



Dutch Hemophilia Registry

Annual Report 2021



HemoNED Foundation
March 2022

<https://hemoned.nl/en>

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Introduction

This annual report describes data from the Dutch Hemophilia Registry ('HemoNED Registry') and the VastePrik digital infusion log for home treatment available on 31 December 2021.

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 Steering Committee of HemoNED, consisting of representatives from all the Dutch Hemophilia Treatment Centers (HTCs), the Dutch Hemophilia Patient Society (NVHP) and the Dutch Hemophilia Nurses Society (NVHV), is responsible for assessing and approving the annual reports and data applications.

The procedure for data applications can be found on the HemoNED website <https://hemoned.nl/en/research/data-application/>.

Dutch Hemophilia Registry

The Dutch Hemophilia Registry was established in 2017 as a joint initiative from the Dutch Hemophilia Treaters Society (NVHB), the NVHP and the 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 HemoNED Registry collects information about the diagnosis, treatment and treatment outcomes of people with hemophilia or related disorders in the Netherlands. 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 2018 both as an app for smartphones and a web page. Participants can register their home treatment (infusions and possible bleeds). VastePrik is mainly used by participants on prophylaxis. The health care provider also has access to the VastePrik data and overview reports of his/her patient through a secured online web page, to evaluate and adjust home treatment if necessary. In agreement with the patient, health care providers can add or change infusions or bleeds in VastePrik.

Inclusion

All national certified HTCs routinely invite possible participants for the Dutch Hemophilia Registry:

- Amsterdam UMC location AMC
- Erasmus MC Rotterdam
- LUMC Leiden & HagaZiekenhuis The Hague
- HTC NEM: 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 VWFact and/or VWFrcf 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 or infusion with thrombocytes at surgery/trauma
- Acquired hemophilia

Adverse events

All HTC's enter adverse events and complications for people with bleeding disorders in the HemoNED Registry. 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.

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 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 provided numbers for the Annual Global Survey 2020 of the World Federation of Hemophilia in collaboration with NVHP (<https://wfh.org/data-collection/#ags>).

Organisation

Board members HemoNED Foundation in 2021:

- **Chair: Dr. F.J.M. (Felix) van der Meer**, Internist LUMC
- **Secretary: Dr. M.H.E. (Mariëtte) Driessens**, Delegate Dutch Hemophilia Patient Society (NVHP)
- **Treasurer: Dr. S.C. (Samantha) Gouw**, Pediatric hematologist Amsterdam UMC

The following representatives were part of the HemoNED Steering Committee in 2021:

- **Dr. F.J.M. (Felix) van der Meer**, chair Steering Committee, Expertise center for hemophilia and related disorders LUMC Leiden & HagaZiekenhuis The Hague
- **Dr. K. (Kathelijn) Fischer**, Van Creveld Clinic UMC Utrecht
- **Dr. S.C. (Samantha) Gouw**, Amsterdam UMC location AMC Hemophilia Treatment Center
- **Dr. M.J.H.A. (Marieke) Kruijff**, 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 / Mrs. M. (Marlène) Beijlevelt**, Dutch Hemophilia Nurses Society (NVHV)

HemoNED Project Office in 2021:

- **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 **2453** (100%)



