HemoNED
Dutch Hemophilia Registry

Dutch Hemophilia Registry

Annual report 2018

HemoNED Foundation

April 2019

www.hemoned.nl/en

Foreword

At the end of 2015, after several years of preparation, the development of a nationwide Hemophilia Registry in the Netherlands was finally started. This initiative was a collaboration of all hemophilia treatment centers (HTCs), the Dutch Hemophilia Treaters Society (NVHB), the Dutch Hemophilia Patient Society (NVHP) and the Dutch Hemophilia Nurses Society (NVHV). To cover the legal aspects, the **HemoNED Foundation** was established in October 2016. 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.

The **Dutch Hemophilia Registry** was established in 2017. Unfortunately, actual inclusion of participants could not start before 2018 as the (many) necessary permissions were delayed. In addition to the Registry, the digital infusion log **'VastePrik'** was launched in 2018. VastePrik is available as an app for smartphones and as an online personal web page in order for patients to register their home treatment and bleeds that occur.

We proudly present the first **Annual Report** over the year 2018! With this report we provide a first impression of the data available from the Dutch Hemophilia Registry and the digital infusion log VastePrik. In the long term these data can be used for the aim of the HemoNED Foundation, that is to contribute to an improvement of the quality of care for people with hemophilia and related disorders. We should, however, point out that in this first annual report the amount and completeness of the data are limited and do not represent the whole group of people with hemophilia.

Felix van der Meer, chair HemoNED Steering Committee

The following representatives were part of the HemoNED Steering Committee on 31 December 2018:

- Dr. F.J.M. van der Meer, chair Steering Committee; Expertise center for hemophilia and related disorders LUMC Leiden & HagaZiekenhuis The Hague
- Dr. K. Fischer, Hemophilia Treatment Center Van Creveld Clinic UMC Utrecht
- Prof. Dr. K. Fijnvandraat, Amsterdam UMC location AMC Hemophilia Treatment Center
- Dr. M. Kruip, Erasmus MC Rotterdam Hemophilia Treatment Center
- Dr. B. Laros, Hemophilia Treatment Center Zuid-Oost Nederland Radboudumc Nijmegen & MUMC+ Maastricht & MMC Eindhoven/Veldhoven
- Dr. R. Tamminga, UMC Groningen Hemophilia Treatment Center
- Dr. J. Schipper, NVHP
- N. Uitslager, NVHV

The Steering Committee is supported by the HemoNED Project Office:

