PedNet Haemophilia Research Foundation

PedNet

Annual report 2025
PedNet cohort studies

Data export January 2026

On behalf of the PedNet study group

Beatrice Nolan, MD
Chair of the management board

Gili Kenet, MD
Director of the PedNet Haemophilia Research Foundation

Contents

PedNet (the European Paediatric Network for Haemophilia Management) started in 1996 as a collaboration of 22 paediatricians in 16 European countries. PedNet was initiated to provide an infrastructure for clinical research on the management of children with haemophilia. Currently the PedNet study group consists of 34 haemophilia treatment centres in 19 countries.

The PedNet Registry started in 2003 and, in order to prevent selection bias, is set up as a birth cohort. It collects real-life data from all newly diagnosed children treated in the participating centres. Data are collected through well-defined e-CRF forms that contain details on all aspects of haemophilia from birth to adolescence and adulthood.
Patients with FVIII/IX levels up to 25%, born from 1 January 2000 are included in the PedNet Registry. Annual data exports are used for analysis of ongoing studies.

The PedNet Haemophilia Research Foundation was founded in December 2016 in The Netherlands and is the legal owner of the database and all its assets.

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Astrid Lindgren Children's hospital
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Ester Zápotocká, MD
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Fernando Pinto, MD
Department of Haematology
Royal Hospital for Sick Children,
Yorkhill
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Key numbers

3104 boys (1942 severe)

27 girls (4 severe)

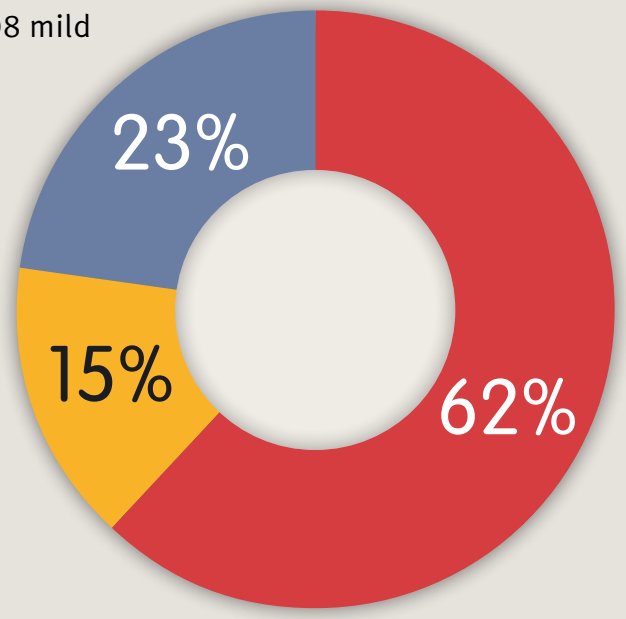
138 new patients included in 2025

Included patients according to disease severity

1946 severe

477 moderate

708 mild



1689 PUPS with severe haemophilia A

64 new severe haemophilia A PUPs in 2025

257 PUPs with severe haemophilia B

20 new severe haemophilia B PUPs in 2025

34 participating centers in 19 countries

Detailed data on gene mutation available in 86% of all patients

Total number of follow up years 31,206

Data export January 2026

Key numbers

Follow up data

82%

severe haemophilia A patients reached 50 exposure days.
Lost to follow up during first 50EDs is 2%

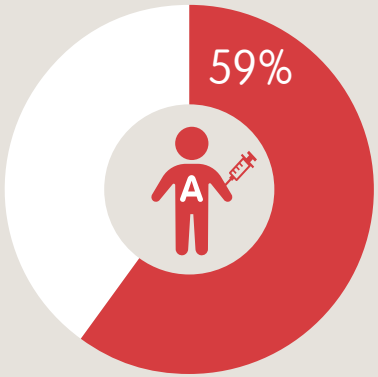
A

86%

severe haemophilia B patients reached 50 exposure days.
Lost to follow up during first 50EDs is 4%

