NHD

U.K.H.C.D.O NATIONAL HAEMOPHILIA DATABASE

UKHCDO Annual Report 2020

& Bleeding Disorder Statistics for the Financial Year 2019/2020

UKHCDO

UNITED KINGDOM HAEMOPHILIA CENTRES DOCTORS' ORGANISATION

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1. Chairperson's Report

It is only about 8 weeks until the end of the year and there are few of us who will be sorry to say goodbye to 2020 and welcome a New Year. This has been my penultimate year as UKHCDO Chair and there are only two issues that are in the forefront of my mind while I write this report; the COVID-19 pandemic and the Infected Blood Inquiry. They are of course unrelated but yet there are underlying similar threads; for example both involve viruses which appeared to come from nowhere and cause/d significant morbidity and mortality. We all know that it took some years for effective treatments for HIV to be available and even longer for HCV and so I am sure we are all anxiously hopeful that our scientific colleagues can make real progress on vaccines and effective treatments to allow inching back to more normal times in 2021 and beyond. Meanwhile the shake-up caused by the pandemic has shown us that we can work effectively but in different ways and for the 1st time in the history of the UKHCDO we will be conducting the AGM virtually by Zoom. We will all miss the benefits of the social interaction and educational networking that is such an important part of a face-to-face AGM but clearly this is all that is currently possible.

In September Counsel for the Infected Blood Inquiry started to present evidence from the enormous volume of documentation they have collected from many sources including the National Haemophilia Database and the hospitals we work in. Ms Richards has also started to take evidence from some of our now retired ex-colleagues who were treating patients during the 80's and 90's and she will continue to do this for the coming months. The evidence is available for all to see on the Inquiry's website. We are early on in this phase of the Inquiry which was delayed 3 months by the pandemic but already we can see an indication of key themes that are being pursued such as the issue of consent, the communication of information by the UKHCDO during those years and whether alternative treatments to un-heated commercial concentrates should have been considered by treating clinicians at the time. It is clear already that the concluding report from the Inquiry will be very extensive and the detailed examination of past practices will undoubtedly provide learning points for us all in our current care of patients.

In April 2020 the National Haemophilia Database received a Rule 9 request to provide a wide-ranging, detailed statistics report to the Inquiry. This work is still ongoing at present but the magnitude of the task has meant that the majority of the NHD staff have been working on this most of the time for 6 months now. The constraints of the Spring lockdown meant that it was not possible for the staff to work onsite or to access any of the paper archive for some months which caused delays but the enormity of the quantity of data required and the need for extensive validation are the main reasons why this is still an ongoing project. We remain committed to provide as much relevant information at our disposal that is required by the Inquiry team.

In my Chairman's report last year I mentioned how the work of the Inquiry had already placed an unprecedented burden on the NHD staff and that was prior to this request for detailed statistics which has increased that many-fold. I would like to commend the dedication and diligence shown by the whole team as they work through this. The previously vacant NHD Manager post was filled at Christmas last year and we have been very fortunate to have Andrew McNally in post who has embarked on his role with true professionalism and competence. We have also recruited another member to help with the analytical side, Mike Grove. His work for the NHD has all been in lockdown but he has provided crucial support for the team in the preparation of the IBI and annual statistics reports.

There have been a number of successive changes in the UKHCDO Executive and NHD senior personnel over the past year; we appointed Professor P Chowdary as the NHD Co-Director to support Professor Hay and to enhance the clinical input and oversight of the NHD and she is the principal author of the Inquiry Statistics report. She therefore stepped down as Treasurer and Dr Rachel Rayment has taken that position. Professor Peter Collins will step down as Vice-Chair at the AGM but will continue to provide an advisory and support role to the Executive which will undoubtedly be of considerable value to us and the membership as a whole. Dr Kate Talks has been appointed to as Vice Chair and her vacated Secretary post has been taken on by Dr Susie Shapiro. A warm welcome and much gratitude to Rachel and Susie for putting their hands up to come onto the Committee and for Kate in agreeing to continue on the Committee; I hope they will find these roles motivating and rewarding over the coming years as we strive to lead in high quality haemophilia care to our patients.

It will come as no surprise that the pandemic and the Infected Blood Inquiry have impacted on UKHCDO business-as-usual but we have tried to keep other matters ticking over. We have made good progress with the Working Party reshuffles that were due this year and it has been a real pleasure to see the enthusiasm from all members including a number who have only recently taken up Consultant posts. We now have newly formed Paediatric, Inhibitor, Genetics and von Willebrand Working Parties with new Chairs in most of those. We also have a new 'Unclassified Bleeding disorder' WP and we will hear brief reports from this and a number of other WPs during the AGM. In the last couple of weeks we have rapidly formed a Task Force to look at what is required in a planned Haemtrack upgrade and we are grateful in advance for help from our nursing colleagues in this and other pieces of UKHCDO work. Next on this agenda is to re-form the Dental and Emergency out of hours Task Forces to update the guidance on these. In addition the need to develop a gene therapy guideline has been highlighted and there was full agreement for this at the last Advisory Committee and so in the next few weeks I will be requesting expressions of interest for these 3 Task Forces. In contrast to progress on the issues mentioned above the next phase of implementation of the Peer review has stalled somewhat for a number of reasons but both the pandemic and the Inquiry are on that list of reasons. As I complete this report the number of COVID-19 cases is continuing on a steep trajectory again and the announcement of a 2nd national lockdown in England looms. Once again haemophilia centres and staff face significant disruption to their working lives and for many there is ongoing disruption to our space and our teams that has not improved through the summer. The current time feels like the wrong time to write to Centres and Trusts to ask them to address the deficiencies revealed by the Peer Review team in 2018-9 but the immense value of the work that was done on the Peer Review is not lost and this will definitely be on the work plan again for 2021.

There are a couple of other issues I would like to mention. NHS England Specialised Commissioning underwent another restructure and a new Clinical Reference Group has been formed – John Hanley is now the Chair - and we were very relieved that Will Horsley was able to continue in his role as Lead Commissioner for Blood Disorders as he has worked energetically and tirelessly to support our patient community and our clinical teams. The CRG now includes TTP and there is representation from TTP clinicians on the CRG. The new tender for all products to treat haemophilia A went live in July 2020 and this was another very successful UK-wide tender run by the NHS England commercial medicines team with clinical input from the CRG and other selected UKHCDO members. This tender has brought new products and therefore expanded the choice available to our patients with new enhanced half-life factor VIII concentrates as well as continued access to Emicizumab / Hemlibra for severely affected and inhibitor patients.

Finally, I would again like to express my gratitude for the continuing support of my team at Great Ormond Street Hospital Haemophilia Centre who support me and allow me to do this national role. Also Sarah Rooney at the NHD – although we have not had a 'normal' AGM to prepare for and she has therefore been doing other NHD duties, she still provides essential assistance for which I remain as ever exceedingly thankful.

Dr Ri Liesner,
UKHCDO Chair
October 2020

Bleeding Disorder Statistics for

April 2019 to March 2020

A report from the UK National Haemophilia Database

February 2021

2. Bleeding Disorder Statistics for 2019 / 2020

Contents

Appendix 1: Glossary

ACMG	American College of Medical Genetics
AGM	Annual General Meeting
APPG	All Party Parliamentary Group
ASH	American Society of Hematology
BCSH	British Committee for Standards in Haematology
BMI	Body mass index
BPG	Best Practice Guidelines
BSH	British Society for Haematology
CCC	Comprehensive Care Centre
CDRF	Clinical Doctoral Research Fellowship
CFC	Clotting factor concentrate
CMU	Commercial Medicines Unit
CMWP	Co-morbidities Working Party
COVID	Corona Virus Disease
CPAG	Clinical Priorities Advisory Group
CPD	Continuing professional development
CQUIN	Commissioning for Quality and Innovation
CRG	Clinical Reference Group
DAG	Data Analysis Group
DMWP	Data Management Working Party
DWP	Department for Work and Pensions
EAHAD	European Association for Haemophilia and Allied Disorders
EHC	European Haemophilia Consortium
EHL	Enhanced Half-life
EIBSS	England Infected Blood Support Scheme
EQA	External quality assessment
EU	European Union
EUHASS	European Haemophilia Safety Surveillance
FIX	Factor nine
FVIII	Factor eight
FXIII	Factor thirteen
GLH	Genomics Laboratory Hub

GLN	Genetic Laboratory Network
GWP	Genetics Working Party
HC	Haemophilia Centre
HCC	Hepatocellular carcinoma
HCIS	Haemophilia Clinical Information System
HCP	Health care professional
HCPA	Haemophilia Chartered Physiotherapists' Association
HCV	Hepatitis C virus
HEE	Health Education England
HIV	Human immunodeficiency virus
HJHS	Haemophilia Joint Health Score
HNA	Haemophilia Nursing Association
ICA	Integrated Clinical Academic
IPOP	Identifying Performance-based Outcome measures of Physical function in people with haemophilia
IPSG	International Prophylaxis Study Group
IQR	Interquartile range
ISO	International Organization for Standardization
ITI	Immune tolerance induction
IU	International units
IU/kg	International units per kilogram
IWP	Inhibitor Working Party
kg	Kilogram
LGTBQ	Lesbian, gay, bisexual, and transgender
MDSAS	Medical Data Solutions and Services
MDT	Multidisciplinary meeting
MLPA	Multiplex ligation-dependent probe amplification
MSK	Musculoskeletal
MTP	Minimally treated patients
NEQAS	National External Quality Assessment Service
NHD	National Haemophilia Database
NHS	National Health Service
NHSE	NHS England
NIBSC	National Institute for Biological Standards and Control
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research

PC	Personal computer
PIP	Personal Independence Payment
PUP	Previously untreated patient
PWP	Paediatric Working Party
QRS	Quality Review Service
RCPCH	Royal College of Paediatrics and Child Health
rFIX	Recombinant factor IX
RfPB	Research for Patient Benefit
rFVIII	Recombinant factor VIII
SHL	Standard Half-life
SOP	Standard operating procedure
UK	United Kingdom
UKAS	United Kingdom Accreditation Service
UKHCDO	United Kingdom Haemophilia Centre Doctors' Organisation
VWD	Von Willebrand disease
VWF	Von Willebrand factor
WAPPS-Hemo	Web-Accessible Population Pharmacokinetic Service—Hemophilia
WHO	World Health Organisation
WMQRS	West Midlands Quality Review Service
WP	Working party

2.0. Comments on the Bleeding Disorder Statistics for 2019 / 2020

The latter part of 2019 and the whole of 2020 has been a very difficult time for the National Database and these difficulties have inevitably delayed the production of this annual report by four months and have also delayed the publication of NHD data in scientific journals by even longer periods of time.

At the start of this period, we had to vacate our office for several weeks because of flooding and as soon as the COVID-19 lockdown started we had to disperse all of our staff and the NHD staff have been working largely or completely from home ever since. It is now almost a year since we have been able to use our office and this has inevitably caused logistic problems.

From the middle of 2019, the work of the database has also been dominated by the requirements of the Infected Blood Inquiry (IBI). We have a paper archive going back to the late nineteen sixties including data and minutes, though the very old data is fragmentary compared with what is collected today. All these old papers had to be scanned and organised. Investigators from the IBI spent several weeks in Autumn of 2019 at the database going through the papers. For most of 2020 almost all the effort of the staff of the database has been directed towards producing a very extensive statistical report to address the Rule 9 requirements of the IBI, often to the exclusion of all other normal activities. This has been extremely costly for the database and has had a major adverse effect on our capacity during this time. Fortunately, this report will be submitted soon and after that we would hope that we can return to more normal working, although it is likely that the IBI will raise supplementary enquiries.

These difficulties have been hugely ameliorated by the appointment of our new manager, Andrew McNally, who joined us from AQA in late 2019 and Mike Grove who also joined us from AQA in mid-summer 2020. These appointments have led to an enormous improvement in management and have also increased analytical capacity. We have also made considerable progress tightening up and documenting information governance.

We have obtained Section 251 exemption from our common law duty of confidentiality for England and Wales under the terms of the 2006 NHS Act, we have an application pending in Scotland and Northern Ireland are still working on an equivalent legal framework to that of England and Wales. For this reason, we no longer need to obtain written consent for research in England and Wales though we must continue to seek written consent in Scotland and Northern Ireland until these issues are also resolved in those administrations. Obtaining written consent has become much more difficult since COVID has severely limited the number of face-to-face interactions with patients. We also have applications pending for resumption in the supply of death certification data from NHS Digital, which is linked to our section 251 exemption. This will considerably strengthen our mortality data.

The following report details the principal registration, treatment, and mortality statistics for the UK for the financial year 2019/20, unless stated otherwise. Most of the commentary appears next to the table or figure to which it relates.

Major therapeutic changes include the widespread adoption of Hemlibra (Emicizumab, Roche) as prophylaxis in factor VIII inhibitor patients and the later and gradual adoption of Hemlibra in non-inhibitor patients with severe haemophilia A. There is an unusual degree of diversity in the approach of different centres to this development. A consensus has not yet formed amongst colleagues about who should and should not be prescribed Hemlibra and a similar dichotomy of therapeutic approach is being observed across Europe and North America. It may take some time and more published data for a consensus approach to emerge.

The current report also enumerates outline data on those patients who have participated in trials of gene-therapy for Haemophilia A or B. Only outline data was sought and obtained because the details of gene therapy are generally covered by confidentiality agreements.

Recent reports from NHD have increasingly minimised numbers of 5 or less, expressing such numbers as 1-5. This is to reduce the chance of any individual being identified. We were increasingly concerned that this rule was being applied uncritically and was reducing the value of the data presented and rendering some tables completely uninformative We have therefore reviewed this blanket policy and have adopted the Guidelines of the Royal Statistical Society (2006). This recommends a case-by-case evaluation of the need to minimise numbers starting with an evaluation of the true need for minimisation based on an assessment of the size of the risk of disclosure and the potential consequences of disclosure. In reality, the risk of identifying an individual from any of our tables, which do not cross reference, is infinitesimally small and most of the data are non-sensitive. Various strategies may also be used to further minimise the risk of disclosure e.g., collapsing groups or categories and avoiding even indirect identifiers or minimising at a lower level (1-2). As a consequence of this more nuanced approach, most of our small numbers will no longer be minimised. We are preparing a number minimising SOP, which will be available on our SharePoint site.

Pharmacovigilance is an increasingly important function of the database especially since the advent of new therapeutic approaches with different safety profiles from traditional replacement therapies e.g. Emicizumab, gene therapy and EHL-IX and VIII. To address this need, we have attempted to improve adverse event reporting. This has been achieved partly by establishing a protocol for the investigation and evaluation of adverse events (AEs) and serious adverse events (SAEs) by the membership of the Co-Morbidities Working Party under the chairmanship of Susie Shapiro. This group meets monthly by Zoom and, amongst other things, score the severity of events and their likelihood of being drug-related using the same scoring framework that would normally be applied in a GCP-standard clinical trial. AEs and SAEs, which are considered drug-related or even possibly or probably drug-related will be reported to the drug manufacturer and through them to the regulators. One consequence of this is the expansion and reformatting of the adverse event section of this report in which AEs are tabulated and SAEs are described in more detail. We hope you find this section interesting and informative.

It only remains for us to thank all the Haemophilia Centre staff for sending us their data despite considerable difficulties encountered at centre level this year, including the temporary redeployment of staff to cope with the COVID pandemic. Without your hard work and forbearance we would have nothing.

We would also like to thank the patients for their Haemtrack data. This data has become increasingly useful in recent years. Although always useful as a tool with which to optimise and individualise a patient's treatment it is also invaluable in helping us to compare treatments at a time of huge therapeutic change. New treatments are changing the face of haemophilia and we need to be able to evaluate these new treatments and compare them with the previous state of the art.

Professor Charles RM Hay,

Lynne Dewhurst,

Ben Palmer, Dr Hua Xiang & Mike Grove

On behalf of the UK National Haemophilia Database

Manchester, January 2021

Important Note: Throughout this report, 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.

Time Periods: Unless otherwise stated, the tables and figures presented in this report relate to the period April 2019 – March 2020 inclusive.

Age is taken at the middle of the financial year, i.e., 30th September 2019

2.1 Haemophilia A

Table 1 People with congenital haemophilia A (including carriers) registered and treated, 2019/20

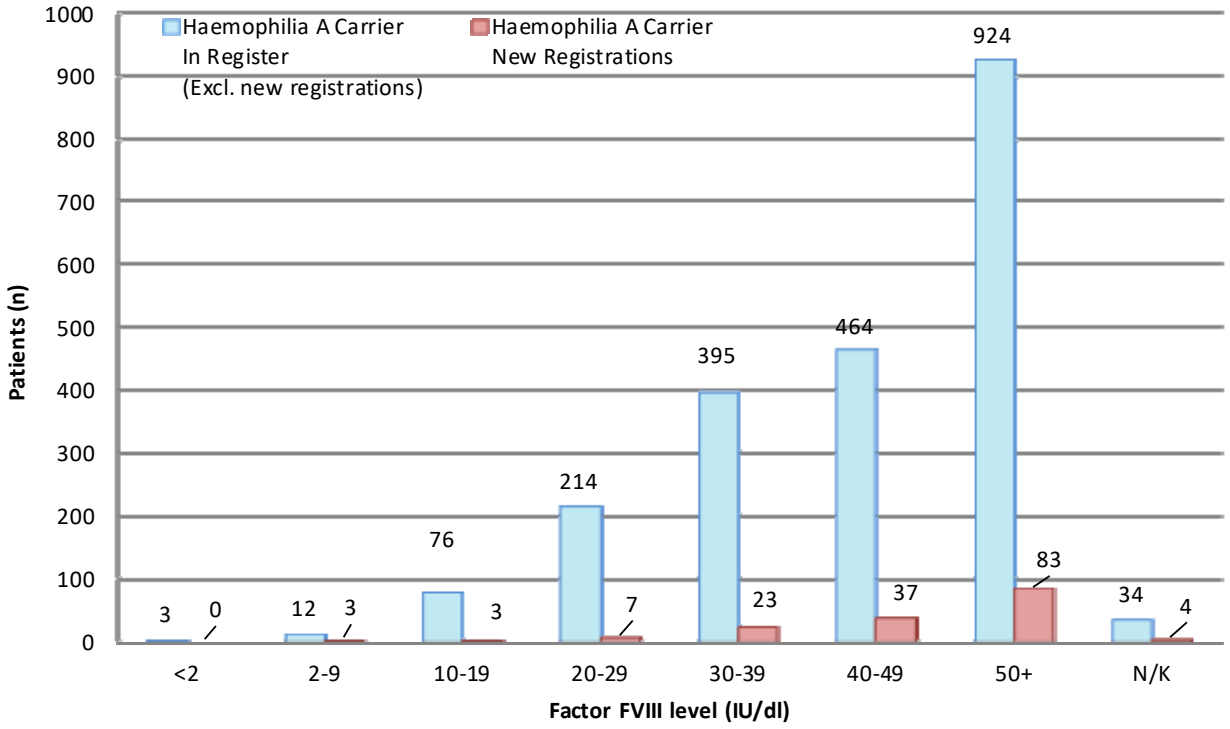
Haemophilia A	Age Range	Number of Patients (Factor VIII level (IU/dl))																	
		< 1			1 - 5			>5 & <40			≥ 40			Unknown Severity			Total		
		M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
Total In Register	<18 years	722	-	722	202	5	207	621	111	732	28	157	185	-	3	3	1,573	276	1,849
	≥18 years	1,382	2	1,384	595	3	598	2,602	614	3,216	182	1,319	1,501	-	68	68	4,761	2,006	6,767
	Total	**2,104**	**2**	**2,106**	**797**	**8**	**805**	**3,223**	**725**	**3,948**	**210**	**1,476**	**1,686**	**-**	**71**	**71**	**6,334**	**2,282**	**8,616**
New Registrations *	<18 years	41	-	41	14	-	14	46	14	60	1	12	13	-	-	-	102	26	128
	≥18 years	14	-	14	9	1	10	38	21	59	7	105	112	-	7	7	68	134	202
	Total	**55**	**-**	**55**	**23**	**1**	**24**	**84**	**35**	**119**	**8**	**117**	**125**	**-**	**7**	**7**	**170**	**160**	**330**
Treated in year**	<18 years	705	-	705	151	3	154	172	9	181	3	-	3	-	-	-	1,031	12	1,043
	≥18 years	1,330	1	1,331	389	3	392	616	49	665	15	17	32	-	1	1	2,350	71	2,421
	Total	**2,035**	**1**	**2,036**	**540**	**6**	**546**	**788**	**58**	**846**	**18**	**17**	**35**	**-**	**1**	**1**	**3,381**	**83**	**3,464**
Treated with concentrate in year**	<18 years	674	-	674	149	3	152	148	5	153	2	-	2	-	-	-	973	8	981
	≥18 years	1,269	1	1,270	367	3	370	506	31	537	12	10	22	-	1	1	2,154	46	2,200
	Total	**1,943**	**1**	**1,944**	**516**	**6**	**522**	**654**	**36**	**690**	**14**	**10**	**24**	**-**	**1**	**1**	**3,127**	**54**	**3,181**

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

*** Treated includes people 'In Register' and 'New Registrations'*

Table 1 shows the total number of people with haemophilia A (including low factor VIII level carriers and factor VIII deficient females) registered in the UK during 2019/20 and broken down by age and disease severity.

Figure 1 Carriers of haemophilia A currently registered and newly registered, broken down by baseline FVIII level, 2019/20



N.B: Includes carriers of haemophilia A and females with FVIII deficiency

Diagnosis	Number of Patients (Factor VIII level (IU/dl))								
	<2	2-9	10-19	20-29	30-39	40-49	50+	N/K	Grand Total
Haemophilia A Carrier In Register (Excl. new registrations)	3	12	76	214	395	464	924	34	2,122
Haemophilia A Carrier New Registrations	0	3	3	7	23	37	83	4	160
Total	**3**	**15**	**79**	**221**	**418**	**501**	**1007**	**38**	**2,282**

Figure 1 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 unaffected carriers continue but are not yet complete.

Table 2 New registrations of haemophilia A (including carriers), by age at mid-year, gender and severity, 2019/20

Haemophilia A	Number of Patients (Factor VIII level (IU/dl))																	
Age (years)	< 1			1 - 5			> 5 & < 40			≥ 40			Unknown			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
0 - < 2	39	-	39	10	-	10	24	2	26	-	2	2	-	-	-	73	4	77
2 - 4	1	-	1	2	-	2	7	1	8	-	2	2	-	-	-	10	3	13
5 - 9	1	-	1	-	-	-	8	4	12	-	2	2	-	-	-	9	6	15
10 - 19	4	-	4	5	-	5	7	8	15	1	9	10	-	-	-	17	17	34
20 - 29	3	-	3	3	1	4	13	7	20	1	30	31	-	3	3	20	41	61
30 - 39	6	-	6	2	-	2	8	9	17	1	37	38	-	2	2	17	48	65
40 - 49	-	-	-	1	-	1	4	2	6	2	11	13	-	-	-	7	13	20
50 - 59	-	-	-	-	-	-	6	1	7	1	14	15	-	2	2	7	17	24
60 - 69	1	-	1	-	-	-	2	-	2	2	6	8	-	-	-	5	6	11
70 +	-	-	-	-	-	-	5	1	6	-	4	4	-	-	-	5	5	10
Total	**55**	**0**	**55**	**23**	**1**	**24**	**84**	**35**	**119**	**8**	**117**	**125**	**0**	**7**	**7**	**170**	**160**	**330**

Table 2: This shows the number of new registrations of haemophilia A broken down by reported severity and age at mid-year (30/09/2019).

The underlying birth rate of people with severe haemophilia A born in the UK runs at 40-45 per year. Over 29% of new registrations of severe haemophilia A were registered aged two years or above. All but two of these are recent migrants to this country (UK = 2, EU = 6, non-EU 8). This has been a stable trend over recent years (see table 3).

Table 3 New registrations of people with severe haemophilia A aged 2 years and over, and subsequent treatment by year

Haemophilia A	Registration year										Total 2010/2020
	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	
New registrations / year	13	18	13	23	22	27	24	24	19	17	183
Treated in each year											
2010/11	12										12
2011/12	11	17									28
2012/13	9	17	12								38
2013/14	10	15	12	22							59
2014/15	10	15	12	22	21						80
2015/16	8	13	11	21	21	26					100
2016/17	7	13	11	21	19	22	24				117
2017/18	7	10	11	20	19	18	24	20			129
2018/19	8	10	10	19	17	15	21	20	16		136
2019/20	8	10	10	18	16	14	20	18	17	15	146
No treatment records	1	0	1	0	0	0	0	2	1	1	6

Table 3: This shows the number of people with severe haemophilia A over two years of age when newly registered (and therefore thought likely to be migrants) each year from 2010/11. It also shows the number treated in each year subsequent to their registration. This shows that potentially at least 200 people with severe haemophilia A have migrated to the UK since 2009/10. This is likely to be an underestimate, since children under two years old are not included in this table. Although six required no treatment, as far as we know, 146 were treated in 2019/20, suggesting that most remain and require regular treatment.

Figure 2a Trend in the number of people with severe haemophilia A, split by HIV status, aged 60 years and above, 1979 – 2019/20

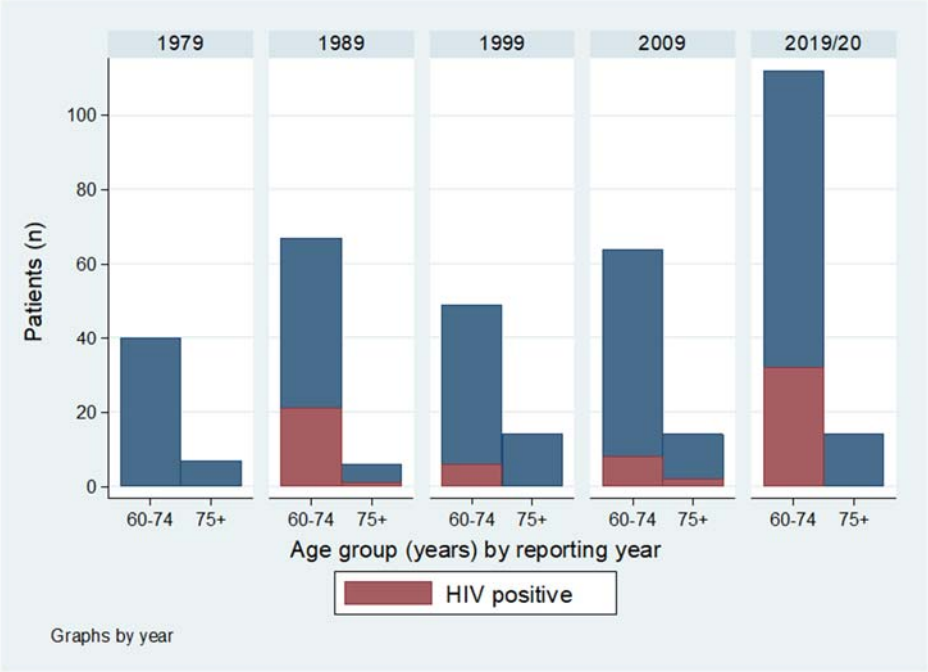


Figure 2a shows a more than doubling in the number of people with severe haemophilia aged 60-74, and aged 75 and above, over the past forty years. The number of elderly people with severe haemophilia A actually declined during the 1990's because of deaths from human immunodeficiency virus (HIV) and hepatitis C virus (HCV), recovering subsequently, as treatment improved.

Figure 2b (overleaf) The effect of HIV is not seen as markedly in moderate severity haemophilia A because proportionately fewer of these individuals were infected. The number of people aged greater than 60 years has increased over the past 40 years. Some of this increase is probably attributable to better diagnosis and more complete registration rather than increasing lifespan.

Figure 2c (overleaf) shows the age trend for mild haemophilia A. This is difficult to interpret since the increased number may reflect increased diagnosis and registration rather than just increased life expectancy.

Figure 2b Trend in the number of people with moderate haemophilia A, split by HIV status, aged 60 years and above, 1979 – 2019/20

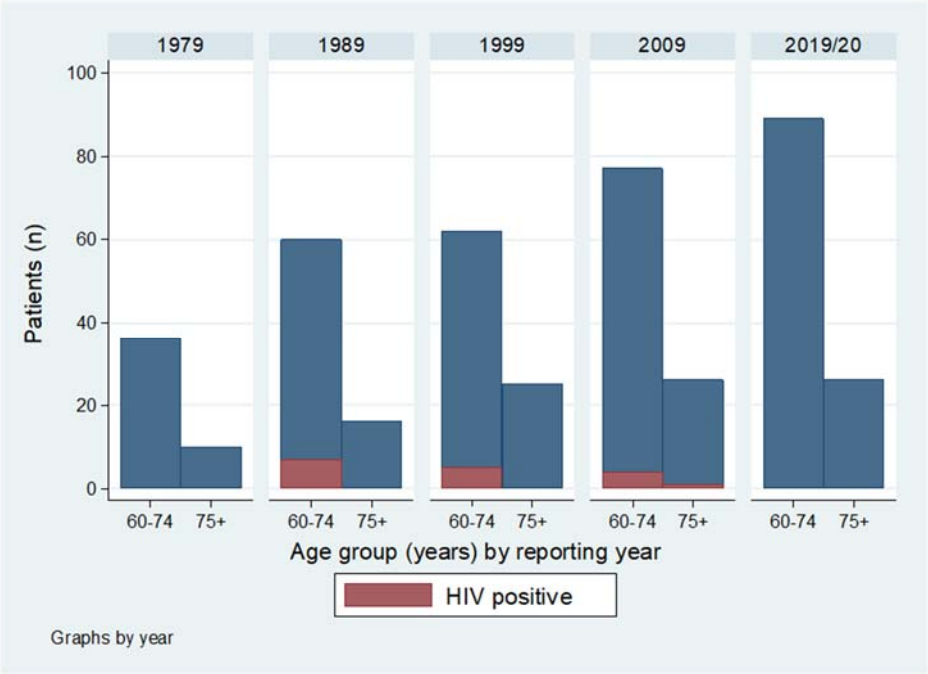
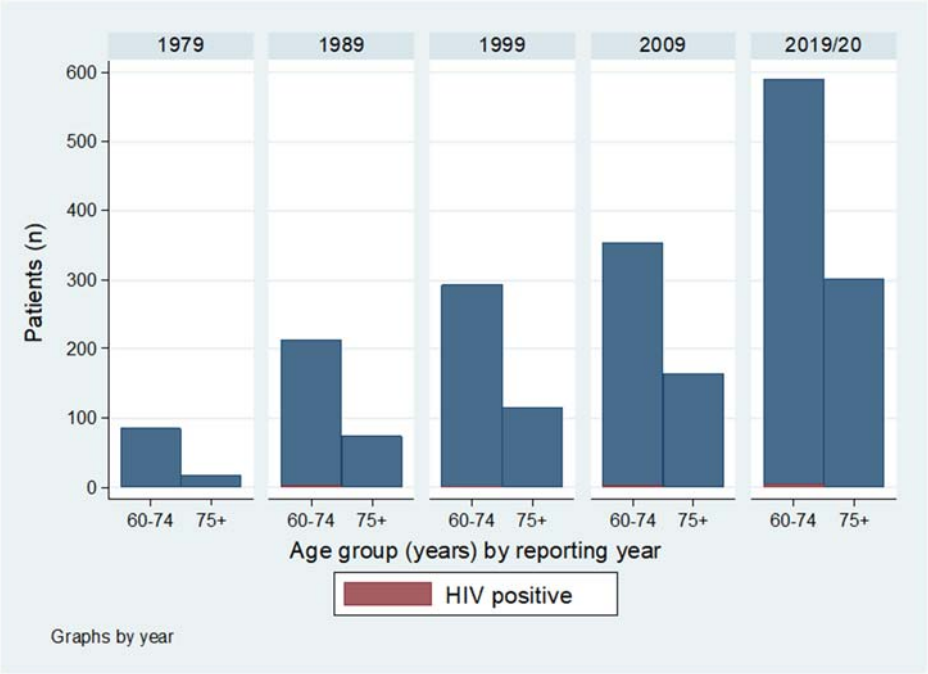


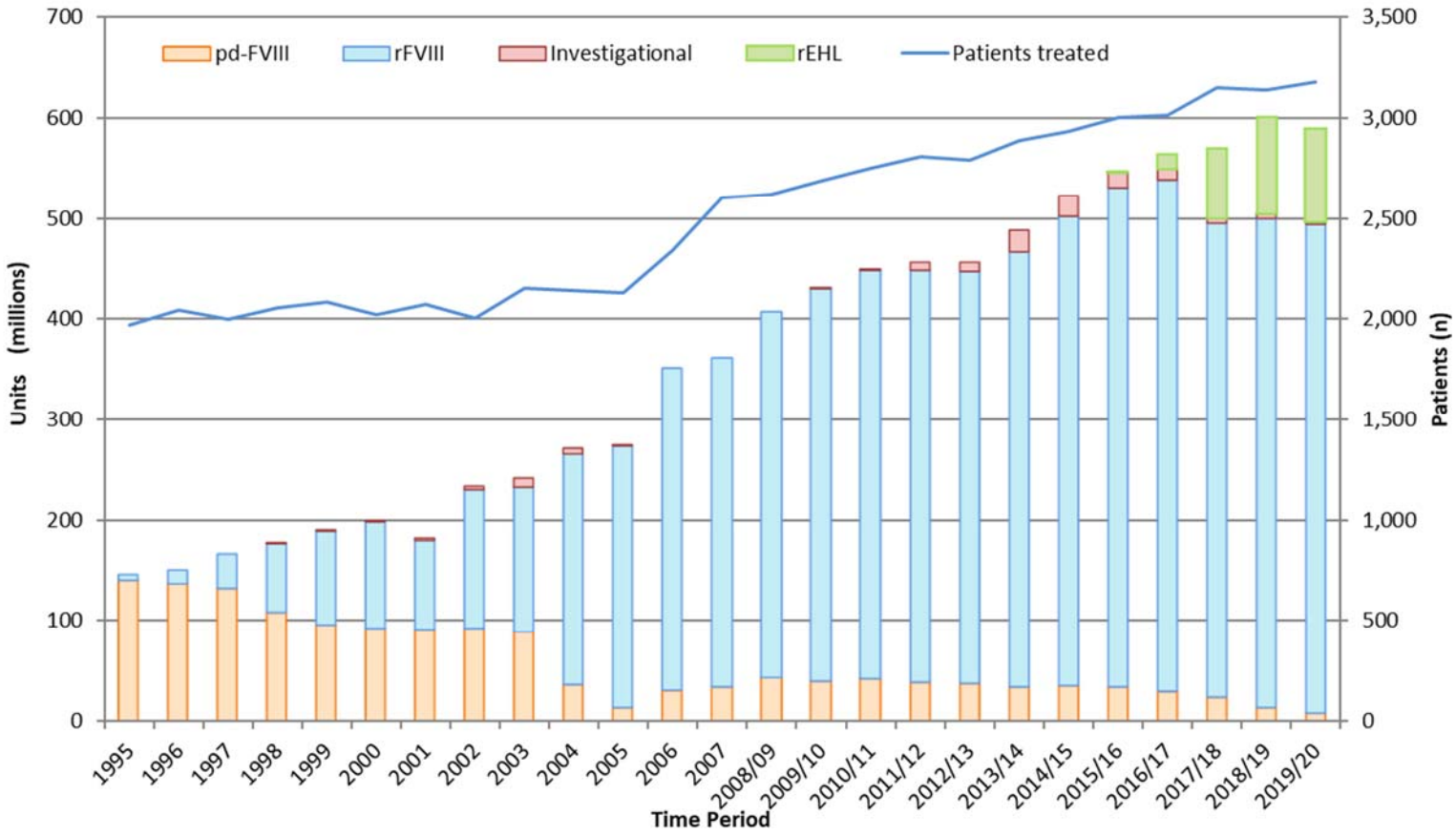
Figure 2c Trend in the number of people with mild haemophilia A, split by HIV status, aged 60 years and above, 1979 – 2019/20



Data table for Figure 2a - c

Year	Severity	Age 60 - 74		Age 75 and over	
		Registered	HIV Positive	Registered	HIV Positive
1979	Severe	40	0	7	0
	Moderate	36	0	10	0
	Mild	85	0	18	0
1989	Severe	67	21	6	1-5
	Moderate	60	7	16	0
	Mild	212	1-5	74	0
1999	Severe	49	6	14	0
	Moderate	62	1-5	25	0
	Mild	293	1-5	114	0
2009	Severe	64	8	14	1-5
	Moderate	77	1-5	26	1-5
	Mild	354	1-5	164	0
2019/20	Severe	112	32	14	0
	Moderate	89	0	26	0
	Mild	590	1-5	302	0

Figure 3 Factor VIII units issued by UK haemophilia centres to treat haemophilia A, 1995 – 2019/20



N.B: Data for St Thomas' were not submitted 1996-2006.