Gender

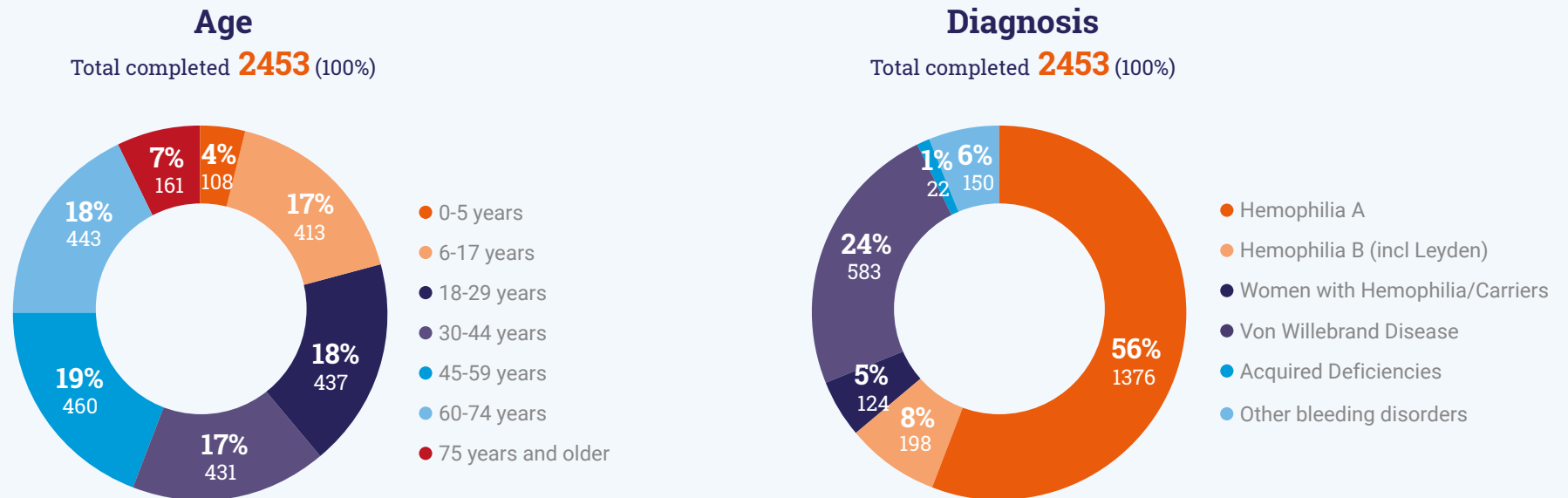
Man **1872** (76%)

Woman **581** (24%)

Results Dutch Hemophilia Registry

General

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



Mortality

2018-2020: 19 participants died. The data of these participants are excluded.
2021: 15 participants died. The data of these participants are included in this report.

Refusals

2018-2021: 132 people who were asked to participate in the HemoNED registry by a health care provider refused to give written informed consent. These are 84 people with hemophilia (35 severe hemophilia) and 48 people with other bleeding disorders.

General

Figure 2a Number of participants included in the HemoNED registry until 31 December 2021

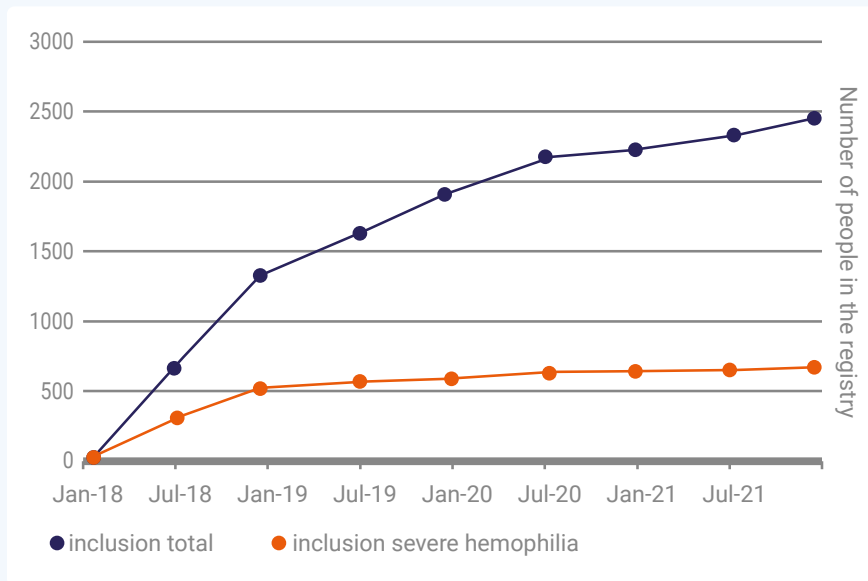
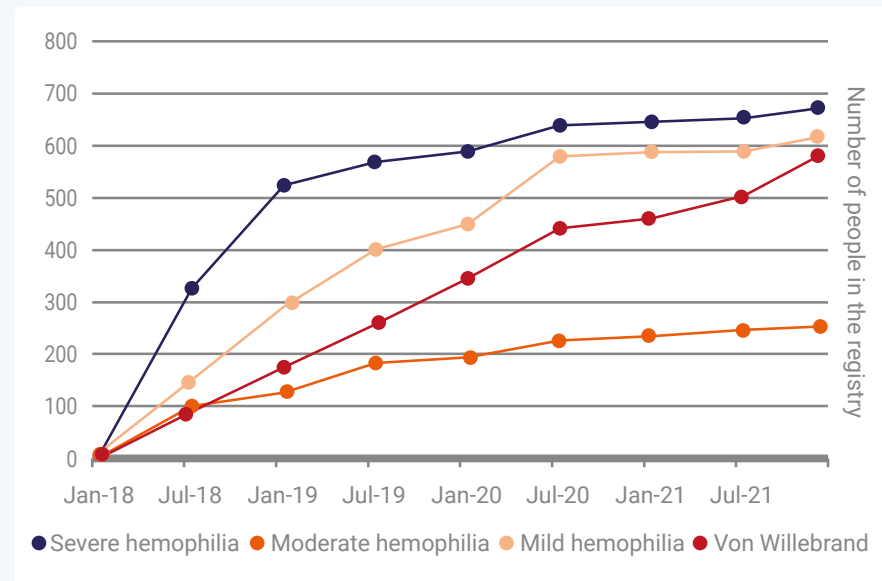