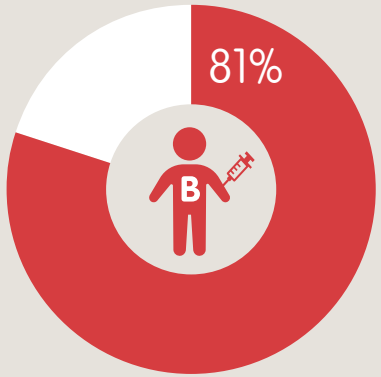
B

Start prophylaxis



1001

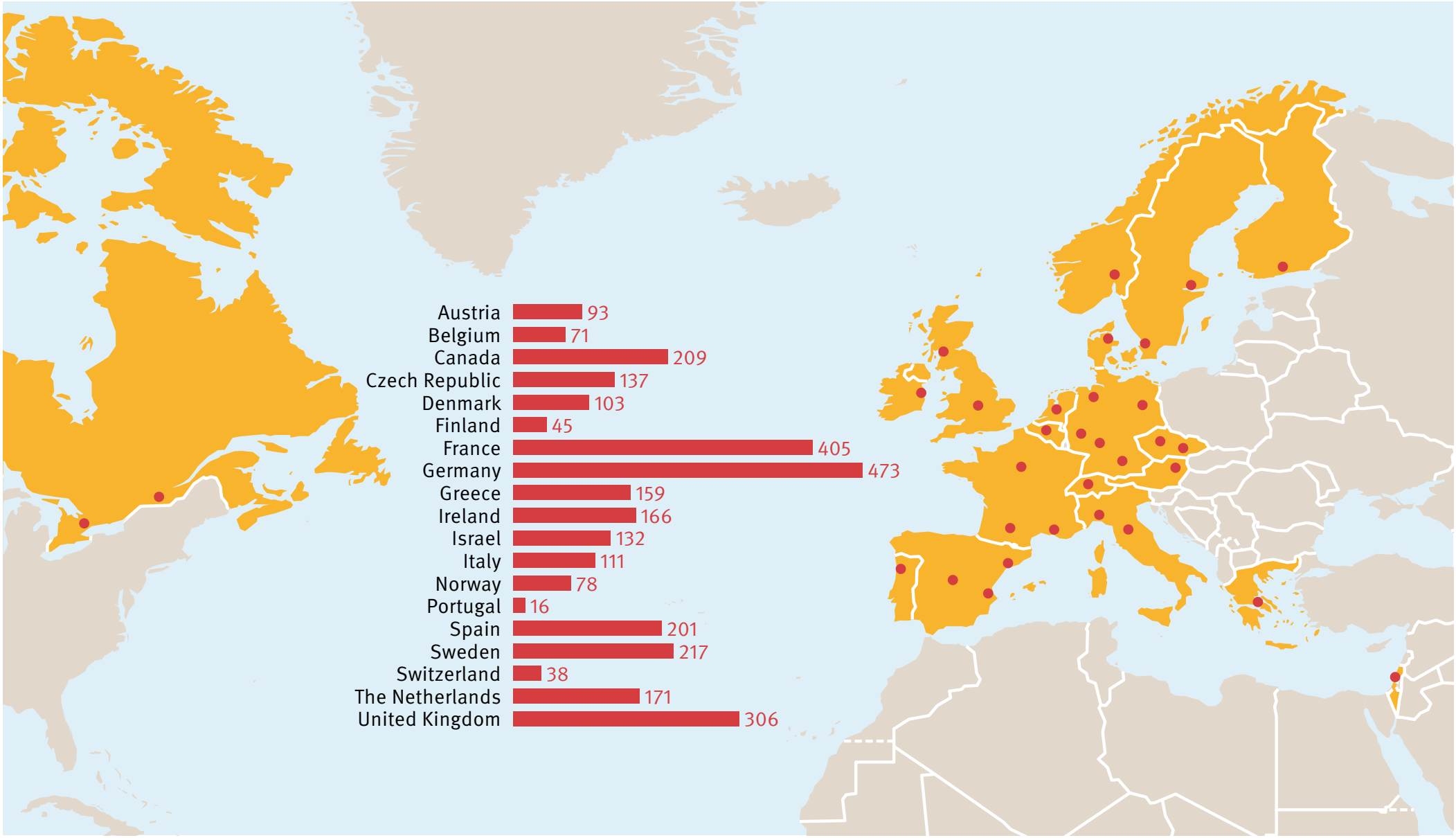
Severe haemophilia A patients started prophylaxis(CFC) before (‹) ED50.
Minimum of 2 consecutive months.
Median age at start in years is 1.2 (IQR 0.9–1.8)