Figure 3 shows FVIII units issued to treat haemophilia A between 1995 to 2019/20. The number of people reported to have been treated is shown by the blue line using a secondary axis. Reporting changed from calendar year to financial year in 2008/09. This chart shows the beginning of a significant fall off in factor VIII usage in 2019/20, which is attributable to the introduction of Hemlibra (Emicizumab, Roche) in September of 2019. This is being introduced relatively gradually in most centres and the full effect will not become apparent until the financial year 2020/21 and thereafter.

Figure 4 Factor VIII units issued by UK haemophilia centres to treat severe haemophilia A, 2014/15 - 2019/20

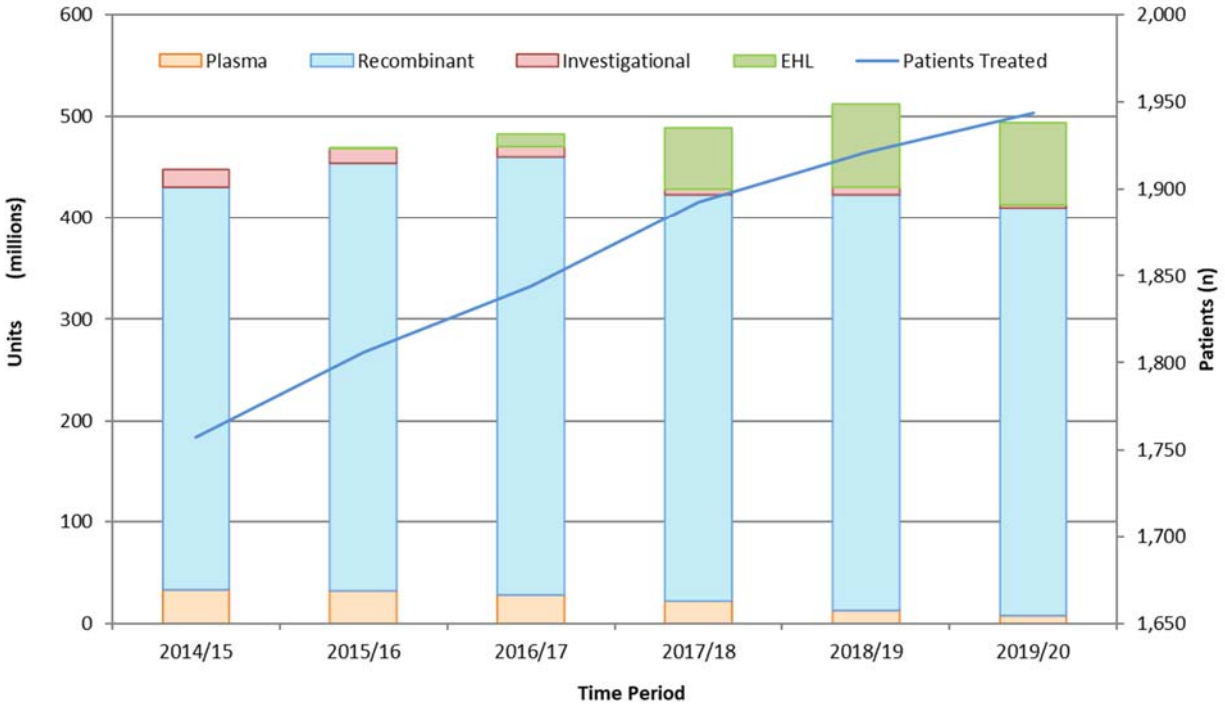


Figure 4 shows a bar diagram of factor VIII issued for *severe haemophilia A* in the UK from 2014/15 to 2019/20 (including inhibitors). The number of people reported to have been treated is shown by the blue line using a secondary axis. This shows, for the first time, an overall reduction in the number of units of factor VIII used, despite an increase in the number of patients. This is attributable to the introduction of Hemlibra. This trend is expected to become far more marked in the financial year 2020/21.

Data table for figure 5 - Factor VIII units issued by UK haemophilia centres to treat severe haemophilia A, 2014/15 - 2019/20

Year	Plasma		Recombinant (excluding investigational)		Investigational rFVIII		Enhanced Half-Life FVIII		Total		Patients Treated	
	IU (000)	% difference since 2014/15	IU (000)	% difference since 2014/15	IU (000)	% difference since 2014/15	IU (000)	% difference since 2016/17	IU (000)	% difference since 2014/15	n	% difference since 2014/15
2014/15	33,434	100.00	397,906	100.00	17,270	100.00	0		448,610	100.00	1,757	100.00
2015/16	32,603	97.52	421,288	105.88	14,419	83.49	285		468,596	104.46	1,806	102.79
2016/17	28,645	85.68	432,147	108.61	9,740	56.40	12,745	100.00	483,277	107.73	1,844	104.95
2017/18	22,301	66.70	401,004	100.78	5,717	33.10	60,346	473.47	489,368	109.09	1,893	107.74
2018/19	12,569	37.59	411,378	103.39	6,493	37.60	81,852	642.21	512,293	114.20	1,921	109.33
2019/20	7,791	23.30	402,604	101.18	3,314	19.19	80,119	628.61	493,828	110.08	1,944	110.64

Figure 5 Numbers of people using different product types issued by UK haemophilia centres to treat severe haemophilia A, 2014/15 – 2019/20

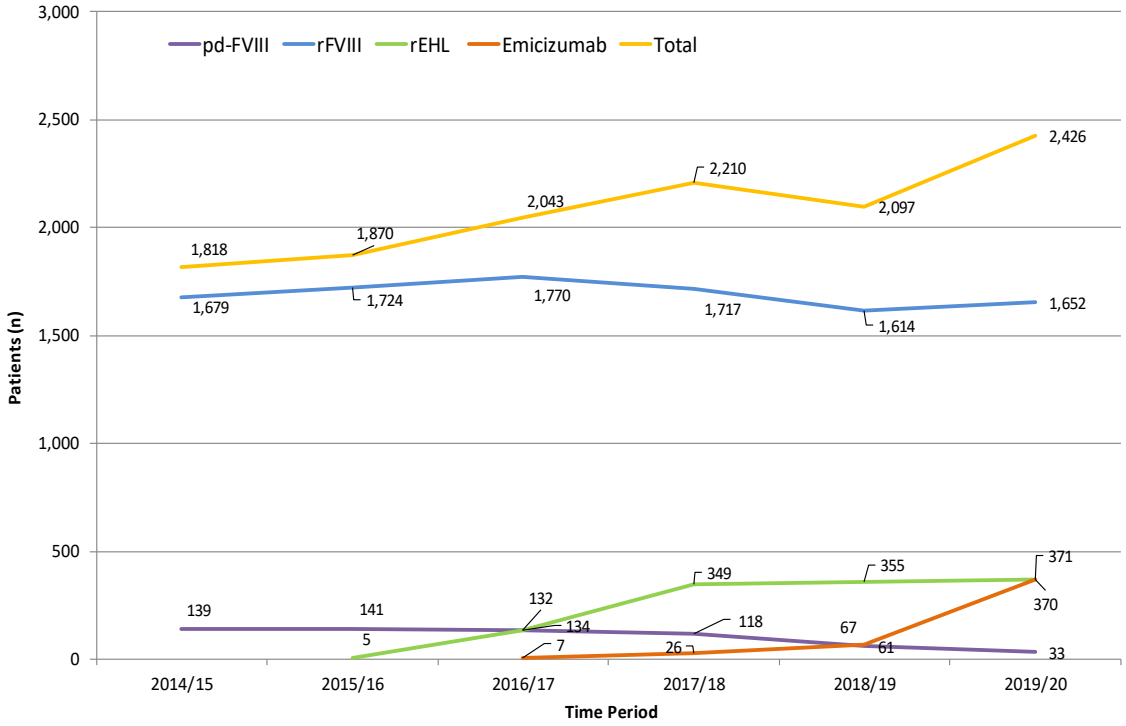


Figure 5 shows the number of people using different product types. This shows a gradual phasing out of the use of plasma-derived factor VIII and the introduction of EHL-VIII in 2016, which started to level off in 2017/18. It also shows an overall reduction in the number of patients treated with factor VIII as Hemlibra was introduced for inhibitor patients in 2018 and for non-inhibitor patients in 2019. This trend is expected to increase considerably in 2021.

Table 4 Factor VIII mean usage by region for people with severe haemophilia A (incl. treatment for inhibitors and EHL- VIII), 2019/20

Health Authority	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20
East Midlands	130,365	137,033	134,304	129,913	138,184	137,016	149,830	141,207	147,750	143,335
East of England	179,557	199,814	210,239	224,451	229,979	238,111	231,127	231,007	214,767	195,263
London	219,241	184,982	180,000	200,850	205,357	202,670	192,970	189,888	188,929	178,080
North East	166,598	186,982	195,902	217,232	218,530	234,500	207,577	211,439	229,603	218,094
North West	118,276	126,120	122,141	125,409	127,585	133,108	125,625	124,259	115,410	105,416
Northern Ireland	191,233	178,963	130,433	129,667	127,776	111,776	109,871	106,031	111,811	118,667
Scotland East	293,306	273,978	243,292	268,370	281,505	255,045	283,922	283,004	299,382	245,107
Scotland West	180,546	191,423	213,693	221,161	219,911	262,232	294,933	285,300	281,500	287,517
South East	132,935	129,765	139,789	145,099	147,791	149,678	148,821	140,807	123,870	127,354
South West	163,468	160,392	155,775	165,784	173,878	185,523	178,276	162,089	183,272	170,704
Wales	176,755	140,135	169,597	170,500	189,734	174,530	196,006	204,732	201,474	196,720
West Midlands	127,419	111,228	118,037	127,479	137,287	117,903	121,357	127,650	138,267	141,474
Yorkshire and the Humber	217,430	219,326	221,724	215,626	202,368	235,548	266,489	219,259	234,043	228,974

Table 4 shows mean FVIII usage by region.

Figure 6 Factor VIII units per kilogram per year issued to treat severe haemophilia A, 2014/15 - 2019/20

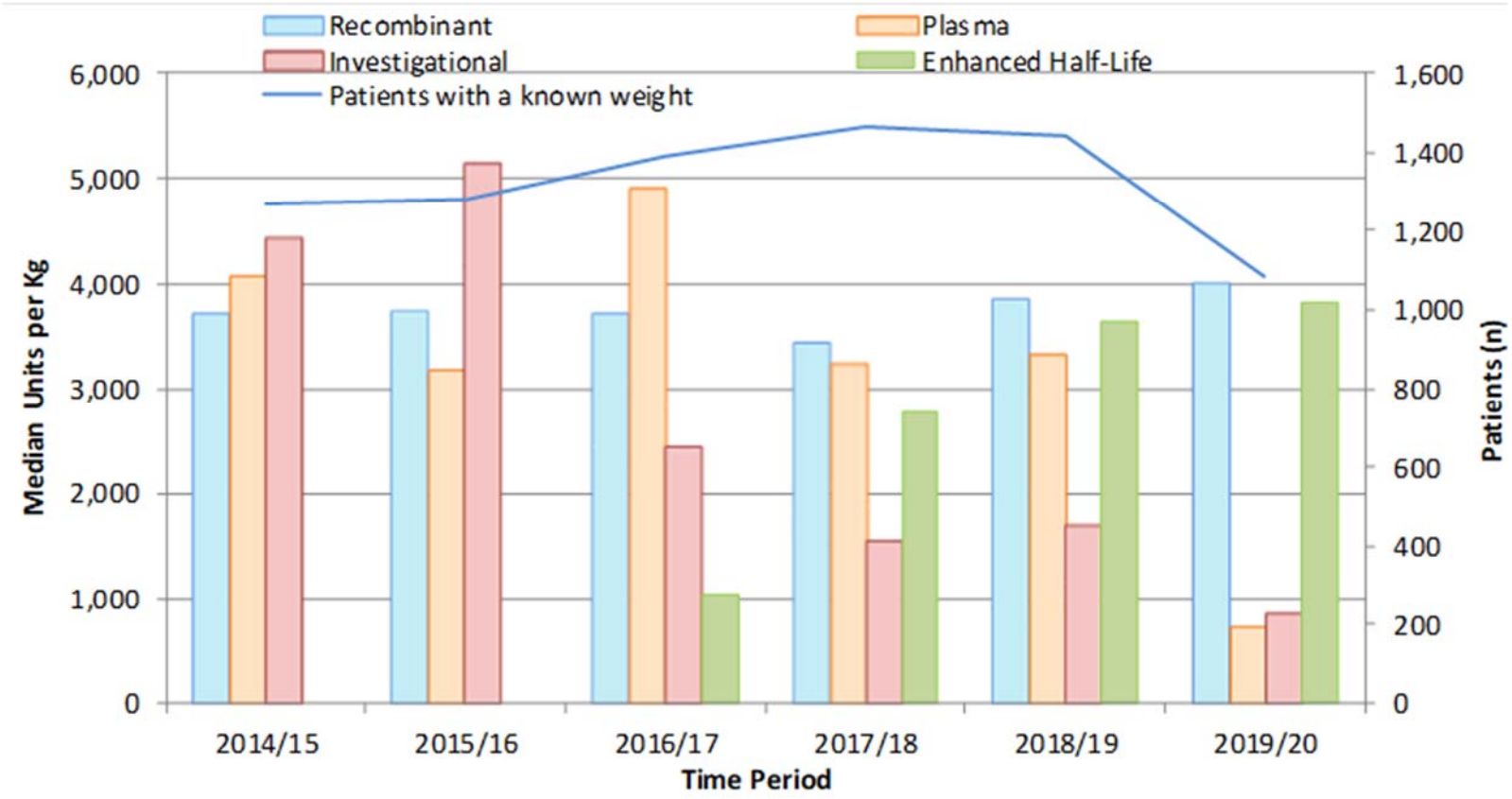


Figure 6 shows a bar diagram of factor VIII usage in IU/kg for people with severe haemophilia A. This table/diagram is not directly comparable with the previous table because bodyweight is not known for all people with severe haemophilia A. This shows that, since 2014/15 the number of eligible people with reported weight has decreased by 14.5%, and now comprises 71.1% of FVIII-treated people with severe haemophilia A. Median usage/Kg has increased by 5.9% during this period. Increased factor VIII usage per-person is thought to be only partly attributable to increased bodyweight. Increased overall usage is largely attributable to increased numbers of people with severe haemophilia A. Investigational products may be underreported, and enhanced half-life (EHL) products cannot be directly compared with standard half-life (SHL) products.

Data table for figure 6 - Factor VIII units per kilogram per year issued to treat severe haemophilia A, 2014/15 - 2019/20

Year	Plasma		Recombinant (excluding investigational)		Investigational rFVIII		Enhanced Half-Life FVIII		Total		Patients with a known weight	
	Median IU/Kg	% difference since 2014/15	Median IU/Kg	% difference since 2014/15	Median IU/Kg	% difference since 2014/15	Median IU/Kg	% difference since 2016/17	Median IU/Kg	% difference since 2014/15	n	% difference since 2014/15
2014/15	4,077	100.00	3,726	100.00	4,449	100.00			3,800	100.00	1,268	100.00
2015/16	3,176	77.90	3,755	100.78	5,164	116.07			3,829	100.76	1,280	100.95
2016/17	4,925	120.80	3,723	99.92	2,438	54.80	1030	100.00	3,862	101.63	1,392	109.78
2017/18	3,256	79.86	3,447	92.51	1,558	35.02	2774	269.32	3,766	99.11	1,464	115.46
2018/19	3,347	82.09	3,864	103.70	1,711	38.46	3638	353.20	3,897	102.55	1,443	113.80
2019/20	734	18.00	4,018	107.84	855	19.22	3810	369.90	4,023	105.87	1,084	85.49

Table 5 People with severe / moderate / mild haemophilia A treated with FVIII by UK haemophilia centres – 2010/11 – 2019/20

Haemophilia A	Number of Patients (Factor VIII level (IU/dl))											
	<1			1 - 5			>5 & <40			≥ 40		
Treatment Year	In Reg n	Treated n (%)	% change since 2010/11	In Reg n	Treated n (%)	% change since 2010/11	In Reg n	Treated n (%)	% change since 2010/11	In Reg n	Treated n (%)	% change since 2010/11
2010/11	1726	1589 (92.1)	100.0	788	494 (62.7)	100.0	3171	643 (20.3)	100.0	605	27 (4.5)	100.0
2011/12	1758	1633 (92.9)	102.8	786	505 (64.2)	102.2	3233	646 (20.0)	100.5	618	23 (3.7)	85.2
2012/13	1791	1649 (92.1)	103.8	785	484 (61.7)	98.0	3357	638 (19.0)	99.2	755	23 (3.0)	85.2
2013/14	1845	1712 (92.8)	107.7	785	510 (65.0)	103.2	3417	648 (19.0)	100.8	875	21 (2.4)	77.8
2014/15	1891	1757 (92.9)	110.6	784	512 (65.3)	103.6	3538	643 (18.2)	100.0	1079	20 (1.9)	74.1
2015/16	1950	1806 (92.6)	113.7	783	509 (65.0)	103.0	3660	659 (18.0)	102.5	1203	26 (2.2)	96.3
2016/17	1986	1844 (92.8)	116.0	781	497 (63.6)	100.6	3712	642 (17.3)	99.8	1335	27 (2.0)	100.0
2017/18	2036	1893 (93.0)	119.1	789	511 (64.8)	103.4	3793	714 (18.8)	111.0	1454	32 (2.2)	118.5
2018/19	2071	1921 (92.8)	120.9	799	497 (62.2)	100.6	3889	691 (17.8)	107.5	1581	28 (1.8)	103.7
2019/20	2106	1944 (92.3)	122.3	806	522 (64.8)	105.7	3950	689 (17.4)	107.2	1686	24 (1.4)	88.9

Table 6a Treatment intensity of people with severe haemophilia A treated with standard half-life FVIII, without inhibitors – 2014/15 - 2019/20

Treatment Period	FVIII Units		Patients (n)		Treatment Intensity (Units/Pt)		Change in treatment intensity since 2014/15 (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2014/15	107,267,253	294,860,523	574	1,086	186,877	271,511	100.0	100.0
2015/16	106,765,940	310,779,731	574	1,124	186,003	276,494	99.5	101.8
2016/17	107,229,167	321,833,376	568	1,163	188,784	276,727	101.0	101.9
2017/18	95,162,764	295,759,676	516	1,141	184,424	259,211	98.7	95.5
2018/19	91,608,117	307,800,548	475	1,055	192,859	291,754	103.2	107.5
2019/20	88,548,567	300,176,846	479	1,084	184,861	276,916	98.9	102.0

Table 6a shows that SHL FVIII treatment intensity (units/person/year) with severe haemophilia A appears to have fallen a little in the last year. The cause for this is not clear but may reflect a tendency to switch the more intensively treated patients to Hemlibra first. The recent fall in overall numbers treated with these products is thought to reflect selective switching of high users from SHL FVIII to EHL FVIII and Hemlibra.

Table 6b Treatment intensity of people with severe haemophilia A treated with enhanced half-life FVIII, without inhibitor – 2017/18 - 2019/20

Treatment Period	Enhanced half-life FVIII Units		Patients (n)		Treatment Intensity (Units/Pt)		Change in treatment intensity since 2017/18 (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2017/18	20,827,736	36,870,348	163	174	127,778	211,899	100.0	100.0
2018/19	24,689,758	52,245,520	144	194	171,457	269,307	134.2	127.1
2019/20	23,947,376	46,056,100	148	199	161,807	231,438	126.6	109.2

Table 6b shows the introduction of EHL FVIII for the treatment of severe haemophilia A from April 2017 to March 2020. There is an apparent reduction in treatment intensity from 2018/19 to 2019/20. This may reflect selective switching of patients with higher intensity treatment to Emicizumab (Hemlibra).

NOTE: Tables 6a & 6b and tables 7a & 7b – People treated with both EHL and non-EHL FVIII and their usage are counted in both tables.

Table 7a Treatment intensity of people with moderate haemophilia A treated with standard half-life FVIII, with no inhibitor – 2014/15 - 2019/20

Treatment Period	FVIII Units		Patients (n)		Treatment Intensity (Units/Pt)		Change in treatment intensity since 2014/15 (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2014/15	16,018,450	38,465,996	154	339	104,016	113,469	100.0	100.0
2015/16	15,271,000	42,432,233	142	352	107,542	120,546	103.4	106.2
2016/17	16,505,470	43,883,871	139	342	118,744	128,315	114.2	113.1
2017/18	13,314,928	38,148,359	136	334	97,904	114,217	94.1	100.7
2018/19	13,639,750	40,899,274	127	313	107,400	130,669	103.3	115.2
2019/20	15,879,250	42,582,766	136	329	116,759	129,431	112.3	114.1

Table 7a: This table shows trends in treatment intensity of moderate severity haemophilia over the last six 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. Hemlibra is not currently licensed for this group.

Table 7b Treatment intensity of people with moderate haemophilia A treated with enhanced half-life FVIII, with no inhibitor – 2017/18 - 2019/20

Treatment Period	Enhanced half-life FVIII Units		Patients (n)		Treatment Intensity (Units/Pt)		Change in treatment intensity since 2017/18 (%)	
	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years	<18 Years	≥18 years
2017/18	1,490,464	6,961,500	12	35	124,205	198,900	100.0	100.0
2018/19	1,824,000	8,703,000	12	33	152,000	263,727	122.4	132.6
2019/20	2,405,500	8,272,250	13	40	185,038	206,806	149.0	104.0

Table 7b Illustrates the introduction of EHL FVIII to a relatively small group of people with moderate severity haemophilia A between April 2017 and March 2020. Their FVIII consumption per year is broadly similar to that found in severe haemophilia.

Figure 7a Treatment intensity (IU/person/year) of people aged under 18 years with severe and moderate severity haemophilia A treated with standard half-life FVIII, with no inhibitor -2019/20

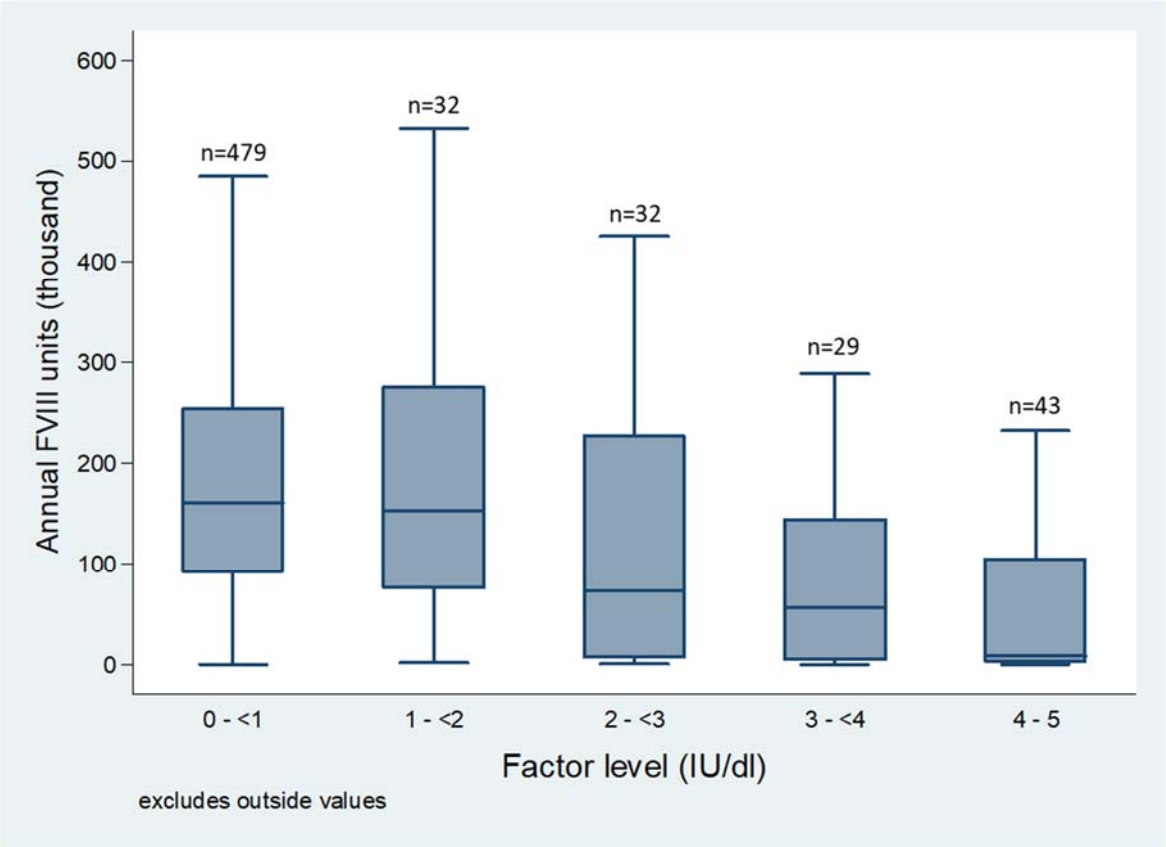


Figure 7a: This box and whisker plot shows the median (Interquartile range (IQR) IU/person/year) and range of FVIII usage broken down by baseline FVIII level in people under 18 years old with severe or moderate haemophilia. This shows that patients with a factor VIII baseline level of 1-2 IU/dl have a similar factor VIII requirement to patients with severe haemophilia but that the factor VIII requirement falls off rapidly at slightly higher factor VIII baseline levels.

Summary statistics for figure 7a

Factor VIII level (IU/dl)	Patients (n)	(median (IQR))
<1	479	(160.0 (91.5;253.5))
1 - <2	32	(152.4 (75.6;274.5))
2 - <3	32	(73.0 (6.8;227.4))
3 - <4	29	(56.0 (4.5;144.5))
4 - 5	43	(9.0 (2.5;104.8))
Total	**615**	**(145.8 (64.5;245.0))**

Figure 7b Treatment intensity (IU/Person/year) of people aged 18 years and above with severe and moderate haemophilia A treated with standard half-life FVIII, with no inhibitor

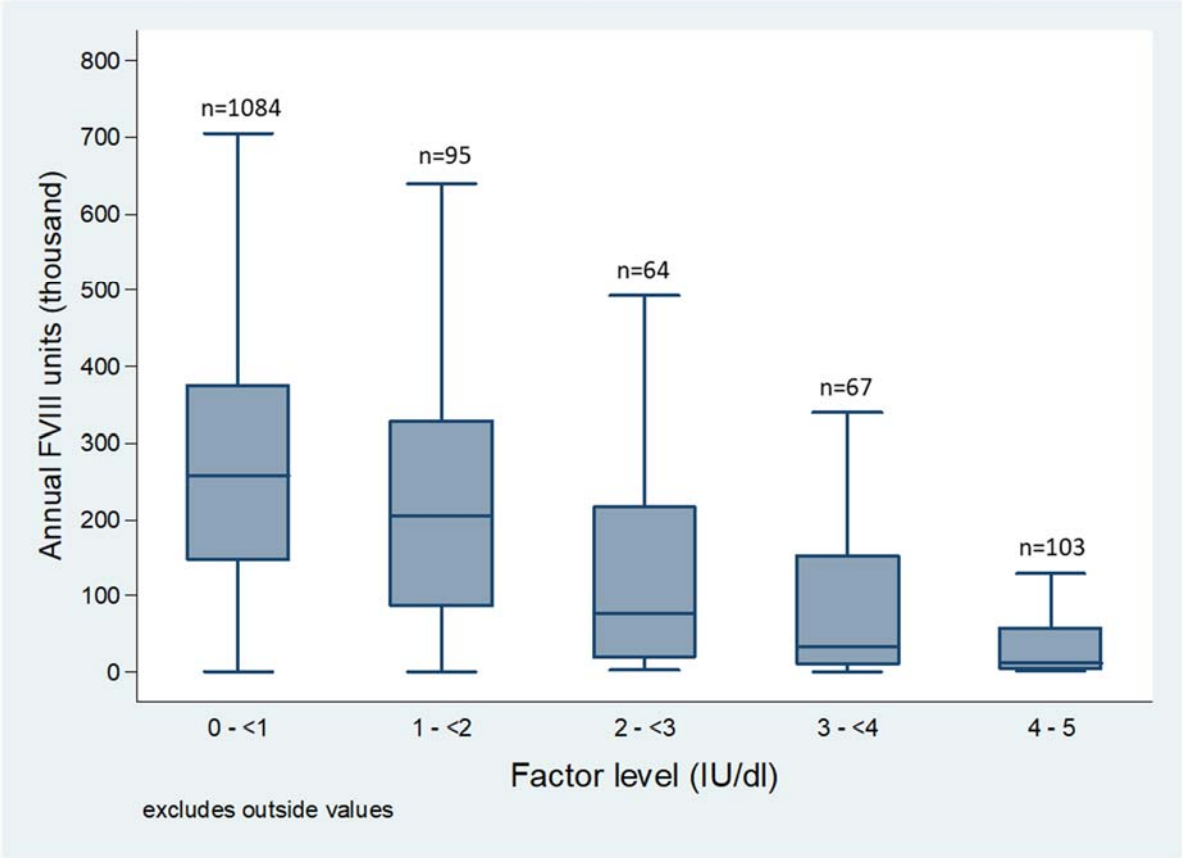


Figure 7b: This box and whisker plot shows the median (Interquartile range (IQR)) and range of FVIII usage broken down by baseline FVIII level in people aged18 years and above with severe or moderate haemophilia A. This shows that although patients with a factor VIII baseline of 1-2 IU/dl have a broadly similar factor VIII requirement to patients with severe haemophilia, the factor VIII requirement falls off dramatically at higher levels of factor VIII.

Summary statistics for figure 7b

Factor VIII level (IU/dl)	Patients (n)	(median (IQR))
<1	1,084	(257.5 (147.0;375.0))
1 - <2	95	(204.8 (86.0;328.0))
2 - <3	64	(76.5 (19.0;217.0))
3 - <4	67	(33.5 (10.0;152.5))
4 - 5	103	(12.0 (4.0;57.5))
Total	**1,413**	**(224.0 (90.0;360.0))**

Figure 8a Annual FVIII usage (IU/Kg/Pt) in people with severe haemophilia A aged under 18 years with no current inhibitor, by centre, ranked by median usage

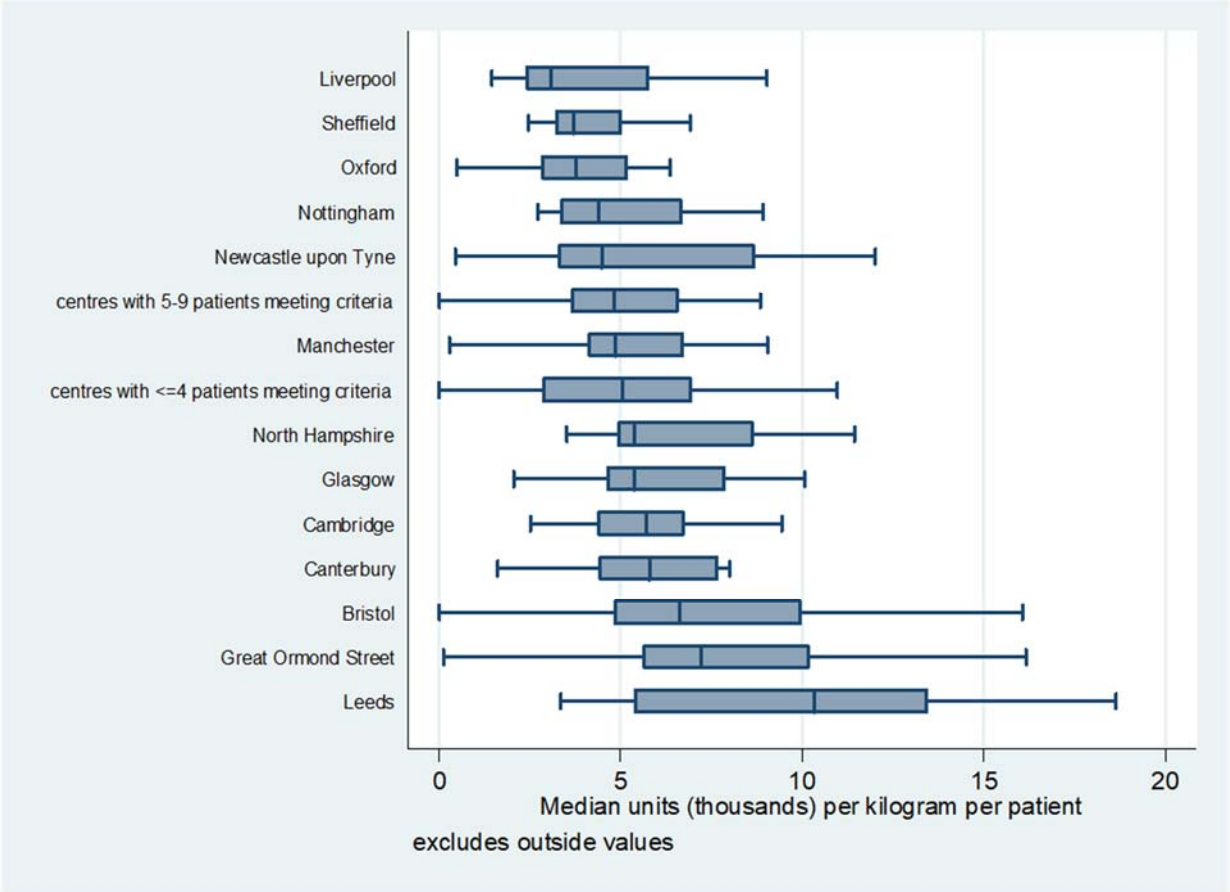


Figure 8a: This shows FVIII usage per kilogram per person by haemophilia centre, ranked by median usage, in people with severe haemophilia A aged under 18 years old with no reported current inhibitor and a bodyweight reported in the previous 12 months.

