HemoNED
Dutch Hemophilia Registry

Dutch Hemophilia Registry
Annual Report 2022

HemoNED Foundation
April 2023

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 2022.

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 Data application HemoNED.

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 and part of the registry is automatically filled with data from Electronic Health Records of the HTCs. 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. In 2022 several promotional activities were developed to increase the use of VastePrik. Short instructional videos were made to explain clearly how to use VastePrik Videos VastePrik.

Inclusion

All national certified HTCs routinely invite possible participants for the HemoNED 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 ≤ 50%
- Von Willebrand disease, VWFag and/or VWFact and/or VWFrcf and /or FVIII levels ≤ 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 HTCs 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 HTCs, the European Haemophilia Safety Surveillance (EUHASS) and the Netherlands Pharmacovigilance Centre Lareb.

Data analysis

The HemoNED project office analyzed the 2022 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 2022 of the World Federation of Hemophilia in collaboration with NVHP (Annual Global Survey -WFH -World Federation of Hemophilia).

Organisation

Board members HemoNED Foundation in 2022:

- **Chair: Dr. F.J.M. (Felix) van der Meer,** Internist LUMC, succeeded in March by **Dr. S.C (Samantha) Gouw**, Pediatric hematologist Amsterdam UMC Hemophilia Treatment Center, in March 2022
- **Secretary: Dr. M.H.E. (Mariëtte) Driessens**, Delegate Dutch Hemophilia Patient Society (NVHP)
- **Treasurer: Dr. S.C. (Samantha) Gouw**, Pediatric hematologist Amsterdam UMC, succeeded by **Prof. Dr. K. (Karina) Meijer**, internist-hematologist UMC Groningen Hemophilia Treatment Center, in March 2022

The following representatives were part of the HemoNED Steering Committee in 2022:

- **Dr. F.J.M. (Felix) van der Meer,** chair Steering Committee Expertise center for hemophilia and related disorders LUMC Leiden & HagaZiekenhuis The Hague, succeeded by **Dr. S.C (Samantha) Gouw**, Amsterdam UMC, location AMC Hemophilia Treatment Center, in March 2022
- **Dr. K. (Kathelijn) Fischer**, Van Creveld Clinic UMC Utrecht
- **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
- **Dr. P.L. (Paul) den Exter**, Hemophilia Treatment Center LUMC Leiden & Hagaziekenhuis The Hague
- **Mr. S.L.A. (Stephan) Meijer**, NVHP
- **Mrs. M. (Marlène) Beijlevelt**, Dutch Hemophilia Nurses Society (NVHV)

HemoNED Project Office in 2022:

- **Dr. G. (Geertje) Goedhart**, Project coordinator HemoNED, succeeded by **Ms. C.M.E. (Caroline) van Veen** in September 2022
- **Mrs. E.M. (Liesbeth) Taal**, Data manager HemoNED

Results Dutch Hemophilia Registry

General

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

Total participants

Total completed 2641 (100%)

Gender

Man 1974 (75%)

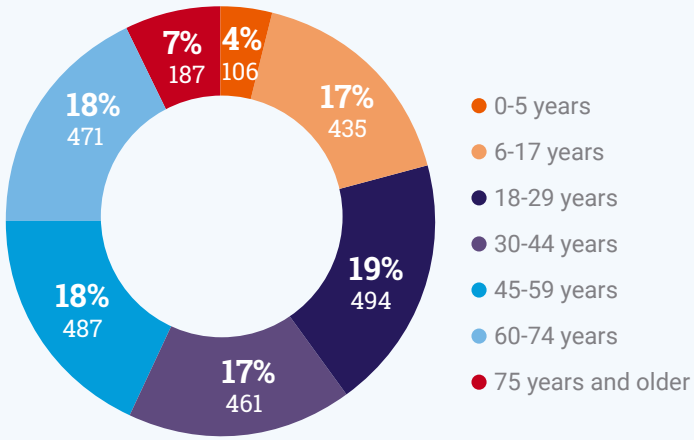
Woman 667 (25%)

