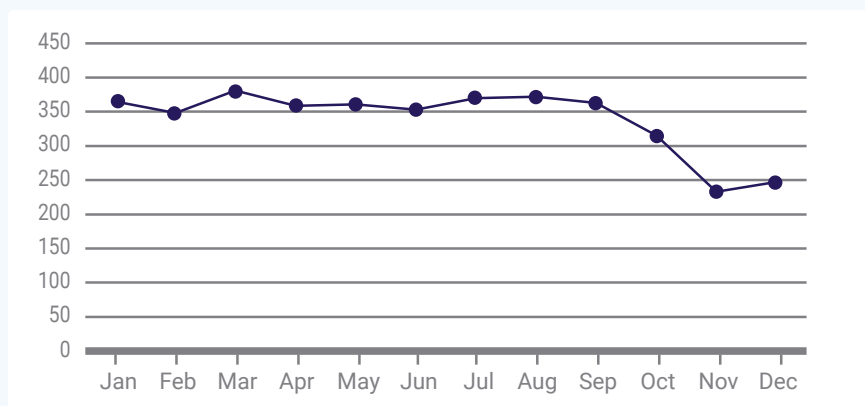


Table 13 Diagnosis of VastePrik users (usage ≥1) in 2020

Diagnosis	Number	%
Total	524	100
Hemophilia A	397	81
Severe	325	
Moderate	45	
Mild	22	
Severity unknown	5	
Hemophilia B (Leyden)	55	11
Severe	44	
Moderate	<10	
Mild	<10	
Severity unknown	<10	
Von Willebrand	25	5
Type 3	12	
Other types/unknown	13	
Other bleeding disorders	13	3
Factor XIII deficiency	<10	
Factor VII deficiency	<10	
Other	<10	
<i>Diagnosis missing</i>	34	

Infusions and bleeds

Table 14 Number of infusions by reason reported in VastePrik in 2020

Reason infusion	Number of infusions	%
Prophylaxis	35559*	92
Precaution (risky activities)	459	1
(Directly following a) Bleed	1445**	4
Aftercare (after a bleed or surgery)	1230	3
Total completed	38693	100

* Prophylaxis reported by 480 of 524 VastePrik users.

**Bleeds reported by 297 of 524 VastePrik users.

Table 15 Type of bleeds reported

Type of bleed	Number of bleeds	%
Joint	651	45
Muscle	240	17
Subcutaneous	132	9
Mucous membranes	107	7
Other	315	22
Total	1445	100

Table 16 Location of joint bleeds

Location	Number of bleeds	%
Ankle	190	29
Elbow	173	27
Knee	159	24
Wrist	38	6
Shoulder	25	4
Hip	15	2
Other	51	8
Total	651	100

Table 17 Bleed severity

Bleed severity	Number of bleeds	%
Low	403	28
Average	774	54
High	268	18
Total	1445	100

Table 18 Cause of bleeds

Cause	Number of bleeds	%
Spontaneously	648	45
Overload	271	18
Accident or trauma	274	19
Postoperative	7	1
Other	245	17
Total	1445	100

Table 19 Reported bleeds in VastePrik in 2020 by users with Hemophilia (selection: regular VastePrik users, mean registration of ≥ 1 prophylaxis infusion each month, N=141)

	Number of participants without bleeds	Number of participants with bleeds	Number of bleeds	A(J)BR*		Number of double bleeds***	A(J)BR without double bleeds	
				median (IQR)**	range		median (IQR)	range
All bleeds	41	100	472	2 (0-5)	(0-36)	60	2 (0-4)	(0-26)
Joint bleeds	65	76	247	1 (0-2)	(0-16)	27	1(0-2)	(0-16)

* Annualized (Joint) Bleeding Rate = median number of (joint) bleeds per person per year.

** Interquartile Range.

***A double bleed is defined as a bleed logged at the same or next day and at the same location of the body as the previous bleed. These data are probably incorrect.

Table 20 Most recently used product reported by VastePrik users with Hemophilia

	Number of users	%
Hemophilia A	397	100
Product a	157	40
Product b	58	15
Product c	57	14
Product d	30	8
Product e	28	7
Product f	22	5
Product g	16	4
Other products*	29	7

	Number of users	%
Hemophilia B (Leyden)	55	100
Product a	36	65
Product b	12	22
Other products*	7	13

*Number of products too small (<10)

Table 21 Most recently used product reported by VastePrik users with Hemophilia, by type of product

	Number of users	%
Hemophilia A	397	100
Standard Half Life	261	66
Extended Half Life	93	23
Non Replacement Therapy	28	7
Plasma derived	<10	
Bypassing Agents	<10	
Desmopressin	<10	
Other	<10	

	Number of users	%
Hemophilia B (Leyden)	55	100
Standard Half Life	14	25
Extended Half Life	41	75

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Support

HemoNED received a grant/research support from the following sponsors:

- Bayer B.V.
- CSL Behring B.V.
- Novo Nordisk B.V.
- Octapharma Benelux N.V.
- Pfizer B.V.
- Roche Netherlands B.V.
- Takeda Netherlands B.V.
- Swedish Orphan Biovitrum BVBA/SPRL

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