This shows a threefold range in median treatment intensity between centres. This implies a wide range in the intensity of prophylaxis used for children with haemophilia in the UK. Most centres have broadly similar treatment intensity, as one would expect, given that prophylaxis is the standard of care. The difference in practice at the extremes, for example St James Hospital Leeds is not easily explained.

Those centres, such as Great Ormond Street, who conduct a far greater number of Immune Tolerance Induction procedures than other paediatric centres, will be expected to have high median usage. 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 eight 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.

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

Data table for figure 8a

Haemophilia Centre	Patients (n)	Median Units/Kg
Bristol	16	6,624
Cambridge	17	5,707
Canterbury	13	5,806
Glasgow	19	5,390
Great Ormond Street	67	7,202
Leeds	20	10,338
Liverpool	22	3,098
Manchester	39	4,851
Newcastle upon Tyne	13	4,480
North Hampshire	15	5,369
Nottingham	14	4,395
Oxford	29	3,780
Sheffield	10	3,711
Centres with <=4 patients meeting criteria	33	5,051
Centres with 5-9 patients meeting criteria	53	4,843

Data table for figure 8b

Haemophilia Centre	Patients (n)	Patients with weight reported	Total Units	Median Units
Belfast Children's	15	9	1,686,500	120,000
Birmingham	27	9	3,885,900	124,250
Bristol	16	16	3,765,500	193,500
Cambridge	17	17	3,465,250	147,250
Canterbury	14	13	2,267,750	130,625
Cardiff	13	2	3,332,250	256,000
Glasgow	19	19	3,381,250	140,000
Great Ormond Street	68	67	18,955,250	264,625
Leeds	20	20	5,616,751	247,626
Liverpool	22	22	2,604,750	97,250
Manchester	43	39	8,320,775	161,000
Newcastle upon Tyne	16	13	3,916,500	220,500
North Hampshire	17	15	4,003,000	249,000
Nottingham	14	14	1,904,008	151,500
Oxford	30	29	5,213,500	180,000
Royal London	17	4	2,231,804	115,500
Sheffield	14	10	2,290,000	131,250
St Thomas'	24	4	2,918,750	134,000
Centres with <=4 patients meeting criteria	28	16	7,043,709	221,875
Centres with 5-9 patients meeting criteria	59	42	12,649,000	166,750

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

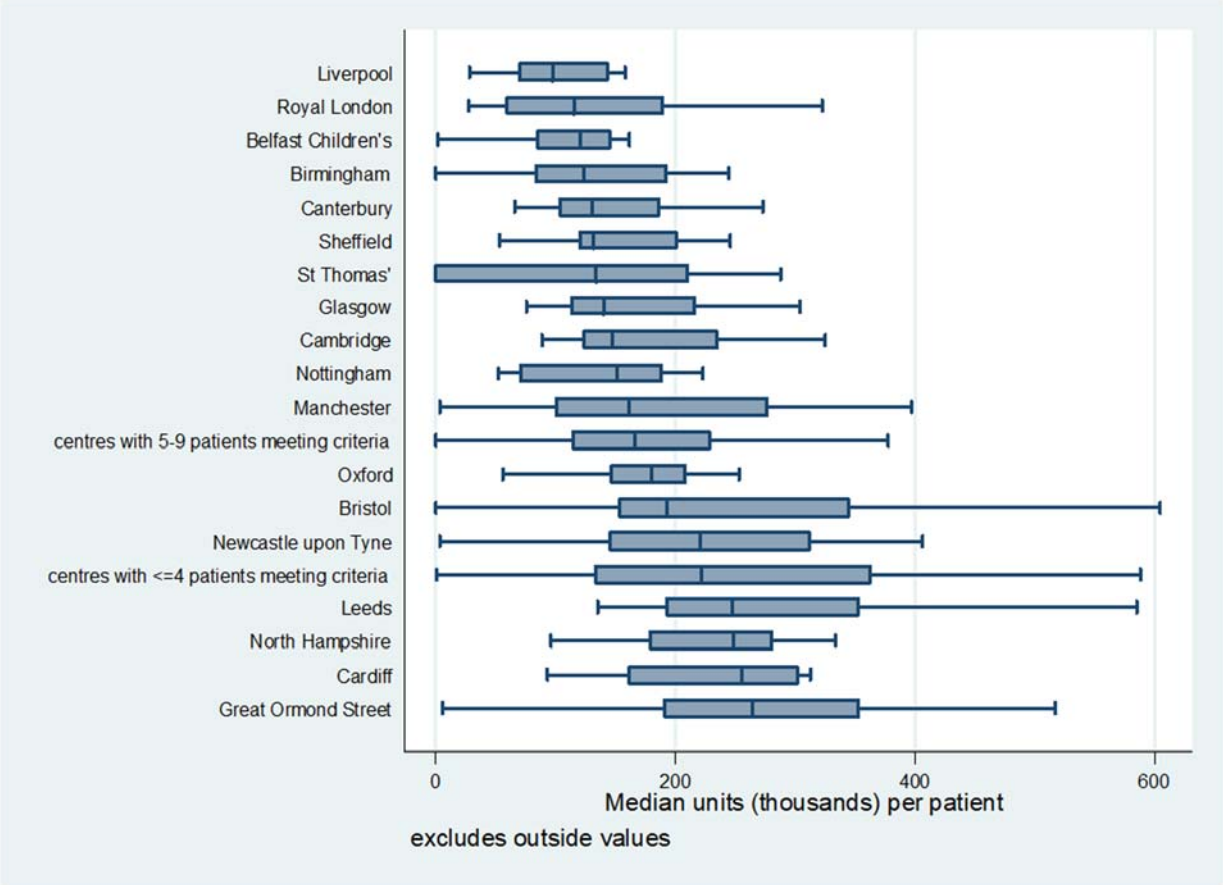


Figure 8b: This shows usage per person with severe haemophilia A, aged under 18 years by centre with no reported current inhibitor, as in the previous figure, but not corrected for bodyweight. It shows a 2.5-fold range in median units used per person between centres. The interpretation is similar to the previous figure. The sample size is slightly larger since the table includes people with and without known bodyweight.

The ranking of centres differs depending on whether it is expressed in IU/Kg/year of IU/Pt per year.

Figure 9a Annual FVIII usage (IU/Kg/Pt) in people with severe haemophilia A aged 18 years or more with no current inhibitor, by centre, ranked by median usage

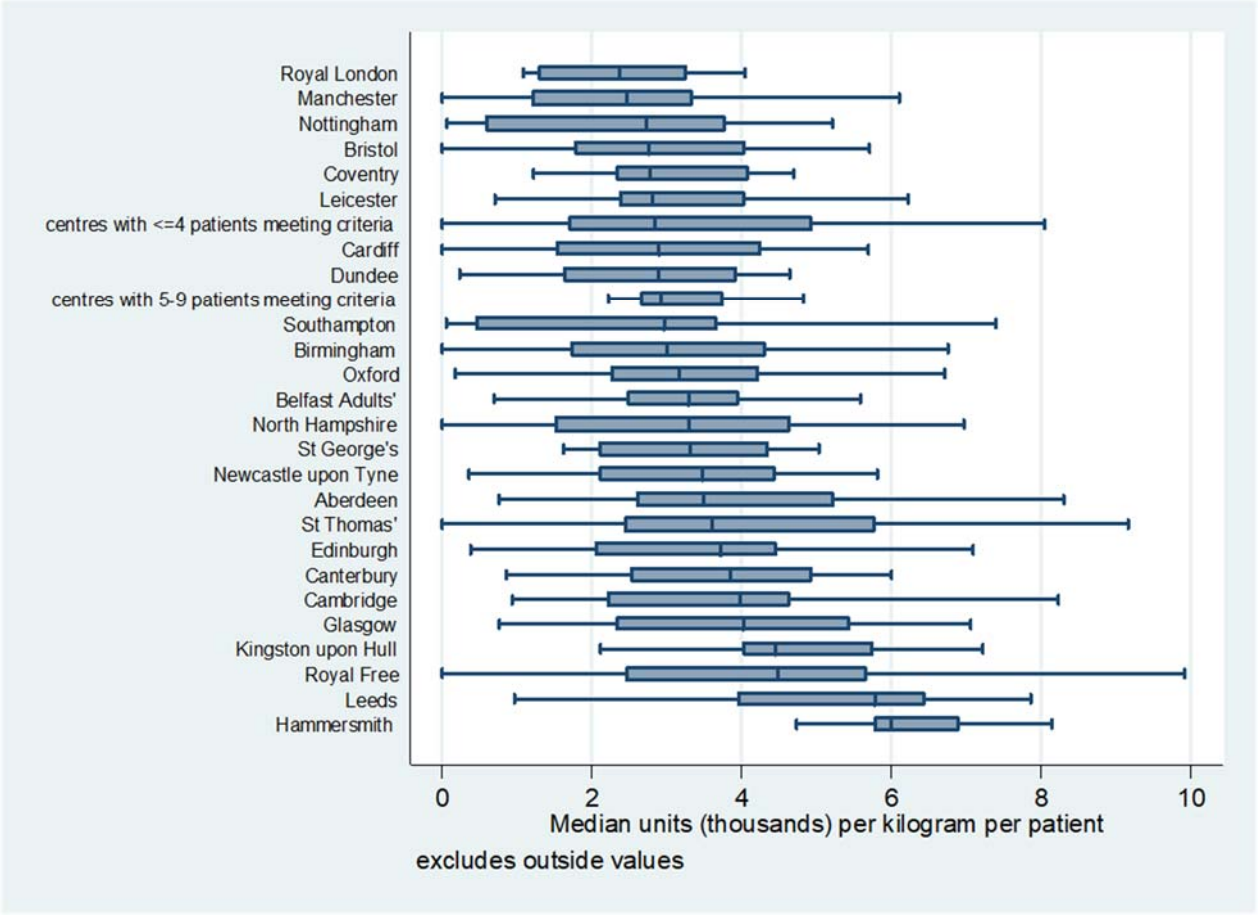


Figure 9a: This shows FVIII usage per kilogram per person by haemophilia centre, ranked by median usage, in people with severe haemophilia A aged 18 years or more with no reported current inhibitor, and an up-do-date bodyweight reported.

Note that the 95th percentile for adults is lower than for children. This is partly a reflection of the shorter half-life found in small children, who require larger doses per kilogram of bodyweight. The adult outliers also show that a small number of people, use a great deal of FVIII, despite having apparently no reported inhibitor in the year.

There is a 2.4-fold range in median treatment intensity. There is still variation in clinical practice from one centre to the next.

Data table for Figure 9a

Haemophilia Centre	Patients with weight reported	Median Units/Kg
Aberdeen	12	3,486
Belfast Adults'	22	3,290
Birmingham	41	3,000
Bristol	26	2,752
Cambridge	18	3,979
Canterbury	24	3,841
Cardiff	21	2,887
Coventry	11	2,772
Dundee	12	2,891
Edinburgh	16	3,711
Glasgow	33	4,023
Hammersmith	13	6,000
Kingston upon Hull	14	4,448
Leeds	15	5,776
Leicester	17	2,805
Manchester	27	2,458
Newcastle upon Tyne	27	3,473
North Hampshire	26	3,299
Nottingham	30	2,714
Oxford	75	3,154
Royal Free	111	4,475
Royal London	16	2,364
Southampton	10	2,962
St George's	15	3,302
St Thomas'	25	3,594
Centres with <=4 patients meeting criteria	31	2,828
Centres with 5-9 patients meeting criteria	5	2,921

Figure 9b Annual FVIII usage (IU/Pt) in people with severe haemophilia A aged 18 years or more with no current inhibitor, by centre, ranked by median usage

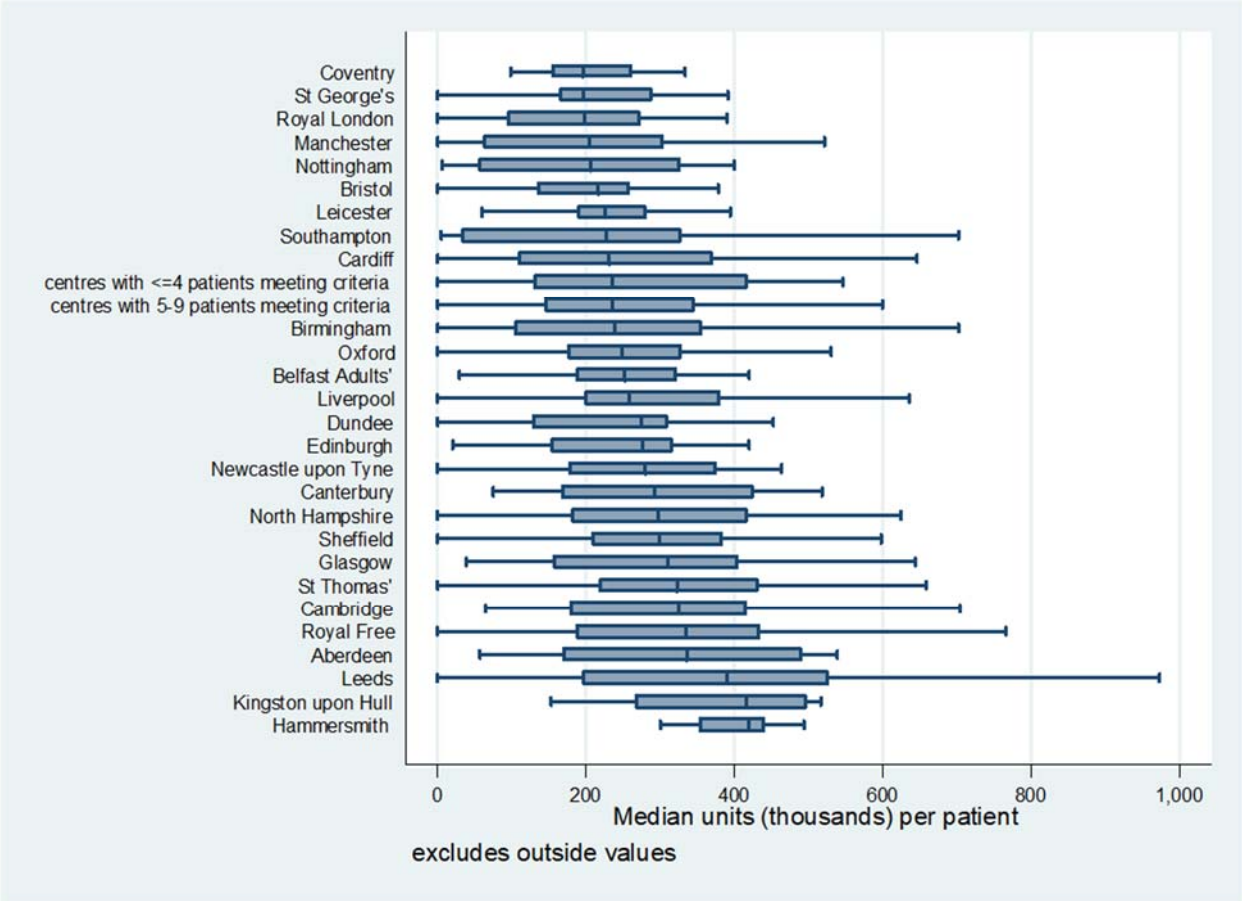
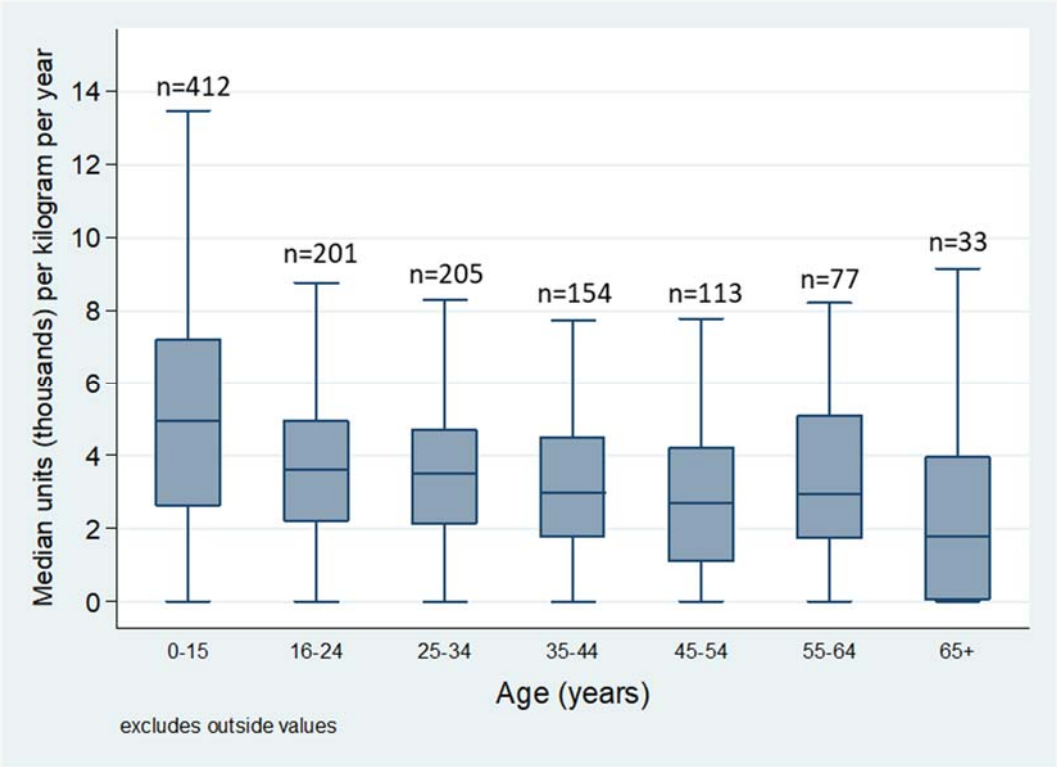


Figure 9b: This shows usage per person aged 18 years or more by centre, for people with severe haemophilia A with no reported current inhibitor not corrected for bodyweight. It shows a wide range in treatment intensity and interpretation is similar to the previous figure, though the sample size is larger since it includes people with and without known bodyweight.

Data table for Figure 9b

Haemophilia Centre	Patients	Patients with weight reported	Total Units	Median Units
Aberdeen	15	12	4,679,750	336,000
Belfast Adults'	47	22	12,193,500	252,000
Birmingham	56	41	13,408,000	238,500
Bristol	27	26	5,939,000	215,500
Cambridge	20	18	6,308,500	326,000
Canterbury	26	24	8,496,500	292,500
Cardiff	31	21	7,474,750	231,000
Coventry	11	11	2,434,700	196,000
Dundee	14	12	3,204,000	275,000
Edinburgh	19	16	5,211,000	277,000
Glasgow	43	33	12,898,000	310,000
Hammersmith	21	13	8,294,000	420,000
Kingston upon Hull	16	14	6,786,000	416,500
Leeds	33	15	13,459,500	390,000
Leicester	21	17	5,818,250	225,000
Liverpool	23	0	6,710,500	258,000
Manchester	43	27	8,733,250	204,000
Newcastle upon Tyne	35	27	9,561,500	280,000
North Hampshire	42	26	12,474,751	297,250
Nottingham	30	30	5,715,032	205,500
Oxford	89	75	22,634,250	248,000
Royal Free	120	111	39,700,021	335,000
Royal London	43	16	8,136,852	197,576
Sheffield	21	3	6,306,000	299,000
Southampton	14	10	3,239,000	228,000
St George's	34	15	7,479,000	196,000
St Thomas'	87	25	28,795,000	322,500
Centres with <=4 patients meeting criteria	20	7	5,150,000	234,750
Centres with 5-9 patients meeting criteria	44	26	12,343,800	236,250

Figure 10 Median FVIII units issued per kilogram body weight per year in people with severe haemophilia A without inhibitors by age



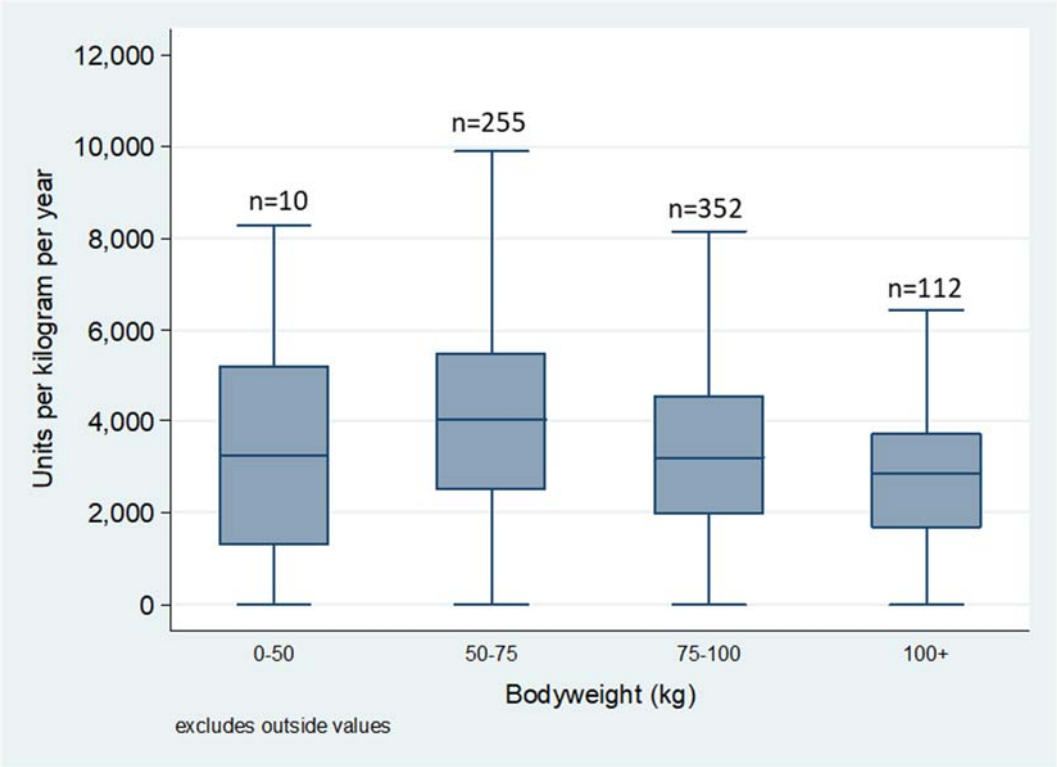
Weight data are missing for n= 512/1708

Figure 10: This shows the median FVIII usage per kilogram bodyweight per year in UK people with severe haemophilia A without inhibitors, broken down by age.

The most intensive general usage appears to be in children, as would be expected. Vial size is also an issue for small children since 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.

Treatment intensity (IU/kg/year) appears to be relatively similar in all adult age-groups except the elderly, which includes a higher-than-average proportion treated on-demand.

Figure 11 Median FVIII units issued (IU/kg) in people with severe haemophilia A without inhibitors aged 16 and over, by bodyweight



Weight data are missing for n= 373/1102

Figure 11: This shows median units per kilogram per year issued to people with severe haemophilia A aged 16 and over without inhibitors, broken down by bodyweight. 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 bodyweight to decline as bodyweight increases. This appears to be the case generally.

It is presumed that the `greater than 100 kg' group will all be obese but since the NHD does not record height, BMI cannot be calculated.

Table 8 Products issued to treat haemophilia A (including inhibitors) - 2018/20

Manufacturer	Product	2018/19 Units (IU)	2018/19 Patients Treated (n)	2019/20 Units (IU)	2019/20 Patients Treated (n)
Bayer	Kogenate	2,079,750	28	808,000	5
Biotest	Haemoctin	358,000	1 - 2	416,000	1 - 2
BPL	FVIII 8Y	324,540	1 - 2	172,000	1 - 2
	Optivate	504,880	3	392,925	3
CSL Behring	Beriplex	-	-	8,000	1 - 2
	Helixate Nexgen	224,500	10	24,000	1 - 2
	Riastap (g)	-	-	20	1 - 2
	Voncento	5,500	1 - 2	72,500	3
Grifols	Alphanate	102,000	1 - 2	135,000	1 - 2
	Fanhdi	9,518,500	22	5,317,500	21
Novo Nordisk	NovoSeven (mg)	10,766	96	6,262	98
	NovoEight	121,188,105	547	123,753,982	539
Octapharma	Nuwiq	12,316,740	70	12,765,310	76
	Octanate	2,506,000	7	1,792,500	7
	Wilate	35,000	1 - 2	2,000	1 - 2
Pfizer	ReFacto AF	173,756,052	1,104	167,649,538	985
Roche	Hemlibra (mg)	187,054	65	907,650	397
SOBI/Biogen	Elocta	93,431,778	407	92,290,296	437
Takeda	Advate	176,356,467	1,152	180,306,002	1,206
	FEIBA	9,121,000	45	2,896,000	22
Various Manufacturers	Desmopressin	21,586	179	21,945	188
	Investigational Factor VIII	6,493,037	38	3,313,886	22
	Investigational Factor VII	*		*	*
	Other Investigational Products	*		*	*

Units in IU unless otherwise stated
** Due to commercial sensitivities, units have been withheld*
Products which include VWF and FVIII are reported in FVIII units

Table 8 (previous page): This shows a breakdown of products, listed by supplier, issued to treat people with haemophilia A during 2019/20, including those with inhibitors but excluding acquired haemophilia. This shows a reduction in the use of all brands of factor VIII as Hemlibra is introduced to both inhibitor and non-inhibitor patients.

These figures have been cross-checked against sales figures supplied by the manufacturers for the same period. Whilst one would not expect a perfect match between NHD figures and the manufacturer's sales figures, there is a very high level of correlation for all but the low usage products. 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. The exception, Fanhdi, is also used for a group of patients without inhibitors attending two centres in the South of England but appears to be being phased out of use.

We have deliberately aggregated and anonymised some investigational products to avoid any breach of individual centre's confidentiality agreements and to take account of commercial sensitivities.

Emicizumab (Hemlibra®) is listed, having previously been unlicensed. This product became available on prescription in September of 2018 for people with an inhibitor and for those lacking an inhibitor in August 2019. Usage is expected to increase.

Table 9 (overleaf): This table shows factor VIII and Hemlibra issues 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 17.

Potentially anomalous use of FVIII in Table 9 is accounted for as follows:

Haemophilia B: treated in error.
Miscellaneous bleeding disorders: thrombotic thrombocytopenia purpura.

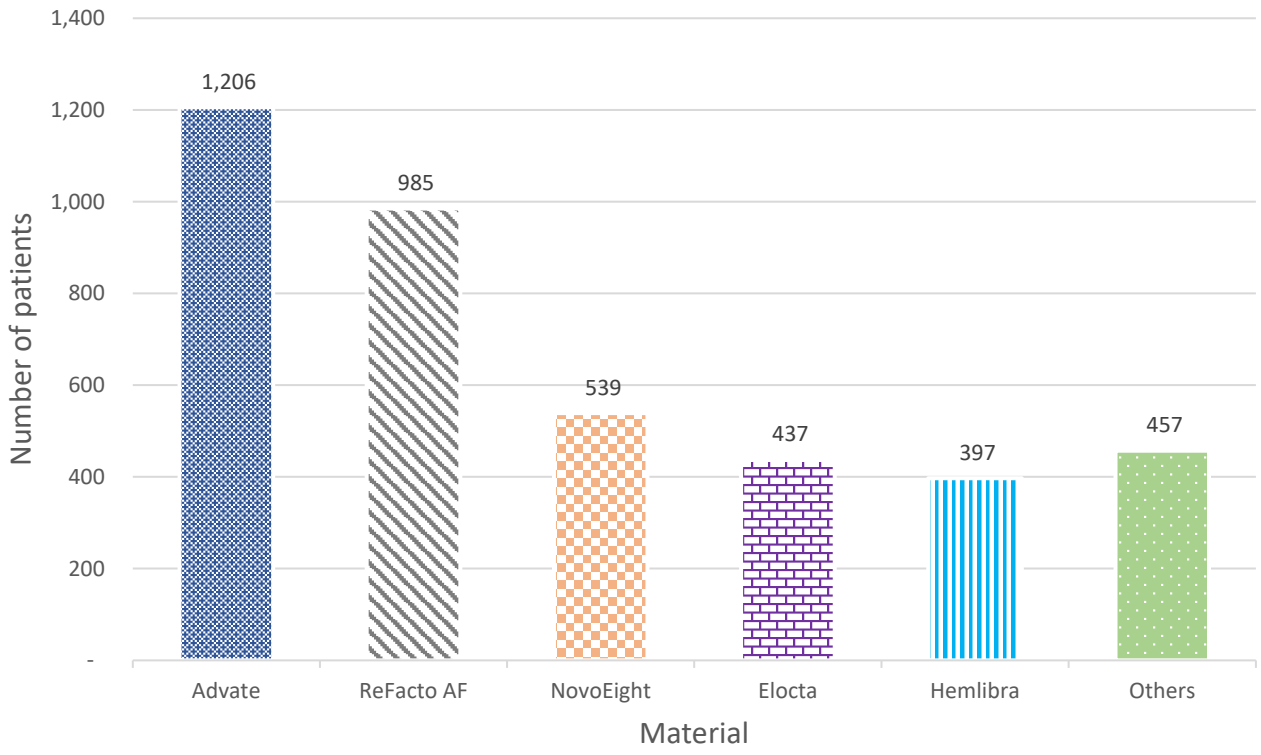
Table 9 Factor VIII and Hemlibra treatment issued by UK haemophilia centres, by diagnosis 2019/20

Coagulation Defect	Patients Treated	FVIII (IU)					Hemlibra	
		Plasma	Recombinant	Investigational	Enhanced Half-Life	Total	Patients Treated	mg
Haemophilia A	3,181	8,300,425	485,306,832	3,313,886	92,290,296	589,211,439	393	907,650
Acquired Haemophilia A	23	-	1,760,000	-	-	1,760,000	-	-
Haemophilia B	n=1 - 2	-	1,000	-	-	1,000	-	-
von Willebrand disease	836	27,208,101	750	-	-	27,208,851	-	-
Acquired von Willebrand Disease	35	1,667,000	-	-	-	1,667,000	-	-
Platelet-type Pseudo von Willebrand Disease	n=1 - 2	2,000	-	-	-	2,000	-	-
Probable von Willebrand disease	4	13,600	-	-	-	13,600	-	-
Combined V+VIII Deficiency	7	-	59,500	-	-	59,500	-	-
Co-inherited diagnoses	19	153,500	1,681,250	-	518,000	2,352,750	n=1 - 2	6,300
Unclassified bleeding disorder	n=1 - 2	1,000	-	-	-	1,000	-	-
Miscellaneous	n=1 - 2	72,000	-	-	-	72,000	-	-
Total	**4105***	**37,417,626**	**488,809,332**	**3,313,886**	**92,808,296**	**622,349,140**	**393***	**913,950**

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

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

Figure 12 Number of people with haemophilia A treated in the UK 2019/20 broken down by product used



The pie chart shows the top five products and is arranged in descending order of percentage of patients treated with the product.

Figure 12: This shows the market breakdown of haemophilia A treatments including those issued to people with an inhibitor.

The data table for this pie chart can be seen overleaf. Patients treated with more than one product in the year will be counted twice. There were 3,604 individual people with haemophilia A treated.

Data table for Figure 12

Manufacturer	Product	Units (IU)	Patients (n)
Takeda	Advate	180,306,002	1,206
Pfizer	ReFacto AF	167,649,538	985
Novo Nordisk	NovoEight	123,753,982	539
SOBI/Biogen	Elocta	92,290,296	437
Octapharma	Nuwiq	12,765,310	76
Bayer	Kogenate	808,000	5
CSL Behring	Helixate Nexgen	24,000	1 - 2
	Beriplex	8,000	1 - 2
Grifols	Fanhdi	5,317,500	21
Octapharma	Octanate	1,792,500	7
Biotest	Haemoctin	416,000	1 - 2
BPL	Optivate	392,925	3
	FVIII 8Y	172,000	1 - 2
Grifols	Alphanate	135,000	1 - 2
CSL Behring	Voncento	72,500	3
Octapharma	Wilate	2,000	1 - 2
	Investigational	3,315,305	26
Takeda	FEIBA	2,896,000	22
Roche	Hemlibra (mg)	907,650	397
	Desmopressin	21,917	188
Novo Nordisk	NovoSeven (mg)	6,262	98
CSL Behring	Riastap (g)	20	1 - 2
	Total	**593,052,708**	**4013***

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

The table is arranged in descending order of recombinant products by volume, then descending order of plasma products by volume

Figure 13 The proportion of people with severe haemophilia A and no-inhibitor issued treatment by product type 2019 Q2-2020 Q3

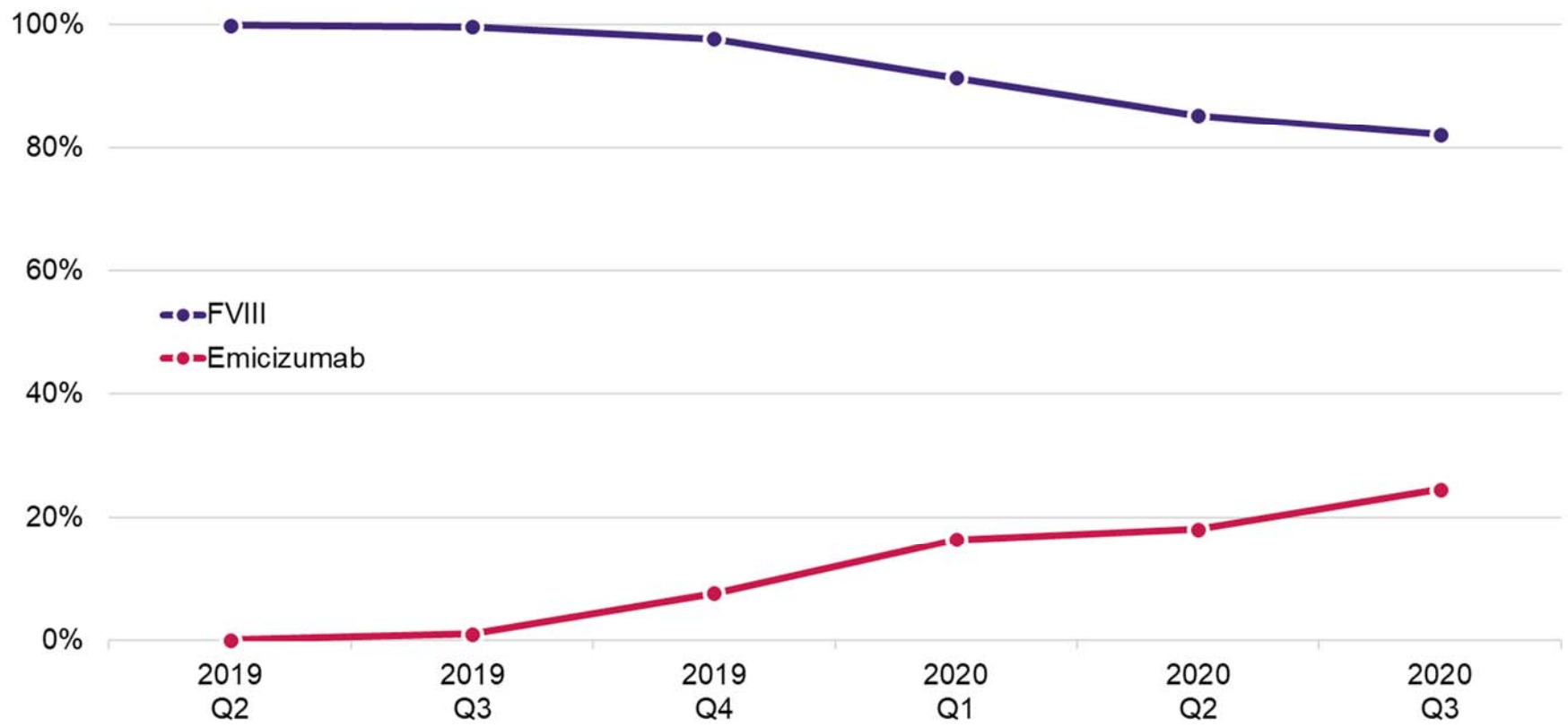


Figure 13 shows a reduction in the proportion of people with severe haemophilia A, without inhibitors, who require factor VIII since Emicizumab was introduced to this group in 2019 Q3. Those not requiring factor VIII at all will be bleed-free on Emicizumab.