General

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

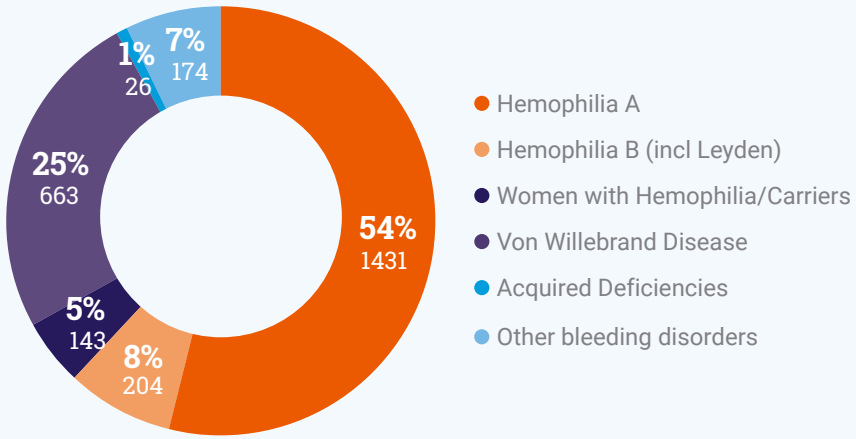
Age

Total completed **2641** (100%)



Diagnosis

Total completed **2641** (100%)



Mortality

2018-2021: 34 participants died. The data of these participants are excluded.

2022: 19 participants died. The data of these participants are included in this report.

General

Figure 2a Number of participants included in the HemoNED registry until 31 December 2022

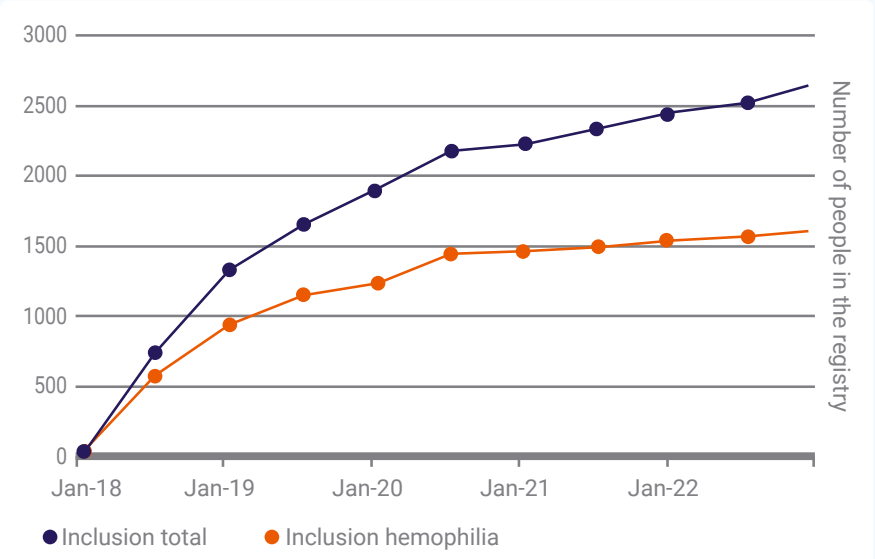
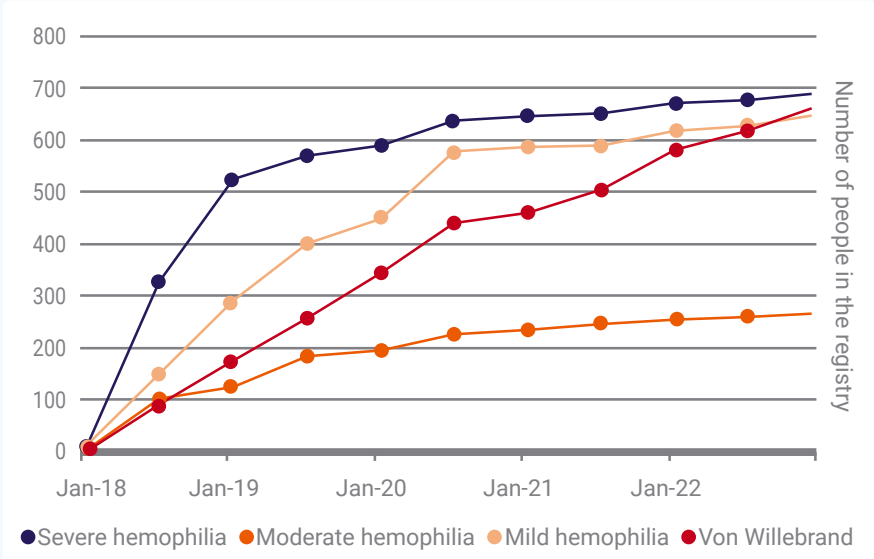


