UKHCDO

UNITED KINGDOM HAEMOPHILIA CENTRES DOCTORS' ORGANISATION

UKHCDO

ANNUAL REPORT 2023

& Bleeding Disorder Statistics for the Financial Year 2022/23

A report from the UKHCDO and NHD

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1.0 Chairperson's Report

A warm welcome to the 24th annual general body meeting as we reflect on the numerous changes over the last year. The executive had some changes, with Mary Mathias and Gary Benson assuming the posts of Secretary and Treasurer. Kate Talks was elected unopposed to the role of Vice-chair for a second term. On behalf of the UKHCDO and its executive, I would like to express our gratitude to Susie Shapiro, our former secretary, and Rachel Rayment, our former treasurer, for their valuable contributions to the long-term goals of the organisation.

As we experience tumultuous times within the NHS, most of us have been stretched to our limits, and I hope some of the challenges are addressed earlier than later. On reflection, this year appears to be one of transition as we prepare for potentially significant changes following the publication of the final report from the Infected Blood Inquiry in March 2024. UKHCDO provided its closing submission in December 2022, followed by a presentation in January 2023. In the interim, we work with other stakeholders to address the second interim recommendation from the Inquiry.

This year, we registered as a stakeholder in several NICE consultations for new therapies in Haemophilia, including gene therapies. The journey is bumpy, and we now face the same challenges as other rare disorders. Through the Clinical Reference Group, we have indicated our intent to develop new policies to support patients with limited therapeutic options. As we develop policies to address unmet needs, we must actively consider generating evidence to support the policies we want in our clinical practice. This needs to be a key focus for us as an organisation with an increase in therapeutic options and a pipeline that might benefit patients with rare disorders.

Several new working parties have been established, reflecting the uncertainties in our clinical practice. The Peer Review working party, currently led by Sarah Mangles, has rationalised and streamlined the standards. We aim to start at the end of the first quarter of 2024, and to this end, a project manager has been appointed. Besides auditing the centres, the peer review will also collect data to help benchmark resources, as the growth in services has not always been matched with increased infrastructure.

The Clinical Reference Group is in the final stages of completing the new national service specifications. We hope that the new services specification will address the gaps identified in previous peer reviews, especially in relation to the provision of comprehensive multidisciplinary care.

Development of the NHD2 software is underway, and we anticipate that it will create new possibilities for research and service reviews, allowing us to make use of data to benefit both services and patients. The launch of the new Haemtrack app has enabled it to be more agile with faster development cycles. A gene therapy registry module with support from industry partners is being developed, and we continue to collaborate actively with the WFH gene therapy registry. NHD is being restructured due to a number of staff changes, which include the retirement of Lynne. We are ever grateful to her for her support of UKHCDO over the past few decades. Indeed, some of the organisational memory has been lost with her. The new structure has seen the separation of the administration and analytic team, with a view to more support to the centres and working parties.

As mentioned last year, the organisation has grown and adapted over time, with its primary aim being to promote the care of patients with bleeding disorders. I am positive that we will endure change and persist with our mission. All of this work would not have been possible without the support of my fellow executive members, Kate, Mary and Gary; a big thank you to them.

Pratima Chowdary
UKHCDO Chair
6 November 2023

Bleeding Disorder Statistics for

April 2022 to March 2023

A report from the UK National Haemophilia Database

October 2023

Appendix 1 Glossary

AE	Adverse Event
AGM	Annual General Meeting
ASH	American Society of Hematology
BCSH	British Committee for Standards in Haematology
BMI	Body mass index
BMS	Biomedical Scientists
BSH	British Society for Haematology
CCC	Comprehensive Care Centre
CEO	Chief executive officer
CMWP	Co-morbidities Working Party
COVID-19	Corona Virus Disease
CPD	Continuing Professional Development
CQUIN	Commissioning for Quality and Innovation
CRG	Clinical Reference Group
DAG	Data Analysis Group
DMWP	Data Management Working Party
EAHAD	European Association for Haemophilia and Allied Disorders
EHL	Enhanced Half-life
EU	European Union
EUHASS	European Haemophilia Safety Surveillance
FEIBA	Factor eight inhibitor bypass agent
FIX	Factor nine
FVII	Factor seven
FVIII	Factor eight
GCP	Good clinical practice
GLH	Genomics Laboratory Hub
GLN	Genetic Laboratory Network
GOSH	Great Ormond Street Hospital
GWP	Genetics Working Party
HC	Haemophilia Centre
HCC	Hepatocellular carcinoma
HCIS	Haemophilia Clinical Information System
HCPA	Haemophilia Chartered Physiotherapists' Association
HCV	Hepatitis C virus

HEE	Health Education England
HJHS	Haemophilia Joint Health Score
HNA	Haemophilia Nursing Association
ICS	Integrated Clinical Academic
IPSG	International Prophylaxis Study Group
IQR	Interquartile range
ISTH	International Society on Thrombosis and Haemostasis
ITI	Immune tolerance induction
IU	International units
IU/dl	International units per decilitre
IU/kg	International units per kilogram
IWP	Inhibitor Working Party
kg	Kilogram
MAHA	Microangiopathic hemolytic anemia
MDSAS	Medical Data Solutions and Services
MDT	Multidisciplinary meeting
MTP	Minimally treated people
NEQAS	National External Quality Assessment Service
NHD	National Haemophilia Database
NHF	National Hemophilia Foundation
NHS	National Health Service
NIBSC	National Institute for Biological Standards and Control
NIHR	National Institute for Health Research
PC	Personal computer
PCC	Prothrombin complex concentrate
PDF	Portable Document Format
pd-FIX	Plasma derived factor nine
PPIE	Patient and Public Involvement and Engagement
PUP	Previously untreated person
PwBD	Person/people with bleeding disorder
PwHA	Person/people with haemophilia A
PwHB	Person/people with haemophilia B
PWP	Paediatric Working Party
PwMHA	Person/people with moderate haemophilia A
PwSHA	Person/people with severe haemophilia A

PwVWD	Person/people with von Willebrand disease
RCEM	Royal College of Emergency Medicine
RCPCH	Royal College of Paediatrics and Child Health
RfPB	NIHR Research for Patient Benefit
rFIX	Recombinant factor IX
rFVIII	Recombinant factor VIII
SAE	Serious Adverse Event
SHA	Severe Haemophilia A
SHL	Standard Half-life
SOP	Standard operating procedure
TF	Task Force
THS	The Haemophilia Society
UK	United Kingdom
UKHCDO	United Kingdom Haemophilia Centre Doctors' Organisation
UKNEQAS	United Kingdom National External Quality Assessment Service
vCJD	Variant Creutzfeldt-Jakob disease
VWD	Von Willebrand disease
VWF	Von Willebrand factor
WAPPS-Hemo	Web-Accessible Population Pharmacokinetic Service—Hemophilia
WFH	World Federation of Hemophilia
WP	Working party

Appendix 2 Participating Centres

Centre Name	
Aberdeen	Lewisham
Bangor	Lincoln
Barnstaple	Liverpool (R. I.)
Belfast - Adult's	Liverpool Children's
Belfast - Children's	Manchester (Adults)
Birmingham (Queen Elizabeth)	Manchester Children's
Birmingham Children's	Newcastle upon Tyne
Bournemouth / Poole	North Hampshire (Basingstoke)
Bradford	North Staffordshire (Stoke on Trent)
Brighton	Norwich
Bristol (Infirmary & Children's)	Nottingham
Cambridge	Oxford
Canterbury	Peterborough
Cardiff	Plymouth
Chichester	Portsmouth
Coventry	Royal Free
Derby	Salisbury
Dundee	Sheffield (Children's)
Edinburgh	Sheffield (Royal Hallamshire)
Exeter	Shrewsbury
Glasgow (R.H.S.C.)	Southampton
Glasgow (R.I.)	St George's Hospital, London
Great Ormond Street	St Thomas' and Guy's Hospital
Hammersmith Hospital, London	Swansea
Inverness	Taunton / Yeovil
Ipswich	The Royal London Hospital
Kettering	Torquay
Kingston upon Hull (Hull)	Truro
Leeds	Wolverhampton
Leicester	York

2.0 Comments on the Bleeding Disorder Statistics for 2022 / 2023

The statistics for the financial year 2022/2023 follow. Most of the explanation and commentary is to be found with the tables and charts themselves.

The main continuing treatment trends are a continued transfer of people with severe haemophilia A to emicizumab and gradual transfer of people with haemophilia B to extended half-life products. In both cases there is a degree of variation in uptake from centre to centre which probably reflecting differences in clinical opinion, since the position of these agents is not settled, either in the UK or abroad.

In the case of emicizumab PWSHA who are considered to be doing well with factor VIII prophylaxis or who have a very low bleeding rate or who have a past history of inhibitors are overall less likely to switch. The proportion of PWSHA switching to emicizumab does not seem to vary greatly with age, those over 50yrs being a little more likely to switch. This may reflect poorer venous access in older PWSHA for whom a sc preparation will be more attractive..

The uptake of extended half-life IX has been relatively slow though the majority of severe haemophilia B people now use these products.

These treatment changes make some of the charts more difficult to interpret. The interpretation of the box and whisker plots showing factor VIII or IX usage per person per year by centre, is distorted by the uptake of EHL products, since there is no unit equivalence with standard half-life products. Unit usage of factor IX appears to be declining as EHL-products are substituted for standard half-life products and people require fewer units/kg because of the extended half-life of the products that they switch to. For Haemophilia A, the distortion is more marked because emicizumab was prescribed first to people with the highest annualised bleed rate and the highest factor VIII use so conversion to emicizumab decreases the number of units of factor VIII prescribed and will also appear to reduce the average factor VIII usage per person. This effect is most marked for those centres who have switched more than 80% of their people with severe Haemophilia A to emicizumab since those centres may have switched all their severe haemophilia A people except those that seldom bleed and treat themselves on-demand. Effectively, mean or median factor IX/VIII use per person can no longer be used to compare treatment intensity of one centre with another.

The data also chart an aging population and increasing numbers of deaths attributed to old age or dementia. There are also increasing reports of the normal degenerative diseases of old-age, the management of which may be complicated by an underlying bleeding disorder. The data presented include causes of death from death certification provided by NHS digital so far fewer causes of death are listed as “unknown”. The adverse event working group are also working on a method to present cause of death going beyond a single principal cause of death so that the effect of contributory causes is not minimised. This suggestion has arisen because death certificates frequently report the mode of death as the principal cause rather than the underlying condition that has led to that mode of death. I have tried to take this into account when reporting the death certification data from NHD digital.

Adverse events reports, assessed monthly by the Adverse Event Panel show the usual range of adverse events. All-drug-related adverse events are reported back to the manufacturer.

Although a number of thrombotic events were reported in the year, these occurred most commonly in people with fibrinogen disorders and von Willebrand's disease and none were attributed to emicizumab. In fact, side effects that were attributed to emicizumab (mostly local reactions and headache) occurred mostly in the first few weeks of use and the drug was generally well tolerated. Adverse event reports also show that, of the almost 100 ex-inhibitor people switching to emicizumab, only 5% had recurrent or resurgent inhibitor activity. This should put this risk into context and inform discussion with people when considering such a switch of products.

There were several reports of loss of efficacy with Esperoct necessitating a change back to their previous product. This is a well-recognised but relatively uncommon adverse event.

I would like to take this opportunity to thank the staff of the Haemophilia centres for collating and sending in all the data and helping us with data cleaning. Without this effort, we would have no report at all. The database and several modules used at a centre level are currently being redeveloped. This development is summarised by the Rob Hollingsworth's MDSAS report elsewhere in the Annual report. When this redevelopment is complete we should be able to collect the data more easily and it will be more readily available and visible for the reporting centres.

The report does not include complete treatment issue data throughout for Birmingham Children's Hospital due to a misunderstanding at centre level, now resolved.

We hope that you find the statistics useful and of interest and if you have any suggestions for future issues, please let us know. We hold a report review meeting usually in January, attended by a group of stakeholders including commissioners, and working party chairs.

Professor Charles RM Hay,
Ben Palmer, Dr Hua Xiang & Hasina Ngyou
On behalf of the UK National Haemophilia Database
Manchester, October 2023

Table 1 People with bleeding disorders by registered diagnosis, 2022/23

Diagnosis	Number of people registered		
	Male	Female	Total*
Haemophilia A	6,609	74	6,683
Haemophilia B	1,305	36	1,341
Haemophilia A carrier	-	1,681	1,681
Females with factor VIII deficiency	-	873	873
Haemophilia B carrier	-	359	359
Females with factor IX deficiency	-	312	312
Factor IX Leyden deficiency	28	-	28
Factor IX Leyden deficiency carrier	-	15	15
Haemophilia A with liver transplant	13	-	13
Haemophilia B with liver transplant	>0 & <3	-	-
von Willebrand disease	4,208	7,375	11,583
von Willebrand disease with liver transplant	>0 & <3	-	-
Probable von Willebrand disease	65	189	254
Factor V deficiency	98	187	285
Factor VII deficiency	1,017	1,191	2,208
Factor X deficiency	146	204	350
Factor XI deficiency	1,693	2,473	4,166
Factor XIII deficiency	52	38	90
Prothrombin (factor II) deficiency	7	12	19
Dysfibrinogenemia	308	500	808
Hypofibrinogenemia	107	153	260
Hypodysfibrinogenemia	21	26	47
Afibrinogenemia	11	6	17
Fibrinogen deficiency	-	3	3
Bleeding disorder of unknown cause	167	1,140	1,307
Glanzmann's thrombasthenia	61	81	142
Bernard-Soulier syndrome	50	51	101
Other severe platelet disorder	60	139	199
Platelet-type pseudo von Willebrand disease	16	27	43
Heritable platelet disorder	201	337	538
Other platelet disorder	895	2,077	2,972
Other disorders**	17	24	41
Acquired haemophilia A	329	328	657
Acquired von Willebrand disease	110	85	195
Other acquired factor deficiency	22	23	45
Combined and miscellaneous disorders	245	517	762
Total*	17,861	20,536	38,397

* This is the total excluding numbers which have been suppressed

**Other disorders include:

Combined factors II, VII, IX and X deficiencies

Combined factors V and VIII deficiencies

Alpha 2-antiplasmin deficiency

Thrombomodulin-associated coagulopathy

***Table 1 (previous page)*:** This shows the number of people registered with the NHD by their registered diagnosis.

Table 2 People with bleeding disorders by nation, 2022/23

Diagnosis	Number of people registered					
	England	Northern Ireland	Scotland	Wales	Not known	Total
Haemophilia A	7,719	360	808	395	34	9,316
Haemophilia B	1,702	43	213	98	14	2,070
von Willebrand disease	9,978	153	1,255	516	70	11,972
Other bleeding disorders	12,733	125	1,566	651	130	15,205
Total*	31,982	681	3,834	1,655	248	38,400

Important Note: Throughout the remainder of this report, haemophilia A results include carriers who have haemophilia A and females with FVIII deficiency. Results for haemophilia B include carriers of haemophilia B, females with FIX deficiency, FIX Leyden and FIX Leyden carriers. People with multiple disorders are included in results for each of their individual blood disorder diagnoses.

Time Periods: The tables and figures presented in this report relate to the period April 2022 – March 2023 inclusive unless stated otherwise.

Age is calculated at the midpoint of the financial year, i.e., 30th September 2022.

Bodyweight measurements were taken from no further back than January 2021 for people aged 18 years and above on the date of measurement, and from no further back than January 2022 for people aged under 18 years on the date of measurement.

2.1 Haemophilia A

Table 3 People with congenital haemophilia A (including carriers) registered and treated, 2022/23

Haemophilia A	Age Range	Number of people by factor VIII level (IU/dl)																	
		<1			1 - 5			>5 & <40			≥ 40			Unknown Severity			Total		
		Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Total Registered	<18 years	719	3	722	221	5	226	650	121	771	30	169	199	10	5	15	1,630	303	1,933
	>=18 years	1,502	6	1,508	641	6	647	2,679	691	3,370	195	1,575	1,770	15	73	88	5,032	2,351	7,383
	Total	**2,221**	**9**	**2,230**	**862**	**11**	**873**	**3,329**	**812**	**4,141**	**225**	**1,744**	**1,969**	**25**	**78**	**103**	**6,662**	**2,654**	**9,316**
New Registrations**	<18 years	33	'1-2	33	17	'1-2	17	38	28	66	4	22	26	7	'1-2	7	99	50	149
	>=18 years	27	'1-2	27	9	'1-2	9	30	57	87	11	87	98	5	12	17	82	156	238
	Total	**60**	**-**	**60**	**26**	**-**	**26**	**68**	**85**	**153**	**15**	**109**	**124**	**12**	**12**	**24**	**181**	**206**	**387**
Treated with concentrate FVIII/Emicizumab in year***	<18 years	695	'1-2	695	158	4	162	140	7	147	4	-	4	4	-	4	1,001	11	1,012
	>=18 years	1,433	'1-2	1,433	405	'1-2	405	558	45	603	22	17	39	3	3	6	2,421	65	2,486
	Total	**2,128**	**-**	**2,128**	**563**	**4**	**567**	**698**	**52**	**750**	**26**	**17**	**43**	**7**	**3**	**10**	**3,422**	**76**	**3,498**

** This is the total excluding numbers which have been suppressed*

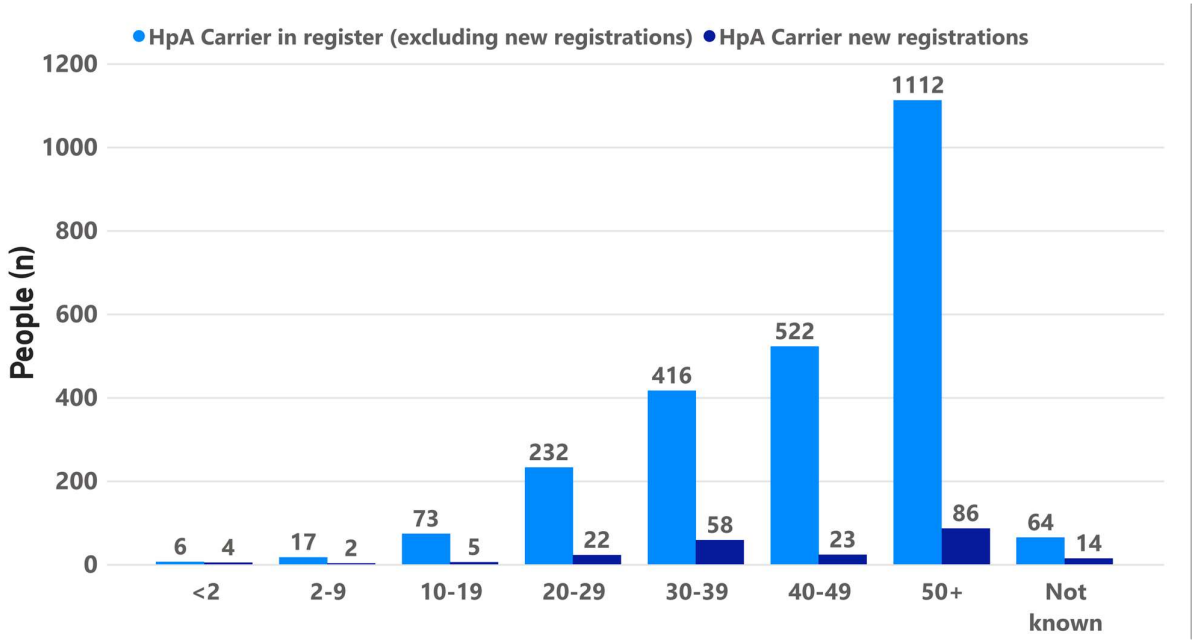
*** New registrations are a subset of the 'In Register' numbers*

**** Excluding people only treated with DDAVP and tranexamic acid*

Table 3: This shows the total number of people with haemophilia A (including low factor VIII level carriers and factor VIII deficient females) registered and/or treated with concentrate in the UK during 2022/23 and broken down by age and disease severity.

There were over 100 people registered with severe haemophilia A who had no recorded treatment with FVIII concentrate or emicizumab within the year. This is under investigation.

Figure 1 Females with FVIII deficiency and carriers of haemophilia A currently registered and newly registered, by baseline FVIII level, 2022/23



Diagnosis	Number of people by factor VIII level (IU/dl)								
	<2	2-9	10-19	20-29	30-39	40-49	50+	Not Known	Total*
Haemophilia A carrier In register (Excluding new registrations)	6	17	73	232	416	522	1,112	64	2,442
Haemophilia A carrier New registrations	4	1-2	5	22	58	23	86	14	212
Total*	**10**	**17**	**78**	**254**	**474**	**545**	**1,198**	**78**	**2,654**

Figure 1: This shows the number of carriers of haemophilia A currently registered with the NHD by baseline FVIII level. This includes females registered by their centre as having FVIII deficiency or haemophilia A. New registrations of carriers with normal FVIII levels continues but is incomplete.

Table 4 New registrations of congenital haemophilia A (including carriers), by age at mid-year, gender and severity, 2022/23

Haemophilia A	Number of people by factor VIII level (IU/dl)																	
Age (years)	< 1			1 - 5			> 5 & < 40			≥ 40			Unknown			Total*		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
0 - < 2	26	'1-2	26	12	'1-2	12	15	4	19	'1-2	3	3	7	-	7	60	7	67
2 - 4	3	-	3	'1-2	-	-	5	3	8	-	3	3	-	-	-	8	6	14
5 - 9	'1-2	-	-	'1-2	-	-	9	9	18	-	5	5	-	'1-2	-	9	14	23
10 - 19	3	-	3	3	-	3	12	14	26	3	12	15	-	'1-2	-	21	26	47
20 - 29	12	-	12	3	'1-2	3	8	15	23	'1-2	26	26	-	4	4	23	45	68
30 - 39	8	-	8	'1-2	-	-	4	15	19	3	28	31	'1-2	3	3	15	46	61
40 - 49	'1-2	-	-	'1-2	-	-	4	7	11	-	13	13	3	'1-2	3	7	20	27
50 - 59	3	'1-2	3	'1-2	-	-	6	7	13	-	10	10	-	'1-2	-	9	17	26
60 - 69	'1-2	'1-2	-	-	-	-	3	5	8	'1-2	3	3	-	-	-	3	8	11
70 +	-	-	-	'1-2	-	-	'1-2	6	6	5	6	11	'1-2	'1-2	-	5	12	17
Total*	**55**	**-**	**55**	**18**	**-**	**18**	**66**	**85**	**151**	**11**	**109**	**120**	**10**	**7**	**17**	**160**	**201**	**361**

**This is the total excluding numbers which have been suppressed*

Table 4: This shows the number of new registrations of haemophilia A broken down by reported severity and age at mid-year (30/09/2022).

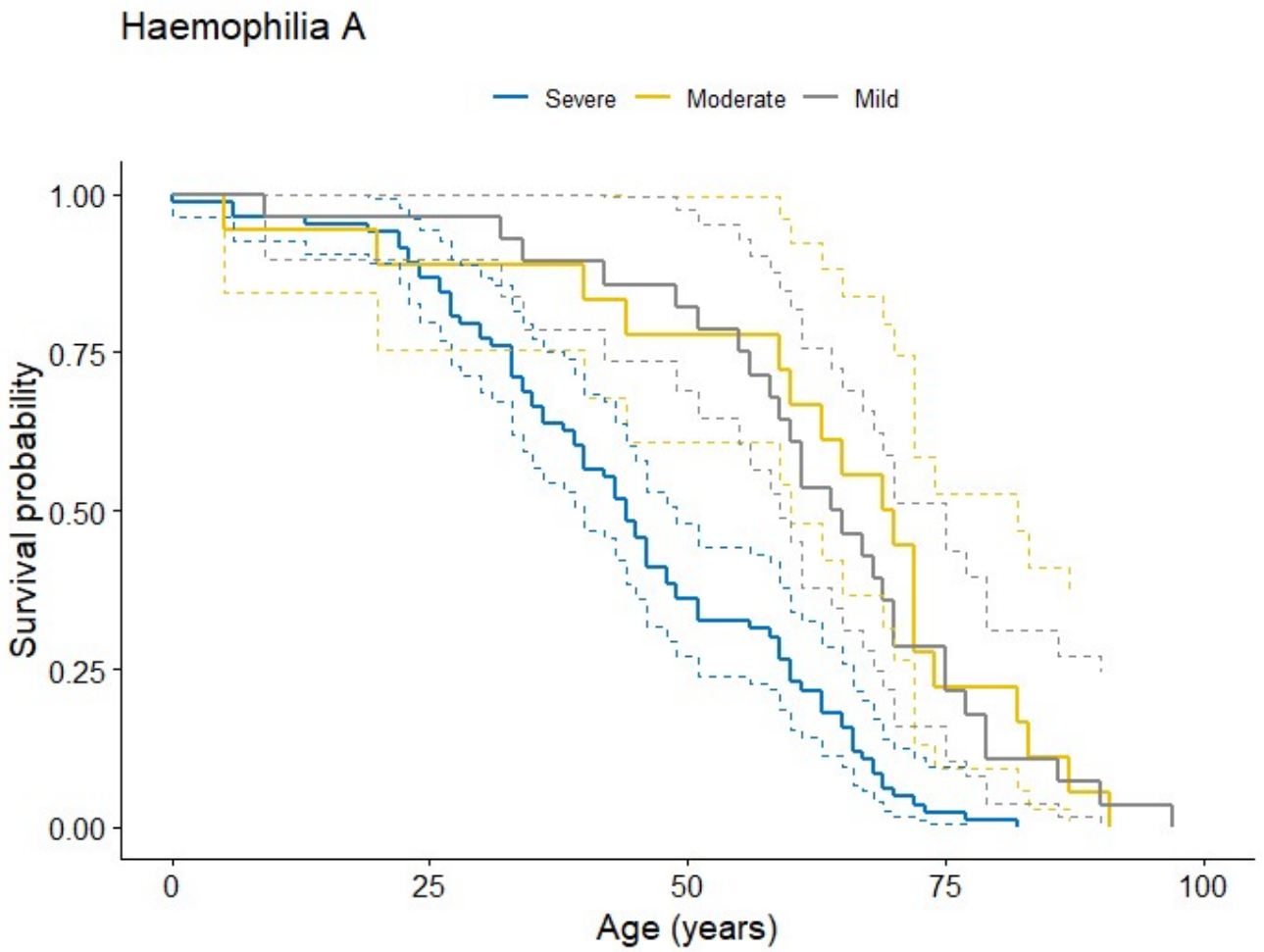
The underlying birth rate of people with severe haemophilia A born in the UK usually runs at 40-45 per year. The proportion of new registration of severe haemophilia A aged two years or above (without suppression of small numbers) in 2022/23 was 44%. It is presumed that most of those with severe haemophilia registered at aged two years or above have migrated or are visitors to the UK.

Table 5 New registrations of people with severe haemophilia A aged 2 years and over, and subsequent treatment by year

	Registration year										Total 2013/2023
	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21	2021/22	2022/23	
New registrations/year	19	17	17	19	21	17	14	15	21	36	196
Treated in each year											
2013/14	19										19
2014/15	18	17									35
2015/16	19	16	16								51
2016/17	19	17	17	19							72
2017/18	19	17	17	19	18						90
2018/19	19	17	16	17	19	14					102
2019/20	18	17	15	17	18	17	13				115
2020/21	17	16	15	16	17	14	12	14			121
2021/22	17	16	16	16	15	14	13	13	18		138
2022/23	16	17	16	17	14	14	12	13	18	31	168
No treatment records	0	0	0	0	1	0	0	0	2	5	8

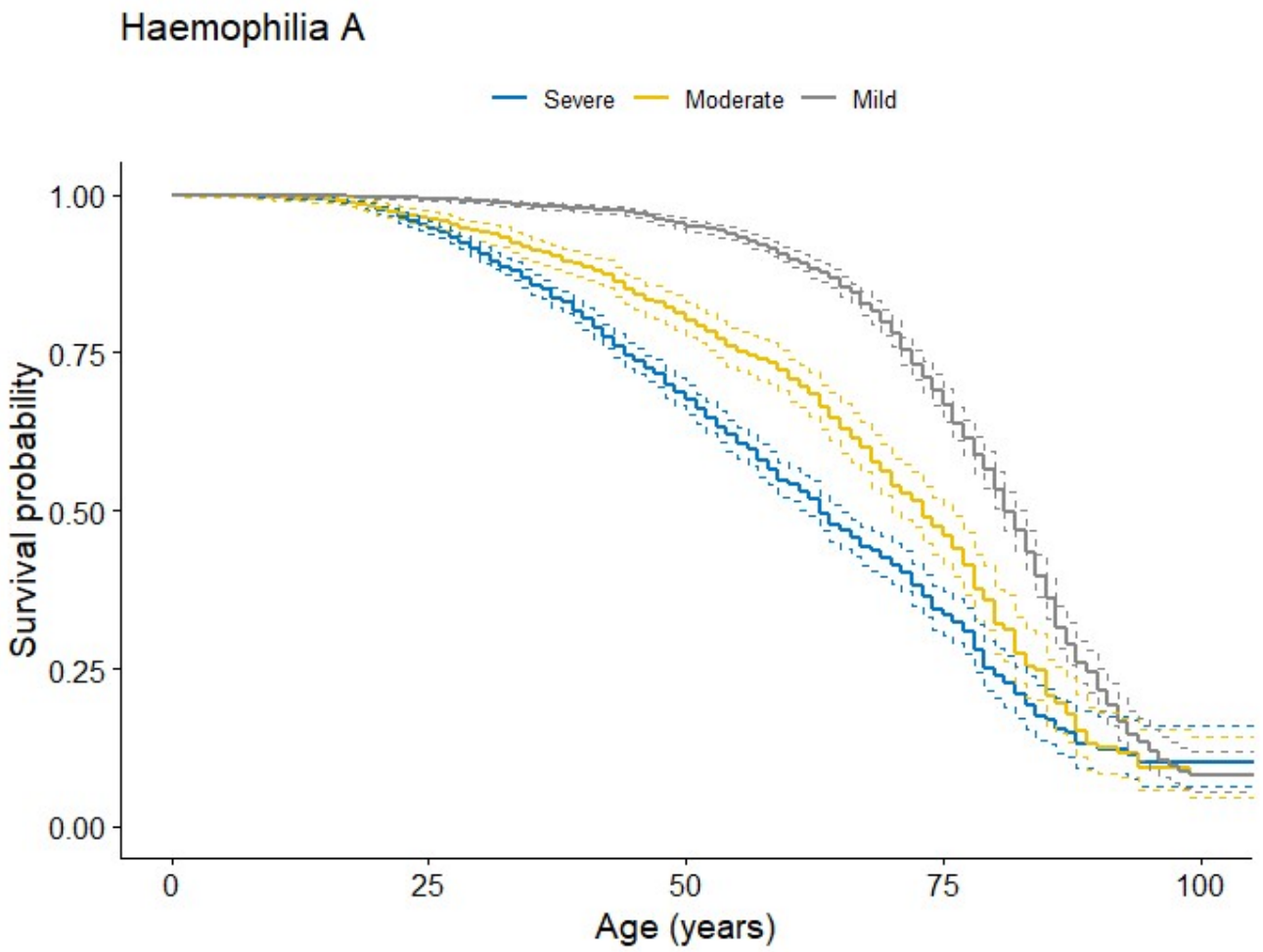
Table 5: This shows the number of people with severe haemophilia A over two years of age when newly registered (and therefore thought potentially to be migrants) each year from 2013/14. It also shows the number treated in each year subsequent to their registration. This shows that up to 196 people with severe haemophilia A may have migrated to the UK since 2013/14. This is may be an underestimate, since children under two years old are not included in this table. 168 were treated in 2022/23, suggesting that most remain and continue to require regular treatment.

Figure 2a Survival of people with haemophilia A by severity, actively registered 1969-1984



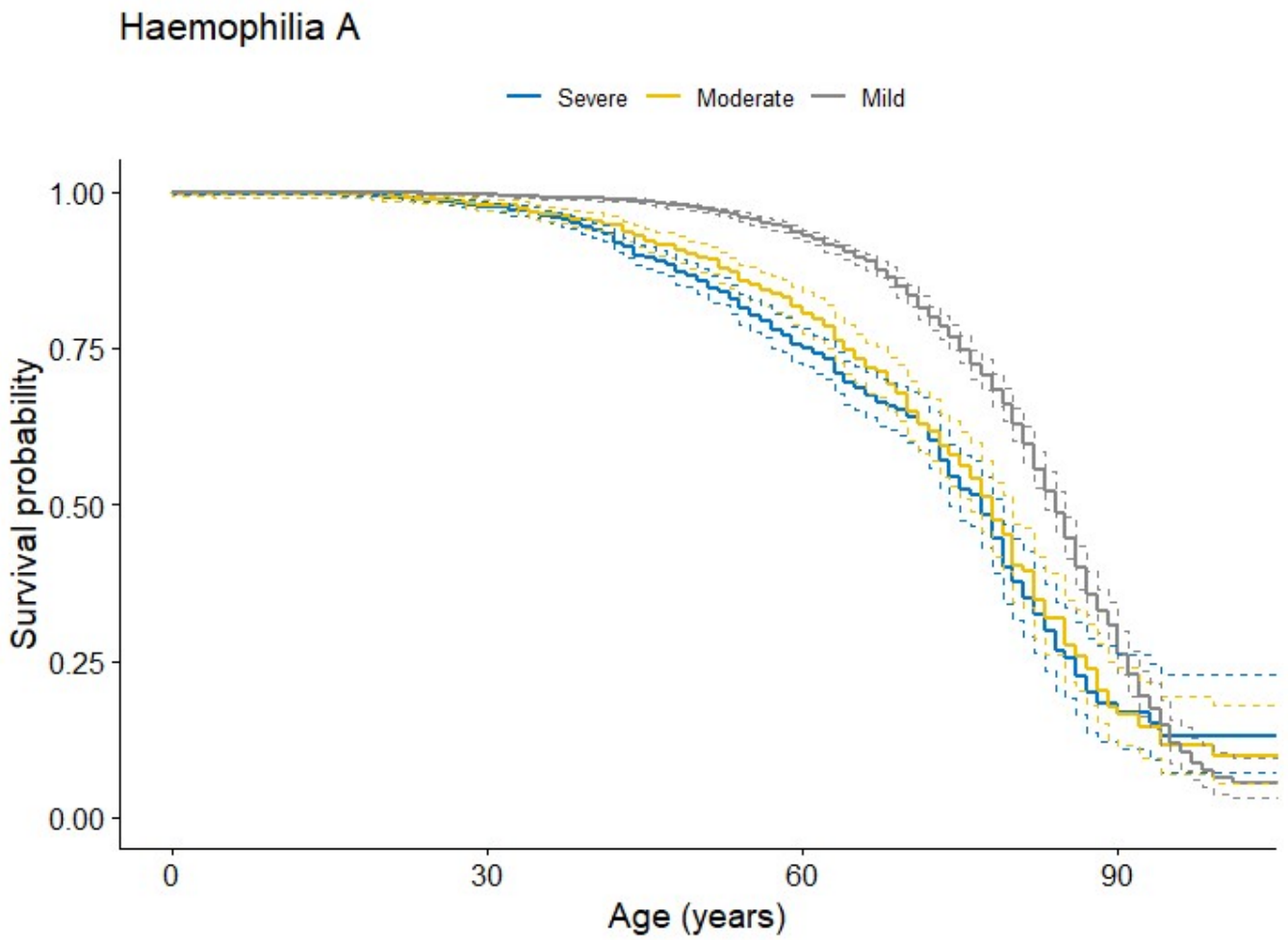
Median survival time (years) for people with haemophilia A: severe: 44, moderate: 69.5, mild: 64

Figure 2b Survival of people with haemophilia A by severity, actively registered 1985-1995



Median survival time (years) for people with haemophilia A: severe: 63, moderate: 73, mild: 81

Figure 2c Survival of people with haemophilia A by severity, actively registered 1996-2023



Median survival time (years) for people with haemophilia A: severe: 77, moderate: 78, mild: 84

***Figures 2a-2c*:** These show survival curves for haemophilia A broken down by severity for the years 1969 to 1984, 1984-96 and 1996-2023 with 95% confidence intervals. Those age ranges were chosen because the database started reporting in 1969, HIV deaths occurred predominantly between 1984 and 1995, when triple-therapy was introduced and the period from 1996 has been characterised by relatively few deaths from HIV and HCV. It should be noted that the survival curve for 1969-84 is based on relatively few people and is subject to a greater degree of uncertainty, as illustrated by the wide confidence intervals shown. However, the median life expectancy for people with severe haemophilia A of 44 years is comparable with published data from that era from the United States. The survival curves show a progressive improvement in life expectancy with time, even during the worst years of the HIV epidemic when older HIV-positive PWHA were disproportionately at risk of dying from AIDS. Subsequent to that there has been significant improvement in median life expectancy of both people with moderate and severe haemophilia A (78 and 77 years, respectively), although it has still not completely corrected to normal levels seen in people with mild haemophilia (median 84 years)."