- G. Goedhart, Project coordinator
- E.M. Taal; K.M. van Beurden, Data manager

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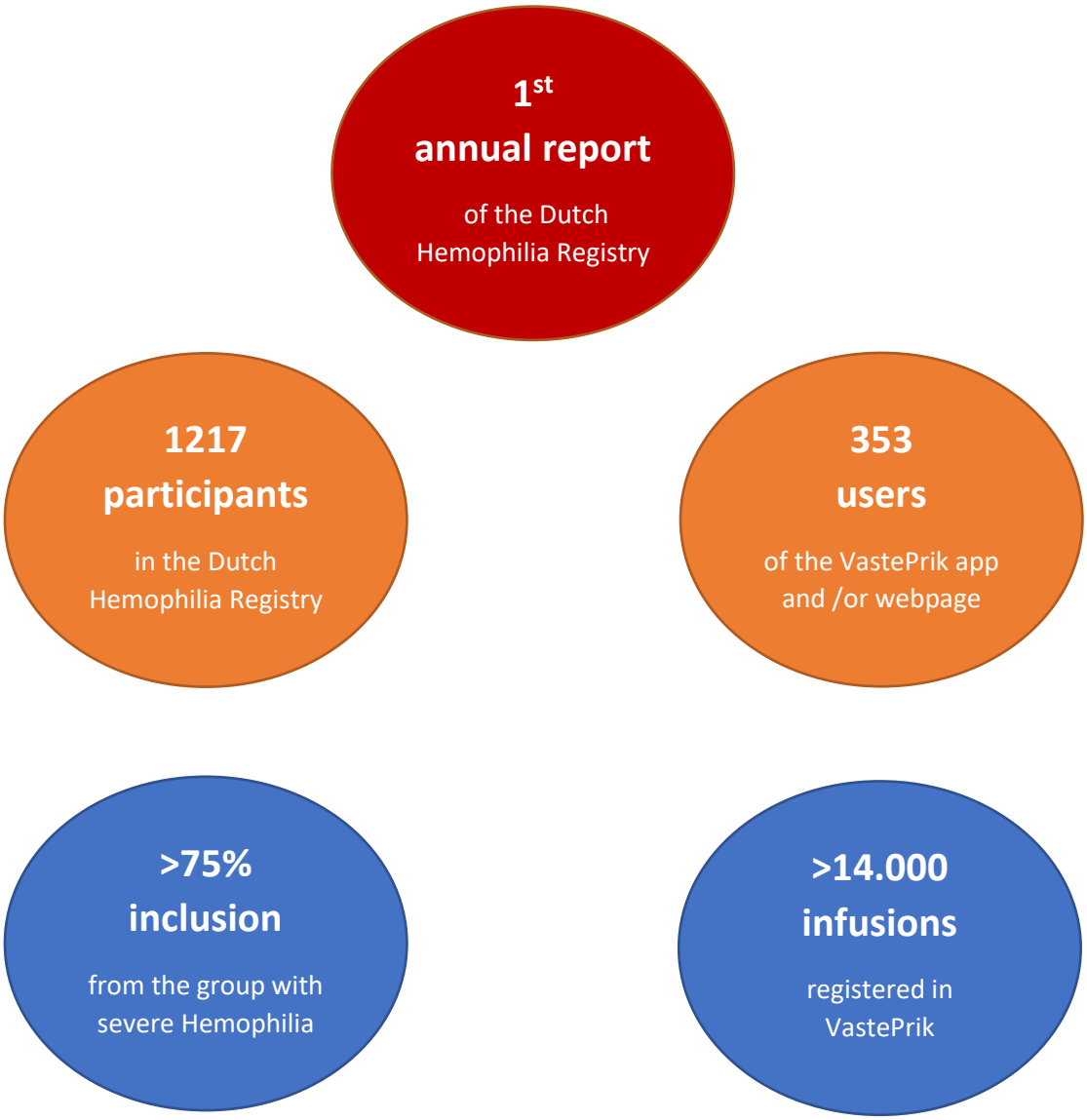

1st
annual report
of the Dutch
Hemophilia Registry
1217
participants
in the Dutch
Hemophilia Registry
353
users
of the VastePrik app
and /or webpage
>75%
inclusion
from the group with
severe Hemophilia
>14.000
infusions
registered in
VastePrik

Introduction

Hemophilia is a congenital anomaly in the body's ability to form blood clots, which can results in bleedings in joints, muscles and organs. Besides Hemophilia A and B there are other bleeding disorders, of which the Von Willebrand disease is the most common form. Nowadays, bleeds can be treated well and even be prevented by administering the missing coagulation factor. However, treatment with coagulation factors is expensive, which is a considerable part of the national care budget.[1]

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. So far, there is a lack of transparency about the total number of people with hemophilia or related disorders in the Netherlands, about coagulation factor use, cost effectiveness and treatment outcomes. Side effects of treatment are being recorded, but the population at risk is unknown. Many other European countries preceded the Netherlands in setting up a national hemophilia registry.

The hemophilia care providers and the hemophilia patient society jointly initiated the set-up of the Dutch Hemophilia Registry ('HemoNED') in 2017. The HemoNED registry aims to document the care and treatment of all people with hemophilia and related disorders with the objective to improve quality of care for this group. By comparing treatments and results the best possible treatments can be searched for. Participants can be compared with each other, but also a comparison between hemophilia treatment centers and with other countries is possible (benchmarking). Side effects of treatment will be registered centrally and forwarded to national (LAREB[2]) and international (EUHASS[3]) safety registries, thereby replacing the registration system of the NVHB ('KWARK'). The anonymized registry data will be used for different purposes such as reports, scientific research and safety studies for drugs. This annual report is a first example of the output.

