NHD

UKHCDO NATIONAL HAEMOPHILIA DATABASE

UKHCDO Annual Report 2014

Including

Bleeding Disorder Statistics for 2013/2014

A report from the UKHCDO and NHD

November 2014

UKHCDO

UNITED KINGDOM HAEMOPHILIA CENTRES DOCTORS' ORGANISATION

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Contents

1. Chairman's Report

Welcome Edinburgh and the 2014 Annual General Meeting of UKHCDO which this year is held in association with the joint scientific meeting between BSHT, UKHCDO and the UK Platelet Group. I hope many of you are able to attend the scientific meeting and I wish to thank Henry Watson and the scientific committee representing all three organisations for producing an excellent programme.

UKHCDO has been very active in the last year, particularly through the working parties. The recently reformed working parties have gathered or maintained momentum with several guidelines published or in development. Brief highlights will be presented at the meeting and more comprehensive descriptions of activity are presented in the Annual Report.

The Advisory Committee has agreed that UKHCDO should set up a Clinical Study Group to lead on the academic aspect of Haemophilia Care and Prof Mike Laffan has agreed to chair this group. He will present the membership and goals of the group. UKHCDO will provide initial funding for the CSG.

UKHCDO will also set up a Haemophilia Therapy Task Force to assess and advise on issues such as options for delivering high quality and cost effective prophylaxis. Another important role of this group will be to assess new therapeutic products and their potential place in UK Haemophilia practice.

With regards to Commissioning, UKHCDO continues to work closely with NHS England through the Clinical Reference Group (CRG) for Haemophilia. In collaboration with the CRG and the Commercial Medicines Unit, we have been very successful in securing another national contract for factor concentrates and, in so doing, have achieved very significant savings for the NHS. Despite this successful joint venture, the environment of NHS England Specialised Commissioning remains very turbulent and difficult to negotiate. Our main dialogue with NHS England is through our engagement with the CRG and it is a major advantage that this group largely consists of clinicians who are also members of UKHCDO. The financial crisis facing the NHS has led to constant reorganization and change of focus of Specialised Commissioning. While quality of care remains an important issue for the CRG, the drive to make financial savings has become a priority. Despite significant savings made with the National Contract for Therapeutic Products, we remain under pressure to achieve further savings. In the face of such pressure, informed bodies such as UKHCDO, HNA and the Haemophilia Society must engage with this process to safeguard haemophilia services in the UK.

In a constantly changing NHS landscape, the long experience of UKHCDO in leading Haemophilia care is particularly valuable and important. Underpinning much of what we do and have achieved is the National Haemophilia Database (NHD). We must continue to support NHD and to help secure funding for future work. I would like to take this opportunity to thank NHD staff, in particular Lynne Dewhurst, Sarah Rooney and Ben Palmer. I wish to thank Charles Hay in particular for his key role in directing the work of NHD on behalf of UKHCDO.

Finally, I wish to thank my colleagues on the Executive of UKHCDO, David Keeling, Ri Liesner and Mike Laffan. We have worked well together and their wisdom and advice has been invaluable.

I welcome your participation in the AGM and hope that you enjoy the scientific meeting.

Dr Gerry Dolan
Chairman, UKHCDO
Nottingham, October 2014

Bleeding Disorder Statistics for

April 2013 to March 2014

A report from the National Haemophilia Database

November 2014

2 Comments on the Bleeding Disorder Statistics for 2013 / 2014

This is the final report for the financial year 2013/14. A draft report had been produced in October to coincide with the AGM, which was held 6 weeks earlier than last year, to coincide with the joint BSHT meeting. Some working party reports had not yet been received at that time and so it had not been possible to produce a complete report by that date. Furthermore, some data cleaning information had still not been received by the database at the time and so work on the national statistics was still ongoing. For that reason we issued a draft report electronically and deferred printing the complete report, including amendments and further data until November.

Consent

The consent process for data entry into the database is under periodic review. The current process was recently approved by the Caldicott inspectors when they inspected the NHD, which we arrange every couple of years. However, we also arranged to review it with the Information Commissioner in early November. The Information Commissioner was happy with our procedure for obtaining implied consent and, given the way in which our data are used for healthcare planning and patient management, questioned whether consent was required. She appeared to believe that we were complying with the principles of fair processing. We are in the process of revising the patient information leaflet for the database and for Haemtrack. We will adopt a "layered" approach so that patients will be presented with a simplified information package but will also have access to more complex and detailed information should they wish to consult this. The Information Commissioner approved of this approach.

Factor Use

Last year, with great fanfare, we reported that factor VIII usage appeared to have stabilised despite increasing numbers of patients treated. This year's report shows an increase in usage for severe haemophilia A (8%) which is only partly accounted for by the increase in patient numbers (4%). Over the past 5 years factor VIII usage for severe haemophilia A has increased 14% whilst patient numbers have increased by 8%. Analysis of Haemtrack data will hopefully provide some insight into this and into the treatment practices of the statistical outliers whose use is greater than the 95th percentile. A great deal of work is going into exploring and cleaning this data.

Patient Demographics: Numbers treated

Patient numbers are increasing more rapidly than they did historically for a number of reasons. Although 22% of new registrations for severe haemophilia A are for immigrants to this country, the underlying birth rate for haemophilia A has increased a little over the years. Until 15 years ago, new registrations for severe haemophilia were running at 40-45 per year. Now a figure of 60-70 per annum would be more typical. Patients are also living longer. Consequently, the number of patients treated for severe haemophilia has increased by 44% in the past decade.

Patient Level Data

Analysis of the enormous volume of Haemtrack data now available is being directed to some degree by the Haemtrack Working Group and we have also appointed a data miner Dr Hua Xiang to analyse these data. Although a short Haemtrack report is presented in this volume, in future it is planned that the Haemtrack report will be longer, require more time to prepare, and will be analysed 4-5 months earlier than the main body of the report.

It is clear from analysing these data so far that data quality is improving and there is a continued reduction in the interval between treatment and data entry. Data completeness is also increasing and it is possible to conduct detailed analysis on data from a growing cohort of patients who are selected using data-completeness criteria. This will enable us to analyse the effect of different treatment patterns and to compare treatment patterns between centres and between types of centres. Although it makes no statistical sense to compare smaller centres because of the relatively small number of patients managed in each centre, their data may be aggregated so that generic comparisons may be made. It is already clear, for example, that although the vast majority of Comprehensive Care Centre patients with severe haemophilia are registered with Haemtrack, that only 50% are registered in Haemophilia Centres.

Leaflets are being printed for patients (and also for centres) to make it clear how Haemtrack may be used, what its value is etc. This is part of a strategy to improve compliance with Haemtrack and to enable centres and patients to use the system optimally to optimise the patient's replacement therapy. Centres vary considerably in the extent to which they utilise Haemtrack, the data from which should be central to any routine outpatient review.

vCJD

We have presented a shorter report on vCJD this year but have added to the tables estimates of the number of patients thought to be 'at risk' for public health purposes based on their factor use as reported to the NHD prospectively through the factor VIII returns. Since this is based on treatment data reported prospectively, we think that these results are likely to be more complete than those based on more recent reports from centres. Older treatment data had often been destroyed at centre level but NHD treatment data goes back to 1969 in some cases. Data on patients exposed to implicated batches is likely to be accurate but incomplete, since the use of some batches cannot be completely accounted for.

We identified and notified centres of patients we thought were potentially no longer considered 'at risk' by virtue of the change in risk period to 1990 to 2001. We asked centres to check their patients' 'at risk' status and to report this back to us. So far we been informed that 21% of patients are no longer 'at risk'.

New Registrations

One recurring theme this year has been that for registration data, disease severity has not always been reported accurately. In medical records full of results of assays which monitor therapy, it can be difficult to find the baseline level and if registration is conducted by staff lacking medical training, the wrong level may be entered. Particularly bad examples of this include patients with severe factor FXIII deficiency, 50% of whom were registered with the incorrect baseline value. Furthermore, only 7 of 24 haemophilia carriers registered with a level <2% were registered with the correct factor VIII or IX baseline value. These apparent anomalies are the subject of ongoing data queries. *The baseline level for patient registration*

should be checked or dictated by a member of nursing or medical staff prior to data entry. In many centres, registrations are always conducted by nursing staff even if all other data is entered by a data manager but practice varies.

We would like to thank Centres and their staff for sending their data in a timely manner and being patient with our data queries. We would also like to thank those working party chairs and commissioners who participated in the annual report review meeting. Their constructive criticism was very valuable in the evolution of the report. Preparing this report is very much a team effort, which involves all the staff of the NHD over a period of months. I would therefore like to take this opportunity, not just to thank Ben Palmer and Lynne Dewhurst but also (in no particular order) Hua Xiang, Helen Brown, Sarah Rooney, Rachel Lockwood, Tom Sharpe, Amy Tidmarsh, Jessica Smith and Rob Hollingsworth and his team.

Professor Charles RM Hay,
Ben Palmer &
Lynne Dewhurst

On behalf of the UK National Haemophilia Database
Manchester, November 2014

Table 1 **In Register – The total number of registered patients with all types of bleeding disorders and carriers as of 31st March 2014 and the number treated between April 2013 & March 2014**

Coagulation Defect	Number of Patients in Register			Treated	% Treated
	Total	Males	Females		
Haemophilia A	5,686	5,686		3,077	54.12%
Haemophilia B	1,205	1,205		662	54.94%
Haemophilia A Carrier	1,377		1,377	66	4.79%
Haemophilia B Carrier	425		425	49	11.53%
Haemophilia A with Liver Transplant	9	9	0	1	11.11%
Haemophilia B with Liver Transplant	6	6	0	0	0.00%
von Willebrand disease	10,178	3,718	6,460	1,161	11.41%
von Willebrand with Liver Transplant	1	1	0	0	0.00%
Probable von Willebrand disease	143	35	108	14	9.79%
Platelet-type Pseudo von Willebrand Disease	6	3	3	0	0.00%
F.V deficiency	164	67	97	12	7.32%
F.VII deficiency	964	461	503	59	6.12%
F.X deficiency	211	88	123	35	16.59%
F.XI Deficiency	2,459	1,051	1,408	78	3.17%
F.XIII Deficiency	63	35	28	52	82.54%
Prothrombin Deficiency	12	6	6	5	41.67%
Dysfibrinogenaemia	291	114	177	24	8.25%
Hypofibrinogenaemia	196	84	112	0	0.00%
Combined II+VII+IX+X Deficiency	4	1	3	0	0.00%
Combined V+VIII Deficiency	27	13	14	5	18.52%
Other combined diagnoses	279	121	158	32	11.47%
Acquired Haemophilia A	388	183	205	73	18.81%
Acquired Haemophilia B	1	1	0	0	0.00%
Acquired von Willebrands	93	50	43	32	34.41%
Acquired Prothrombin Deficiency	1	1	0	0	0.00%
Acquired F.XIII Deficiency	3	1	2	0	0.00%
Acquired F.V Deficiency	4	0	4	1	25.00%
Acquired Deficiency (other)	9	8	1	3	33.33%
Glanzmann's Thrombasthenia	119	50	69	35	29.41%
Bernard Soulier	73	34	39	13	17.81%
Other platelet defects	1,768	570	1,198	93	5.26%
Miscellaneous	208	63	145	6	2.88%
Unclassified bleeding disorder	208	31	177	20	9.62%
Total	**26,581**	**13,696**	**12,885**	**5,608**	**21.10%**

Table 1: Lists the patients registered with the database in 2013/14 (26,581) and shows the proportion which required treatment during the course of that financial year.