Figure 3 Factor VIII units issued by UK haemophilia centres to treat severe haemophilia A, 2013/14 - 2022/23

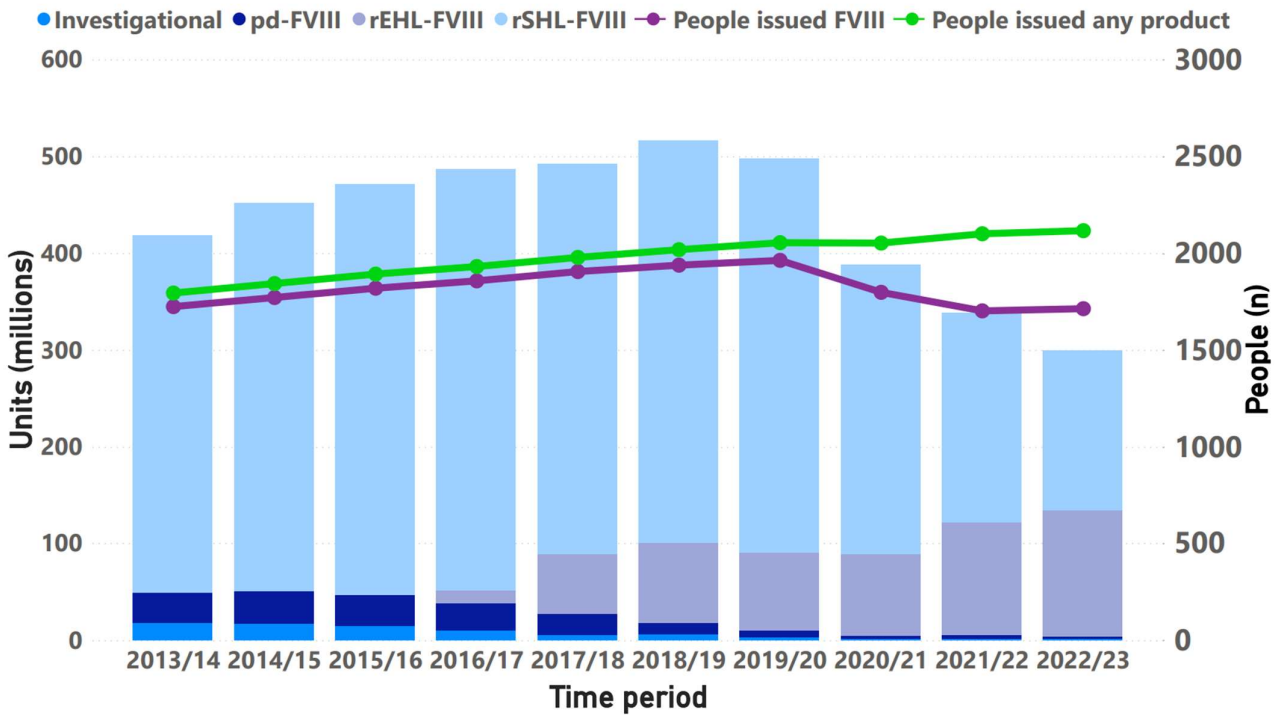


Figure 3: This shows reported FVIII units issued to treat PwSHA between 2013/14 to 2022/23, including people with FVIII inhibitors. The number of people reported to have been treated with FVIII (standard and extended half-life) is shown by the purple line using a secondary axis, and the total number of people treated with any product (including emicizimab and novoseven) is shown by the green line. This chart shows the beginning of a significant fall off in overall FVIII issues from 2020/21, which is attributable to the introduction of emicizumab prophylaxis from September of 2019. There has also been a dramatic fall-off in the use of plasma-derived products over the past few years, which have almost completely fallen out of use. However the proportion of EHL-FVIII has increased rapidly, first with the introduction of Elocta and more recently Esperoct..

Figure 4 Factor VIII units issued by UK haemophilia centres to treat non-severe haemophilia A, 2013/14 - 2022/23

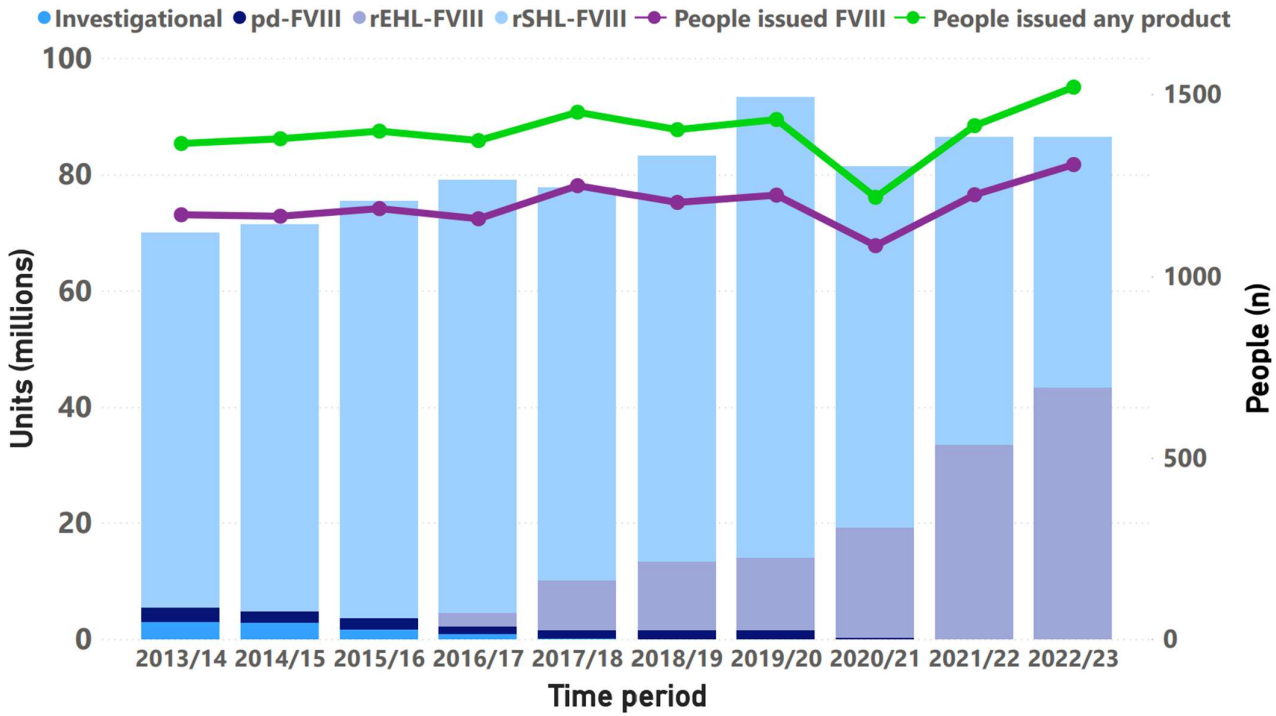


Figure 4: This shows FVIII units issued to treat people with non-severe haemophilia A in the UK from 2013/14 to 2022/23, including people with FVIII inhibitors. The number of people reported to have been treated with FVIII is shown by the purple line using a secondary axis, and the total number of people treated with any product is shown by the green line. Emicizumab is currently not licensed for use in this group. Note also the declining proportion of SHL-rFVIII issued, and increasing issues of EHL-rFVIII. There has been no use of pd-VIII in this group since 2020/21.

Data table for Figure 3: Factor VIII units issued by UK haemophilia centres to treat severe haemophilia A, 2013/14 - 2022/23

Year	pd FVIII		Standard half-life FVIII (excluding investigational)		Investigational rFVIII		Enhanced half-life FVIII		People issued FVIII		People issued any product	
	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2016/17	n	% difference since 2013/14	n	% difference since 2013/14
2013/14	31.3	-	369.2	-	18.1	-	-	-	1724	-	1794	-
2014/15	33.4	6.9	400.9	8.6	17.3	-4.6	-	-	1771	2.7	1843	2.7
2015/16	32.6	4.2	424.3	14.9	14.4	-20.2	-	-	1819	5.5	1892	5.5
2016/17	28.6	-8.4	435.1	17.8	9.7	-46.1	12.9	-	1857	7.7	1931	7.6
2017/18	21.8	-30.2	403.8	9.4	5.7	-68.4	60.9	370.8	1905	10.5	1978	10.3
2018/19	11.8	-62.4	416.3	12.7	6.5	-64.1	81.8	531.8	1938	12.4	2018	12.5
2019/20	6.7	-78.7	407.6	10.4	3.3	-81.7	80.2	519.5	1962	13.8	2054	14.5
2020/21	3.4	-89.1	299.3	-18.9	1.5	-91.6	83.9	548.0	1797	4.2	2052	14.4
2021/22	3.8	-87.7	218.5	-40.8	1.7	-90.8	116.6	800.8	1704	-1.2	2114	17.8
2022/23	2.9	-90.7	165.6	-55.1	1.2	-93.6	129.7	902.3	1717	-0.4	2139	19.2

Data table for Figure 4: Factor VIII units issued by UK haemophilia centres to treat non-severe haemophilia A, 2013/14 - 2022/23

Year	pd FVIII		Standard half-life FVIII (excluding investigational)		Investigational rFVIII		Enhanced half-life FVIII		People issued FVIII		People issued any product	
	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2016/17	n	% difference since 2013/14	n	% difference since 2013/14
2013/14	2.5	-	64.5	-	3.0	-	-	-	1169	-	1365	-
2014/15	1.9	-24.5	66.6	3.2	2.9	-3.8	-	-	1165	-0.3	1378	1.0
2015/16	1.9	-22.5	71.8	11.3	1.7	-42.3	-	-	1186	1.5	1399	2.5
2016/17	1.3	-45.4	74.5	15.4	0.9	-70.5	2.3	-	1158	-0.9	1373	0.6
2017/18	1.5	-39.4	67.7	4.9	0.1	-97.0	8.5	268.5	1249	6.8	1451	6.3
2018/19	1.6	-34.7	69.9	8.3	0.0	-100.0	11.7	407.0	1203	2.9	1403	2.8
2019/20	1.6	-33.3	79.3	22.8	0.0	-100.0	12.4	434.9	1223	4.6	1431	4.8
2020/21	0.3	-88.6	62.2	-3.6	0.0	-99.6	18.9	713.7	1084	-7.3	1217	-10.8
2021/22	0.1	-95.7	53.7	-16.8	0.0	-99.7	33.5	1346.5	1225	4.8	1414	3.6
2022/23	0.0	-99.3	43.1	-33.2	0.0	-99.7	43.4	1772.6	1307	11.8	1520	11.4

Figure 5 Number of people with haemophilia A issued product, 2013/14 - 2022/23

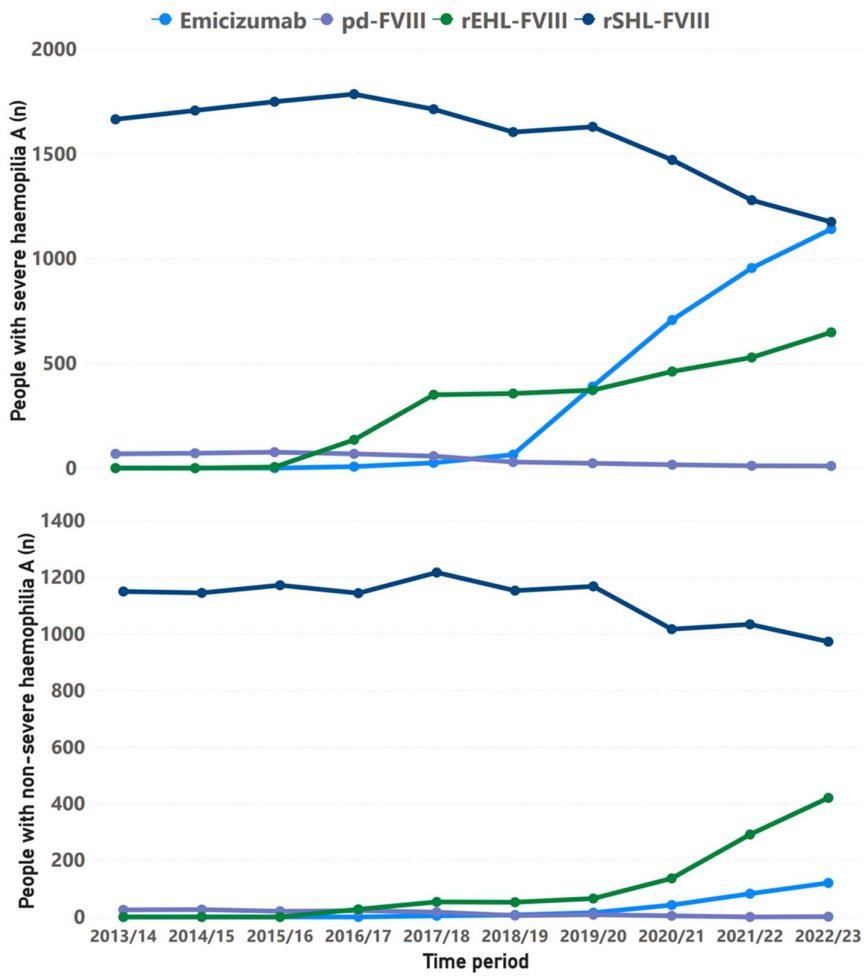


Figure 5: This shows the number of people with haemophilia A (with and without FVIII inhibitors) using different product types, by severity. This shows a gradual introduction of enhanced half-life (EHL) FVIII from 2016. It also shows an overall reduction in the number of people with severe haemophilia A treated with standard half-life (SHL) FVIII as emicizumab was introduced for people with inhibitors in 2018 and for people with severe haemophilia A without inhibitors in 2019. As people may be issued with more than one product type in any given year, there is some double counting of people between product groups within years.

Table 6 Factor VIII mean issues by region for people with severe haemophilia A (including treatment for inhibitors and EHL-FVIII), 2013/14 - 2022/23

Country	Region	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21	2021/22	2022/23
England	North East & Yorkshire	261,475	259,215	291,575	303,843	294,707	318,577	305,860	242,553	194,925	182,337
	North West	192,345	208,117	219,172	225,109	226,156	218,378	198,362	115,678	81,308	66,306
	Midlands	179,937	189,962	185,792	189,881	193,194	204,555	206,058	152,986	127,781	118,458
	East of England	262,953	265,370	274,063	291,560	287,620	239,310	210,763	196,372	150,152	105,368
	London	309,448	329,803	328,459	318,175	302,795	311,835	279,968	263,737	261,958	226,249
	South East	210,798	227,414	241,870	242,747	245,653	250,223	251,473	214,704	202,342	187,654
	South West	200,055	211,572	216,984	228,146	225,444	254,787	238,486	195,827	167,183	118,094
Wales	Wales	209,025	209,704	217,153	237,842	241,798	256,926	273,408	222,801	221,561	140,254
Scotland	East of Scotland	288,029	262,718	266,772	283,500	287,079	289,642	268,399	259,069	217,566	215,917
	West of Scotland	210,545	231,047	267,070	311,664	281,492	284,933	255,053	231,885	205,134	138,182
Northern Ireland	Northern Ireland	254,554	232,332	215,088	205,823	205,560	228,285	228,478	242,710	241,557	269,691

Table 6: This shows mean FVIII issues by region. Units are assigned to region by haemophilia centre rather than home postcode, as requested by the Lead Commissioner. There appears to have been a decline in FVIII issues over the last three years in all regions except Northern Ireland, where it has increased. The magnitude of this decline, which is attributable to significant numbers of people switching to emicizumab prohylaxis, varies considerably between regions.

Table 7 People with haemophilia A issued with FVIII by severity, 2013/14 – 2022/23

Treatment Year	Number of people with haemophilia A by factor VIII level (IU/dl)											
	<1			1 - 5			>5 & <40			≥ 40		
	Registered	Issued FVIII	% change	Registered	Issued FVIII	% change	Registered	Issued FVIII	% change	Registered	Issued FVIII	% change
	n	n (%)	since 2013/14	n	n (%)	since 2013/14	n	n (%)	since 2013/14	n	n (%)	since 2013/14
2013/14	1844	1726 (93.6)	-	778	504 (64.8)	-	3281	642 (19.6)	-	821	25 3	-
2014/15	1894	1772 (93.6)	2.7	779	505 (64.8)	0.2	3425	639 (18.7)	-0.5	1029	23 2.2	-8.0
2015/16	1953	1820 (93.2)	2.7	783	507 (64.8)	0.4	3554	654 (18.4)	2.3	1150	27 2.3	17.4
2016/17	1992	1858 (93.3)	2.1	784	492 (62.8)	-3.0	3608	640 (17.7)	-2.1	1276	28 2.2	3.7
2017/18	2043	1906 (93.3)	2.6	794	508 (64.0)	3.3	3708	713 (19.2)	11.4	1395	32 2.3	14.3
2018/19	2079	1939 (93.3)	1.7	805	490 (60.9)	-3.5	3811	684 (17.9)	-4.1	1527	31 2	-3.1
2019/20	2117	1963 (92.7)	1.2	817	516 (63.2)	5.3	3887	686 (17.6)	0.3	1635	23 1.4	-25.8
2020/21	2144	1798 (83.9)	-8.4	830	505 (60.8)	-2.1	3945	567 (14.4)	-17.3	1694	19 1.1	-17.4
2021/22	2179	1705 (78.2)	-5.2	846	532 (62.9)	5.3	4022	663 (16.5)	16.9	1850	32 1.7	68.4
2022/23	2229	1717 (77.0)	0.7	872	517 (59.3)	-2.8	4145	744 (17.9)	12.2	1967	44 2.2	37.5

Table 7: This table shows factor VIII issued in any amount during the year, broken down by severity. The number of PwSHA NOT issued factor VIII has increased year on year and is now in excess of 500. This is attributable to switching to emicizumab. People issued emicizumab who are bleed free may be issued a contingency stock of rFVIII only when their current stock goes out of date.

Table 8a Treatment intensity of people with severe haemophilia A without inhibitors issued with standard half-life FVIII, 2013/14 - 2022/23

Treatment period	FVIII units		People (n)		Treatment intensity (units/person/year)		Change in treatment intensity year on year (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2013/14	98,000,847	252,291,254	522	975	187,741	258,760	-	-
2014/15	102,848,472	275,520,775	521	1017	197,406	270,915	5.1	4.7
2015/16	100,937,490	289,422,170	513	1,033	196,759	280,176	-0.3	3.4
2016/17	91,110,048	290,102,711	454	1,036	200,683	280,022	2	-0.1
2017/18	81,854,418	259,664,470	393	952	208,281	272,757	3.8	-2.6
2018/19	84,936,367	290,806,198	411	974	206,658	298,569	-0.8	9.5
2019/20	71,821,893	254,992,176	336	864	213,756	295,130	3.4	-1.2
2020/21	53,279,806	176,918,381	239	639	222,928	276,868	4.3	-6.2
2021/22	43,061,200	122,748,908	179	450	240,565	272,775	7.9	-1.5
2022/23	32,198,506	93,175,958	133	350	242,094	266,217	0.6	-2.4

Table 8a: This shows that the number of people issued SHL alone has reduced dramatically over the last ten years. For those who continue to use SHL rFVIII, treatment intensity has increased in children and remained stable in adults.

NOTE - exclusions from this analysis:

People issued with emicizumab, people issued with both EHL- and SHL-FVIII, people using gene therapy, people resident overseas, people not registered for full treatment period, people for whom inhibitors are reported within the treatment period

Table 8b 2022/23 Treatment intensity of people with severe haemophilia A without inhibitors treated with enhanced half-life FVIII, 2017/18-

Treatment Period	Enhanced half-life FVIII Units		People (n)		Treatment Intensity (units/person/year)		Change in treatment intensity year on year (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2017/18	13,336,000	17,809,810	70	62	190,514	287,255	-	-
2018/19	20,386,258	45,800,020	115	166	177,272	275,904	-7.0	-4.0
2019/20	20,329,710	34,819,480	112	131	181,515	265,798	2.4	-3.7
2020/21	14,865,325	34,546,000	86	131	172,853	263,710	-4.8	-0.8
2021/22	17,890,545	68,859,400	88	213	203,302	323,284	17.6	22.6
2022/23	18,595,750	75,683,240	99	248	187,836	305,174	-7.6	-5.6

Table 8b: This shows some fluctuation in the treatment intensity (units/person/year) of EHL-FVIII for the treatment of severe haemophilia A from April 2017 to March 2023. The apparent increase in treatment intensity from 2020/21 to 2021/22 has to some extent reversed over the last year. The increase in the number of PwSHA issued EHL, and the increased treatment intensity in 2021/22 corresponds with the widespread uptake of Esperoct.

NOTE - exclusions from this analysis:

People issued with emicizumab, people issued with both EHL- and SHL-FVIII, people using gene therapy, people resident overseas, people not registered for full treatment period, people for whom inhibitors are reported within the treatment period

Table 9a Treatment intensity of people with moderate haemophilia A (0.01 - 0.03 IU/ml) treated with standard half-life FVIII, with no inhibitor, 2013/14 - 2022/23

Treatment Period	FVIII Units		People (n)		Treatment Intensity (units/person/year)		Change in treatment intensity year on year (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2013/14	10,397,250	29,357,249	88	213	118,151	137,827	-	-
2014/15	12,836,450	29,428,296	92	214	139,527	137,515	18.1	-0.2
2015/16	13,553,500	31,851,233	94	220	144,186	144,778	3.3	5.3
2016/17	12,357,750	30,434,121	83	203	148,889	149,922	3.3	3.6
2017/18	10,861,650	26,207,859	88	189	123,428	138,666	-17.1	-7.5
2018/19	10,686,250	28,361,274	75	190	142,483	149,270	15.4	7.6
2019/20	12,792,750	28,994,766	77	190	166,140	152,604	16.6	2.2
2020/21	8,686,500	22,988,750	61	168	142,402	136,838	-14.3	-10.3
2021/22	7,045,500	18,101,718	48	129	146,781	140,323	3.1	2.5
2022/23	4,591,000	15,723,500	42	119	109,310	132,130	-25.5	-5.8

Table 9a: This table shows the trend in treatment intensity in people with haemophilia A and factor level between 0.01 - 0.03 IU/ml over the last ten years. Only people treated during this time are included. However, the range of baseline FVIII levels and bleeding phenotypes included in this data ranges from those on regular prophylaxis to those requiring only occasional treatment. This renders the data more difficult to interpret and impossible to compare directly with the relatively more homogeneous group of people with severe haemophilia A. Emicizumab is not currently licensed for this group. This shows that treatment intensity fluctuates over time in both age groups. The number of both adults and children issued product has reduced over recent years, as people have been switched to EHL.

NOTE - exclusions from this analysis: People issued with emicizumab, people issued with both EHL- and SHL-FVIII, people using gene therapy, people resident overseas, people not registered for full treatment period, people for whom inhibitors are reported within the treatment period

Table 9b Treatment intensity of people with moderate haemophilia A (0.01 - 0.03 IU/ml) treated with enhanced half-life FVIII, with no inhibitor, 2017/18 - 2022/23

Treatment Period	Enhanced half-life FVIII Units		People (n)		Treatment Intensity (units/person/year)		Change in treatment intensity year on year (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2017/18	597,464	3,499,000	4	12	149,366	291,583	-	-
2018/19	1,499,750	8,145,000	7	29	214,250	280,862	43.4	-3.7
2019/20	2,005,750	7,615,750	8	31	250,719	245,669	17.0	-12.5
2020/21	1,146,750	7,375,750	7	27	163,821	273,176	-34.7	11.2
2021/22	1,289,100	12,235,500	17	44	75,829	278,080	-53.7	1.8
2022/23	2,278,500	16,204,754	25	61	91,140	265,652	20.2	-4.5

Table 9b: This illustrates the introduction of EHL-FVIII to a relatively small group of people with haemophilia A and a factor level between 0.01 - 0.03 IU/ml between April 2017 and March 2023.

NOTE - exclusions from this analysis:

People issued with emicizumab, people issued with both EHL- and SHL-FVIII, people using gene therapy, people resident overseas, people not registered for full treatment period, people for whom inhibitors are reported within the treatment period,

Figure 6a Treatment intensity (IU/person/year) of people *aged under 18 years* with haemophilia A treated with standard half-life FVIII, with no inhibitor by severity, 2022/23

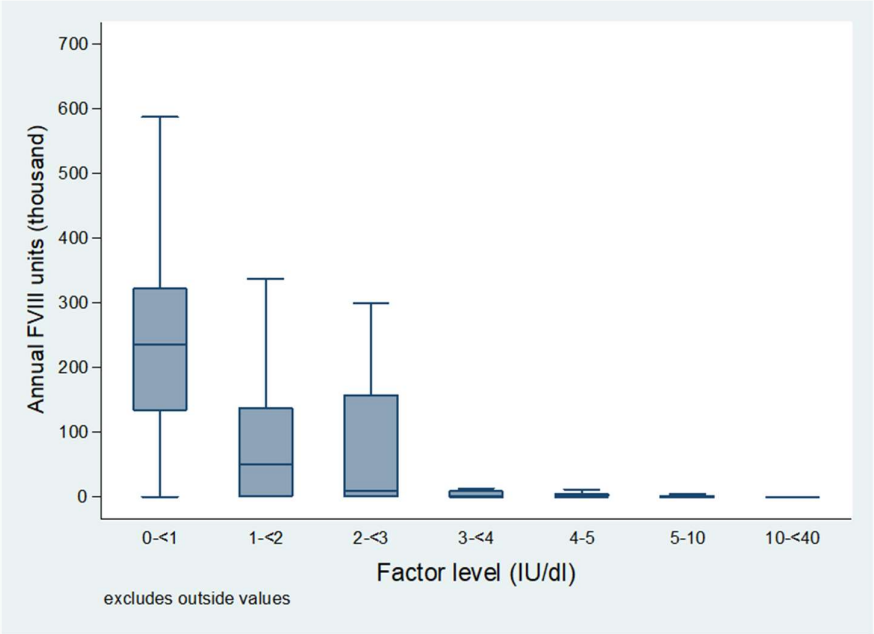


Figure 6a: This box and whisker plot shows the median, IQR and range of SHL-FVIII (IU/person/year) broken down by baseline FVIII level in people under 18 years old with haemophilia A. This shows that young people with a FVIII baseline level of 1 - <2 IU/dl have a greater median factor VIII requirement than those with 2 - <3 IU/dl, although this difference is not significant (Wilcoxon rank-sum p=0.53). The factor VIII requirement falls off rapidly at higher factor VIII baseline levels.

Summary statistics for figure 6a

Factor VIII level (IU/dl)	People (n)	Annual FVIII units (thousands) (median, (IQR))
<1	124	235.0 (134.5; 322.5)
1 - <2	17	50.0 (0.0; 138.0)
2 - <3	27	10.5 (0.0; 157.5)
3 - <4	25	0.0 (0.0; 9.0)
`4 - 5	51	0.0 (0.0; 5.0)
`5 - 10	119	0.0 (0.0; 2.0)
`10 - 40	534	0.0 (0.0; 0.0)
Total	**897**	**0.0 (0.0; 2.0)**

Exclusions from this analysis:
Issued emicizumab or EHL 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy
Issued trial product 2022/23
Issued plasma 2022/23

Figure 6b Treatment intensity (IU/person/year) of people *aged 18 years and above* with haemophilia A treated with standard half-life FVIII, with no inhibitor by severity, 2022/23

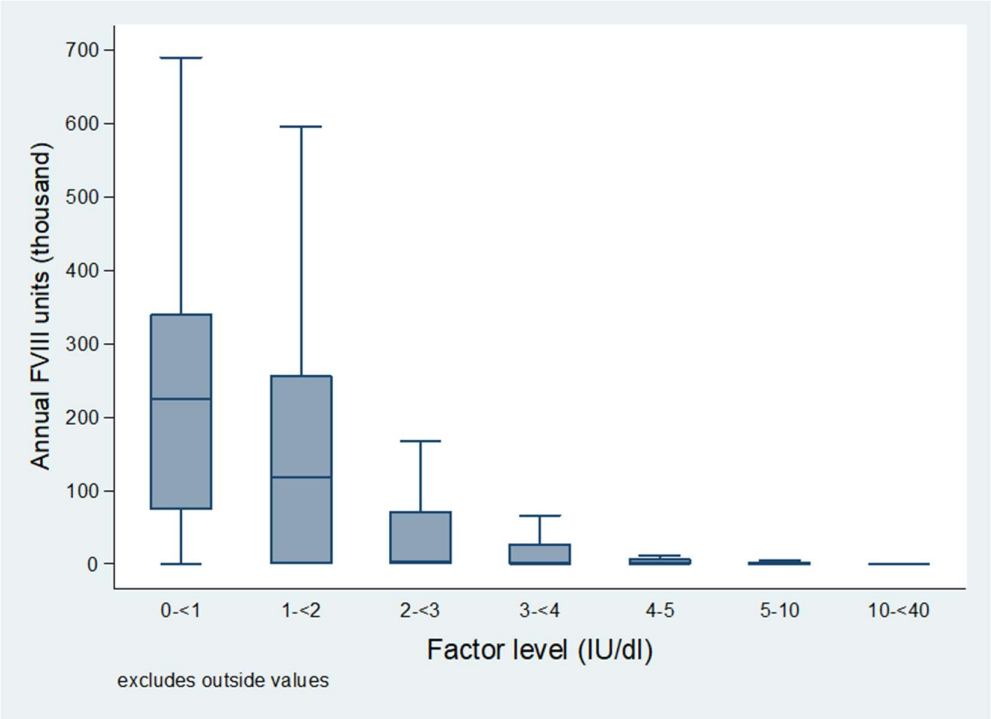


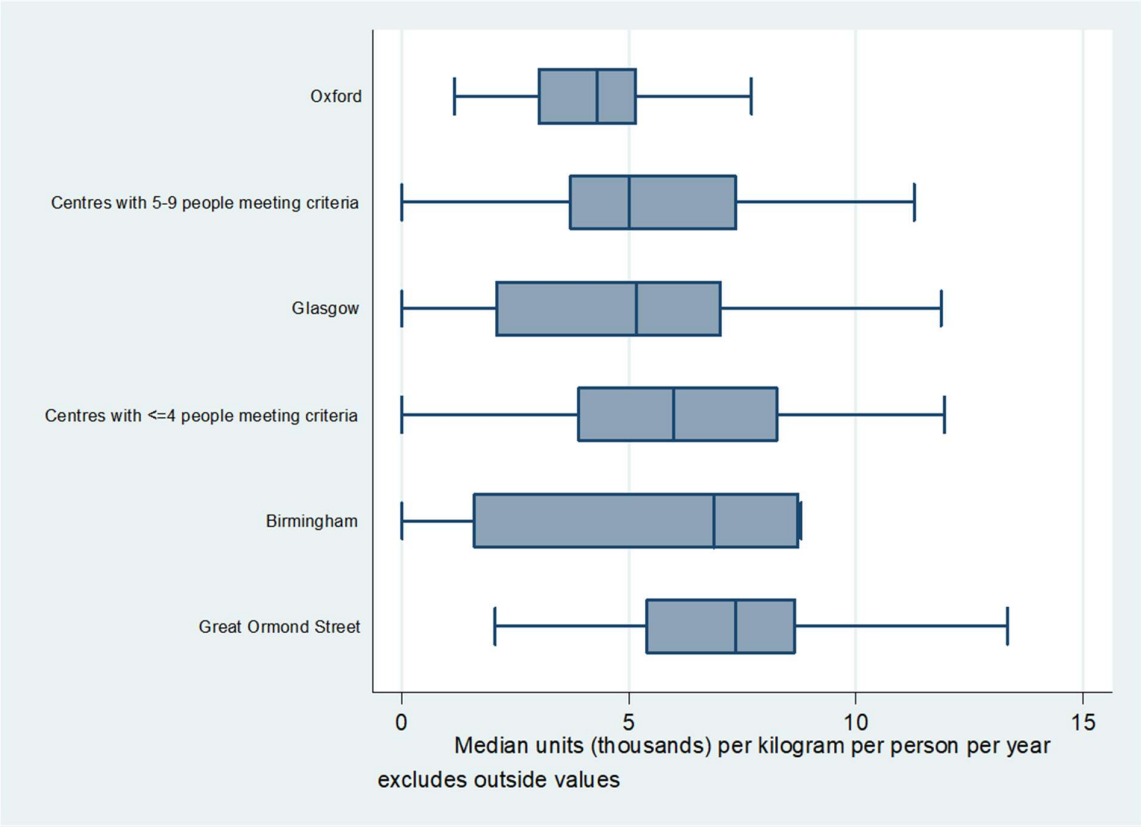
Figure 6b: This box and whisker plot shows the median, IQR and range of SHL-FVIII (IU/person/year) broken down by baseline FVIII level in people aged 18 years and above with haemophilia A. This shows that adults with a FVIII baseline of <1 and 1 - <2 IU/dl have substantial factor VIII requirements, and the factor VIII requirement falls off dramatically at higher levels of baseline factor VIII. Adults with a FVIII baseline level of 1 - <2 IU/dl have a significantly greater median factor VIII requirement than those with 2 - <3 IU/dl (Wilcoxon rank-sum p<0.005).

Summary statistics for figure 6b

Factor VIII level (IU/dl)	People (n)	Annual FVIII units (thousands) (median, (IQR))
<1	386	225.5 (76.0; 340.0)
1 - <2	46	119.0 (0.0; 256.5)
2 - <3	80	3.3 (0.0; 70.5)
3 - <4	89	0.0 (0.0; 27.0)
`4 - 5	196	0.0 (0.0; 6.0)
`5 - 10	441	0.0 (0.0; 2.0)
`10 - 40	2,583	0.0 (0.0; 0.0)
Total	**3,821**	**0.0 (0.0; 0.0)**

Exclusions from this analysis:
Issued emicizumab or EHL 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy
Issued trial product 2022/23
Issued plasma 2022/23

Figure 7a Annual FVIII issues (IU/kg/person) in people with severe haemophilia A aged under 18 years with no current inhibitor, by centre, ranked by median issues per person



Summary statistics for this chart are presented in the data table below.

Data table for Figures 7a & b

Haemophilia Centre	People (n)	People with weight reported	Total Units	Median Units	Median Units / Kg
Belfast	15	0	2,900,250	195,000	-
Birmingham	12	5	2,089,250	72,000	6879
Glasgow	14	13	2,446,800	150,750	5163
Great Ormond Street	49	49	15,492,250	304,000	7347
Oxford	25	25	5,022,250	225,500	4298
Royal London	14	0	1,709,000	119,750	-
St Thomas'	11	0	2,320,000	204,500	-
Centres with <=4 people meeting criteria	35	29	8,892,256	219,000	5972
Centres with 5-9 people meeting criteria	58	39	14,749,750	223,000	5019

**Median units/kg is not presented for centres with fewer than three people with weight reported*

Exclusions from this analysis:
Issued emicizumab 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy
Issued trial product 2022/23

Figure 7a: This shows FVIII issues per kilogram per person by haemophilia centre, ranked by median issues, in people with severe haemophilia A aged under 18 years old with no reported current inhibitor and a body weight reported in 2022/23. Centres with fewer than three people with weight reported are excluded. This figure should be interpreted with extreme caution since the median factor VIII usage is likely to be significantly distorted by the very variable uptake of emicizumab from centre to centre and also by variations in prescribing policy for this drug. In general, when new treatments are introduced, heavy users of factor VIII and those with the most severe bleeding phenotype tend to be switched first. This policy has also been adopted for emicizumab resulting in a reduction in the median factor VIII consumption in those not switched to emicizumab

This shows an almost twofold range in median treatment intensity between centres. This is a much lower range than in the past, suggesting greater uniformity in prophylaxis and possibly switching of high users and outliers to emicizumab. Most centres have broadly similar treatment intensity, as one would expect, given that prophylaxis is the standard of care.

Centres such as Great Ormond Street, which conduct a far greater number of immune tolerance induction procedures than other paediatric centres, will be expected to have high median issues but the difference is not dramatic. Although this chart excludes people with a reported current inhibitor, they may have a higher proportion of people with unreported low-level inhibitors following immune tolerance induction. It is now well recognised that some people who fulfil the internationally recognised criteria for tolerance (half-life greater than seven hours), and who have traditionally been thought to be inhibitor-free, continue to have low level inhibitor activity, which is too low to detect in the Bethesda assay but high enough to impair FVIII pharmacokinetics and increase FVIII consumption.

Figure 7b Annual FVIII issues (IU/person) in people with severe haemophilia A aged under 18 years with no current inhibitor, by centre, ranked by median issues per person

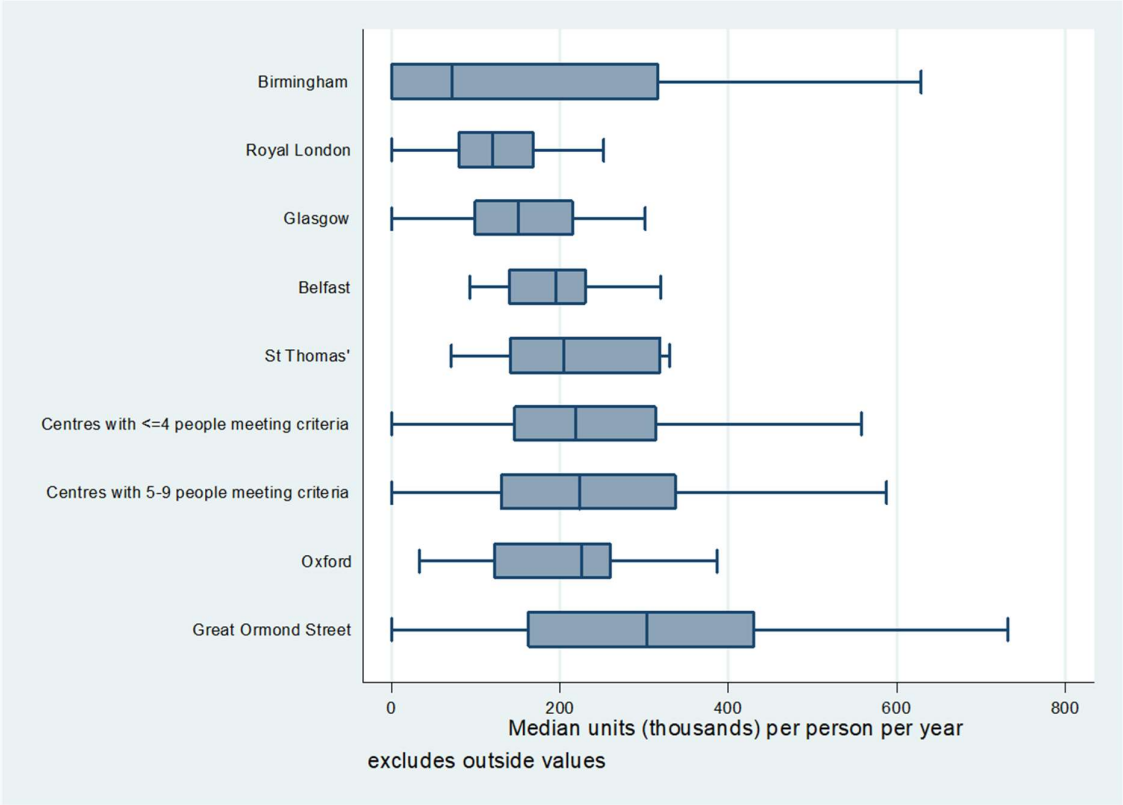


Figure 7b: This shows issues per person with severe haemophilia A, aged under 18 years by centre with no reported current inhibitor, as in the previous figure, but not corrected for body weight. It shows a more than fourfold range in median units used per person between centres. The interpretation is similar to the previous figure. The sample size is larger since the table includes people with and without known body weight.

The ranking of centres differs depending on whether it is expressed in IU/kg/person/year or IU/person/year.