In April 2018, the digital infusion log 'VastePrik' became available in the form of an app and an online web page. Participants on home treatment can use VastePrik to easily keep track of their infusions and bleeds. The digital infusion log is developed to replace the paper log book (lower workload for care providers who used to manually enter the paper logbook into the computer) and other existing apps (most of them were developed by pharmaceutical companies, data were not available for the care providers). Both the participant and his/her treater have access to an online overview of the registered infusions and bleeds. This is for example used during a consultation with the hemophilia treater to evaluate treatment. VastePrik aims to make the communication between patient and treater easier and clearer, which will improve the quality of care.

Methods

For the Dutch Hemophilia Registry the following participants are eligible: All people in the Netherlands with hemophilia or a related bleeding disorder who are now or in the future documented by one of the national certificated HTCs:

- 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)

Before the inclusion of patients could stared, a lot of approvals had to be obtained: METC (Medical Ethics Review Committee) approval in all hospitals involved, a Study Collaboration Agreement between the HemoNED Foundation in each hospital, and a Data Processing Agreement between MRDM[4] (the developer of the registry and processor of personal data according to the General Data Protection Regulation) and the Board of Directors of all participating centers. After METC approval, a hospital could start to invite possible participants for the Registry. In 2017 the first HTCs started inclusion, the last HTC started in April 2018. As soon as the Data Processing Agreement had been signed, the hemophilia treaters could start to enter data of participants who had signed informed consent in the Registry. The last hospital gained access to the Registry in August 2018. In 2018 the inclusion of people with severe Hemophilia was given priority as agreed with sponsor ZonMw.[5]

The data manager of the HemoNED Foundation visited 5 HTCs in October and November 2018 to monitor the quality of the registration. Apart from the Informed Consent Forms, 5% of the records in the Registry were checked on completeness and accuracy. These control visits were completed satisfactorily.

The data from the Registry and VastePrik are saved into a central database which is hosted by the company MRDM. MRDM provides the HemoNED Foundation with a coded dataset to, among others, compile this annual report. The project office (data manager and project coordinator) analyzed the data as requested by the Steering Committee. The statistical software SPSS was used to perform describing statistical analyses (crosstabs, bar charts). The HemoNED Foundation ensures that all information exported for research and publications will be fully anonymized. To prevent indirect traceability of data to individuals we choose in this annual report to present cells with values lower than 10 as ‘<10’ or to aggregate data with other (sub)categories.[6]

In 2018, the focus was on the inclusion of participants for the Registry and VastePrik and the registration of basic data (demographics, diagnosis). Other variables in the Registry, like treatment plan and viral infections, are not yet completed into the database by some HTCs. Therefore, in each table in this report it is mentioned with ‘total entries completed’ how complete the variable is entered in the Registry.