Figure 2b Number of participants with severe, moderate and mild hemophilia and von Willebrand disease included in HemoNED until 31 December 2021



Hemophilia

Diagnosis and demographic data

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

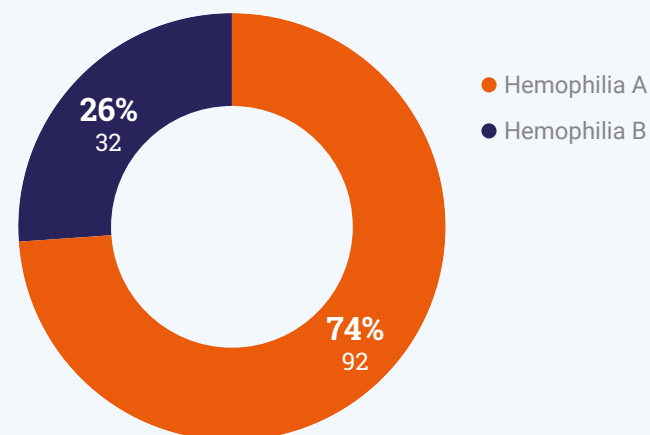
Diagnosis	Number	%
Hemophilia A	1376	100
Severe	586	43
Moderate	219	16
Mild	562	41
Severity unknown	9	

Diagnosis	Number	%
Hemophilia B	176	100
Severe	86	49
Moderate	34	19
Mild	55	32
Severity unknown	1	