Figure 2b Number of participants with severe, moderate and mild hemophilia and von Willebrand disease included in HemoNED until 31 December 2022



Hemophilia

Diagnosis and demographic data

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

Diagnosis	Number	%
Hemophilia A*	**1431**	**100**
Severe	605	42
Moderate	230	16
Mild	589	41
Severity unknown	7	

Diagnosis	Number	%
Hemophilia B**	**204**	**100**
Severe	86	42
Moderate	36	18
Mild	60	29
Leyden	22	11

Diagnosis	Number	%
Hemophilia Carriers	**143**	**100**
Hemophilia A	104	73
Hemophilia B	39	27

* 1414 men, 17 women

** 197 men, 7 women

Hemophilia

Figure 3a Participants with Hemophilia A by severity

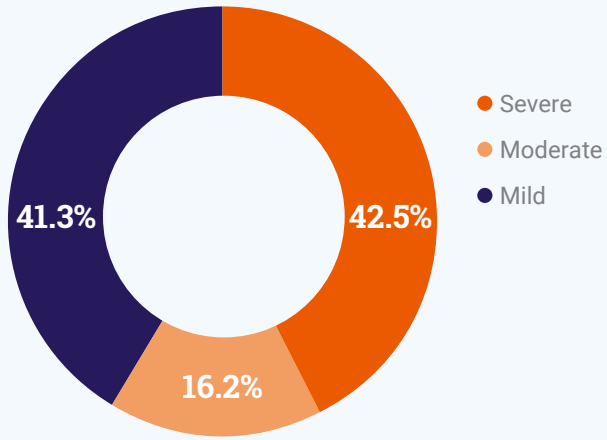
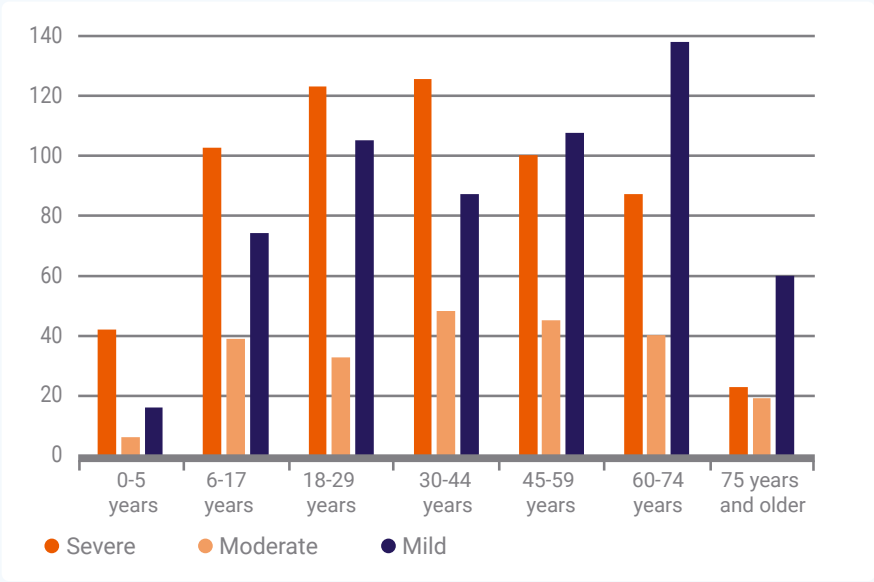