Figure 14 The proportion of people with severe haemophilia A, without inhibitors treated with Emicizumab by centre

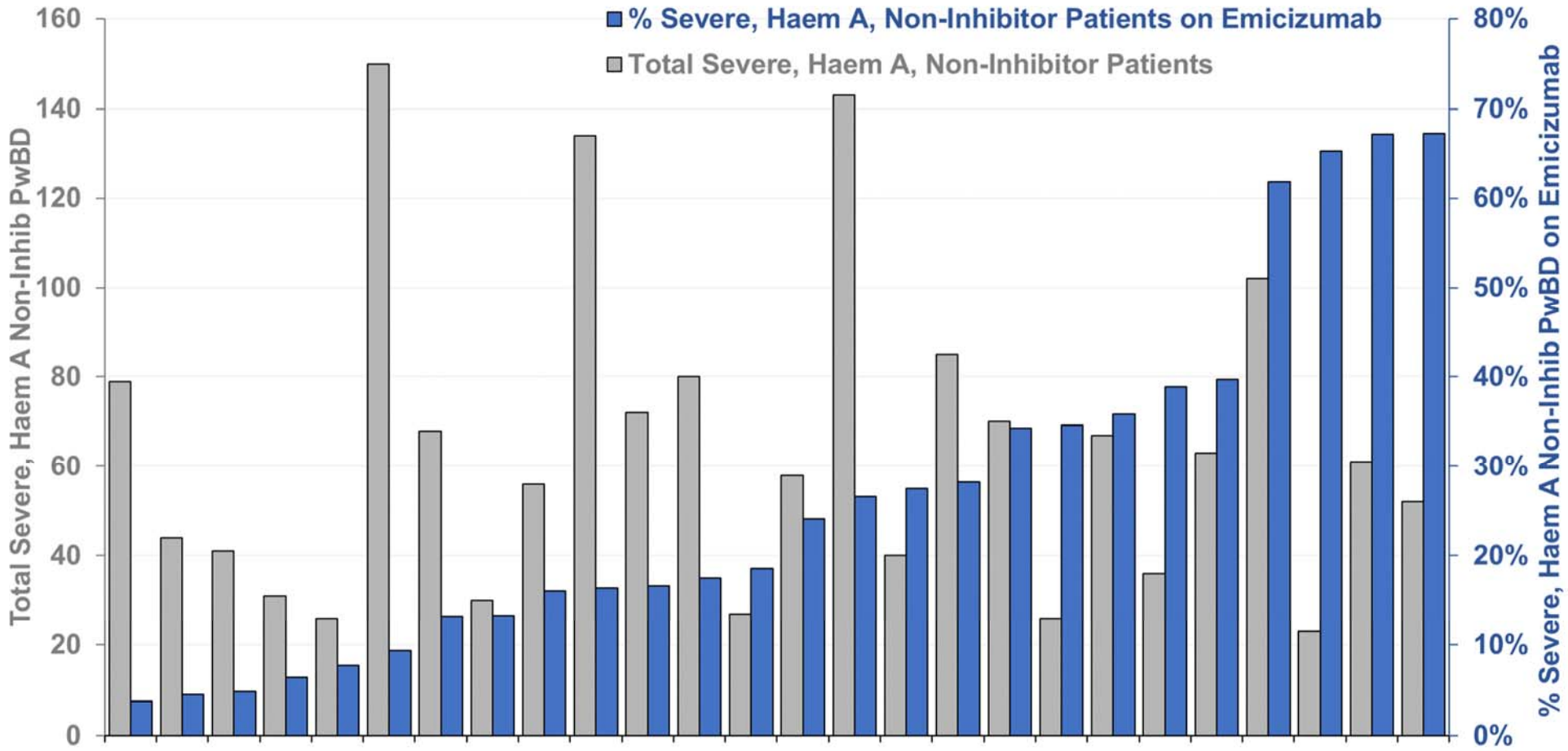


Figure 14 shows the number of people registered with each centre with severe haemophilia A without an inhibitor, and therefore potentially eligible for treatment with Hemlibra (grey bars) and the percentage of those issued Hemlibra in September 2020 (blue bars) ranked by % of potentially eligible patients treated with Emicizumab. This shows considerable centre-to-centre variation in the early adoption of Hemlibra.

2.2 Haemophilia B

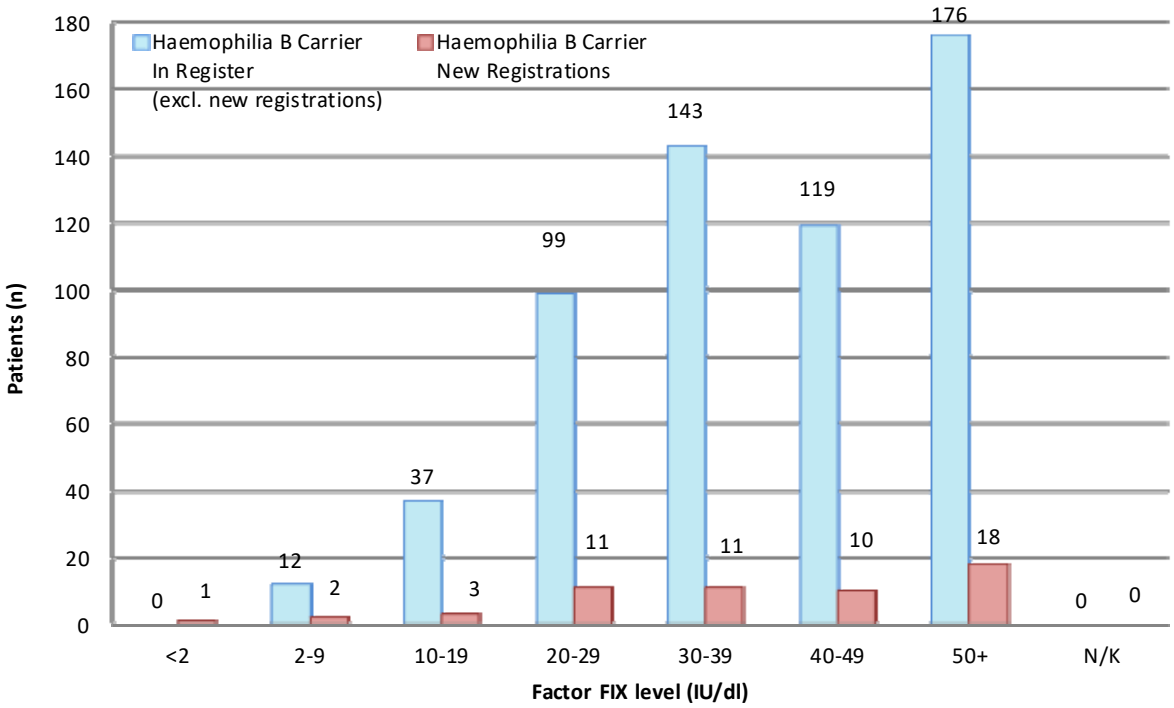
Table 10 People with congenital haemophilia B (including carriers) registered and treated, 2019/20

Haemophilia B	Age Range	Number of Patients (Factor IX level (IU/dl))																	
		< 1			1 - 5			>5 & <40			≥ 40			Unknown			Total		
		M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
Total In Register	<18 years	125	-	125	73	-	73	110	80	190	7	37	44	-	-	-	315	117	432
	≥18 years	243	1	244	265	6	271	412	232	644	37	283	320	-	3	3	957	525	1,482
	Total	**368**	**1**	**369**	**338**	**6**	**344**	**522**	**312**	**834**	**44**	**320**	**364**	**-**	**3**	**3**	**1,272**	**642**	**1,914**
New Registrations *	<18 years	7	-	7	6	-	6	11	20	31	3	6	9	-	-	-	27	26	53
	≥18 years	-	1	1	4	-	4	6	7	13	1	22	23	-	-	-	11	30	41
	Total	**7**	**1**	**8**	**10**	**-**	**10**	**17**	**27**	**44**	**4**	**28**	**32**	**-**	**-**	**-**	**38**	**56**	**94**
Treated in year**	<18 years	117	-	117	44	-	44	25	4	29	1	1	2	-	-	-	187	5	192
	≥18 years	222	-	222	137	2	139	102	21	123	5	8	13	-	-	-	466	31	497
	Total	**339**	**-**	**339**	**181**	**2**	**183**	**127**	**25**	**152**	**6**	**9**	**15**	**-**	**-**	**-**	**653**	**36**	**689**
Treated with concentrate in year**	<18 years	114	-	114	43	-	43	25	4	29	1	1	2	-	-	-	183	5	188
	≥18 years	216	-	216	137	2	139	102	21	123	4	8	12	-	-	-	459	31	490
	Total	**330**	**-**	**330**	**180**	**2**	**182**	**127**	**25**	**152**	**5**	**9**	**14**	**-**	**-**	**-**	**642**	**36**	**678**

** New registrations are a subset of the 'In Register' numbers*
*** Treated includes those 'In Register' and 'New Registrations'*

Table 10: This shows the number of people with haemophilia B (including 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 treated. The number of people registered with haemophilia B continues to rise, especially non-severe haemophilia B, which may previously have been underdiagnosed.

Figure 15 Carriers of haemophilia B currently registered and newly registered, by baseline FIX level, 2019/20



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+	N/K	Grand Total
Haemophilia B Carrier In Register (excl. new registrations)	0	12	37	99	143	119	176	0	586
Haemophilia B Carrier New Registrations	1	2	3	11	11	10	18	0	56
Total	**1**	**14**	**40**	**110**	**154**	**129**	**194**	**0**	**642**

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

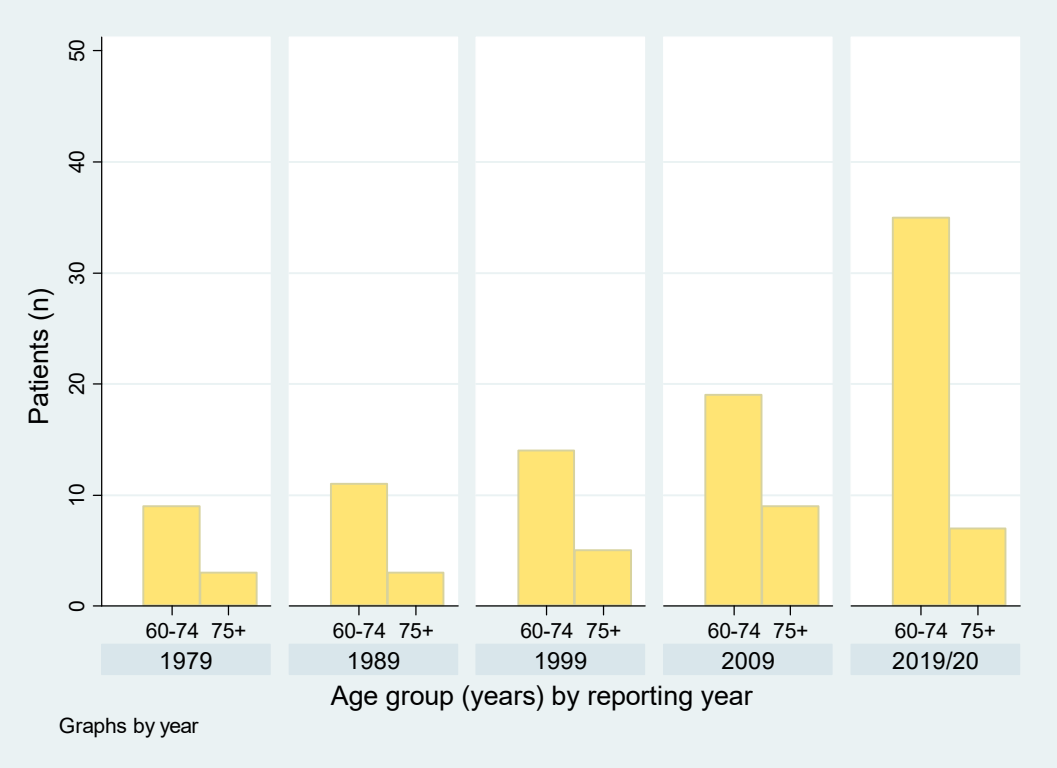
It is interesting that there is a relatively large number of very low-level carriers. These mostly have an extreme degree of lyonisation, but some are homozygous products of consanguineous unions.

Table 11 New registrations of haemophilia B (including carriers), by age at mid-year, gender and severity, 2019/20

Haemophilia B	Number of Patients (Factor IX level (IU/dl))														
Age (years)	< 1			1 - 5			> 5 & < 40			≥ 40			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
0 - < 2	5	-	5	2	-	2	3	3	6	-	1	1	10	4	14
2 - 4	2	-	2	3	-	3	2	4	6	-	1	1	7	5	12
5 - 9	-	-	-	1	-	1	3	7	10	1	1	2	5	8	13
10 - 19	-	-	-	-	-	-	3	7	10	2	7	9	5	14	19
20 - 29	-	1	1	1	-	1	1	1	2	-	5	5	2	7	9
30 - 39	-	-	-	1	-	1	2	4	6	-	4	4	3	8	11
40 - 49	-	-	-	2	-	2	-	1	1	1	4	5	3	5	8
50 - 59	-	-	-	-	-	-	-	-	-	-	3	3	-	3	3
60 - 69	-	-	-	-	-	-	2	-	2	-	1	1	2	1	3
70 +	-	-	-	-	-	-	1	-	1	-	1	1	1	1	2
Total	**7**	**1**	**8**	**10**	**0**	**10**	**17**	**27**	**44**	**4**	**28**	**32**	**38**	**56**	**94**

Table 11: This shows new registrations of haemophilia B broken down by reported severity and age at mid-year year (30/09/2019). 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. Of the two people registered after the age of two, one has FIX Leyden and the other was born outside the EU.

Figure 16a Trend in numbers of people with severe haemophilia B aged 60 years and above, 1979 – 2019/20



N.B. Carriers are included in Figures 16a - 16c

Figure 16a: This shows the trend in numbers of people aged over 60 years with severe haemophilia B since 1979. This shows a 3.5-fold increase over the past 40 years, presumably attributable to increased life-expectancy.

Figure 16b (overleaf): This shows a similar bar diagram of people with moderate severity haemophilia B showing a 3.5-fold increase in those aged over 60 years during the past 40 years. This will reflect a combination of better diagnosis, more complete registration and improved life expectancy.

Figure 16c (overleaf): This shows the trend in numbers of people aged over 60 years with mild haemophilia B in the register since 1979. This shows an 8.4-fold increase over the past 40 years. This probably reflects a relatively modest increase in life expectancy coupled with increased diagnosis and reporting of mild haemophilia B.

Figure 16b Trend in numbers of people with moderate haemophilia B aged 60 years and above, 1979 – 2019/20

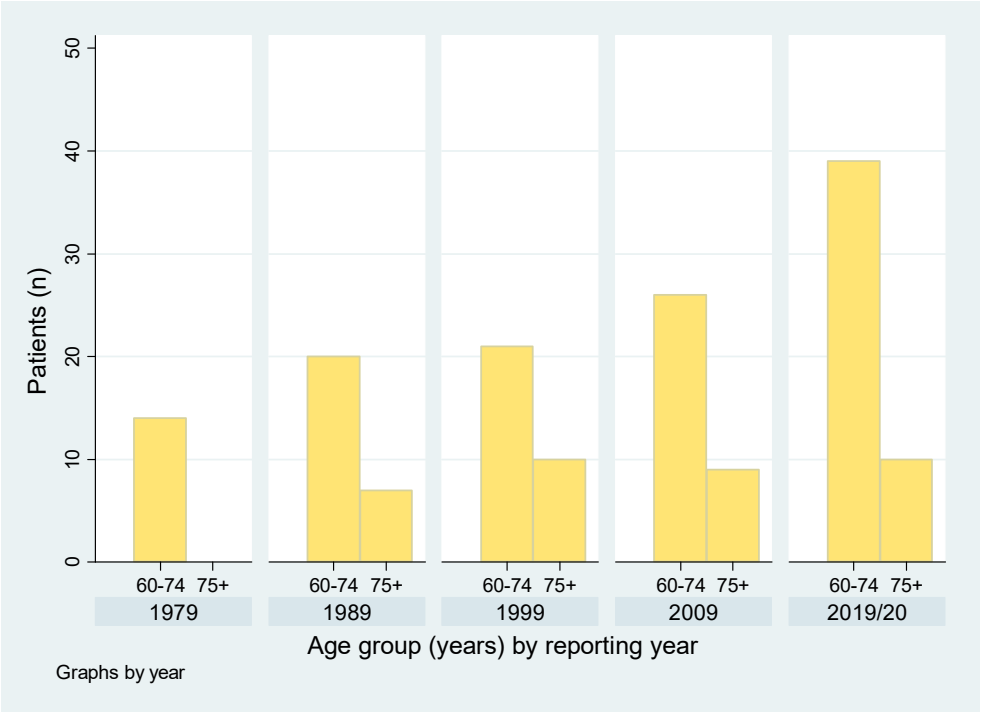


Figure 16c Trend in numbers of people with mild haemophilia B aged 60 years and above, 1979 – 2019/20

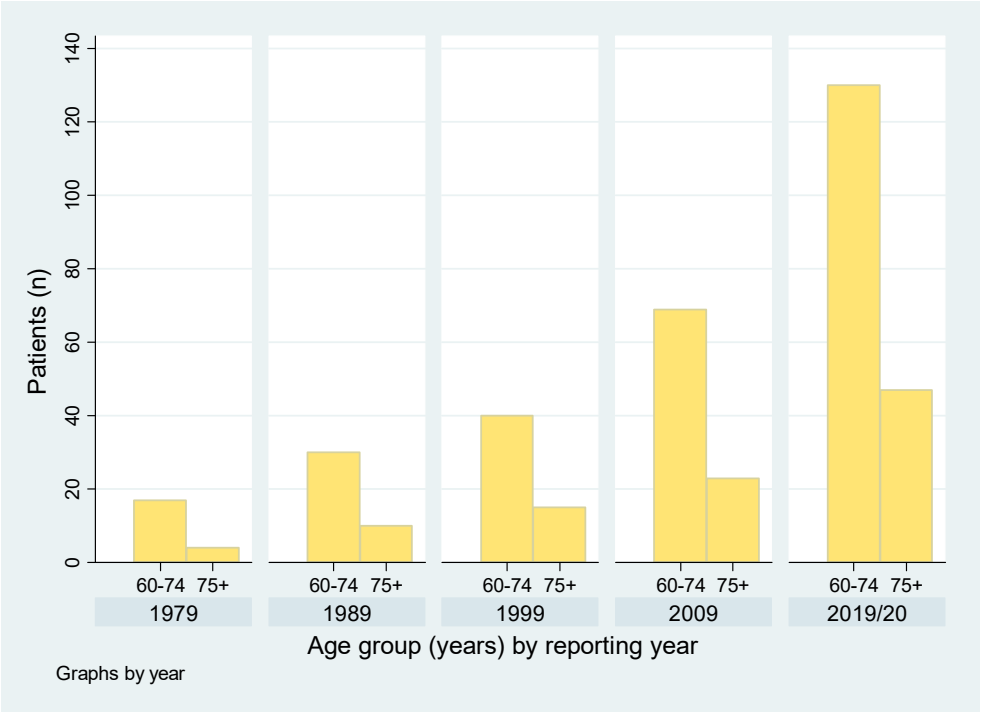


Figure 17 Factor IX units issued by UK haemophilia centres to treat haemophilia B, 1995 – 2019/20

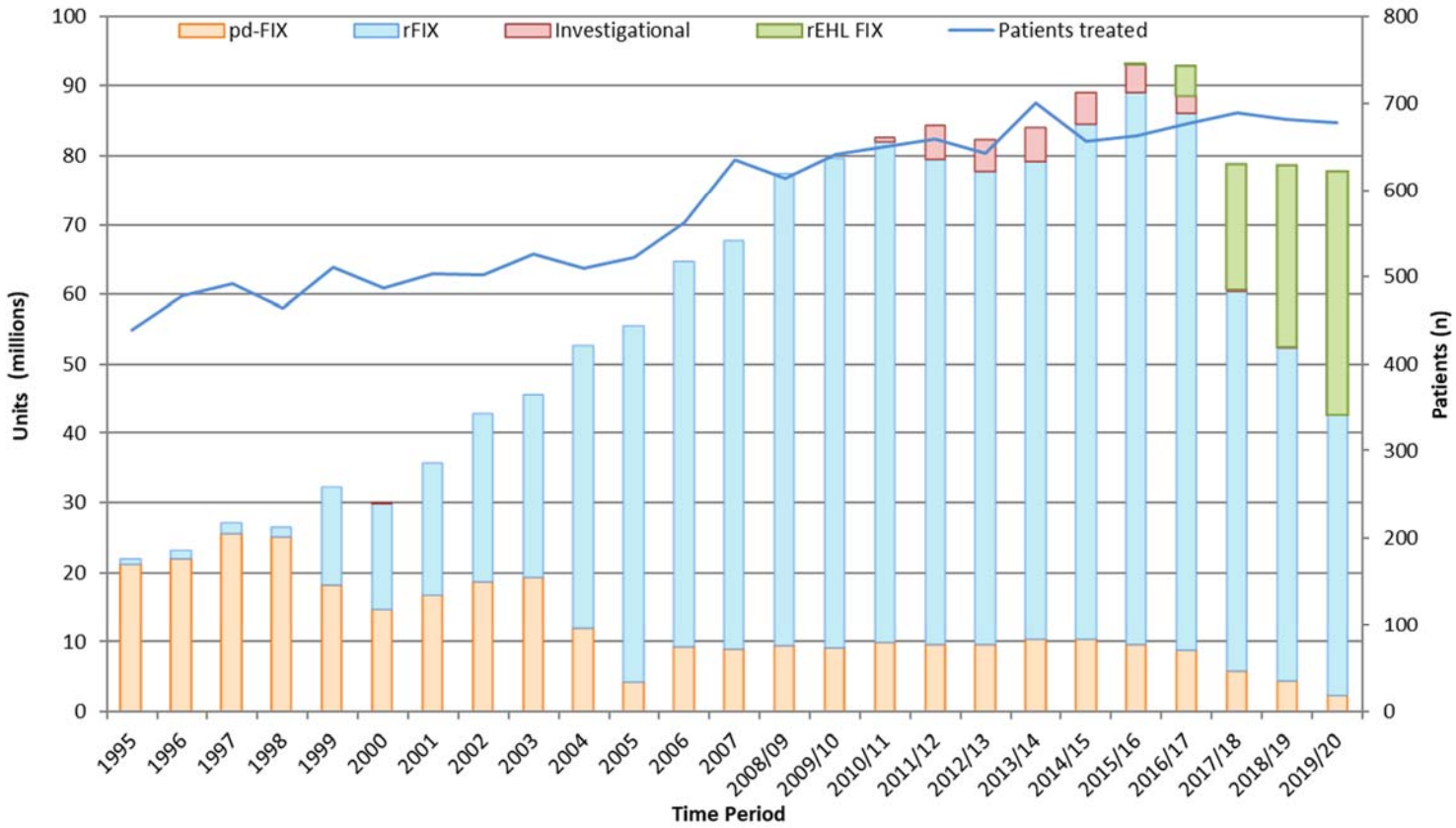


Figure 17: Shows FIX usage for Haemophilia B 1995 to 2019/20. The number of people reported to have been treated is shown by the blue line using a secondary axis. Use of recombinant SHL FIX reduced by 16% between 2018/19 and 2019/20 and use of EHL FIX (shown in green) increased by 34% in the same period. Overall, FIX units consumed has declined as a direct consequence of switching to EHL FIX products, which are prescribed generally in lower doses/kg/week than standard products because of their longer half-life. Gene therapy is also reducing the numbers requiring FIX to some degree.

Figure 18 Numbers of people using different product types issued by UK haemophilia centres to treat haemophilia B, 2015/16 – 2019/20

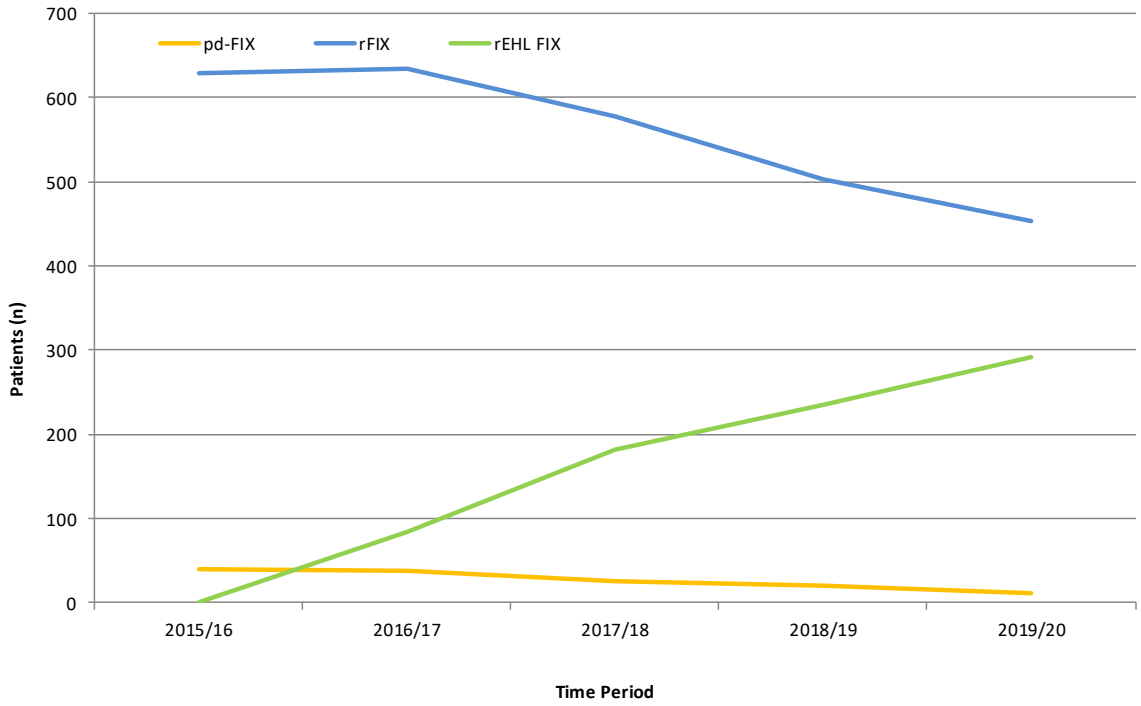


Figure 18: Shows a steady decline in the number of patients using both plasma-derived and recombinant standard half-life factor IX corresponding with, and probably caused by, the increasing use of extended half-life rFIX. It is interesting that, in contrast with some other markets, patients have not switched to EHL-IX to a greater extent. Personal experience leads me to believe that this is attributable in general to patient choice.

Table 12 Factor IX mean usage by region for people with severe haemophilia B (incl. treatment for inhibitors and EHL-FIX), 2019/20

Health Authority	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20
East Midlands	152,777	144,795	154,136	177,142	179,386	199,323	161,714	122,027	107,924	97,400
East of England	225,893	214,500	211,405	194,150	199,871	173,450	167,654	169,568	179,971	172,250
London	209,131	197,044	165,763	180,511	206,134	201,764	191,217	179,765	181,598	163,922
North East	157,667	176,136	161,583	167,038	205,346	271,917	223,958	138,712	104,788	86,231
North West	140,926	198,457	209,373	185,190	180,135	225,401	199,339	182,955	166,067	149,070
Northern Ireland	208,708	202,889	193,781	225,188	200,563	236,388	239,688	201,563	121,031	185,156
Scotland East	256,164	257,271	253,781	229,936	184,679	208,857	171,250	124,000	126,429	125,964
Scotland West	220,500	247,500	327,250	287,250	291,000	342,250	313,000	320,250	298,500	296,000
South East	160,251	146,370	136,858	136,738	143,788	154,728	159,535	133,837	136,360	126,036
South West	199,472	229,472	280,065	222,591	246,222	231,722	247,912	216,981	245,188	228,231
Wales	119,682	157,476	158,307	156,144	153,342	142,414	160,071	141,200	122,364	151,577
West Midlands	185,616	173,379	219,034	189,116	190,999	198,389	182,470	153,771	170,415	139,769
Yorkshire and the Humber	134,357	168,058	175,261	199,903	193,961	227,503	254,821	163,808	152,587	174,288

Table 12: Shows mean FIX usage by region. This shows similar variation in treatment intensity to that observed with haemophilia A, although the number of people with this diagnosis are 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.

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Table 13 Products issued to treat haemophilia B (including inhibitors), 2018/20

Manufacturer	Product	2018/19		2019/20	
		Units (IU)	Patients Treated (n)	Units (IU)	Patients Treated (n)
BPL	Replenine	393,940	3	826,055	3
CSL Behring	IDELVION	7,429,250	83	8,152,750	90
Grifols	Alphanine	3,857,000	18	1,473,000	11
Novo Nordisk	NovoSeven (mg)	13,401	10	7,541	9
	Refixia	1,058,507	14	3,594,500	36
Pfizer	BeneFIX	46,700,500	485	39,781,750	447
	ReFacto AF	-	-	1,000	1 - 2
SOBI/Biogen	ALPROLIX	17,593,950	143	23,278,750	176
Takeda	FEIBA	1,417,000	4	873,000	3
	RIXUBIS	1,116,500	14	489,000	6
Various Manufacturers	Desmopressin	-	-	72	1 - 2
	Investigational Factor IX	*	*	*	*
	Investigational Other	*	*	*	*

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

Table 13 This gives a breakdown of the products issued to treat haemophilia B in the UK in 2018/19 and 2019/20, organised by supplier. These figures have been cross-checked with sales figures provided by the suppliers. Whilst a perfect match between manufacture's sales figures and NHD usage figures would not be expected, there was a high level of correlation except for low-usage products. Sales figures are not reported here for reasons of confidentiality.

There is a continued marked reduction in the proportion of investigational FIX use as these clinical trials come to an end. Investigational products have been deliberately aggregated and anonymised to avoid any breach of confidentiality agreements and to take account of commercial sensitivities. It is not possible to distinguish between standard and extended half-life investigational products for that reason. *It is advised that data on trial products should be shared with 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.*

A significant proportion of plasma-derived FIX was used, mainly for people who do not “get on with” BeneFIX. The proportions of plasma-derived FIX supplied by Grifols has declined, with people being switched to EHL FIX. The number of patients treated with EHL FIX continues to increase.

One person was issued ReFacto AF in error.

Table 14 Factor IX units issued by UK haemophilia centres, by diagnosis, 2019/20

Coagulation Defect	Patients Treated	FIX (IU)				
		Plasma	Recombinant	Investigational	Enhanced Half-Life	Total
Haemophilia B	678	2,299,055	40,270,750	**	35,026,000	77,595,805
Co-inherited diagnoses	n=1 - 2	-	-	-	60,000	60,000
Total	**678***	**2,299,055**	**40,270,750**	**-**	**35,086,000**	**77,655,805**

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

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

Table 14: This shows FIX issued in 2019/20, broken down by product type and diagnosis. Note that this includes the use of 182,359 units of investigational recombinant FIX. This represents a smaller proportion of the total FIX units issued compared to last year.

Figure 19 Number of people with haemophilia B treated in the UK 2019/20 broken down by product used

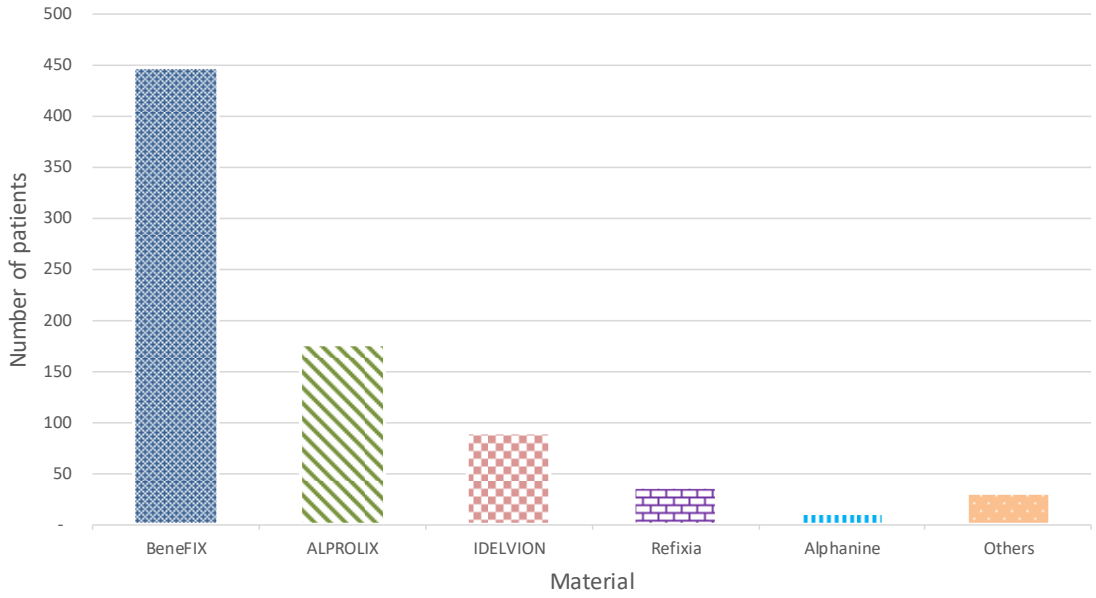

Figure 19: This shows the market breakdown of haemophilia B treatments, including those issued to people with an inhibitor. This includes double counting where patients are treated with more than one product.