Figure 8a Annual FVIII issues (IU/kg/person) in people with severe haemophilia A aged 18 years or more with no current inhibitor, by centre, ranked by median issues per person

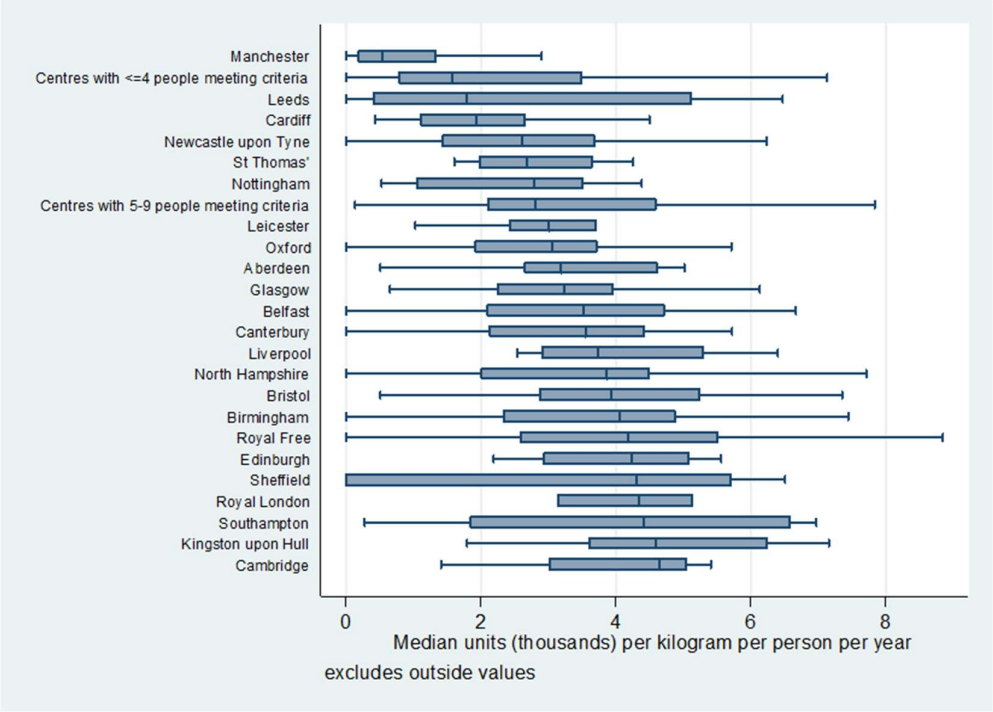


Figure 8a: This shows FVIII issues per kilogram per person by haemophilia centre, ranked by median issues, in people with severe haemophilia A aged 18 years or more with no reported current inhibitor, and an updated body weight reported. Bodyweight measurements were taken from no further back than January 2021 for people aged 18 years and above on the date of measurement, and from no further back than January 2022 for people aged under 18 years on the date of measurement.

Although it appears, superficially, that there is a wide range in factor VIII treatment intensity from centre to centre, these figures are now grossly distorted by the variable uptake of emicizumab from centre to centre. Manchester, for example, has switched about 85% of its people with severe Haemophilia A to emicizumab and those that continue to use factor VIII as their primary treatment are mostly those with a mild bleeding phenotype and/or treating themselves on-demand. Consequently, median factor VIII issues per kilogram (based on only seven people) appears to have reduced dramatically from year to year for that centre.

Exclusions from this analysis:
Issued emicizumab 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy
Issued trial product 2022/23

Data table for Figures 8a & b

Haemophilia Centre	People (n)	People with weight reported	Total Units	Median Units	Median Units / Kg
Aberdeen	10	10	2,812,000	303,500	3186
Belfast	47	43	13,115,000	292,000	3525
Birmingham	31	21	8,738,000	292,000	4056
Bristol	13	12	4,259,500	336,000	3927
Cambridge	15	4	3,031,000	132,000	4655
Canterbury	11	9	3,552,500	252,000	3555
Cardiff	19	10	3,680,500	194,000	1941
Edinburgh	10	9	4,143,500	308,500	4232
Glasgow	18	10	4,175,250	234,000	3233
Kingston upon Hull	10	10	4,829,000	450,000	4597
Leeds	19	13	4,285,500	77,000	1799
Leicester	10	6	2,252,000	244,500	3015
Liverpool	13	4	4,161,500	286,000	3744
Manchester	11	7	657,500	35,000	549
Newcastle upon Tyne	20	20	5,060,500	250,000	2607
North Hampshire	34	32	9,843,500	317,500	3872
Nottingham	11	11	2,305,000	182,000	2791
Oxford	63	62	15,339,750	237,000	3055
Royal Free	100	93	31,360,500	307,500	4190
Royal London	44	3	9,285,141	224,000	4349
Sheffield	15	7	3,041,000	156,000	4311
Southampton	12	11	4,078,500	367,500	4420
St George's	31	0	6,753,000	236,000	-
St Thomas'	64	4	16,762,500	266,250	2689
Centres with <=4 people meeting criteria	26	19	5,269,500	139,250	1578
Centres with 5-9 people meeting criteria	29	27	7,634,888	238,240	2809

Figure 8b Annual FVIII issues (IU/person) in people with severe haemophilia A aged 18 years or more with no current inhibitor, by centre, ranked by median issues per person

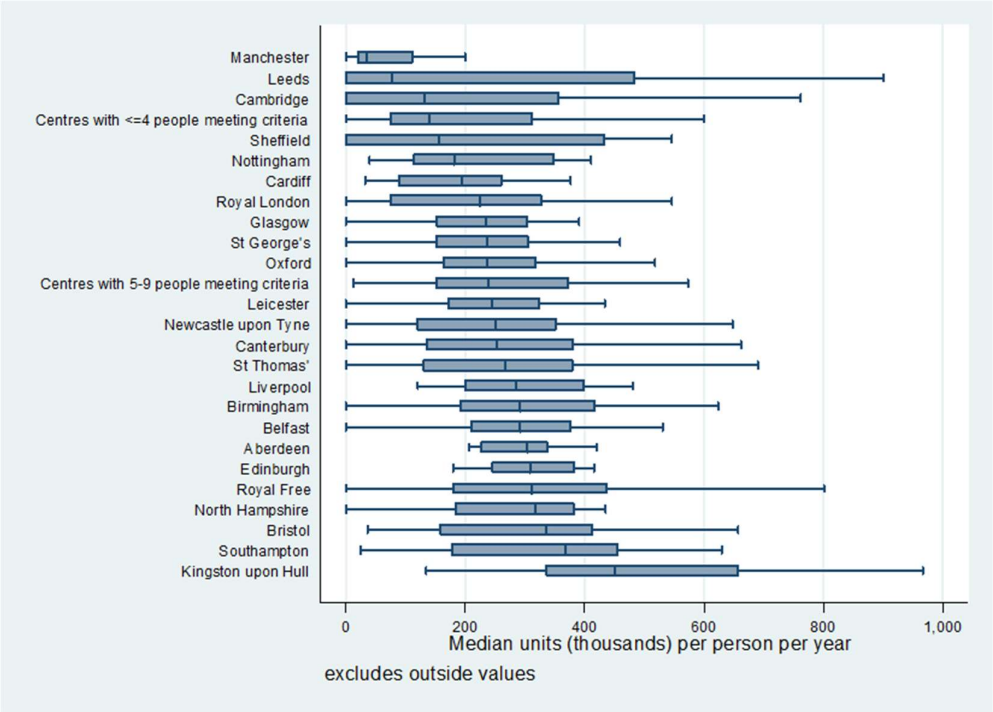
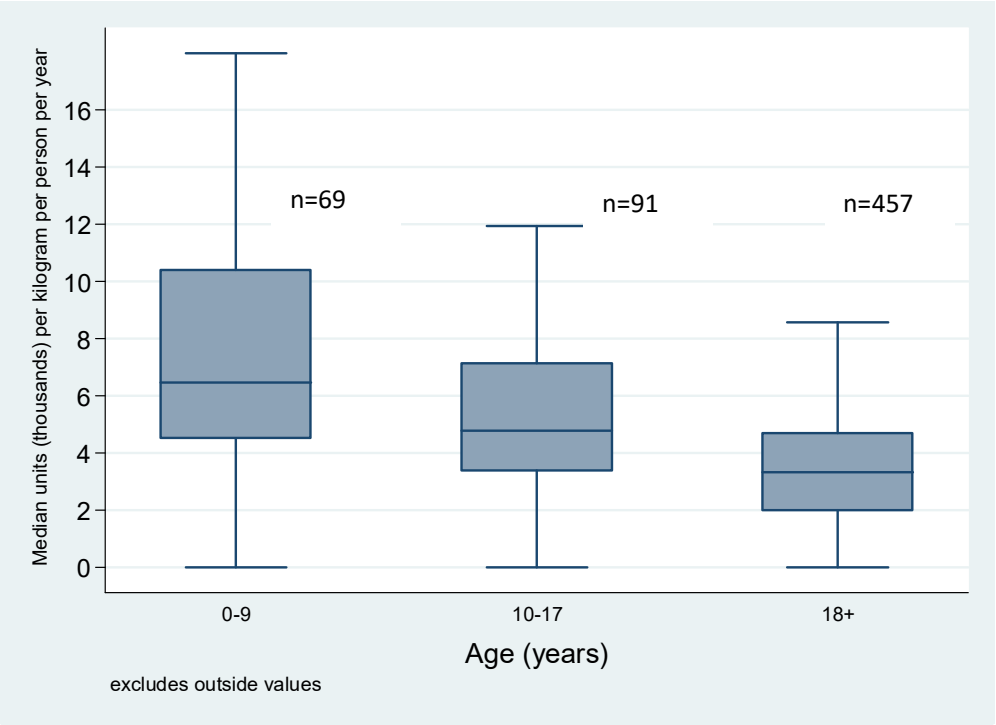


Figure 8b: This shows annual FVIII issues per person aged 18 years or more by centre, for people with severe haemophilia A with no reported current inhibitor not corrected for bodyweight. It shows a wide range in treatment intensity and interpretation is similar to the previous figure, though the sample size is larger since it includes people with and without a known bodyweight.

Figure 9 Median FVIII units issued per kilogram body weight per year in people with severe haemophilia A without inhibitors, by age



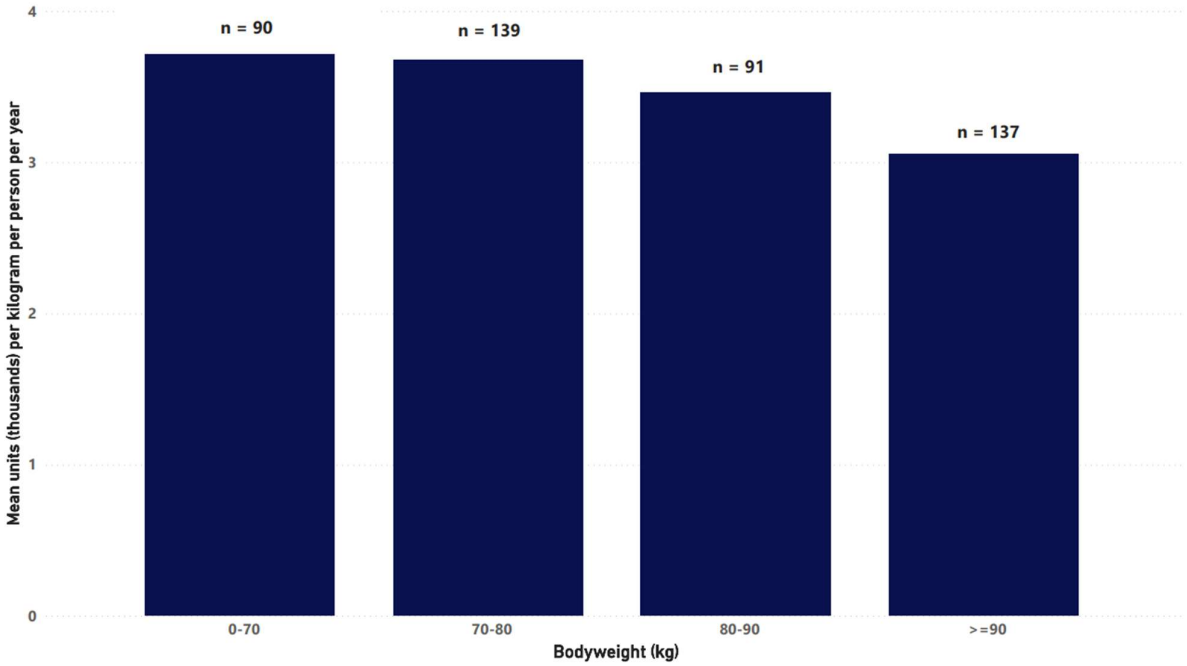
Weight data are missing for n= 302/919

Figure 9: This shows the median FVIII issues per kilogram body weight per year in people with severe haemophilia A without inhibitors, broken down by age.

The most intensive treatment appears to be in children aged under 10 years, as would be expected, given their shorter FVIII half-life. Vial size is also an issue for small children. Doses will often be rounded up because the range of available vial sizes does not make it possible to make small dose adjustments in very small individuals.

Exclusions from this analysis:
Issued emicizumab 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy
Issued trial product 2022/23

Figure 10 Mean annual FVIII units issued per kilogram body weight in people with severe haemophilia A without inhibitors aged 18 and over



Weight data are missing for n= 229/686

Spearman's rank correlation coefficient: p<0.005

Figure 10: This shows mean units per kilogram per person issued to people with severe haemophilia A aged 18 and over without inhibitors, broken down by body weight. The total number of people in each group is indicated by the number over each box. Since FVIII recovery increases progressively as Body Mass Index (BMI) increases, one would expect FVIII consumption per kilogram body weight to decline as body weight increases. This appears to be the case generally.

It is presumed that the '>= 90 kg' group will all be overweight, but the NHD does not record height, and therefore we cannot calculate BMI.

Exclusions from this analysis:
Issued emicizumab 2022/23
Registered for only part of the year 2022/23
Inhibitor 2022/23
Resident overseas
Gene therapy

Table 10 Products issued to treat people with haemophilia A (including inhibitors), 2021/22 and 2022/23

Product Type	Manufacturer	Product	2021/22 Units (IU)	2021/22 People (n)	2022/23 Units (IU)	2022/23 People (n)
Non-factor	Roche	Hemlibra (mg)	4,076,180	1,077	5,115,838	1,261
Recombinant	Novo Nordisk	Esperoct	72,609,400	378	90,114,294	539
		NovoEight	53,779,400	330	34,227,000	270
		NovoSeven (mg)	11,918	119	7,763	117
		Refixia	36,000	`1-2	-	-
	Octapharma	Nuwiq	10,666,500	88	9,909,000	98
	Pfizer	ReFacto AF	84,940,470	778	60,996,946	648
	SOBI/Biogen	Elocta	73,475,295	436	75,741,721	529
	Takeda	Advate	123,139,350	1,161	104,029,418	1,150
		ADYNOVI	4,042,000	16	7,348,500	19
		Veyvondi	-	-	4,550	3
		OBIZUR	14,000	`1-2	-	-
	Withheld	Investigational FVII	-	-	Withheld	Withheld
		Investigational FVIII	Withheld	Withheld	Withheld	Withheld
Plasma-derived	BPL	BPL FVIII 8Y	446,525	`1-2	235,000	`1-2
		Optivate	-	-	205,000	`1-2
	Biotest	Haemoctin	384,000	`1-2	413,000	`1-2
	CSL Behring	Voncento	147,800	11	129,500	5
		Fibrogammin P	10,000	`1-2	8,008	`1-2
		Riastap	3	`1-2	-	-
	Grifols	Fanhdi	1,478,000	5	378,000	4
	Octapharma	Octanate	1,525,000	4	1,558,000	5
		Octaplex	-	-	2,000	`1-2
	Takeda	FEIBA	1,265,000	23	1,035,000	20
Other	Withheld	Investigational other	Withheld	Withheld	Withheld	Withheld
Not known	Withheld	Investigational not known	-	-	Withheld	Withheld

Units in IU unless otherwise stated
Products which include VWF and FVIII are reported in FVIII units

Table 10 (previous page): This shows a breakdown of product volumes, listed by supplier, issued to treat people with haemophilia A during 2021/22 and 2022/23, including those with inhibitors but excluding acquired haemophilia. Please note these include people with haemophilia A combined with other blood disorders, e.g. haemophilia B and von Willebrand disease. People may be issued multiple products. This reflects the reduction in FVIII issues in recent years, as emicizumab is introduced to treat people with severe haemophilia A with and without inhibitors. Furthermore, there appears to be fluctuation in volumes issued between FVIII brands over the last two years.

These figures have yet to be cross-checked against sales figures supplied by the manufacturers for the same period. Whilst one would not expect a perfect match between NHD figures based on issues and the manufacturers' sales figures, there is usually a high level of correlation for all but the low usage rFVIII products, as well as emicizumab. These sales figures are not reported, by agreement with suppliers, for reasons of commercial sensitivity.

By and large, the plasma-derived products listed were used for immune tolerance induction. In general, there is a very steep decline in the use of plasma-derived factor VIII, which has largely fallen out of use altogether.

We have deliberately aggregated and anonymised investigational products to avoid any breach of confidentiality agreements and to take account of commercial sensitivities, although their use has declined steeply in recent years.

Figure 11 Number of people with haemophilia A treated in the UK 2022/23 broken down by product used

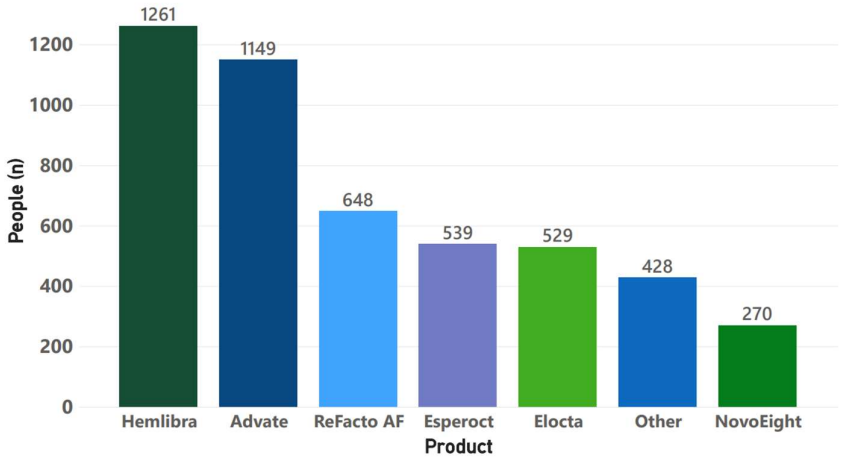


Figure 11: This shows the number of people with haemophilia A issued each product during the course of the year, including those issued to people with an inhibitor. The data that informs this graph can be found in Table 10. People issued multiple products in the year are included in the numbers for each product, so there is some double counting. There were 3,654 individual people with haemophilia A treated during the year

Table 11 Factor VIII and emicizumab treatment issued by UK haemophilia centres, by diagnosis 2022/23

Coagulation Defect	FVIII (IU)						Hemlibra		Total*
	People (n)	Plasma	Standard half-life recombinant	Enhanced half-life recombinant	Investigational **	Total	People (n)	mg	People (n)
Haemophilia A	3,037	2,916,500	209,156,364	173,182,515	Withheld	385,255,379	1,261	5,115,838	3,504
von Willebrand disease	748	30,580,100	246,900	651,500	-	31,478,500	`1-2	5,145	748
Combined factors V and VIII deficiencies	5	-	36,500	34,000	-	70,500	`1-2	30	5
Acquired haemophilia A	40	-	2,702,500	31,000	-	2,733,500	`1-2	5,760	40
Acquired von Willebrand disease	47	1,749,700	15,000	-	-	1,764,700	-	0	47
Platelet-type pseudo von Willebrand disease	`1-2	5,500	-	-	-	5,500	-	0	`1-2
Probable von Willebrand disease	`1-2	1,000	-	-	-	1,000	-	0	`1-2
Haemophilia B	`1-2	6,000	-	24,000	-	30,000	-	0	`1-2
Factor X deficiency	`1-2	-	-	14,000	-	14,000	-	0	`1-2
Miscellaneous	3	94,380	-	-	-	94,380	-	0	3
Bleeding disorder of unknown cause	`1-2	2,000	-	-	-	2,000	-	0	`1-2
Multiple diagnoses	3	-	27,000	565,500	-	592,500	-	0	3
Total*	**3,883**	**35,355,180**	**212,184,264**	**174,502,515**	**Withheld**	**422,041,959**	**1,261**	**5,126,773**	**4,354**

** Excludes suppressed numbers*

*** Due to commercial sensitivities, units have been withheld*

Products containing VWF as well as FVIII are reported in FVIII units

Table 11: This table shows factor VIII and emicizumab treatment use broken down according to diagnosis, including any apparently anomalous use reported to the NHD. Products used to treat von Willebrand disease which include VWF and FVIII are included and are reported in FVIII units. More detail on the use of these products to treat VWD is given in Table 21. Please note people issued with both FVIII and emicizumab are counted only once in the final column.

Issues of emicuzimab for von Willebrand disease, acquired haemophilia A and combined factors V and VIII deficiencies are presumed to be related to individual funding requests, since these indications are unlicensed and not yet subject to NHSE policy documents.

Figure 12 The proportion of people with severe haemophilia A and no inhibitor issued treatment by product type 2019 Q2 – 2023 Q1 Q2

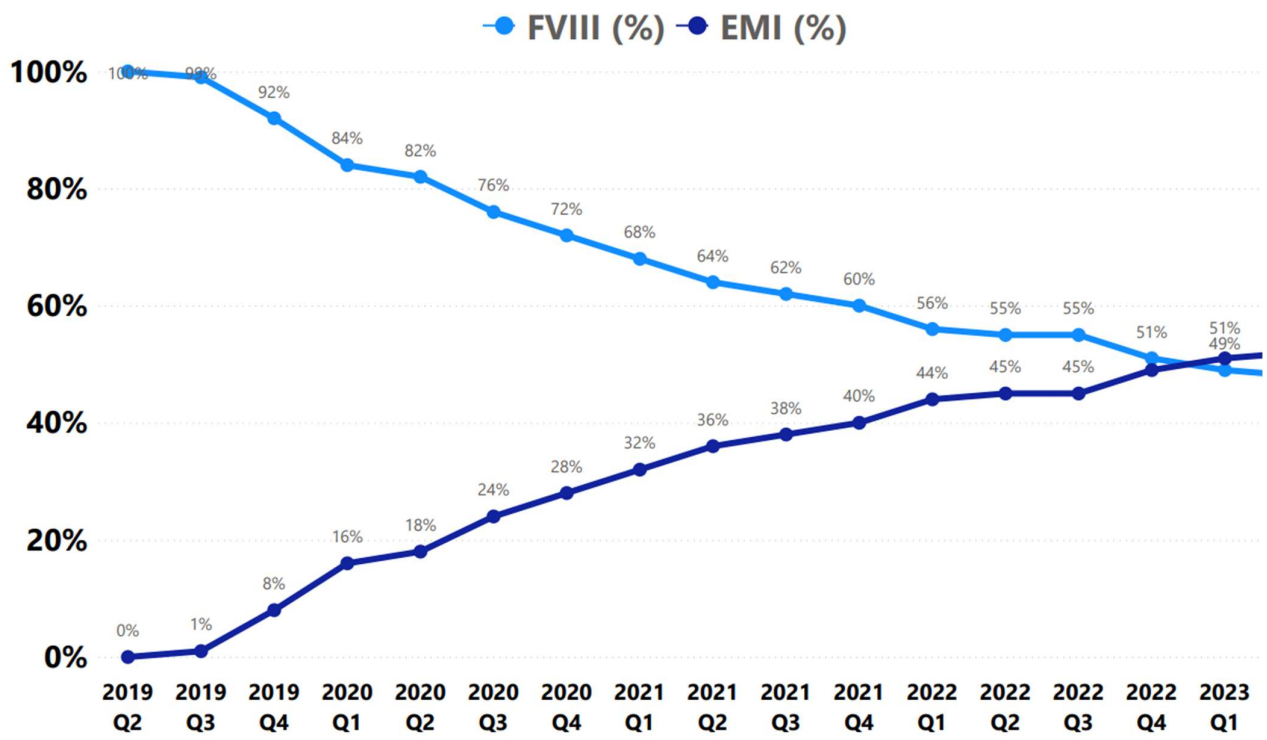


Figure 12: This shows a reduction in the proportion of people with severe haemophilia A, without inhibitors, who require factor VIII since emicizumab was introduced to this group in 2019 Q2. Please note that issue data from one haemophilia centre is incomplete.

Figure 13 The proportion of people with severe haemophilia A without inhibitors issued emicizumab by centre

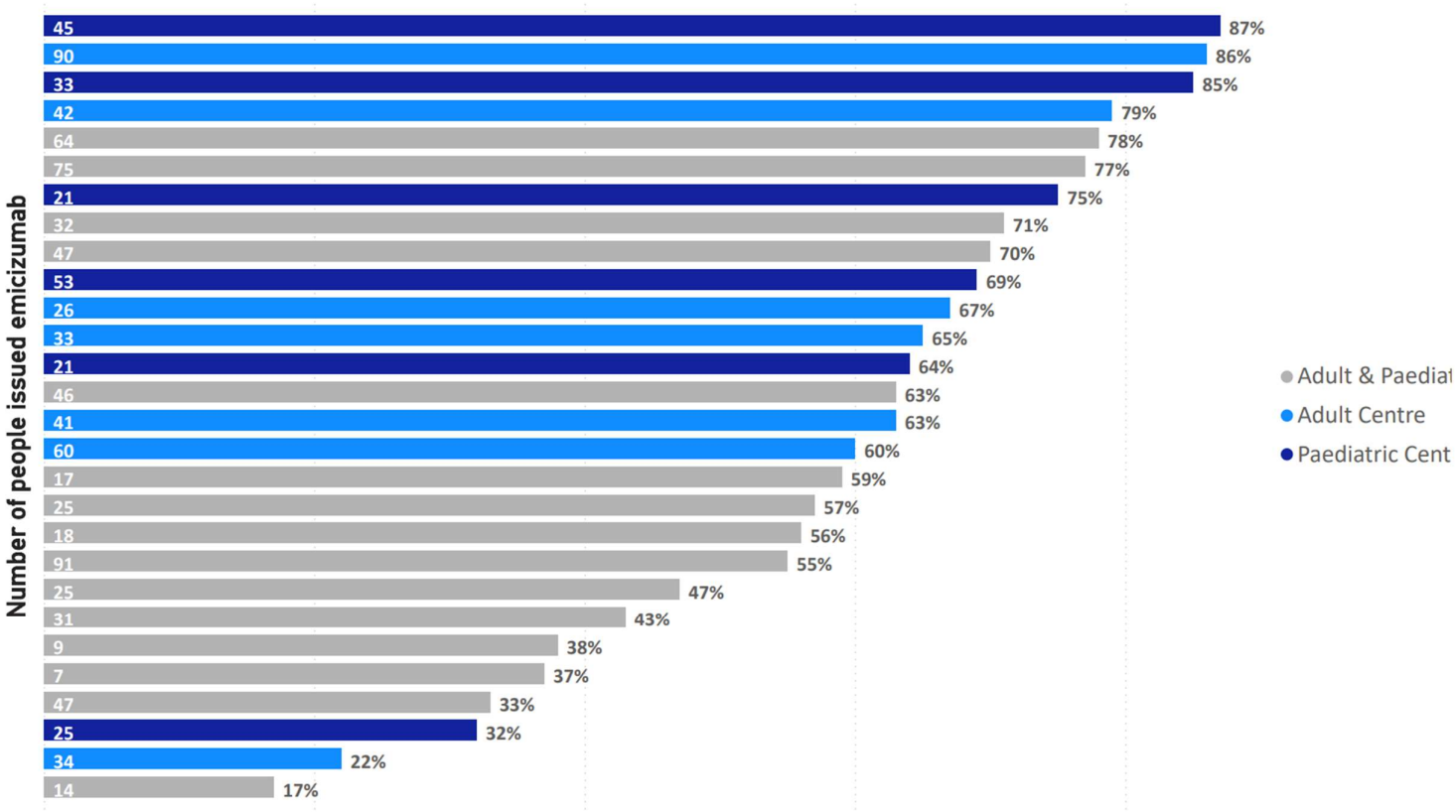


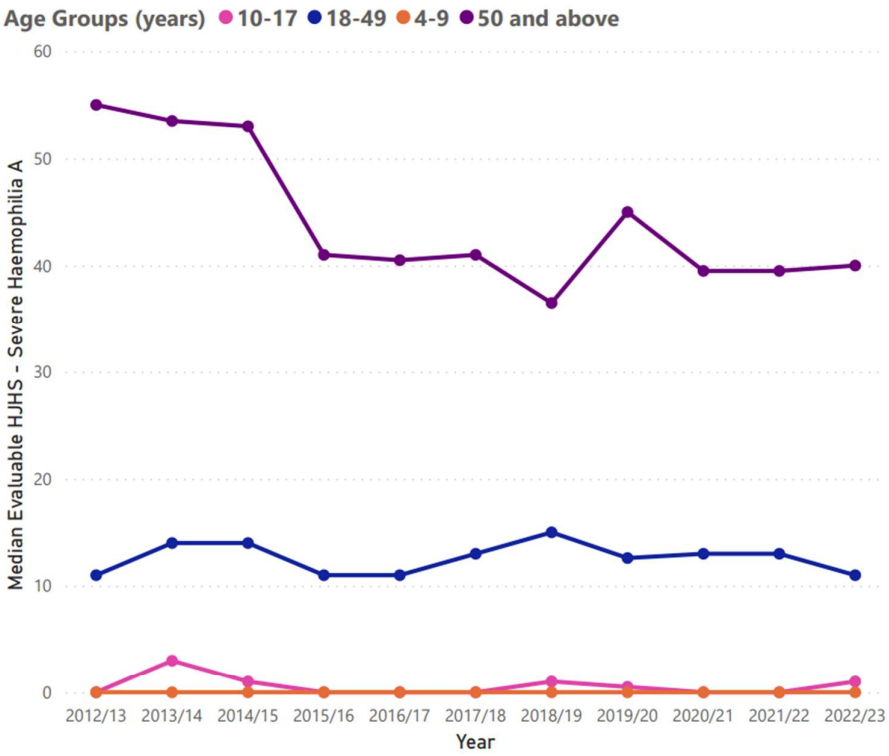
Figure 13: This shows the ranked proportion of people with severe haemophilia A without an inhibitor who were issued emicizumab, by centre, in 2022/23. This shows considerable centre-to-centre variation (median 59%, IQR 37-70%), which reflects diversity of clinical opinion.

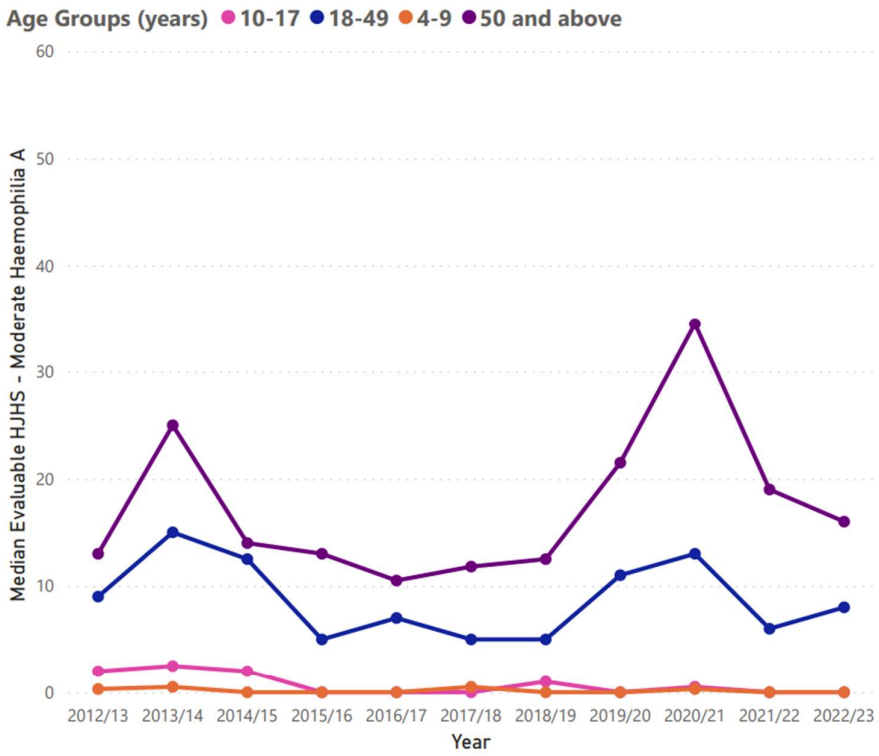
Table 12 Haemophilia joint health scores for people with haemophilia A without inhibitors 2012/13 - 2022/23

Severity (IU/dl)	Age (years)	Year	Registered, n	HJHS submitted, n (% of registered)	HJHS evaluable, n (% of submitted)	HJHS = 0, n (% of submitted)	Median (iqr) evaluable HJHS
<1 IU/dl	'4-9	2012/13	184	20 (10.9)	20 (100.0)	15 (75.0)	0.0 (0.0 -0.8)
		2017/18	210	85 (40.5)	81 (95.3)	53 (62.4)	0.0 (0.0 -0.9)
		2022/23	235	67 (28.5)	66 (98.5)	49 (73.1)	0.0 (0.0 -1.0)
	'10-17	2012/13	263	28 (10.6)	25 (89.3)	15 (53.6)	0.0 (0.0 -5.0)
		2017/18	262	129 (49.2)	125 (96.9)	63 (48.8)	0.0 (0.0 -3.6)
		2022/23	284	90 (31.7)	89 (98.9)	36 (40.0)	1.0 (0.0 -2.6)
	18-49	2012/13	877	68 (7.8)	63 (92.6)	7 (10.3)	11.0 (3.8 -32.6)
		2017/18	1,019	367 (36.0)	308 (83.9)	29 (7.9)	13.0 (4.9 -26.4)
		2022/23	1,096	269 (24.5)	256 (95.2)	44 (16.4)	11.0 (2.4 -24.5)
	50 and above	2012/13	177	17 (9.6)	17 (100.0)	0 (0.0)	55.0 (47.6 -63.7)
		2017/18	257	90 (35.0)	64 (71.1)	0 (0.0)	41.0 (28.7 -55.4)
		2022/23	325	100 (30.8)	73 (73.0)	0 (0.0)	40.0 (25.9 -51.1)
1-5 IU/dl	'4-9	2012/13	73	4 (5.5)	4 (100.0)	2 (50.0)	0.3 (0.0 -0.5)
		2017/18	65	21 (32.3)	21 (100.0)	10 (47.6)	0.5 (0.3 -2.3)
		2022/23	71	15 (21.1)	15 (100.0)	12 (80.0)	0.0 (0.0 -0.3)
	'10-17	2012/13	90	9 (10.0)	9 (100.0)	3 (33.3)	2.0 (0.6 -5.8)
		2017/18	100	28 (28.0)	26 (92.9)	14 (50.0)	0.0 (0.0 -3.8)
		2022/23	103	24 (23.3)	24 (100.0)	13 (54.2)	0.0 (0.0 -2.5)
	18-49	2012/13	368	18 (4.9)	16 (88.9)	2 (11.1)	9.0 (5.4 -10.1)
		2017/18	364	56 (15.4)	47 (83.9)	16 (28.6)	5.0 (1.2 -15.8)
		2022/23	388	56 (14.4)	54 (96.4)	13 (23.2)	8.0 (1.1 -16.9)
	50 and above	2012/13	198	6 (3.0)	5 (83.3)	0 (0.0)	13.0 (7.0 -26.0)
		2017/18	204	29 (14.2)	24 (82.8)	0 (0.0)	11.8 (6.0 -21.7)
		2022/23	231	28 (12.1)	25 (89.3)	1 (3.6)	16.0 (8.6 -24.2)

Table 12 and Figure 14 (overleaf): These shows HJHS for PwHA without inhibitors over the last ten years. It is hoped that the low submission of HJHS data for people with severe or moderate haemophilia can be improved. This shows that reported HJHS scores for children have been stable and close to zero for the 10-year period shown. It would appear that joint scores for older patients with severe haemophilia improved in mid decade. If true, this may be a response to increasing intensity and antedates the introduction of emicizumab. This is not seen in non-severe haemophilia. It is notable that older patients with non-severe haemophilia also have significant arthropathy, albeit with slightly lower joint scores than are observed in severe haemophilia.

Figure 14 Median evaluable HJHS of people with severe haemophilia A without inhibitors 2012/13 – 2022/23





2.2 Haemophilia B

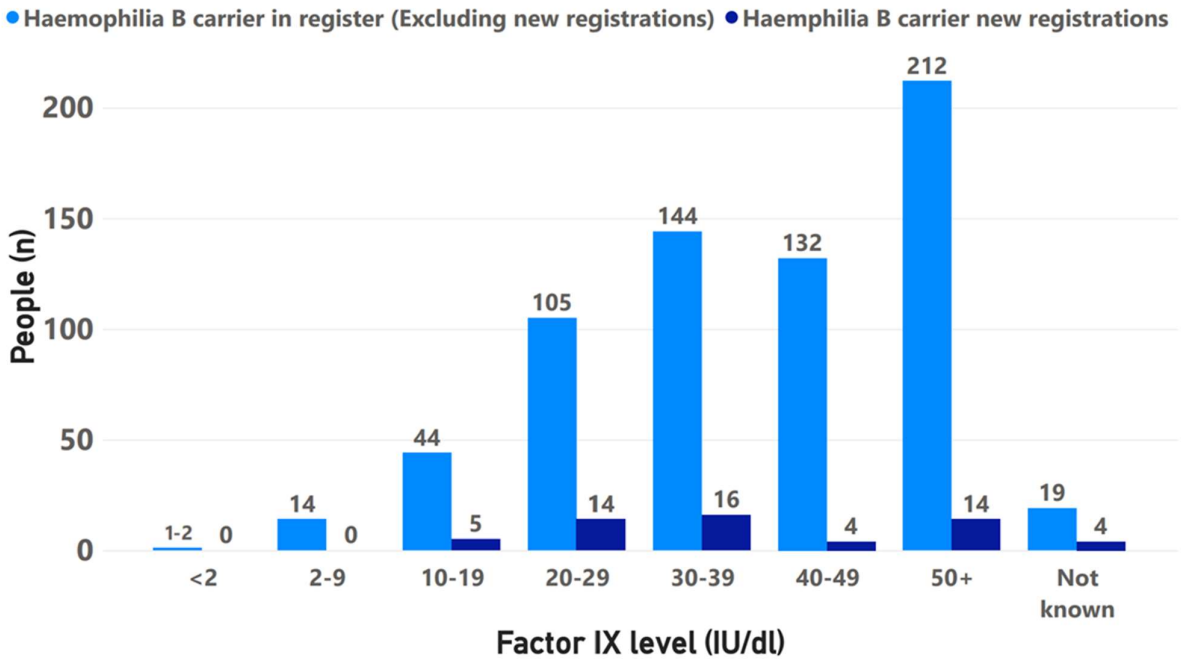
Table 13 People with congenital haemophilia B (including carriers) registered and treated, 2022/23

Haemophilia B	Age Range	Number of people by factor IX level (IU/dl)																	
		< 1			1 - 5			>5 & <40			≥ 40			Unknown			Total		
		Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
Total In Register	<18 years	125	-	**125**	75	-	**75**	107	81	**188**	9	47	**56**	4	6	**10**	320	134	**454**
	≥18 years	249	'1-2	**249**	270	6	**276**	450	255	**705**	46	315	**361**	7	17	**24**	1,022	593	**1,615**
	Total	**374**	**-**	**374**	**345**	**6**	**351**	**557**	**336**	**893**	**55**	**362**	**417**	**11**	**23**	**34**	**1,342**	**727**	**2,069**
New Registrations **	<18 years	6	-	**6**	'1-2	-	**-**	10	16	**26**	'1-2	5	**5**	'1-2	3	**3**	16	24	**40**
	≥18 years	3	-	**3**	4	-	**4**	10	19	**29**	3	13	**16**	'1-2	'1-2	**-**	20	32	**52**
	Total	**9**	**-**	**9**	**4**	**-**	**4**	**20**	**35**	**55**	**3**	**18**	**21**	**-**	**3**	**3**	**36**	**56**	**92**
Treated with concentrate FIX in year***	<18 years	115	-	**115**	50	-	**50**	37	4	**41**	'1-2	-	**-**	-	-	**-**	202	4	**206**
	≥18 years	214	'1-2	**214**	144	'1-2	**144**	121	40	**161**	'1-2	8	**8**	'1-2	'1-2	**-**	479	48	**527**
	Total	**329**	**-**	**329**	**194**	**-**	**194**	**158**	**44**	**202**	**-**	**8**	**8**	**-**	**-**	**-**	**681**	**52**	**733**

** This is the total excluding numbers which have been suppressed*
*** New registrations are a subset of the 'In Register' numbers*
**** Excluding people only treated with DDAVP and tranexamic acid*

Table 13: This shows the number of people with haemophilia B (including FIX Leyden, carriers and females with factor IX deficiency), broken down by severity, gender and age. The number of new registrations is also shown, as are the numbers issued concentrate.