Figure 3b Participants with Hemophilia A by age and severity



Hemophilia

Figure 4a Participants with Hemophilia B by severity

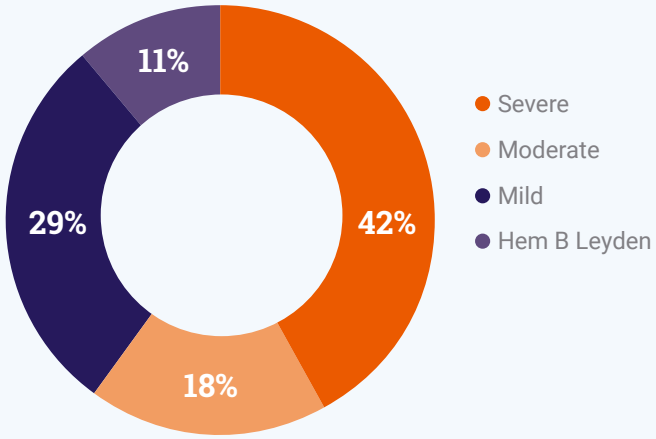
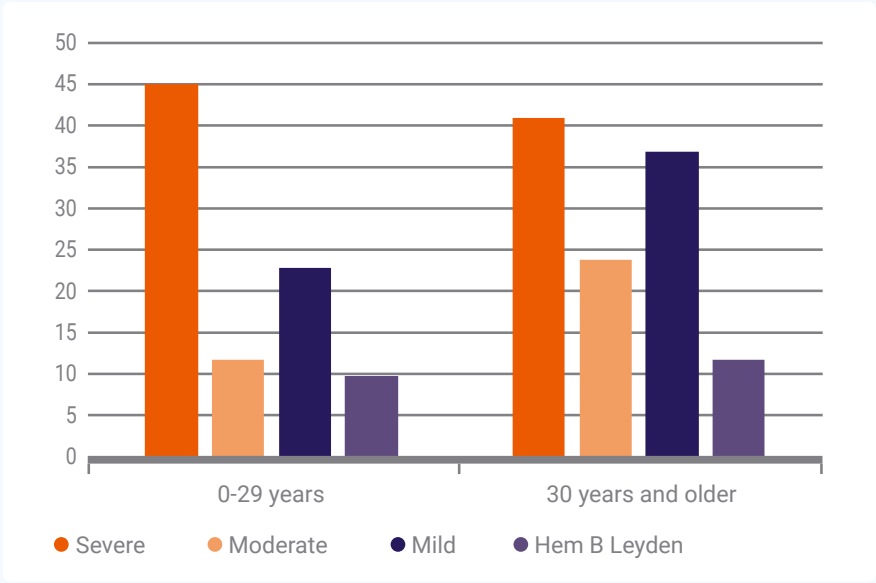


Figure 4b Participants with Hemophilia B by age and severity



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 participants with hemophilia born before 1992	**980**	
Not completed	**446**	
Total completed	**534**	**100**
Unknown*	44	8
No	265	50
Yes**	225	42

Viral infection	Number	%
HIV infection	**<10**	

Viral infection	Number	%
Hepatitis B infection	**69**	**13**

Viral infection	Number	%
Hepatitis C	**197**	**100**
Successfully treated	165	84
Spontaneously cleared	11	6
Still infected	13	7
Unknown	8	4

* 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*	**784**	**100**
Never	662	84
Current or past inhibitor	108	14
Unknown**	14	2

Inhibitors and Hemophilia B	Number	%
Total completed*	**107**	**100**
Never	106	99
Current or past inhibitor	0	0
Unknown**	1	1

* Data available for 784 of 1431 participants with Hemophilia A.
** Classified by a health care provider as 'Unknown'.
*** Data available for 107 of the 182 participants with Hemophilia B.

Hemophilia

Treatment

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

Prophylaxis	Number	%
Severe Hemophilia A		
Total completed	**604**	**100**
No	17	3
Yes	587	97
Moderate Hemophilia A		
Total completed	**228**	**100**
No	174	76
Yes	54	24
Mild Hemophilia A		
Total completed	**588**	**100**
No	580	99
Yes	8	1

Prophylaxis	Number	%
Severe Hemophilia B		
Total completed	**86**	**100**
No	5	6
Yes	81	94
Moderate Hemophilia B		
Total completed	**36**	**100**
No	23	64
Yes	13	36
Mild Hemophilia B		
Total completed	**60**	**100**
No	56	93
Yes	4	7

Hemophilia

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

Hemophilia A	Number
Total completed	**1925 (for 1427 participants)***
Product A	800
Product B	322
Product C	233
Product D	196
Product E	161
Product F	64
Product G	56
Product H	35
Product I	20
Product J	14
Product K	12
Other products***	12

Hemophilia B	Number
Total completed	**203 (for 204 participants)****
Product A	84
Product B	69
Product C	43
Other products***	<10

* for 4 participants the treatment plan is missing; for some of the participants more than one treatment product was prescribed.