208

Severe haemophilia B patients started prophylaxis (CFC) before (‹) ED50.
Minimum of 2 consecutive months.
Median age at start in years is 1.3 (IQR 0.9–2.0)

Participating countries and numbers of included patients



Data export January 2026

Introduction

The PedNet study group (the European Paediatric Network for Haemophilia Management) is a collaboration of now 34 haemophilia treatment centres (HTCs) in 19 countries, including Canada (Montreal and Toronto) and Israel. The PedNet cohort studies include all patients with FVIII/IX levels up to 25%, born from 1 January 2000 onwards and treated at one of the participating HTCs.
On 16 December 2016, the PedNet Haemophilia Research Foundation was founded in Amsterdam. The Foundation was instituted to incorporate the PedNet study group and to ascertain that it can continue to function in the future. More information can be found on the PedNet website: www.pednet.eu.
This report provides an overview of the status of the PedNet registry up to January 2026 and of the research activities performed by the PedNet study group in 2025. More information on all research activities can be found in the Research programme 2024-2026, see https://pednet.eu/pednet-group.

Mission of the PedNet Haemophilia Research Foundation

The mission of the PedNet Foundation is to improve the current and future care of children with haemophilia by collecting of high-quality data from a large cohort of unselected previously untreated children with haemophilia A and B, thus enabling front-line research projects on inhibitor development, safety, efficacy of replacement and non-replacement therapies, and long-term outcome. The foundation is not-for-profit and publishes annual reports on activities and financial reports. The reports can be found on https://pednet.eu/foundation/anbi.

PedNet Registry

The protocol of the PedNet Registry follows the EMA guideline on registry-based studies (EMA/426390/2021). Well-defined clinical parameters are collected through a secured data capture system (Castor EDC). For participating centres a minimum inclusion rate of 90% of all newly diagnosed patients is mandatory.
PedNet has consortium agreements with the participating centres and they are compensated for the new inclusions and follow-up data entry.
Data of all included patients are regularly updated and they are checked for validity and completeness during the year. Yearly data exports are performed every January and used for new studies in that particular year.

Monitoring

Data collected in the PedNet Registry are monitored to improve data quality.
This is done by built-in checks in the e-CRF and regular data checks on exports.
Coordinators employed by the foundation are in frequent contact with centres and perform regular checks on the inclusion of new patients and follow-up data entry.
On-site monitoring of source data and informed consent is performed by an independent research organisation according to a predefined monitor plan.
The PedNet centres agreed together that 100% of baseline data and informed consent forms are checked with the medical files in the centres. For 10% of the patients, all exposure days and follow-up data are checked.

Current status

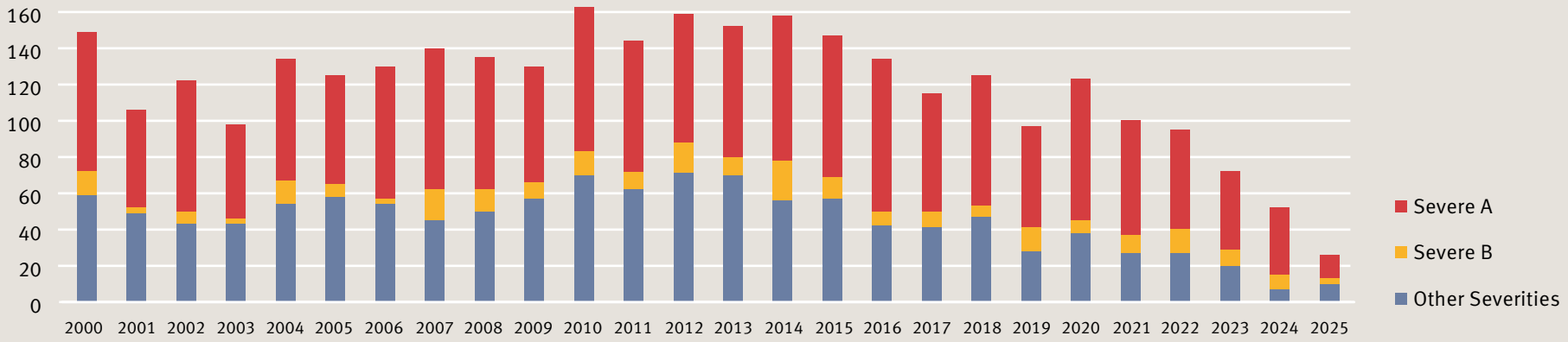
As of 1 January 2026, a total of 3131 previously untreated patients (PUPs) with haemophilia A or B are included in the registry. Of these, 1689 have severe haemophilia A (64 more than last year) and 257 have severe haemophilia B (20 more than last year) (see Appendix 1). 1609 (83%) of the severe haemophilia patients (A plus B) have reached 50 exposure days. Data on gene defects are available for 2707 (86%) patients included in the registry.