For the first time, both asymptomatic and low-level carriers are included. Previously, only low-level carriers were registered. Asymptomatic carriers are still under-represented, since they have only recently been included and carrier testing is usually deliberately deferred until the patient requires surgery or reaches their mid-teens.

671 patients were removed from the register for various reasons: -

- 363 moved centre or were lost to follow-up
- 221 died and 51 changed diagnosis
- 23 diagnosis were updated or are no longer current
- 7 died prior to April 2012 but the database was not informed until 2013
- 6 were entered in error or their record was duplicated

There are, despite these deletions, 1,395 more patients in the register than last year.

For simplicity, Haemophilia B Leyden has been aggregated with Haemophilia B in this table. Haemophilia B Leyden is under-reported. It has become clear that some of these patients have previously been reported as Haemophilia B (subtype not stated). Software changes are being undertaken to HCIS and NHD to make it easier to report Haemophilia B Leyden and we would ask centres to check the registration of any patients that they have with this diagnosis and to amend the registration if necessary.

We suspect that liver transplantation is under-reported. We have only registered unclassified bleeding disorders for the past two years and suspect that the number of those patients registered (currently 208 patients) will increase markedly.

Up to now we have registered only severe platelet defects with a specific diagnosis. Mild defects are far commoner, however, and we await further guidance on how these should be reported from the Rare Diseases Working Party.

N.B:

Haemophilia A Carriers includes females with factor VIII deficiency and females registered by their Haemophilia Centre as Haemophilia A

Haemophilia B includes patients with FIX Leyden

Haemophilia B Carrier includes females with factor IX deficiency, females registered by their Haemophilia Centre as Haemophilia B and FIX Leyden carriers

Table 2 **New Registrations - Number of patients newly registered at UK Haemophilia Centres between April 2013 & March 2014 showing their coagulation defect and gender**

Coagulation Defect	Male	Female	Total
Haemophilia A	221		221
Haemophilia B	55		55
Haemophilia A Carrier		180	180
Haemophilia B Carrier		47	47
von Willebrand disease	201	357	558
von Willebrand with Liver Transplant	1	0	1
Probable von Willebrand disease	7	21	28
Platelet-type Pseudo von Willebrand Disease	2	1	3
F.V deficiency	5	9	14
F.VII deficiency	58	56	114
F.X deficiency	8	7	15
F.XI Deficiency	116	126	242
F.XIII Deficiency	2	2	4
Dysfibrinogenaemia	21	43	64
Hypofibrinogenaemia	6	16	22
Acquired Haemophilia A	39	28	67
Acquired von Willebrands	7	6	13
Acquired F.V deficiency	0	1	1
Acquired Deficiency (other)	3	1	4
Glanzmann's Thrombasthenia	3	3	6
Bernard Soulier	3	4	7
Other platelet defects	85	124	209
Combined V+VIII Deficiency	1	1	2
Other combined diagnoses	6	16	22
Miscellaneous	9	12	21
Unclassified bleeding disorder	3	56	59
Total	**862**	**1,117**	**1,979**

Table 2: This table lists new registrations during the year. The 1,979 new registrations during the course of 2013/14 include 66 previously registered patients in whom a change of diagnosis was registered. There were 98 fewer new registrations than in 2012/13.

There is also a considerable increase in the number of Haemophilia A carriers registered, since the current policy is to register all haemophilia carriers and not just low level carriers. A large number (227) of female Haemophilia carriers were registered during the year, reflecting the policy change to register all carriers.

As usual, this continues to show a consistent excess of female registrations for all autosomal disorders, presumably reflecting referral and diagnostic bias of women with menorrhagia

N.B:

Haemophilia A Carrier includes females with factor VIII deficiency and females registered by their Haemophilia Centre as Haemophilia A

Haemophilia B includes patients with FIX Leyden

Haemophilia B Carrier includes females with factor IX deficiency, females registered by their Haemophilia Centre as Haemophilia B and FIX Leyden carriers

Table 3 **New Registrations of Haemophilia A & B between April 2013 & March 2014, by age at the end of September 2013 and disease severity**

Coagulation Defect	Age (years)	Number of Patients (factor level iu/dl)			
		≤1	>1 & <5	≥5	Total
Haemophilia A	0 : 4	53	8	44	105
	5 : 9	4	1	14	19
	10 : 19	6	0	16	22
	20 : 29	6	2	17	25
	30 : 39	3	1	11	15
	40 : 49	1	1	7	9
	50 : 59	0	0	5	5
	60 : 69	0	0	11	11
	70 : +	0	0	10	10
Total		**73**	**13**	**135**	**221**
Haemophilia B	0 : 4	8	6	14	28
	5 : 9	0	1	4	5
	10 : 19	1	1	4	6
	20 : 29	0	0	5	5
	30 : 39	0	1	4	5
	40 : 49	0	0	2	2
	50 : 59	0	0	0	0
	60 : 69	0	0	3	3
	70 : +	0	0	1	1
Total		**9**	**9**	**37**	**55**

Table 3: This shows the number of new registrations of haemophilia A and B broken down by reported severity and age at mid-year (30/09/2013). This shows a significant increase in new registrations of haemophilia of all degrees of severity.

The underlying birth rate of patients with severe haemophilia A born to UK-born mothers used to run at 40-45 patients per year until relatively recently. This table suggests an increase in the birth rate for severe haemophilia, since new registrations of young children is almost 60 in the last 12 months.

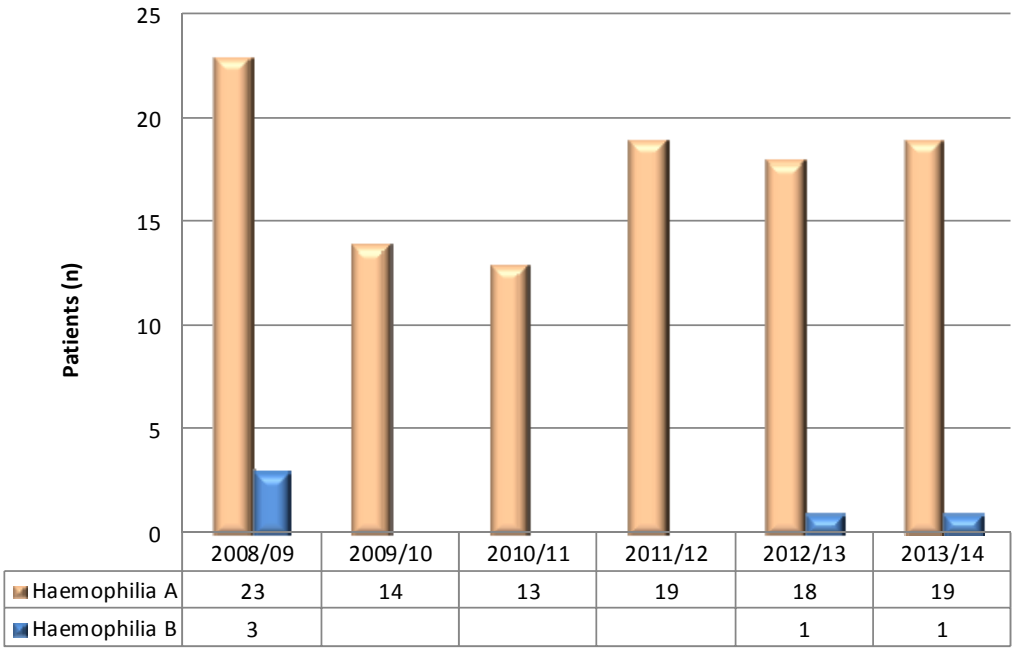
All those patients with severe haemophilia A or B (17/82 (20.7%)) first registered with the database after the age of 9 years were immigrants to this country. Some of the younger patients were also immigrants. About half of these patients come from the wider EU, many

of whom stay for only a few months to a year or so. The remainder originate from the rest of the world.

However, between 20 and 30% of all new registrations for severe Haemophilia has been accounted for by immigration in recent years (see Figure 1). Although we have a good handle on the extent of immigration, we cannot estimate emigration and so are not in a position to estimate net immigration (immigration *minus* emigration).

N.B: Haemophilia B includes patients with FIX Leyden

Figure 1 **New Registrations of Haemophilia A & B - Patients with Severe Haemophilia A or B over 5 years old at registration**



	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14
Haemophilia A	23	14	13	19	18	19
Haemophilia B	3				1	1

Figure 1 suggests that about 25% of all new registrations of severe haemophilia A and B have been immigrants in the past five year. However, a proportion of these are students or come to work in the UK for a short time or are visitors and so this figure overestimates the number that settle here and who require treatment in the long term. A more detailed analysis of the patients treated for more than 12 months may be helpful for the purpose of healthcare planning. We have no data on emigration of patients born in the UK.