** For 1 participant the treatment plan is missing.

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

Hemophilia

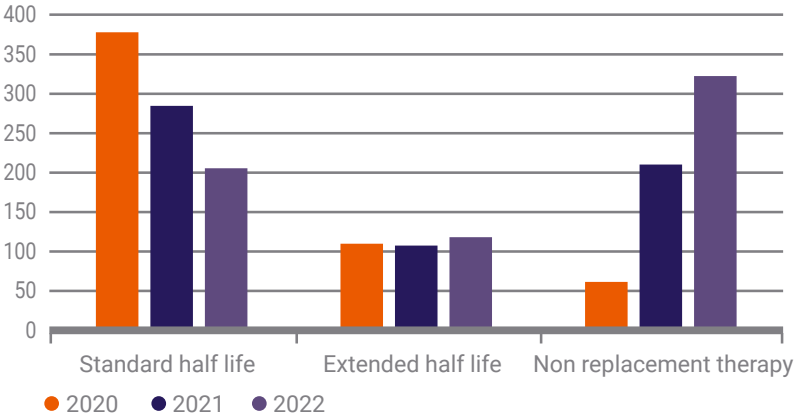
Table 6 Number of participants with diagnosis Hemophilia A or B by type of product*

Hemophilia A	Number	%	Number on prophylaxis	%
Total completed	**1427**	**100**	**650**	**100**
Standard Half Life	923	65	205	31.5
Extended Half life	122	9	118	18.2
Non Replacement Therapy	322	23	322	49.5
Bypassing Agents	29	2	<10	0.3
Plasma derived	14	1	<10	0.2
Only Desmopressin	15	1	0	0
Other	2	2	<10	0.3

Hemophilia B	Number	%	Number on prophylaxis	%
Total completed	**203**	**100**	**99**	**100**
Standard Half Life	112	55	17	17
Extended Half life	91	45	82	83

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

Figure 5 Number of persons with Hemophilia A on prophylactic treatment, by type of prescribed product in 2020, 2021 and 2022



Tabel 7 Reason to start with Non Replacement therapy

Reason to start Non Replacement therapy	Number	%
Total completed	**281**	**100**
Preference of both patient and physician, non-specific	103	37
Recurring bleeds despite regular prophylaxis	66	23
Venous access problems	61	22
Inhibitor with bleeding tendency	26	9
Very active life (sports, travelling)	14	5
Not being able to administer regular prophylaxis	11	4

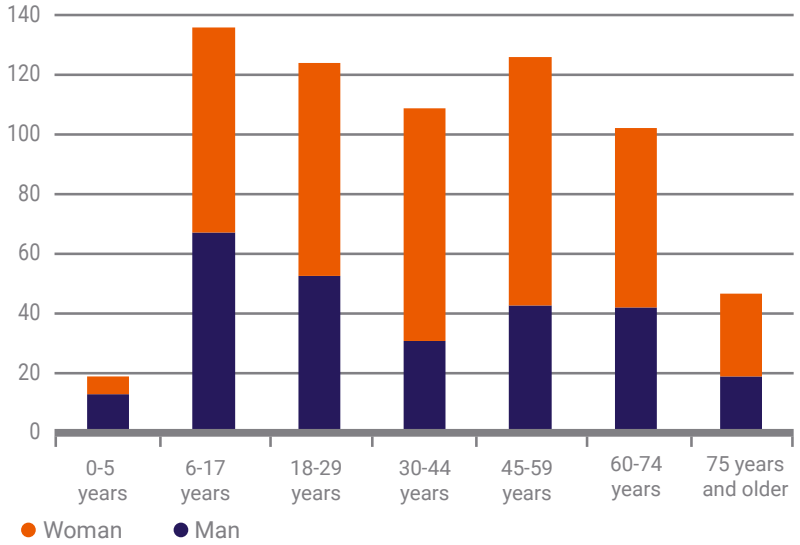
Von Willebrand Disease

Diagnosis and demographic data

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

Diagnosis	Number	%
Von Willebrand disease	**663**	**100**
Type I	366	55
Type 2A	108	16
Type 2B	62	9
Type 2M	45	7
Type 2N	17	3
Type 3	34	5
Other unknown/type	31	5

Figure 6 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	**357***	**100**
Never	338	94.7
Current or past inhibitor	<10	<1
Unknown**	17	4.7

* Data available for 357 of 583 participants with Von Willebrand disease.