Start prophylaxis

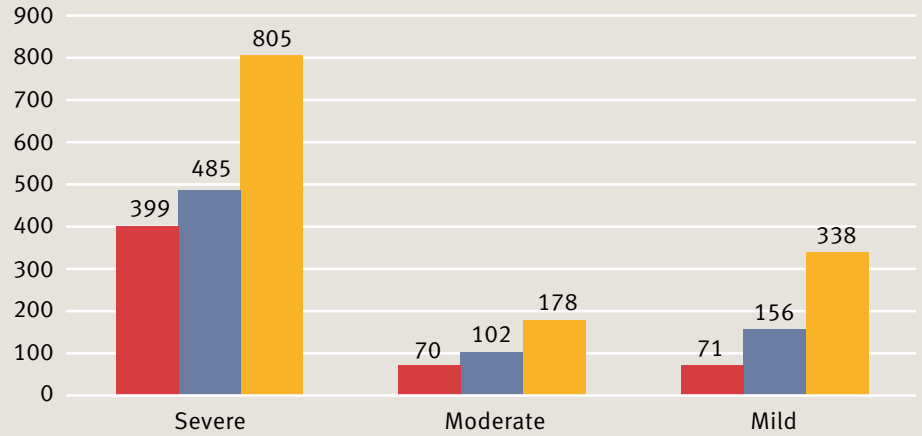
A total of 1402 patients started prophylactic treatment with clotting factor concentrate before ED50 and with a minimum duration of 2 months. Of these, 1001 were severe A patients and 208 were severe B patients. The median age at start prophylaxis was 1.2 years for severe A and 1.3 years for severe B patients.

Tables & Figures

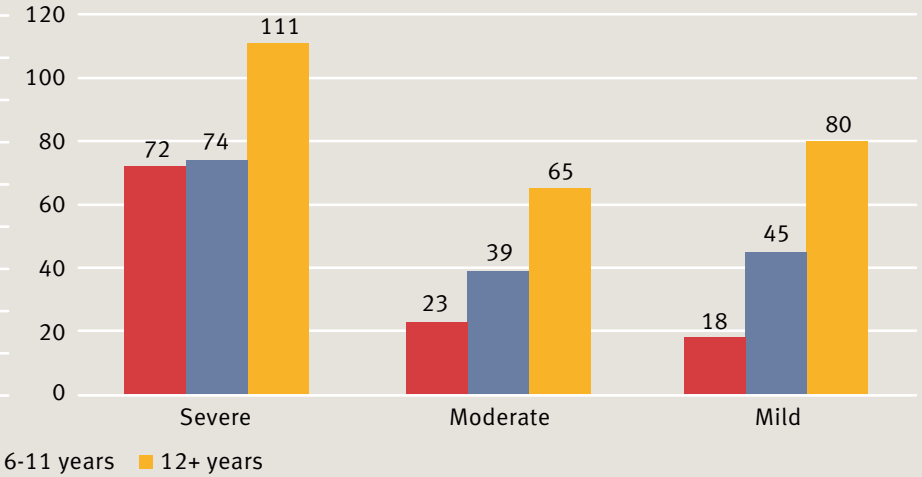
N Patients per birth year



Current age haemophilia A



Current age haemophilia B



Tables & Figures

Haemophilia A

	Severe	Moderate	Mild	Total HA
Baseline	1,689	350	565	2,604
Girls	3	4	10	17
Known gene mutations	1,541	278	439	2,258 (87%)
At least 50 EDs	1,387 (82%)	193	77	1,657
Inhibitors	486	32	12	530
Follow-up data	1,649	341	558	2,548 (98%)
Total FU years	17,251	3,397	5,595	26,243
Lost to follow-up during first 50 EDs*	41 (2%)	36	166	243 (9%)