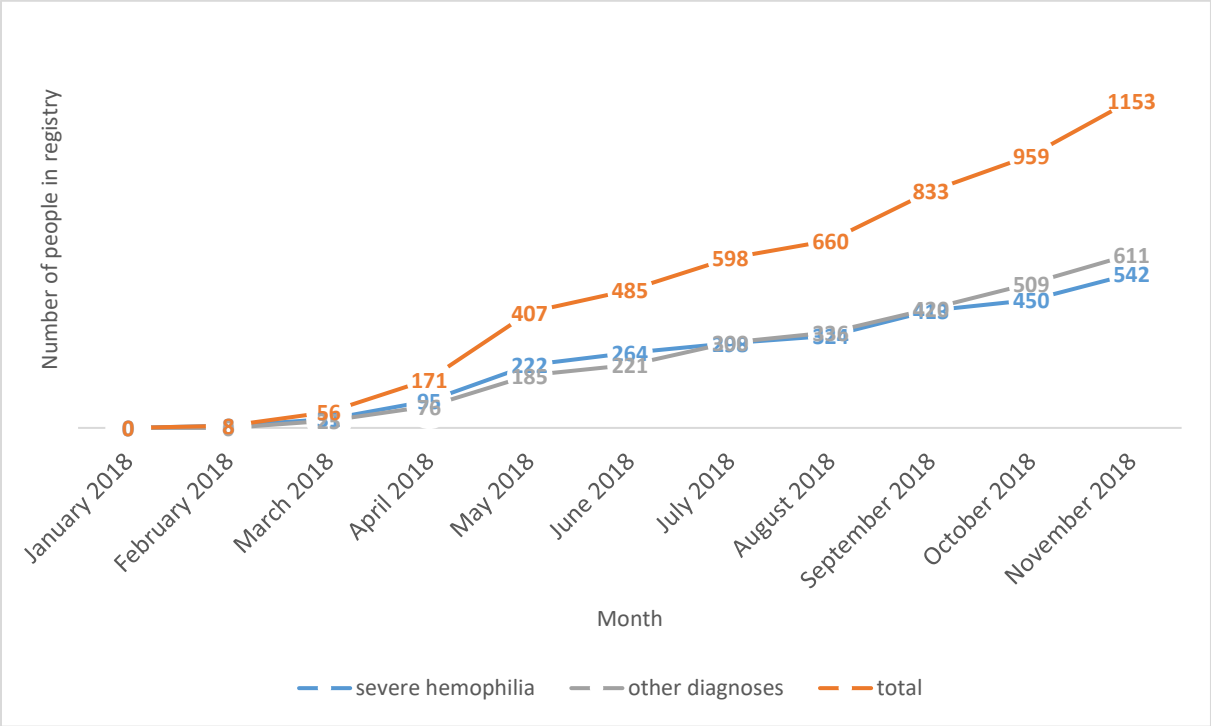
The data of this annual report are from 31 December 2018.

Results Dutch Hemophilia Registry

Please be aware that the tables and figures in this report should be interpreted with great caution! The incomplete data do not represent the total population of people with hemophilia and related disorders.

In 2018, all Hemophilia Treatment Centers in The Netherlands have started enthusiastically to invite and include people with hemophilia and related disorders for the Dutch Hemophilia Registry. Figure 1 shows the timeline of inclusions per month in 2018 as reported by the HTCs. As agreed with the main sponsor ZonMw[5], the priority was set to the inclusion of people with severe Hemophilia; in November 2018, more than 75% of this group had been included. The HTCs counted 62 people who refused to participate in the registry.

Figure 1. Timeline: number of participants included in the HemoNED registry per month in 2018



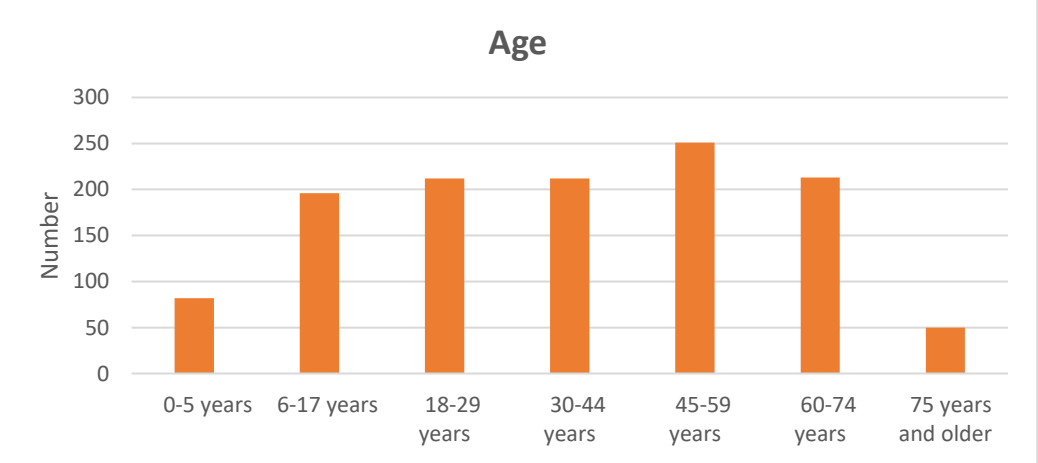
Demographic data

On 31 December 2018 1217 participants were registered in the HemoNED registry. Table 1 and Figure 1 show some demographic characteristics of this group. The vast majority (1060, 87%) of participants is male. With regard to age, there are 278 children (0-17 years) and 938 adults registered. A relatively small percentage (4%) is 75 years or older. The mean age was 38 years.