Diagnosis	Number	%
Hemophilia B Leyden	22	

Figure 3 Women with Hemophilia/Carriers of Hemophilia A and B

Women with Hemophilia/Carriers



Hemophilia

Figure 4a Participants with Hemophilia A by severity

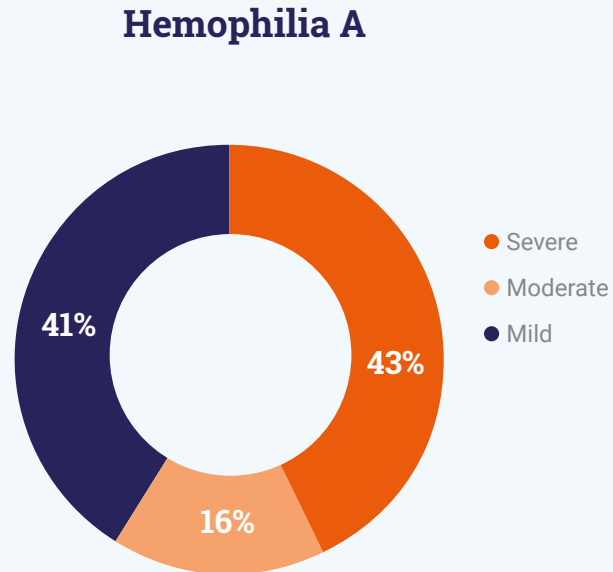
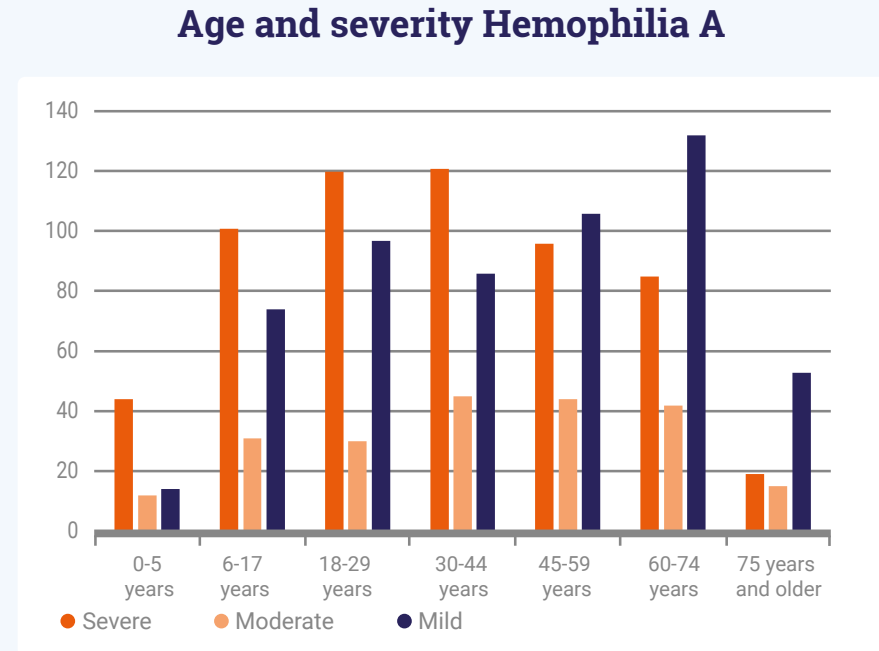


Figure 4b Participants with Hemophilia A by age and severity



Hemophilia

Figure 5a Participants with Hemophilia B by severity

Hemophilia B (Leyden)

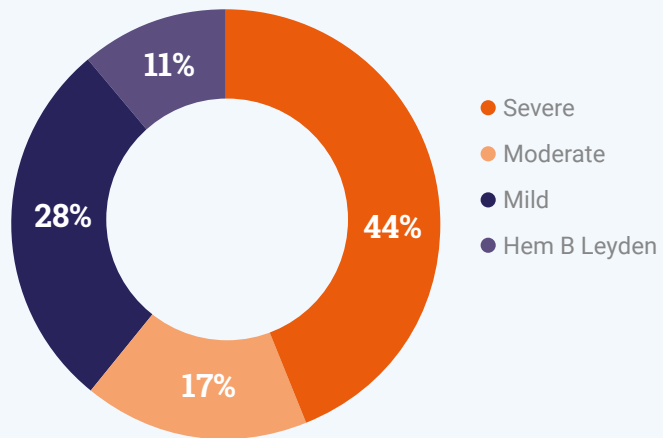
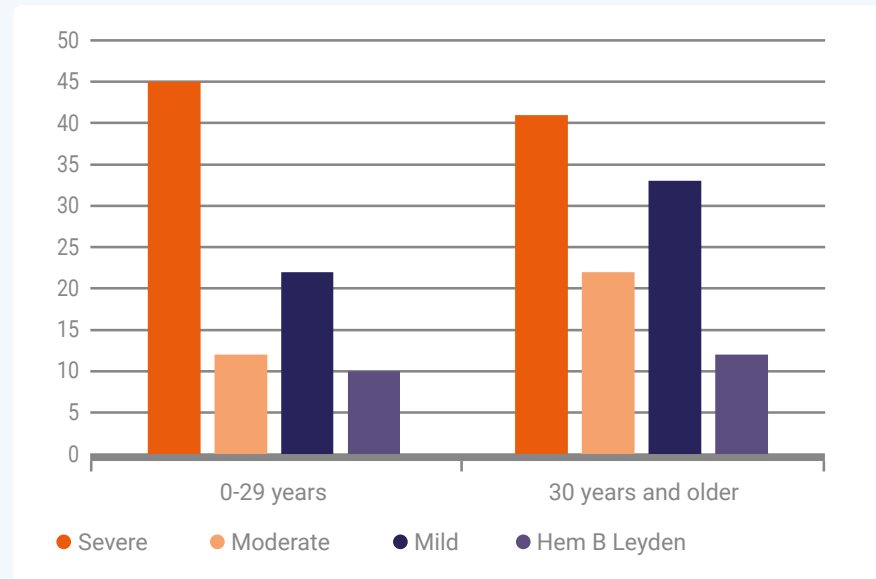