Figure 15 Females with FIX deficiency and carriers of haemophilia B currently registered and newly registered, by baseline FIX level, 2022/23



N.B: Includes carrier of haemophilia B and females with FIX deficiency

Diagnosis	Number of Patients (Factor IX level (IU/dl))								
	<2	2-9	10-19	20-29	30-39	40-49	50+	Not Known	Total*
Haemophilia B carrier In register (excluding new registrations)	1-2	14	44	105	144	132	212	19	670
Haemophilia B carrier New registrations	0	0	5	14	16	4	14	4	57
Total*	**0**	**14**	**49**	**119**	**160**	**136**	**226**	**23**	**727**

** This is the total excluding numbers which have been suppressed*

Figure 15: This shows the distribution of reported FIX levels amongst registered carriers of haemophilia B in the UK. All carriers should be registered.

It is interesting that there is a relatively large number of very low-level carriers. These mostly have an extreme degree of lyonisation, but some are homozygous daughters from consanguineous unions.

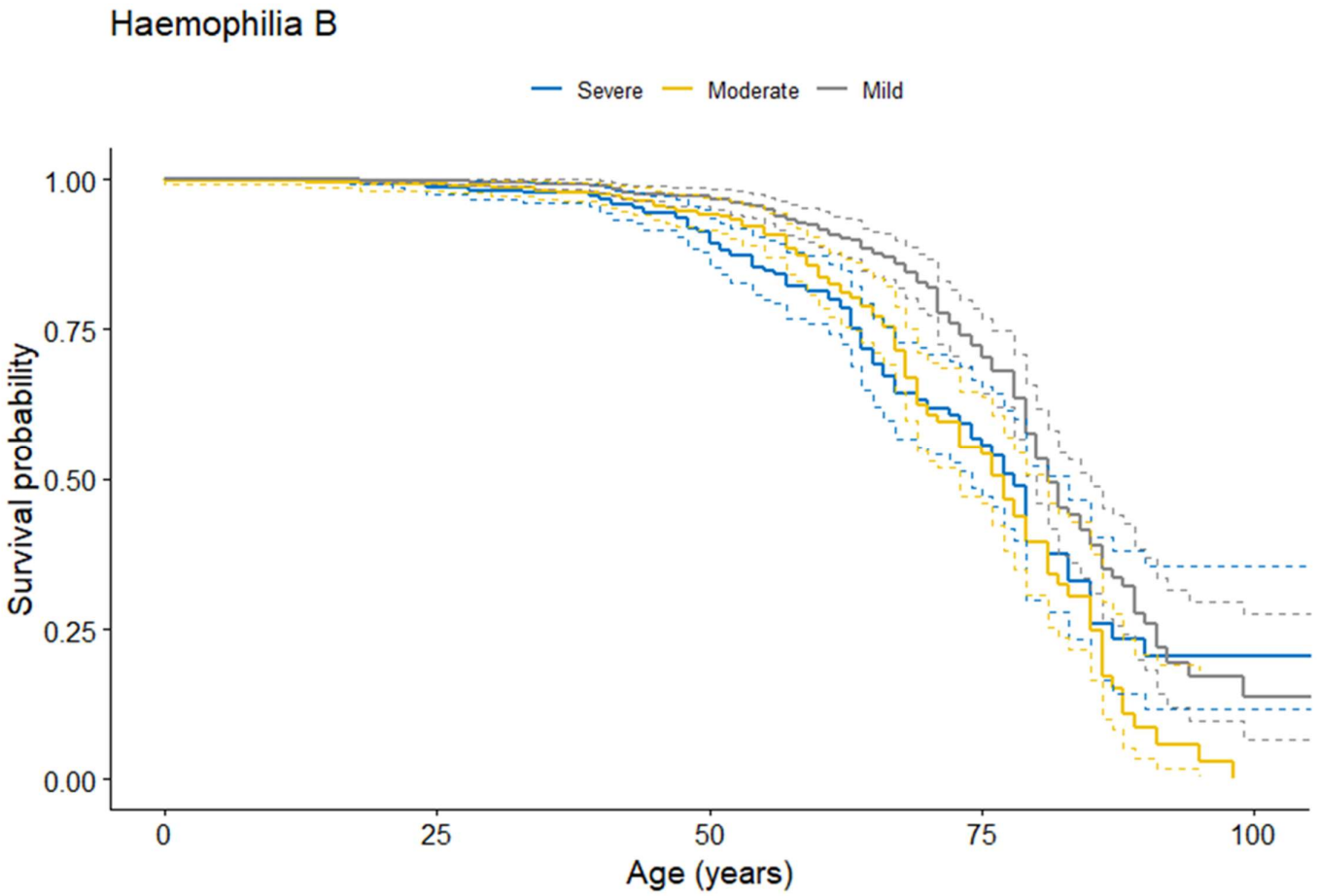
Table 14 New registrations of haemophilia B (including carriers), by age at mid-year, gender and severity, 2022/23

Haemophilia B	Number of people by factor IX level (IU/dl)																	
Age (years)	< 1			1 - 5			> 5 & < 40			≥ 40			Unknown			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total
0 - 1	6	-	6	'1-2	-	-	'1-2	'1-2	-	'1-2	'1-2	-	'1-2	'1-2	-	6	-	6
2 - 19	'1-2	-	-	'1-2	-	-	10	18	28	-	3	3	-	'1-2	-	10	21	31
20 and above	'1-2	-	-	3	-	3	9	16	25	3	13	16	'1-2	'1-2	-	15	29	44
Total*	**6**	**-**	**6**	**3**	**-**	**3**	**19**	**34**	**53**	**3**	**16**	**19**	**-**	**-**	**-**	**31**	**50**	**81**

**This is the total excluding numbers which have been suppressed*

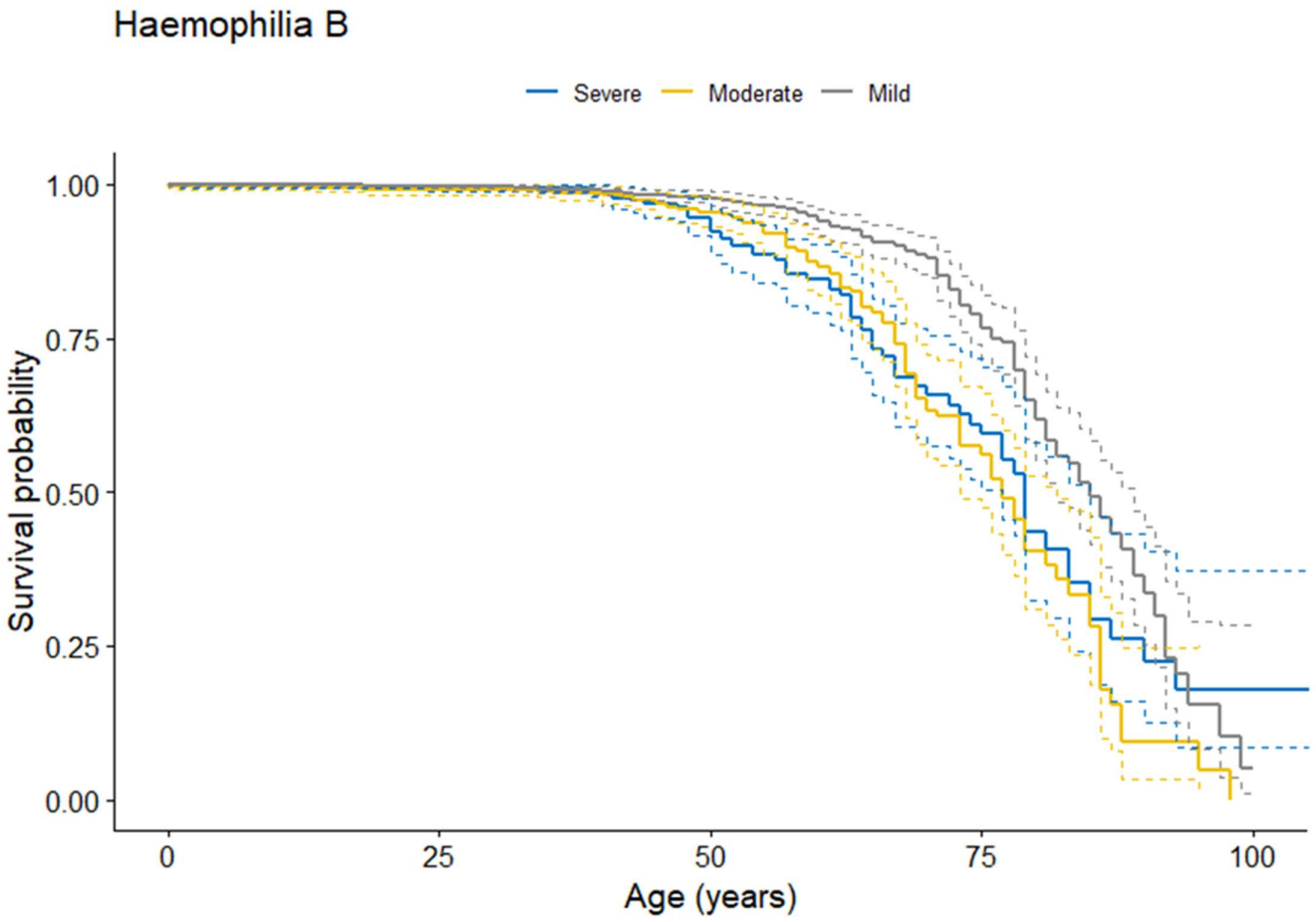
Table 14: This shows new registrations of haemophilia B broken down by reported severity and age at mid-year. Less severe disease will often present at a later age and the proportion of that group not native to the UK has not been investigated. It is presumed that most of those with severe haemophilia registered at aged two years or above have migrated or are visitors to the UK.

Figure 16a Survival of people with haemophilia B by severity, actively registered 1985-1995



Median survival time (years) for people with haemophilia B: severe: 78, moderate: 77, mild: 81

Figure 16b Survival of people with haemophilia B by severity, actively registered 1996-2023



Median survival time (years) for people with haemophilia B: severe: 79, moderate: 77, mild: 85

***Figure 16a and 16b*:** These show survival curves with 95% confidence intervals for severe, moderate and mild haemophilia B for the period 1985-95 and 1996-2023. This shows better life expectancy during 1985-95 for people with severe haemophilia B (median survival 78 years) than for severe haemophilia A (median 63 years) during that period. This may reflect the lower incidence of HIV in haemophilia B. These curves do not show a significant improvement in survival of people with severe haemophilia B during the period 1985-2023, which has not normalised relative to the survival of people with mild haemophilia B (median 85 years for people actively registered 1996-2023).

Figure 17 Factor IX units issued by UK haemophilia centres to treat severe haemophilia B, 2013/14 – 2022/23

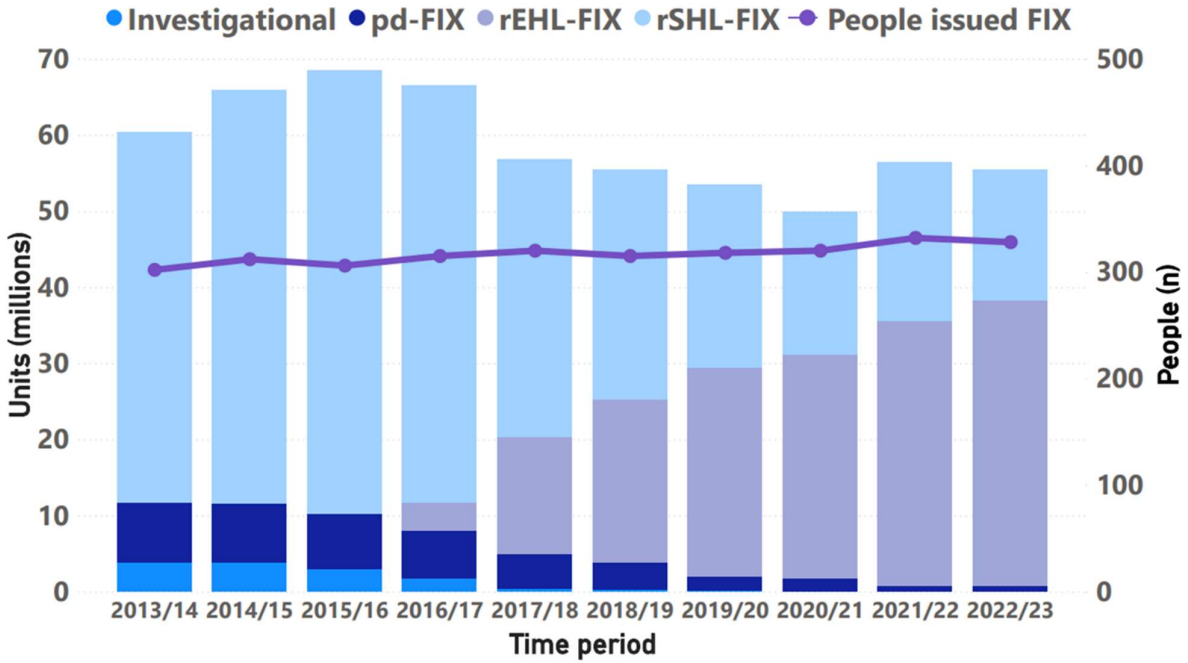


Figure 17: This shows FIX issues for severe haemophilia B 2013/14 to 2022/23. The number of people reported to have been issued FIX is shown by the purple line using a secondary axis and shows a gradual, fluctuating increase. Generally, FIX units issued have declined as a direct consequence of the switch to EHL-FIX products, which are generally prescribed in lower doses than standard products due to their longer half-life. There may also have been a temporary decline in issues associated with the general reduction in surgical interventions attributable to COVID-19 restrictions. This shows that people continue to switch from standard half-life to extended half-life products and plasma-derived factor IX concentrate is now used by relatively few people with severe haemophilia B. Gene therapy is also reducing the numbers requiring FIX to some degree but is not a marked trend.

Figure 18 Factor IX units issued by UK haemophilia centres to treat non-severe haemophilia B, 2013/14 - 2022/23

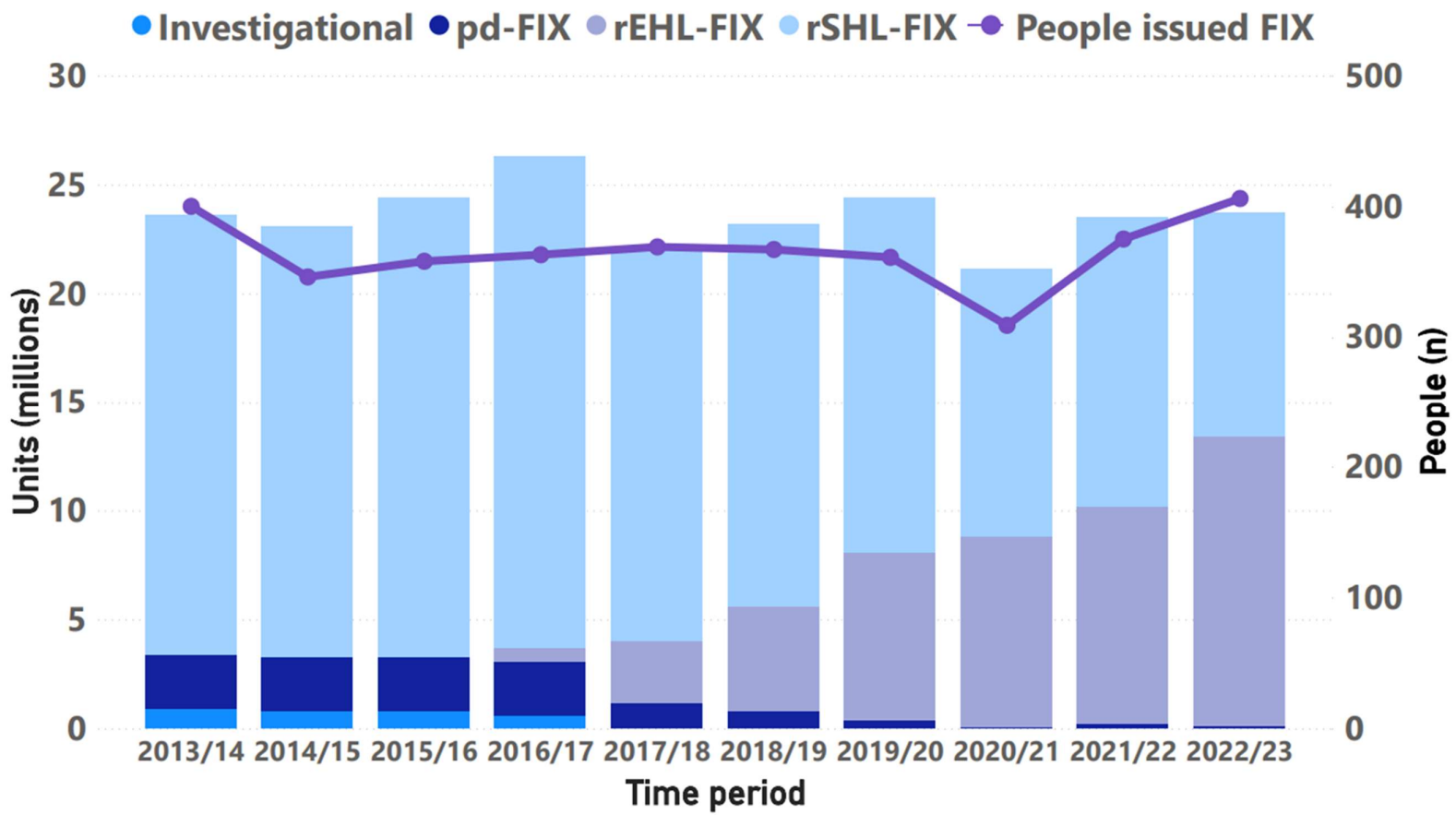


Figure 18: This shows FIX issues for non-severe haemophilia B 2013/14 to 2022/23. The number of people reported to have been issued FIX is shown by the purple line using a secondary axis.

Data table for Figure 17: Factor IX units issued by UK haemophilia centres to treat severe haemophilia B, 2013/14 - 2022/23

Year	pd FIX		Standard half-life rFIX (excluding investigational)		Investigational rFIX		Enhanced half-life rFIX		People issued FIX	
	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2016/17	n	% difference since 2013/14
2013/14	7.8	-	48.6	-	3.9	-	-	-	302	-
2014/15	7.8	-0.2	54.3	11.6	3.8	-4.6	-	-	312	3.3
2015/16	7.2	-8.3	58.3	20.0	3.0	-24.7	-	-	306	1.3
2016/17	6.2	-20.6	54.8	12.7	1.8	-54.3	3.7	-	315	4.3
2017/18	4.6	-41.1	36.5	-24.9	0.4	-90.8	15.3	316.6	320	6.0
2018/19	3.6	-53.6	30.2	-37.9	0.3	-93.5	21.3	480.2	315	4.3
2019/20	1.8	-76.4	24.0	-50.7	0.2	-95.4	27.4	645.7	318	5.3
2020/21	1.6	-79.1	18.7	-61.5	0.1	-98.1	29.5	701.7	320	6.0
2021/22	0.7	-90.6	20.9	-56.9	0.0	-99.9	35.1	854.2	332	9.9
2022/23	0.8	-89.4	17.3	-64.4	0.0	-100.0	38.1	937.5	330	9.3

Data table for Figure 18: Factor IX units issued by UK haemophilia centres to treat non-severe haemophilia B, 2013/14 - 2022/23

Year	pd FIX		Standard half-life rFIX (excluding investigational)		Investigational rFIX		Enhanced half-life rFIX		People issued FIX	
	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2013/14	IU (millions)	% difference since 2016/17	n	% difference since 2013/14
2013/14	2.5	-	20.2	-	0.9	-	-	-	400	-
2014/15	2.5	2.2	19.8	-1.9	0.8	-17.0	-	-	346	-13.5
2015/16	2.5	-0.8	21.1	4.4	0.8	-12.7	-	-	358	-10.5
2016/17	2.5	1.6	22.6	12.2	0.6	-34.9	0.6	-	363	-9.3
2017/18	1.2	-53.1	18.1	-10.2	0.0	-100.0	2.8	337.5	369	-7.8
2018/19	0.8	-65.9	17.6	-12.6	0.0	-100.0	4.8	653.5	367	-8.3
2019/20	0.4	-81.8	16.3	-19.2	0.0	-99.9	7.7	1116.6	361	-9.8
2020/21	0.1	-94.1	12.3	-39.1	0.0	-100.0	8.7	1272.5	309	-22.8
2021/22	0.2	-92.6	13.3	-34.0	0.0	-97.4	10.1	1503.9	376	-6.0
2022/23	0.1	-94.1	10.5	-48.1	0.0	-99.8	13.6	2050.1	411	2.8

Figure 19 Number of people with haemophilia B issued product by severity, 2013/14 - 2022/23

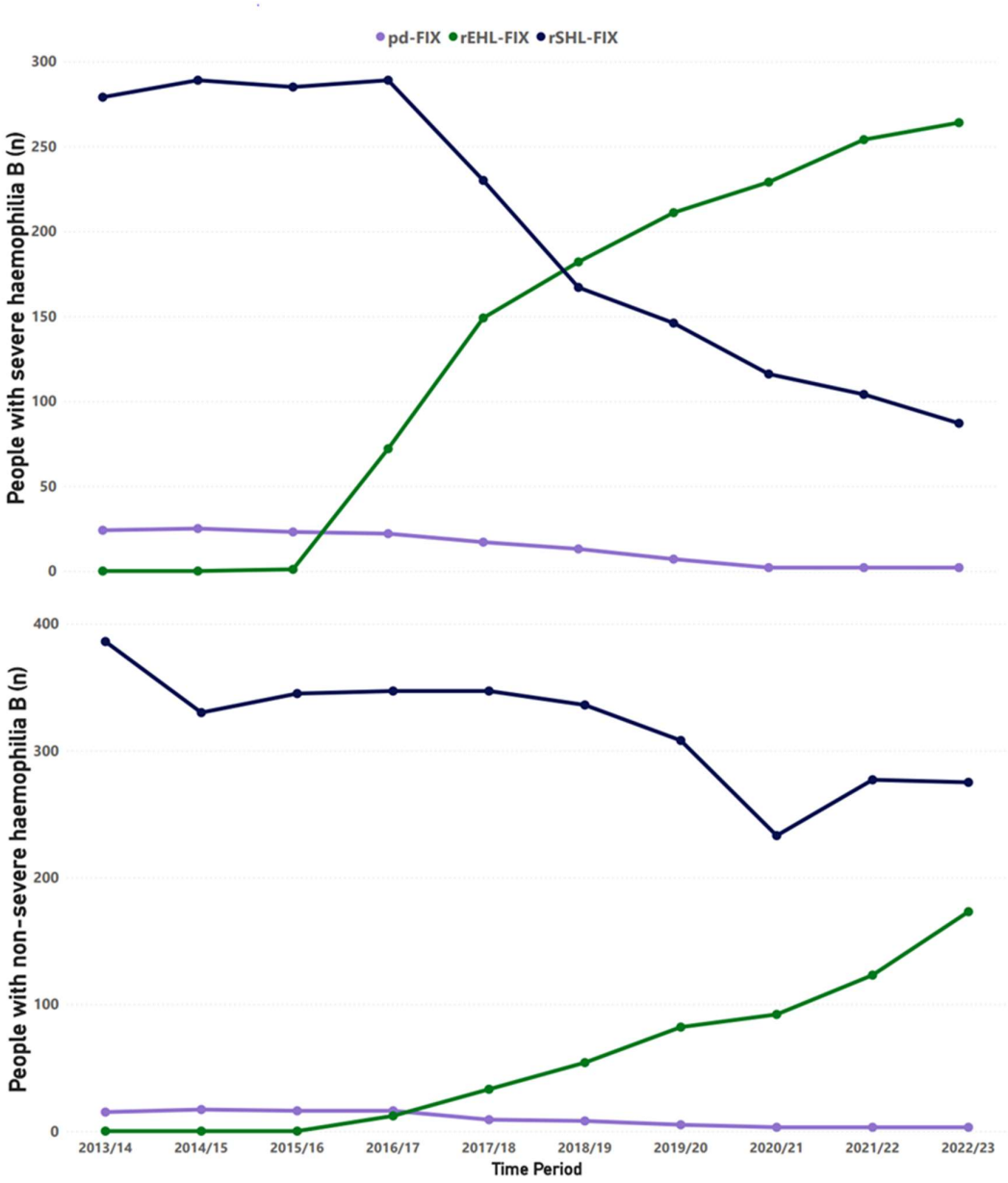


Figure 19: This shows a decline in the number of people with severe haemophilia B issued SHL-FIX, probably caused by the increasing use of EHL-FIX. Plasma-derived IX issues have also declined to a very low level and have almost fallen out of use.

Table 15 Factor IX mean issues by region for people with severe haemophilia B (including treatment for inhibitors and EHL-FIX), 2022/23

Country	Region	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21	2021/22	2022/23
England	North East & Yorkshire	208,243	221,835	232,559	215,202	188,713	179,493	164,138	149,526	157,404	145,962
	North West	218,573	209,088	241,317	232,160	206,333	173,598	174,033	156,910	151,888	135,509
	Midlands	192,222	204,069	225,171	192,419	153,993	137,821	135,128	98,872	128,454	144,955
	East of England	185,276	195,458	180,250	177,190	170,917	195,250	197,155	183,071	183,988	182,500
	London	227,257	250,677	254,066	225,728	200,205	212,171	182,997	178,216	196,544	188,598
	South East	168,590	185,200	193,711	209,040	154,866	158,845	146,055	145,341	168,000	160,198
	South West	183,140	229,958	189,964	231,909	249,000	237,591	277,037	342,492	236,136	210,100
Wales	Wales	152,501	166,419	146,046	156,337	136,909	147,727	146,854	122,792	209,308	140,250
Scotland	East of Scotland	237,554	205,222	278,000	196,278	86,477	78,250	100,227	81,917	79,139	100,028
	West of Scotland	167,333	158,288	178,717	164,450	146,500	140,567	155,567	153,875	152,054	189,031
Northern Ireland	Northern Ireland	241,188	261,643	278,888	258,438	245,417	158,531	215,906	191,531	194,833	218,525

Table 15: This shows mean FIX issues by region. This shows similar variation in treatment intensity to that observed with haemophilia A, although the number of people with this diagnosis is very much smaller and so between-region comparisons of treatment intensity cannot really be made. Also, there is greater interpersonal variation in clinical phenotype for this condition than for haemophilia A. Overall issues, when expressed in terms of units per person per year, have declined overall, reflecting the switch to EHL products.

Table 16 Products issued to treat people with haemophilia B (including inhibitors), 2021/22 – 2022/23

Product Type	Manufacturer	Product	2021/22		2022/23	
			Units (IU)	People (n)	Units (IU)	People (n)
Recombinant	CSL Behring	IDELVION	8,805,750	98	9,329,550	112
	Novo Nordisk	Refixia	6,825,500	63	8,545,000	82
		NovoSeven (mg)	8,350	11	168,926	12
	Pfizer	Benefix	33,158,050	375	27,143,150	360
	SOBI/Biogen	ALPROLIX	29,562,650	226	33,830,250	264
		Elocta	-	-	24,000	'1-2
	Takeda	RIXUBIS	1,107,000	4	640,000	4
	Withheld	Investigational FIX	Withheld	Withheld	Withheld	Withheld
Plasma-derived	BPL	BPL Replenine	920,360	5	979,000	5
	Octapharma	Wilate	-	-	6,000	'1-2
	Takeda	FEIBA	689,000	3	471,000	3
Other	Withheld	Investigational other	Withheld	Withheld	Withheld	Withheld

Units in IU unless otherwise stated
** Due to commercial sensitivities, units have been withheld*

Table 16: This gives a breakdown of the products issued to treat people with haemophilia B in the UK in 2021/22 and 2022/23, presented by supplier. Please note these may include people with haemophilia B combined with other blood disorders, e.g. haemophilia A and von Willebrand disease. These figures have yet to be cross-checked with sales figures provided by the suppliers. Whilst a perfect match between manufacturers sales figures and NHD issue figures would not be expected, there is a high level of correlation for the rFIX products. Sales figures are not reported here for reasons of confidentiality. The use of EHL-FIX continues to increase.

The use of investigational FIX has largely ceased due to clinical trials coming to an end. *It is advised that data on trial products be reported to the NHD, anonymising the product, and at a local level with commissioners so that they have a realistic estimate of future product consumption and avoid any inadvertent reduction in future budget.*

Potentially anomalous use is accounted for as follows:
Elocta was presumed to have been issued in error.

Table 17 Factor IX units issued by UK haemophilia centres, by diagnosis, 2022/23

Coagulation Defect	People (n)	FIX (IU)				
		Plasma	Standard half-life recombinant	Extended half-life recombinant	Investigational**	Total
Haemophilia B	741	979,000	27,783,150	51,704,800	Withheld	80,466,950
Acquired haemophilia B	1-2	-	20,000	-	-	20,000
Total*	**741**	**979,000**	**27,803,150**	**51,704,800**	**Withheld**	**80,486,950**

** Excludes suppressed numbers*

*** Due to commercial sensitivities, units have been withheld*

Table 17: This shows FIX issues reported to the NHD in 2022/23, broken down by product type and diagnosis.

Figure 20a Number of people with haemophilia B treated in the UK 2022/23 broken down by product used

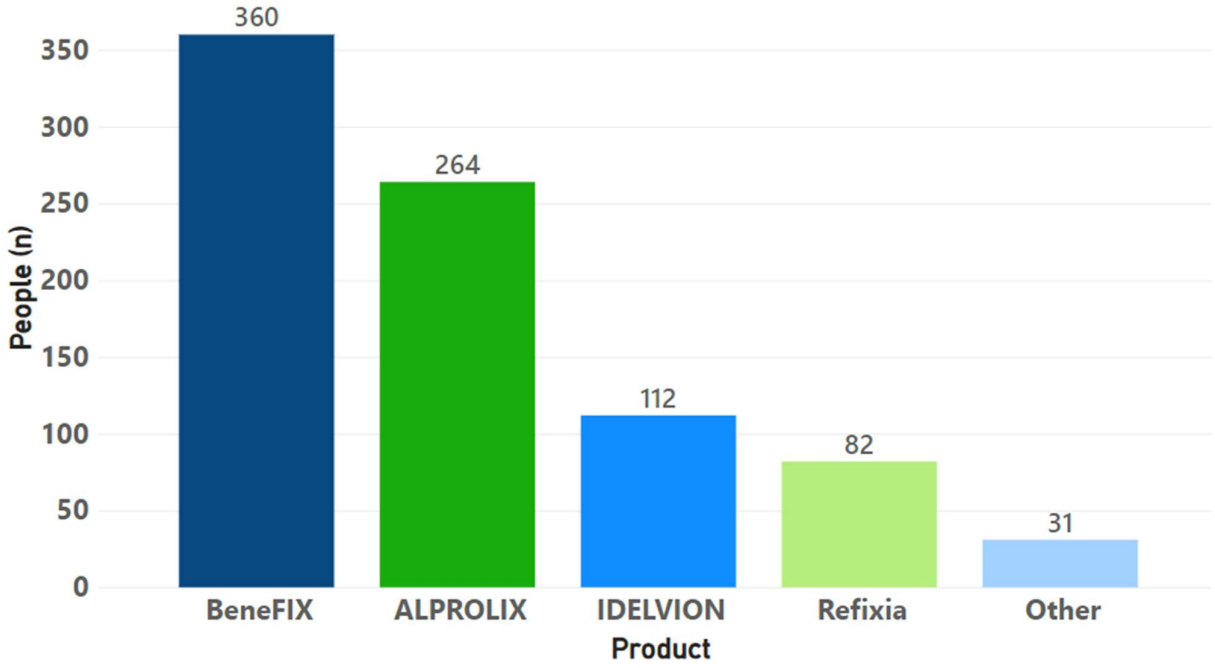


Figure 20a: This shows the number of people with haemophilia B treated by product, including those issued to people with an inhibitor. The data that informs this graph can be found in Table 16. People issued multiple products in the year are included in the numbers for each product, resulting in some double counting. There were 752 individual people with haemophilia B treated during the year. The large number of people using Benefix is a reflection of its episodic use for non-severe haemophilia B as well as its continued use for a declining proportion of people with severe haemophilia B.

Figure 20b The proportion of people with severe haemophilia B, without inhibitors issued with EHL products by centre

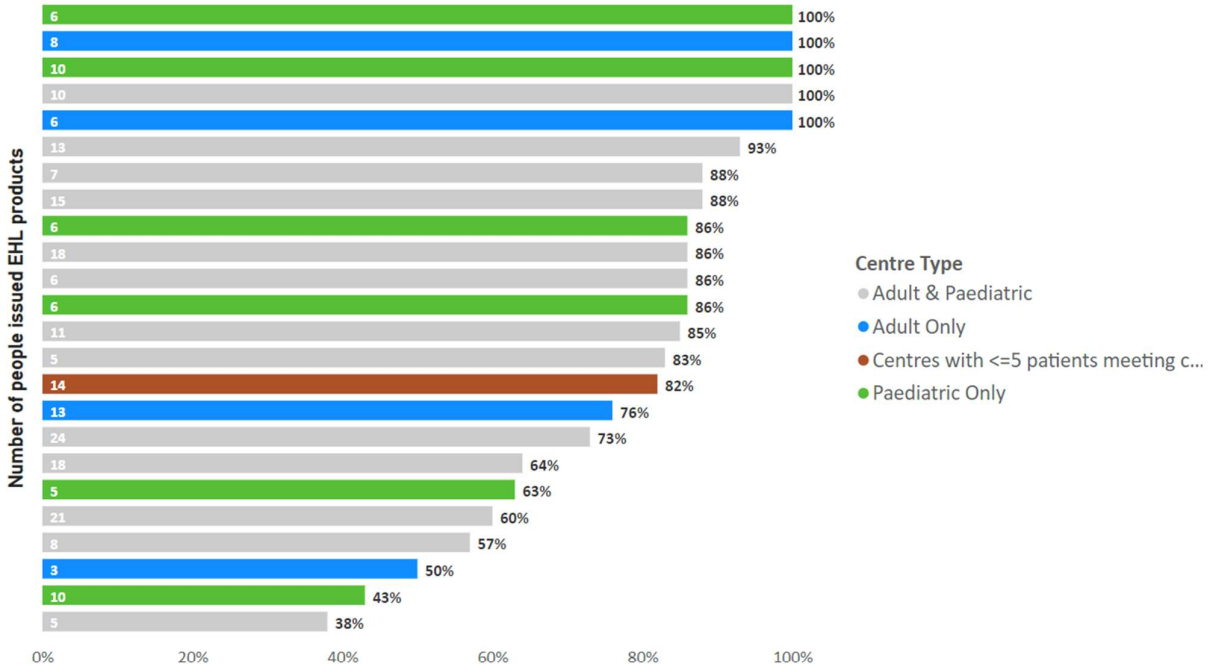


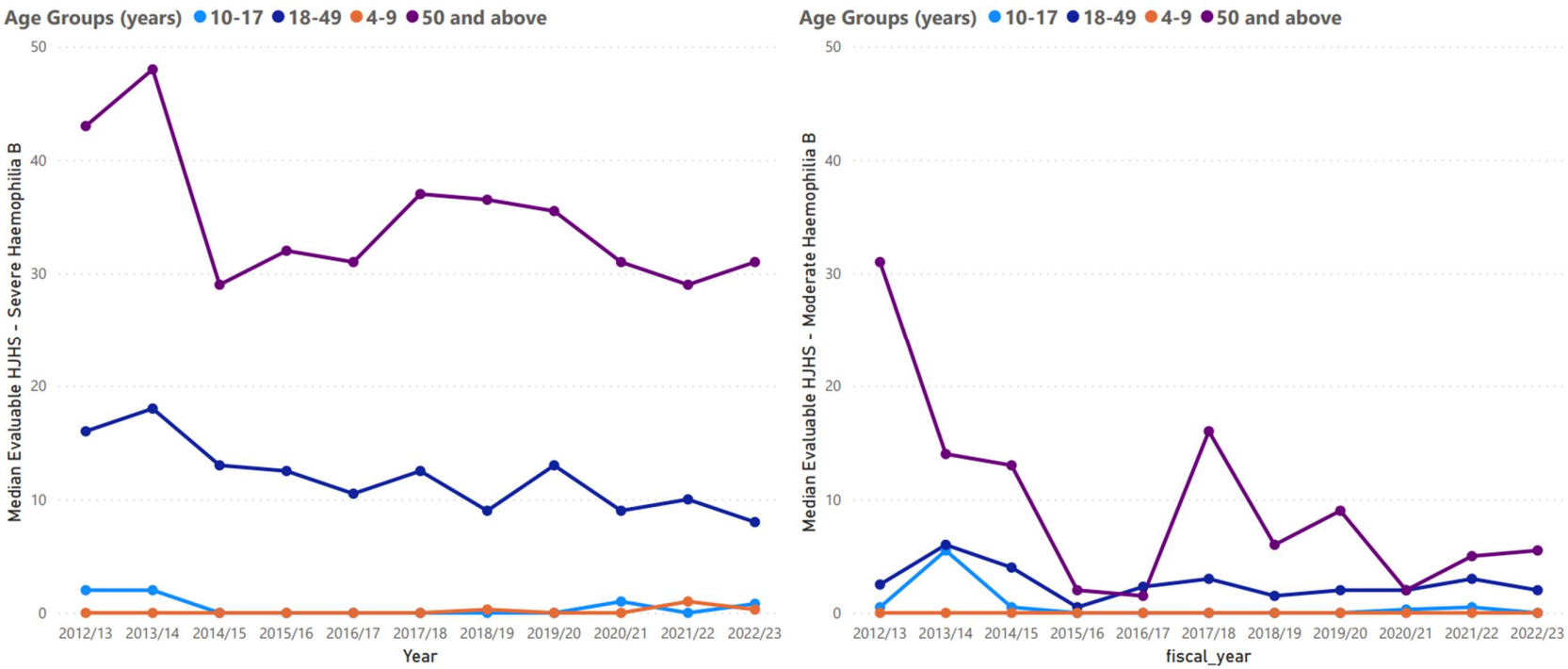
Figure 20b: This shows the ranked proportion of people with severe haemophilia B without an inhibitor who were issued EHL products, by centre, in 2022/23. The centres are not identified. The number of people per centre (presented on each bar) is, in many cases, small. Proportional uptake of EHL FIX concentrates appears to vary considerably amongst centres, although it is increasing.