Table 1. Number of unique participants in the HemoNED registry, by gender and age.

Gender/Age	Number of participants	%
Total in registry	**1217**	**100**
Gender		
Total completed	1215	100
Man	1060	87
Woman	155	13
Age (years)		
Total completed	1216	100
0-5	82	7
6-17	196	16
18-29	212	17
30-44	212	17
45-59	251	21
60-74	213	18
≥75	50	4

Figure 2. Age distribution of participants in the HemoNED registry.



Diagnosis

About 80% of participants in the HemoNED registry have the diagnosis Hemophilia A or B; more than half of them (57-59%) have the severe form (*Table 2; Figure 3*). The number of participants with severe Hemophilia in table 2 (source: registry data) does not correspond with figure 1 (source: reports from HTCs) because the diagnostic information in the registry is incomplete. Twelve percent of the participants have Von Willebrand disease, about half of them (49%) type 1 (*Figure 4*).

Table 2. Number of participants in the HemoNED registry by diagnosis.

Diagnosis	Number of participants	%
Total Diagnosis completed	**1134**	**100**
Hemophilia A	**797**	**70**
Total Severity completed	779	100
Severe	444	57
Moderate	109	14
Mild	226	29
Hemophilia B	**109**	**10**
Total Severity completed	107	100
Severe	63	59
Moderate	17	16
Mild	26	25
Hemophilia B Leyden	**16**	**1**
Von Willebrand Disease	**140**	**12**
Total Type completed	139	100
Type I	68	49
Type 2A	20	14
Type 2B	20	14
Type 3	20	14
Other (sub)types*	11	8
Other bleeding disorders	**38**	**3**
Total disorders completed	38	100
Factor VII deficiency	10	26
Other bleeding disorders*	28	74
Acquired bleeding disorders	**< 10**	**< 1**
Carrier	**32**	**3**
Total diagnosis completed	32	100
Hemophilia A	22	69
Hemophilia B	10	31

**Subcategories <10*

Figure 3. Participants in the HemoNED registry, by diagnosis and severity (Hemophilia A & B).