* excl. patients =›16 yrs & discontinued centres

Haemophilia B

	Severe	Moderate	Mild	Total HB
Baseline	257	127	143	527
Girls	1	3	6	10
Known gene mutations	230	108	111	449 (85%)
At least 50 EDs	222 (86%)	70	15	307
Inhibitors	22	0	0	22
Follow-up data	251	125	140	516 (98%)
Total FU years	2,412	1,221	1,329	4,962
Lost to follow-up during first 50 EDs*	9 (4%)	28	43	80 (15%)

* excl. patients =›16 yrs & discontinued centres

Display of PedNet Numbers

	2020	2021	2022	2023	2024	2025	2026
Baseline	2,304	2,409	2,576	2,759	2,886	2,933	3,131
Known gene mutations	1,958	2,071	2,219	2,373	2,479	2,601	2,707
At least 50 exposure days	1,483	1,550	1,653	1,737	1,844	1,893	1,964
Patients with follow-up data	2,203	2,314	2,472	2,633	2,790	2,909	3,064

Adverse events in 2024 & 2025*

		Inhibitor	No inhibitor	Total
Total events		5	5	10
Type of adverse event	Allergic reaction	3	2	5
	Thromboembolic event	0	0	0
	Thrombotic microangiopathy	0	0	0
	Neurological event (other than ICH**)	0	1	1
	Local subcutaneous reaction	1	1	2
	Death	0	0	0
	Other	1	1	2

* reporting of adverse events may be delayed, as centres first report to national and local authorities

** ICH = intracranial haemorrhage

Activities of PedNet Working Groups

Research projects are structured into working groups, each with one chair, 5-8 members, and analytic and administrative support from the study staff in The Netherlands. All planned research activities of the PedNet study group can be found in the Research Programme 2024-2026 https://pednet.eu/pednet-group. For full publication list see https://pednet.eu/publications.

Genetic working group

Haemophilia B Leyden is a unique form of haemophilia B in which the endogenous factor IX levels rise over time. The genetic working group aimed to explore the natural history of these patients, assess the association between genetic variants, follow the rise in endogenous factor IX levels over time, and explore treatments and bleeding phenotype. Twenty four children with the HB Leyden phenotype were identified. The variant c.-36G>A was found in over 50% of the cases, FIX increase occurred at a very young age, and this variant was associated with low bleeding rates in contrast to children with a non-c.-35G>A variant. The manuscript has been accepted for publication in Journal of Thrombosis and Haemostasis (doi: 10.1016/j.jtha.2024.12.020).

Haemophilia B working group

In 2020, a paper on the inhibitor incidence in severe haemophilia B was published: Inhibitor incidence in an unselected cohort of previously untreated patients with severe haemophilia B: A PedNet Study *(Male et al., Haematologica 2020)*. A manuscript on patients with severe haemophilia B and an inhibitor and their response to ITI is underway.

Working group on long-term outcome

Children in PedNet are followed from diagnosis until adulthood. The collection of data on validated outcome tools started in 2018. In 2021, a pilot project was performed on data of 141 patients (100 without inhibitors, and 41 with current/past inhibitors) from 5 PedNet centres with the aim to explore the feasibility to answer several research questions on long-term outcome. The results showed that most adolescents had a favourable joint health, while patients with inhibitors showed a two-fold increased proportion with joint deterioration as assessed by Haemophilia Joint Health Score. Project results are described in the article: *Long-term joint outcomes in adolescents with moderate or severe haemophilia A (Schmidt et al)*, which has been published in Haemophilia in 2022.
The succeeding project started in 2022: to compare treatment and joint health status in Greek and Swedish children with severe haemophilia on prophylactic treatment. The results have recently been published in Haemophilia (http://doi.org/10.1111/hae.70140).

Working group on intracranial haemorrhage

Intracranial haemorrhage (ICH) is a major bleed causing morbidity and death. Children with haemophilia have a significantly higher risk of ICH compared to the normal population. Neonatal ICH has the highest known incidence for ICH. Prophylaxis with factor concentrate reduces the risk for ICH. New treatment options (non-replacement therapies such as emicizumab) have reached the market and could be given early in life. The aim of the study was to assess how many ICHs in children with haemophilia could be prevented by earlier start of prophylaxis.
It has recently been accepted for publication by Haematologica (doi: 10.3324/haematol.2024.285874). The succeeding project started in 2025. This project aims to shine light on bleeding in the first 3 months of life in children with haemophilia.