The data table for this pie chart can be seen overleaf. Patients treated with more than one product in the year will be counted twice. There were 689 individual people with haemophilia B treated.

Data table for Figure 19

Manufacturer	Product	Units (IU)	Patients (n)
Pfizer	BeneFIX	39,781,750	447
SOBI/Biogen	ALPROLIX	23,278,750	176
CSL Behring	IDELVION	8,152,750	90
Novo Nordisk	Refixia	3,594,500	36
Takeda	RIXUBIS	489,000	6
Novo Nordisk	NovoSeven (mg)	7,541	9
Pfizer	ReFacto AF	1,000	1 - 2
Grifols	Alphanine	1,473,000	11
Takeda	FEIBA	873,000	3
BPL	Replenine	826,055	3
	Investigational	*	*
	Desmopressin	72	1 - 2

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

2.3 Gene Therapy

Outline data was requested from those centres active in gene therapy for Haemophilia A and B. Since none of these products are licensed, detailed data is still covered by study confidentiality agreements. For that reason, only outline data was requested and we suspect that even that is probably incomplete from some centres.

We requested details of who had undergone gene therapy at any time. In some cases, we have the date of gene therapy and an outline of the course subsequently pursued but, in most cases, far less data has been submitted. In all cases we have record of factor VIII/IX concentrate issued to people through the normal quarterly returns. We strongly suspect that far more people with Haemophilia B have undergone gene therapy than have been reported to us, since only nine subjects undergoing Haemophilia B gene-therapy have been reported to us. One wonders if all the people from the earliest trials have been reported. We have no record of the product used or dosage administered since such details are still covered by confidentiality agreements held between the investigator and the manufacturer.

We are not in a position to estimate the overall failure rate, based on the number who require regular conventional replacement therapy or Hemlibra after undergoing gene therapy, that does not give a meaningful estimate of overall efficacy because some of the dose-ranging phase 1 studies started with very low “safety” doses of the IP. Furthermore, we suspect that not all cases have been reported to the database.

It is important that all cases, including relatively historic cases, are reported to us so that we can reconcile our data and account for people who no longer use replacement therapy.

A total of 31 people who underwent gene therapy have been reported to us, 9 Haemophilia B and 22 Haemophilia A.

2.4 Von Willebrand's Disease

Table 15 People with von Willebrand disease registered and treated 2019/20

von Willebrand disease	VWD Activity IU/dl										Total	Treated with Concentrate	Treated with Desmopressin
	<10	10 - <30	≥30	N/K	Sub Total	<10	10 - <30	≥30	N/K	Sub Total			
	<18 years					≥18 years							
Males													
Type 1	22	201	260	9	**492**	97	408	649	91	**1,245**	**1,737**	**77**	**31**
Type 2A	43	38	7	0	**88**	106	96	40	3	**245**	**333**	**73**	**5**
Type 2A, 2M	0	0	0	0	**0**	0	0	1	0	**1**	**1**	**1**	**1**
Type 2B	9	9	4	0	**22**	16	40	20	0	**76**	**98**	**21**	**1**
Type 2M	19	11	3	1	**34**	41	38	14	1	**94**	**128**	**26**	**1**
Type 2N	1	0	2	0	**3**	3	4	25	3	**35**	**38**	**4**	**1**
Type 2 Unspecified	9	13	3	0	**25**	26	18	12	0	**56**	**81**	**14**	**3**
Type 3	25				**25**	65				**65**	**90**	**65**	**0**
Type Unreported	49	120	190	2	**361**	146	286	540	45	**1,017**	**1,378**	**90**	**20**
Low VWF	3	2	46	0	**51**	1	5	105	0	**111**	**162**	**1**	**5**
										Sub Total Males	**4,046**	**372**	**68**
Females													
Type 1	23	144	184	3	**354**	144	743	1,695	167	**2,749**	**3,103**	**120**	**91**
Type 2A	38	34	10	0	**82**	132	135	68	3	**338**	**420**	**84**	**9**
Type 2B	8	11	6	0	**25**	18	45	43	3	**109**	**134**	**24**	**2**
Type 2M	10	24	2	0	**36**	67	83	29	3	**182**	**218**	**34**	**6**
Type 2N	1	1	5	0	**7**	9	11	69	3	**92**	**99**	**13**	**5**
Type 2 Unspecified	9	10	2	0	**21**	28	30	20	0	**78**	**99**	**12**	**3**
Type 3	23				**23**	57				**57**	**80**	**55**	**0**
Type Unreported	50	122	158	4	**334**	182	553	1,424	126	**2,285**	**2,619**	**132**	**61**
Low VWF	1	1	36	0	**38**	0	6	256	2	**264**	**302**	**2**	**17**
										Sub Total Females	**7,074**	**476**	**194**
										Grand Total - Males and Females	**11,120**	**848**	**262**

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Table 15 (previous page): This shows the number of people registered with von Willebrand disease 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 in 64% of registrations, almost the same proportion as last year (61%). Efforts are ongoing to tidy up this part of the database, but problems include repeatedly changing classification over time; some very old data entries; and changing opinion in relation to the diagnosis of mild type 1 VWD, which may have been over-diagnosed in the past. It is nevertheless disappointing that over one third of registrations lack a subtype. This may be because the diagnostic process for VWD is frequently in two stages (basic diagnosis and then sub-typing) and the registration may be submitted to the NHD half-way through this process. The registration should be updated when the subtype becomes known.

There remains a relative excess of adult females, reflecting referral bias of women with menorrhagia and possibly also over-diagnosis of mild type 1 VWD. 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 16 (overleaf)*:* This shows that 401 people with von Willebrand disease were newly registered in the past year. Only 12% of these were registered without indicating a subtype, which is encouraging.

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

Table 16 New registrations of von Willebrand disease between 2019/20, by age at mid-year, severity, and gender

von Willebrand disease	VWF Activity IU/dl										Total
	<10	10 - 29	≥30	N/K	Sub Total	<10	10 - 29	≥30	N/K	Sub Total	
	<18 years					≥18 years					
Males											
Type 1	3	23	21	0	**47**	5	11	9	0	**25**	**72**
Type 2A	5	8	1	0	**14**	3	7	1	0	**11**	**25**
Type 2B	0	0	0	0	**0**	0	1	1	0	**2**	**2**
Type 2M	3	1	1	1	**6**	2	1	1	0	**4**	**10**
Type 2N	0	0	0	0	**0**	1	1	1	0	**3**	**3**
Type 2 Unspecified	2	1	0	0	**3**	3	2	1	0	**6**	**9**
Type 3	1				**1**	0				**0**	**1**
Type Unreported	3	4	4	0	**11**	1	3	1	0	**5**	**16**
Low VWF	0	0	9	0	**9**	1	1	7	0	**9**	**18**
										Sub Total Males	**156**
Females											
Type 1	4	14	16	0	**34**	0	28	42	0	**70**	**104**
Type 2A	4	5	1	0	**10**	0	6	2	0	**8**	**18**
Type 2B	0	1	0	0	**1**	0	1	3	0	**4**	**5**
Type 2M	2	5	1	0	**8**	5	5	1	0	**11**	**19**
Type 2N	1	1	1	0	**3**	1	1	3	0	**5**	**8**
Type 2 Unspecified	3	2	1	0	**6**	1	1	1	0	**3**	**9**
Type 3	3				**3**	2				**2**	**5**
Type Unreported	1	3	9	0	**13**	0	3	14	0	**17**	**30**
Low VWF	0	0	13	0	**13**	0	2	30	2	**34**	**47**
										Sub Total Females	**245**
										Grand Total - Males and Females	**401**

Figure 20 Units of Von Willebrand Factor issued by UK haemophilia centres to treat von Willebrand disease 2014/15 - 2019/20

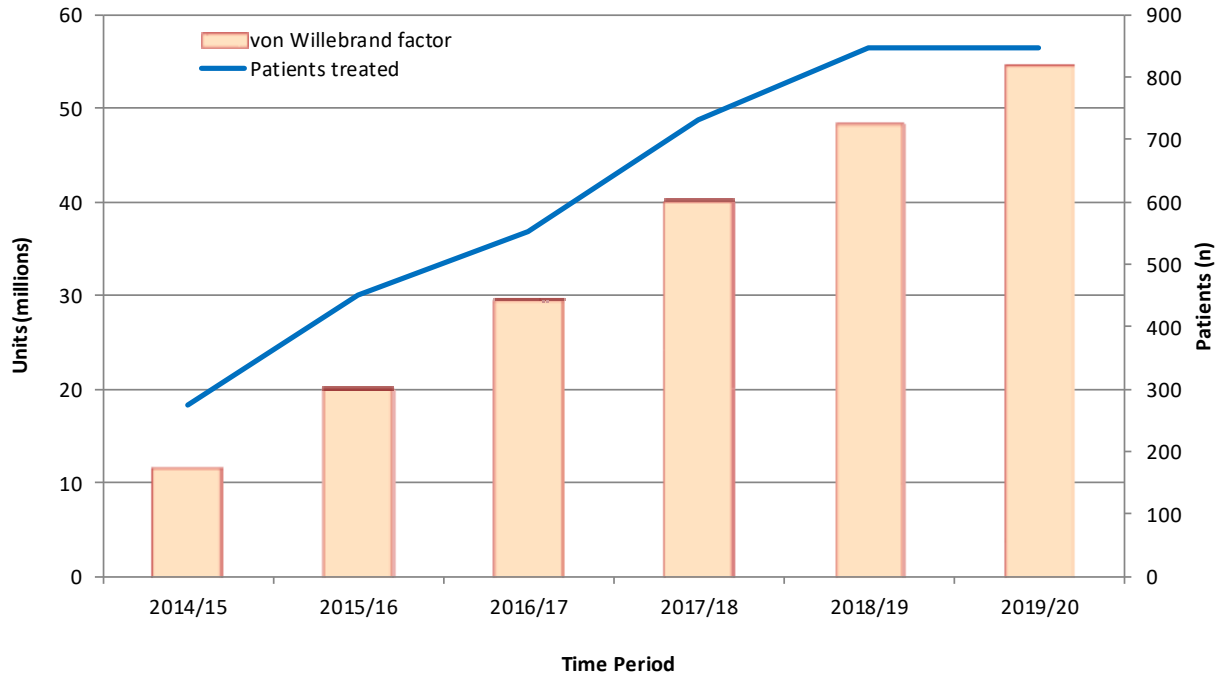

Figure 20 shows von Willebrand factor units issued to treat von Willebrand disease from 2014/15 to 2019/20. Usage has increased almost five-fold during that time and number of patients treated about threefold. Von Willebrand prophylaxis has increased considerably during that period.

Table 17 Products issued to treat von Willebrand disease (including inhibitors), 2018/20

Manufacturer	Product	2018/19		2019/20	
		Units (IU)	Patients Treated (n)	Units (IU)	Patients Treated (n)
CSL Behring	Haemate P	205,000	7	135,000	1 - 2
	Voncento	16,723,500	607	18,966,001	619
LFB Biomedicaments	Willfact /Wilfactin	1,068,000	20	1,026,000	15
Novo Nordisk	NovoEight	-	-	4,000	1 - 2
	NovoSeven (mg)	2,560	8	801	4
Octapharma	Wilate	6,973,000	245	8,107,100	222
Takeda	Advate	70,000	4	750	1 - 2
	Veyvondi	-	-	7,150	1 - 2
	Desmopressin	16,058	264	27,094	262

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

Table 17: This shows a breakdown of concentrates issued to treat von Willebrand disease in the UK by supplier. These 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. Haemate P has now been withdrawn. Veyvondi was introduced for surgery and on-demand treatment in late 2020 and so there was very little of this product used during this reporting period. This is expected to change in the next reporting period.

Potentially anomalous product use in Table 17 is accounted for as follows:

Advate: Allergic to VWF products
Advate: Small dose for a procedure

2.5 Congenital and Acquired factor VIII, IX and VW Inhibitors

Table 18 Inhibitors by disease severity – congenital haemophilia A, haemophilia B & von Willebrand disease

Coagulation Defect	Severity (IU/dl) / Subtype	In Register *	Inhibitors n (%)			
			Newly Reported	Ongoing	Historical	Total
Haemophilia A	< 1	2,106	12 (0.6)	161 (7.6)	320 (15.2)	493 (23.4)
	1 - 5	805	3 (0.4)	29 (3.6)	46 (5.7)	78 (9.7)
	>5	5,705	7 (0.1)	9 (0.2)	46 (0.8)	62 (1.1)
	Total	**8,616**	**22 (0.3)**	**199 (2.3)**	**412 (4.8)**	**633 (7.3)**
Haemophilia B	Severe	369	0 (0.0)	9 (2.4)	8 (2.2)	17 (4.6)
	Non-Severe	1,545	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.1)
	Total	**1,914**	**0 (0.0)**	**10 (0.5)**	**8 (0.4)**	**18 (0.9)**
Von Willebrand disease	Type 1	4,808	0 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)
	Type 3	168	0 (0.0)	6 (3.6)	1 (0.6)	7 (4.2)
	Others	6,141	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Total	**11,117**	**0 (0.0)**	**6 (0.1)**	**2 (0.0)**	**8 (0.1)**

** Including those not regularly treated*

New=newly reported in year
Ongoing=inhibitor in year but not new in year
Historical=history of inhibitor, but not current

Table 18 (previous page): This table shows the incidence of new inhibitors in the past year, the prevalence 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.

Those labelled "new" were reported for the first time in the year 2019/20. Those labelled "ongoing" are those reported in previous years which have not been eradicated and which remain clinically significant and reported in 2019/20. Those reported as "historical" are those reported in previous years but not reported to be ongoing in 2019/20.

An inhibitor is designated as historical if it is no longer reported in the quarterly returns within 2019/20. It should be recognised that there is necessarily some softness or lack of precision surrounding this judgement because inhibitors thought to have been eradicated may persist at a variable low level below the level of detection of the Bethesda assay but high enough to shorten the FVIII half-life. This uncertainty will only increase with the introduction of Emicizumab. Inhibitors usually decline during treatment with Emicizumab but cannot be said to have disappeared unless the person is re-challenged with FVIII without a subsequent anamnestic inhibitor recurrence. We have received at least two reports in the last year of inhibitors, probably incompletely tolerised which have recurred after the patient was switched to Emicizumab and regular factor VIII prophylaxis stopped.

The table shows that a history of inhibitor is over twice as prevalent in severe as in moderate haemophilia A and twenty 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, fortunately, far less common, with a prevalence of 0.9% of people registered with haemophilia B. These arise early in the persons treatment and occur only in-patients with severe haemophilia B caused by factor IX gene deletions.

Inhibitors in von Willebrand disease appear in our cohort almost exclusively in type 3 VWD and, judged by the very low number of inhibitors marked as "historical" (2 of 8), are very difficult to eradicate.

Table 19 (overleaf): Shows products reported to have been issued to people with a current inhibitor during 2018/19 and 2019/20, broken down by diagnosis, supplier and product.

Table 19 Products issued to people with congenital bleeding disorders reported to have a positive inhibitor during 2018/20

Manufacturer	Product	2018/19		2019/20	
		Units (IU)	Patients Treated (n)	Units (IU)	Patients Treated (n)
Haemophilia A					
BPL	FVIII 8Y	324,540	1	171,500	1 - 2
	Optivate	361,880	1	372,925	1 - 2
Grifols	Fanhdi	3,323,000	5	231,000	1 - 2
Novo Nordisk	NovoSeven (mg)	10,653	92	5,982	89
	NovoEight	1,662,573	10	2,169,250	8
Octapharma	Nuwiq	2,632,500	10	3,035,750	8
	Octanate	2,258,500	6	1,512,500	4
Pfizer	ReFacto AF	6,832,250	26	11,043,500	25
Roche	Hemlibra (mg)	187,054	66	351,878	113
SOBI/Biogen	Elocta	5,571,000	19	10,929,070	27
Takeda	Advate	12,930,500	37	12,593,500	37
	FEIBA	9,081,000	44	2,825,000	18
Various Manufacturers	Desmopressin	124	2	258	5
	Investigational FVIII	3,228,132	10	925,539	3
	Investigational Other	412	2	728	1 - 2
Haemophilia B					
Novo Nordisk	NovoSeven (mg)	13,401	10	7,541	9
Takeda	FEIBA	1,417,000	4	873,000	3
	Investigational Other	-	0	560	1 - 2
von Willebrand Disease					
CSL Behring	Voncento	458,000	4	387,900	3
Novo Nordisk	NovoSeven (mg)	1,184	4	262	3
F.VII deficiency					
Novo Nordisk	NovoSeven (mg)	592	1	1,576	1 - 2
Takeda	FVII	-	-	39,600	1 - 2
Co-inherited diagnoses					
Novo Nordisk	NovoSeven (mg)	-	-	6	1 - 2
Roche	Hemlibra (mg)	5,880	1	6,300	1 - 2
Takeda	FEIBA	178,000	1	157,500	1 - 2
Unclassified					
Novo Nordisk	NovoSeven (mg)	-	-	40	1 - 2

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Table 20 Products issued to people with acquired inhibitors 2019/20

Manufacturer	Product / Patients (n)	Acquired Haemophilia A	Acquired von Willebrands	Acquired FXIII Deficiency	Acquired Deficiency - Other
CSL Behring	Fibrogammin P (1)	-	-	8,750	-
	Voncento (27)	-	1,422,000	-	-
Novo Nordisk	NovoEight (1)	66,000	-	-	-
	NovoSeven (mg) (13)	3,620	-	-	-
Octapharma	Wilate (12)	-	245,000	-	-
Takeda	Advate (3)	78,500	-	-	-
	FEIBA (100)	9,015,150	15,000	-	-
	OBIZUR (20)	1,615,500	-	-	-
Various Manufacturers	Desmopressin (3)	-	48	-	150
	Investigational (3)	187	-	-	-

Units in IU unless otherwise stated

Table 20: This shows reported products issued for people with an acquired inhibitor reported or ongoing during 2019/20, broken down by diagnosis and supplier.

Table 21 FEIBA® usage: breakdown by diagnosis 2018/20

Coagulation Defect	2018/19		2019/20	
	Units (IU)	Patients Treated (n)	Units (IU)	Patients Treated (n)
Haemophilia A	9,121,000	45	2,896,000	22
Acquired Haemophilia A	8,738,000	95	9,015,150	97
Haemophilia B	1,417,000	4	873,000	3
Acquired von Willebrand disease	-	-	15,000	1 - 2
Co-inherited diagnoses	178,000	1 - 2	157,500	1 - 2
Total	**19,454,000**	**144***	**12,956,650**	**122***

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

Table 22 NovoSeven® usage: breakdown by diagnosis 2018/20

Coagulation Defect	2018/19		2019/20	
	mg	Patients Treated (n)	mg	Patients Treated (n)
Haemophilia A	10,766	96	6,262	98
Haemophilia B	13,401	10	7,541	9
von Willebrand disease	2,560	8	801	1 - 5
Acquired Haemophilia A	1,724	15	3,620	13
F.VII deficiency	2,978	72	4,195	62
F.XI Deficiency	150	4	42	1 - 5
Co-inherited diagnoses	1	1 - 2	6	1 - 5
Hypodysfibrinogenemia	-	-	1	1 - 5
Bernard Soulier	150	9	223	8
Glanzmann's Thrombasthenia	2,313	43	8,855	49
Platelet defects	13	1 - 2	26	1 - 5
Miscellaneous	-	-	207	1 - 5
Unclassified bleeding disorder	6	1 - 2	69	6
Total	**34,056**	**257***	**31,848**	**245***

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

Tables 21, 22 (previous page) *& 23* show in greater detail how much FEIBA, NovoSeven and Hemlibra were issued for each diagnosis in 2018/20. 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 usage occurs outside haemophilia centres and is consequently not systematically collected. The usage of FEIBA and factor VIII in congenital Haemophilia A with inhibitors has declined markedly since last year, as people start using Hemlibra. In contrast, the fall in the use of NovoSeven is less marked, probably because it is now used in preference to FEIBA for surgery in people with FVIII inhibitors who are co-prescribed Hemlibra.

Table 23 Hemlibra® usage: breakdown by diagnosis 2018/20

Coagulation Defect	2018/19		2019/20	
	mg	Patients Treated (n)	mg	Patients Treated (n)
Haemophilia A	187,054	65	897,750	393
Co-inherited diagnoses	5,880	1 - 2	6,300	1 - 5
Total	**192,934**	**65***	**904,050**	**393***

This is the total excluding numbers which have been suppressed.

Figure 21 The proportion of people with haemophilia A and an inhibitor broken down by treatment product used

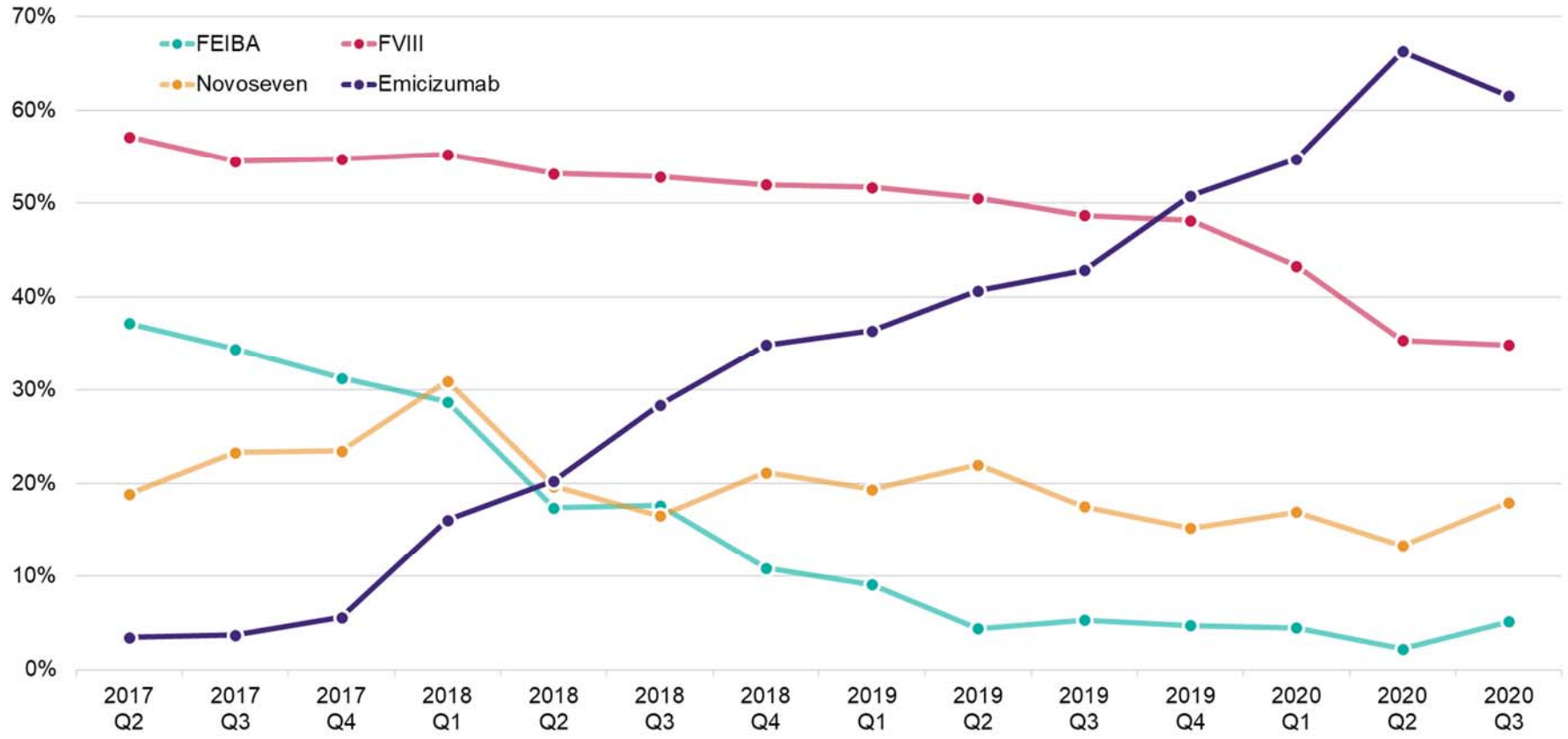


Figure 21 shows the change in the percentage of patients with haemophilia A and an inhibitor treated with FEIBA, NovoSeven, factor VIII and Emicizumab in the two years since Emicizumab was licensed for use in this group of patients. Patients treated with more than one product are double counted. The introduction of Emicizumab has led to a marked reduction in the use of factor VIII and FEIBA in inhibitor patients but less change in the use of NovoSeven, which may be used for surgery and intercurrent bleeding in preference to FEIBA in patients co-prescribed Emicizumab.

Figure 22 The number of people with haemophilia A and inhibitors and the proportion who switched to Emicizumab by centre2019-2020

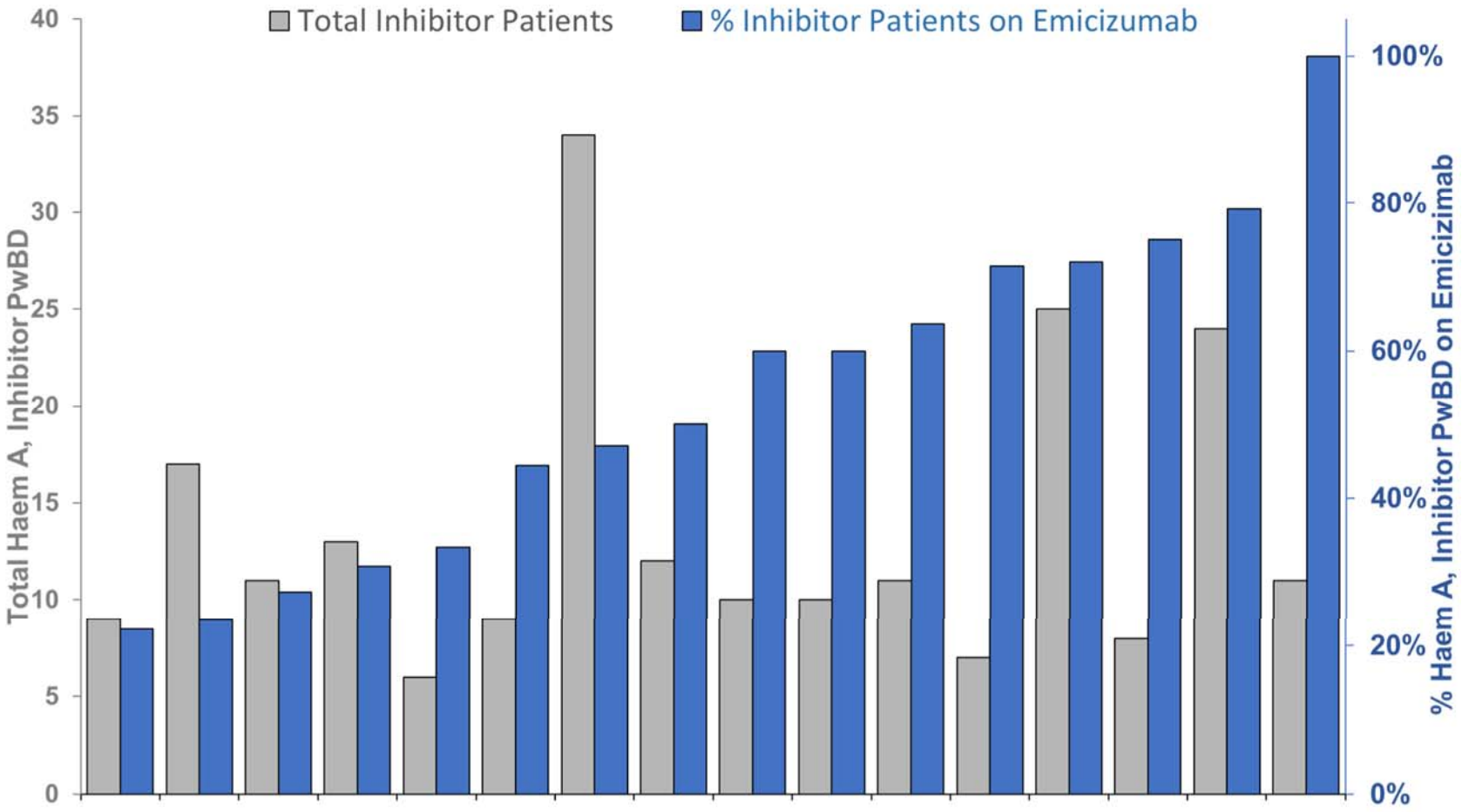


Figure 22 shows the number of patients with active inhibitors registered in each centre with inhibitors (grey bars) and the percentage of those changed to Hemlibra (blue bars). This shows that about 50% of factor VIII inhibitor patients have changed to Hemlibra with some centre to centre variation.

2.6 Rarer Bleeding Disorders

Table 24 People with rarer types of bleeding disorders registered and treated 2019/20

Coagulation Defect	Number of Patients in Register		Treated with		
	Males	Females	Any Product	Concen-trate	Desmo-pressin
Probable von Willebrand disease	64	180	10	4	6
Platelet-type Pseudo von Willebrand Disease	16	24	1 - 2	1 - 2	0
F.V deficiency	92	158	3	0	0
F.VII deficiency	841	945	68	65	1 - 2
F.X deficiency	129	176	40	38	1 - 2
F.XI Deficiency	1,496	2,160	59	44	1 - 2
F.XIII Deficiency	44	36	66	66	0
Combined II+VII+IX+X Deficiency	1 - 2	1 - 2	0	0	0
Combined V+VIII Deficiency	12	15	7	7	1 - 2
Co-inherited diagnoses	150	171	30	23	8
Prothrombin Deficiency	8	9	1 - 2	1 - 2	0
Afibrinogenemia	9	7	12	11	0
Dysfibrinogenemia	259	391	16	15	1 - 2
Hypofibrinogenemia	85	119	9	9	0
Hypodysfibrinogenemia	18	20	3	3	0
Fibrinogen Deficiency	5	1 - 2	0	0	0
Acquired Haemophilia A	300	284	110	106	0
Acquired Haemophilia B	1 - 2	0	0	0	0
Acquired von Willebrands	98	66	36	35	1 - 2
Acquired Prothrombin Deficiency	4	4	0	0	0
Acquired F.XIII Deficiency	0	1 - 2	1 - 2	1 - 2	0
Acquired F.V Deficiency	1 - 2	6	0	0	0
Acquired Deficiency (other)	11	4	1 - 2	0	1 - 2
Glanzmann's Thrombasthenia	69	85	52	49	1 - 2
Bernard Soulier	50	52	12	9	1 - 2
Other platelet defects	962	2,153	98	4	87
Thrombomodulin-associated Coagulopathy	1 - 2	1 - 2	0	0	0
Miscellaneous	83	255	15	6	7
Unclassified bleeding disorder	115	778	38	7	28
Haemophilia A with Liver Transplant	13	0	0	0	0
Haemophilia B with Liver Transplant	1 - 2	0	0	0	0
von Willebrand with Liver Transplant	1 - 2	0	0	0	0
Total	**4933***	**8098***	**684***	**501***	**136***

This is the total excluding numbers which have been suppressed.

Table 24: This shows the number of people registered with rarer disorders and the proportion treated during the year. It is suspected that liver transplantation is under-reported.

Table 25 People with selected rarer bleeding disorders registered and treated 2019/20, by disease severity

Coagulation Defect	Number of Patients (factor level IU/dl)							
	<5		≥5		N/K		Total	
	In Reg	Treated	In Reg	Treated	In Reg	Treated	In Reg	Treated
F.V deficiency	52	3	198	0	0	0	250	3
F.VII deficiency	144	29	1638	39	4	0	1786	68
F.X deficiency	40	29	265	11	0	0	305	40
F.XI Deficiency	269	28	3384	31	3	0	3656	59
Total	**505**	**89**	**5,485**	**81**	**7**	**-**	**5,997**	**170**

Table 25: It is acknowledged that these rarer disorders have no recognised classification of disease severity. However, the table above gives an idea of the range of registered levels.

Table 26 New registrations of rarer bleeding disorders 2019/20, by coagulation defect and gender

Coagulation Defect	Male	Female	Total
Platelet-type Pseudo von Willebrand Disease	1	4	5
Probable von Willebrand disease	4	9	13
F.V deficiency	6	13	19
F.VII deficiency	97	112	209
F.X deficiency	10	19	29
F.XI Deficiency	100	165	265
F.XIII Deficiency	2	1	3
Co-inherited diagnoses	10	20	30
Afibrinogenemia	1	-	1
Dysfibrinogenemia	21	46	67
Hypofibrinogenemia	13	19	32
Hypodysfibrinogenemia	2	1	3
Prothrombin Deficiency	-	1	1
Acquired Haemophilia A	73	46	119
Acquired F.V deficiency	1	1	2
Acquired von Willebrand disease	16	10	26
Acquired Deficiency (other)	1	1	2
Glanzmann's Thrombasthenia	3	2	5
Bernard Soulier	3	4	7
Other platelet defects	90	194	284
Thrombomodulin-associated Coagulopathy	2	2	4
Miscellaneous	11	42	53
Unclassified bleeding disorder	22	147	169
Total	**489**	**859**	**1,348**

Table 26: This table shows new registrations of rarer 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 27 Concentrates used to treat rarer bleeding disorders between 2019/20

Manufacturer	Product	F.V Deficiency		F.VII Deficiency		F.X Deficiency		F.XI Deficiency		F.XIII Deficiency	
		Pts treated (n)	Units	Pts treated (n)	Units	Pts treated (n)	Units	Pts treated (n)	Units	Pts treated (n)	Units
BPL	COAGADEX	-	-	-	-	4	118,750	-	-	-	-
	FIX	-	-	-	-	-	-	-	-	-	-
	FXI	-	-	-	-	-	-	24	50,945	-	-
CSL Behring	Beriplex	-	-	-	-	16	929,500	-	-	-	-
	Fibrogammin P	-	-	-	-	-	-	-	-	64	1,113,002
	FXIII	-	-	-	-	-	-	-	-	1 - 2	32,500
LFB Biomedicaments	Hemoleven	-	-	-	-	-	-	19	78,000	-	-
Novo Nordisk	NovoSeven (mg)	-	-	62	4,195	-	-	1 - 2	42	-	-
	NovoThirteen	-	-	-	-	-	-	-	-	1 - 2	40,000
Octapharma	Octaplas (units)	3	409	-	-	1 - 2	29,000	9	840	-	-
	Octaplex	-	-	1 - 2	16,500	18	1,390,500	-	-	-	-
Takeda	FEIBA	-	-	-	-	-	-	-	-	-	-
	FVII	-	-	3	657,000	-	-	-	-	-	-
	Desmopressin	-	-	1 - 2	91	1 - 2	30	1 - 2	3,750	-	-

Units in IU unless otherwise stated

Table 27: This gives a breakdown of products issued during 2019/20 for people with rarer bleeding disorders, broken down by diagnosis and supplier.