Figure 5b Participants with Hemophilia B (Leyden) by age and severity

Age and severity Hemophilia B (Leyden)



Hemophilia

Viral infections

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

Viral infection	Number	%
Total completed*	525	100
Unknown**	44	8
No	263	50
Yes***	218	42

Viral infection	Number	%
HIV infection	<10	

Viral infection	Number	%
Hepatitis B infection	64	

Viral infection	Number	%
Hepatitis C infection	192	100
Successfully treated	161	84
Spontaneously cleared	11	6
Still infected	12	6
Unknown**	<10	

* Data available for 525 of 959 participants with hemophilia born <1992.

** Classified by a health care provider as 'Unknown'.

*** 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*	753	100
Never	634	84
Current or past inhibitor	105	14
Unknown**	14	2

Inhibitors and Hemophilia B	Number	%
Total completed***	103	100
Never	102	99
Current or past inhibitor	0	0
Unknown**	<10	

* Data available for 745 of 1376 participants with Hemophilia A.

** Classified by a health care provider as 'Unknown'.

*** Data available for 103 of the 176 participants with Hemophilia B.

Hemophilia

Treatment

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

Prophylaxis	Number	%
Severe Hemophilia A		
Total completed	586	100
No	36	6
Yes	550	94
Moderate Hemophilia A		
Total completed	219	100
No	171	78
Yes	48	22
Severe Hemophilia B		
Total completed	85	100
No	8	9
Yes	77	91
Moderate Hemophilia B		
Total completed	34	100
No	23	68
Yes	11	32



Hemophilia

Table 5 All prescribed treatment products for participants with diagnosis Hemophilia A or B (Leyden)

Hemophilia A	Number	Hemophilia B (Leyden)	Number
Total completed	1840 (for 1375 participants)*	Total completed	201 (for 196 participants)*
Product A	608	Product A	90
Product B	293	Product B	66
Product C	219	Product C	37
Product D	209	Other products**	<10
Product E	190		
Product F	126		
Product G	75		
Product H	48		
Product I	27		
Product J	15		
Product K	12		
Other products**	18		

* 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 (Leyden) by type of product*

Hemophilia A	Number	%	Number on prophylaxis	%
Total completed	1375	100	604	100
Standard Half Life	989	72	284	47
Extended Half life	115	8	108	18
Non Replacement Therapy	209	15	209	35
Bypassing Agents	26	2	0	0
Plasma derived	15	1	<10	
Only Desmopressin	20	2	0	0
Other	<10		<10	

Hemophilia B (Leyden)	Number	%	Number on prophylaxis	%
Total completed	196	100	95	100
Standard Half Life	125	64	28	29
Extended Half life	71	36	67	71
Other	<10		0	0

* If more than one product was prescribed to a participant, the main product is shown.