Working group on novel therapies

As many new concentrates and alternative therapies are currently entering the market for haemophilia, the PedNet study group sees the need to study both the safety and the efficacy of these new therapies. The study group conducted a survey on the implementation of emicizumab in the PedNet centres. The results of the survey were accepted for publication in Haemophilia (doi: 10.1111/hae.14847).
A project on 80 previously untreated patients (PUPs) and minimally treated patients (≤5 EDs to FVIII; MTPs) using emicizumab, was started in 2025, presented during the ASH conference in December 2025, and is currently under review for publication.
A project on previously treated patients (PTP) and inhibitor development and recurrence, while on emicizumab prophylaxis is currently in progress.

Working group on bleeding

Bleeding in non-severe haemophilia

Novel therapies, including modified replacement therapy and gene therapy, provide an opportunity to substantially increase baseline FVIII activity levels, or to (partially) correct haemostasis. Information on bleeding phenotype in non-severe haemophilia provides the best possible information regarding the optimum target for prophylactic treatment. The aim of this project is to assess bleeding according to baseline FVIII activity in children with non-severe haemophilia A. Data on comparing non-severe haemophilia A and B was presented at the ISTH in July 2022. At the same congress, a poster focused on bleeding in non-severe haemophilia A was presented. The manuscript has been accepted for publication by Journal of Thrombosis and Haemostasis (doi: 10.1016/j.jtha.2024.05.030). A manuscript on prophylaxis in non-severe haemophilia is currently in preparation for publication.

Bleeding pattern in severe haemophilia A and B on prophylaxis

Few data exist on long-term follow-up of type and frequency of bleedings in children up to 18 years with severe haemophilia on primary prophylaxis with FVIII/FIX.
The aim of this study is to compare real-world data of bleeds between different age groups in children with severe haemophilia A or B on primary prophylaxis. Data was presented at the ISTH in July 2022. A full manuscript was accepted by JTH in 2025 (https://doi.org/10.3324/haematol.2025.288101).

Publications PedNet study group 2024 & 2025

2025

Michalopoulou A, Ranta S, G. Andersson N, Fischer K, de Kovel M, de Boer-Verdonk E, Motwani J, Kenet G, Pergantou H.
Differences between Sweden and Greece in joint outcomes assessed by ultrasound in adolescents with severe hemophilia on prophylaxis: Data from the PedNet Registry.
http://doi.org/10.1111/hae.70140 PMID: 41069334

Ranta S, de Kovel M, Olivieri M, Fischer K, Castaman G, Königs C, Oldenburg J, Pergantou H, Male C, van den Berg HM.
Benchmarking prophylaxis with factor concentrates: reference data on annualized bleeding rates in children with severe hemophilia.
https://doi.org/10.3324/haematol.2025.288101 PMID: 40874346

Carcao M, Königs C, G. Andersson N, de Kovel M, de Boer-Verdonk E, Motwani J, Blatny J, Olivieri M, van den Berg HM, Fischer K.
Predictors of ITI success in 231 children with severe hemophilia A with high titer inhibitors – lessons learned from the PedNet prospective cohort study.
https://doi.org/10.1016/j.jtha.2025.07.010 PMID: 40706963

Mendoza A, Rivas I, Benítez Hidalgo O, Rosa Cid AR, Olivieri M, Ranta A, Labarque V, G. Andersson N, de Kovel M, Álvarez-Román MT, the PedNet Study Group.
Impact of Family History of Haemophilia on Diagnosis, Management and Outcomes in Severe Haemophilia.
http://doi.org/10.1111/hae.70018 PMID: 40444652

de Kovel M, van Haaster AC, Carcao M, Ranta S, Glosli H, Rivard GE, Kenet G, Kurnik K, Van Geet C, Carvalho M, G. Andersson N, Kartal-Kaess M, Ljung R, van den Berg HM, the PedNet Study Group
Blood Group O does not increase the risk of inhibitors in severe haemophilia A: Data from the PedNet Study Group.
https://doi.org/10.1111/hae.70035 PMID: 40123267