2.7 Adverse Events

Introduction:

Pharmacovigilance has become an increasingly important function of the database. Treatments are monitored for safety signals and drug-related adverse events are reported to the manufacturer and, through them, to the regulators. Licensing studies for rare disease therapeutics are, by their nature, small and uncommon side effects may only be discovered when new drugs are prescribed to larger numbers of people, post-licensure. 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 drugs with novel modes of action with side effect profiles very different from the products 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 and working closely with the Co-Morbidity Working Party (CMWP), we have written an SOP for managing and investigating adverse events. Adverse Events (AEs) and Serious Adverse Events (SAEs) are defined as for GCP clinical trials. Where required, adverse event reports are further investigated by the CMWP. The CMWP meets once a month by Zoom and adjudicates on repeated AEs and all SAEs and scores their severity (1-5) and potential relationship to drug therapy (unrelated; possibly related; probably drug-related and definitely drug-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.

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!): -

Deaths	Malignancy
Thrombotic events (incl. MAHA)	Acute or Allergic reactions
Infections	COVID-19 infection
Inhibitors	Unexpected poor efficacy
Intracranial Haemorrhage (paediatric and adult)	Other Neurological events
Neurological Events	Other

We are very concerned to try to minimise the “Weber Effect”. This is the tendency to report adverse events in relation to newer products in preference to adverse events in relation to well established products. Whilst understandable, this is a form of reporting bias which may inadvertently lead to the impression that newer agents have more frequent or more severe side effects than those they replace or compete with. It is therefore extremely important that *ALL* drug-related side effects are reported, to facilitate objective safety comparisons of new and established agents.

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.

Table 28 Adverse Events reported between April 2019 & March 2020

Table 28 summarises the number and category of adverse events reported to the database during 2019/20. 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.

Adverse Event	Number of Patients	Number of Events
Allergy Event	12	12
COVID-19	0	0
Infection Event	0	0
Inhibitor Event	22	22
Intracranial Haemorrhage	11	12
Malignancy Event	33	34
Neurological Event	1	1
Other Event	2	2
Poor Efficacy Event	2	2
Thrombotic Event	10	10
Total	**93**	**95**

Further details of these events are as follows.

Table 29 Allergic / Other Reactions

Event	Diagnosis	Material	Relationship to material	Outcome
Rash 28 days after starting	Severe Haemophilia A	NovoEight	Probable	Resolved
Rash 150 mimutes after administration	von Willebrand disease	Wilate	Possible	Resolved
Rash 15 mimutes after administration	von Willebrand disease	Voncento	Probable	Resolved
Rash 45 mins after administration	von Willebrand disease	Voncento	Possible	Resolved
Pruritis and urticaria 15 mins after administration	von Willebrand disease	Voncento	Probable	Resolved
Dizziness. visual disturbance	F.XI Deficiency	Hemoleven	Possible	Resolved
Frontal headache and visual disturbance 24 hrs after dosing	Severe Haemophilia A	Hemlibra	Probable	Resolved
Injection site reaction	Severe Haemophilia A	Hemlibra	Probable	Resolved
Injection site reaction	Severe Haemophilia A	Hemlibra	Probable	Resolved
Headache/migraine	Severe Haemophilia A	Hemlibra	Possible	Resolved
Headache	Severe Haemophilia A	Hemlibra	Possible	Resolved
Single episode headache/confusion 7 hrs after 4th dose.	Severe Haemophilia A	Hemlibra	Possible	Resolved

Table 30 Thrombotic Events

Event	Diagnosis	Material	Relationship to material	Outcome
Mild DIC	Severe Haemophilia A	FEIBA	Probable	Resolved when FEIBA stopped
Myocardial Infarct 17 hours after administration	Severe Haemophilia B	Idelvion	Possible	Resolved
Myocardial infraction	Acquired Haemophilia	None	N/A	Resolved
Angina pectoris (New) Smoker, hypertension, high BMI	Mild Haemophilia A	None	N/A	Ongoing
Myocardial infarct after third loading dose. Coronary arteries appeared clear despite smoking and diabetes. Subendocardial infarct	Severe Haemophilia A	Hemlibra	Probable	Resolved. Hemlibra stopped
Thrombotic stroke (recurrence; AF)	Mild Haemophilia A	None	N/A	Ongoing
Superior mesenteric artery thrombosis with established collaterals (incidental finding 15 months after starting Emicizumab)	Severe haemophilia A	Hemlibra	Possible contributor. Relationship uncertain.	Resolved
Poor efficacy Haematoma after line insertion	Severe Haemophilia A with inhibitor	Hemlibra and Novoseven	Probably unrelated	Resolved
Poor efficacy. Excessive intercurrent bleeding	Severe Haemophilia A, bleed-free on Elocta	Hemlibra	No anti-drug antibodies. Poor efficacy of drug.	Reverted to Elocta prophylaxis and now bleed-free

Table 31 Factor VIII Inhibitors

Patient Number	1	2	3	4	5	6	7	8	9	10	11	12	13
Product in use at time of inhibitor development	*N/K	Advate	Advate	Advate	Advate	Advate	Advate	Advate	Nuwiq	Nuwiq	Elocta	ReFacto AF	ReFacto AF
Age at time of inhibitor development (years)	*21	9 mths	7 mths	11 mths	5	70	25	68	1	10 mths	11 mths	12	53
Haemophilia Severity (IU/dl)	0	0	0	1	0	1	0	15	0	0	0	11	7
Maximum Inhibitor titre	2.8	15.7	0.6	17.9	0.6	36.1	2.6	2.4	3.4	2.2	1.0	0.9	2.4

Twenty-two factor VIII inhibitors and no factor IX or VW inhibitors were reported between April 2019 and March 2020. Outline data for those where a full report was submitted is summarised in the table above.

* One of these was a pre-existing inhibitor in a person with severe haemophilia A who had recently migrated to this country. He developed an inhibitor to an unknown product after 36 exposure-days.

See table 18 for breakdown of inhibitors by disease severity.

Table 32 Intracranial Haemorrhage

Diagnosis	Age	Trauma present	Drug therapy	Outcome
Severe Haemophilia B Intracerebral bleed	1 day	None	-	Gross motor Weakness Alive
Severe Haemophilia A Subdural and intracranial bleeding	21	Major trauma	Factor VIII prophylaxis	Full recovery
Moderate severity Von Willebrand's disease	24	Major trauma	No regular treatment	Incomplete neurological recovery
Mild Haemophilia A Spontaneous catastrophic subarachnoid bleed	51	Spontaneous (no trauma)	No regular treatment	Died without regaining consciousness
Dysfibrinogenaemia Intracerebral bleed	63	Spontaneous no trauma	No regular treatment	Hemiplegia. Died
Mild Haemophilia A Spontaneous intracerebral bleeding	69	Spontaneous (no trauma)	No regular treatment	Died from unrelated malignancy
Mild von Willebrand's disease Subdural haematoma	74	Minor head bump	No regular treatment	Surgical evacuation Hemiplegia
Moderate haemophilia B Subarachnoid and intracerebral bleeding	76	Trauma	No previous regular treatment	Hemiplegia now on prophylaxis
Severe haemophilia B Intracranial Haemorrhage	78	None	On demand	Died
Mild Haemophilia A Recurrent intracerebral bleeding	82	Minor head bump	No regular treatment	Hemiplegia. Died
Mild von Willebrand's disease Subarachnoid bleed	88	Minor head bump	No regular treatment	Full recovery

Table 33 Malignancy events

Diagnosis	Malignancy	Number
Haemophilia A	Hepatocelular carcinoma	6
Haemophilia A	Colorectal carcinoma	6
Haemophilia A	Lymporoliferative malignancy	4
Haemophilia A	Prostatic carcinoma	4
Haemophilia A	Transitional carcinoma of the bladder	1
Haemophilia A/B	Skin (Melanoma, BCC, Squamous Ca.)	4
Haemophilia B	Hepatocellular carcinoma	1
Acquired von Willebrand's disease	Multiple myeloma	2
Various	Other (cancer of unknown origin, AML,Breast and endometrial carcinoma, Cholangiocarcinoma, astrocytoma)	6

Table 34 Other Events

Event	Diagnosis	Material	Relationship to material	Outcome
Osteonecrosis in Tibia	Severe Haemophilia A	Hemlibra	Possible	Resolved
Appendicitis	Severe Haemophilia A	Hemlibra	unrelated	Surgery
Guillaine Barre	Severe Haemophilia A	ReFacto AF	Unrelated	Resolved
Poor efficacy Haematoma after line insertion	Severe Haemophilia A with inhibitor	Hemlibra and Novoseven	Probably unrelated	Resolved
Poor efficacy. Excessive intercurrent bleeding	Severe Haemophilia A, bleed-free on Elocta	Hemlibra	No anti-drug antibodies. Poor efficacy of drug.	Reverted to Elocta prophylaxis and now bleed-free.

2.8 Mortality

Table 35 Causes of death in people with haemophilia A and B between April 2019 & March 2020

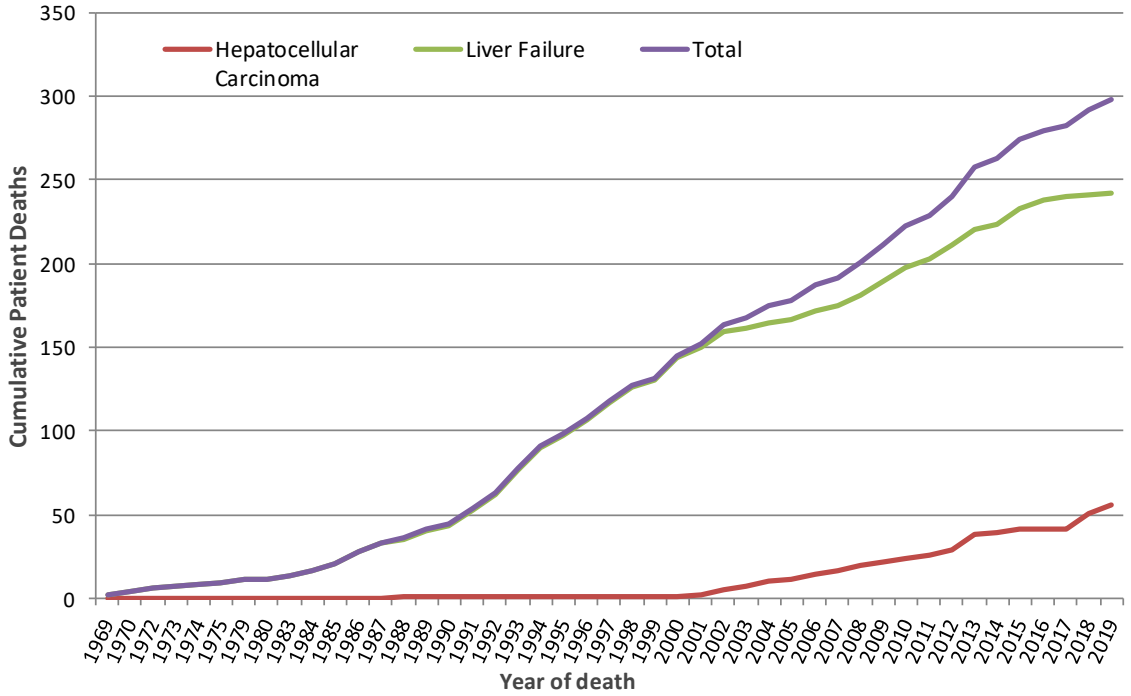
Cause of Death	Haemophilia A			Haemophilia B		
	Severe	Non-Severe	Total	Severe	Non-Severe	Total
Accident	-	1	1	-	-	-
Carcinoma	1	11	12	-	-	-
Cerebral haemorrhage	2	4	6	1	-	1
COAD	-	1	1	-	-	-
Haemorrhage (misc)	2	-	2	-	-	-
Hepatocellular Carcinoma	3	1	4	-	-	-
Infection (Bacterial)	-	1	1	-	1	1
Ischaemic Heart Disease	1	1	2	-	1	1
Ruptured Aorta (Peripheral vascular disease)	-	1	1	-	-	-
Suicide	-	1	1	-	-	-
Unknown	2	25	27	-	4	4
Totals	**11**	**47**	**58**	**1**	**6**	**7**

Tables 35 & 36 (overleaf) show the causes of death amongst people with haemophilia A and B (including carriers), broken down by severity (table 35) and for other bleeding disorders (table 36) during 2019/20. At present, it can be ascertained who has died from the NHS spine but the only source of cause of death data is from haemophilia centres themselves. All causes of death should be reported to the database, where this is known. An application to NHS digital to renew the contract to receive death certification data has been submitted.

Table 36 Causes of death in other coagulation defects between April 2019 & March 2020

Coagulation Defect	Cause of Death	Total
F.V deficiency	Unknown	1
F.VII deficiency	Unknown	7
F.X deficiency	Unknown	4
F.XI Deficiency	ARDS	1
	Carcinoma	3
	COAD	1
	COVID-19	1
	Infection (Bacterial)	5
	Ischaemic Heart Disease	2
	Liver Failure	1
	Suicide	1
	Unknown	22
Dysfibrinogenemia	Cerebral haemorrhage	1
	Unknown	2
Co-inherited diagnoses	Unknown	4
Haemophilia A with Liver Transplant	Hepatocellular Carcinoma	1
	Unknown	2
Acquired Haemophilia A	ARDS	2
	Carcinoma	2
	Cerebral haemorrhage	1
	COAD	2
	COVID-19	1
	Dementia/Alzheimer's disease	2
	Haemorrhage (misc)	3
	Infection (Bacterial)	14
	Intestinal Obstruction	1
	Ischaemic Heart Disease	5
	Unknown	50
Acquired von Willebrand Disease	Infection (Bacterial)	1
	Unknown	7
Acquired Deficiency (other)	Unknown	1
Bernard Soulier	Unknown	1
Glanzmann's Thrombasthenia	COAD	1
Other platelet defects	Benign Tumour	1
	Infection (Bacterial)	2
	Unknown	14
Miscellaneous	Carcinoma	1
	Ischaemic Heart Disease	1
	Unknown	4
Unclassified bleeding disorder	COVID-19	1
	Ischaemic Heart Disease	1
	Unknown	6
von Willebrand disease	Accident	1
	Carcinoma	5
	Cerebral haemorrhage	1
	Dementia/Alzheimer's disease	1
	Epilepsy	1
	Haemorrhage (Misc)	1
	Infection (Bacterial)	2
	Liver Failure	1
	Suicide	1
	Unknown	55
Probable von Willebrand disease	Unknown	1
	Total	**254**

Figure 23 Cumulative incidence chart of deaths from hepatocellular carcinoma or liver failure in people with bleeding disorders in the UK 1969 - 2019



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

Year	Hepatocellular Carcinoma	Liver Failure	Total
1998	0	9	9
1999	0	4	4
2000	0	14	14
2001	1	6	7
2002	3	9	12
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	9	1	10
2019	5	1	6
Total	**56**	**242**	**298**

Figure 23 (previous page): This shows deaths directly attributable to liver disease.

The above 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 but was not listed as the primary cause.

This appears to show some levelling-off of deaths from hepatocellular failure. This may be a reporting artefact in that the NHD has not received death certification data from NHS Digital for six years, although reports of death are collected directly from the haemophilia centres. However, as HCV has now been eradicated from almost all surviving patients, one would expect a reduction in the incidence of hepatocellular carcinoma (HCC), which declines dramatically after viral eradication, even in the presence of ongoing cirrhosis. There may be a delay before a further reduction in deaths from hepatocellular failure is seen since 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 for those with early cirrhosis or less advanced liver disease and they should not go on to develop advanced cirrhosis or die from complications of HCV in future.

Table 37 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	660	295	1885	2840
	Dead	147	91	556	794
	Total	807	386	2441	3634
Sex	M	767	304	2021	3092
	F	40	82	420	542
Current age band of living 'at risk' patients	0-19	0	0	0	0
	20-39	271	106	576	953
	40-59	271	117	750	1138
	60-79	111	64	474	649
	80+	n=1-5	8	85	100
	Not known	0	0	0	0

These data were last updated on 30/12/2019
**Not updated by UKHCDO*

Table 37: This summary of vCJD surveillance is sent to Public Health England every six months. 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. Patients 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. Patients identified as at risk 1990-2001 via 1990-2001 NHD treatment records but not via risk assessment exercise.

Figure 24 Total number of people with haemophilia A, haemophilia B or von Willebrand disease treated by UK haemophilia centres

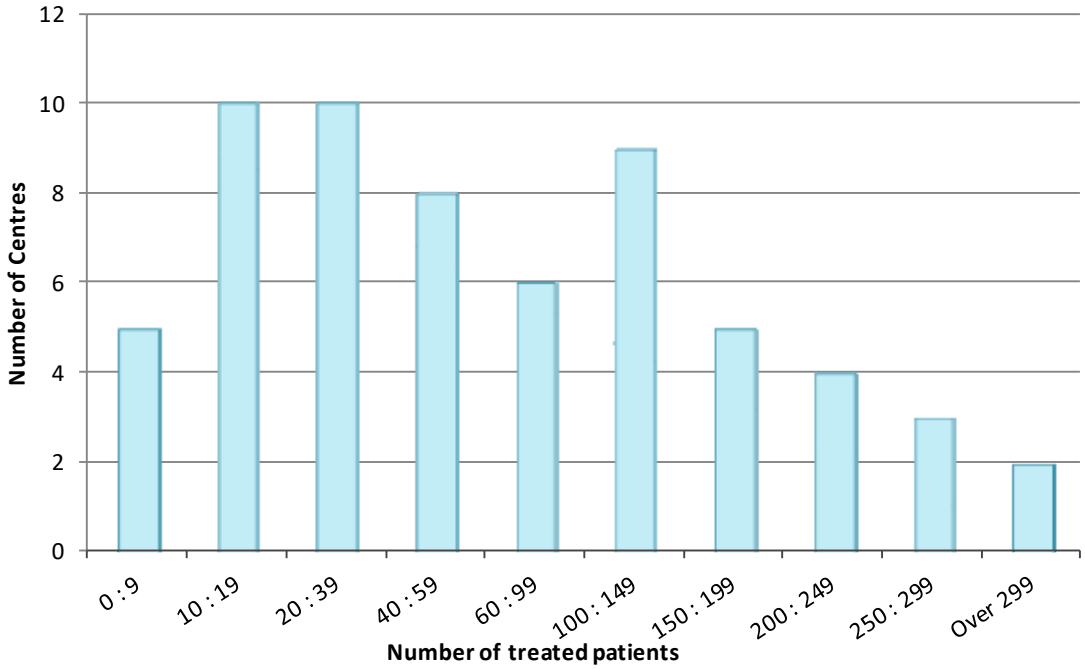
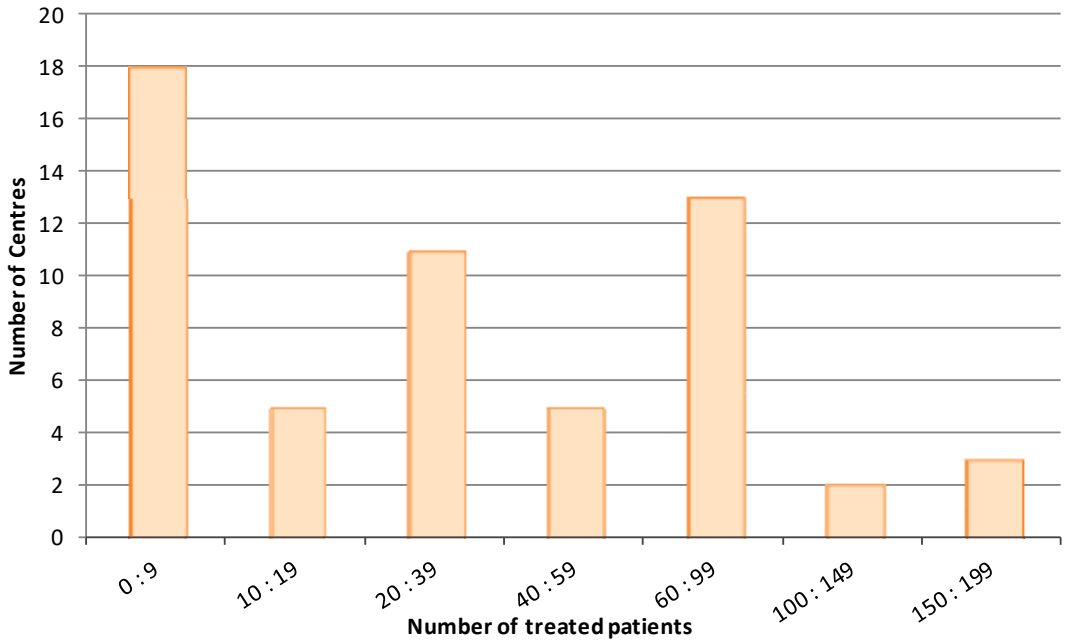


Figure 25 Total number of people with severe haemophilia A and haemophilia B treated by UK haemophilia centres



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

Appendix 2: Participating Centres

Centre Name	
Aberdeen	Leicester
Abergavenny	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
Lancaster	Wolverhampton
Leeds	York

3. Haemtrack Annual Report for the calendar year 2019

Introduction

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

Haemtrack is used by patients 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 patients also use home therapy. Both haemophilia centres and patients vary in their reporting compliance with Haemtrack and so the quality of individual patient self-reported data varies and the proportion of patients using the system also varies from centre to centre. In general, data quality is improving and the proportion of patients using the system is increasing.

Our aim is that Haemtrack should become a routine part of home-therapy management and a valuable tool for the review and optimisation of home-therapy and for patient education. For that to happen, compliance will have to improve and be reinforced by Health Care Professionals (HCP's) reviewing Haemtrack records with patients in clinic and checking the data for accuracy before downloading into Haemophilia Clinical Information System (HCIS), where it should be checked by Health care professionals (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 patients. It is important to demonstrate to the patient, 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 has come 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 more expensive new treatments such as Hemlibra® and EHL-IX. NHS England require hard proof that these drugs are cost effective in normal use and that they improve outcome.

For that reason, it is necessary to be able to demonstrate that the use of resources is being closely monitored and the way in which these resources are used can be accounted for. Patient-reported data, such as Haemtrack, is an important element of this and so it is important that centres take steps to obtain more complete data from a higher proportion of their patients. This may require significant effort and may also have staffing implications at a centre level, which will have to be addressed but which could be funded from the CQUIN budget or as part of the forthcoming service review.

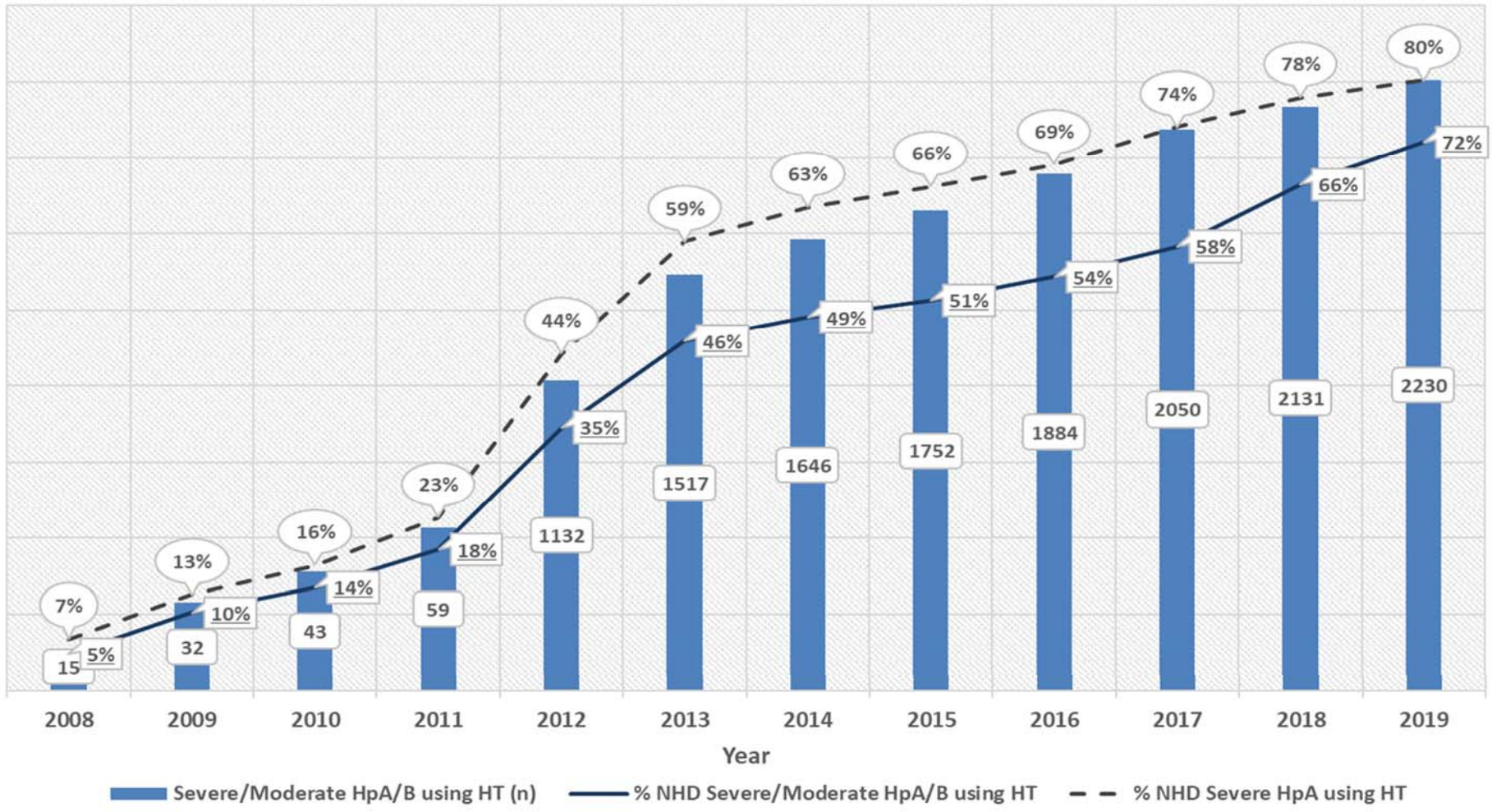
Section 1: Patients' Haemtrack Usage Analysis

1.1 Overall

Figure 1 presents an overview of severe and moderate patients with haemophilia A or haemophilia B using Haemtrack from 2008 to 2019. The blue columns give the numbers of patients using 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 slower continued growth in usage particularly since NHSE have made access to EHL-VIII and IX and Hemlibra conditional on Haemtrack reporting compliance. Figure 1 also reveals that there has been a gradual rise in the rate of recruitment, especially in severe haemophilia A cohort.

Haemtrack is also used for rarer bleeding disorders requiring home therapy, such as VWD and factor XIII deficiency (not shown).

Figure 1 Number of patients using Haemtrack and recruitment rate, 2008-2019



1.2 Haemtrack usage analysis at centre level - patients with severe Haemophilia

Use of Haemtrack has increased at a rapid rate in recent years and most Comprehensive Care Centres (CCCs) use Haemtrack to some degree, though far fewer Haemophilia Centres (HCs). This may relate to staffing issues and perhaps a lower degree of engagement in HCs who in some cases have only have a few patients suitable for the system.

Figures 2 and 3 display the proportion of patients with severe haemophilia A/B using Haemtrack in each CCC (Figure 2) and HC (Figure 3). Recruitment is a little better in CCCs than in HCs. The centre is identified with number of severe haemophilia and B patients treated in parenthesis. The blue bars illustrate the proportion (%) of those patients using Haemtrack in 2019.

Figure 2 Comparison of recruitment to Haemtrack by centre for patients with severe haemophilia A/B: Comprehensive Care Centres (CCCs) in 2019

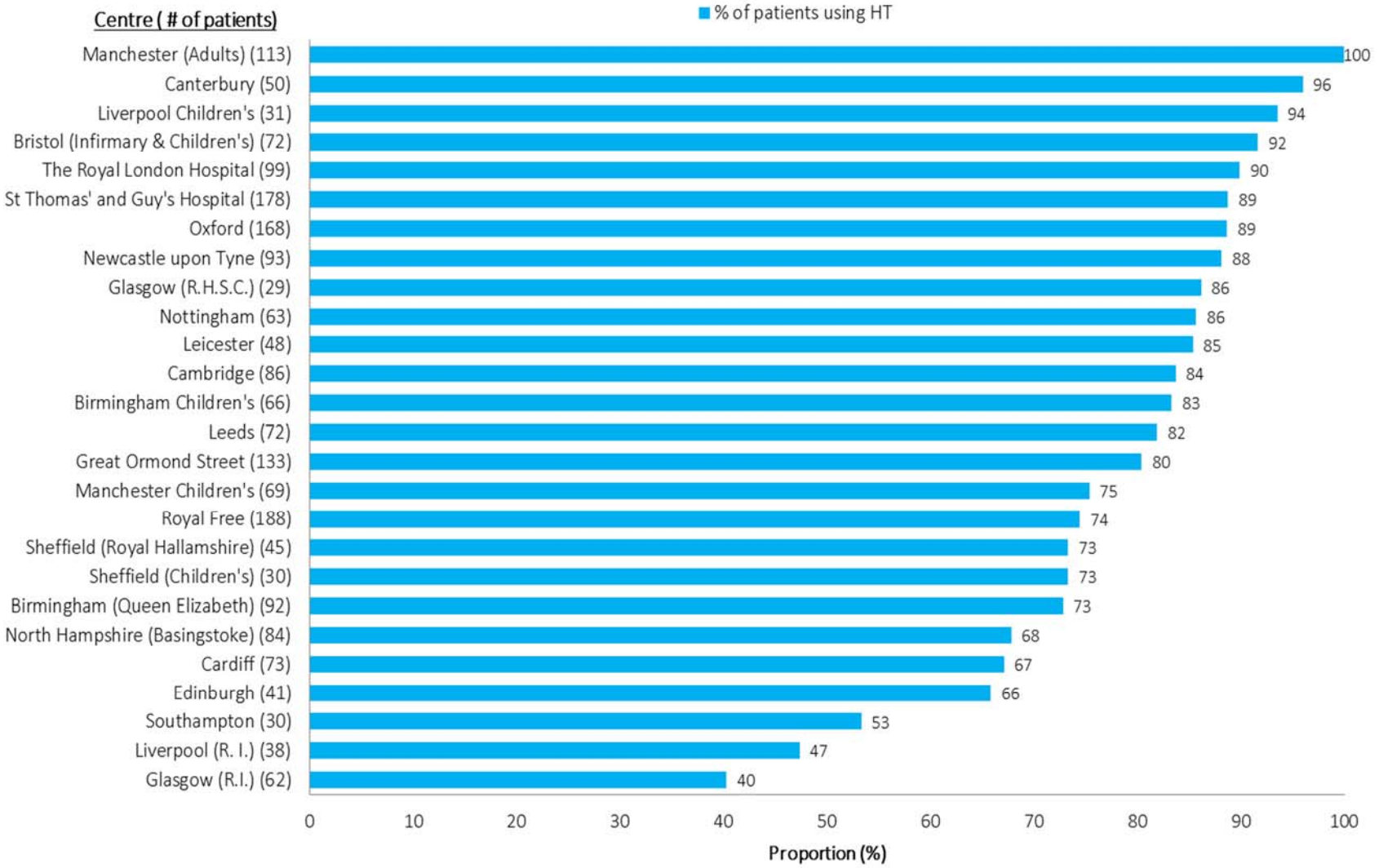
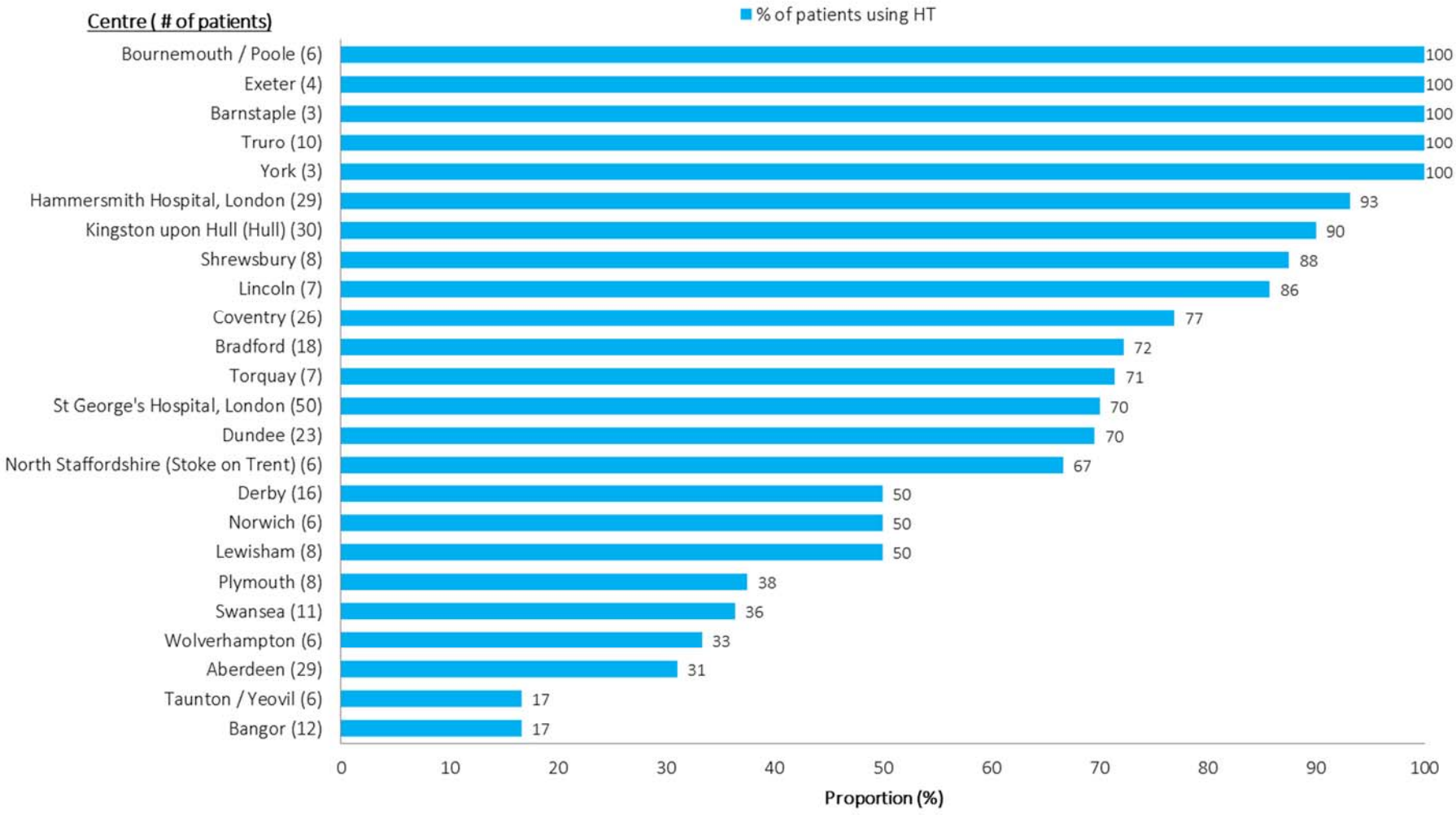


Figure 3 Comparison of recruitment to Haemtrack by centre for patients with severe haemophilia A/B: Haemophilia Centres (HCs) in 2019



Compliance with record keeping amongst patients using Haemtrack also varied considerably. For the purposes of this report, compliance is estimated by comparison of the patient's annual product usage reported through Haemtrack as a proportion of the factor issued to the patient, as reported quarterly to the NHD. Good compliance has been arbitrarily defined as Haemtrack reporting of use of >75% of replacement issued by the centre.