Table 18 Haemophilia joint health scores for people with haemophilia B without inhibitors 2012/13 - 2022/23

Severity (IU/dl)	Age (years)	Year	Registered, n	HJHS submitted, n (% of registered)	HJHS evaluable, n (% of submitted)	HJHS = 0, n (% of submitted)	Median (iqr) evaluable HJHS
<1 IU/dl	'4-9	2012/13	39	3 (7.7)	3 (100.0)	3 (100.0)	0.0 (0.0 -0.0)
		2017/18	43	25 (58.1)	25 (100.0)	16 (64.0)	0.0 (0.0 -2.2)
		2022/23	37	12 (32.4)	12 (100.0)	6 (50.0)	0.3 (0.0 -1.9)
	'10-17	2012/13	38	3 (7.9)	3 (100.0)	1 (33.3)	2.0 (0.0 -2.0)
		2017/18	48	30 (62.5)	29 (96.7)	15 (50.0)	0.0 (0.0 -2.1)
		2022/23	57	24 (42.1)	24 (100.0)	11 (45.8)	0.8 (0.3 -2.3)
	18-49	2012/13	158	7 (4.4)	6 (85.7)	2 (28.6)	16.0 (15.3 -21.0)
		2017/18	160	57 (35.6)	52 (91.2)	5 (8.8)	12.5 (4.5 -22.1)
		2022/23	152	52 (34.2)	51 (98.1)	10 (19.2)	8.0 (2.0 -17.2)
	50 and above	2012/13	66	3 (4.5)	3 (100.0)	0 (0.0)	43.0 (36.0 -43.0)
		2017/18	72	18 (25.0)	11 (61.1)	0 (0.0)	37.0 (31.4 -59.2)
		2022/23	89	20 (22.5)	17 (85.0)	1 (5.0)	31.0 (27.1 -46.0)
1-5 IU/dl	'4-9	2012/13	19	2 (10.5)	2 (100.0)	2 (100.0)	0.0 (0.0 -0.0)
		2017/18	30	8 (26.7)	8 (100.0)	7 (87.5)	0.0 (0.0 -0.3)
		2022/23	28	11 (39.3)	11 (100.0)	7 (63.6)	0.0 (0.0 -0.3)
	'10-17	2012/13	32	4 (12.5)	4 (100.0)	2 (50.0)	0.5 (0.0 -1.0)
		2017/18	27	5 (18.5)	5 (100.0)	5 (100.0)	0.0 (0.0 -0.0)
		2022/23	38	9 (23.7)	9 (100.0)	5 (55.6)	0.0 (0.0 -1.8)
	18-49	2012/13	188	8 (4.3)	8 (100.0)	3 (37.5)	2.5 (0.3 -6.3)
		2017/18	170	22 (12.9)	22 (100.0)	6 (27.3)	3.0 (0.6 -6.0)
		2022/23	163	13 (8.0)	13 (100.0)	3 (23.1)	2.0 (0.6 -10.6)
	50 and above	2012/13	80	1 (1.2)	1 (100.0)	0 (0.0)	31.0 (31.0 -31.0)
		2017/18	92	9 (9.8)	6 (66.7)	1 (11.1)	16.0 (5.0 -15.7)
		2022/23	113	17 (15.0)	16 (94.1)	3 (17.6)	5.5 (1.2 -12.0)

Table 18 and Figure 21 (overleaf): This shows HJHS for PwHB without inhibitors over the last ten years. It is hoped that the low submission of HJHS data for people with severe or moderate haemophilia can be improved. It can be observed above that although data from ten years ago is scarce, joint health in PwHB aged over 50 years has improved over the last five years.

Figure 21 Median evaluable HJHS of people with severe haemophilia B without inhibitors 2012/13 - 2022/23



2.3 Von Willebrand Disease

Table 19 People with von Willebrand disease registered and treated 2022/23

Type of von Willebrand disease	VWD Activity IU/dl										Total*	Treated with Concentrate	Treated with Desmopressin
	<10	10 - <30	≥30	N/K	Subtotal*	<10	10 - <30	≥30	N/K	Subtotal*			
	<18 years					≥18 years							
Males													
1	18	214	258	5	**495**	107	444	681	90	**1,322**	**1,817**	**96**	**23**
2A	51	43	11	`1-2	**105**	107	109	44	`1-2	**260**	**365**	**84**	**3**
2B	11	10	5	-	**26**	19	41	22	-	**82**	**108**	**24**	-
2M	19	14	4	-	**37**	49	52	13	`1-2	**114**	**151**	**30**	**`1-2**
2N	`1-2	`1-2	4	-	**4**	3	4	29	`1-2	**36**	**40**	**8**	-
2 unspecified	12	15	`1-2	-	**27**	35	27	10	`1-2	**72**	**99**	**16**	**4**
3	22	`1-2	`1-2	-	**22**	62	15	`1-2	`1-2	**77**	**99**	**81**	-
Low VWF	`1-2	6	81	-	**87**	`1-2	13	150	`1-2	**163**	**250**	**6**	**3**
Other	-	-	`1-2	-	**-**	-	`1-2	`1-2	-	**-**	**-**	**-**	**-**
Unreported	42	110	165	12	**329**	138	291	560	63	**1,052**	**1,381**	**99**	**22**
										Total males*	**4,310**	**444**	**55**
Females													
1	29	164	172	6	**371**	157	819	1,761	149	**2,886**	**3,257**	**140**	**75**
2A	46	41	11	-	**98**	155	152	76	3	**386**	**484**	**101**	**13**
2B	10	15	6	-	**31**	19	52	40	3	**114**	**145**	**34**	-
2M	18	23	3	-	**44**	78	90	33	3	**204**	**248**	**43**	**3**
2N	`1-2	`1-2	7	3	**10**	8	10	76	7	**101**	**111**	**14**	**`1-2**
2 unspecified	12	12	3	-	**27**	32	44	21	-	**97**	**124**	**18**	**`1-2**
3	27	`1-2	`1-2	-	**27**	51	10	-	-	**61**	**88**	**62**	-
Low VWF	`1-2	4	78	-	**82**	`1-2	25	397	6	**428**	**510**	**7**	**17**
Other	-	-	-	-	**-**	-	-	`1-2	`1-2	**-**	**-**	**-**	**-**
Unreported	45	99	123	7	**274**	177	577	1,478	152	**2,384**	**2,658**	**130**	**34**
										Total females*	**7,625**	**549**	**142**
										Total males and females*	**11,935**	**993**	**197**

** Please note that totals and subtotals exclude suppressed numbers*

Table 19: (previous page): This shows the number of people with von Willebrand disease registered and/or treated broken down by age, activity level, subtype, gender and treatment. Whilst there is no generally agreed severity classification for VWD, the data are reported by the subdivisions <10, 10-<30 and ≥30% VW activity to give some indication of the distribution of severity amongst the UK cohort.

A VW subtype is reported for approximately 66% of registrations. Efforts are ongoing to tidy up this part of the database, but challenges include changing classification over time, old data, and changing opinion in relation to the diagnosis of mild type 1 VWD, which may have been over-diagnosed in the past. The diagnostic process for VWD is frequently in two stages (basic diagnosis and then subtyping) and the registration may be submitted to the NHD part-way through this process. The registration should be updated when the subtype becomes known. Type 1 defects should be reported at the time of original registration. The new database will send automatic reminders to complete registration of subtypes after initial incomplete registration. Changes in diagnosis should also be registered with the database. It is also going to be possible to capture temporal change in levels.

There remains a relative excess of adult females especially for type 1 VWD, reflecting referral bias of women with menorrhagia and possible over-diagnosis of mild type 1 VWD in the past. Some people have been de-registered or their diagnosis changed when they are re-investigated or when their VW activity level normalises with increasing age.

Table 20 (overleaf)**:** This shows that at least 356 people with von Willebrand disease were newly registered in the past year, of whom 15% were registered without a reported subtype.

This table supports previous reports of an apparent relative excess of female registrants after menarche, which reflects referral bias. New registrations of von Willebrand disease are more equally distributed between genders in people under 18 years of age.

Table 20 New registrations of von Willebrand disease between 2022/23, by age at mid-year, severity and gender

Type of von Willebrand disease	VWD Activity IU/dl								Total*
	<30	≥30	N/K	Subtotal*	<30	≥30	N/K	Subtotal*	
	<18 years				≥18 years				
Males									
1	15	27	-	**42**	6	7	-	**13**	**55**
2A	6	`1-2	`1-2	**6**	3	3	-	**6**	**12**
2B	`1-2	`1-2	-	**-**	`1-2	`1-2	-	**0**	**0**
2M	`1-2	-	-	**-**	`1-2	-	-	**0**	**0**
2N	`1-2	`1-2	-	**-**	-	`1-2	`1-2	**0**	**0**
2 unspecified	`1-2	-	-	**-**	`1-2	-	-	**0**	**0**
3	`1-2	-	-	**-**	`1-2	-	-	**0**	**0**
Low VWF	`1-2	13	-	**13**	`1-2	10	-	**10**	**23**
Unreported	5	6	`1-2	**11**	4	7	-	**11**	**22**
								Total males*	**112**
Females									
1	23	22	3	**48**	17	34	`1-2	**51**	**99**
2A	10	`1-2	-	**10**	7	6	-	**13**	**23**
2B	`1-2	-	-	**-**	4	`1-2	-	**4**	**4**
2M	4	-	-	**4**	`1-2	`1-2	-	**0**	**4**
2N	-	`1-2	`1-2	**-**	-	5	`1-2	**5**	**5**
2 unspecified	`1-2	`1-2	-	**-**	8	-	-	**8**	**8**
3	3	-	-	**3**	-	-	-	**0**	**3**
Low VWF	`1-2	20	-	**20**	5	38	`1-2	**43**	**63**
Unreported	6	4	-	**10**	12	13	`1-2	**25**	**35**
								Total females*	**244**
								Total males and females*	**356**

** Please note that totals and subtotals exclude suppressed numbers*

Table 21 Products issued to treat people with von Willebrand disease (including inhibitors), 2021/22 and 2022/23

Product Type	Manufacturer	Product	2021/22		2022/23	
			Units (IU)	People (n)	Units (IU)	People (n)
Non-factor	Roche	Hemlibra (mg)	7,980	4	11,985	3
Recombinant	Baxter	Recombinate (IU)	-	-	1,000	`1-2
	Novo Nordisk	Esperoct (IU)	-	-	19000	`1-2
		NovoEight (IU)	5,500	`1-2	2500	`1-2
		NovoSeven (mg)	2,604	7	1,610	7
	Pfizer	ReFacto AF (IU)	106,500	8	99,000	9
	SOBI/Biogen	Elocta (IU)	951,500	5	726,750	7
	Takeda	Veyvondi (IU)	3,008,250	181	5,262,392	315
		Advate (IU)	857,750	33	1,146,900	64
Plasma-derived	CSL Behring	Voncento - FVIII (IU)	20,708,650	557	22,311,100	521
		Voncento - VWF (IU)	49,700,760	557	53,546,640	521
	Grifols	Fanhdi (IU)	8,000	`1-2	-	-
	LFB Biomedicaments	Willfact (IU)	1,232,000	19	1,810,000	18
	Octapharma	Wilate - FVIII (IU)	8,161,500	208	8,273,500	180
		Wilate - VWF (IU)	8,161,500	208	8,273,500	180
		Octaplex (IU)	-	-	3000	`1-2
	Takeda	FEIBA (IU)	155000	`1-2	371000	4
Unknown	Unknown	Unknown	-	-	160	`1-2

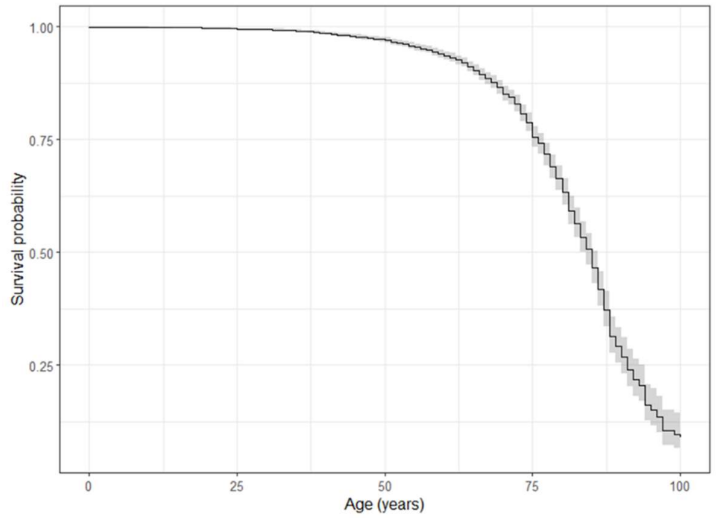
Units in IU unless otherwise stated

Products containing VWF and FVIII are reported separately in VWF and FVIII units

Table 21: This shows a breakdown of products issued to treat people with von Willebrand disease in the UK by supplier. Please note these include people with von Willebrand disease combined with other blood disorders, e.g. haemophilia A. These products are generally listed by and priced by their labelled FVIII content, with the exception of Willfact (LFB) and Veyvondi (Takeda), which are labelled and priced only by VWF content. Veyvondi is currently licensed for surgery and on-demand use only, which may have limited market penetration following its launch in the UK. Where factor VIII and VW units are shown for Voncento, Alphanate and Willate, the VW units have been derived by converting the factor VIII units issued, using the published FVIII:VWF ratio.

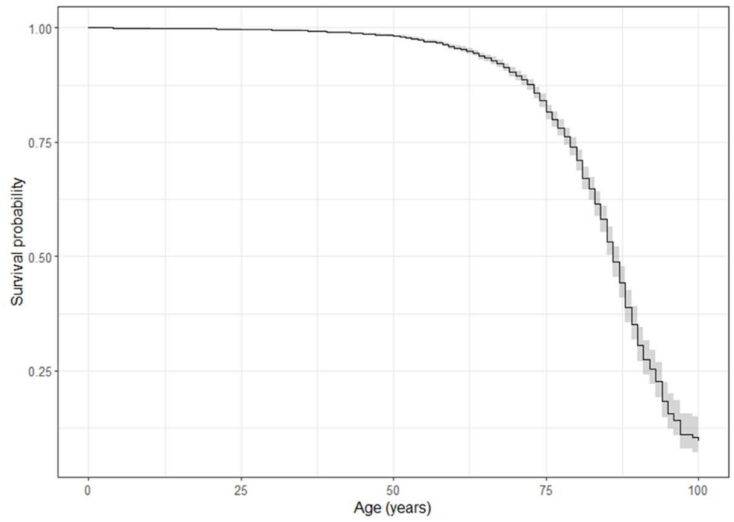
Advate was issued to 84 PwVWD over the last two years, of whom nine also had haemophilia A. Elocta was issued to eight PwVWD over the last two years. Emicuzimab was issued to people who also had haemophilia A, or was presumed to have been issued to PwVWD following individual funding requests.

Figure 22a Survival of people with VWD, actively registered 1985-1995.



Median survival time (years) for people with Von Willebrand disease is 85.

Figure 22b Survival of people with VWD, actively registered 1996-2023.



Median survival time (years) for people with Von Willebrand disease is 86.

Figures 22a and 22b: These show the survival curves (and 95% confidence intervals) for people registered with any type of von Willebrand disease, with a median survival of 85-86 years. Too few people are registered with subtypes of VWD for survival curves to be constructed for these groups. Consequently, the survival curve will be heavily weighted by people with type 1 VWD and milder type 2 phenotypes. People with von Willebrand disease, as a group, appear to have a normal life expectancy.

Figure 23 Units of von Willebrand Factor issued by UK haemophilia centres to treat von Willebrand disease 2013/14 – 2022/23

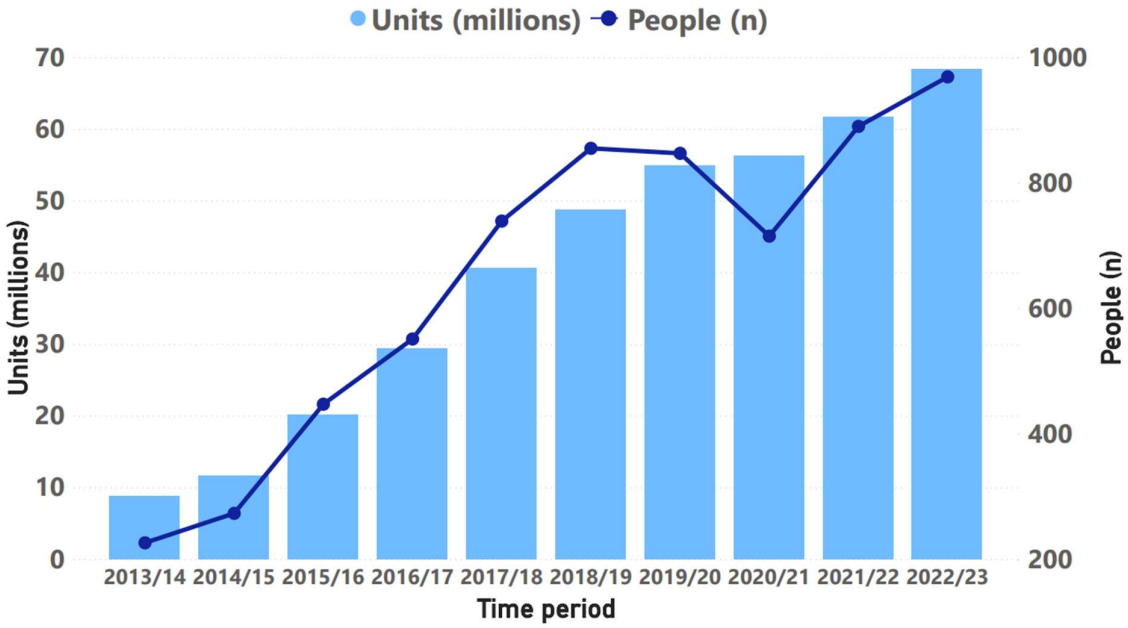


Figure 23: This shows von Willebrand factor units issued to treat von Willebrand disease from 2013/14 to 2022/23. This shows a steady and marked increase in the use of von Willebrand factor concentrate over this time period, probably attributable to increased surgical need and the greater use of prophylaxis in people with type 2 and type 3 VWD. The apparent fall in the number of people issued VWF in 2020/21 is probably attributable to deferral of surgery and other procedures during the COVID-19 pandemic.

2.4 Congenital and Acquired factor VIII, IX and VW Inhibitors

Table 22 Inhibitors by disease severity – congenital haemophilia A, haemophilia B & von Willebrand disease

Diagnosis	Severity (IU/dl) / Subtype	In Register *	Inhibitors n (%)							
			Newly Reported		Ongoing		Historical		Total**	
Haemophilia A	< 1	2,230	13	(0.6)	169	(7.6)	343	(15.4)	525	(23.5)
	`1-5	873	3	(0.3)	34	(3.9)	56	(6.4)	93	(10.7)
	>5	6,213	`1-2	(-)	20	(0.3)	42	(0.7)	62	(1.0)
	Total	**9,316**	**16**	**(0.2)**	**223**	**(2.4)**	**441**	**(4.7)**	**680**	**(7.3)**
Haemophilia B	< 1	374	`1-2	(-)	14	(3.7)	6	(1.6)	20	(5.3)
	`1-5	351	0	(0.0)	0	(0.0)	`1-2	(-)	0	(0.0)
	>5	1,344	0	(0.0)	0	(0.0)	`1-2	(-)	0	(0.0)
	Total	**2,069**	**0**	**(0.0)**	**14**	**(0.7)**	**6**	**(0.3)**	**20**	**(1.0)**
Von Willebrand disease	Type 1	5,074	0	(0.0)	0	(0.0)	`1-2	(-)	0	(0.0)
	Type 3	187	3	(1.6)	6	(3.2)	4	(2.1)	13	(7.0)
	Other/ unreported	6,674	0	(0.0)	`1-2	(-)	`1-2	(-)	0	(0.0)
	Total	**11,935**	**3**	**(0.0)**	**6**	**(0.1)**	**4**	**(0.0)**	**13**	**(0.1)**

** Including those not regularly treated*

*** Please note that totals exclude suppressed numbers*

New: Reported this year and not in previous years
Ongoing: Reported this year and in previous years
Historical: Reported in previous years and not in this year

Table 22 (previous page): This table shows the incidence of new inhibitors in the past year, the history of inhibitors ever registered and the prevalence of those still considered active for haemophilia A, B and von Willebrand disease, broken down by disease severity. There has been a downward trend in the number of reports of new inhibitors in PwSHA over the last few years, from 24 in 2016/17 to twelve in the past year.

Those labelled "new" were reported for the first time in the year 2022/23. Those labelled "ongoing" are reported in previous years and have not been eradicated and remain clinically significant in 2022/23. Those reported as "historical" were reported in previous years and not reported to be ongoing in 2022/23 and are therefore assumed to have been tolerised.

An inhibitor is designated as historical if it is no longer reported in the quarterly returns within 2022/23. There is necessarily some lack of precision surrounding this categorisation, as inhibitors thought to have been eradicated may persist at a variable low level, below the level of detection of the Bethesda assay although high enough to shorten the FVIII half-life. These inhibitors may re-emerge as have up to 25% of inhibitors after tolerisation (International ITI registry data) or after FVIII prophylaxis is replaced with emicizumab. We have received a number of reports of recurring inhibitors after switching to emicizumab. Some of these were clearly ongoing. To add to the "softness" of the "historical inhibitor" designation, it is clear anecdotally that there may be inconsistency in reporting that an inhibitor has been eliminated when, in some cases, the factor VIII half-life remains very short.

The table shows that a history of inhibitor is over twice as prevalent in severe as in moderate haemophilia A and twenty over times more prevalent than in mild haemophilia A. The proportion of people with non-severe haemophilia A thought to have eliminated their inhibitor cannot be known with certainty, however, since some may have an undetectable inhibitor which may reappear as soon as they have FVIII replacement. Similarly, many "ex-inhibitor" people with severe haemophilia probably continue to have some low-level inhibitor activity, below the level of detection of the Bethesda assay.

Inhibitors in haemophilia B are far less common, with a prevalence of 1.0% of people registered with severe haemophilia B, and 0% for people registered with non-severe haemophilia B. These arise early in the person's treatment and usually only in people with severe haemophilia B caused by FIX gene deletions. Inhibitors in von Willebrand disease appear in our cohort almost exclusively in type 3 VWD. The relatively low numbers of inhibitors in haemophilia B and von Willebrand disease marked as "historical" suggest these inhibitors are difficult to eradicate.

Table 23 (overleaf): This shows products reported to have been issued to people with a current inhibitor during 2020/21 and 2022/23, broken down by diagnosis, supplier and product.

Table 23 Products issued to people with congenital bleeding disorders reported to have a positive inhibitor, 2021/22 and 2022/23

Product type	Manufacturer	Product	2021/22		2022/23	
			People (n)	Units (IU)	People (n)	Units (IU)
Haemophilia A						
Non-factor	Roche	Hemlibra (mg)	148	547,094	149	561,121
Recombinant	Novo Nordisk	Esperoct	5	1,086,000	10	2,020,500
		NovoEight	8	2,735,500	5	1,725,500
		NovoSeven (mg)	101	10,308	98	7,056
	Octapharma	Nuwiq	7	1,994,250	9	2,055,750
	Pfizer	ReFacto AF	16	2,153,750	13	1,433,250
	SOBI/Biogen	Elocta	30	5,250,750	33	4,994,580
	Takeda	Advate	27	3,953,300	26	3,973,250
		ADYNOVI	-	-	`1-2	448,000
		OBIZUR	`1-2	14,000	-	-
	Withheld	Investigational FVII	-	-	Withheld	Withheld
Plasma-derived	BPL	BPL FVIII 8Y	`1-2	444,525	`1-2	221,000
	Grifols	Fanhdi	`1-2	306,000	`1-2	70,000
	Octapharma	Octanate	3	1,200,000	3	982,000
	Takeda	FEIBA	18	1,016,000	16	799,000
Not known	Withheld	Investigational not known	-	-	Withheld	Withheld
Haemophilia B						
Recombinant	Novo Nordisk	NovoSeven (mg)	11	8,350	10	13,146
	Pfizer	Benefix	3	1,355,800	`1-2	582,000
	SOBI/Biogen	ALPROLIX	`1-2	2,000	`1-2	499,000
Plasma-derived	Takeda	FEIBA	3	689,000	3	471,000
Other	Withheld	Investigational other	Withheld	Withheld	Withheld	Withheld
von Willebrand disease						
Non-factor	Roche	Hemlibra (mg)	`1-2	840	`1-2	5,145
Recombinant	Novo Nordisk	NovoSeven (mg)	4	2,590	5	1,305
	SOBI/Biogen	Elocta	`1-2	619,500	3	447,000
	Takeda	Advate	`1-2	6,750	`1-2	24,000
		Veyvondi	`1-2	26,000	`1-2	18,200
Plasma-derived	CSL Behring	Voncento	3	233,000	3	328,000
	Takeda	FEIBA	-	-	`1-2	288,000
FVII deficiency						
Recombinant	Novo Nordisk	NovoSeven (mg)	`1-2	2,619	`1-2	2,148
FXI deficiency						
Recombinant	Novo Nordisk	NovoSeven (mg)	-	-	`1-2	4
Combined haemophilia A + von Willebrand disease						
Non-factor	Roche	Hemlibra (mg)	`1-2	4,320	`1-2	5400
Recombinant	Novo Nordisk	NovoSeven (mg)	`1-2	3	-	-
Plasma-derived	Takeda	FEIBA	`1-2	155,000	`1-2	81000
Bleeding disorder of unknown cause						
Plasma-derived	Takeda	FEIBA	-	-	`1-2	10000

Units in IU unless otherwise stated

Table 24 Products issued to people with acquired disorders, 2021/22 and 2022/23

Product type	Manufacturer	Product	2021/22		2022/23	
			People (n)	Units (IU)	People (n)	Units (IU)
Acquired haemophilia A						
Non-factor	Roche	Hemlibra (mg)	`1-2	1,680	`1-2	5,760
Recombinant	Novo Nordisk	Esperoct	-	-	`1-2	31,000
		NovoSeven (mg)	19	2,053	14	3,076
		NovoEight	-	-	`1-2	2,000
	Takeda	OBIZUR	29	1,315,000	37	2,673,500
		Advate	6	130,500	3	27,000
Plasma-derived	Octapharma	Wilate	`1-2	5,000	-	-
	Takeda	FEIBA	96	9,269,000	81	6,599,900
Acquired haemophilia B						
Recombinant	Pfizer	Benefix	-	-	`1-2	20,000
Acquired von Willebrand disease						
Recombinant	Pfizer	ReFacto AF	`1-2	22,000	`1-2	2,000
	Takeda	Veyvondi	11	104,650	14	207,350
		Advate	`1-2	6,000	3	13,000
Plasma-derived	CSL Behring	Voncento	24	1,226,800	36	1,627,700
		Riastap	-	-	`1-2	4
	LFB Biomedicaments	Willfact /Wilfactin	`1-2	424000	`1-2	454,000
	Octapharma	Wilate	13	265,000	9	122,000
Acquired FXIII deficiency						
Plasma-derived	CSL Behring	Fibrogammin P	3	27,750	-	-
Other acquired factor deficiency						
Plasma-derived	BPL	COAGADEX	`1-2	161,250	`1-2	1,000

Units in IU unless otherwise stated

Table 24: This shows products issued for people with an acquired inhibitors in 2022/23, broken down by diagnosis and supplier.

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Table 25 FEIBA® issues: breakdown by diagnosis, 2020/21 – 2022/23

Diagnosis	2020/21		2021/22		2022/23	
	People (n)	Units (IU)	People (n)	Units (IU)	People (n)	Units (IU)
Haemophilia A	16	535500	22	1,110,000	19	954000
Haemophilia B	4	414000	3	689,000	3	471000
von Willebrand disease	-	-	-	-	3	290000
Factor VII deficiency	-	-	-	-	`1-2	500
Bleeding disorder of unknown cause	-	-	-	-	`1-2	10000
Glanzmann's thrombasthenia	`1-2	104000	-	-	-	-
Acquired haemophilia A	82	7391500	96	9,269,000	81	6599900
Combined haemophilia A and von Willebrand disease	`1-2	145000	`1-2	155,000	`1-2	81000
Miscellaneous	-	-	-	-	`1-2	9000
Total*	**102**	**8,590,000**	**121**	**11,223,000**	**106**	**8,415,400**

** This is the total excluding numbers which have been suppressed.*

Table 26 NovoSeven® issues: breakdown by diagnosis, 2020/21 – 2022/23

Diagnosis	2020/21		2021/22		2022/23	
	People (n)	Units (mg)	People (n)	Units (mg)	People (n)	Units (mg)
Haemophilia A	92	6,817	118	11,915	117	7,763
Haemophilia B	11	5,412	11	8,350	12	13,204
von Willebrand disease	5	449	6	2,601	7	1,610
Factor V deficiency	-	-	3	58	3	81
Factor VII deficiency	64	4,680	84	5,955	79	9,399
Factor X deficiency	-	-	`1-2	2	`1-2	1
Factor XI deficiency	3	15	-	-	`1-2	26
Factor XIII deficiency	-	-	-	-	`1-2	2
Bleeding disorder of unknown cause	`1-2	10	5	42	`1-2	8
Glanzmann's thrombasthenia	42	16,361	54	6,797	49	28,528
Bernard-Soulier syndrome	9	112	15	1,093	8	296
Heritable platelet disorder	-	-	`1-2	59	4	39
Other platelet disorder	`1-2	9	3	22	`1-2	6
Acquired haemophilia A	16	2,767	19	2,053	14	3,076
Other acquired factor deficiency	`1-2	15	-	-	-	-
Combined haemophilia A and von Wille	-	-	`1-2	3	-	-
Multiple diagnoses	`1-2	2	`1-2	2	`1-2	2
Miscellaneous	5	14	-	-	`1-2	9
Total*	**247**	**36,663**	**318**	**38,952**	**293**	**64,050**

** This is the total excluding numbers which have been suppressed.*

Tables 25, 26 (previous page) ***& 27*** show in greater detail how much FEIBA, NovoSeven and emicizumab were issued for each diagnosis over the last three years. People with any hereditary or acquired bleeding disorder, either with or without inhibitors, are included. There is no estimate given for off-label usage or usage for reversal of over-anticoagulation as this occurs outside haemophilia centres and is consequently not systematically collected. FEIBA issued for congenital haemophilia A with inhibitors has declined markedly as people started using emicizumab, , although it has fluctuated in the last three years. NovoSeven issues for congenital haemophilia A have increased, probably because it is now used in preference to FEIBA for surgery in people with FVIII inhibitors who are co-prescribed emicizumab.

Table 27 Emicizumab issues: breakdown by diagnosis, 2020/21 – 2022/23

Diagnosis	2020/21		2021/22		2022/23	
	People (n)	Units (mg)	People (n)	Units (mg)	People (n)	Units (mg)
Haemophilia A	750	2,598,185	1073	4,064,990	1258	5,102,413
von Willebrand disease	-	-	`1-2	840	`1-2	5,145
Acquired haemophilia A	-	-	`1-2	1,680	`1-2	5,760
Combined haemophilia A and von Willebrand disease	`1-2	5,760	3	10,890	3	13,425
Combined factors V and VIII deficiencies	-	-	-	-	`1-2	30
Total*	**750**	**2,603,945**	**1,076**	**4,078,400**	**1,261**	**5,126,773**

** This is the total excluding numbers which have been suppressed.*

Table 27: This includes emicizumab issues for people with and without inhibitors, and off-license issues to isolated people with von Willebrand disease and acquired haemophilia. Issues of emicuzimab for von Willebrand disease, acquired haemophilia A and combined factors V and VIII deficiencies are presumed to be related to individual funding requests.

Figure 24 The proportion of people with haemophilia A and an inhibitor issued treatment products by quarter

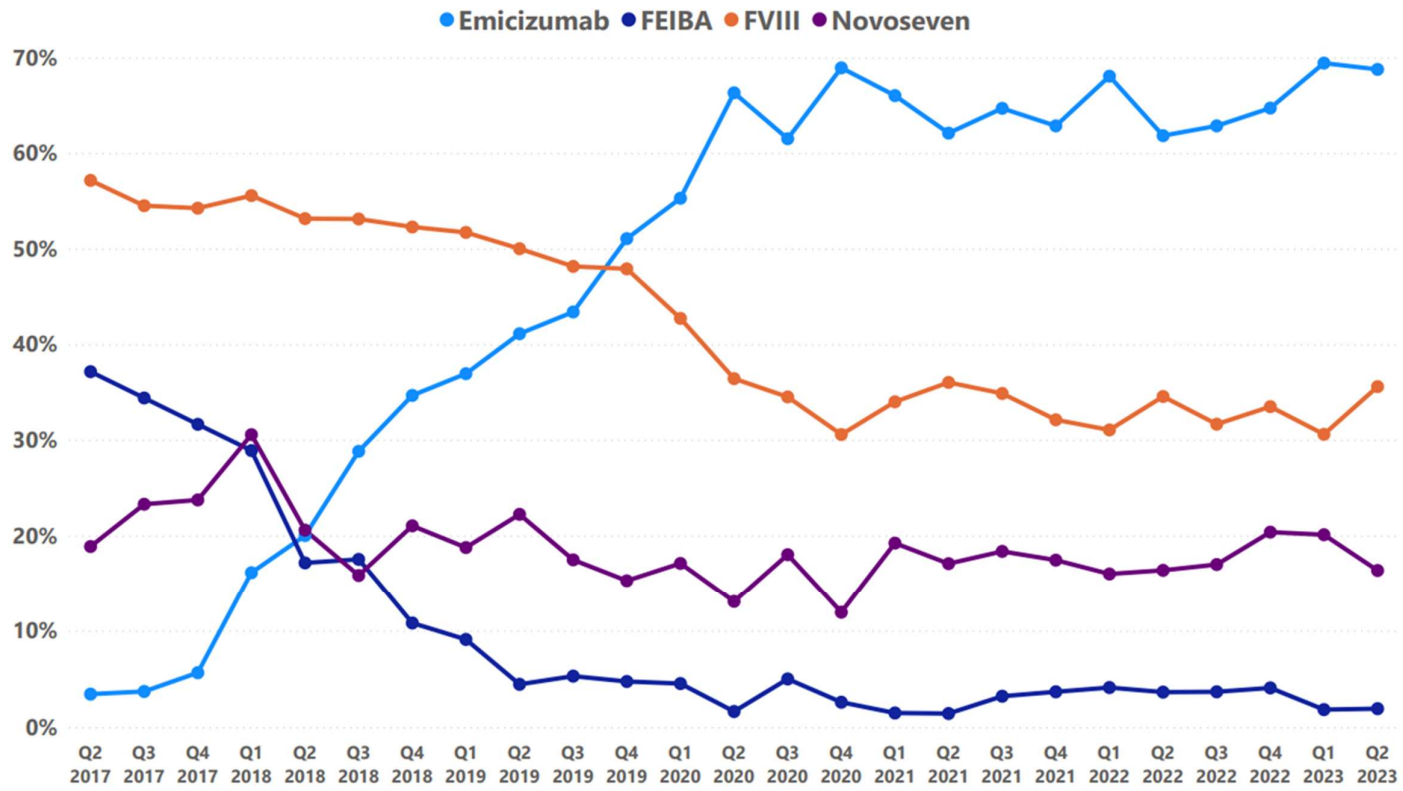


Figure 24: This shows the change in the proportion of PwHA and an inhibitor issued with FEIBA, NovoSeven, FVIII and emicizumab since emicizumab was licensed for use in this group. People may be issued with more than one product during a given quarter. Novoseven, in particular, is often used in people treated also with other products. The introduction of emicizumab has led to a marked reduction in the use of FVIII and FEIBA in this group, although not in the use of NovoSeven, which may be used for surgery and intercurrent bleeding in preference to FEIBA in people prescribed emicizumab. The proportion of PwHA with inhibitors issued emicizumab appears to have stabilised.