Table 4 **In Register – The total number of patients with Haemophilia A & B currently in the register, by severity and age group**

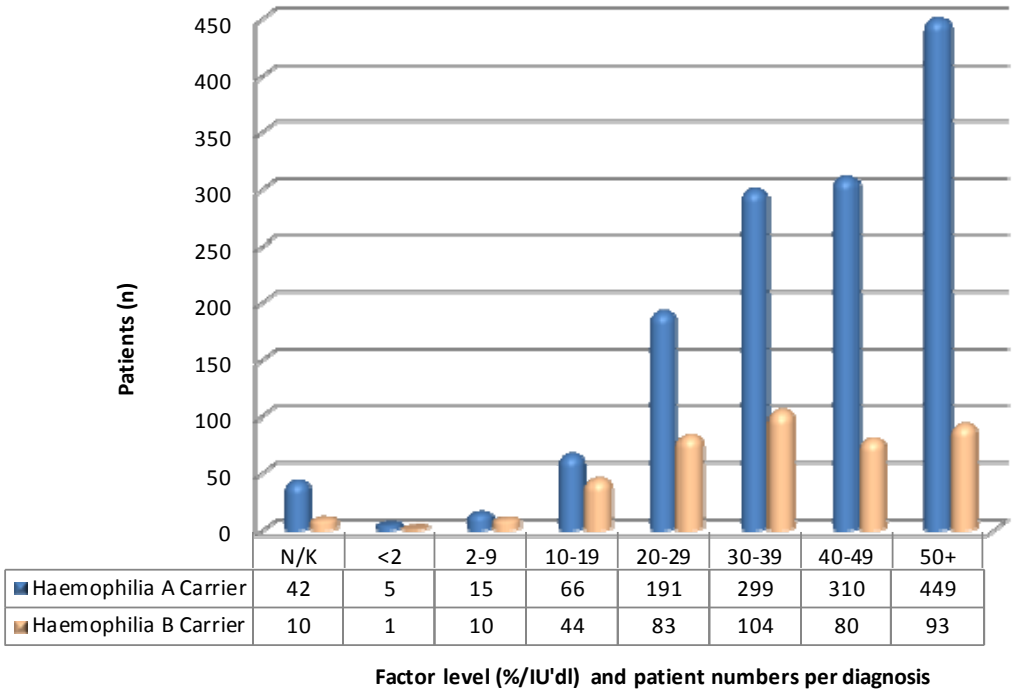
Coagulation Defect	Age Range	Factor level iu/dl			
		≤ 1	>1 & <5	≥ 5	Total
Haemophilia A	<18 years	709	128	648	**1485**
	≥18 years	1293	384	2524	**4201**
	Sub Total	**2002**	**512**	**3172**	**5686**
Haemophilia B	<18 years	121	66	116	**303**
	≥18 years	289	183	430	**902**
	Sub Total	**410**	**249**	**546**	**1205**

Table 4: This shows a breakdown of the number of patients in the register with haemophilia A and B, broken down by severity, age and gender. Patients with von Willebrand disease Normandy, acquired haemophilia and combined factor VIII and V deficiency are excluded from this table.

N.B:

Haemophilia B includes patients with FIX Leyden (9 aged <18 years old and 12 aged ≥18 years)

Figure 2 **In Register – The total number low level Carriers of Haemophilia A & B currently in the register, by severity**



	N/K	<2	2-9	10-19	20-29	30-39	40-49	50+
Haemophilia A Carrier	42	5	15	66	191	299	310	449
Haemophilia B Carrier	10	1	10	44	83	104	80	93

Figure 2: This figure shows the distribution of reported severity amongst low level carriers in the UK. Of interest is the relatively large number of very low level carriers. Most of these have an extreme degree of lyonisation but one or two are either homozygous products of consanguineous unions or are compound heterozygotes.

This dataset required a lot of data cleaning. Many of the very low-level registrations were incorrect and have now been corrected. As for all other patients, the level requested at the time of registration is that of the patient and not of any other family member. In some cases, the level is not known either because the patient is too young to be tested or because a test has been inadvertently omitted.

New registrations should be checked by a nurse specialist or member of medical staff to ensure that the level reported to the database is, in fact, the patient's baseline level and not a level taken to monitor replacement therapy.

N.B:

Haemophilia A Carrier includes:
Females registered by their Haemophilia Centre as Females with VIII deficiency
Females registered by their Haemophilia Centre as Haemophilia A (1 aged <18 years old and 2 aged ≥18 years)

Haemophilia B Carrier includes:
Females registered by their Haemophilia Centre as Females with IX deficiency
Females registered by their Haemophilia Centre as Haemophilia B (1 aged ≥18 years)
FIX Leyden carriers (5 aged ≥18 years)

Table 5 **In Register – The total number of patients with Von Willebrand Disease currently in the register, by severity, age group and gender**

von Willebrand disease	<18 years (VWD Activity iu/dl)				≥18 years (VWD Activity iu/dl)				Total
	<30	≥30	N/K	Sub Total	<30	≥30	N/K	Sub Total	
Males									
Type 1	109	215	31	**355**	241	397	70	**708**	**1,063**
Type 2A	33	6	1	**40**	56	14	1	**71**	**111**
Type 2B	9	3	0	**12**	13	12	1	**26**	**38**
Type 2M	12	5	0	**17**	29	4	2	**35**	**52**
Type 2N	0	1	0	**1**	4	10	3	**17**	**18**
Type 2 Unspecified	10	10	2	**22**	21	7	1	**29**	**51**
Type 3	24			**24**	26			**26**	**50**
Type Unreported	201	316	68	**585**	727	854	167	**1,748**	**2,333**
Females									
Type 1	80	186	17	**283**	354	1,107	168	**1,629**	**1,912**
Type 2A	27	7	1	**35**	82	30	4	**116**	**151**
Type 2B	6	6	1	**13**	28	17	2	**47**	**60**
Type 2M	9	3	1	**13**	62	19	4	**85**	**98**
Type 2N	0	0	0	**0**	7	28	6	**41**	**41**
Type 2 Unspecified	6	2	1	**9**	32	21	5	**58**	**67**
Type 3	9			**9**	26			**26**	**35**
Type Unreported	222	295	61	**578**	1,103	2,020	394	**3,517**	**4,095**
Grand Total - Males and Females				**1,996**				**8,179**	**10,175**

Table 5: This shows a breakdown of Von Willebrand disease registrations broken down by age, severity subtype and gender.

More than a third have a reported subtype and this is improving year by year.

As one would expect, the previously reported disparity in the gender of registrants with a relative excess of female registrants is much more marked with mild von Willebrand disease than in patients with more severe forms of the disease and only becomes apparent after menarche. Registrations of VWD are equally distributed between genders in patients under 18 years of age.

N.B:

There are:

8 patients where the sex or age (or both) are missing
1 patient with age unknown
1 patient who needs re-registering as Platelet-type Pseudo von Willebrand Disease
In total there are 10,185 patients registered with VWD

Table 6 **In Register – The number of patients with selected rarer bleeding disorders currently registered and the number treated between April 2013 & March 2014, 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	46	11	118	1	0	0	164	12
F.VII deficiency	113	31	845	28	6	0	964	59
F.X deficiency	38	27	172	8	1	0	211	35
F.XI Deficiency	207	28	2241	50	11	0	2459	78
Total	**404**	**97**	**3,376**	**87**	**18**	**-**	**3,798**	**184**

Coagulation Defect	<2		≥2		N/K		Total	
	In Reg	Treated	In Reg	Treated	In Reg	Treated	In Reg	Treated
F.XIII Deficiency	37	33	26	19	0	0	63	52
Total	**37**	**33**	**26**	**19**	**-**	**-**	**63**	**52**

Table 6: This table shows the number of patients with rarer disorders currently registered and the number reported to have required treatment during the year. In the absence of an internationally agreed severity classification, this is broken down by less than 5 IU/dl or 5 IU/dl and over, except for factor XIII deficiency, which is reported as less than 2 IU/dl or 2 IU/dl and over.

Almost all patients receiving treatment regularly have severe deficiency. Many of these were registered with Factor XIII levels which, on review, reflected ongoing treatment rather than their true baseline and which were therefore misleading. One patient with confirmed 16% factor XIII level is treated on-demand for trauma with factor XIII concentrate.

New registrations should be checked by a nurse specialist or member of medical staff to ensure that the level reported to the database is, in fact, the patient's baseline level and not a level taken to monitor replacement therapy.

F.XIII Deficiency IU/dl	In Register	Treated	Treated %
<1 - 2	39	35	89.7
>2 - 5	7	7	100.0
>5 - 10	8	8	100.0
>10 - 15	2	2	100.0
>15 - 25	1	0	0.0
>25	6	0	0.0
Total	**63**	**52**	

Table 7a Inhibitors by Disease Severity – Haemophilia A and B

Coagulation Defect	Inhibitor Status	≤ 1 iu/dl			>1 and <5 iu/dl			≥ 5 iu/dl		
		In Reg *	Inhib. Pts	%	In Reg *	Inhib. Pts	%	In Reg *	Inhib. Pts	%
Haemophilia A	Inhibitor ever reported	2002	425	21.23%	514	37	7.20%	3173	72	2.27%
	Inhibitor still present		161	8.04%		14	2.72%		27	0.85%
Haemophilia B	Inhibitor ever reported	410	16	3.90%	250	1	0.40%	546	0	0.00%
	Inhibitor still present		10	2.44%		0	0.00%		0	0.00%

** Including patients not regularly treated*

N.B:
Haemophilia B includes patients with FIX Leyden

Table 7b Inhibitors by Disease Severity – Von Willebrand Disease

von Willebrand disease	In Reg*	Inhibitor ever reported	%	Inhibitor still present	%
Type 1	2,975	1	0.03%	0	0.00%
Type 3	85	7	8.24%	7	8.24%

** Including patients not regularly treated*

Tables 7a & 7b - These tables show 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.

This shows that inhibitors are about seven times commoner in severe than non-severe haemophilia A and that about 60% of inhibitors remit, either spontaneously or following immune tolerance induction in patients with both severe and mild or moderate severity haemophilia A. There remains a suspicion, however, which is difficult to substantiate, that a proportion of patients with haemophilia A, thought to have eliminated their inhibitor, continue to have some low-level inhibitor activity, below the level of detection of current conventional tests.

Inhibitors in haemophilia B are fortunately far less common, occurring in about 4% of patients with severe haemophilia B, but about 60% persist long term. These arise almost invariably very early in the patient's treatment history and only very rarely (one patient) occur in non-severe haemophilia B.

None of the seven inhibitors reported in patients with type 3 von Willebrand Disease has remitted. One transient inhibitor has been reported in a patient with severe type 1 VWD. This has been confirmed by the centre.

Figure 3a **Trend in numbers of Severe Haemophilia A patients aged 60 years and above (HIV negative), 1982 – 2013/2014**

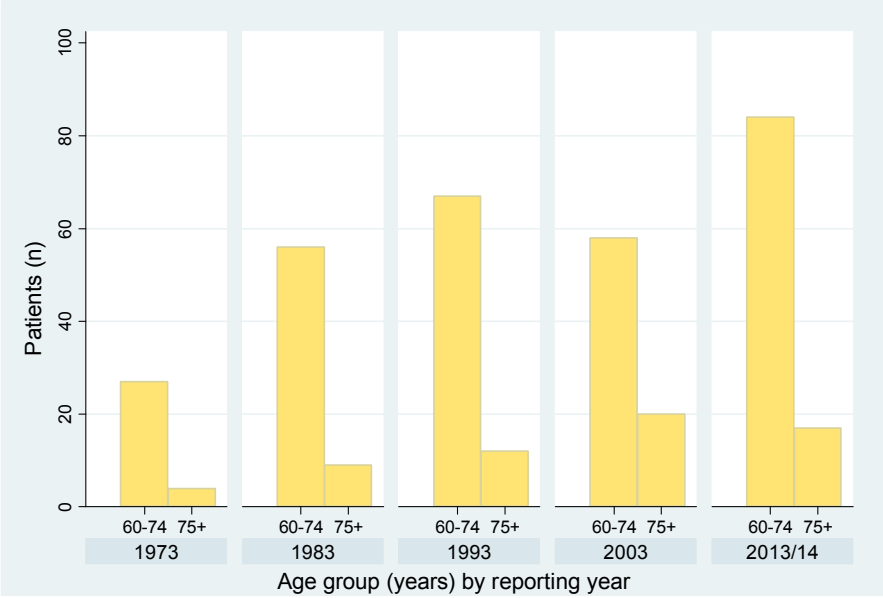


Figure 3a: This shows the number of HIV negative patients in the register aged 60-74 years and 75 and over with severe haemophilia A from 1973 until the present day. It can be seen that the number of such patients has tripled during this period, reflecting therapeutic improvements and increased life expectancy. The dip in numbers in 2003 reflects the effect of HIV, which had a poorer prognosis in older patients.