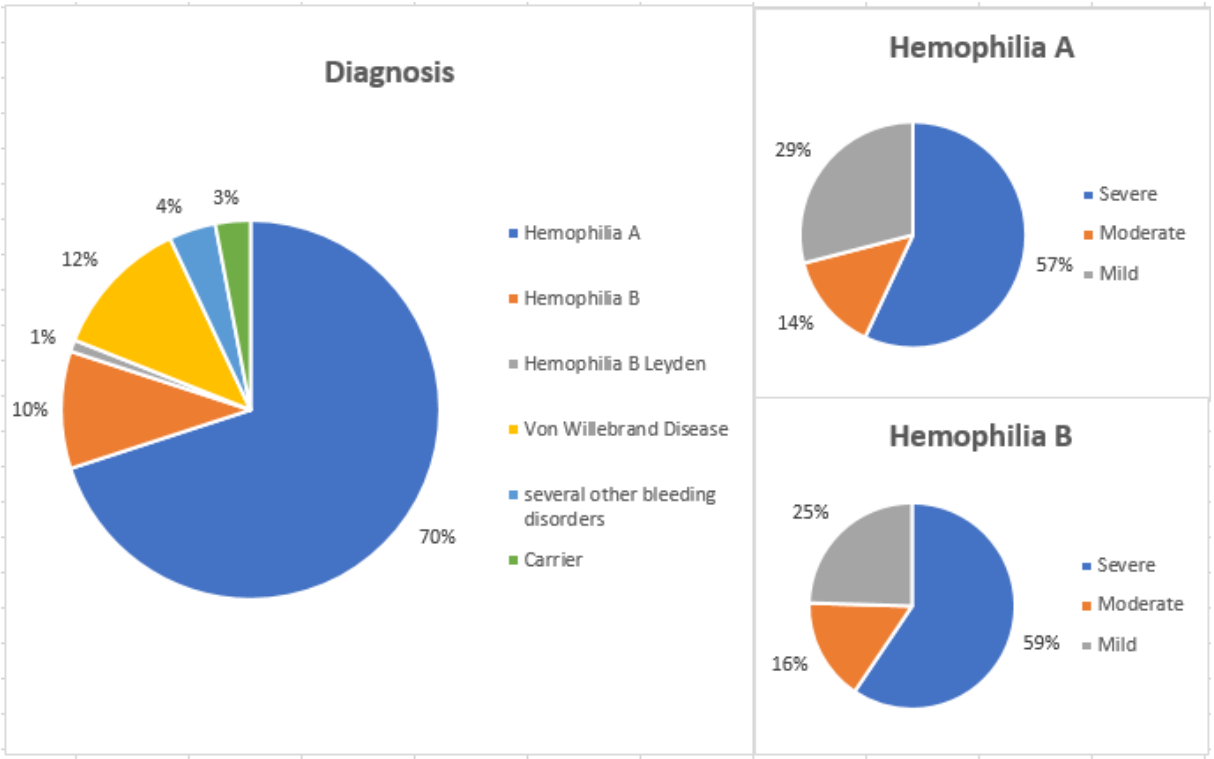
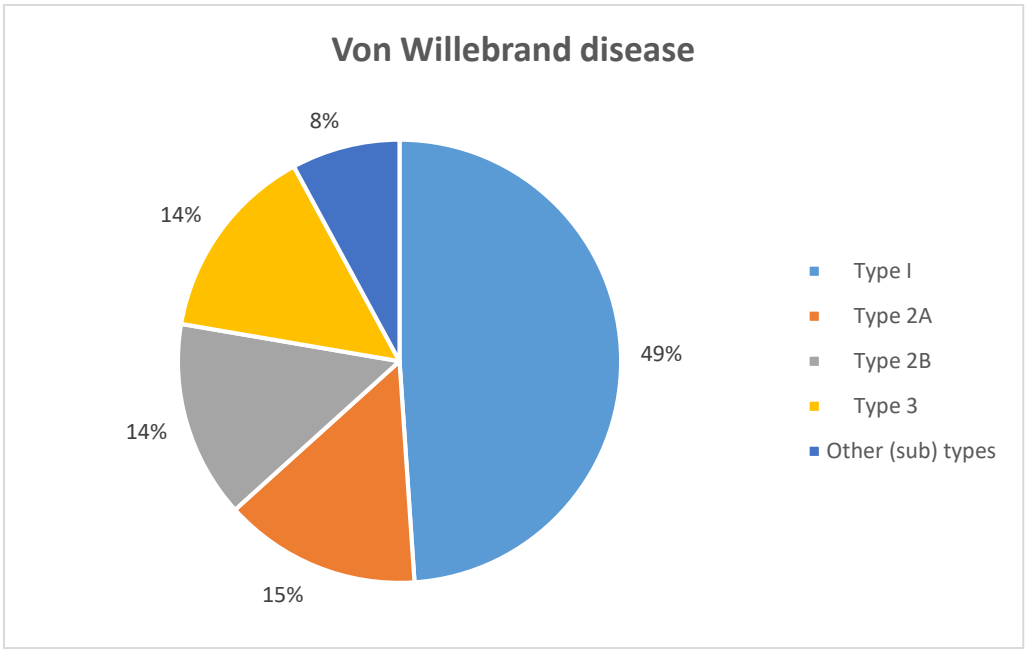


Figure 4. Participants with Von Willebrand disease, by type of the disease.