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

Treatment

Table10 All prescribed treatment products for participants with diagnosis Von Willebrand disease

Products and Von Willebrand	Number
Total completed	**765 (for 633 participants)***
Product A	429
Product B	182
Product C	120
Product D	18
Other products**	16

* For 30 participants the treatment plan is missing; 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	**28**
Factor VIII	<10
Combination Factor VIII/VWF	26
VWF	<10

Other bleeding disorders

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

Diagnosis	Number	%
Other bleeding disorder	**200**	**100**
Factor VII deficiency	31	16
Factor XI deficiency	25	13
Glanzmann's disease	19	10
Acquired Hemophilia A	18	9
Factor XIII deficiency	14	7
Storage Pool Disease	14	7
Afibrinogenemia/hypofibrinogenemia Hypodysfibrinogenemia/dysfibrinogenemia	13	6
Other bleeding disorders	66	33
Various other platelet disorders	33	
Rare factor deficiencies	20	
Other acquired bleeding disorders	8	
Other or disorder not specified	5	

Other platelet disorders include Gray platelet syndrome, Bernard-Soulier syndrome, May-Hegglin syndrome

Rare factor deficiencies include Factor II deficiency, Factor V deficiency, combined Factor V and Factor VIII deficiency, Factor X deficiency

Other bleeding disorders include alpha-2-antiplasmin deficiency

Adverse events

Table 13 Adverse events and complications reported in HemoNED registry

Adverse events and complications	Number
Reported in 2022*	**66**
Mortality**	37
Malignancy	<10
Inhibitor	<10
Allergic or other acute event	<10
Poor efficacy	0
Severe bleeding	<10
Other	10

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

** 19 events reported from participants.

Results VastePrik

Diagnosis and demographic data

Table 14 Diagnosis of VastePrik users (usage ≥1 in 2022) related to prophylactic treatment

Diagnosis	Number	% from number	Number on prophylaxis (table 4, table 11)	% of number of patients on prophylaxis
Total	**429**	**100**		
Hemophilia A	**362**	**84**		**52**
Severe	302	83		
Registration prophylaxis	295		587	50
Moderate	49	14		
Registration prophylaxis	33		54	61
Mild	11	3		
Registration prophylaxis	<10		<10	
Hemophilia B	**43**	**10**		**44**
Severe	35		81	43
Moderate	<10		13	38
Mild	<10		<10	
Leyden	<10			
Von Willebrand disease	**10**	**2**	**28**	**36**
Type 3	<10			
Other types/unknown	<10			
Other bleeding disorders	**13**	**4**		
Factor XIII deficiency	<10			
Factor VII deficiency	<10			
Afibrinogenemia / hypofibrinogenemia	<10			
Other	<10			

Diagnosis and demographic data

Figure 7 Age distribution of the VastePrik users (N=429) in 2022

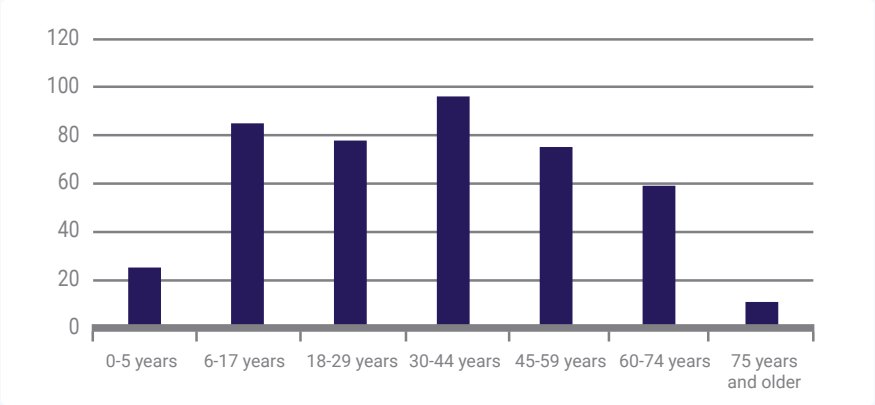
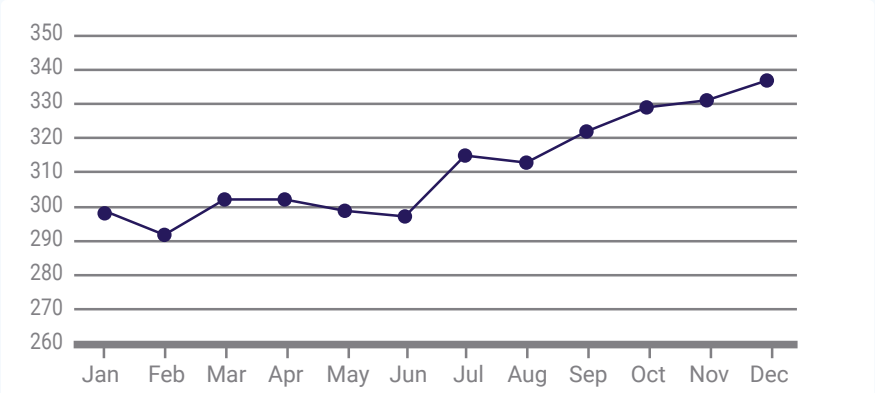