Figure 6 Switch in prescribed products in Hemophilia A: number of persons on prophylactic treatment by type of prescribed product in 2020 and 2021.

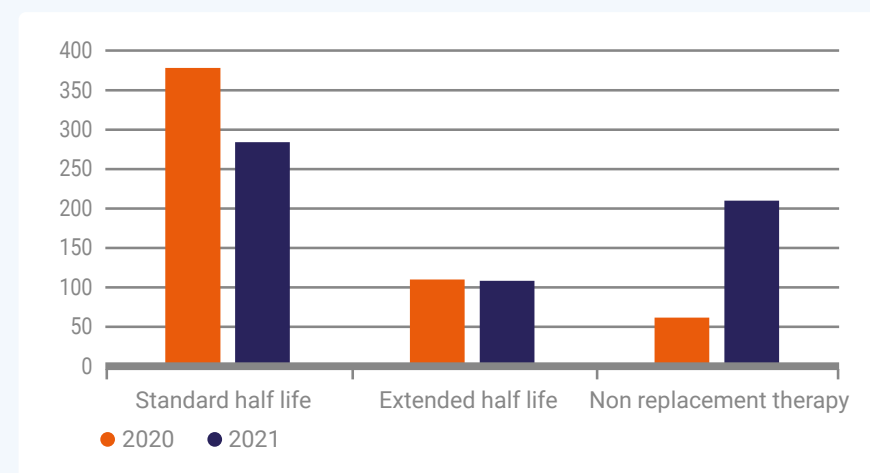


Table 7 Reasons to switch to Non Replacement therapy

Reason to start Non Replacement therapy	Number	%
Total completed	181	100
Inhibitor with bleeding tendency	19	10
Venous access problems	27	15
Not being able to administer regular prophylaxis	10	5
Recurring bleeds despite regular prophylaxis	16	9
Very active life (sports, travelling)	<10	
Preference of both patient and physician, non-specific	102	56

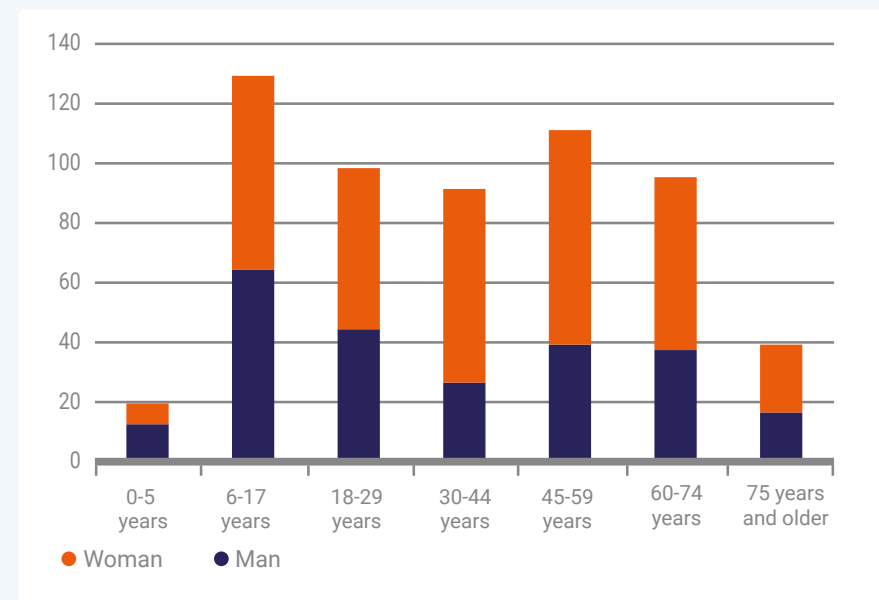
Von Willebrand Disease

Diagnosis and demographic data

Table 8 Number of participants in HemoNED registry with diagnosis Von Willebrand disease

Diagnosis	Number	%
Von Willebrand disease	583	100
Type 1	311	53
Type 2A	97	17
Type 2B	59	10
Type 2M	42	7
Type 2N	13	2
Type 3	33	6
Other/unknown type	28	5

Figure 7 Participants with Von Willebrand disease by age and gender



Von Willebrand Disease

Inhibitors

Table 9 Inhibitor status of participants with diagnosis Von Willebrand disease

Inhibitors and Von Willebrand	Number	%
Total completed	301*	100
Never	282	94
Current or past inhibitor	<10	
Unknown**	17	5

* Data available for 301 of 583 participants with Von Willebrand disease.