Viral infections

Up to now for 384 (42%) participants with Hemophilia A or B it is completed in the HemoNED registry if they suffer or suffered from an infection with HIV, Hepatitis B or Hepatitis C. Nearly 30% of the participants with Hemophilia have experienced one or more viral infections (*Table 3*).

Table 3. Number of participants – with diagnosis Hemophilia – that suffer(ed) from a viral infection.

Viral infection (now/in the past)	Number of participants	%
Total completed	**384**	**100**
Suffer(ed) from viral infection		
No	241	63
Yes	111	29
HIV infection*	<10	
Hepatitis B infection*	39	
Hepatitis C infection*	103	
Unknown	32	8

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

Treatment

For 32 percent of the participants with severe Hemophilia A or B it is recorded in the registry if they use prophylactic treatment. Within this group 93% is on prophylaxis *(Table 4)*.

Table 4. Number of participants – with diagnosis severe Hemophilia – on prophylaxis.

Prophylaxis	Number of participants	%
Total completed	**164**	**100**
Prophylactic treatment		
No	11	7
Yes	153	93

For nearly 30 percent of the participants a treatment plan has been registered in the HemoNED registry, including the prescribed treatment product *(Table 5)*. This does not imply that the participant really used this product in the year 2018.

Table 5. Number of participants in HemoNED registry by prescribed treatment product.

Product	Number of participants	%
Total completed	**347**	**100**
FVIII		
Product A	114	33
Product B	75	22
Product C	28	8
Product D	13	4
Product E	11	3
Product F	11	3
FIX		
Product H	35	10
Product I	11	3
Other products*	49	14

**Number of other products to small (<10)*

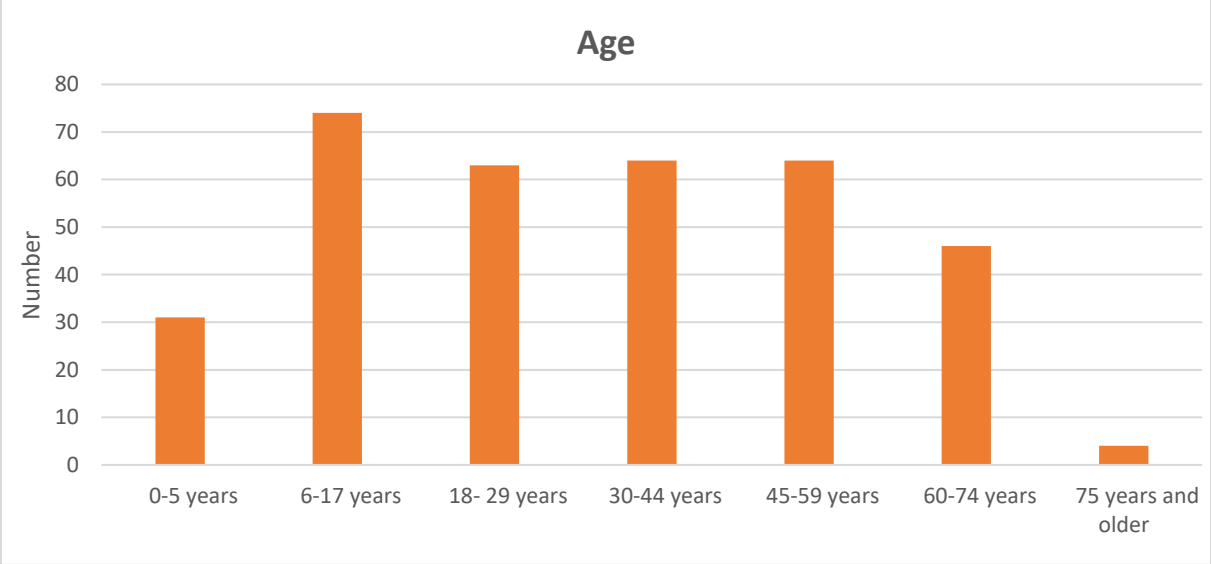
Results VastePrik

From April 2018 more than 900 participants of the HemoNED registry requested a personal account for using VastePrik, the digital infusion log. December 31st 2018 353 unique participants had registered one or more infusions or bleeds in VastePrik. Since VastePrik is only used for a short period now and the number of users is relatively small, only part of the VastePrik data is presented in this annual report.