Figure 3b **Trend in numbers of Non-Severe Haemophilia A patients aged 60 years and above (HIV negative), 1982 – 2013/2014**

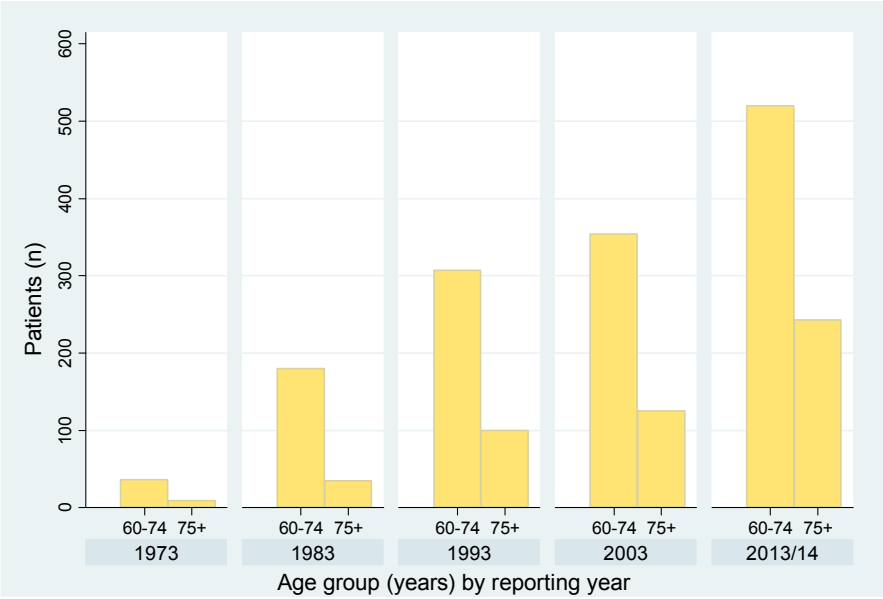


Figure 3b: This shows the number of HIV negative patients in the register aged 60-74 years and 75 and over with non-severe haemophilia A from 1973 until the present day. It can be seen that the number of such patients has increased more than tenfold during this period. This probably reflects a combination of improved diagnosis and reporting as well as therapeutic improvements and increased background life expectancy.

Figure 4a **Trend in numbers of Severe Haemophilia B patients aged 60 years and above (HIV negative), 1982 – 2013/2014**

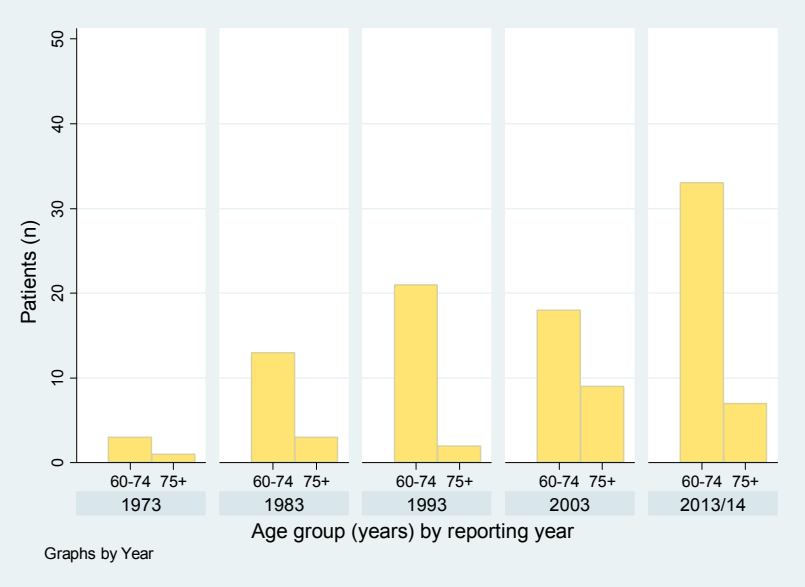


Figure 4a: This shows the number of HIV negative patients in the register aged 60-74 years and 75 and over with Severe haemophilia B from 1973 until the present day. It can be seen that the number of such patients has increased tenfold during this period. This probably reflects therapeutic improvements and increased background life expectancy. Similar to haemophilia A, there is a dip in numbers in patients aged 60-74 years between the early 1990's and early 2000's, although the incidence of HIV was very much lower in haemophilia B than haemophilia A.

Figure 4b **Trend in numbers of Non-Severe Haemophilia B patients aged 60 years and above (HIV negative), 1982 – 2013/2014**

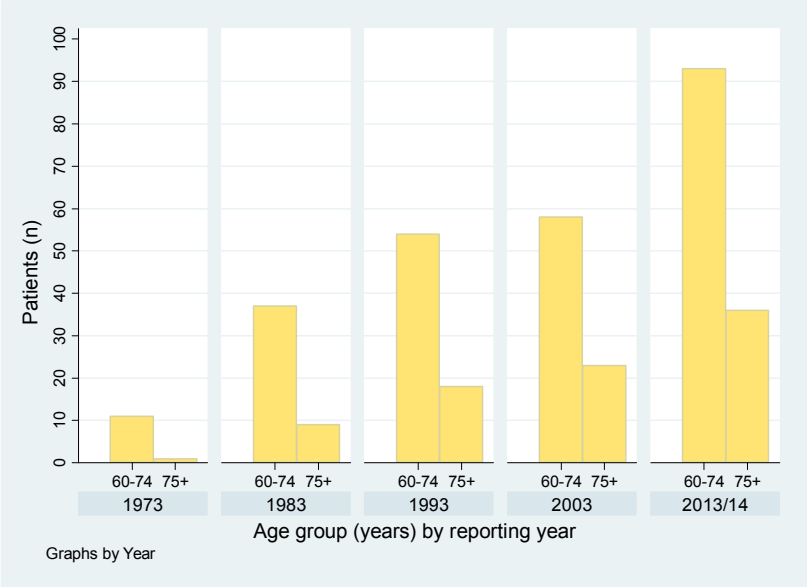


Figure 4b: This shows the number of HIV negative patients in the register aged 60-74 years and 75 and over with non-severe haemophilia B from 1973 until the present day. It can be seen that the number of such patients has increased more than tenfold during this period. This probably reflects a combination of improved diagnosis and registration as well as therapeutic improvements and increased background life expectancy.

Table 8 **Factor VIII units used by UK Haemophilia Centres between April 2013 and March 2014, broken down by diagnosis**

Coagulation Defect	Patients Treated	Plasma FVIII (IU)	Recombinant FVIII (IU)	Investigational FVIII (IU)	Total FVIII (IU)
Haemophilia A	2,861	33,587,330	432,036,007	21,120,111	486,743,448
Haemophilia A Carrier	32	-	586,500	-	586,500
Acquired Haemophilia A	8	14,000	365,500	-	379,500
Haemophilia A with Liver Transplant *	1	-	1,000	-	1,000
von Willebrand disease	581	16,124,920	55,000	-	16,179,920
Probable von Willebrand disease	3	7,500	-	-	7,500
Acquired von Willebrand Disease	21	132,000	2,000	-	134,000
Combined V+VIII Deficiency	4	-	36,000	-	36,000
Other combined diagnoses	15	239,000	1,193,000	-	1,432,000
Miscellaneous *	7	125,500	-	-	125,500
Total	**3,533**	**50,230,250**	**434,275,007**	**21,120,111**	**505,625,368**

Table 8: This shows plasma derived and recombinant factor VIII concentrate usage for 2013/14 broken down by diagnosis. Investigational factor VIII use is also indicated separately. This shows factor VIII usage increased from last year, perhaps reflecting the unusual 4% increase in the number of patients treated in the year.

***** Apparently anomalous use of factor VIII included 8Y usage in seven patients variously diagnosed with either Miscellaneous bleeding disorder or platelet defect. On further investigation, however, all seven turned out to have Thrombotic Thrombocytopaenia Purpura, a diagnosis which we have agreed not to register.

N.B: Haemophilia A Carrier includes females with factor VIII deficiency

Table 9 **Products used to treat Haemophilia A (including inhibitors) between April 2013 and March 2014**

Manufacturer	Product	Total Units
Baxter	Advate	54,909,057
	FEIBA	26,153,490
Bayer	Kogenate	119,282,940
Biotest	Haemoctin	428,000
BPL	FVIII 8Y	468,030
	Optivate	264,000
CSL Behring	Haemate P	10,500
	Helixate Nexgen	56,657,898
Grifols	Alphanate	98,000
	Fanhdi	28,075,300
Novo Nordisk	NovoSeven (mg)	19,231.00
Octapharma	Octanate	4,243,500
	Octaplas (units)	1,800
	Octaplex	2,000
Pfizer	ReFacto AF	201,298,612
Various Manufacturers	Investigational FVIIa (mg)	13
	Investigational Factor VIII	21,120,111

Units in IU unless otherwise stated

Table 9: shows a breakdown of products, listed by supplier, used to treat UK patients with haemophilia A, including those with inhibitors, during the financial year 2013/14.

These figures have been cross-checked against sales figures for the same period supplied by the manufacturers. 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. Sales figures are not reported for reasons of confidentiality.

Note that the use of over 21,000,000 units of investigational factor VIII was reported to us during the year, more than twice last year's total. We have deliberately aggregated and anonymised these products to avoid any breach of individual centre's confidentiality agreements and to take account of commercial sensitivities. Some centres would have refused to share these data with us had we not agreed to this compromise.

Potentially anomalous product use in Table 9 is accounted for as follows: -

BPL 8Y was all administered to a single patient with haemophilia A for immune tolerance induction of a factor VIII inhibitor.

BPL Optivate was administered to a single patient undergoing immune tolerance induction.

Haemate P was administered to four different patients with haemophilia A (lacking inhibitors) in four different centres. In three cases, this was given in error and in the fourth case administered because the centre was running out of rFVIII

Alphanate was administered to a single patient with moderate severity Haemophilia A using this as his routine replacement therapy. He does not have an inhibitor.

Octanate was used for ten patients for immune tolerance induction for factor VIII inhibitors.