** Classified by a health care provider as 'Unknown'.

Treatment

Table 10 All prescribed treatment products for participants with diagnosis Von Willebrand disease

Products and Von Willebrand	Number
Total completed	735 (for 558 participants)*
Product A	453
Product B	223
Product C	21
Product D	17
Product E	13
Other products**	<10

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

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

Table 11 Prescribed type of treatment products for participants with Von Willebrand disease on prophylaxis

Product types and Von Willebrand	Number
Total completed	21
Factor VIII	<10
Combination Factor VIII/VWF	18
VWF	<10

Other bleeding disorders

Table 12 Number of participants in HemoNED registry with other bleeding disorders

Diagnosis	Number	%
Other bleeding disorder	172	100
Factor VII deficiency	28	16
Factor XI deficiency/Hemophilia C	22	13
Glanzmann's disease	17	10
Acquired Hemophilia A	15	9
Factor XIII deficiency	14	8
Storage Pool Disease	12	7
Other bleeding disorders*	64	38
Various platelet disorders	24	
Rare factor deficiencies	31	
Other acquired bleeding disorders	<10	
Bleeding disorder not specified	<10	

* Bleeding disorders with < 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
- Alpha-2-antiplasmin deficiency
- Other factor deficiency
- Other platelets disorder

Adverse events

Table 13 Adverse events and complications reported in HemoNED registry

Adverse events and complications	Number
Reported in 2021*	52
Mortality	29
Malignancy	<10
Inhibitor	<10
Allergic or other acute event	<10
Poor efficacy	<10
Severe bleeding	<10
Other	<10

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



Results VastePrik

Diagnosis and demographic data

Table 14 Diagnosis of VastePrik users (usage ≥ 1) in 2021

Diagnosis	Number	%
Total	424	100
Hemophilia A	352	83
Severe	250	
Moderate	37	
Mild	12	
Severity missing*	53	
Hemophilia B (Leyden)	44	10
Severe	28	
Moderate	<10	
Mild	<10	
Severity missing*	13	
Von Willebrand disease	10	2
Type 3	<10	
Other types/unknown	<10	
Other bleeding disorders	16	4
Factor XIII deficiency	<10	
Factor VII deficiency	<10	
Other	<10	
<i>Diagnosis missing</i>	2	

* Diagnosis derived from the product used.

Figure 8 Age distribution of the VastePrik users (N=379, missing 45) in 2021

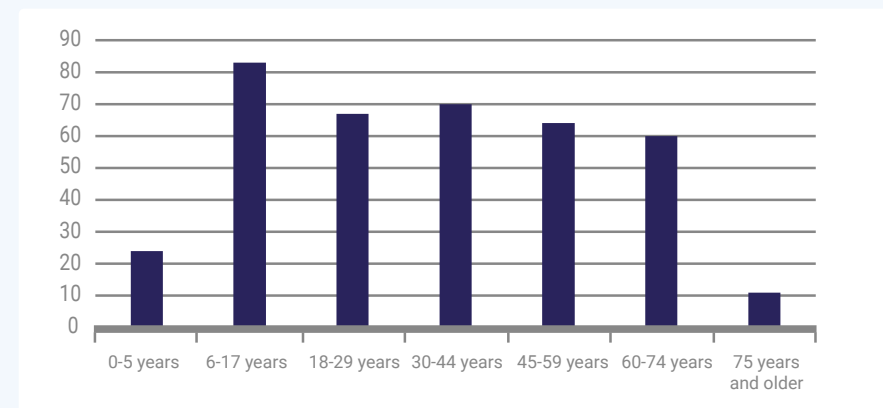
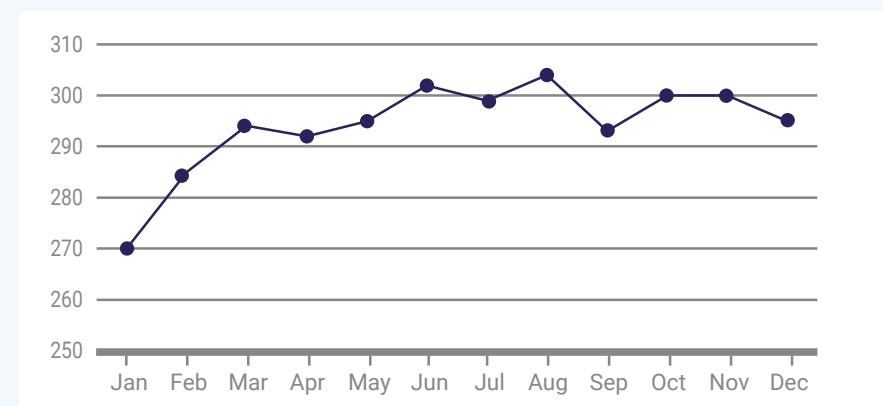