Figure 8 Number of unique VastePrik users each month in 2022



Infusions and bleeds

Table 15 Number of infusions by reason reported in VastePrik in 2022

Reason infusion	Number of infusions	%
Prophylaxis*	19565	90
Precaution (risky activities)	542	2
(Directly following a) Bleed**	1008	5
Aftercare (after a bleed or surgery)	738	3
Total	**21853**	**100**

* Prophylaxis reported by 398 of 429 VastePrik users.
** Bleeds reported by 235 of 429 VastePrik users.
Joint bleeds reported by 154 of 429 VastePrik users.

Table 16 Type of bleeds reported

Type	Number of bleeds	%
Joint	504	50
Muscle	187	19
Subcutaneous	86	8
Mucous membranes	59	6
Other	172	17
Total	**1008**	**100**

Table 17 Location of joint bleeds

Location	Number of bleeds	%
Elbow	142	28
Knee	132	26
Ankle	128	25
Shoulder	29	6
Wrist	17	3
Hip	<10	2
Other	47	10
Total	**504**	**100**

Table 18 Bleed severity

Severity*	Number of bleeds	%
Low	288	29
Average	546	54
High	154	15
Missing	20	2
Total	**1008**	**100**

* Self-report of the VastePrik user.

Table 19 Cause of bleeds

Cause	Number of bleeds	%
Spontaneously	312	31
Overload	268	27
Accident, trauma	260	26
Postoperative	<10	1
Other or missing	163	16
Total	**1008**	**100**

Table 20 Severity of joint bleeds

Severity*	Number of bleeds	%
Low	136	27
Average	278	55
High	87	17
Missing	<10	1
Total	**504**	**100**

* Self-report of the VastePrik user.

Table 21 Cause of joint bleeds

Cause	Number of bleeds	%
Spontaneously	184	36
Overload	161	32
Accident or trauma	103	20
Postoperative	<10	1
Other or missing	53	11
Total	**504**	**100**

Table 22 Reported bleeds in VastePrik in 2022 by user with Hemophilia A or B (selection: regular VastePrik user, mean registration of ≥ 1 prophylaxis infusion each month, N=196).

	Number of participants without bleeds	Number of participants with bleeds	Number of bleeds*	A(J)BR**	
				median (IQR)***	range
All bleeds	70	126	400	1 (0-2.7)	(0-26)
Joint Bleeds	113	83	199	0 (0-1.0)	(0-17)

* Bleeds logged at the same or next day and at the same location are probably incorrectly labelled as 'bleed' instead of 'aftercare' and not counted in.

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

*** Interquartile Range.

Table 23 Most recently used prophylaxis product by VastePrik users with Hemophilia

	Number of users	%
Hemophilia A	**336**	**100**
Product a	187	56
Product b	70	21
Product c	43	13
Product d	19	6
Product e	16	5
Other products*	<10	

	Number of users	%
Hemophilia B	**43**	**100**
Product a	36	84
Other products*	<10	16

* Number of users to small (<10)

Table 24 Most recently used prophylaxis product by VastePrik users with Hemophilia, by type of product

	Number of users	%
Hemophilia A	**336**	**100**
Standard Half Life	89	26
Extended Half Life	59	18
Non Replacement Therapy	187	56
Bypassing Agents	<10	

	Number of users	%
Hemophilia B	**43**	**100**
Standard Half Life	<10	7
Extended Half Life	40	93

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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

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