Octaplex was used to correct coagulation in a patient with haemophilia A and liver failure prior to a procedure.

Figure 5 Market Share of factor VIII concentrates known to have been used by UK Haemophilia Centres during 2013/14

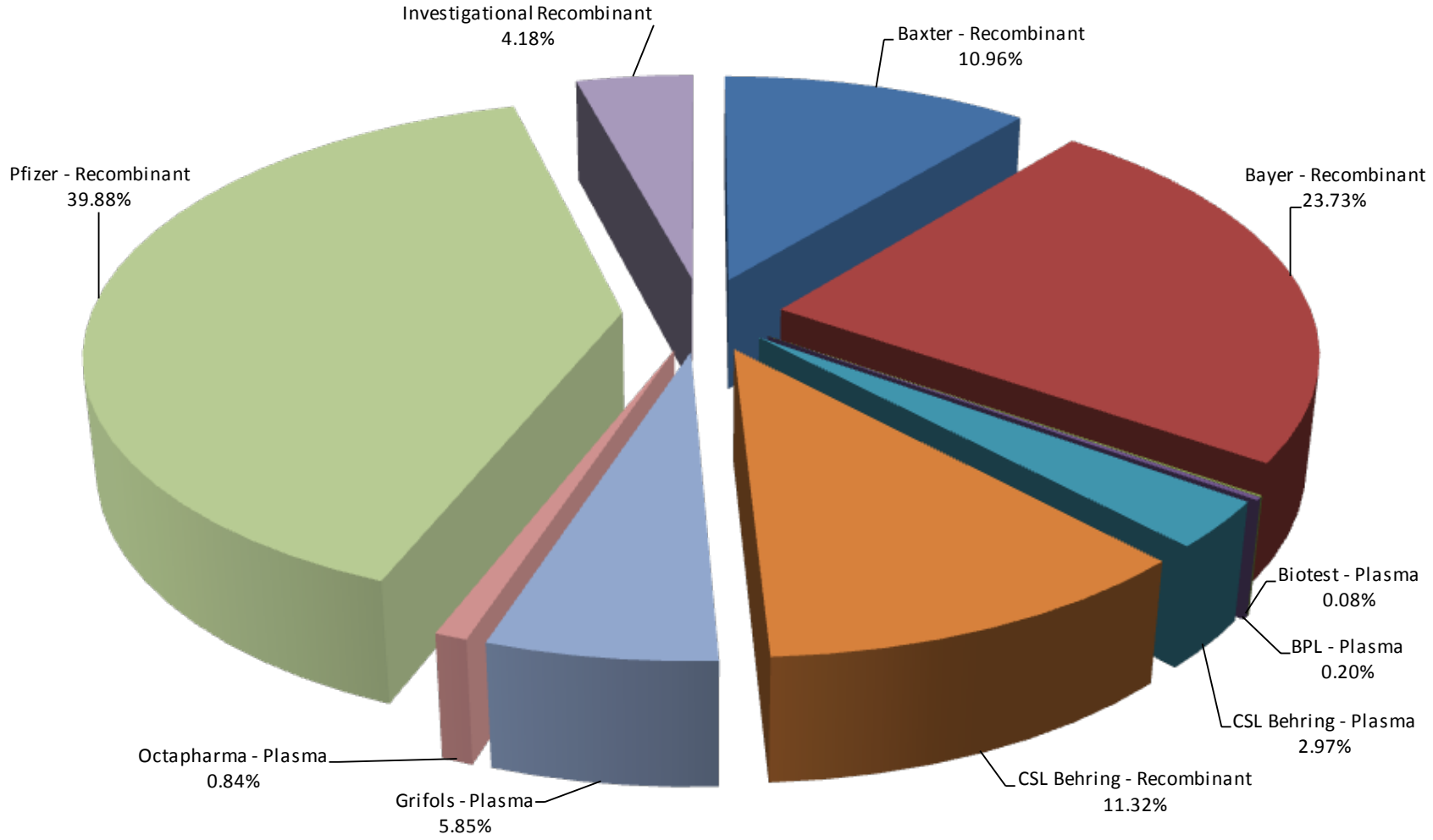


Figure 5: This shows 4.18% of market share taken up with investigational FVIII. Plasma-derived factor VIII is generally used for treatment of von Willebrand disease or for immune tolerance induction but one centre has a significant use of Fanhdi for non-inhibitor patients with haemophilia A and one or two other, isolated patients in other centres use plasma-derived products as their routine replacement therapy.

Figure 6 **Factor VIII units used by UK Haemophilia Centres 1990-2013/14 (by calendar year between 1990 and 2007 and by financial year from April 2008 onwards)**

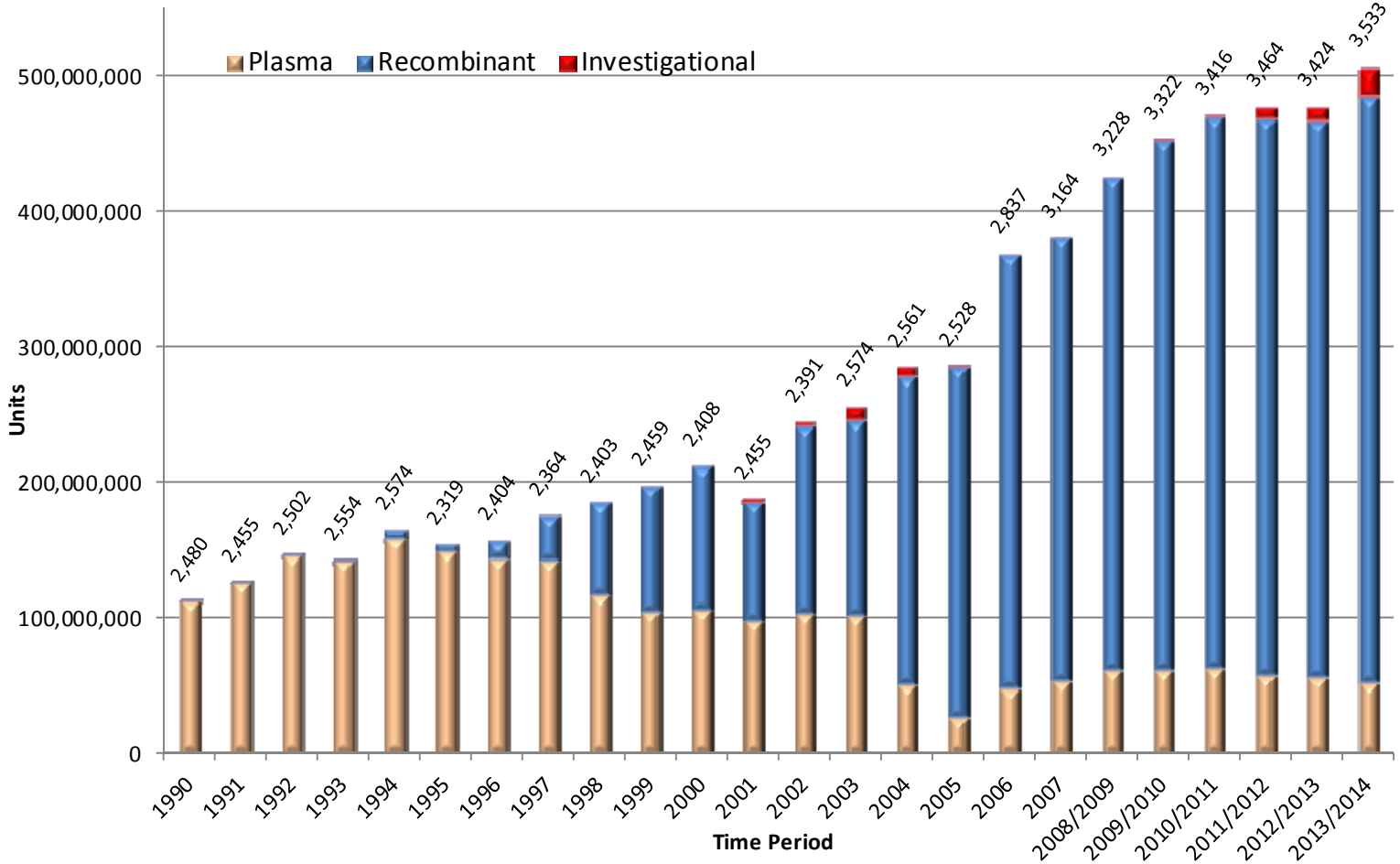


Figure 6: This shows annual UK factor VIII concentrate use for all diagnoses between 1990 and 2013/14. The numbers above each column are the numbers of patients with any diagnosis treated with factor VIII concentrate during the course of the year. This was reported by calendar year up to 2007 and by financial year thereafter.

We have taken care to include in these figures the currently very significant use of investigational drugs.

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

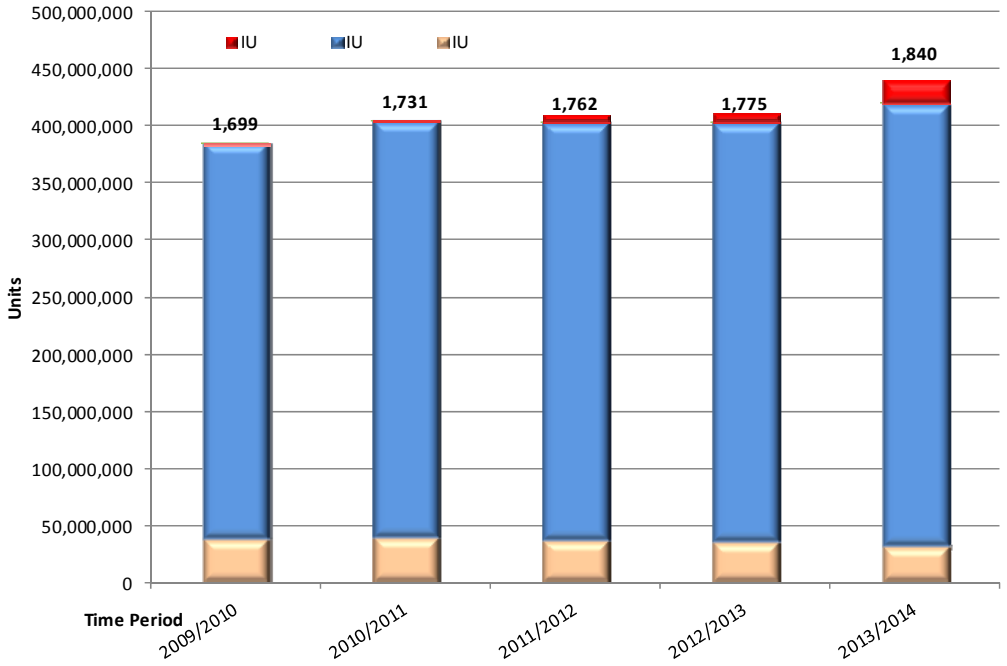
Figure 7: This bar diagram shows the last 5 years (2009-2013/14) of usage for severe haemophilia A only. The numbers over the bars are the number of such patients treated within year. Those patients with severe haemophilia not treated in year are excluded. The accompanying table gives the actual numbers and trends for both usage and patient numbers.