Figure 25 The proportion of people with severe haemophilia A and an inhibitor issued with emicizumab by centre 2022/23

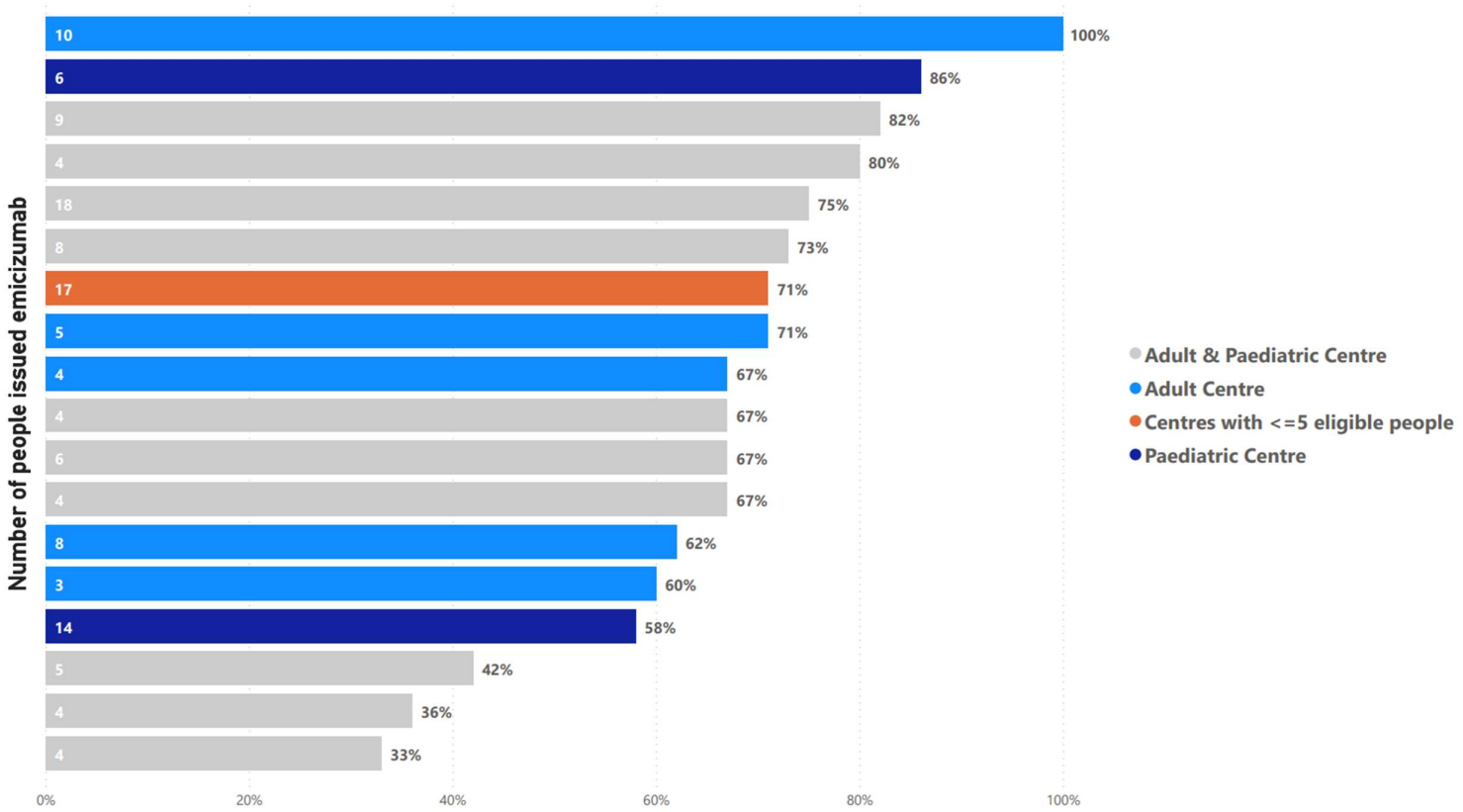


Figure 25: This bar diagram shows the proportion of people with severe haemophilia A and inhibitors issued with emicizumab, broken down by centre. Centres with five or fewer eligible people are aggregated and shown as the orange bar. This shows considerable centre to centre variation in clinical practice (median 67%, IQR 61-75%).

2.5 Other Bleeding Disorders

Table 28 People with other bleeding disorders registered and issued treatment products 2022/23

Diagnosis	People in Register		Treatment product issues		
	Males	Females	Any Product	Concentrate	Desmopressin
Haemophilia A with liver transplant	13	-	-	-	-
Haemophilia B with liver transplant	`1-2	-	-	-	-
von Willebrand disease with liver transplant	`1-2	-	-	-	-
Factor V deficiency	107	194	3	3	-
Factor VII deficiency	1,038	1,216	88	82	`1-2
Factor X deficiency	155	214	37	37	-
Factor XI deficiency	1,751	2,544	71	59	3
Factor XIII deficiency	52	38	66	66	-
Prothrombin (factor II) deficiency	7	12	5	5	-
Dysfibrinogenemia	308	500	30	29	-
Hypofibrinogenemia	107	153	12	11	-
Hypodysfibrinogenemia	21	26	3	3	-
Afibrinogenemia	11	6	14	14	-
Fibrinogen deficiency	-	3	`1-2	`1-2	-
Bleeding disorder of unknown cause	167	1,140	46	`1-2	41
Glanzmann's thrombasthenia	61	81	48	48	-
Bernard-Soulier syndrome	50	51	9	8	-
Other severe platelet disorder	60	139	4	-	4
Platelet-type pseudo von Willebrand disease	16	27	3	3	-
Heritable platelet disorder	202	337	15	4	8
Other platelet disorder	903	2,090	73	3	65
Other disorders	17	24	7	6	`1-2
Acquired haemophilia A	329	328	99	44	-
Acquired von Willebrand disease	110	85	47	47	`1-2
Other acquired factor deficiency	22	23	`1-2	`1-2	`1-2
Multiple diagnoses	46	77	4	4	-
Miscellaneous	91	322	15	4	9
Factor XII (Hageman) defect	3	7	-	-	-
Total*	**5,613**	**9,598**	**697**	**479**	**129**

** This is the total excluding numbers which have been suppressed.*

Table 28: This shows the number of people registered with other disorders and the proportion issued products during the year. It is suspected that liver transplantation is under-reported.

Table 29 a, b People with selected other bleeding disorders registered and treated 2022/23, by disease severity

Diagnosis	People in register by factor level (IU/dl)							
	<5		≥5		Not known		Total	
	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products
Factor V deficiency	59	3	235	-	7	-	301	3
Factor VII deficiency	180	42	2065	47	9	-	2254	89
Factor X deficiency	45	33	322	7	`1-2	-	367	40
Factor XI deficiency	333	30	3874	39	88	3	4295	72
Total*	**617**	**108**	**6,496**	**93**	**104**	**3**	**7,217**	**204**

** Small numbers have been suppressed.*

Table 29a: It is acknowledged that these other disorders have no recognised classification of disease severity. However, the table above gives an idea of the range of registered levels.

Diagnosis	People in register by factor level (IU/dl)											
	<2		2-<10		10-<15		≥15		Not known		Total	
	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products	Registered	Issued treatment products
Factor XIII deficiency*	**37**	**37**	**29**	**25**	**3**	**`1-2**	**19**	**3**	**`1-2**	**`1-2**	**88**	**65**

** Small numbers have been suppressed.*

Table 29b: The table above gives an idea of the range of registered levels for factor XIII deficiency.

Table 30 New registrations of other bleeding disorders 2022/23, by coagulation defect and gender

Diagnosis	Male	Female	Total
Haemophilia A with liver transplant	`1-2	-	-
Factor V deficiency	5	8	13
Factor VII deficiency	88	89	177
Factor X deficiency	7	11	18
Factor XI deficiency	108	151	259
Factor XIII deficiency	5	3	8
Prothrombin (factor II) deficiency	-	`1-2	-
Dysfibrinogenemia	29	46	75
Hypofibrinogenemia	9	19	28
Hypodysfibrinogenemia	3	6	9
Fibrinogen deficiency	-	`1-2	-
Bleeding disorder of unknown cause	15	168	183
Bernard-Soulier syndrome	`1-2	`1-2	-
Platelet-type pseudo von Willebrand disease	-	`1-2	-
Heritable platelet disorder	120	215	335
Other platelet disorder	6	21	27
Other disorders	-	`1-2	-
Acquired haemophilia A	59	52	111
Acquired von Willebrand disease	13	8	21
Other acquired factor deficiency	3	3	6
Multiple diagnoses	6	5	11
Miscellaneous	8	32	40
Factor XII (Hageman) defect	`1-2	`1-2	-
Total*	478	834	1,312

** Small numbers have been suppressed.*

Table 30: This table shows new registrations of other bleeding disorders during the year. This shows a large number of newly registered females for all autosomal disorders, presumably reflecting referral and diagnostic bias of women with menorrhagia.

Table 31 Concentrates used to treat selected other bleeding disorders between 2022/23

Product type	Manufacturer	Product	Factor V deficiency		Factor VII deficiency		Factor X deficiency		Factor XI deficiency		Factor XIII deficiency	
			Units (IU)	People (n)	Units (IU)	People (n)	Units (IU)	People (n)	Units (IU)	People (n)	Units (IU)	People (n)
Recombinant	Novo Nordisk	NovoSeven (mg)	81	3	9,399	79	1	`1-2	26	`1-2	2	`1-2
		NovoThirteen	-	-	-	-	-	-	-	-	95,000	8
	Pfizer	Benefix	-	-	-	-	2,000	`1-2	3,000	`1-2	-	-
		ReFacto AF	-	-	-	-	-	-	2,500	`1-2	-	-
	SOBI/Biogen	Elocta	-	-	-	-	14,000	`1-2	-	-	-	-
	Takeda	Advate	-	-	-	-	-	-	35,000	`1-2	-	-
	Withheld	Investigational FVII	-	-	123	`1-2	-	-	-	-	-	-
Plasma-derived	BPL	BPL FXI	-	-	-	-	-	-	120,075	42	-	-
		COAGADEX	-	-	-	-	2,606,000	28	-	-	-	-
	Baxter	Com FVII	-	-	760,800	4	-	-	-	-	-	-
	CSL Behring	Beriplex	-	-	-	-	158,000	7	-	-	-	-
		FXIII	-	-	-	-	-	-	-	-	44,000	`1-2
		Fibrogammin P	-	-	-	-	-	-	-	-	1,124,900	63
	LFB Biomedicaments	Hemoleven (LFB XI)	-	-	-	-	-	-	31,000	16	-	-
	Octapharma	Octaplas (bags)	-	-	-	-	-	-	2,804	3	-	-
		Octaplex	-	-	-	-	289,000	5	-	-	-	-
	Takeda	FEIBA	-	-	500	`1-2	-	-	-	-	-	-

Units in IU unless otherwise stated.
Small numbers have been suppressed.

Table 31: This gives a breakdown of products issued during 2022/23 for people with other bleeding disorders, broken down by diagnosis and supplier.

2.6 Adverse Events

2.6.1 Introduction and Adverse Event Assessment Panel

Pharmacovigilance is an increasingly important function of the database. Treatments are monitored for safety signals and drug-related adverse events, including poor efficacy, are reported to the manufacturer and, through them, to the regulators. Consequently, the conduct of post-license safety and efficacy studies has become a routine for the database. This function has assumed even greater prominence as we enter a new therapeutic era, using non-replacement drugs and antibodies with novel modes of action and with side effect profiles very different from the traditional replacement therapies that we are used to and which they may replace.

In response to this increasing need and the need for an objective, independent and robust evaluation of adverse events an SOP was developed for managing and evaluating adverse events in 2019 and 2021. Adverse Events (AEs) and Serious Adverse Events (SAEs) were defined as for GCP clinical trials. Where required, adverse event reports are further investigated by the Adverse Event Panel.

The Adverse Event Panel meet once a month by video conference to adjudicate on all SAEs. scoring their severity (1-5) and the potential relationship to drug therapy (unrelated; possibly related; probably related or definitely related), again using the same framework that would apply for AE and SAE reporting in GCP-standard clinical trials. Serious Adverse events may be evaluated more urgently by e-mail and ad-hoc meetings, if necessary. All adverse events are reviewed by the panel.

The NHD Adverse Event Assessment Panel membership is as follows:

Prof Charles RM Hay Co-Chair, Representing NHD
Prof Pratima Chowdary, Co-Chair representing NHD
Sharon Thind, representing the HNA
Prof Mike Makris, representing EUHASS (retired 2023)
Dr Sarah Mangles
Dr Mary Mathias, Representing the Paediatric Working Party
Dr Charles Percy, Representing the Inhibitor Working Party
Dr Kate Talks, representing the Data Management Working Party

The group meets once a month by video conference and the meetings are recorded to facilitate production of accurate minutes. The group may meet or communicate between meetings if required.

All adverse events reported to the database are considered by the group. Where further enquiries or follow up are required to resolve issues in relation to reported events, these are delegated to panel members to follow up and events are not “closed” until data queries have been resolved or exhausted.

Where adverse events are considered possibly or definitely drug-related, the event is reported on to the manufacturer and through them to the regulator. The adverse event forms are currently being redesigned and reviewed to ensure they are up to date, to reduce the work for the reporting centre and to minimise the need for follow-up enquiries.

Most adverse events are reported to the database spontaneously soon after they occur, using the electronic reporting system. Many adverse events are unresolved at the time of reporting and require follow up from the database and CMWP before the report can be concluded.

Reports on the following events are actively solicited with monthly reminder “orange email*”. (*successor to the orange reminder postcard!):

Acute or Allergic reactions
Deaths
Infections

Malignancy
Inhibitors and anti-drug abs
Intracranial Haemorrhage (paediatric and adult)
Neurological Events
Thrombotic events (including MAHA)
Unexpected poor efficacy
Other events

Adverse events are summarised overleaf, and serious adverse events described in more detail. Personal details have been supressed to minimise the risk of a breach of confidentiality.

All adverse events reported by centres who participate in the European Haemophilia Safety Surveillance (EUHASS) program are anonymised and automatically forwarded via the NHD website to avoid the need for double-reporting.

Table 32 Summary of Adverse Events reported between April 2022 & March 2023

Adverse Event	People (n)	Number of Events
Allergic or Other Acute Event	4	4
Death Event	132	132
ICH Event	15	16
Infection Event	2	2
Inhibitor Event	14	14
Malignancy Event	16	16
Neurological Event	0	0
Other Event	5	5
Poor Efficacy Event	2	2
Thrombotic Event	10	10
Total	**190**	**191**

Table 32: This summarises the number and category of adverse events reported to the database during 2022/23. These events are reported in greater detail in the tables that follow. Covid events are no longer collected and will not appear in future reports.

In future, events of special interest should probably not merely be broken down by bleeding diagnosis, treatment, and treatment-relationship, if any, but also expressed in events per period of risk so that it is possible to compare the incidence of such events in different treatment risk-groups.

Further details of these events are provided in the following tables.

Table 33 Allergic / Other Reactions

Diagnosis	Event	Material	Relationship to material	Outcome
Haemophilia A	Shortness of breath	Esperoct	Definite	Resolved
Haemophilia A	Shortness of breath	Esperoct	Definite	Resolved
Haemophilia B	Anaphylaxis, rash to torso, face & neck coughing crying +++	ALPROLIX	Definite	Resolved
von Willebrand disease	See comment	Desmopressin (4mcg/ml)	Possible	Resolved
Acquired von Willebrands	Headaches and sweats	Voncento	Definite	Resolved

Table 33: In each case the events were evaluated by the Adverse Events Assessment Panel and are reported on to the manufacturer. Emicizumab-related allergy events appear to occur almost exclusively in the first few weeks of treatment.

Table 34 Intracranial Haemorrhage (all ages)

Diagnosis	Severity	Age (years)	Material	Trauma Present	Maintenance therapy	Outcome
Acquired von Willebrands	Unknown	79	Wilate	Minor head bump	On demand	Deceased
Haemophilia A	Mild	64	Cryoprecipitate	Minor head bump	Prophylaxis	Unknown
Haemophilia A	Severe	72	BPL FVIII	Unknown	Prophylaxis	Unknown
Haemophilia A	Severe	51	BPL Replenate	Major trauma	Prophylaxis	Unknown
Haemophilia A	Normal	23	Advate	Major trauma	On demand	Unknown
Haemophilia A	Severe	0	Nuwiq	Major trauma	Prophylaxis	Unknown
Haemophilia A	Mild	86	Elocta	Unknown	On demand	Unknown
Haemophilia A	Severe	0	Nuwiq	Unknown	Prophylaxis	Unknown
Haemophilia B	Mild	73	Refixia	Minor head bump	On demand	Unknown
Haemophilia B	Mild	20	Refixia	Major trauma	On demand	Unknown
Haemophilia B	Severe	0	Benefix	Unknown	Prophylaxis	Unknown
von Willebrand disease	Moderate	65	Cryoprecipitate	Minor head bump	On demand	Deceased due to ICH
von Willebrand disease	Normal	34	Alphanate	Unknown	Prophylaxis	Unknown
von Willebrand disease	Mild	76	Voncento	Major trauma	On demand	Unknown
von Willebrand disease	Mild	12	Wilate	Unknown	On demand	Unknown

Table 35 Infection Events

Diagnosis	Event	Material	Relatedness to material	Outcome
Afibrinogenemia	Hepatitis E	None	Probably contributing factor	Unknown
Females with VIII deficiency	Hepatitis C	None	Unrelated	Unknown

Table 36 Inhibitors

Bleeding disorder	Age at time of inhibitor development	Product(s) in use at time of inhibitor detection	Exposure days	Maximum inhibitor titre
Severe Haemophilia A	0	Nuwiq	<=50	2
Severe Haemophilia A	46	Esperoct	>50	2
Severe Haemophilia A	24	Unknown	>50	5
Severe Haemophilia A	22	Advate	>50	Unknown
Severe Haemophilia A	12	Emicizumab	>50	Unknown
Severe Haemophilia A	3	Hemlibra	>50	0
Severe Haemophilia A	1	Nuwiq	<=50	66
Severe Haemophilia A	30	Unknown	>50	1
Severe Haemophilia A	67	ReFacto AF	>50	41
Non-Severe Haemophilia A	10	Elocta	Unknown	2
Non-Severe Haemophilia A	12	ReFacto AF	Unknown	7
Non-Severe Haemophilia A	67	ReFacto AF	Unknown	41
Non-Severe Haemophilia A	84	Unknown	Unknown	Unknown
Haemophilia B	3	ALPROLIX	Unknown	4

Table 36: Full reports were submitted for thirteen factor VIII inhibitors, one FIX inhibitor and no VW inhibitors between April 2022 and March 2023. Outline data is summarised in the table above.

Inhibitors appearing or re-appearing after switching to emicizumab are probably recurrences of inhibitors that were already present at a relatively low level below the level of detection of the Bethesda assay at the time of switching. In some of these cases there is direct evidence that this is the case in the form of an abnormally short FVIII half-life and breakthrough bleeding on factor VIII prophylaxis prior to initiation of emicizumab.

There was also a single report of a emicizumab anti-drug antibody during this 12-month period. This reduced circulating emicizumab levels but so far has not led to any loss of efficacy. It was picked up by routine surveillance. A total of three anti-drug antibodies have been reported since emicizumab was commissioned in 2018, only one of which led to complete loss of efficacy.

See Table 22 for further details of new, ongoing and historic inhibitors.

Table 37 Malignancy Events

Malignancy	People
Esophageal cancer	3
Grade 2 atypical meningioma	1
Hepatocellular carcinoma	1
Invasive mammary carcinoma of breast	1
Metastatic cancer of unknown primary	1
Metastatic mucinous adenocarcinoma	1
Multi-focal glioblastoma multiforme	1
Non small cell lung cancer	1
Penile cancer	1
Prostate cancer	2
Rectosigmoid adenocarcinoma	1
Squamous cell carcinoma of the vulva stage 1b	1
Tongue - squamous cell carcinoma	1

Table 37: The bleeding diagnosis has not been shown since the malignancies reflect both the types and frequencies seen in the general population, as a broad generalisation, and are found in all groups of people with bleeding disorders with no specific associations. The exception to this is hepatocellular carcinoma, which was found exclusively in haemophilia A and B and which relates to previous infection with hepatitis C or B in almost all cases. The HCC event reported above relates to a PwBD with a history of HCV.

Table 38 Poor Efficacy Events

Diagnosis	Event	Material	Trauma Present	Outcome
Haemophilia A	Haemuturia	Emicizumab	None	Unknown
Haemophilia A	Haemuturia	Emicizumab	None	Unknown

Table 39 Thrombotic Events

Diagnosis	Event	Material	Relationship to material	Outcome
Haemophilia A	Thrombotic stroke	None	Unrelated	Unknown
Haemophilia A	Angina - first occurrence only	None	Unrelated	Unknown
von Willebrand disease	Thrombotic stroke	Voncento	Unlikely	Unknown
von Willebrand disease	Transient ischemic attack (tia) - first occurrence only	None	Unrelated	Unknown
von Willebrand disease	Pulmonary embolism (pe)	None	Unrelated	Unknown
von Willebrand disease	Thrombotic stroke	None	Unrelated	Unknown
Acquired F.V deficiency	Thrombotic stroke	None	Unrelated	Deceased
Acquired Haemophilia A	Pulmonary embolism (pe)	None	Unrelated	Deceased
F.VII deficiency	Pulmonary embolism (pe)	None	Unrelated	Deceased
Glanzmanns Thrombasthenia	Pulmonary embolism (pe)	FVII - Novo FVIIA	Probably contributing factor	Unknown

Table 40 Other Events

Diagnosis	Event	Material	Relationship to material	Outcome
Haemophilia A	Left sided facial cellulitis requiring admission and IV antibiotics Previous HCV Ab+ve, PCR -ve	Emicizumab (ACE910)	Probably related	Unresolved
Haemophilia A	Fatigue and headache	Emicizumab	Probably related	Unresolved
Haemophilia A	Fractured skull, large haematoma on head. Cause of injury not known.	NovoEight	Probably related	Unresolved
Haemophilia A	Incorrect Emi dose for a number of unspecified months. No reported side effects	Emicizumab	Probably related	Unresolved

These events were adjudicated by the membership of the Co-Morbidities Working Party.

2.7 Mortality

Table 41 Causes of death in people with haemophilia A and B between April 2022 & March 2023

Cause of Death	Haemophilia A					Haemophilia B		
	Severe	Non-Severe	Severity not known	Liver transplant	Total	Severe	Non-Severe	Total
Chronic obstructive airways disease	1	-	-	0	1	-	-	-
Cancer	-	8	-	0	8	1	1	2
Hepatocellular carcinoma	2	-	-	1	3	1	-	1
Lymphoproliferative malignancy	-	1	-	0	1	-	-	-
Haemorrhage	-	1	-	0	1	1	-	1
Cerebral haemorrhage	1	-	-	0	1	-	-	-
Infection (bacterial)	2	2	-	0	4	-	-	-
Ischaemic heart disease	-	1	-	0	1	-	-	-
Stroke (thrombotic)	-	1	-	0	1	-	-	-
Liver failure	-	-	-	0	-	-	1	1
Suicide	-	-	-	0	-	1	1	2
Peripheral vascular disease	-	1	-	0	1	-	-	-
Not known	-	8	1	0	9	1	1	2
Total	**6**	**23**	**1**	**1**	**31**	**5**	**4**	**9**

Tables 41 & 42 (overleaf): These show the causes of death amongst people with haemophilia A and B (including carriers), broken down by haemophilia severity (table 39) and for other bleeding disorders (table 40) during 2022/23. This table includes death certification data from NHS digital.. Consequently, the proportion of PwBD whose cause of death is unknown has reduced dramatically, but even NHS digital are unable to provide the cause of death in all people with bleeding disorders.

Table 42 Causes of death in other coagulation defects between April 2022 & March 2023

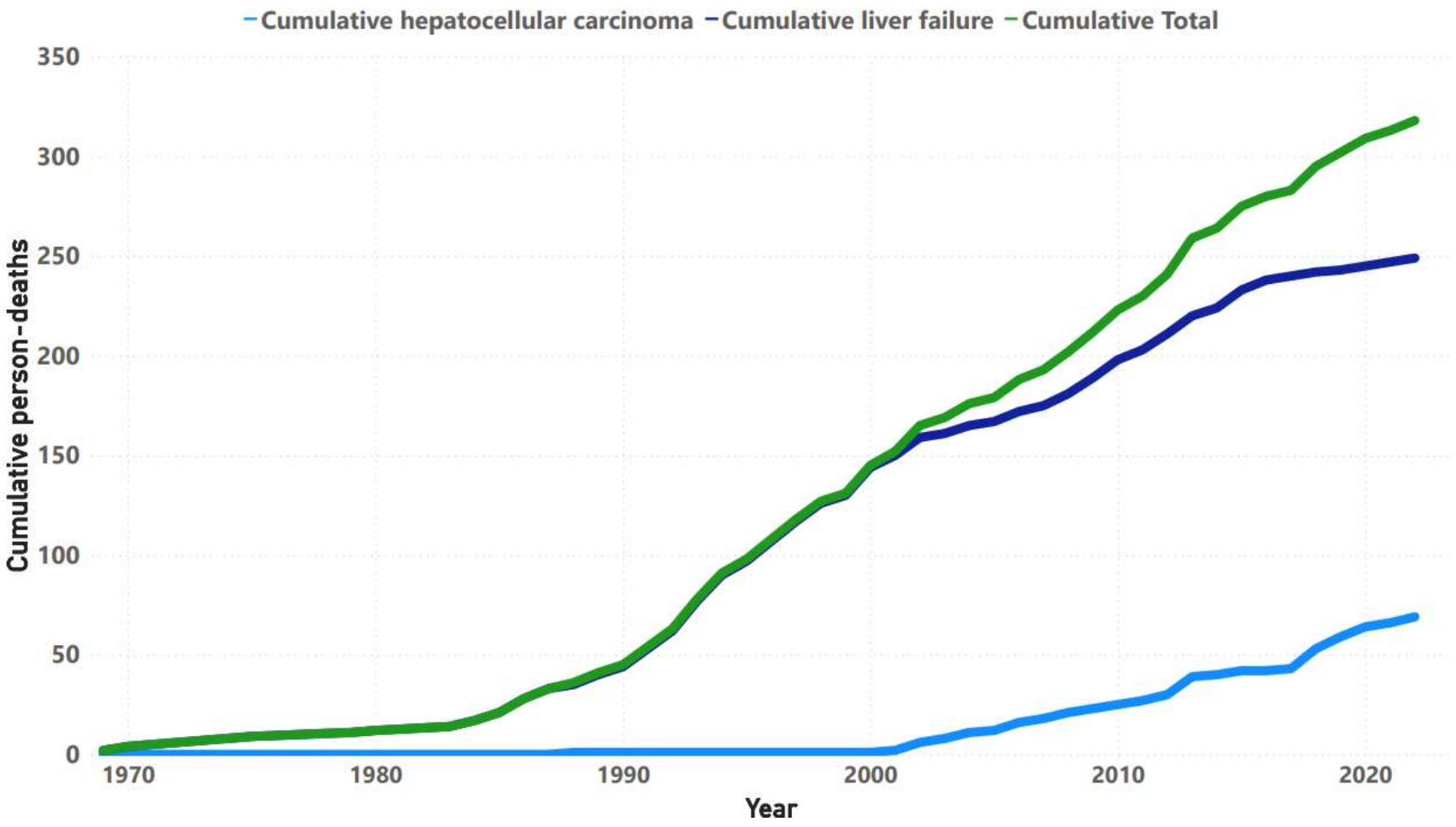
Diagnosis	Cause of Death	Total
von Willebrand disease	Chronic obstructive airways disease	1
	Cancer	2
	Cerebral haemorrhage	3
	Infection (bacterial)	3
	Ischaemic heart disease	2
	Liver failure	1
	Hypoglycaemia	1
	Not known	5
von Willebrand disease with liver transplant	Acute respiratory distress syndrome	1
Factor VII deficiency	Infection (bacterial)	1
	Not known	3
Factor X deficiency	Not known	2
Factor XI deficiency	Acute respiratory distress syndrome	1
	Chronic obstructive airways disease	1
	Cancer	3
	Infection (bacterial)	3
	Ischaemic heart disease	1
	Stroke	1
	Liver failure	1
	Asphyxia	1
	Not known	3
Dysfibrinogenemia	Infection (bacterial)	1
Bleeding disorder of unknown cause	Disseminated intravascular coagulation	1
	Not known	2
Glanzmann's thrombasthenia	Cerebral haemorrhage	1
Bernard-Soulier syndrome	Not known	1
Other severe platelet disorder	Infection (bacterial)	1
Heritable platelet disorder	Cancer	1
	Ischaemic heart disease	1
	Suicide	1
Other platelet disorder	Infection (bacterial)	1
	Not known	4

Continued overleaf

Causes of death in other coagulation defects between April 2021 & March 2022 continued

Diagnosis	Cause of Death	Total
Acquired haemophilia A	Cancer	5
	Haemorrhage	2
	Venous thromboembolism	1
	Infection (bacterial)	13
	Ischaemic heart disease	3
	Stroke	1
	Renal failure	1
	Pneumocephalus	1
	Cachexia	1
	Not known	16
Acquired von Willebrand disease	Cancer	2
	Infection (bacterial)	1
	Ischaemic heart disease	1
	Not known	5
Other acquired factor deficiency	Acute respiratory distress syndrome	1
	Not known	1
Total	**Total**	**110**

Figure 26 Cumulative incidence chart of deaths from hepatocellular carcinoma or liver failure in people with bleeding disorders in the UK 1969 - 2022



Data table for Figure 26: Cumulative incidence chart of deaths from hepatocellular carcinoma or liver failure in people with bleeding disorders in the UK 1969 - 2022

Year	Hepatocellular Carcinoma	Liver Failure	Total
1969	0	2	2
1970	0	2	2
1972	0	2	2
1973	0	1	1
1974	0	1	1
1975	0	1	1
1979	0	2	2
1980	0	1	1
1983	0	2	2
1984	0	3	3
1985	0	4	4
1986	0	7	7
1987	0	5	5
1988	1	2	3
1989	0	5	5
1990	0	4	4
1991	0	9	9
1992	0	9	9
1993	0	15	15
1994	0	13	13
1995	0	7	7
1996	0	10	10
1997	0	10	10
1998	0	9	9
1999	0	4	4
2000	0	14	14
2001	1	6	7
2002	4	9	13
2003	2	2	4
2004	3	4	7
2005	1	2	3
2006	4	5	9
2007	2	3	5
2008	3	6	9
2009	2	8	10
2010	2	9	11
2011	2	5	7
2012	3	8	11
2013	9	9	18
2014	1	4	5
2015	2	9	11
2016	0	5	5
2017	1	2	3
2018	10	2	12
2019	6	1	7
2020	5	2	7
2021	2	2	4
2022	3	2	5
Total	**69**	**249**	**318**

Figure 26 (previous page): This shows deaths directly attributable to liver disease. The table documents the number whose death certificate listed liver disease as the principal cause of death or who were reported to the NHD by their centre as having died from complications of HCV. Liver disease may have been a subsidiary contributory factor in other deaths although not listed as the primary cause. Please note these results may vary from those produced for the NHD & UKHCDO report "Bleeding disorder statistics for the Infected Blood Inquiry 2020" because the extensive bespoke data collection and cleaning for the latter has yet to be incorporated into the National Haemophilia Database.

This appears to show no levelling-off of deaths from hepatocellular failure despite successful HCV eradication from almost all people with bleeding disorders infected with that agent. As HCV has now been eradicated from almost all surviving people, one might expect a reduction in the incidence of hepatocellular carcinoma (HCC), which declines after viral eradication, even in the presence of ongoing cirrhosis. It is sobering, however, that new cases of hepatocellular carcinoma continue to be reported, occurring as a consequence of the legacy of serious liver disease in some PwBD. A reduction in this complication of hepatitis C may take some time to become evident. There may also be a delay before a further reduction in deaths from hepatocellular failure is seen, as some people have advanced cirrhosis with hepatocellular failure and not all are suitable for transplantation or have a donor. However, successful viral eradication will result in complete recovery of early cirrhosis or less advanced liver disease, and they should not go on to develop advanced cirrhosis and will have a greatly reduced risk of HCC, which usually complicates cirrhosis.

Table 43 Summary of people 'at risk' of vCJD for public health purposes who received UK sourced plasma products as reported by centres

Summary table of people with bleeding disorders 'at risk' who received UK sourced plasma products					
		Implicated batches	Non-implicated batches	Batches not known	Combined
Current status of 'at risk' patients	Alive	638	281	1816	2735
	Dead	168	105	625	898
	Total	806	386	2441	3633
Sex	Male	765	305	2020	3090
	Female	41	81	421	543
Current age band of living 'at risk' patients	0-19	0	0	0	0
	20-39	206	79	452	737
	40-59	306	126	733	1165
	60-79	117	63	536	716
	80+	9	13	95	117
	Not known	0	0	0	0

These data were last updated on 31/12/2022

Table 43: This summary of vCJD surveillance is sent to the UK Health Security Agency regularly. It lists the number of people exposed to UK-sourced blood products or components, according to NHD treatment records, during the period of risk (1990-2001) broken down by those who were known to have received an implicated batch and those not known to have been exposed to an implicated batch. Implicated batches of factor concentrates were those batches which included a donation of plasma from a donor known to have subsequently developed vCJD. In some cases, red-cell donations from those donors are known to have caused vCJD transmission to recipients. So far, there is no evidence of any transmission of vCJD through clotting factor concentrates and no people with bleeding disorders have developed the disease. Given the known incubation period for this condition, it seems increasingly unlikely that people exposed to UK-sourced blood products or components will be affected by vCJD, but the population will continue to be monitored for this.

Batches not known comprises:

1. People presumed as at risk 1990-2001 because they were classified as at risk via the 1980-2001 risk assessment exercise although they have no 1980-2001 NHD treatment records.
2. People identified as at risk 1990-2001 via 1990-2001 NHD treatment records but not via risk assessment exercise.

Figure 27 Total number of people with haemophilia A, haemophilia B or von Willebrand disease issued product by UK haemophilia centres

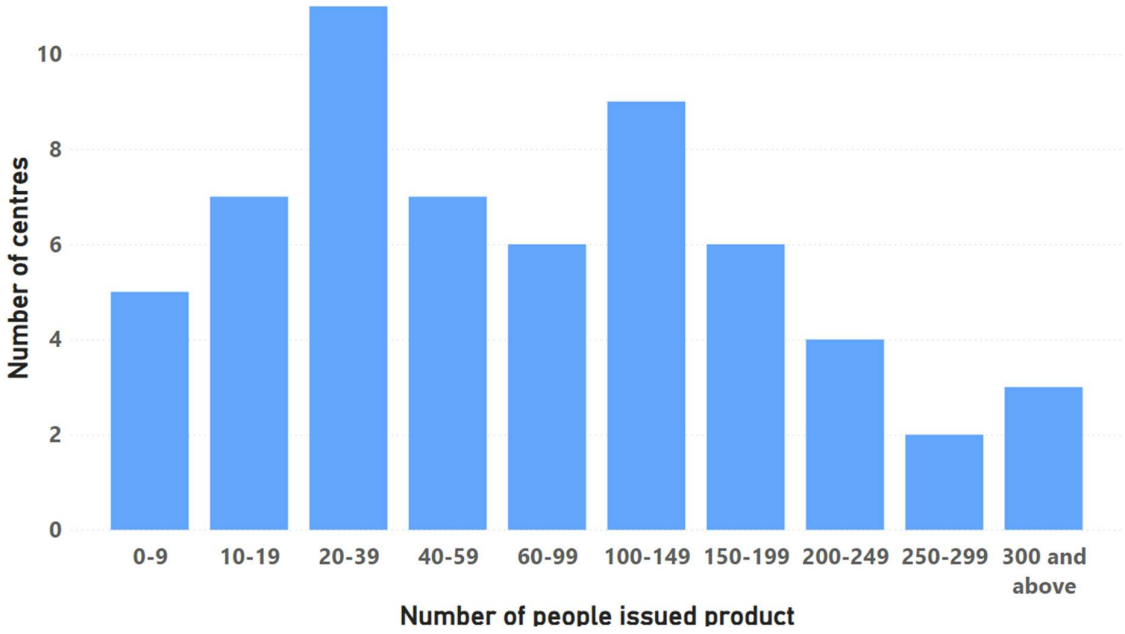
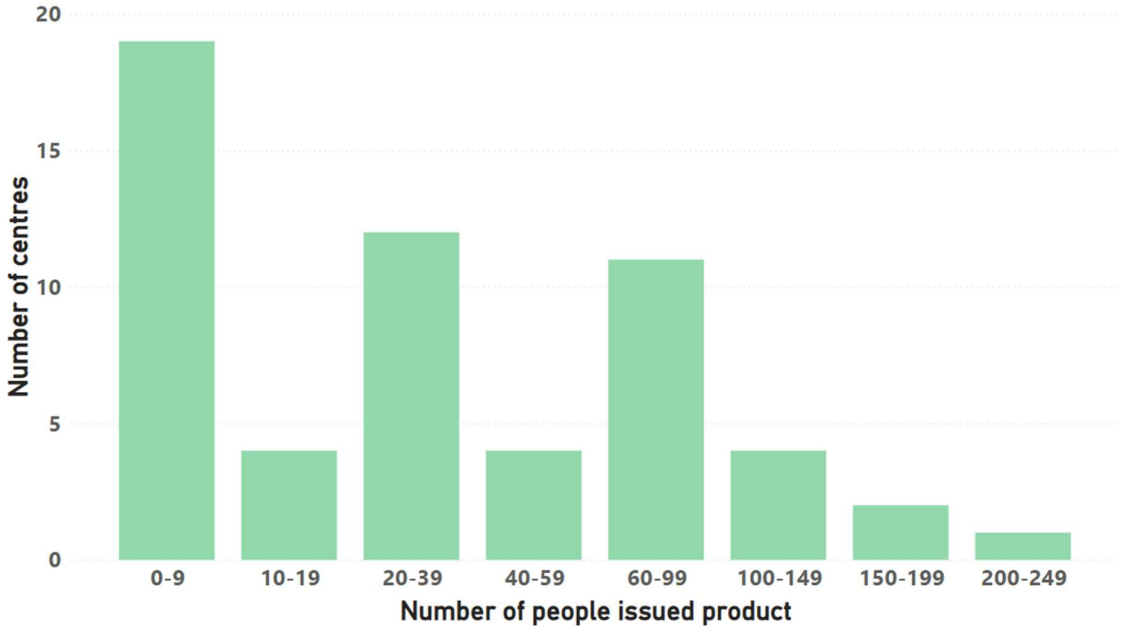


Figure 28 Total number of people with severe haemophilia A and haemophilia B issued product by UK haemophilia centres



NB: Haemophilia A includes carriers of haemophilia A and females with FVIII deficiency
Haemophilia B includes carriers of haemophilia B, females with FIX deficiency, FIX Leyden and FIX Leyden carriers.

3. Haemtrack Annual Report for the calendar year 2022

Introduction

This report is reported by calendar year rather than by financial year since 10% of the data is reported on paper, incurring a significant delay.

Haemtrack is used by people to report home therapy to their haemophilia centre and so its use is not limited to haemophilia A or B but includes other, rarer, bleeding disorders for which people also use home therapy. Both haemophilia centres and people vary in their reporting compliance with Haemtrack and so the quality of individual person self-reported data varies and the proportion of people using the system also varies from centre to centre.

In general, data quality is improving *but for the first time since the system was introduced, we are observing a slight reduction in the proportion of people using the system*. I would attribute this largely to PwBD becoming bleed-free on emicizumab. With little to report other than their weekly or fortnightly injection, some people stop reporting altogether. It remains important that they continue to report, however, because we need to document their drug compliance and their bleed rate and use of Haemtrack remains a condition of access to the drug.

Broadly speaking, reporting compliance is best for severe haemophilia A and B and less good for von Willebrand's disease and rarer conditions but is improving in those conditions This data is extremely valuable however and we would urge centres to press their PWBD to report in all their home therapy so that we are in a better position to assess relative efficacy of different products and regimens.