Figure 9 Number of unique Age VastePrik users each month in 2021



Infusions and bleeds

Table 15 Number of infusions by reason reported in VastePrik in 2021

Reason infusion	Number of infusions	%
Prophylaxis*	24503	90
Precaution (risky activities)	643	2
(Directly following a) Bleed**	1138	4
Aftercare (after a bleed or surgery)	1034	4
Total completed	27318	100

* Prophylaxis reported by 398 of 424 VastePrik users.

** Bleeds reported by 228 of 424 VastePrik users.

Joint bleeds reported by 156 of 424 VastePrik users.

Table 16 Type of bleeds reported

Type of bleed	Number of bleeds	%
Joint	566	50
Muscle	204	18
Mucous membranes	54	5
Subcutaneous	86	8
Other	228	20
Total	1138	100

Table 17 Location of joint bleeds

Location	Number of bleeds	%
Ankle	157	28
Elbow	148	26
Knee	119	21
Wrist	39	7
Shoulder	32	6
Hip	21	4
Other	50	8
Total	566	100

Table 18 Bleed severity

Severity*	Number of bleeds	%
Low	374	33
Average	557	49
High	180	16
Missing	27	2
Total	1138	100

* Self-report of the VastePrik user.

Table 19 Cause of bleeds

Cause	Number of bleeds	%
Spontaneously	477	42
Overload	278	24
Accident or trauma	232	20
Postoperative	<10	
Other or missing	144	13
Total	1138	100

Table 20 Reported bleeds in VastePrik in 2021 by users with Hemophilia (selection: regular VastePrik users, mean registration of ≥ 1 prophylaxis infusion each month, N=146)

	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	54	92	529	2 (0-5)	(0-31)	117	1 (0-4)	(0-29)
Joint bleeds	72	74	297	1 (0-3)	(0-25)	80	1 (0-2)	(0-9)

* 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 21 Most recently used product reported by VastePrik users with Hemophilia

	Number of users	%
Hemophilia A	352	100
Product a	137	39
Product b	97	28
Product c	51	15
Product d	22	6
Product e	20	6
Product f	10	3
Other products*	<10	
Missing	<10	


	Number of users	%
Hemophilia B (Leyden)	44	100
Product a	34	77
Other products*	<10	
Missing	<10	

* Number of users too small (<10)

Table 22 Most recently used product reported by VastePrik users with Hemophilia, by type of product

	Number of users	%
Hemophilia A	352	100
Standard Half Life	132	38
Extended Half Life	73	21
Non Replacement Therapy	137	39
Bypassing Agents	<10	
Plasma derived	<10	
Desmopressin	0	0
Missing	<10	

	Number of users	%
Hemophilia B (Leyden)	44	100
Standard Half Life	<10	
Extended Half Life	38	86
Missing	<10	

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Support

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

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

Contact

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