This shows an increase of 141 patients (8.3%) in patients with severe haemophilia treated and a 55,622,403 million unit increase (14.4%) in factor VIII use within that period.

During this period, the usage of plasma-derived factor VIII for severe haemophilia A has declined by 17%.

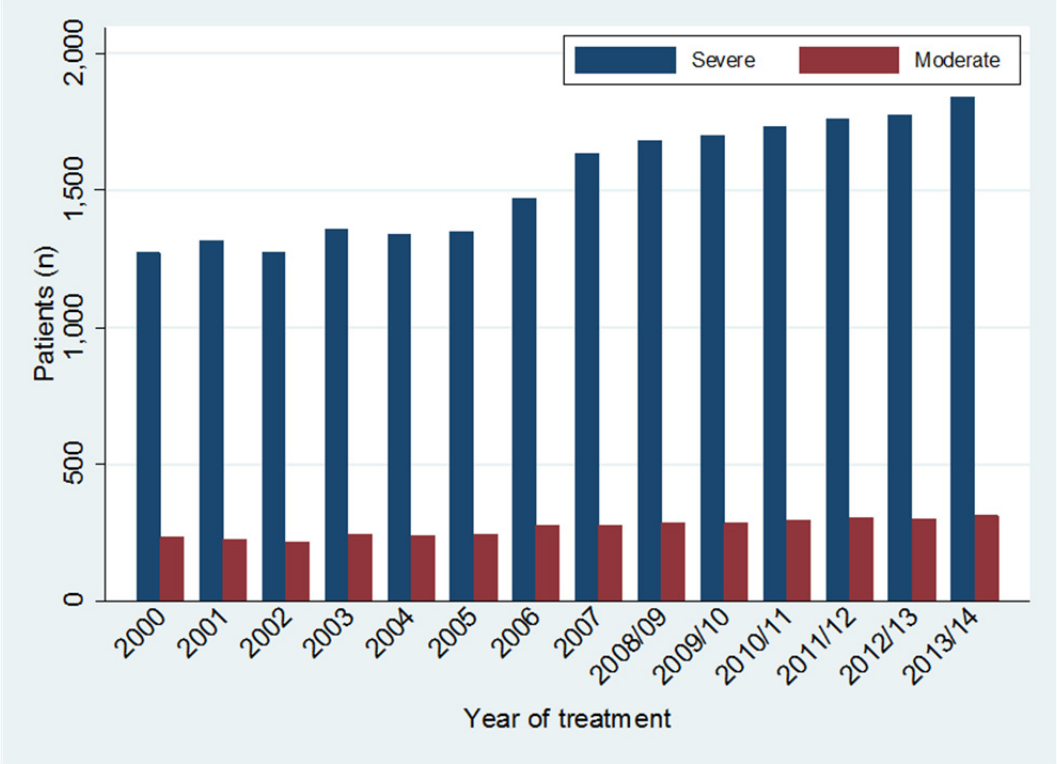
At the same time, the use of investigational factor VIII has increased almost 40-fold from 549,623 to 21,073,111 and more than doubled in the last 12 months. Overall usage of factor VIII for severe haemophilia A currently stands at over 441 million units.

Figure 7 Factor VIII units used by UK Haemophilia Centres to treat Severe Haemophilia A – 2009/10 - 2013/14



Year	Plasma		Recombinant (excluding investigational)		Investigational rFVIII		Total		Patients	
	IU	% difference since 2009/10	IU	% difference since 2009/10	IU	% difference since 2009/10	IU	% difference since 2009/10	n	% difference since 2009/10
2009/2010	38,144,300	100.00%	346,689,442	100.00%	549,623	100.00%	385,383,365	100.00%	1,699	100.00%
2010/2011	39,954,241	104.74%	364,017,724	105.00%	1,224,384	222.77%	405,196,349	105.14%	1,731	101.88%
2011/2012	36,510,299	95.72%	366,180,151	105.62%	7,947,007	1445.90%	410,637,457	106.55%	1,762	103.71%
2012/2013	35,194,265	92.27%	367,091,549	105.88%	9,183,346	1670.84%	411,469,160	106.77%	1,775	104.47%
2013/2014	31,646,330	82.96%	388,286,327	112.00%	21,073,111	3834.10%	441,005,768	114.43%	1,840	108.30%

Figure 8 **Patients with Severe or Moderate Haemophilia A treated by UK Haemophilia Centres - 2000-2013/14**



Treatment Year	Severe Haemophilia A Patients		Moderate Haemophilia A Patients	
	n	% difference since 2000	n	% difference since 2000
2000	1273	100	233	100
2001	1316	103.4	226	97
2002	1275	100.2	216	92.7
2003	1358	106.7	242	103.9
2004	1338	105.1	240	103
2005	1349	106	246	105.6
2006	1470	115.5	278	119.3
2007	1634	128.4	278	119.3
2008/09	1681	132.1	287	123.2
2009/10	1700	133.5	284	121.9
2010/11	1731	136	294	126.2
2011/12	1762	138.4	307	131.8
2012/13	1775	139.4	301	129.2
2013/14	1840	144.5	312	133.9

Figure 8 shows the change in the number of patients with severe or moderate severity haemophilia A treated in the UK since 2000. Taking the year 2000 as 100%, there has been a 44% increase in the number of patients with severe haemophilia A treated and a 34% increase in the number of patients with moderate severity haemophilia treated since 2000. This increase is presumably due to the cumulative effect of a modest increase in birth-rate and life expectancy and net immigration of patients with haemophilia.

Note on Figures 9 – 11 and 21 – 23 (Maps)

The commissioning regions shown in these maps are those used under the new commissioning arrangements for England and have therefore changed from previous reports. Furthermore, patients are allocated to the haemophilia centre treating them and not allocated to a commissioning region by way of their GP practice code as in previous years under different commissioning arrangements. This change will tend to increase the apparent concentration of patients in central London, since the London tertiary referral centres see patients from a very wide area.

Figure 9 **Factor VIII Usage (including Inhibitor) divided by number of Severe Haemophilia A patients by commissioning region**

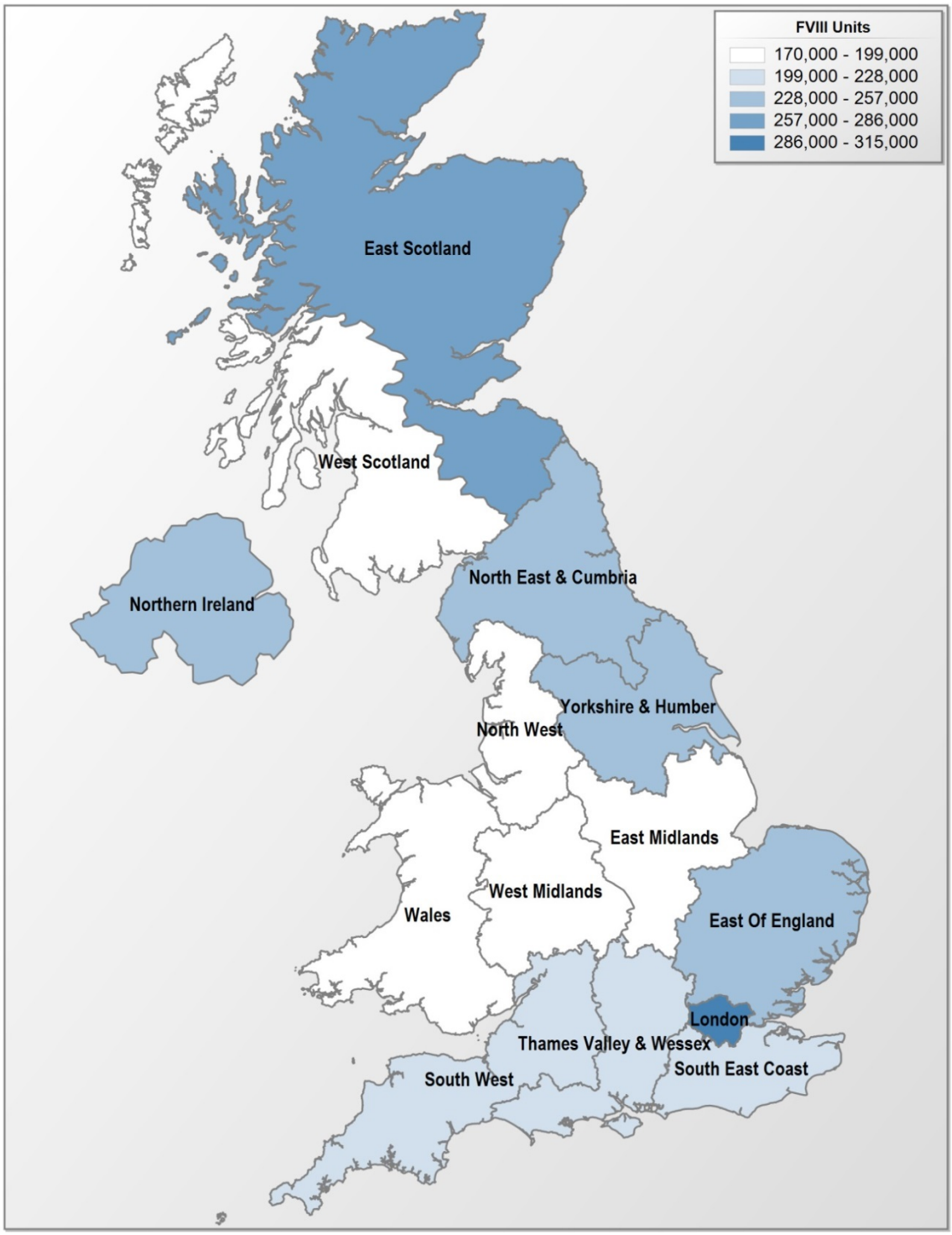


Figure 9: This map shows factor VIII usage divided by the number of severe haemophilia A patients, including those with a current inhibitor, by commissioning region. This gives a measure of the intensity of replacement therapy for severe Haemophilia A and shows considerable regional variation.