Haemtrack should become a routine part of home-therapy management and a valuable tool for the review and optimisation of home-therapy and for person education. For that to happen, compliance will have to be reinforced by Health Care Professionals (HCP's) reviewing Haemtrack records with people in clinic and checking the data for accuracy before downloading into HCIS, where it should be checked by HCPs prior to uploading into the National Haemophilia Database.

Haemtrack should also be used in multidisciplinary team meetings (MDTs). Many haemophilia centres already do this and in those centres recruitment and data quality are steadily improving. This requires a consistent investment in time by the centre staff which results in improving compliance with both home therapy and record keeping.

Some haemophilia centres appear not to have realised the full clinical utility of this reporting system and consequently return sub-optimal data, which may reflect some degree of non-engagement by both HCPs and their PWBD. It is important to demonstrate to the person, by referring to Haemtrack data on screen in clinics, that collecting and reporting treatment data is useful for their clinical management, and that its collection is not just an empty bureaucratic exercise.

NHS funding is always under extreme pressure and NHS England, desiring responsible use of drugs and accountability, have made it clear that compliant use of Haemtrack will be a prerequisite for access to new treatments such as emicizumab and EHL-FIX and Veyvondi®. NHS England require evidence that new drugs are cost effective and lead to better clinical outcomes in normal use. Haemtrack provides such evidence.

Haemtrack Update

Haemtrack continues to be a fundamentally important component of the UKHCDO Haemophilia IT Strategy. It integrates with the Haemophilia Clinical Information System (HCIS) and the National Haemophilia Database (NHD) providing PwBD-entered data on treatments and bleeds that is unavailable from any other source. The data from Haemtrack is invaluable to support centres in the management of therapy for PwBD and optimising treatment regimens, whilst also providing its data nationally to support research and introduction of new treatments and regimens.

Haemtrack now has over 2 million PwBD-recorded entries, with over 100 thousand bleeds recorded. On average between 15 and 20 thousand entries a month are being added by people. The majority of people using the system are severe as would be expected, though some people with mild or moderate severity disease also use the system. The main diagnosis of people using the system are Haemophilia A, Haemophilia B, von Willebrand disease, Factor VII deficiency and Factor X deficiency. A video for PwBD explaining its use is available on-line (https://youtu.be/MVQbhJe7Rmk).

Haemtrack currently has a number of different platforms for people to enter their data, phone apps, website and paper. These are being rapidly phased out as the new web-based Haemtrack 3 system has been introduced, which can be used with any smartphone. Although this requires Wifi access, it is easy to use and is much easier to maintain and update.

The majority of entries are made by people using the Haemtrack apps. People using the Haemtrack app enter their data nearest to the point of treatment with nearly 80% entered within 7 days, comparatively paper records can take up to 3 months to reach a similar level of completeness.

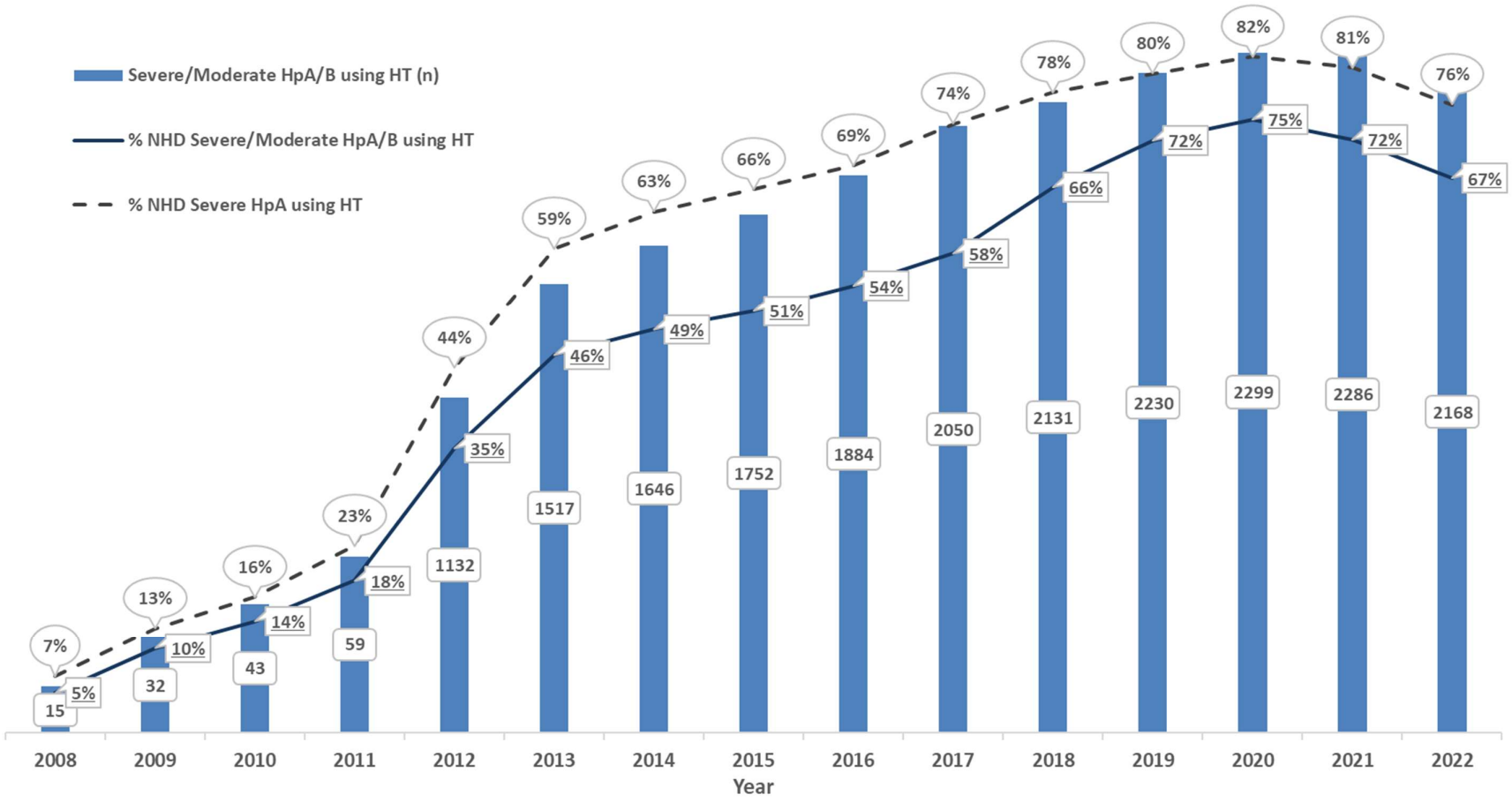
We have extended the use of Haemtrack to inpatient use (data entered by centre staff) so that it will provide a complete treatment record. Some centres are using this routinely and others not. We would encourage the universal adoption of inpatient use of Haemtrack so that the treatment record becomes complete.

3.1 People's Haemtrack Usage Analysis

3.1.1 Overall

Figure 1 (overleaf) presents an overview of severe and moderate patients with haemophilia A or haemophilia B using Haemtrack from 2008 to 2022. The blue columns give the numbers of patients that use Haemtrack, and the lines show the proportion of NHD patients who use Haemtrack. This illustrates rapid growth in 2012, when recruitment was the subject of a CQUIN and increased growth from 2017 when Haemtrack became a condition for access to new treatments. Figure 1 also reveals that there has been a gradual rise in the rate of recruitment, especially in severe haemophilia A cohort but that this has tailed off over the past year during which time the proportion of patients using the system has declined for the first time (see comments above).

Figure 1 Number of people using Haemtrack and recruitment rate, 2008-2022



3.1.2 Haemtrack usage analysis at centre level - people with severe Haemophilia

Figures 2 and 3 display the proportion of people with severe haemophilia A/B using Haemtrack in each CCC (Figure 2) and HC (Figure 3). Use of Haemtrack has increased at a rapid rate in recent years.

Figure 2 Comparison of recruitment to Haemtrack by centre for people with severe haemophilia A/B: Comprehensive Care Centres (CCCs) in 2022

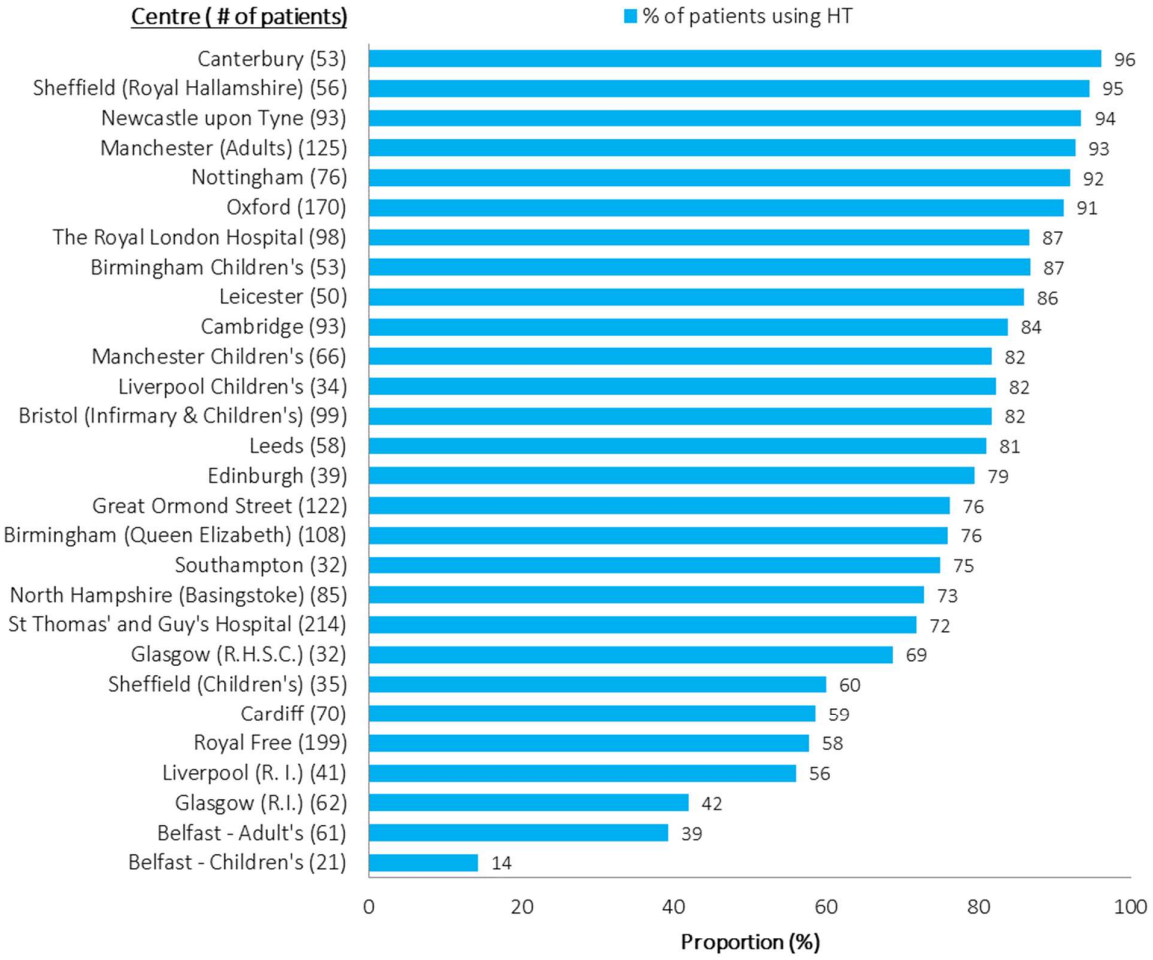
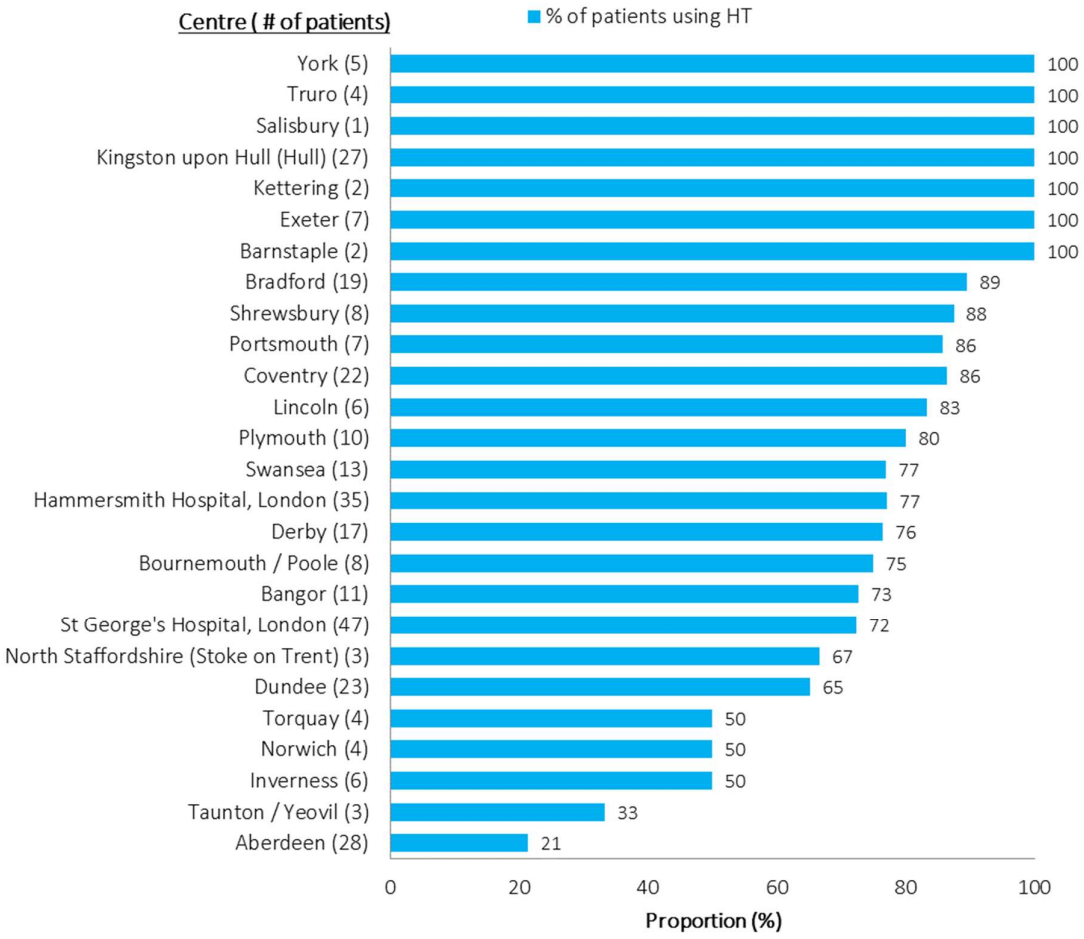


Figure 3 Comparison of recruitment to Haemtrack by centre for people with severe haemophilia A/B: Haemophilia Centres (HCs) in 2022



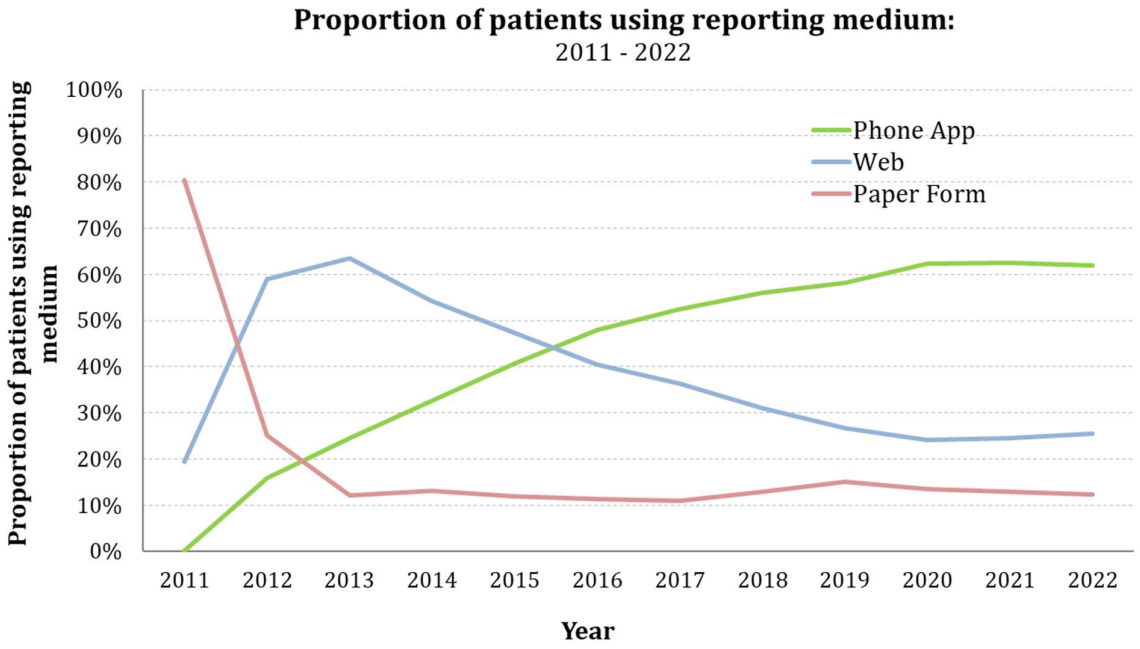
3.2 Haemtrack Users' Reporting Analysis

3.2.1 Reporting Medium

Figure 4 shows the proportion of Haemtrack users using different reporting methods between 2011 and 2022. This shows an initial rapid uptake of the use of the web application at the expense of paper reporting. Subsequently, when the iPhone and then the Android app were introduced, they rapidly gained popularity at the expense of the web application. Oddly, the use of paper has remained stable over the past several years. This is curious given that electronic data can be very quickly quality-checked and rapidly imported into the haemophilia Centre Information System (HCIS) whereas paper records need to be laboriously keyed in by centre personnel. Most centres have a small proportion of PwBD using paper, but some centres still have most of their PwBD reporting on paper even though this creates more work for centre staff. The number of PwBD who are statistical outliers for compliance and use a paper reporting system suggests that some of these records had

been manually entered by centres without checking or reconciliation. More recently, there seems to be a considerable increased in checking at centre level since there are far fewer obvious errors.

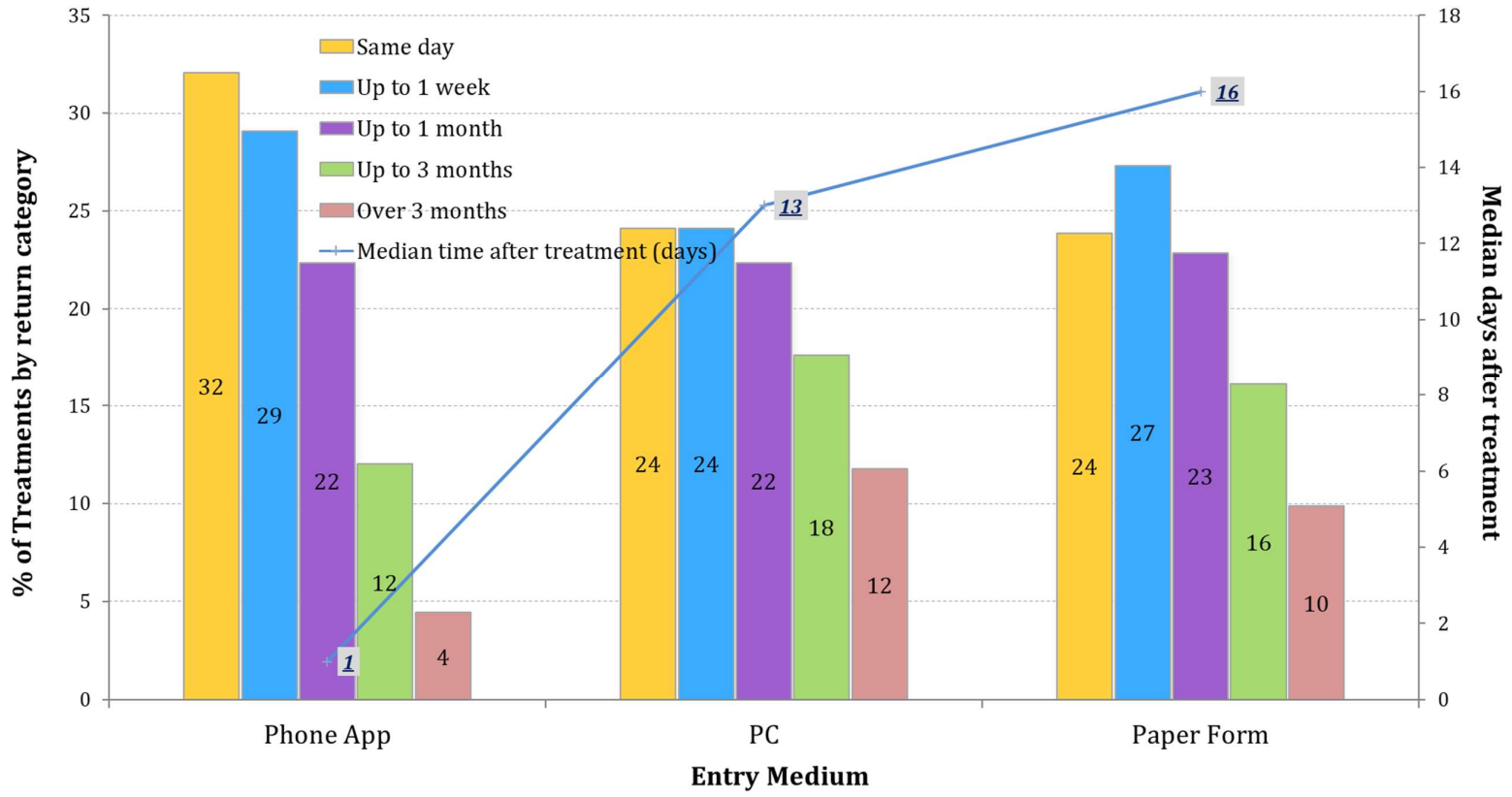
Figure 4 Change in the use of different Haemtrack Reporting Media: 2011- 2022



This is further analysed in Figure 5 (overleaf), which breaks down the interval between treatment and reporting by the reporting method used (smartphone apps, web/PC and paper). Use of phone apps is associated with the most rapid reporting, with 32% of data being recorded on the day of treatment and a further 29% within a week. In contrast, only 24% of treatments were reported the same day and a further 24% within a week using web. Most data submitted on paper was reported after an interval of up to one month, either by post or at the next review clinic. Data reported by phone app was returned after a median of only 1 day, whereas paper-recorded data was reported after a median of 16 days with the web/PC being intermediate. There is slight difference in the median age of patients using phone app, web, and paper form. The median age being 26, 33 and 28 years for phone app, web and paper reporters, respectively.

We are actively promoting the use of the phone apps in preference to other methods of reporting because we believe that the data are not only available to centres more quickly but are likely to be more accurate and will be of greater utility for the centre. Data reported on the day of treatment may be used by centres to identify abnormal treatment patters within a clinically useful timeframe.

Figure 5 Haemtrack Reporting Delay by Reporting Medium 2022



4. Data Management Working Party

Membership

Chair:	Dr Kate Talks
Commissioner representative:	Will Horsley
Co-Director of the National Haemophilia Database:	Professor Charles Hay
Co-Director of the National Haemophilia Database:	Prof Pratima Chowdary
Haemophilia Nurses Association representative:	Emma Franklin
Haemophilia Physiotherapists Group representative:	Dr David Stephensen
Haemophilia Society representative:	Kate Burt
MDSAS representative:	Dr Rob Hollingsworth
PwBD representatives:	William McKeown
	Paul Sartain

Representatives of Northern Ireland, Scotland and Wales:

Northern Ireland	Dr Gary Benson
Scotland	Dr Ryan Rodgers
Wales	Professor Peter Collins

UKHCDO Working Party Chairs/ co-chairs:

Co-morbidities Working Party	Dr Susie Shapiro
Genetics Working Party	Dr Keith Gomez
Inhibitor Working Party	Dr Charles Percy
Musculoskeletal Working Party	Dr G Benson
Paediatric Working Party	Dr Mary Mathias
Von Willebrand Working Party	Dr Carolyn Millar
Laboratory Working Party	Dr Will Lester
Women and Bleeding disorder Working Party	Dr Nicola Curry

UKHCDO Executive Committee:

Chair	Prof Pratima Chowdary
Secretary	Dr Mary Mathias
Treasurer	Dr Gary Benson

Members of the NHD as nominated by the Director(s) of the National Haemophilia Database:

NHD Manager	Andrew McNally
Business Support Partner - Administration & Executive Support	Alex Goodall
Business Support Partner – Governance (P/T)	Liz Ardern
Data and General Administrator	Blanca Martinez
	James McKenna
Head of Data Analytics	Dr Hua Xiang
Data Scientist	Paul Twine

Data Analyst	Ben Palmer
	Hasina Ngyou
Project Manager Peer Review	Harry Evans

Meetings

Since the last report the UKHCDO Data Management Working Party (DMWP) has met twice via TEAMS on 21st April 2023 and 18th October 2023. In the course of the year there have been a number of changes in roles and new members welcomed; the list provided reflects the current membership.

The DMWP oversees the data collection and analysis of people with inherited bleeding disorders undertaken by the National Haemophilia Database (NHD). The DMWP and NHD are jointly responsible for the accuracy and completeness of the data collected. The DMWP has delegated most of the responsibility for assessing and overseeing requests for analysis of NHD data to the Data Analysis Group (DAG), which is a subcommittee of the DMWP.

The DMWP reviews the information that is collected on PwBD and revises this as necessary. Any member of UKHCDO can suggest changes to the data that are collected which will be considered by the DMWP. The Database governance arrangements and information governance compliance are reviewed at each meeting and the database remains compliant with all the relevant information governance regulations: Data Protection Act 2018 (DPA); General Data Protection Regulation (2016), Caldicott Principles and NHS Information Governance guidance, legislation, and good practice. The NHD have successfully reapplied to the Health Research Authority (HRA) Confidentiality Advisory Group (CAG) in England and Wales for section 251 support, which is required by NHS Digital to supply mortality data. The Scottish Public Benefit and Privacy Panel for Health and Social Care have provided approval for Haemophilia Centres in Scotland to share data with the NHD. Consent of people in Northern Ireland is required for mortality data to be shared. The HRA CAG have recently confirmed that a mixed model of consent use within the database is acceptable and will not put the section 251 application at risk. Agreement reached to restart a consent process to ensure people are fully informed of their options and how their data may be used by the NHD. Proposals from a number of working parties to set up registries with new data sets have been discussed over the year with a new process agreed for the working parties to develop draft forms and pilot these. Development of a gene therapy database has been started to support prospective clinical data collection when the provision of this is agreed. Data from people who have participated in gene therapy clinical studies will be provided by manufacturers.

The Adverse Events Panel supports the consistent and timely assessment of all Adverse Events (AE) reported electronically to the NHD. The panel meets monthly and is co-chaired by an NHD director and the DMWP chair with additional UKHCDO members including representation from the paediatric and inhibitor working parties. Summary reports are provided to the DMWP and included in the annual NHD report.

Examples of Current UKHCDO projects supported by NHD include:

Real world experience of Emicizumab for people with and without inhibitors
Immune Tolerance Induction registry
The previously untreated patient (PUP) registry

Haemtrack

Commissioners for England and the devolved countries of the UK continue to encourage the use of Haemtrack as a means of capturing individual PwBD events and treatment. This has allowed important information about the impact of enhanced half-life factor VIII and IX and Emicizumab to be collated.

A new web-based version, Haemtrack 3 was launched in September 2023 and will increase connectivity between the other NHD systems, HCIS2 and NHD2.

Pharmacokinetic analyses through NHD

A system has been developed whereby individual pharmacokinetic data can be entered through NHD into the WAPPs-Hemo system. This supports tailoring and personalisation of prophylaxis for individual people. The system functions for all licensed brand of factor VIII and factor IX.

The UKHCDO would like to thank the Co-directors of NHD, Professor Charles Hay and Professor Pratima Chowdary, and all the other staff within the NHD for their commitment to collecting and analysing the data on behalf of the UKHCDO and Rob Hollingsworth and MDSAS for their continued support and maintenance of our national information systems.

We also wish to acknowledge and thank staff in the Haemophilia Centres and PwBD for their ongoing support providing data.

Dr Kate Talks,
Chair UKHCDO Data Management Working Party

November 2023

5. Data Analysis Group

Membership

Co-Chair (ex-Chair of Data Management Working Party)	Professor Peter Collins
Co-Chair (Director of NHD)	Professor Charles Hay
Co-Chair (Chair of Data Management Working Party)	Dr Kate Talks
User representatives:	Paul Sartain Dr Richard Gorman
UKHCDO members:	Dr Charles Percy Professor Pratima Chowdary Dr Susie Shapiro Dr Mary Mathias Dr Kate Talks Dr Gillian Lowe
Haemophilia Nurses and physiotherapy representatives:	Dr David Stephensen
National Haemophilia Database:	Ben Palmer Dr Martin Scott Dr Caroline Wall Dr Hua Xiang Hasina Ngyou Alex Godsall Andrew McNally James McKenna Blanca Martinez

Meetings

The Data Analysis Group (DAG) is a subgroup of the Data Management Working Party. Its role is to assess and prioritise applications to analyse data held by NHD, including Haemtrack and joint score data. Applications are assessed based on data governance considerations, scientific merit and available resources. The group meets once a month by videoconference which last on average 60-90 mins. The terms of reference of the DAG are available on the UKHCDO website.

Requests for analyses are submitted on a standardised form. This form is available from NHD and has been updated recently.

The DAG reviews and discusses all applications. It provides feedback to the applicant and works with them to refine the proposal, if necessary. The contributions from the user representatives have

been particularly useful in assessing the applications and interpreting results. Some straight forward requests, for example, those from NHS commissioners are often progressed on chair action and discussed at the next meeting.

The data analyses that are generated from the requests are reviewed and commented on by the group and may be further revised, if necessary, before release. Reports often contain caveats about data limitations that impact on the interpretation of reports.

The DAG acts the steering committee for a study that is analysing data held on the NHD relating to the introduction of Emicizumab. A paper about people with haemophilia and inhibitors has been published (C Wall et al Haemophilia 29:743-752, 2023) and one reporting on people without inhibitors is under development. This project is likely to be extended to cover people with moderate haemophilia A.

Requests for data analyses have been submitted by individual members of UKHCDO, UKHCDO working parties, Haemophilia Centres, NHS England, NHS Wales and pharmaceutical companies. A number of requests have been made to support applications to NICE appraisals.

All members of UKHCDO and UKHCDO working parties are encouraged to suggest analyses and are invited to collaborate with the DAG on these projects. The number of UKHCDO members on the DAG has fallen over the last 2-3 years due to retirement and changes in career path. Members of UKHCDO are encouraged to join the DAG and anyone interested should contact Kate Talks. The DAG is also looking for a nurse to join the group to replace Simon Fletcher.

Dr Kate Talks,
Chair UKHCDO Data Management Working Party

Prof Peter Collins
Prof Charles Hay
Director NHD

October 2023

6. Co-Morbidities Working Party

Membership

Chair	Dr Susie Shapiro, Oxford
UKHCDO representatives:	Dr Gary Benson, Belfast Dr Gillian Evans, Canterbury Dr Sarah Mangles, Basingstoke
Haemophilia Nurses Association Representative:	Cathy Harrison, Sheffield

Remit

To consider comorbidity issues in people with bleeding disorders (PwBD) within the UK and review any unmet need with respect to data collection, guidelines and PwBD-related information / material.

To develop a Work Plan for the CMWP.

To advise the DMWP as to what data the NHD should collect regarding comorbidities in people with haemophilia and bleeding disorders.

Any publications arising from the CMWP should be approved by the UKHCDO Executive in line with the UKHCDO publication policy.

Meetings

Discussions have been held via email April 2022 – April 2023 to support progression of Work Plan.

Activities

1. The group previously agreed that the initial focus of the Work Plan would be on cardiovascular disease and bleeding disorders.

2. The group previously agreed to initially write an up-to-date review on cardiovascular disease in people with haemophilia (prevalence and management) in order to highlight areas of unmet need/lack of data and potential areas for future data collection/research/service improvement. The review was published in the British Journal of Haematology May 2022; 197(4):397-406: “Cardiovascular disease in hereditary haemophilia: The challenges of longevity.”

3. Following this review, the group have agreed that a key area of need is to improve data and further understanding for PWH with AF (prevalence, use of anti-thrombotics, risk of bleeding and stroke). This is also a James Lind Alliance top 10 research priority 2019. The group would like to initiate a national registry for PWH with AF to prospectively record AF management including antithrombotics, bleeds, strokes. The group have approached UKHCDO and NHD with regards to the possibility of support of data collection through

NHD; NHD are reviewing consent process for prospective research registries and will hopefully be a suitable platform once this is established.

Dr Susie Shapiro,
Chair, Co-Morbidities Working Party
October 2023

7. Genetics Working Party

Membership

Keith Gomez	Chair
Vicky Cloke	Representing Genetics Laboratory Network
Nicola Curry	
Claire Forrester	
Mike Laffan	
Jayashree Motwani	
Suthesh Sivapalaratnam	
Megan Sutherland	Representing Genetics Laboratory Network
Kate Talks	
Claire Lentaigne	

Remit

1. Provide oversight of issues related to genetics in haemophilia
2. Review guidance on genomic testing and update as required
3. Support genetic analysis of all people with heritable haemostatic disorders and facilitate recording of data on NHD

Meetings and main work streams

Provision of Genetic Services

Testing is available for all NHS-registered people with heritable bleeding or thrombotic disorders. The genes that can be tested are listed in the following panels:

- Bleeding and platelet disorders (R90) https://panelapp.genomicsengland.co.uk/panels/545/
- Thrombophilia (R97) https://panelapp.genomicsengland.co.uk/panels/516/

The NHS service is provided through Genomic Laboratory Hubs in England and Regional Centres in Scotland, Wales and Northern Ireland.

Newborn Screening Programme

The Generation Study is due to start recrutitment in the next few months. The project is run by Genomics England and the aim is to screen 100,000 newborns for specific genetic diseases. Several haemostatic diseases are included. Further details of the study are available at https://www.genomicsengland.co.uk/initiatives/newborns

Dr Keith Gomez,
Chair, Genetics Working Party
October 2023

8. Genetic Laboratory Network (UKHCDO-GLN)

Background

The UKHCDO GLN was formed in 2002, arising out of the UKHCDO Genetic Working Party (UKHCDO GWP), with the aim of improving collaboration between laboratories and of ensuring quality and equity of service across the U.K. The network currently comprises 8 laboratories, 7 across the UK plus Dublin, involved in the molecular genetic analysis of haemophilia and other inherited bleeding and thrombotic disorders (many of the laboratories are also involved in other areas as well).

Representatives of the Network attend meetings of the UKHCDO Genetics Working Party.

Meetings

The UKHCDO GLN holds bi-annual meetings. The GLN met virtually on 13th December 2022 and on 19th June 2023. The next meeting is scheduled to be another virtual meeting in December 2023.

Chair & Secretary

Megan Sutherland and Catriona Keenan continue in their roles as Chair and Secretary, respectively.

Current activities

1. **NHS England Genetic Laboratory Hubs:** The new structure of service provision in England went live in February 2021. The NHS England genomic test directory now specifies which disorders and gene targets will be investigated under this new service model and by which methodologies they should be performed (https://www.england.nhs.uk/publication/national-genomic-test-directories/). The 'Non-malignant Haematology' service, including the investigation of bleeding and thrombotic disorders, is provided by four Genomic Laboratory Hubs.

2. **Laboratory Audit – ISO 15189**: Laboratories in the Network are accredited by the United Kingdom Accreditation Service (UKAS). Laboratories are required to adhere to ISO 15189 quality standards. The GLN continues to share examples of good practice, practical advice and knowledge as the inspection process is applied to member laboratories. The Network continues to provide an informal sample exchange scheme between its members for disorders and methodologies that are not provided for by UK NEQAS. All laboratories continue to participate in the UKAS inspection process cycle.

3. **Von Willebrand disease (VWD) Genetic Analysis Best Practice Guidelines:** The UK Best Practice Guidelines (BPG) for phenotypic and genetic analysis of VWD have been incorporated into a single guideline this year which is currently under review prior to publication. Two members of the GLN were involved in writing the genetic testing section for this guideline, and the content was reviewed by the remainder of the group. Merging

the two lab diagnosis pathways into one guideline has aimed to enable a more comprehensive route to diagnosis of VWD.

4. **Other Bleeding Disorder Genetic Analysis Best Practice Guidelines:** The UK Best Practice Guidelines (BPG) for Haemophilia A and Haemophilia B are in the process of being reviewed and updated in accordance with the NHS England genomic test directory In addition, a working group has been established to produce a BPG for the genetic investigation of rare bleeding disorders. Due to the recent reconfiguration of genetic services in England and the ongoing effects of the pandemic, the updates to these guidelines have stalled, however we anticipate that progress will be made in the coming year.

5. **UK NEQAS Genetics of Heritable Bleeding and Thrombotic Disorders scheme:** The UK NEQAS Genetics of Heritable Bleeding and Thrombotic Disorders EQA scheme provides four EQA exercises per year, two of these are the traditional 'wet' exercises which always include analysis of one of *F8*, *F9* or *VWF*. The two additional 'paper' exercises provide a clinical scenario and genetic variant for a PwBD which are to be interpreted by the participants and a report produced. The paper exercises aim to expand the scope of gene targets for interpretation to include rare bleeding and thrombotic disorders. The UK NEQAS paper exercises also include analysis of MLPA data and to provide an interpretative report for the clinical scenario. The results for each round of the scheme are reviewed and discussed at the following GLN meeting and any relevant comments fed back to the steering group.

6. **Participation in other groups:** Representatives of the Network input to the UKHCDO GWP. A representative of the Network is a member of the World Federation of Hemophilia Laboratory Science committee.
7. **General:** At each of the GLN meetings there is an open forum to discuss scientific and technical issues. We also aim to include an educational session at least once a year to focus on difficult areas for interpretation. Our main focus continues to be on the classification of rare or novel variants with reference to the current ACMG variant classification guidelines, and the sharing of this information throughout the network. It is recognised within the group that the sharing of knowledge and expertise is an essential mechanism for the interpretation of previously uncharacterised genetic variants.

Megan Sutherland,
Chair, UKHCDO Genetic Laboratory Network
October 2023

9. Inhibitor Working Party

Membership

Charles Percy (Chair)

John Grainger

Mike Makris

Mary Mathias

Ben Palmer

Anne Riddell

Kate Talks

Meetings

There have been three online meetings of the inhibitor working party (IWP) since December 2022. All of these have focused on updating the guideline on acquired coagulation factor inhibitors. The first draft is about to be submitted to the BSH Taskforce for initial review. Other activities have included the following:

1. In conjunction with the paediatric working party (PWP) and the National Haemophilia Database (NHD), reports of new or recurrent factor VIII inhibitors in PwBD continue to be reviewed, with a particular emphasis on those receiving prophylaxis with emicizumab.