Demographic data

Although participants of all ages use VastePrik it is most commonly used by (parents from) children between 6 and 17 years old (*Figure 5*). The number of users in the oldest age group (75 years and older) is limited.

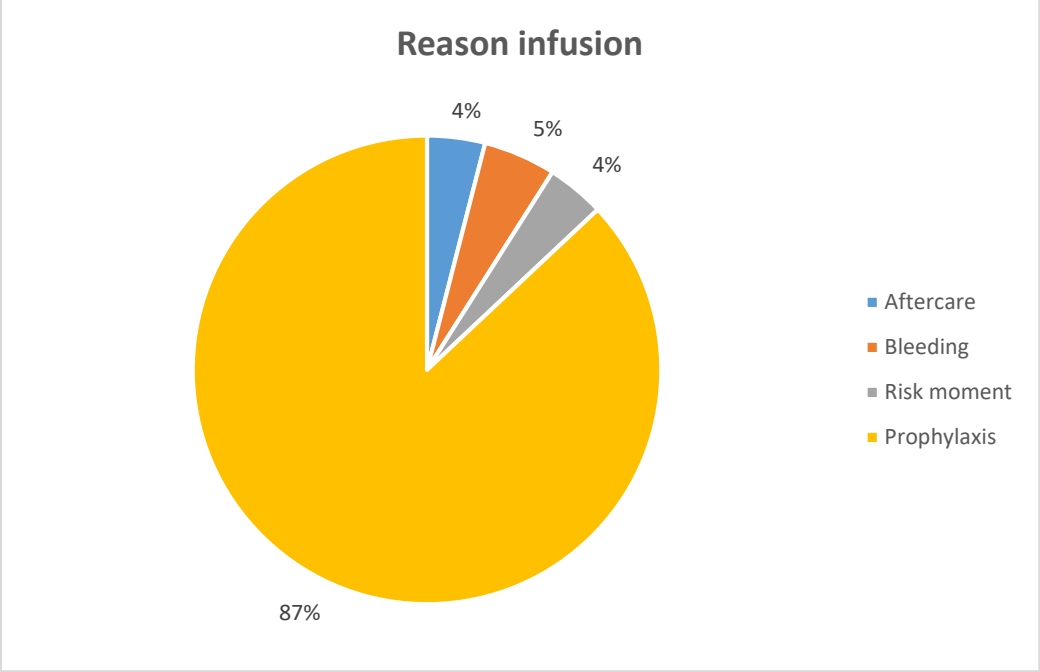
Figure 5. Age distribution of the VastePrik users.



Treatment

In total, more than 14.000 infusions have been registered in VastePrik. Most infusions (87%) were prophylactic treatment (*Figure 6*).

Figure 6. VastePrik registrations, reasons of infusion (n=14.539).



Conclusion

The first annual report from the Dutch Hemophilia Registry is now a fact. Although the presented data are limited, it gives insight into the available data and the possibilities for the future. In 2019, inclusion of participants continues and completeness of variables in the registry will be improved. Furthermore, adverse drug reactions will be registered and VastePrik will start to provide valuable data.

Reference list

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2. https://www.lareb.nl/en/
3. http://web.euhass.org/
4. https://mrdm.nl/en/
5. https://www.zonmw.nl/nl/onderzoek-resultaten/doelmatigheidsonderzoek/programmas/project-detail/goed-gebruik-geneesmiddelen/dutch-registry-of-patients-with-hemophilia-and-associated-disorders/
6. Washington State Department of Health. *Guidelines for Working with Small Numbers.* Revised October 2012.

Support

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

- The Netherlands Organisation for Health Research and Development (ZonMw), programme 'Goed Gebruik Geneesmiddelen'[5]
- Bayer
- CSL Behring
- Novo Nordisk
- Octapharma
- Pfizer
- Sanquin
- Shire/Takeda
- Sobi

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