Figure 10 **Total Number of Severe Haemophilia A patients by commissioning region**

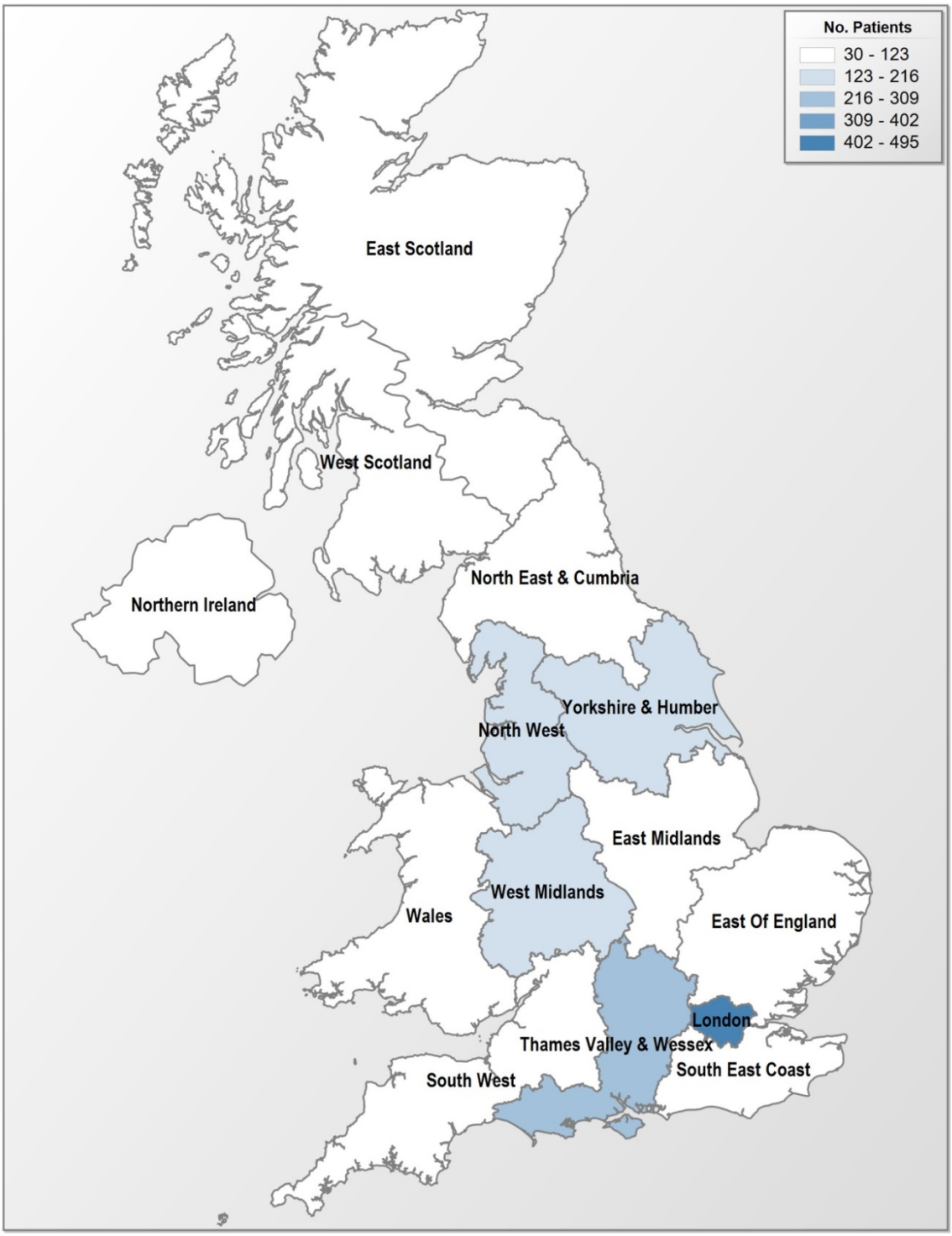


Figure 10: This map shows the regional distribution of severe haemophilia A. This also shows considerable regional variation but this is at least partly attributable to differences in population density, since this map is not corrected for population density.

Figure 11 FVIII Units – usage per capita of general population by administration

Figure 11: shows usage of factor VIII per capita of population. This corrects usage for population density and should give a measure of the intensity of treatment per capita of population. Unfortunately, the new Specialist Commissioning regions in England do not correspond with administrative regions and so it is no longer possible for us to correct for population density by Specialist Commissioning region. Treatment intensity per capita of population is therefore shown for the whole of England and is not broken down regionally.

Table 10 Factor VIII usage by region for Severe Haemophilia A patients only (incl. treatment for inhibitors)

Region	General Population *	Patients treated (n) Severe Haemophilia A	Total FVIII Units (IU) Severe Haemophilia A	Mean Usage Severe Haemophilia A	FVIII Units Per Capita Severe Haemophilia A
London		486	146,278,874	300,985	
South Yorkshire & Bassetlaw		183	46,759,331	255,515	
East Anglia		56	13,088,500	233,723	
Cumbria, Northumberland & Tyne and Wear		74	17,076,500	230,764	
Surrey & Sussex		34	7,738,000	227,588	
Wessex		232	47,332,550	204,020	
Bristol, North Somerset & South Gloucestershire		87	17,687,250	203,302	
Cheshire, Warrington & Wirral		178	31,869,000	179,039	
Leicestershire & Lincolnshire		93	16,227,208	174,486	
Birmingham & Black Country		143	24,466,950	171,098	
England	**53,493,729**	**1,525**	**368,524,163**	**241,655**	**6.89**
Northern Ireland	1,823,634	68	16,656,100	244,943	9.13
Scotland East	2,885,570	94	24,944,505	265,367	8.64
Scotland West	2,428,030	73	13,981,000	191,521	5.76
Wales	3,074,067	85	16,900,000	198,824	5.50
United Kingdom	**63,705,030**	**1,840**	**441,005,768**	**239,677**	**6.92**

English regions ranked by mean usage

* Source: ONS, Mid-2012 Population estimate based on the 2011 census: Adapted from data from the Office for National Statistics licensed under the Open Government Licence v.1.0.
Population data for Scotland supplied by National Records of Scotland © Crown Copyright 2012

Table 10: shows factor VIII usage by country and commissioning region, ranked by number of units per patient with severe haemophilia. This suggests a narrower range of clinical practice from region to region than observed in earlier years though there is still a 75% range.

Usage per capita of population is reported for the whole of England since the administrative regions do not match Specialist Commissioning regions for England. This means that population cannot be calculated by Specialist commissioning region. Usage per capita for Scotland and England are fairly closely matched though per capita usage in Northern Ireland is noticeably higher.

Please note, that the figures are based on severe haemophilia A patients treated and not on the number of patients registered. The allocation of patient's to regions is explained below.

N.B:

Patients resident in England are reported against all English commissioning areas in which they were treated, so may be counted more than once.

The total number of severe Haemophilia A patients treated in the UK in 2013/14 was 1840.

Patients resident in Wales, Scotland or Northern Ireland are reported against their devolved administrations, regardless of where they were treated.

Patients resident in Scotland are reported against East/West Scotland according to their home postcode, rather than where they were treated.

Patients resident in England and treated in Wales, Scotland or Northern Ireland are reported against the devolved administration in which they were treated.

Patients resident outside the UK are reported against the commissioning areas in which they were treated.

Figure 12 **Annual FVIII usage 2013/14 in Severe Haemophilia A patients *aged under 18 years* with no current inhibitor, by centre, ranked by median usage**

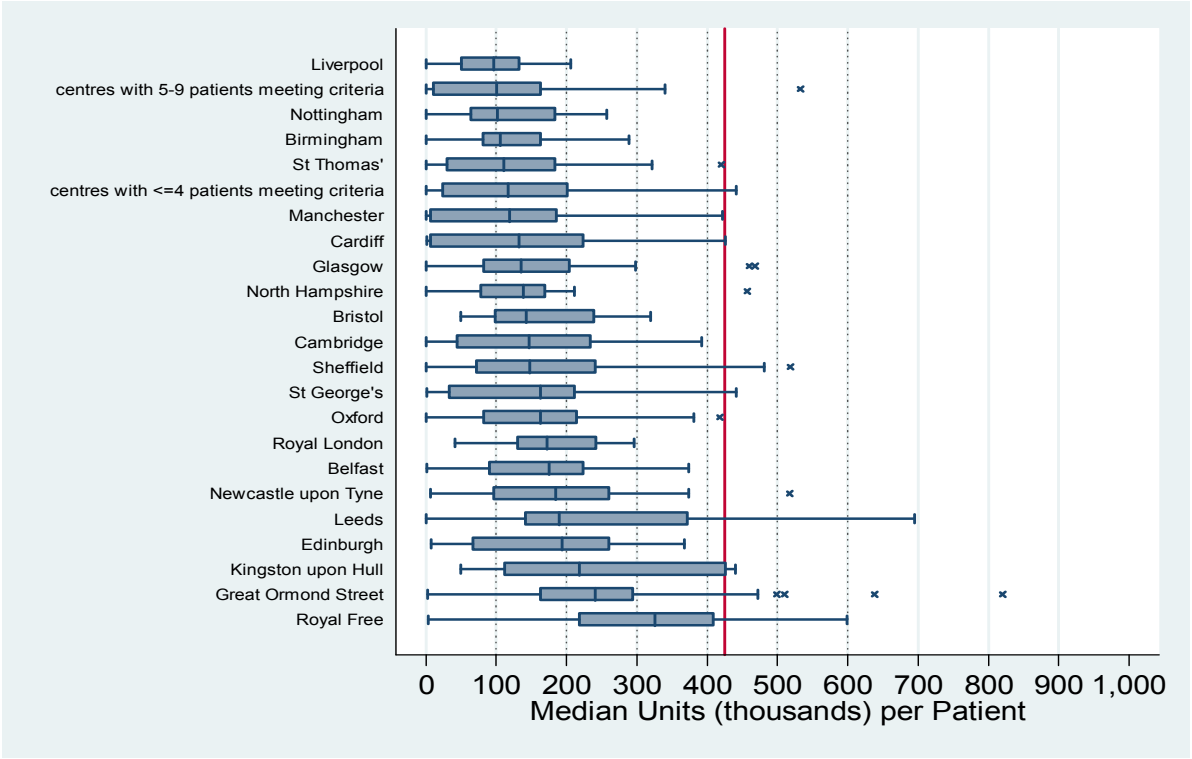


Figure 12: shows a box and whisker plot of factor VIII usage by Haemophilia Centre in patients with severe haemophilia A aged less than 18 years with no current inhibitor. Centres are ranked by median annual usage per patient with severe haemophilia A. The boxes show the 25th and 75th percentiles and the whiskers show the arithmetic range of use excluding outliers.

Outliers are identified by the statistical software by reference to the usage in that individual centre where the patient's usage is greater than 1.5 times the interquartile range (IQR) from the nearest quartile at centre level. They are outliers from the normal practice of the centre rather than by reference to practice in the UK as a whole. Some outliers in some centres therefore use less than patients not deemed to be outliers in other centres.

The vertical red line (436.450 IU/patient/year) indicates the 95th percentile of units used for the whole UK.

It should be noted that usage for the Royal Free Hospital is skewed, since they manage no children younger than 11 years of age.