Ranta S, Zapotocka E, G. Andersson N, Fischer K, Kenet G, de Kovel M, Königs C, Labarque V, Male C, Olivieri M, Motwani J, the PedNet Study Group.
A survey on clinical practice in monitoring and management of bleeding in children with haemophilia A on emicizumab prophylaxis in the PedNet centres.
https://www.sciencedirect.com/science/article/pii/S0049384825000568
PMID: 40120320

2024

Kartal-Kaess K, Pinto F, Labarque V, de Kovel M, Nolan B, Carcao M, d'Oiron R, Stamm Mikkelsen T, Ljung R, G. Andersson N, the PedNet Study Group.
Hemophilia B Leyden: Characteristics and natural history in the PedNet Registry.
https://www.sciencedirect.com/science/article/abs/pii/S1538783624007694
PMID: 39742973

G. Andersson N, de Kovel M, Castaman G, d'Oiron R, Kenet G, Königs C, Male C, Nolan B, Olivieri M, Pinto F, Sigurgisladottir S, Zapotocka E, Fischer K, the PedNet Study Group.
Intracranial hemorrhage before start of prophylaxis in children with hemophilia: incidence, timing, and potential for prevention.
https://pubmed.ncbi.nlm.nih.gov/39605212/ PIMD: 39605212

de Kovel M, Escuriola-Ettingshausen C, Königs C, Ranta S, Fischer K, the PedNet Study Group.
Bleeding phenotype according to factor level in 825 children with non-severe hemophilia; data from the PedNet cohort.
https://doi.org/10.1016/j.jtha.2024.05.030 PMID: 38866249

Van der Zwet K, de Kovel M, Motwani J, Van Geet C, Nolan B, Glosli H, Escuriola Ettingshausen C, Königs C, Kenet G, Fischer K, the PedNet Study Group. *Bleeding control improves after switching to emicizumab: Real-world experience of 177 children in the PedNet registry.* https://onlinelibrary.wiley.com/doi/10.1111/hae.15015 PMID: 38578720

Fischer K, Kenet G, Kurnik K, Carcao M, Oldenburg J, Stamm-Mikkelsen T, Cid Haro AR, Koskenvuo M, Blatny J, Königs C, the PedNet Study Group. *Determinants of bleeding before and during immune tolerance in 222 boys with severe hemophilia A and inhibitors >5BU.* https://www.sciencedirect.com/science/article/pii/S2473952923006249 PMID: 38214949

For full publication list see www.pednet.eu/publications

Abstracts & Presentations

EAHAD 2025 Milan	Poster	Real world experience of emicizumab prophylaxis started in PUPs and MTPs with severe haemophilia A
EAHAD 2025 Milan	Poster	Association of bleeding rate and ABO blood group with prophylaxis in non-severe haemophilia A
GTH 2025 Lausanne	Poster	Haemophilia B Leyden: Characteristics and natural history in the PedNet Registry
ASH 2025 Orlando	Oral	Emicizumab prophylaxis in PUPs and MTPs with severe haemophilia: the PedNet real world experience in 80 infants

Sponsor page

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- Swedish Orphan Biovitrium AB
- Takeda

Correspondence

PedNet Haemophilia Research Foundation
Mollerusstraat 1
3743 BW Baarn
The Netherlands
info@pednet.eu

Study staff

Gili Kenet, MD
Director

Angelique Hermeling
Foundation Coordinator

Marloes de Kovel, MSc
Epidemiologist / Data Manager

Marieke Blom-Smink, MSc
Registry Coordinator

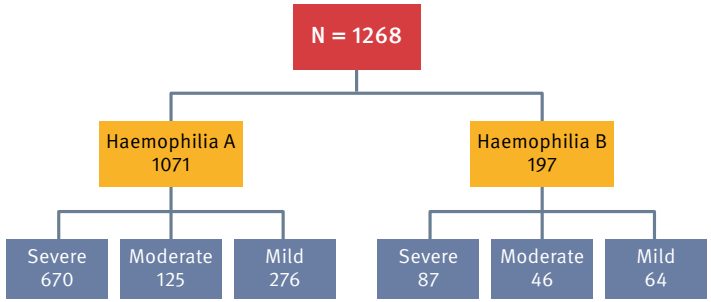
Kathelijn Fischer MD, PhD
Senior Epidemiologist