Figure 4 and 5 exhibit the overall compliance by severe haemophilia A patients for CCCs and HCs respectively. The compliance value closer to 100 indicates better usage compliance. The figures show the mean (diamond), median (vertical line), interquartile range (bar) and range (whiskers) compliance.

Compliance has improved considerably in recent years, both in CCCs and HCs, and is generally good but requires constant checking and follow up with patients to maintain. However, compliant Haemtrack data, reviewed with the patient in clinic, is a very valuable tool to use in optimising prophylaxis and reinforcing drug compliance.

Figure 4 Overall compliance in patients with severe haemophilia A, by Comprehensive Care Centre

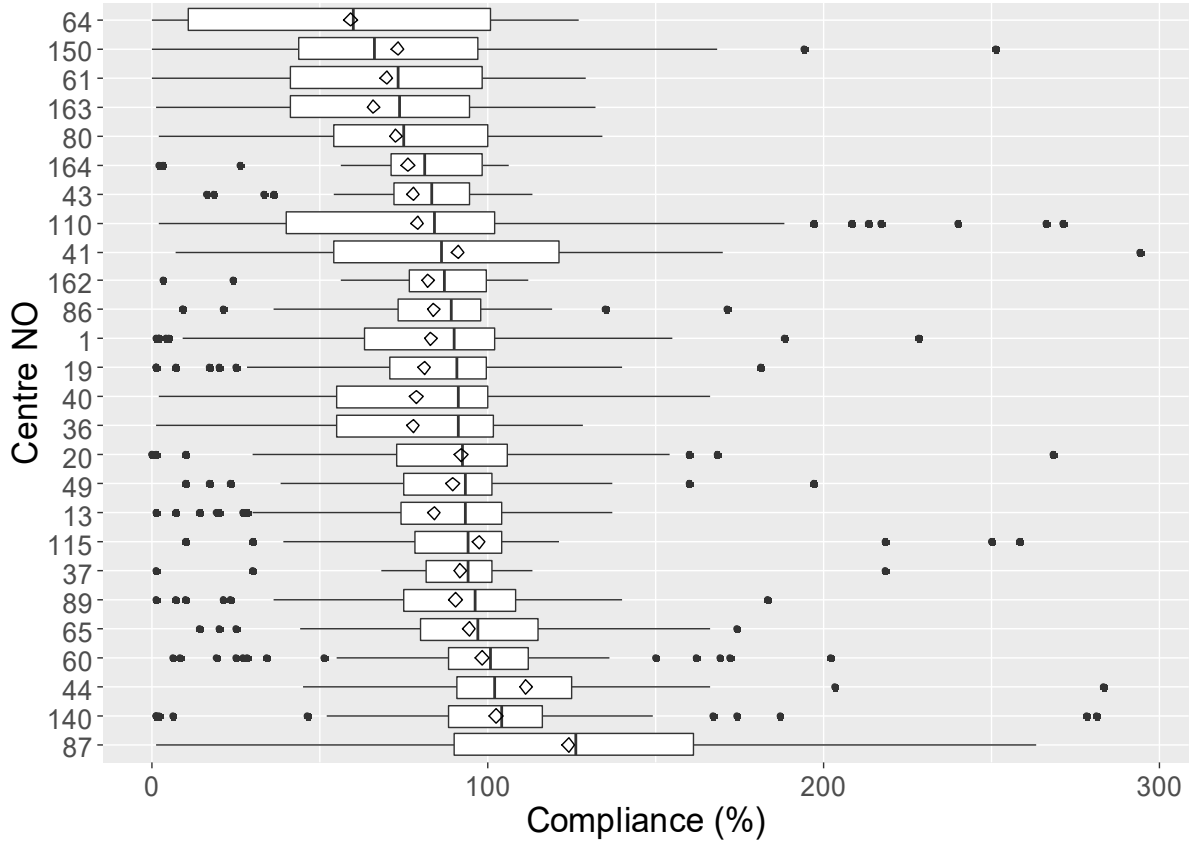
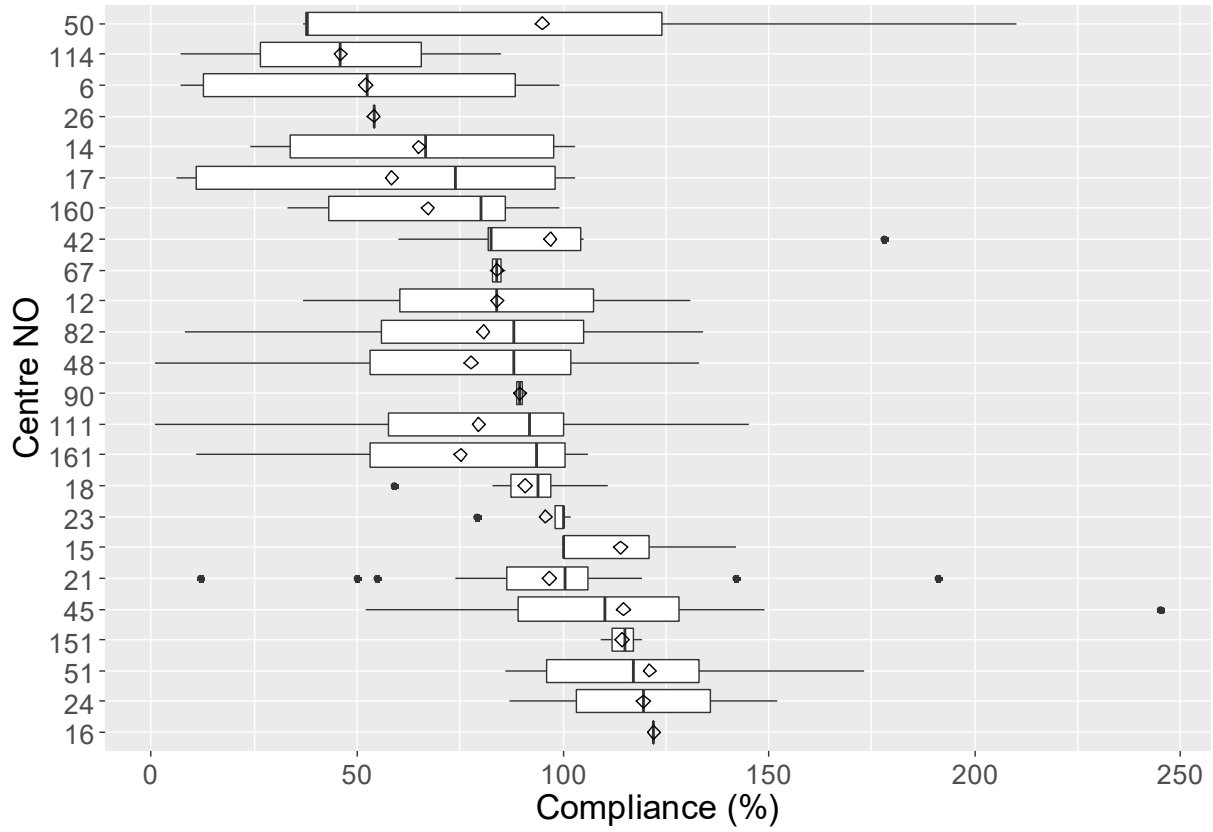


Figure 5 Overall compliance in patients with severe haemophilia A, by Haemophilia Centre



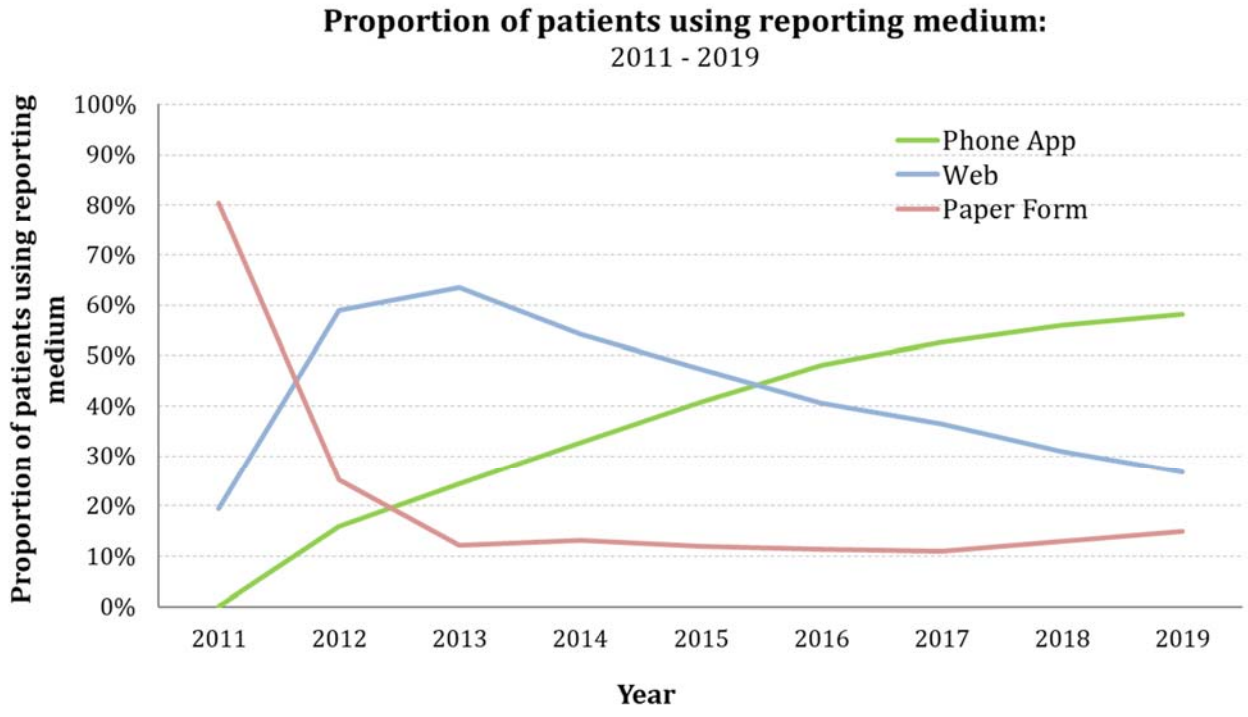
Section 2: Patients' Reporting Analysis

2.1 Patients' Reporting Medium

Figure 6 shows the proportion of Haemtrack users using different reporting methods between 2011 and 2019. This shows an initial rapid uptake of the use of the web application (PC) 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 even though almost all patients have a smart phone they could use for Haemtrack. 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 patients using paper, but some centres still have most of their patients reporting on paper even though this creates more work for centre staff themselves. The number of patients 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 data-reconciliation. More recently, there seems to be a considerable increased in checking at centre level since there are far fewer obvious errors.

We hope and expect that the use of a phone-app for Haemtrack will continue to increase as we introduce the web-based Haemtrack 2 phone-app. Although this requires internet access, it can be used on any smart phone and will be much easier for MDSAS to maintain.

Figure 6 Change in the use of different Haemtrack Reporting Media: 2011- 2019



This is further analysed in Figure 7, which breaks down the interval between treatment and reporting by the reporting method used (smartphone apps, web and paper). Use of phone apps is associated

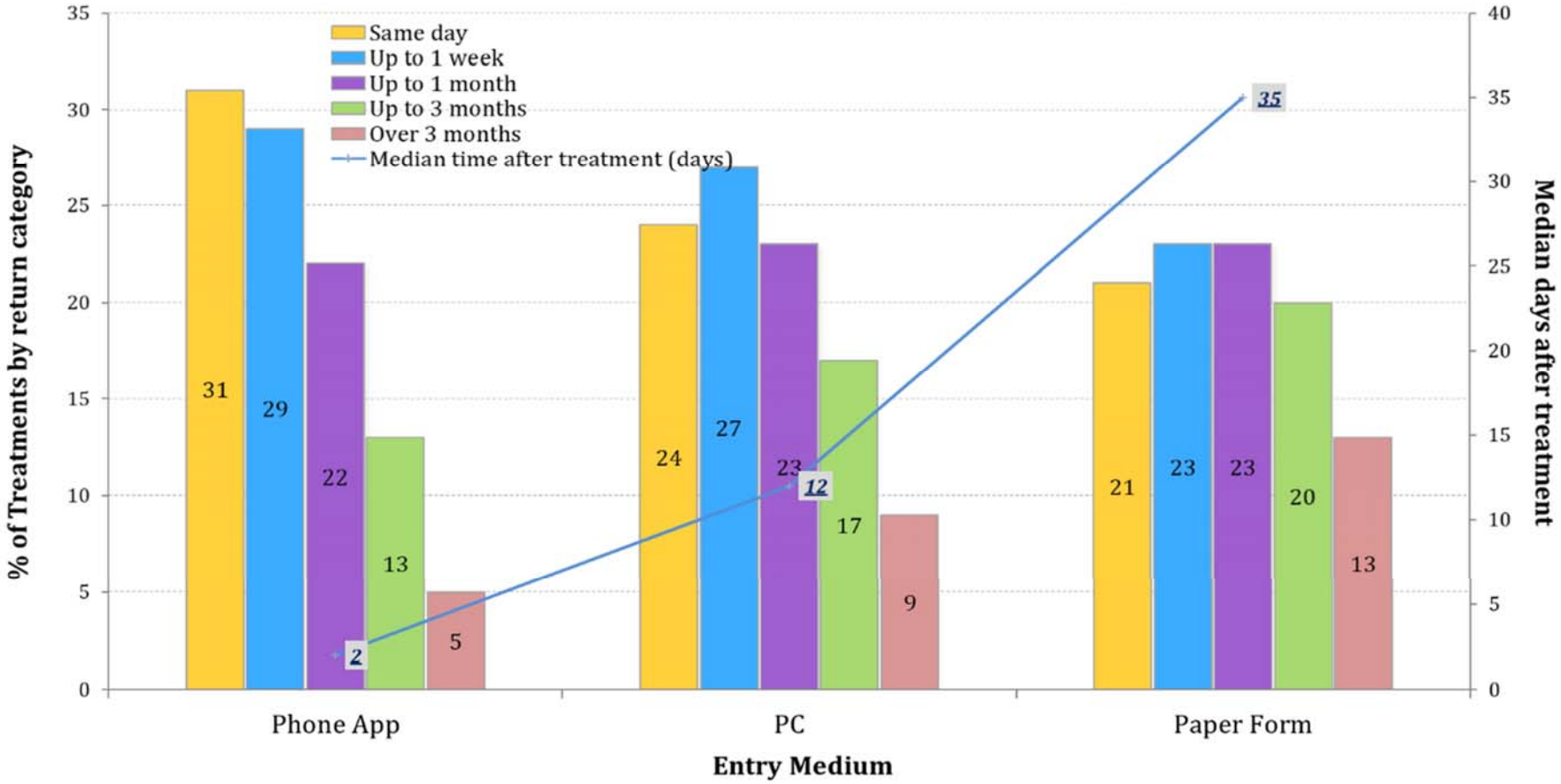
with the most rapid reporting, with 30% of data being recorded on the day of treatment and a further 29% within a week. In contrast, 24% of treatments were reported the same day and a further 27% within a week using the web. Most data submitted on paper was reported after an interval of over one month, either by post or at the next review clinic. Data reported by phone app was returned after a median of only 2 days, whereas paper-recorded data was reported after a median of 35 days with the web being intermediate. There is no difference in the median age of patients using the paper form and web, while the patients using phone app are younger than those two groups, the median age being 24, 31 and 31 years for phone app, web and paper reporters, respectively.

We are actively promoting the use of Haemtrack 2, which is web based and can be used on any smartphone or PC (or Mac), in preference to existing android and i-phone apps because we believe that the data are not only available to centres more quickly but are likely to be more accurate.

Haemtrack 2 has been launched in 2019 and patients are slowly changing to this. Being completely web-based, it may be used on any smartphone or personal computer and will synch automatically but is dependent on having a Wi-Fi connection. This version is also easier to use than previous versions.

We have extended the use of Haemtrack to inpatient use (data entered by centre staff) so that it will provide a complete treatment record.

Figure 7 Haemtrack Reporting Delay by Reporting Medium 2019



4. Data Management Working Party

Membership

Chair:	Professor Peter Collins
Commissioner representative:	Will Horsley
Co-Director of the National Haemophilia Database:	Professor Charles Hay
Co-Director of the National Haemophilia Database:	Professor Pratima Chowdary
Data Managers' Forum representative:	Lynne Dewhurst
Haemophilia Nurses Association representative:	Emma Franklin
Haemophilia Physiotherapists Group representative:	David Stephensen
Haemophilia Society representative:	Role open at present
MDSAS representative:	Dr Rob Hollingsworth
Patient representatives:	Barry Flynn
	Paul Sartain

Representatives of Northern Ireland, Scotland and Wales:

Northern Ireland	Dr Gary Benson
Scotland	Dr Elizabeth Chalmers
Wales	Professor Peter Collins

UKHCDO Working Party Chairs:

Co-morbidities Working Party	Dr Susie Shapiro
Genetics Working Party	Dr Keith Gomez
Inhibitor Working Party	Drs Dan Hart and Charles Percy
Musculoskeletal Working Party	Professor Pratima Chowdary
Paediatric Working Party	Dr Elizabeth Chalmers
Peer Review Working Party	Dr John Hanley
Von Willebrand Working Party	Professor Mike Laffan
Unclassified Bleeding Disorder Working Party	Dr William Thomas

UKHCDO Executive Committee:

Chair	Dr Ri Liesner
Secretary	Dr Kate Talks
Treasurer	Dr Rachel Rayment

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

Working Party Secretary	Lynne Dewhurst
	Ben Palmer
	Dr Hua Xiang

Meetings

The UKHCDO Data Management Working Party (DMWP) met on 24th April 2020 (virtual) and 17th Sept 2019 (virtual). The terms of reference for the Working Party are available on the UKHCDO website and have been reviewed.

The DMWP oversees data collection and analysis of patients 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 patients and revises this as necessary. Any member of UKHCDO can suggest changes to the data that are collected and these will be considered by the DMWP. Recently the way that platelet disorders are recorded has been updated. NHD has started to collect limited information on gene therapy.

Examples of current UKHCDO projects supported by NHD are:

The Acquired Haemophilia A registry
Real world experience of Emicizumab for people with and without inhibitors
Immune Tolerance Induction registry
Enhanced half-life factor VIII and IX registry
Mortality in severe haemophilia

The DMWP and NHD are ensuring that the Infected Blood Inquiry has full access to the information held by the NHD. In June 2020 UKHCDO received a rule 9 request from the Infected Blood Inquiry that asked for a number of statistical analyses to be reported. NHD staff have worked with UKHCDO to prepare the reports. This work is ongoing at present.

Haemtrack

Commissioners for England and the devolved countries of the UK continue to encourage the use of Haemtrack as a means of capturing individual patient 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 group is being established to review the current version of Haemtrack and recommend whether any updates in functionality are required.

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 patients. The system functions for all licensed brand of factor VIII and factor IX.

UKHCDO would like to thank many individuals involved in the work of the NHD. Professor Hay and Professor Pratima Chowdary are the clinical co-directors of NHD working on behalf of UKHCDO.

The following people work for the National Haemophilia Database and have been invaluable in their commitment to collecting and analysing the data on our behalf. Their role in supporting the aims of the Infected Blood Inquiry has been especially important.

Katie Allen
Liz Ardern
Lynne Dewhurst
Mike Grove
Rachel Lockwood
Andrew McNally
Ben Palmer
Sarah Rooney
Tom Sharpe
Hua Xiang

We also thank Rob Hollingsworth and MDSAS for their continued support and maintenance of our national information systems.

We also wish to acknowledge all the important work done at the Centre level and for the support of all the patients for supporting this important work.

Professor Peter Collins,
Chair UKHCDO Data Management Working Party

October 2020

5. Data Analysis Group

Membership

Co-Chair (Chair of Data Management Working Party)	Professor Peter Collins
Co-Chair (Director of NHD)	Professor Charles Hay
User representatives:	Dr Ryan Cheal Paul Sartain
UKHCDO members:	Dr Elizabeth Chalmers Professor Pratima Chowdary Dr Dan Hart Dr Ri Liesner Dr Susie Shapiro Dr Kate Talks
Haemophilia Nurses and Physiotherapy representatives:	Simon Fletcher Dr David Stephensen
National Haemophilia Database:	Lynne Dewhurst Ben Palmer Dr Martin Scott Dr Hua Xiang Andrew McNally

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 and meeting last on average 60-90 mins.

Requests for analyses are submitted on a standardised form. This form is available from NHD. The DAG particularly welcomes applications from UKHCDO working parties. 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 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.

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.

All reports are made available to UKHCDO members through the UKHCDO website.

The DAG leads an investigator-led proposal to Roche/Chugai to analyse data held on the NHD relating to the introduction of Emicizumab in both the inhibitor and non-inhibitor groups.

Requests for data analyses have been submitted by individual members of UKHCDO, UKHCDO working parties, Haemophilia physiotherapy group, researchers external to UKHCDO, UK Haemophilia Society, NHS England and pharmaceutical companies.

The DAG is open to new members from UKHCDO and anyone interested should contact Charlie Hay and Peter Collins.

Prof Peter Collins,
Chair UKHCDO Data Management Working Party

Prof Charles RM Hay,
Director NHD

October 2020

6. Co-Morbidities Working Party

Membership

Chair	Dr Susie Shapiro, Oxford
UKHCDO representatives:	Dr Gary Benson, Belfast Dr Gillian Evans, Canterbury Prof Charles Hay, Manchester Prof Mike Makris, EUHASS Dr Rhona Maclean, Sheffield Dr Sarah Mangles, Basingstoke
Haemophilia Nurses Association Representative:	Cathy Harrison, Sheffield

Remit

To review reported adverse events of special interest potentially related to products (including thrombotic events, mortality, allergy): to agree consensus on severity and outcome of event and evaluate any potential relationship to treatment (New remit – Jan 2020)

To consider comorbidity issues in patients with bleeding disorders within the UK and review any unmet need with respect to data collection, guidelines and patient 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 patients 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

Since January 2020 we have held scheduled monthly online video meetings in order to review new adverse events of special interest related to any product (as well as reviewing historical events reported with Emicizumab); and to agree and progress further Work Plan.

Activities

Adverse events of special interest. Agreed process for reviewing adverse events of special interest, including SOP and new forms to request additional information via NHD. The decision with regards to causality and relationship to product requires minimum of 3 members of the group to be present. All relevant historic reported events on Emicizumab have been reviewed and the group is up-to-date with newly reported events (any product). The consensus decision of reported events is included in this annual report. In the future the plan will be that any serious adverse events will be fed back rapidly to UKHCDO membership, and otherwise a regular report will be sent round, frequency dependent on number of events reported.

Cardiovascular events and bleeding disorders. The group agreed to perform and write-up a systematic review on cardiovascular events in patients with bleeding disorders (prevalence and treatment) in order to highlight areas for future work. This is currently underway.

Dr Susie Shapiro,
Chair, Co-Morbidities Working Party
October 2020

7. Genetics Working Party

Membership

Keith Gomez	Chair
Nicola Curry	
Gerry Dolan (stood down March 2020)	
Steve Keeney (stood down March 2020)	Representing Genetics Laboratory Network
Mike Laffan	
Megan Sutherland	Representing Genetics Laboratory Network
Kate Talks (joined Sept 2020)	
Jayashree Motwani (joined Sept 2020)	
Gavin Ling (joined Sept 2020)	

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 patients with heritable haemostatic disorders and for results to be recorded on NHD

Meetings and main work streams

The working party last met by teleconference in October 2019. The 3 year term came to an end at the March advisory committee meeting and was reformed with new members joining following the advisory committee meeting in September 2020

There are three main work streams at the moment.

Reconfiguration of Genetic Services by NHS England

The four Genomics Laboratory Hubs (GLH) providing testing for haemostatic disorders under the national contract in England, at no charge to NHS requestors, are:

- Wessex and West Midlands GLH (led by Oxford)
- London South GLH (led by St Thomas')
- North West GLH (led by Manchester)
- Yorkshire and North East GLH (led by Newcastle/Sheffield).

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/

Oversight of the service is provided through Non-Malignant Haematology Genomics workshops that met in January and July 2020. The transition period for testing to move to this framework commenced on April 1st 2020. In the last few months most hubs have been validating their panels which has been delayed by redeployment of staff away from genomic testing during the pandemic.

Consent

A revised information sheet and consent form for genomic testing to cover bleeding and thrombotic disorders is now available at http://www.ukhcdo.org/wp-content/uploads/2020/02/Genomics-Information-Sheet-and-Consent-Form_02-2020.docx

A UK working group for discussion of consent in children was being formed prior to the pandemic and work is expected to continue on this next year.

Creation of new category of Heritable Platelet Disorders on NHD

In conjunction with the Data Mangement Working Party the NHD has been revised with a new category of Heritable Platelet Disorder to replace the following categories: Platelet defects (misc), Glanzmann thrombasthenia, Bernard Soulier Syndrome, Severe Platelet Disorders – Other, Heritable Platelet Function Disorder and Platelet-type Pseudo von Willebrand Disease. The new category went live on 21st September.

Other work streams

The working party has updated factsheets provided by Health Education England on haemophilia and von Willebrand Disease. These are aimed at non-specialists, predominantly in primary care and can be accessed at https://www.genomicseducation.hee.nhs.uk/news/new-conditions-factsheets/.

The table shows the capture of genetic diagnosis for haemophilia in the NHD. Having seen annual increases in previous years the numbers are relatively unchanged compared with 2019.

Dr Keith Gomez,
Chair, Genetics Working Party
October 2020

Number of patients with a genetic diagnosis by region (based on patient's postcode and not registered centre)

Diagnosis	Region	Patients with a genetic diagnosis (% of registered patients)									
		Factor VIII / IX level (iu/dl)									
		< 1		1 & 5		> 5		40+		N/K	
		All Variants	Validated Variants	All Variants	Validated Variants	All Variants	Validated Variants	All Variants	Validated Variants	All Variants	Validated Variants
Haemophilia A	East Midlands	88 (49.4%)	68 (38.2%)	9 (15.3%)	8 (13.6%)	85 (25.8%)	66 (20.1%)	21 (11.8%)	10 (5.6%)	1 (12.5%)	1 (12.5%)
	East of England	27 (18.4%)	26 (17.7%)	14 (16.1%)	9 (10.3%)	41 (10.3%)	36 (9.1%)	4 (2.5%)	3 (1.9%)	0 (0.0%)	0 (0.0%)
	London	109 (30.4%)	107 (29.9%)	30 (36.6%)	28 (34.1%)	93 (20.8%)	90 (20.1%)	11 (6.7%)	9 (5.5%)	0 (0.0%)	0 (0.0%)
	North East	10 (15.9%)	8 (12.7%)	8 (20.5%)	8 (20.5%)	42 (29.0%)	37 (25.5%)	23 (16.8%)	20 (14.6%)	0 (0.0%)	0 (0.0%)
	North West	64 (29.0%)	59 (26.7%)	30 (35.7%)	26 (31.0%)	103 (27.3%)	86 (22.8%)	43 (28.9%)	24 (16.1%)	1 (14.3%)	1 (14.3%)
	Northern Ireland	42 (56.0%)	42 (56.0%)	18 (56.3%)	18 (56.3%)	64 (41.8%)	64 (41.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Scotland East	7 (8.8%)	7 (8.8%)	4 (10.8%)	4 (10.8%)	19 (10.5%)	16 (8.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Scotland West	2 (3.1%)	0 (0.0%)	2 (6.3%)	2 (6.3%)	3 (2.2%)	3 (2.2%)	3 (2.3%)	3 (2.3%)	0 (0.0%)	0 (0.0%)
	South East	131 (40.4%)	103 (31.8%)	37 (43.5%)	30 (35.3%)	131 (21.5%)	88 (14.4%)	51 (23.8%)	19 (8.9%)	0 (0.0%)	0 (0.0%)
	South West	39 (26.4%)	36 (24.3%)	8 (11.9%)	2 (3.0%)	37 (11.0%)	21 (6.3%)	13 (16.5%)	5 (6.3%)	0 (0.0%)	0 (0.0%)
	Wales	36 (40.0%)	34 (37.8%)	9 (31.0%)	8 (27.6%)	39 (19.6%)	38 (19.1%)	4 (6.9%)	4 (6.9%)	0 (0.0%)	0 (0.0%)
	West Midlands	39 (21.9%)	37 (20.8%)	5 (8.2%)	4 (6.6%)	15 (5.8%)	13 (5.0%)	2 (1.9%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
	Yorkshire and the Humber	22 (14.0%)	19 (12.1%)	4 (3.7%)	3 (2.8%)	32 (8.8%)	20 (5.5%)	13 (8.7%)	8 (5.4%)	0 (0.0%)	0 (0.0%)
Haemophilia A Total		**616 (29.6%)**	**546 (26.2%)**	**178 (22.2%)**	**150 (18.7%)**	**704 (17.9%)**	**578 (14.7%)**	**188 (11.2%)**	**106 (6.3%)**	**2 (2.8%)**	**2 (2.8%)**
Haemophilia B	East Midlands	10 (33.3%)	8 (26.7%)	4 (22.2%)	1 (5.6%)	7 (12.7%)	6 (10.9%)	2 (9.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	East of England	0 (0.0%)	0 (0.0%)	3 (10.7%)	2 (7.1%)	2 (2.5%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	London	8 (12.1%)	3 (4.5%)	6 (11.1%)	4 (7.4%)	9 (7.1%)	7 (5.6%)	2 (4.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)
	North East	3 (21.4%)	3 (21.4%)	1 (7.1%)	1 (7.1%)	3 (9.7%)	1 (3.2%)	3 (8.1%)	1 (2.7%)	0 (0.0%)	0 (0.0%)
	North West	13 (37.1%)	9 (25.7%)	14 (35.9%)	14 (35.9%)	18 (27.7%)	13 (20.0%)	18 (38.3%)	10 (21.3%)	0 (0.0%)	0 (0.0%)
	Northern Ireland	2 (25.0%)	2 (25.0%)	1 (25.0%)	1 (25.0%)	4 (22.2%)	4 (22.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Scotland East	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Scotland West	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	South East	21 (33.3%)	10 (15.9%)	15 (26.8%)	6 (10.7%)	24 (20.2%)	11 (9.2%)	13 (28.9%)	3 (6.7%)	0 (0.0%)	0 (0.0%)
	South West	3 (15.8%)	1 (5.3%)	4 (20.0%)	2 (10.0%)	10 (13.7%)	6 (8.2%)	1 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Wales	4 (30.8%)	4 (30.8%)	12 (54.5%)	12 (54.5%)	11 (25.0%)	10 (22.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	West Midlands	8 (26.7%)	5 (16.7%)	6 (31.6%)	6 (31.6%)	2 (3.0%)	2 (3.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Yorkshire and the Humber	2 (7.7%)	2 (7.7%)	1 (3.8%)	0 (0.0%)	2 (3.9%)	2 (3.9%)	4 (13.3%)	3 (10.0%)	0 (0.0%)	0 (0.0%)
Haemophilia B Total		**74 (20.2%)**	**47 (12.8%)**	**67 (19.5%)**	**49 (14.3%)**	**92 (11.1%)**	**63 (7.6%)**	**43 (11.9%)**	**18 (5.0%)**	**0 (0.0%)**	**0 (0.0%)**

Patients registered with the NHD 2019/20
Haemophilia A includes females with FVIII deficiency & haemophilia A carriers.
Haemophilia B includes females with FIX deficiency, haemophilia B carriers, FIX Leyden & FIX Leyden carriers
Genetic variants entered on the NHD require a second-person entry as a validation check. This table shows all Genetic variants and validated entries separately by disease severity

8. Genetic Laboratory Network

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 13 laboratories, 12 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 on 28 November 2019 in Edinburgh and we held our first virtual meeting on 03 June 2020. The next meeting is scheduled to be another virtual meeting in November 2020.

Chair & Secretary

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

Current activities

1. *NHS England genetic laboratory re-designation exercise* In August 2018 the tenders for the provision of genetics services across England were awarded. 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 'Specialist Haematology' service, including the investigation of bleeding and thrombotic disorders, is to be provided by four entities. An expert group representing the four service providers and NHS England have agreed the content of relevant gene panels for Next Generation Sequencing investigation, including a 'Bleeding and Platelet Disorders' panel and a 'Thrombophilia' panel. This will represent a major change in genomic service configuration within England and was scheduled to "go-live" in April 2020. However due to current National budgetary NHS restrictions we are still awaiting National and Local agreement to implement.
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 has implemented an informal sample exchange scheme between members of the GLN for disorders and methodologies that are not provided for by UK NEQAS. All laboratories continue to participate in the inspection process cycle.
3. *National Haemophilia Database (NHD) Genetics Portal*: The NHD Genetics Portal allows members of the GLN to upload genetic variant data for patients they have

investigated into the patient's record on the NHD. The Genetics Portal is used by members of the GLN to see if a variant they have found has been reported by other centres, thereby providing evidence for pathogenicity calculations of genetic variation. During these searches the patient details are not shown. Members are also able to search for patients to confirm which centre they are registered at, and if a genetic variant has been reported, prior to contact for release of relevant details if appropriate (no further information regarding the variant is made available at this time).

4. *Bleeding Disorder Genetic Analysis Best Practice Guidelines*: The UK Best Practice Guidelines for genetic analysis of Haemophilia A, Haemophilia B and VWD are in the process of being reviewed and updated in accordance with the NHS England genomic test directory and associated changes in service re-designation (see item 1). The classification of genetic variation will also be considered and implemented in the guidelines. Working groups have been assigned to each of the guidelines to be produced – those for VWD, and a combined BPG for haemophilia A and B. In addition, a working group has been established to produce a BPG for the genetic investigation of rare bleeding disorders.

5. *UK NEQAS Genetics of Heritable Bleeding and Thrombotic Disorders scheme*: The UK NEQAS Genetics of Heritable Bleeding and Thrombotic Disorders EQA scheme was expanded in 2019 to include the analysis of heritable thrombotic disorders, in line with the published NHS England genomic test directory. The scheme now 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 new additional 'paper' exercises provide a clinical scenario and genetic variant for a patient 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. A further EQA requirement for the analysis of MLPA data has been identified by the GLN in response to UKAS findings. The UK NEQAS paper exercises are to be expanded from October 2020 to 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, a main focus this year has been on the approach to classification of rare or novel variants with reference to the current ACMG variant classification guidelines, and the sharing of this information throughout the network. With the increasing availability of service provision and gene panels for very rare heritable bleeding and thrombotic disorders, the sharing of knowledge and expertise will become an essential mechanism for the interpretation of previously uncharacterised genetic variants.