2. Review of all adverse event report forms with the NHD, which will hopefully result in forms which are more user friendly, whilst capturing relevant information.

3. Meetings continue to be held with the NHD to find a way forward for analysis of data from acquired haemophilia A project.

4. Participation in other meetings: Data Management Working Party, NHD Adverse Events Review Panel.

Dr Charles Percy
Chair, Inhibitor Working Party
October 2023

10. Laboratory Working Party

Membership

Dr Will Lester	Co-Chair
Annette Bowyer	Co-Chair

Laboratory

Annette Bowyer	Royal Hallamshire Hospital, Sheffield
Caroline Lawrence	Glasgow Royal Infirmary
Stephen MacDonald	Cambridge University

Hospitals

Jill Morris	Aberdeen Royal Infirmary
Sean Platton	Royal London Hospital
Anne Riddell	Royal Free Hospital, London
Janenne Sanders	Hull Royal infirmary

Clinical

Dr Mohammed Khan	Aberdeen Royal Infirmary, Aberdeen
Dr Will Lester (Co-chair)	Birmingham Women's and Children's Hospital
Dr Andrew Page	Edinburgh Royal Infirmary

Invited representation

UKNEQAS Blood Coagulation	Anna Williams
NIBSC	Stella Williams

Activities

The group held three online meetings over the past 12 months 22/3/23, 14/06/23 and 04/10/23.

The VWD laboratory guidelines ready for submission. This is a UKHCDO/BSH guideline which is separated from the clinical guidelines.

The working party has also contributed to discussions on whether to recommend that factor assay results are issued to users in iu/dl rather than iu/ml for consistency and safety. There is a now a BSH good practice paper in progress which will include representation from the UKHCDO working party, BSH and NEQAS blood coagulation.

A survey of laboratories has been designed along with proposals for the test repertoire expected in CCC and HC laboratories and a list of which laboratories can provide rarely requested tests

Items in progress

New collaborations between laboratories and with UKNEQAS are currently being discussed

An ambition of the group is to create stronger links between laboratory scientists who are responsible for delivering haemostasis testing in their labs. The intention is for more senior scientists to help upskill the next generation and provide a support network for advice. A list of e mail contacts for lead coagulation scientists in UK CCC and HC laboratories has been made predominantly for the purpose of education and networking. A proposal for consideration by UKHCDO is to incorporate sessions for senior scientists (joint and/or parallel) at the UKHCDO educational meeting in 2024.

Dr Will Lester Co-Chair, Laboratory Working Party November 2023

11. Musculoskeletal Working Party

Co-chairs:

- Dr Gary Benson
- Dr Paul McLaughlin

Members:

- Trupti Bhandari (Physiotherapist, Evelina)
- Dr Nicola Curry (Haematologist, Oxford)
- Dr Emma Fosbury (Haematologist, Manchester)
- Jessica Hedden (Physiotherapist, Swansea)
- Dr Emily Symington
- Dr Thynn Thynn Yee

The MSK WP had just recently been reconvened after an open call for applications. We have yet to arrange the first meeting of the group, although the aim is to have this before the end of December 2024. Once terms of reference have been reviewed and agreed, the group will aim to review the work to date from the previous WP, and instigate a work plan for the upcoming 24 months.

Dr Gary Benson
Co-chair, Musculoskeletal Working Party
November 2023

12. Paediatric Working Party

Membership

Mary Mathias	Chair, London (GOSH)
Jeanette Payne	Secretary, Sheffield
Jayanthi Alamelu	London (Evelina)
Neha Bhatnagar	Oxford
Tina Biss	Newcastle
Jayashree Motwani	Birmingham
John Grainger	Manchester
Simone Greene	Hull
Simone Stockley	Nottingham
Anne Kelly	GOSH

Meetings

Since the last AGM the PWP has held 3 teleconference meetings in January, May and September

Summary of activities

1. We are now collecting data on **emicizumab PUPs and MTPs** at a national level. We have a list of PwBD from the database team and have devised a data set including bleeds, bleed treatment and adverse reactions. The WP members are capturing their own PwBD data and MM has sent requests to the other centres with PwBD requesting their input. We hope to be able to start collating this data before the end of the year.
2. **PUP registry on the NHD.** The data collection process via the NHD/MDSAS has now been streamlined as much as possible prior to the new version the NHD. Reminders for PwBD updates are sent quarterly.
3. **Access to Veyvondi for children.** Veyvondi is now commissioned for adolescent children on the same basis as adults (surgery and bleed treatment) after completion of a Blueteq form. MM submitted a Preliminary Policy Proposal for use in younger children in March 2023 and is awaiting a response.
4. **The national advisory group/MDT** continues to run smoothly with 3 monthly teleconferences with terms of reference for discussion and recording of outcome. Calls for cases to discuss are sent out to paediatric treating centres prior to the dates with a data pro forma. The feedback continues to be positive in terms of support for centres and allows for ad hoc emailing of complex cases in between meetings if there is a clinical necessity with follow up and minuting at the next meeting. Minutes are circulated and saved at the NHD.
5. **PWP membership at other UKHCDO meetings:** Inhibitor WP, DMWP, DAG and Adverse events panel.

Dr Mary Mathias
Chair, Paediatric Working Party
October 2023

13. Peer Review Working Party

Membership

Chair Dr Sarah Mangles Southern Haemophilia Network (Basingstoke)

UKHCDO representatives

Pratima Chowdary	(Royal Free)
Kate Talks	(Newcastle)
Gary Benson	(Belfast)
John Grainger	(Manchester Childrens)
Joannes Hermans	(Nottingham)
Gillian Lowe	(Birmingham)
Gillian Evans	(Kent and Canterbury)
Keith Sibson	(GOSH)

Haemophilia Nurse Association representatives

Elsa Aradom	(Royal Free)
Amy Conquergood	(Oxford)
Kate Forsyth	(Barts and Royal London)
Emma Franklin	(Bristol)
Lara Oyesiku	(Basingstoke and SHN)
Julie Spiers	(GOSH)

HCPA representatives

David Hopper	(Newcastle)
Stephanie Taylor	(Oxford)

Psychology representatives

Grainne O'Brien	(Edinburgh)

PwBD representatives

Nigel Miller	(Haemophilia Wales)
Debra Morgan	(Haemophilia Society - England)
Alan Martin	(Haemophilia Society – Scotland)

Project manager

Harry Evans

Remit

To review previous peer review standards and update

To work with project manager to set up peer review in 2024 for all CCC, interim CCC and HC who wish to be audited

To ensure training of all peer reviewers

To write summary report once all peer reviews completed

Meetings

Regular virtual meetings to discuss peer review standards, report templates, plan for peer review, as well as email review of documentation.

Activities

I took over as chair of the peer review working party in February 2023. It has been a busy 8 months to update and finalise the standards to enable peer review to start Spring 2024.

1. The group have reviewed the peer review standards from 2019, edited, updated and standards have been sent to all members of UKHCDO for review.
2. A project manager has been appointed
3. Report templates are being developed
4. Project manager planning actual visits
5. List of volunteers for peer review collected
6. Training being developed – compulsory virtual training for all reviewers
7. Working with PwBD representatives to ensure PwBD on each centre review have appropriate training

Dr Sarah Mangles

Chair, Peer Review Working Party

October 2023

14. Von Willebrand Working Party

Membership

Dr Carolyn Millar Chair

Cathy Farrelly
Vince Jenkins
Will Lester
Shapiro Susie
Thynn Thynn Yee

Mike Laffan retired in December 2022 and has stepped down from the Working Party. Vince Jenkins was re-instated in September 2023.

The principal focus of the VWD working party continues to be the revision and update of the BCSH/UKHCDO 2014 guidelines. A writing group has formed to develop a BSH guideline for the clinical diagnosis and management of VWD, and approval obtained from the BSH taskforce and guideline committee. It is anticipated that this will be completed and published mid 2024 and complements the guidelines for the laboratory diagnosis and monitoring of VWD.

Work continues on the update, reclassification and removal of PwVWD from the NHD. Discussions with the NHD regarding the most suitable approach for centres are ongoing.

Dr Carolyn Millar,
Chair, Von Willebrand Working Party
October 2023

15. Dental Task Force

Membership

Dr Julia Anderson	(Chair)
Mr Andrew Brewer	(Associate Specialist, Oral Surgery)
Dr Lochana Nanayakkara	(Consultant Dental Surgeon)
Dr Emily Symington	(Consultant Haematologist)
C/N Jayne Keaney	(Haemophilia Nurses Association)
Dr Janet Davies	(British Paediatric Dental Association representative)
Dr Alice Taylor	(Consultant Paediatric Haematologist)
Dr Sara Boyce	(Consultant Haematologist)
Dr Bella Madan	(Consultant Haematologist)
Dr Albert Yeung	(Public Health Dentist)

Dr Anderson chairs the Dental Task Force. The Task Force met on 7 February 2023, 9 May 2023, 29 August 2023 and a date is to be scheduled for November 2023.

The group membership consists of adult and paediatric haemophilia consultants, adult and paediatric dental and oral surgeons, and nurse representatives. Invited guests have discussed ongoing audits, and raised discussion on issues surrounding dental implants.

The group is focussing on the update of the 2013 guideline with a view to re-publication in the British Dental Journal and will be adding sections on gene therapy, extended half life products, emicizumab and local anaesthesia.

The guidance is primarily intended for dental practitioners, with a separate publication aimed at haemophilia treaters either in Haemophilia or the British Journal of Haematology.

The task force has written a first draft and is working towards further drafts and sending to the Advisory Panel by Spring 2024 prior to publication.

Thereafter the aim is to focus on audits of access to dental services across the UK, and an update of leaflets.

Julia A M Anderson

Chair, UKHCDO Dental Task Force

November 2023

16. Emergency Care Guideline Re-write Task Force

Over the last year our group has made progress on updating most of the standards for emergency care. Significant work has been done engaging with emergency medicine specialists and we have gained good insights into mechanisms for improving care for patients with bleeding disorders in the emergency department and we are making progress with insight into pre-hospital care (ambulance services and paramedics).

A manuscript has been prepared for submission as a practice review to the Emergency Medicine Journal. This is a narrative, pragmatic clinical review aimed at emergency medicine professionals emphasising rapid triage and assessment and prioritisation of haemostatic support. A talk about emergency care for haemophilia and bleeding disorders has also been presented at the British Association for Immediate Care Conference in October 23. Arrangements are being made for a priority meeting to discuss achieving an entry in Joint Royal Colleges Ambulance Liaison Committee pocket guideline book.

Our group is aiming to complete a new guideline/standards document for submission for publication to a haemophilia journal by the end of 2023. Liaison with the peer review working party has taken place to ensure compatibility of standards.

Dr Lishel Horn
Chair, Emergency Care Guideline Re-Write Task Force
Lead Clinician for the NW Yorkshire Haemophilia Network
November 2023

17. Gene Therapy Guideline Task Force

Prof Pratima Chowdary, Chair

Medical

Dr Gillian Lowe

Dr Jayshree Motwani

Dr Kathryn Musgrave

Dr Sara Boyce

Dr Susie Shapiro

Dr Paul Batty

Nursing

Debra Pollard

April Jones

Physiotherapy

David Hopper

Stephen Classey

Pharmacy and ATMP expertise

Bea Duran

Psychologists

Nicola Dunn

Sarah Whitaker

There have been several changes in the membership over the last year. John Hanley, Anne Black and Gavin Ling have stepped down and been replaced by Paul Batty and Kathryn Musgrave. The group has expanded its expertise by recruiting two psychologists, making it genuinely multidisciplinary. A first draft was completed and discussed before the summer, and a second draft in October 23. A final draft for stakeholder comments is expected at the end of November. The intention was to publish by the second quarter of 2023, with slippage secondary to the gene therapy tender. The next few months will involve working on several items. First, we must develop patient information in collaboration with the Haemophilia Society. Second, we should create a standardized consent form. Lastly, it is essential to define the roles and responsibilities of a national MDT clearly.

Prof Pratima Chowdary

Chair, Gene Therapy Guideline Task Force

November 2023

18. Haemophilia Nurses' Association

Committee:

Julia Spires	Chair (Great Ormond Street)
Sharon Thind	Vice Chair (Alder Hey Children's hospital)
Debra Pollard	Secretary (Royal Free and Director of Education HNA-UK)
Marie Eales	Treasurer (John Radcliffe, Oxford)
Helen Hupston	Queen's Medical Centre, Birmingham
Siwan Owen	Betsi Cadwaladr University Health Board
Molly Ndebele	Royal Free Hospital

The Haemophilia Nurses Association -UK (HNA) continues to represent specialist nurses who care for people with bleeding disorders in the UK.

We ran our highly successful annual meeting in January 2023. This was well attended by nurses representing all haemophilia centres across the country. We had a vast array of speakers from our nursing body as well as PwBD representatives and external speakers for academic support and planning. The planning for 2024 is well underway and the focus is well being for staff as well as families and looking at how we can work with our Neurodivergent population. We have launched a quarterly 'Bulletin' providing information to nurses about developments, opportunities and a morale boost cheerleading proactive members.

Last year we spent a great deal of time working on Charitable status for the HNA-UK, however after 2 failed applications we approached the Haemophilia Society to suggest that we support each other, and this was well received and they now hold our finances and have supported us with much of our accountancy and organisational activities while we as a nursing body have offered them support in the education, providing nurse representation at their meetings, PwBD support groups and events.

The CCC continues to be exceptionally well attended and has maintained its accreditation through Middlesex University, providing this with the academic validation it deserves. It is truly a practical, hands-on course developed and run by nurses from four key haemophilia centres, supplemented by external invited speakers, covering all aspects of nursing care in bleeding disorders.

Over the year, we have lost members of our community to retirement, changes in service and brighter futures and to say these individuals and their expertise will be a loss to our community is an understatement. However, we do wish them all the best in their chosen pathways. We have welcomed many new members and continue to offer support to them as they develop their Haemophilia Nursing careers.

2024 brings with it opportunities for education and networking through international meetings, such as EAHAD and ISTH. As always, we ask the centre directors for their support for their nursing colleagues in being able to access the opportunities these meetings afford.

As well as being active on the steering committees of EAHAD and WFH committees, our members are active on other initiatives within the UK haemophilia treaters community, including the CRG, and various UKHCDO working parties. I thank all those who have participated in these groups and those who respond to questions to ensure that the national voice of haemophilia nursing is represented at these events.

JULIA SPIRES, Chair, Haemophilia Nurses Association-UK

November 2023

19. Haemophilia Chartered Physiotherapists' Association

The HCPA consists of specialist physiotherapists working in haemophilia and allied bleeding disorders services across the UK and Ireland. We aim to define, promote and encourage best practice for physiotherapy within haemophilia care, providing professional leadership and directing national physiotherapy policy.

Executive Committee

David Hopper	Chair
Stephen Classey/Paula Loughnane	Vice-Chair
David Stephensen	Research Lead
Katie Lindsay	Secretary
Steph Taylor	Treasurer

The committee was re-elected at the 2023 AGM in June and the positions will be held for a two-year period before another election at the 2025 AGM.

Peer Review 2024

David Hopper and Steph Taylor have been working with the UKHCDO and the peer review working party over the last year. The HCPA have played an active role in helping look at how each CCC will be assessed.

Members of the HCPA have also volunteered their services to take part the actual peer review process in 2024.

National Service Specification

David Hopper and a HCPA working party (Dr Paul McLaughlin, Fionnula Sayers, Thuvia Flannery, Melanie Bladen, and Victoria Morris) have helped rewrite the physiotherapy section in the revised national service specification which will hopefully be completed later this year.

The HCPA has actively been involved in helping rewrite the document and as a result we have also updated the HCPA adult and paediatric standards of care guidelines.

Working Parties

MSK Working Party	Dr Paul Mclaughlin (Co-Chair)
Peer Review Working Party	David Hopper

	Steph Taylor
Emergency Guidelines Working Party	David Hopper
National Service Specifications Working Party	David Hopper
Care of the Elderly Working Party	Fionnula Sayers
Data Management Working Party	Dr David Stephensen
Gene Therapy Working Party	Steve Classey David Hopper

Research

The HCPA is proud to support and facilitate a thriving research environment. Members have successfully received NIHR and commercial grant funding. Current NIHR/Grant funded research includes:

- David Hopper - The development of a self-ASSESSment decision aid to enable people with haemophilia (PWH) to detect and manage acute musculoskeletal bleeding events utilising ultrasound technology. (ASSESS)
- Anna Wells - "Exploring Post-traumatic Stress Symptoms and Pain Memories in People with Haemophilia and the influence on current pain experience"
- Paula Loughnane - Physical Fitness And Physical Activity In Children And Adolescents With Haemophilia In Ireland (ActFit-H).
- Melanie Bladen -
- Stephanie Taylor (ARC) – Evidence based co-design of and exercise intervention for PWH.
- Development of a haemophilia physiotherapy intervention for optimum musculoskeletal health in children (DOLPHIN-II) - a randomised controlled trial.NIHR Research for Patient Benefit (RfPB) Programme, NIHR-201588 David Stephensen, Melanie Bladen, Liz Carroll, Ferhana Hahsem, Tracy Pellat-Higgins, Eirini Saloniki
- The Irish Personalised Approach to the Treatment of Haemophilia (iPATH) Study Supported by Science Foundation Ireland (SFI) Strategic Partnership Programme Grant (16/SPP/3303) and Shire US Inc., a Takeda company, Lexington, MA, USA.Research Physiotherapist: Megan Kennedy (Principal Investigator: Professor James O'Donnell)

AGM and Educational Meeting

This Year the AGM was held separately to the educational meeting, this was held online via Zoom. At the AGM the positions of Chair, Vice Chair and Treasurer were extended for a further two years and Katie Lindsay was appointed as the new secretary.

The annual education meeting 2023 was held in Birmingham at the La Tour Hotel face to face with a virtual option, with over 40 physiotherapists attending (38 F2F 10 Virtually). The first day included a half-day session focussed on HJHS training for new and existing members of the HCPA. The second day included a range of national and international speakers and a free papers session for members to showcase their work in the format of a five-minute assessed oral presentation. This will take place again next year 2024 as we intend to host this meeting face to face whilst also offering the virtual options as well.

The meeting was kindly sponsored by Pharma (Roche Sobi Pfizer CSL).

HEAD-US (Haemophilic Early Arthritic Detection with Ultrasound) Training Birmingham July 2023

The HCPA organised an ultrasound (HEAD-US) training course for beginners and an update course for experienced therapists in Birmingham in July 2023. This event was delivered by Dr David Stephensen and Steve Classey and was sponsored by Pharma. Over 15 people attended over the two days.

EAHAD

The HCPA currently have three of its members sitting on the EAHAD committee;

- Dr Paul McLaughlin Chair of EAHAD Physiotherapy Committee
- Dr David Stephensen Physiotherapy Committee
- Paula Loughnane Physiotherapy Committee

Presentations/Posters EAHAD 2023

At EAHAD in February 2023, HCPA members contributed to numerous poster presentations and 5 presentations three of which were in the main programme. The HCPA encourages collaboration and members continue to initiate, present and publish key papers on an international level.

International Prophylaxis Study Group (IPSG)

Melanie Bladen is currently a member of the International Prophylaxis Study Group (the IPSG), a collaborative group of health care professionals involved with the assessment and care of individuals with inherited bleeding disorders, which is currently exploring the utility and modification of the Haemophilia Joint Health Score (HJHS) this is ongoing.

Dr David Stephensen is also a member of the Musculoskeletal Health Expert Working Group with the IPSG.

Publications in 2022/23:

1. Bladen M, Drechsler W, Duport G, Harbidge H, Mahaffey R, van der Net J, Perez-Alenda S, Sayers F, Strike K, Timmer M, Stephensen D. Identifying performance-based outcome measures of physical function in people with haemophilia (IPOP). Haemophilia (In Press). DOI: 10.1111/hae.14886

2. Boban A, Baghaei F, Fijnvandraat K, Klamroth R, Miesbach W, Stephensen D, Kavanagh M, Noone D, Crato M, Peyvandi F. Accreditation model of European Haemophilia centres in the era of novel treatments and gene therapy. Haemophilia (In Press).

3. Dodd C, Hashem F, Bassett P, Stephensen D. Wearable activity trackers in young people with haemophilia: What needs to be considered? Haemophilia. 2023;29(3):942-945.

4. Wall C, Xiang H, Palmer B, Chalmers E, Chowdary P, Collins P, Fletcher S, Hall G, Hart D, Mathias M, Sartain P, Shapiro S, Stephensen D, Talks K, Hay C. Emicizumab prophylaxis in haemophilia A with inhibitors: three years follow-up from the UK Haemophilia Centre Doctors' Organisation (UKHCDO). Haemophilia 2023;29(3):743-752.

5. Minno MNDD, Martinoli C, Pasta G, la Corte-Rodriguez H, Samy I, Stephensen D, Timmer MA, Winburn I. How to assess, detect, and manage joint involvement in the era of transformational therapies: Role of point-of-care ultrasound. Haemophilia. 2023;29(1):1-10. doi: 10.1111/hae.14657.

6. de Kleijn P, Duport G, Jansone K, Marinić M, McLaughlin P, Noone D, Ramishvili L, Tollwé A, Stephensen D; European Haemophilia Consortium and EAHAD Physiotherapy Committee. European principles of care for physiotherapy provision for persons with inherited bleeding disorders: Perspectives of physiotherapists and patients. Haemophilia. 2022;28(4):649-655.

7. Chugh, D., Thorpe, N., Alderson, L., Main, E. and **Bladen, M.** (2022), Reliability of the submaximal iSTEP performance test in children with haemophilia. Haemophilia, 28: e5-e8. https://doi.org/10.1111/hae.14436

8. **Bladen, M.,** Thorpe, N., Ridout, D., Barrie, A., McGibbon, E., Mance, A., Watson, L. and Main, E., 2022. Autism Spectrum Disorders in boys at a major UK hemophilia center: prevalence and risk factors. *Research and Practice in Thrombosis and Haemostasis*, p.100013.

9. **Bladen M,** Alderson L, Thorpe N, Cortina-Borja M, Main E. Performance on the iSTEP and 10 m-ISWT in boys with haemophilia. Haemophilia. 2023 Sep;29(5):1343-1350. doi: 10.1111/hae.14833. Epub 2023 Aug 12. PMID: 37572336.

10. Frailty and Haemophilia; speaking the language of geriatricians. Sangha, Gavinda; Obeidalla, Abubaker; **Taylor, Stephanie**; McKeown, William; Shapiro, Susie Haemophilia 2023. **DOI:** 10.1111/hae.14839

11. HA HA study: A single centre, open label, pilot study evaluating the effect of intra articular hyaluronic acid injection on pain and functionality into the ankle joint in patients with haemophilia arthropathy. **Taylor S,** David J, Partington K, Pemberton S, Mangles S, Wells A, Curry N. Haemophilia 2022. DOI: 10.1111/hae.14639

12. St-Louis, J., Abad, A., Funk, S. et al. The Hemophilia Joint Health Score version 2.1 Validation in Adult Patients Study: A multicenter international study. *Research and Practice in Thrombosis and Haemostasis*, 2022; 6; e: 12690, doi.org/10.1001/rth2.12690

13. de Kleijn, P., Duport, G., Jansone, K., Marinic, M., McLaughlin, P., Noone, D., Ramishvilli, L., Tollwe, A., Stephensen, D. European Principles of care for physiotherapy provision for persons with inherited bleeding disorders: Perspectives of physiotherapists and patients. *Haemophilia*, 2022; 28;4: 649-655. doi:10.1111/hae.14566

14. Matlary, R.E.D., Grinda, N., Sayers, F., Versloot, o., **McLaughlin, P**. Promoting physical activity for people with haemophilia in the age of new treatments. *Haemophilia* (2022), 28:6:885-890. doi: 10.1111/hae.14641

15. Burke, T,. Rodriguez-Santana, I., Chowdary, P., Curtis, R., Khair, K., Laffan, M., **McLaughlin, P**., et al. Humanistic burden of problem joints for children and adults with haemophilia. *Haemophilia* (2023), 29;2: 608-618. doi: 10.1111/hae.14731

16. Khair, K; **McLaughlin, P**., Roussel, N., Boyton, M., Holland, M. Prevalence and perceptions of pain in people with haemophilia: A UK study. Haemophilia, 2023; 1-10. doi:10.1111/hae.14860

17. **Wilkins, RA**., Siddle, HJ., Chapman, GJ., Horn, E., Walwyn, R. and Redmond, AC.. (2023) 'Decline in health related quality of life and foot and ankle patient reported outcomes measures in patients with haemophilia and ankle haemarthropathy.', *Journal of foot and ankle research*, 16(1).

18. Wells AJ, Whitaker S, Gray D, Mangles S, Hislop-Lennie K, Stephensen D. (2022). Pain memories: A new concept to consider in the management of chronic pain in people with haemophilia. Haemophilia, 28: e46-e48. https://doi.org/10.1111/hae.14480

EAHAD 2024 Frankfurt

At the AGM in June 2023 the committee were encouraging attendance and abstract submissions to next year's EAHAD.

WFH 2024 Madrid

At the AGM in June 2023 the committee were encouraging attendance and abstract submissions to next year's WFH event.

HCPA Meetings

- June 2024 AGM (Virtual) and Educational meeting Face to Face in Birmingham with a virtual option over two days with national and international speakers on the agenda.
- Northern Physiotherapy Group – Monthly CPD sessions 2023 and Northern face to face meeting planned for 2024.
- Southern Physiotherapy Group – Monthly CPD sessions 2023

Future Meetings

- 2024 – HCPA training days – Topic to be determined (Face to Face)

HCPA Logo Design

The HCPA have decided to change their logo to make it more up to date and recognisable. We hope to have this completed by the end of 2023.

UK Standards of Care

- http://www.ukhcdo.org/wp-content/uploads/2020/06/2020v1-Children-Service-Provision-of-Physiotherpay-in-Haemophilia.pdf
- http://www.ukhcdo.org/wp-content/uploads/2020/06/2020v1-Adult-Service-Provision-of-Physiotherapy-in-Haemophilia.pdf

These Standards of Care have recently been updated and will be ratified by the HCPA and sent to the UKHCDO for approval to go on the website.

HCPA Constitution

- http://www.ukhcdo.org/wp-content/uploads/2019/01/FINAL_HCPA_Constitution.pdf

David Hopper,
Chair, Haemophilia Chartered Physiotherapists' Association
October 2023

20. British Society for Haematology Haemostasis & Thrombosis Task Force

Membership

Dr Keith Gomez	Chair
Dr Will Lester	Deputy-Chair
Dr Ian Jennings	UK NEQAS representative
Dr Stella Williams	NIBSC representative
Dr Karen Breen	
Dr Lara Roberts	
Dr Jayashree Motwani	
Dr Julia Anderson	UKHCDO representative
Mr Sean Platton	
Mr Peter Baker	
Dr Renu Riat	
Dr Khalid Saja	
Dr Christina Crossette-Thambiah	Task Force Trainee

Meetings

Dr Gomez chairs the BSH H&T Task Force, and Dr Lester is Vice-Chair. The Task Force met on 24 January 2023, 22 April 2022, 17 May 2023, 14 September 2023 and scheduled to meet on 3 November 2023.

UKHCDO Guidelines and other publications published 2022/2023:

Laboratory coagulation tests and recombinant porcine factor VIII: A United Kingdom Haemophilia Centre Doctors' Organisation guideline. A Bowyer, E Gray, P Murphy et al. Haemophilia 2022 May 28 (3) 515-519

Twelve month prevalence of haemarthrosis and joint disease using the Haemophilia Joint Health Score: evaluation of the UK National Haemophilia Database and Haemtrack patient reported data: an observational study. R A Wilkins, D Stephensen, H Siddle, M J Scott, H Xiang, E Horn, B Palmer, GJ Chapman, M Richards, R Walwyn, A Redmond. BMJ Open 2022; 12: e052358. Doi: 10.1136/bmjopen-2021-052358.

Gynaecological management of women with inherited bleeding disorders. A UK Haemophilia Centres Doctors' Organisation Guideline. N Curry, L Bowles, T Justin Clark, G Lowe, J Mainwaring, S Mangles, B Myers, R Abdul Kadir. Haemophilia 2022; 28 (6) 917 – 937.

BSH Guidelines Published 2022/2023

Position paper: Joint guidance from the British Societies of Interventional Radiology and Haematology on managing Bleeding Risk during Procedures in Interventional Radiology, date 31 January 2023.

Haematological evaluation of bruising and bleeding in children undergoing child protection investigation for possible physical maltreatment: A British Society for Haematology Good Practice Paper. T Biss, K Sibson, P Baker et al. B J Haem 2022 Oct; 199(1) 45-53

Guidelines in Preparation:

The laboratory diagnosis of von Willebrand disease (Joint BSH/UKHCDO guideline, writing group chair: Mr Sean Platton)

Investigation and Management of Acquired Coagulation Factor Inhibitors: A joint BSH/UKHCDO guideline. C Percy, A Riddell, K Talks, J Anderson, S Cotton, R Riat, K Saja, M Makris. Writing group chair: Dr C Percy.

Guidance on the Dental Management of Patients with Haemophilia and Inherited Bleeding Disorders (UKHCDO guideline: working party members: Chair: Dr J Anderson, Sara Boyce, Andrew Brewer, Janet Davies, Jayne Keaney, Bella Madan, Lochana Nanayakkara, Emily Symington, Alice Taylor, Albert Yeung.

Guidance on the Management of Patients with Congenital Bleeding Disorders in Emergency Medicine (UKHCDO guideline, chair Dr E Horn)

Dr Julia A M Anderson
UKHCDO Representative for BSH Haemostasis & Thrombosis Task Force
November 2023

21. Haemophilia Society

The last financial year was one in which the charity sector continued to feel the after-effects of the pandemic combined with the cost-of-living crisis impacting income, and inflation adding to costs.

In spite of these challenges the Haemophilia Society (THS) continued to deliver free services to members including new events focused on VWD and rare bleeding disorders, Haemophilia Live and HaemFest, a weekend of camping in Derbyshire. We were also pleased to offer free to members our annual women and girl-focused Talking Red Live event, Newly Diagnosed weekends and Youth Camp, all of which were over-subscribed.

We represented the UK bleeding disorder community on the global stage at the World Federation of Hemophilia's Congress in Montreal, Canada, the first in-person congress since the UK hosted the WFH in Glasgow in 2018. The UK has representatives on the European Haemophilia Consortium's (EHC) von Willebrand disorder and Youth committees and we attended the EHC annual conference in Copenhagen. The war in Ukraine has touched so many of us, and we were proud to provide financial support to the Duisburg Haemophilia Centre in Germany, which was supporting a large number of displaced families with bleeding disorders in desperate need of treatment.

Nationally we represented the community's interests through influencing the NHS' new service specification for care in haemophilia centres. We have representatives on the new Clinical Reference Group which provides advice to NHS England in various areas such as commissioning policies, innovation and quality of services. We have developed a major new campaign to assess the provision of service and care for women and girls across the UK.

We're encouraged by progress in bringing gene therapy in both haemophilia A and B to the market, with significant steps being made globally. We, alongside many of our members who have been involved in research, will continue to work with the organisations involved in supplying, commissioning and delivery of gene therapy to ensure it will be available as a treatment option in the UK in the near future.

Six years after the Infected Blood Inquiry was announced, an important milestone was reached when the hearings came to an end in February 2023. The payment of interim compensation in October 2022 to those registered on UK support schemes was an important step forward, but there is much to do in ensuring full compensation is paid to everyone infected and affected by the contaminated blood scandal. THS continues to offer its full support to those impacted until justice is delivered and beyond.

As we look forward to 2024, the 60th anniversary of THS being granted charitable status, we do not take for granted your support.

Thank you.

Kate Burt,
CEO, The Haemophilia Society
October 2023

The Haemophilia Society

22. Haemophilia Scotland

Haemophilia Scotland's vision is for Scotland to be a place where people with haemophilia, Von Willebrand's and other rare bleeding disorders, along with their families and carers, are fully supported to live healthy, happy lives.

Membership of our organisation is completely free and open to anyone that is affected by a bleeding disorder, their family, friends, carers and healthcare professionals.

Events and Projects

Our 2022 events programme began with the launch of our Women's Group exhibition at the Glasgow Gallery of Modern Art to coincide with World Haemophilia Day. This was the first opportunity for our members to attend an in-person event since the onset of the global pandemic. As the year progressed, we continued to offer new opportunities to our members to meet and share experiences once more.

2022 also saw the launch of our Scottish Bleeding Disorders Needs Assessment survey. This ran from September 2022 to February 2023 and was available to anyone in Scotland living with a bleeding disorder or is the parent or carer for someone who does. The report was published in August 2023 and is available, along with our other publications, on our website.

In March 2023, we were delighted to launch our multi-year Comic Book project for our young members which will help raise awareness of the challenges of living with a bleeding disorder as a child and will be a valuable education tool to distribute to distribute to haemophilia centres, schools and clubs.

Engagement with Other Organisations

Throughout its history, Haemophilia Scotland has developed strong relationships with other organisations that share its aims on relevant health, social welfare or educational areas. This includes other haemophilia societies in the UK and beyond.

We continued to work closely with The Haemophilia Society on several collaborations this year, including a joint social media campaign to help raise awareness of misconceptions around bleeding disorders in early 2023 and have begun working on new education materials for upcoming future treatments for PwBD.

We continue to actively engage with all six Scottish haemophilia centres and have a strong PwBD representation within the Scottish Inherited Bleeding Disorders Network Steering Group which promotes the strategic direction of care for people with inherited and acquired bleeding disorders in Scotland. These relationships are vital to ensure we continue to provide a PwBD voice and highlight any unmet needs of PwBD effectively.

Advocacy

Advocacy remains a crucial role for our organisation as we strive to ensure equitable access to care and treatments for PwBD across Scotland. From representing an individual member to lobbying for improved levels of service and accessibility nationwide, Haemophilia Scotland continues to be the voice for the people in Scotland affected by bleeding disorders.

As the UK Infected Blood Inquiry entered its fifth year, Haemophilia Scotland continued to represent our members as a Core Participant to the Inquiry and providing ongoing support, information and advice to our members. We await the publication of the final report and being actively involved in campaigning for the conclusions and any recommendations made to be resolved as soon as possible.

Our organisation also had the opportunity to meet with the Scottish Minister for Public Health, Women's Health and Sport twice during the past twelve months to discuss matters relating to the Infected Blood Inquiry and about compensation. We also raised concerns over the long-term access to psychological support in Scotland, improved access to physiotherapy services and improvements needed in palliative care.

Throughout the year, the organisation has been very active in supporting our members in many different areas and have recently published our new Strategic Plan for 2023-2026 which will allow us which identifies our priorities over the coming years to ensure we continue to improve the health and wellbeing of people in Scotland living with or affected by a bleeding disorder.

Alan Martin
Haemophilia Scotland
October 2023

23. NHD technical development

It has been an extremely busy period at the database with a great deal of progress made in relation to re-development of NHD IT systems. This work has involved updates on all infrastructure and IT platforms utilised by the database.

During the year we have also undertaken an office move to a new location which has required the setup of new operational IT infrastructure including networking and PC setups for staff members.

Cloud Migration

Historically the database and all related IT systems where held on local servers which restricted the scalability of the database and the ability to adopt the latest technologies. We are pleased to be able to update that the migration of all existing NHD IT systems to the cloud has now been completed.

This has been done in a way that maintains the highest level of security with core database systems still protected from external Internet access within the secure internal NHS Health and Social Care IT Network (HSCN).

Data Warehousing

We have introduced data warehousing technology for the NHD Database. Operational effectiveness of NHD analytical work has been greatly enhanced through this development, with faster and simpler access to data.

An added benefit of the data warehousing approach is that it has reduced the risk of potential data issues resulting from access to live operational databases.

HCIS 2

Development of the new HCIS system which collects data from Haemophilia Centres at source has now been completed.

This system offers multiple advantages over the previous version, including automated updates, ability to collect data at a more detailed level, and ability to take data on a more frequent basis. The rollout of this system to Haemophilia Centres is now underway.

Data Transfer Web Services

A key aim of the new NHD IT strategy is the reduction in manual effort to obtain, validate and analyse data.

With the introduction of the new HCIS 2 system, multiple new web services have been developed in the latest technologies, that manage the flow of data between Haemophilia Centres and the NHD.

These new web services are essential to feed data to the new NHD API data manager which will automate validation and data processing activities.

Haemtrack 3

A new version of the hugely successful PwBD home therapy system has been developed and implemented recently.

The very latest technologies have been adopted in the new system and with its implementation we have hugely improved the scope and capability of the system. We now have the ability to release updates to the system within days, whereas previously it would take several months.

The new system can also be extended and tailored for multiple use cases, including new developments such as gene therapy, PwBD reported outcome measures and clinical studies.

Haemtrack 3 is a core component on the NHD re-development strategy and it's successful development and implementation is a huge achievement.

API Data Manager

The API data manager will provide the mechanism for the automated validation of data, improving data quality and reducing manual effort.

We have undertaken significant design work required for the introduction of this system, defining the automated rule bases that will be run against the incoming data from Haemophilia centres.

This includes validation of factor levels, diagnoses, inhibitors, product usage etc.

Output from the API Data Manager will be visible directly by Haemophilia Centres and NHD, speeding up the process of data cleaning and improving access to data.

Power BI

We have begun the work to introduce Power BI reporting to the NHD. Initial work is focussed on the development of data validation dashboards built on the output of the API data manager.

Power BI will offer the NHD a huge technological advancement in its ability to provide stakeholders with visibility of data within the NHD and reported to it.

Over the coming months we will begin to implement online Power BI reporting tools.

Gene therapy

With the advent of gene therapy PwBD therapy the NHD is establishing itself as the leading national source for gene therapy data.

NHD is developing a new gene therapy database in the new NHD 2 platform technologies. This will ensure that NHD is able to monitor and provide analysis on the introduction of gene therapy at a level of detail that will not be possible from any other source.

Adverse events

Significant work has been undertaken by the working parties to review and update the existing adverse event forms. There is a desire to improve the completeness, validity and timeliness of adverse event reporting to NHD.

This piece of work is increasingly important with the advent of new therapy options that will require long-term follow-up.

The revised adverse event forms will also be developed using the new NHD 2 platform technologies.

Security

NHD is currently updating all systems to the latest database technologies. This allows us to take advantage of new encryption technologies that provide an extra level of security for the database.

In addition the database has in place operational tools to monitor and defend against threats and vulnerabilities.

It is essential that the database continues to evolve and adopt the latest technologies to ensure it remains secure and stable.

Dr Rob Hollingsworth,

Head of Medical Data Solutions and Services

October 2023