Marjolein Blits, MSc
Data Manager / Junior Epidemiologist

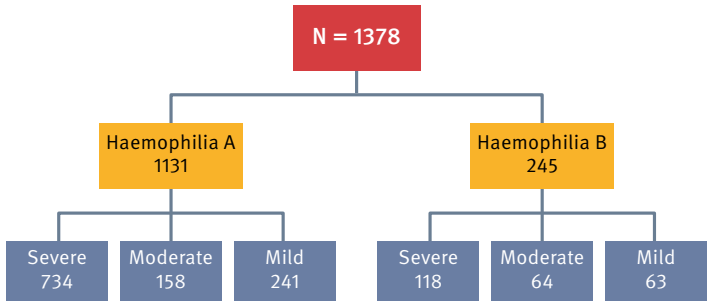
Participants PedNet Annual Meeting Vienna, 2025

Appendix 1 Flowcharts January 2025

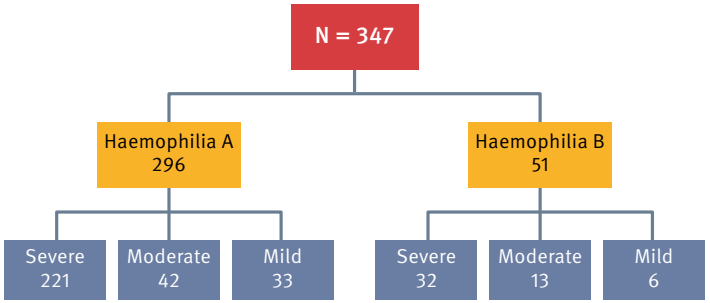
PedNet Birth Cohort 1 (2000 - 2009)



PedNet Birth Cohort 2 (2010 - 2019)

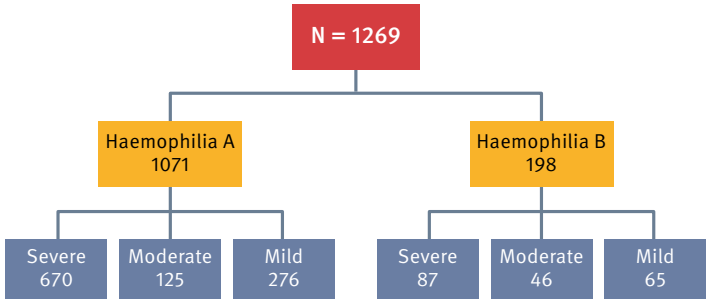


PedNet Birth Cohort 3 (2020 - 2029)



Appendix 2 Flowcharts January 2026

PedNet Birth Cohort 1 (2000 - 2009)



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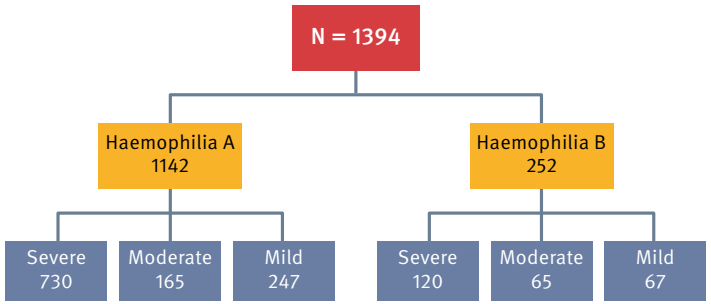

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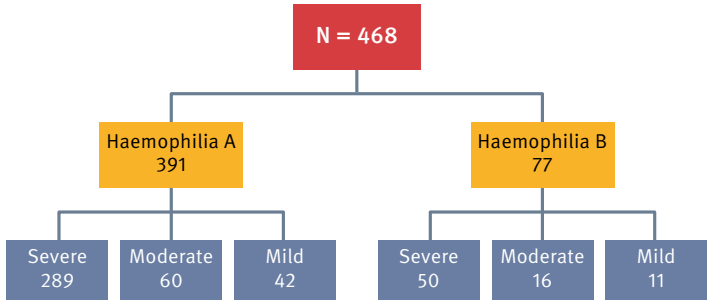

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PedNet

www.pednet.eu

info@pednet.eu