Megan Sutherland,
Chair, UKHCDO Genetic Laboratory Network
October 2020

9. Inhibitor Working Party now dissolved

Membership

Dr Dan Hart	Chair
Dr Kate Talks	Secretary

Prof Peter Collins
Dr Georgina Hall
Prof Charles Hay
Dr Ri Liesner
Prof Mike Makris
Ben Palmer
Dr Charles Percy
Dr Anne Riddell

The Inhibitor working party (IWP) met virtually in Q1 of 2020 to conclude this cycle of work under Dan Hart's chairmanship. The group was then dissolved and will be reconstituted with Charles Percy as chair.

Anne Riddell continued to facilitate communication with all Comprehensive care centre (CCC) laboratory chiefs, monitoring their new assay development and availability for Bethesda assays whilst on Emicizumab; chromogenic FVIII assays with human or bovine reagents and porcine FVIII (Obizur®) inhibitor assays. Upon request, this data repository remains available to colleagues, needing access to assays or technical advice. The direct communication between the IWP and CCC laboratory staff has been an important step forward in recent years as we enter a more challenging landscape of laboratory monitoring for different therapeutics. A collaborative project with NEQAS highlights the ongoing variability between comprehensive care centres in their standard inhibitor assay practices. This was recently accepted for publication by Haemophilia journal.[1] Ongoing dialogue between labs will be an important support to minimize further methodological variability as more assays emerge.

Acquired Haemophilia A enhanced data collection has concluded after 4 years of prospectively collected data. Analysis will commence in early 2021 after all patients have completed 12 months follow up. This will be overseen by Charles Percy and Dan Hart. A snapshot of Obizur® use in the first 18 months after NHS England commissioning approval is also underway in collaboration with NHS England.

Indications for Emicizumab continued to be a significant workstream. Georgina Hall and Liz Chalmers head the continuing prospective collection of Immune Tolerance Induction (ITI) data. Revised guidance for ITI has been agreed between the IWP and Paediatric Working party[2]. This revision of ITI guidance incorporates the option to use the bi-phenotypic antibody, Emicizumab, as a prophylaxis haemostatic agent to reduce bleeding rates and to facilitate low dose and reduced frequency of FVIII CFC for ITI in the majority of children. The consensus being FVIII ITI remains the gold standard for a newly detected inhibitor with an expectation that upon tolerisation FVIII concentrate would remain the preferred prophylaxis agent thereafter. For those failing ITI, Emicizumab would be the preferred prophylaxis agent.

I wish to thank all the working party and NHD staff for their hard work, support and enthusiasm during the last cycle of activity whilst I was chair. I wish Charles Percy well as he takes over as chair of this working party.

Publications

1 Factor VIII/IX Inhibitor Testing Practices in the United Kingdom: Results of a UKHCDO and UKNEQAS National Survey

Batty P, Riddell A, Kitchen S, Sardo Infirri S, Walker I, Woods T, Jennings I, Hart DP

Accepted for publication in Haemophilia

2 Immune tolerance induction in severe haemophilia A: A UKHCDO inhibitor and paediatric working party consensus update.

Hart DP, Alamelu J, Bhatnagar N, Biss T, Collins PW, Hall G, Hay CR Liesner R, Makris M, Mathias M, Motwani J, Palmer B, Payne J, Percy C, Richards M, Riddell A, Talks K, Tunstall O, Chalmers EA

Submitted for publication in Haemophilia

Dr Dan Hart
Outgoing Chair, Inhibitor Working Party
October 2020

10. Inhibitor Working Party reconstituted

The Inhibitor Working Party has recently been re-constituted with the following membership:

Membership

Dr Charles Percy	Chair
Dr John Grainger	
Dr Dan Hart	
Prof Mike Makris	
Dr Mary Mathias	
Ben Palmer	
Dr Anne Riddell	
Dr Kate Talks	

The group have yet to meet but a date is the process of being finalised. The initial priorities are to review and update relevant guidelines, particularly relating to the management of acquired coagulation inhibitors.

Dr Charles Percy
Incoming Chair, Inhibitor Working Party
October 2020

11. Laboratory Working Party

Membership

Dr Vincent Jenkins	Co-Chair
Dr Will Lester	Co-Chair

Dr Annette Bowyer
Clive Burgess
Prof Pratima Chowdary
Dr Elaine Gray
Dr Steve Kitchen
Paul Murphy
Sean Platton
Dr Anne Riddell

Activities

The main output of the working group has been the publication of two laboratory-based guidelines to address new treatment options for haemophilia. The group held one meeting this year 12/02/2020, although there has been e-mail correspondence between group members.

Publications. Gray E, Kitchen S, Bowyer A, Chowdary P, Jenkins PV, Murphy P, Platton S, Riddell A, Lester W. Laboratory measurement of factor replacement therapies in the treatment of congenital haemophilia: A United Kingdom Haemophilia Centre Doctors' Organisation guideline. Haemophilia. 2020 Jan;26(1):6-16. doi:10.1111/hae.13907

Jenkins PV, Bowyer A, Burgess C, Gray E, Kitchen S, Murphy P, Platton S, Riddell A, Chowdary P, Lester W. Laboratory coagulation tests and emicizumab treatment A United Kingdom Haemophilia Centre Doctors' Organisation guideline. Haemophilia. 2020 Jan;26(1):151-155. doi: 10.1111/hae.13903

Meeting attended: WHO meeting regarding Factor Product Specific Standards. Anne Riddell attended the meeting in November 2019 as a member of the Lab WP on behalf of the UKHCDO.

Items in progress

Guideline for the measurement of recombinant Porcine Factor VIII (Obizur) (Annette Bowyer Lead).

Laboratory Survey: A survey of current practice in haemophilia related testing (Annette Bowyer, Anne Riddell).

Planned scientific guideline or review

A requirement for updated guideline for detection and quantification of inhibitors to coagulation factors has been recognised by both the Lab WP and the Inhibitor WP.

Similarly update of VWF testing guidelines is required. Sean Platton has liaised with the BSH and it has been agreed there will be a joint approach between BSH and UKHCDO with input from the VWF WP. Sean Platton and Vince Jenkins to lead.

Other plans

To develop small practical educational meetings for coagulation laboratory scientists to complement existing meetings and to allow sharing of experience peer to peer. The aim is to reduce isolation and encourage best practice across the UK.

Dr Vincent Jenkins & Dr Will Lester
Co-Chairs, Laboratory Working Party
October 2020

12. Musculoskeletal Working Party

Membership

Dr Pratima Chowdary	Chair
Melanie Bladen	Great Ormond Street, Hospital
Mr Peter Briggs	Royal Victoria Infirmary, Newcastle
Dr Elizabeth Chalmers	Glasgow Children's
Mr Stephen Classey	St Thomas' Hospital, London
Dr Desmond Creagh	Royal Cornwall Hospital
Dr Gerry Dolan	St Thomas' Hospital, London
Prof Simon Frostick	Royal Liverpool University Hospital
Mr Nicholas Goddard	Royal Free Hospital, London
Dr John Hanley	Royal Victoria Infirmary, Newcastle
Dr Angela McKernan	Royal Derby Hospital
Paul McLaughlin	Royal Free Hospital, London
Dr David Stephensen	Kent & Canterbury
Angela Westoby	St James' University Hospital, Leeds
Anna Wells	North Hampshire Hospital, Basingstoke

The Musculoskeletal working party has met on one occasion and has undertaken one round of Delphi to establish standards for MSK care. The aim of the guidance is to Improve patient experience, improve clinical outcomes, improve equity of access to specialist services and Identify optimal service requirements.

The planned title is Musculoskeletal care in patients with Haemophilia and related bleeding disorders – Care standards and core outcomes: UKHCDO guideline.

The Delphi was suspended pending COVID 19 crisis and will be restarted in a few weeks. The new working party will start in April 2021.

Prof Pratima Chowdary
Chair, Musculoskeletal Working Party
October 2020

13. Paediatric Working Party

Membership

Dr Mary Mathias	Chair, London (GOSH)
Dr Jeanette Payne	Secretary, Sheffield
Dr Jayanthi Alamelu	London (Evelina)
Dr Neha Bhatnagar	Oxford
Dr Tina Biss	Newcastle
Dr Elizabeth Chalmers	Glasgow
Dr John Grainger	Manchester
Dr Simone Greene	Hull
Dr Anne Kelly	Addenbrookes
Dr Jayashree Motwani	Birmingham
Dr Mike Richards	Leeds (outgoing)
Dr Simone Stockley	Nottingham
Dr Oliver Tunstall	Bristol (outgoing)

The working party membership was renewed in October 2020.

Meetings

Since the last AGM the PWP has held 3 teleconference or virtual meetings.

Summary of activities

Immune Tolerance Induction (ITI) consensus update post emicizumab commissioning.

This was developed in conjunction with the Inhibitor Working Party and has now been submitted for publication to Haemophilia and will be available on the UKHCDO website.

ITI outcomes

ITI outcome data using the previous UKHCDO ITI protocol was presented at the UKHCDO Education meeting in 2018. Data collection was from 2015 to Dec 2019. This data is now being analysed but this will be time consuming due to presentation and need to data clarify.

Emicizumab PUP and MTP data

Given the delay in starting the NHD PUP registry data collection caused by the enquiry, the Chair asked the NHD to request a 'snap-shot' of data on use of emicizumab in children under 12 years with and without inhibitors. This has been collated by Liz Chalmers and will be submitted as an abstract for EAHAD 2021. No children under 4 months have received emicizumab. There is considerable centre variation in the use of emicizumab for non-inhibitor children.

A National Advisory Group/MDT

This has now been established 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.

Other projects

Data collection has inevitably been delayed by the COVID epidemic and prior to that by uncertainty around the NHD research database in terms of requirement for consent. We will now continue to pursue:

a. PUP registry- a template for data collection has been created within the NHD with the plan to ask for data to be collected every 3 months
b. Inhibitors in Haemophilia B.
c. Outcomes and prophylaxis in Moderate Haemophilia A and B.
d. Bleeding and treatment in children with rare coagulation disorders starting with severe FVII deficiency.

Dr Mary Mathias
Chair, Paediatric Working Party
October 2020

14. Von Willebrand Working Party

Membership

Prof Mike Laffan Chair

Anne Goodeve
Keith Gomez
Henry Watson
Carolyn Millar
Shapiro Susie
Thynn Thynn Yee
Vince Jenkins
Will Lester

The VWD working party has not met formally since the last AGM.

However, the WP has worked on the following projects:

1. The new registration process and forms for VWD has been implemented but remains under review. A recent request for the addition of VWD Type 1C (eg Vicenza) has been received. Implementation of rules to avoid nonsense entries remains.
2. The NHD have compiled lists of patients whose entries require review by the registering centre with a view to updating, reclassifying or removing. Some centres have large numbers and a stepwise plan has been drawn up.
3. Several members of the WP took part in the submission and resubmission of recombinant VWF to the CPAG via a NICE consultation process. This has now been approved.
4. The WP is awaiting the publication of ASH guidelines on Diagnosis and on Management of VWD before reviewing the need to update the UK guidelines or write a position paper in conjunction with the BSH Haemostasis and Thrombosis Working Party. The ASH guidelines are expected to be in press within a few weeks.

Prof Laffan is stepping down as chair of the WP and Dr Millar will be taking over following the AGM. The revised membership will also be announced.

Prof Mike Laffan,
Chair, Von Willebrand Working Party
October 2020

15. Peer Review Working Party

Membership

Dr John Hanley	Chair
Dr Julia Anderson	UKHCDO Member
Dr Gillian Evans	UKHCDO Member
Dr Lishel Horn	UKHCDO Member
Dr Ri Liesner	UKHCDO Member
Dr Rhona MacLean	UKHCDO Member
Dr Tim Nokes	UKHCDO Member
Anna Wells	Lead Physio HCPA
Sarah Bowman	Social Worker
Cathy Harrison	Chair HNA
Liz Carroll	CEO Haemophilia Society
Graham Knight	Patient Representative
Dr Kate Khair	Past Chair HNA
Dr Anne Yardumian	Peer Review Programme Clinical Lead
Rachael Blackburn	Assistant Director QRS

Since the 2019 AGM, the UKHCDO Peer Review programme has been completed. In total 37 sites were visited – all 28 Comprehensive Care Centre and 9 haemophilia centres. The Peer Review programme was a collaborative project with the Quality Review Service (QRS – formally the West Midlands Quality Review (WMQRS)).

The reports on the 37 visits have been published on the QRS website:

https://qualityreviewservicewm.nhs.uk/reviews/?search=IABD

In addition, an overview report has been published:

https://qualityreviewservicewm.nhs.uk/news/overview-report-inherited-and-acquired-haemophilia-and-other-bleeding-disorders/

The peer review programme has highlighted that the service provided in the UK is of high quality with many examples of good and innovative practice.

Visits identified 7 immediate risks all of which were rapidly addressed by the centres involved.

Concerns identified were in the following areas:

1. Staffing
2. Emergency Care
3. Date collection and sharing
4. Clinical Guidelines
5. Governance arrangements
6. Environment and facilities
7. IT support
8. Network arrangements

The nature of concerns varied considerably from Centre to Centre. It is clear that there are wide differences in the provision of staffing infrastructure particularly in relation to physiotherapy, clinical psychology and social work although there are also shortfalls in medical and nursing provision in some Centres.

Unfortunately, the plan to organise a "good practice sharing event" coincided with the first wave of COVID19, so did not happen.

Individual Centres and Networks should draw up a plan to address the concerns raised in the Peer Review reports. This will involve discussion at Trust and Local Commissioner Level. Feedback will be requested by the UKHCDO and be monitored via the Clinical Reference Group.

Further discussion will be needed to decide on the next round of Peer Review. Prior to this a review of the standards will need to be undertaken. Some of the standards need to be more explicit and some more detailed standards in relation to staffing requirements and facilities would strengthen the process.

Dr John Hanley,
Chair, Peer Review Working Party
November 2020

16. Gynaecology Guideline Task Force

Membership

Dr Nicola Curry Chair

Dr Rezan Abdul-Kadir, Consultant Obstetrician and Gynaecologist, Royal Free
Dr Louise Bowles, Consultant Haematologist, Royal London
Professor Justin Clark, Consultant Obstetrician and Gynaecologist, Birmingham
Dr Gill Lowe, Consultant Haematologist, Birmingham
Dr Jason Mainwaring, Consultant Haematologist, Bournemouth
Dr Sarah Mangles, Consultant Haematologist, Basingstoke
Dr Bethan Myers, Consultant Haematologist, Leicester

The literature search has been completed and the first draft of the guideline is being written at present. The guideline writing was disrupted by COVID-19, meaning that we are now writing the final version of the paper prior to updating the literature search appropriately and submitting it for peer review.

Dr Nikki Curry
Chair, Gynaecology Task Force writing committee
October 2020

17. Prophylaxis Task Force

Membership

Dr Rachel Rayment (adult)	Co-Chair
Dr Tina Biss (paediatric)	Co-Chair

Dr Steve Austin
Dr Elizabeth Chalmers
Dr Richard Gooding
Dr Anne Kelly
Dr Susie Shapiro
Dr Kate Talks
Dr Oliver Tunstall

Remit of the group

The remit of this task force was to revise and update the UKHCDO/BSH guideline on the use of prophylactic factor concentrate in children and adults with haemophilia that was published in 2010.

The guideline has been published (10.5.20) and the Task force has disbanded.

Dr Tina Biss & Dr Rachel Rayment,
Co-Chairs, Prophylaxis Task Force
October 2020

18. Haemophilia Nurses' Association

Membership

Simon Fletcher	Chair
Vacant	Vice-Chair
Shaun Emmitt	Secretary
Julia Spires	Treasurer

Marie Eales
Helen Hupston
Molly Musarara
Sharon Thind

The Haemophilia Nursing Association (HNA) represents and supports specialist nurses who care for people with bleeding disorders in the UK.

For the HNA (as for everyone) the past year has been one of disruption, change and accommodation as a result of the COVID-19 pandemic. The courses and the lines of support that we would normally have been able to offer to the association members have not been available and we have had to move everything online. As a result, we have been unable to run our yearly conference which has been postponed until the latter half of 2021. We have though continued to run ongoing training courses, including a new Introduction to Haemophilia Care course, the Contemporary Care course and ASPIRE, utilising various online platforms. We hope that in future years we may be able to offer these courses in a face to face format once again.

Following the release of the Peer Review reports back in April 2020, the HNA was pleased to see the excellent service provision offered by both Comprehensive Care Centres (CCCs) and Haemophilia Treatment Centres (HTCs) around the country. It was though disappointing to see the reports highlight that there was not always a parity of service across the whole of the UK in areas including, staffing levels to patient numbers, care provided to extended specialities, support of the wider multi professional teams, such as psychology support. The COVID-19 pandemic and the local preparedness changes (the redeployment of staff to other specialties, the need to work from home, and the movement of some centres wholesale to facilities little suited to the level of service required) have in some ways exacerbated this lack of parity. The committee have therefore been looking at how best to support its members during this time and have been sharing standards, individual job descriptions and matrices of responsibilities/duties across all of its platforms (Haemnet, Facebook and Twitter), so that individual centres and nursing teams can further evidence the level of care being provided in centres and advocate for parity within their Trusts.

During the past year HNA members have continued to be key stakeholders in the ongoing care of people living with bleeding disorder and have continued to be active participants within the UK haemophilia treaters community, including in the CRG, CMU, NHDDAG, and various UKHCDO working parties.

On behalf of the HNA committee, I would like to thank all the members who work within the field and whose passion for their role continues to ensure that the national voice of haemophilia nursing is heard.

Simon Fletcher
Chair, Haemophilia Nurses' Association
October 2020

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

Anna Wells	Chair:
David Hopper	Vice-Chair
David Stephensen	Research Lead
Elizabeth Bradshaw & Sarah Jones	Secretary
Joanne Minshall	Treasurer

Peer Review

The peer review process has highlighted inadequate levels of physiotherapy provision in 60% of the haemophilia services reviewed across the UK. HCPA members have been able to use the reports to raise the profile of this problem to local senior managers and commissioners. To date, of the 22 centres where provision was assessed as inadequate, 9% have achieved a significant improvement, 59% are in progress with on-going meetings and business cases being put in place, and 32% remain with significant barriers.

Research

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

- Haemarthrosis of the ankle in haemophilia A and B: prevalence, impact and intervention.
  NIHR Academy HEE/NIHR ICA Clinical Doctoral Academic Fellowship, ICA-CDRF-2015-01-012
  Richard Wilkins
- Developing a rehabilitation intervention for the management of chronic arthritic joint pain in people with haemophilia.
  NIHR Academy HEE/NIHR ICA Clinical Doctoral Academic Fellowship, ICA-CDRF-2017-03-050
  Paul McLaughlin
- 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 annual meeting includes a half-day session focussed on sharing and developing research activity, as well as a free papers session for members to showcase their work in the format of a five minute assessed oral presentation. The HCPA encourages collaboration and members continue to

initiate, present and publish key papers on an international level. Melanie Bladen has been invited to join 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).

At EAHAD in February 2020, HCPA members contributed 20 posters and six presentations. In the Physiotherapy SLAM Oral presentation session five of the seven abstracts selected were from HCPA members.

- Physical activity and cardiometabolic risk profiles amongst Irish adults with severe haemophilia: the Irish personalised approach to the treatment of haemophilia (iPATH) study, M Kennedy
- Project gym: promoting fitness in haemophilia, P McLaughlin
- DOLPHIN: development of a haemophilia physiotherapy intervention for optimum musculoskeletal health – interim results of a randomised controlled trial, D Stephensen
- Identifying performance-based outcome measures of physical function in people with haemophilia (IPOP), M Bladen
- Reliability of the i-step in children with haemophilia, D Chugh
- Prevalence of haemarthrosis and clinical impact on the musculoskeletal system in people with haemophilia in the United Kingdom; evaluation of NHD and Haemtrack patient reported data, R Wilkins.

Melanie Bladen won first prize for her presentation on the IPOP (Identifying Performance-based Outcome measures of Physical function in people with haemophilia) study and David Stephensen second prize for the interim results of the DOLPHIN study which explored feasibility of a randomised controlled trial of an exercise programme for children with haemophilia. Megan Kennedy won third prize for her poster on Physical activity and cardiometabolic risk profiles amongst Irish adults with severe haemophilia: The Irish Personalised approach to the treatment of Haemophilia (iPATH) study.

Publications in 2020:

1. Flannery T, Bladen M, Hopper D, Jones S, McLaughlin P, Penn A, Sayers F, Wells A & Stephensen D (2020). Physiotherapy after COVID-19 – "Zoom or room". *Haemophilia*, Early view. https://doi.org/10.1111/hae.14166
2. McLaughlin P, Aspdahl M, Matlary RED, Grinda N, Katzerova M, O'Mahony B, Stephensen D, Lobet S. (2020) Comprehensive care on paper only? The challenge for physiotherapy provision in day to day haemophilia practice. *Haemophilia*. Early view. https://doi.org/10.1111/hae.14150
3. Kuijlaars IAR, van der Net J, Feldman BM, Aspdahl M, Bladen M, et al. (2020) Evaluating international Haemophilia Joint Health Score (HJHS) results combined with expert opinion: Options for a shorter HJHS. Haemophilia. Early view. https://doi.org/10.1111/hae.14180
4. Wells AJ & Stephensen D (2020). The role of the physiotherapist in the management of people with haemophilia: defining the new normal. *Br J Hosp Med*, *81*(8). https://doi.org/10.12968/hmed.2020.0016

5. Bladen M, Carroll L, Dodd C, Drechsler WI, Hashem F, Patel V, Pellatt-Higgins T, Saloniki E, Stephensen D (2020). Results of feasibility and safety of randomised controlled trial of a musculoskeletal exercise intervention versus usual care for children with haemophilia. *Haemophilia*. 26(5): e223-225. https://doi.org/10.1111/hae.14026

6. McLaughlin P, Hurley M, Chowdary P, Khair K & Stephensen D (2020). Physiotherapy interventions for pain management in haemophilia: a systematic review. *Haemophilia*, 26(4):667-684. https://doi.org/10.1111/hae.14030

7. Taylor S, Room J, Barker K (2020). Physical activity levels in men with Haemophilia–A single centre UK survey. *Haemophilia*, 26(4): 718-725. https://doi.org/10.1111/hae.14009

8. Hashem F, Bladen M, Carroll L, Dodd C, Drechsler WI, Patel V, Pellatt-Higgins T, Saloniki E, Stephensen D (2020). Muscle strengthening intervention for children with haemophilia: co-designing a best-practice exercise programme with children, families and healthcare professionals. *Health Expectations*. https://doi.org/10.1111/hex.13119

9. O'Donovan M, Buckley C, Benson J, Roche S, McGowan M, Parkinson L et al. (2020). Telehealth for delivery of haemophilia comprehensive care during the COVID-19 pandemic. *Haemophilia,* 00:1-7. https://doi.org/10.1111/hae.14156

10. Bradshaw E, McClellan, Whybrow P, Cramp F (2019). Physiotherapy outcome measures of haemophilia acute bleed episodes: What matters to patients? *Haemophilia,* 25(6): 1066-1072. https://doi.org/10.1111/hae.14180

Covid-19

At the beginning of lockdown HCPA members worked quickly to provide online resources for both patients and fellow clinicians. Members have supported one another with the move to virtual consultations, alongside the challenges of redeployment and for some, significant changes to departmental infrastructure. The adaptability and positivity shown is a credit to HCPA members whose focus is always on providing the highest quality of patient care.

Meetings

1. 5th -6th March 2020 Annual educational meeting & AGM, Birmingham. Brenda Buzzard award & CPD bursary winner for best free paper: Steph Taylor 'Past the tipping point: a qualitative study of the views and experiences of men with haemophilia regarding mobility, balance and falls'.
2. 2nd July 2020 Virtual educational meeting
3. November 2020 Virtual educational meeting
4. 5th March 2021 Virtual annual educational meeting & AGM

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

HCPA Constitution

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

Anna Wells,
Chair, Haemophilia Chartered Physiotherapists' Association
October 2020

20. BCSH Haemostasis and Thrombosis Task Force

Membership

Dr Keith Gomez	Chair
Dr Will Lester	Vice-Chair
Dr Raza Alikhan	
Dr Julia Anderson	UKHCDO representative
Dr Deepa Arachillage	
Mr Peter Baker	
Dr Tina Biss	
Dr Elaine Gray	NIBSC representative
Dr Ian Jennings	UK NEQAS representative
Mr Sean Platton	
Dr Renu Riat	
Dr Khalid Saja	

Dr Gomez now chairs the H&T Task Force, taking over from Professor Mike Laffan, and Dr Lester is Vice-Chair. The Task Force met on 22 November 2019, 6 March, 12 June and 14 September 2020.

UKHCDO Guidelines Published 2019/2020

Laboratory coagulation tests and emicizumab treatment. A UKHCDO guideline. P V Jenkins, A Bowyer, C Burgess, E Gray, S Kitchen, P Murphy, S Platton, A Riddell, P Chowdary, W Lester. Haemophilia 2020 26 (1) 151-155.

Laboratory measurement of factor replacement therapies in the treatment of congenital haemophilia. A UK Haemophilia Centre Doctors' Organisation guideline. E Gray, Kitchen S, Jenkins PV, Bowyer A, Riddell A, Platton S, Murphy P, Chowdary P, W Lester. Haemophilia 2019 26 (1) 6-16.

Recombinant factor VIII products and inhibitor development in previously untreated patients with severe haemophilia A: Combined analysis of three studies. P Volkers, K-M Hanschmann, T Calvez, H Chambost, P W Collins, V Demiguel, D P Hart, C R M Hay, J Goudemand, R Ljung, B P Palmer, E Santagostino, E M van Hardeveld, M van den Berg, B Keller-Stanislawski. Haemophilia 2019;25:398-407

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Guidelines for the laboratory investigation of platelet function disorders. BSH approved; guideline writing group convened. Guideline chair: K Gomez

RCPCH guidelines on the haematological investigation within child protection investigation of possible physical maltreatment. Proposal for RCPCH & BSH Good Practice Paper submitted. Guideline chair: J Grainger

Dr Julia A M Anderson
UKHCDO Representative for BSH Haemostasis & Thrombosis Task Force
October 2020

21. Haemophilia Society

We are the only UK-wide charity for all those affected by a genetic bleeding disorder: a community of individuals and families, healthcare professionals and supporters.

For almost 70 years we have campaigned for better treatment, been a source of information and support, and raised the awareness of bleeding disorders.

We:

- Raise awareness about bleeding disorders
- Provide support throughout members lives
- Influence and advocate for the community on health and social care policy and access to treatment

More than 36,000 men, women and children in the UK have a diagnosed bleeding disorder and the number rises every year. Membership of The Haemophilia Society is free and open to all.

Our peer support – through local groups around the UK and our online community – offers friendship and a listening ear when needed, as well as enabling people to share their views and experiences. By bringing people together for information and support at events tailored to all life stages, we amplify their voices to reduce isolation and influence government, welfare and health care policy.

Our community is at the heart of everything we do – we work collaboratively with members and health professionals to ensure we make decisions influenced by their valued input and direction.

As bleeding disorders are rare, many people will never encounter The Haemophilia Society; we are largely invisible beyond the communities we serve. So, we must work doubly hard to raise both awareness and understanding of bleeding disorders and vital funds needed to give those affected the services they deserve and need to live the best life they can.

Activities

Members Conference

This year we held our members conference in Liverpool with almost 400 people attending over the two days. There was a packed agenda as always with updates in new advances in services and treatments as well as sessions on women's issues and health and wellbeing.

We held a gala dinner with a lively auction and the chance to socialise with other members and build connections to others in the community. Children's activities included a trip to Chester Zoo and bowling on Sunday.

Newly Diagnosed Family Weekends

Our weekends for parents of recently diagnosed children are free to attend and enable new parents to learn more about what to expect when raising a child with a bleeding disorder. It is a chance to meet others who are experiencing the same emotions and spend time hearing from and talking to experts, helping them build a foundation of knowledge and support as they start their journey as a family.

Specialist bleeding disorder physiotherapists, nurses, doctors, psychologists and play specialists facilitate sessions alongside our trustees and Youth Ambassadors.

This year we held three weekends for families with a newly diagnosed child, with one focusing specifically on mild and moderate bleeding disorders, while the others focused on children with a severe bleeding disorder. This year we have included information on women with bleeding disorders, recognising that the needs of girls ought to be highlighted and addressed at an early stage.

Youth Activities

This year our younger children attended summer camp at a dedicated outdoor activity centre in Surrey. Attending camp reduces the isolation of living with a bleeding disorder and raises the confidence levels of our younger members. Siblings are invited to attend as it is important that the impact of living with a brother or sister who has a bleeding disorder are understood and managed.

From learning to give your treatment for the first time and understanding what your condition really means for you, to understanding how teamwork and determination can help you make huge leaps and in some cases learn new skills such as those who learnt to ride a bike for the first time this year.

Youth Ambassador Engagement

Our Youth Ambassadors have attended two training weekends to enhance their skills in communication and storytelling, learning about clinical trials structure, personality types and teamwork. They have been developing three works teams concentrating on mental health, exercise and wellbeing and women's bleeding disorders.

They continue to support us at all of our events talking about their experiences, engaging with the community and helping staff deliver services as well as engaging in social media and advocating for our community.

Two of the Youth Ambassadors attended the EHC Conference, one as part of the Youth development programme and one representing us at the inhibitor working group. We also had one youth ambassador attending the EHC new technologies workshop.

Additionally, they organised the 'Lads and Dads' activity weekend in the Brecon Beacons continuing the friendly rivalry between parents and their children across a range of outdoor events and activities.

Talking Red Programme

This year we held two Talking Red conferences in Belfast and Birmingham with tailored sessions from a range of health care professionals talking about the challenge's women with bleeding disorders face, from diagnosis and dentistry to periods, pregnancy and childbirth.

These events allow women living with bleeding disorders to connect with others who understand their challenges and provide a safe environment to share their experiences, reducing the isolation some people feel.

We surveyed women to understand more comprehensively the issues that were important to women living with bleeding disorders and the issue of 'period poverty'. The findings were to be presented at our third Talking Red event scheduled for March 2020 but due to COVID-19 this had to be cancelled and rescheduled for 2021.

Family Days

We held 7 family days at various fun locations across the UK from Zoo's and Aquariums to Science Parks. These were attended by over 250 people and is a great way for families to get to know each other share experiences and build support networks over lunch. Some of the families had met previously at newly diagnosed weekends and had the chance to meet up again a few years later to compare their journeys.

Service of Thanksgiving and Remembrance

With the start of the Inquiry hearings and it was of particular importance this year to remember those who could not be with us and lost their lives through contaminated blood. The personal testimonies heard this year have been deeply moving and for many have brought back many painful memories so therefore it was not surprising that we had 150 people attending this year to honour lost friends and family.

Publications

We produced this year new booklets on dental care for adults, sex and bleeding disorders as well as factsheets on applying for PIP. An updated version of the understanding VWD was released and work started on a series of rare disease factsheets.

Volunteering

As always, we rely on the generosity of so many volunteers to help us run our events and support us in a range of amazing ways. Without the help of the many healthcare professionals who give up their time to speak at events for us, the Youth Ambassadors and newly appointed LGTBQ Ambassador, local group volunteers, reading panels and a whole host of volunteers who rise to the challenge we would not be able to deliver the range of services we do.

This year we began a plan to expand our volunteering process to offer a larger range of opportunities, however due to COVID-19 this process was put on hold at the end of the financial year and will be initiated again in the future.

Advocacy

This year we have continued to advocate for access to new treatments for people with bleeding disorders, responding to NICE consultations, NHSE consultations on new treatments and as part of the NHS Tender Boards for treatment and home delivery. As members of the Clinical Reference Group in England (which is attended by Welsh and Scottish clinicians' representatives too) we bring the collective patient voice, along with two patients, to provide advice to the decision makers in the NHS on what matters to our members about treatment, care and support.

Issues highlighted included access to innovative new treatments, access to specialist nursing and physio care, and sharing people's experiences of their haemophilia centres.

We have also represented patients' views on the Welsh Inherited bleeding disorder project board, which is redesigning care for people in Wales with a bleeding disorder. We also worked closely with the DWP to highlight concerns over benefits, particularly for those with a bleeding disorder who are routinely being refused PIP but are successful on appeal. We have worked with DWP on developing training for providers and with the assessment providers to improve education.

We have also worked closely with EIBSS (and the associated devolved nations support organisations) and the APPG on Haemophilia and Contaminated Blood to challenge decisions on support for those affected by contaminated blood and called on governments to end the disparity between nations.

We have worked with the APPG to investigate the challenges people living with bleeding disorders face whether access to improved treatment, access to quality service or disparity of services across the UK. This has been collated, however launch was postponed due to timings with Brexit, General election and the COVID-19 situation.

Database and Processes

We have been working hard this year to examine our background processes and database and ensure we have a solid foundation to move forward from. It is vital for us that we have good procedures in place and the right information to allow us to engage effectively with our community. This work is ongoing to help us become more efficient in the future and provide the right information to our members.

Public inquiry into infected blood

This year saw the start of the hearings of the Statutory Public Inquiry into Infected Blood. We heard from personal witnesses across the devolved nations. It was both heart-breaking and yet inspirational to hear the experiences of people and their families of living through the impact of contaminated blood and losing loved ones. No one attending could help but be moved by the bravery of those who spoke out, vividly bringing to life the tragedy they had lived through.

We have continued to keep our members updated via a dedicated section on our website, producing newsletters and articles in HQ, daily updates on social media during the hearings and meeting with people attending the hearings around the UK. We have ensured all our documentation was provided to the Inquiry and have waived legal privilege on all of our documents. We have inputted to the experts reports and attended the hearings of these in February.

We continue to campaign for increased expert psychological support for those affected by contaminated blood and to support our members through these difficult times.

Fundraising

Our fundraisers have been active throughout the year organising sports days, baking, knitting, hosting brunches and initiating a range of fun activities. We welcome your feedback about different activities and stories of success, especially with the ongoing challenges of COVID-19.

We are grateful that people are running, walking, cycling and swimming to raise money for us and we thank you all for your commitment and the personal sacrifices and hours of training you have put in.

We have launched our virtual shop so you can buy merchandise from us including Christmas cards and are looking to expand this in the future to include our publications. Thank you to all who have contributed to our campaigns so we can continue to provide information and support to our members free of charge.

This year we held our Big Red Glasgow Bridge Walk but unfortunately had to cancel our Big Red London Walk due to COVID-19 lockdown restrictions. This was a real blow for us as it was such a great event attended by so many the year before. We hope we can reinstate this event.

Debra Morgan& Kate Burt,
The Haemophilia Society
October 2020