Data table for Figure 12

Haemophilia Centre	Patients treated	Patients treated with weight reported	Total Units	Median Units
Royal Free	21	21	6,148,000	326,000
Great Ormond Street	80	80	19,500,750	241,125
Kingston upon Hull	11	11	2,557,000	218,250
Edinburgh	11	9	1,835,920	194,000
Leeds	29	25	7,495,750	189,250
Newcastle upon Tyne	22	21	4,212,500	184,500
Belfast	24	22	4,081,700	175,100
Royal London	15	12	2,758,000	172,000
Oxford	44	44	7,299,750	163,250
St George's	11	11	1,639,000	163,000
Sheffield	28	26	4,765,750	147,250
Cambridge	25	23	3,702,750	146,250
Bristol	21	21	3,410,750	142,750
North Hampshire	19	18	2,656,750	138,000
Glasgow	32	32	4,944,000	135,625
Cardiff	15	13	2,151,750	132,500
Manchester	44	37	5,074,772	118,750
Centres with <=4 patients meeting criteria	48	44	6,356,200	116,625
St Thomas'	22	21	2,765,000	111,250
Birmingham	41	41	4,691,250	106,000
Nottingham	18	16	2,015,500	101,625
Centres with 5-9 patients meeting criteria	55	53	6,107,975	100,500
Liverpool	20	18	1,910,500	96,500

Figure 13 **Annual FVIII usage 2013/14 in Severe Haemophilia A *patients aged 18 years or more* with no current inhibitor, by centre, ranked by median usage**

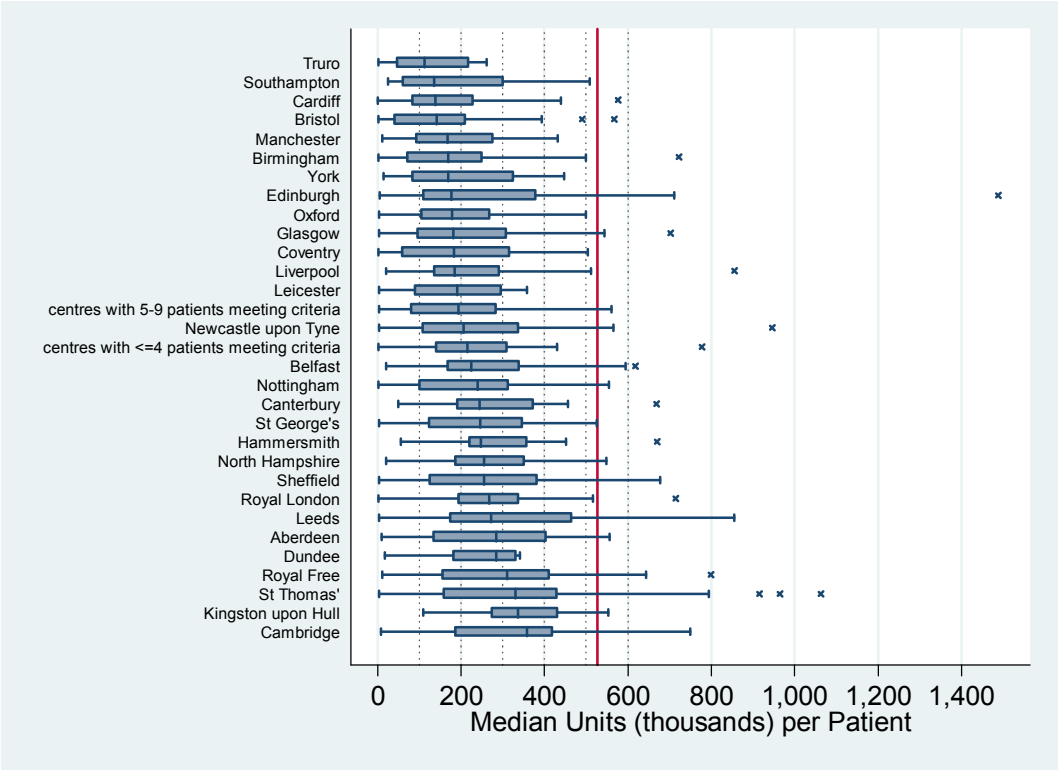


Figure 13: shows a box and whisker plot of factor VIII usage per patient by centre, ranked by median usage (IU per patient per year), for severe haemophilia A patients with no inhibitor reported in-year, aged 18 years and over. Again, the boxes show the 25th to 75th percentile, the whiskers show the arithmetic range and the median appears as a line in the box. The 95th percentile of usage for the whole group, regardless of centre (526,000 IU) is indicated by the red line.

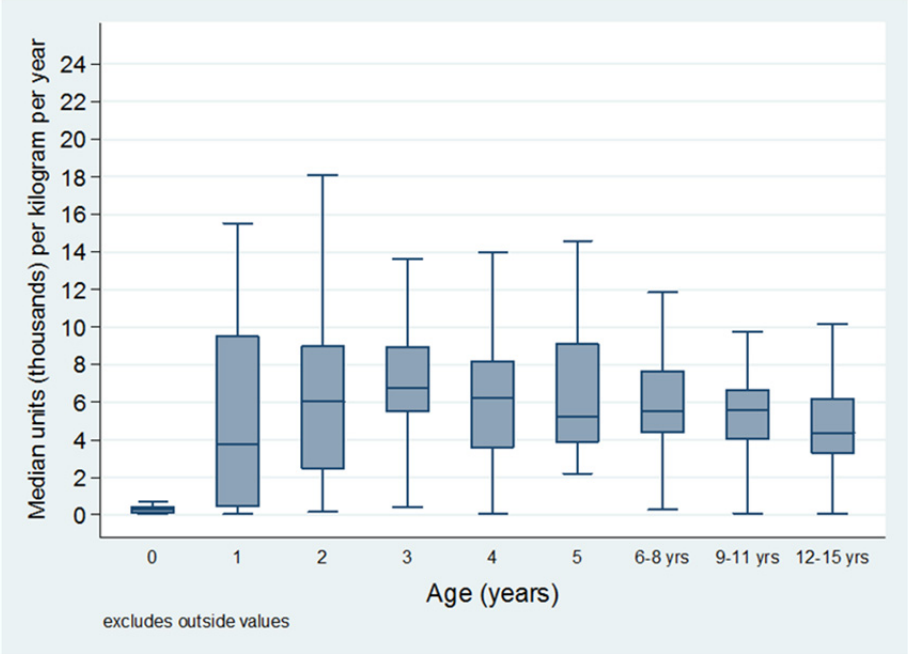
The adult outliers also show that a small number of patients, maybe one or two in each centre, use a great deal of factor VIII, despite having apparently no reported inhibitor in year. Two of these patients use in excess of a million units per year and 19 use in excess of 700,000 units per year. They used a mean of 844,868 units per year, and median 787,500 units (IQR 722,000 to 915,000 units per year). This group will be the subject of separate study, to better understand the reasons for their factor usage.

Data table for Figure 13

Haemophilia Centre	Patients treated	Patients treated with weight reported	Total Units	Median Units
Cambridge	24	24	7,720,750	358,500
Kingston upon Hull	10	10	3,474,500	336,000
St Thomas'	103	102	34,011,750	330,000
Royal Free	114	114	33,230,344	311,250
Dundee	14	14	3,264,330	284,815
Aberdeen	10	10	2,724,010	284,000
Leeds	31	19	9,854,000	271,500
Royal London	41	39	11,063,000	267,500
Sheffield	41	41	10,590,831	256,000
North Hampshire	54	53	14,629,000	255,500
Hammersmith	21	21	6,036,500	247,500
St George's	28	28	6,802,500	245,500
Canterbury	17	17	4,712,000	244,000
Nottingham	24	24	5,529,548	240,500
Belfast	42	42	10,819,400	224,000
Centres with <=4 patients meeting criteria	17	17	4,107,500	216,000
Newcastle upon Tyne	47	47	11,341,500	206,000
Centres with 5-9 patients meeting criteria	76	61	15,378,500	194,000
Leicester	20	20	3,728,160	191,000
Liverpool	29	25	6,688,000	184,000
Coventry	12	12	2,347,000	183,000
Glasgow	50	50	10,145,000	182,000
Oxford	86	85	17,099,300	177,750
Edinburgh	28	28	7,560,770	176,275
York	10	1	2,032,450	170,000
Birmingham	67	62	12,490,500	169,000
Manchester	87	87	15,615,228	168,500
Bristol	28	28	4,420,000	142,000
Cardiff	33	32	5,793,000	138,000
Southampton	14	14	2,637,000	136,000
Truro	11	10	1,304,500	112,000

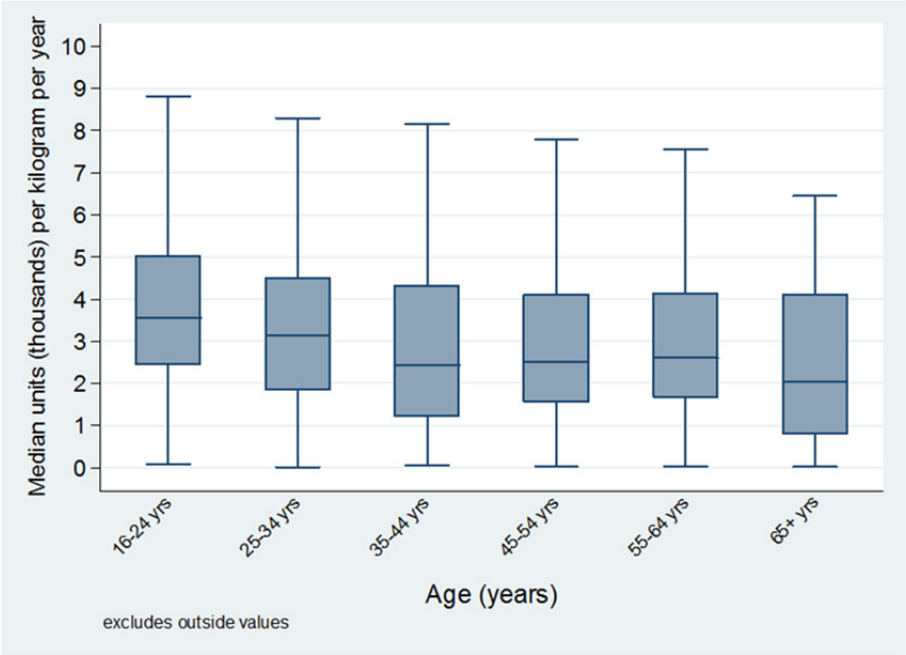
Figures 14a&b Median factor VIII units used per kilogram body weight per year in Severe Haemophilia A patients without inhibitors, 2013/14, broken down by decades of life

14a. Paediatrics



Weight data are missing for 33/523 patients, including 21/35 children aged <12m

14b. Adults



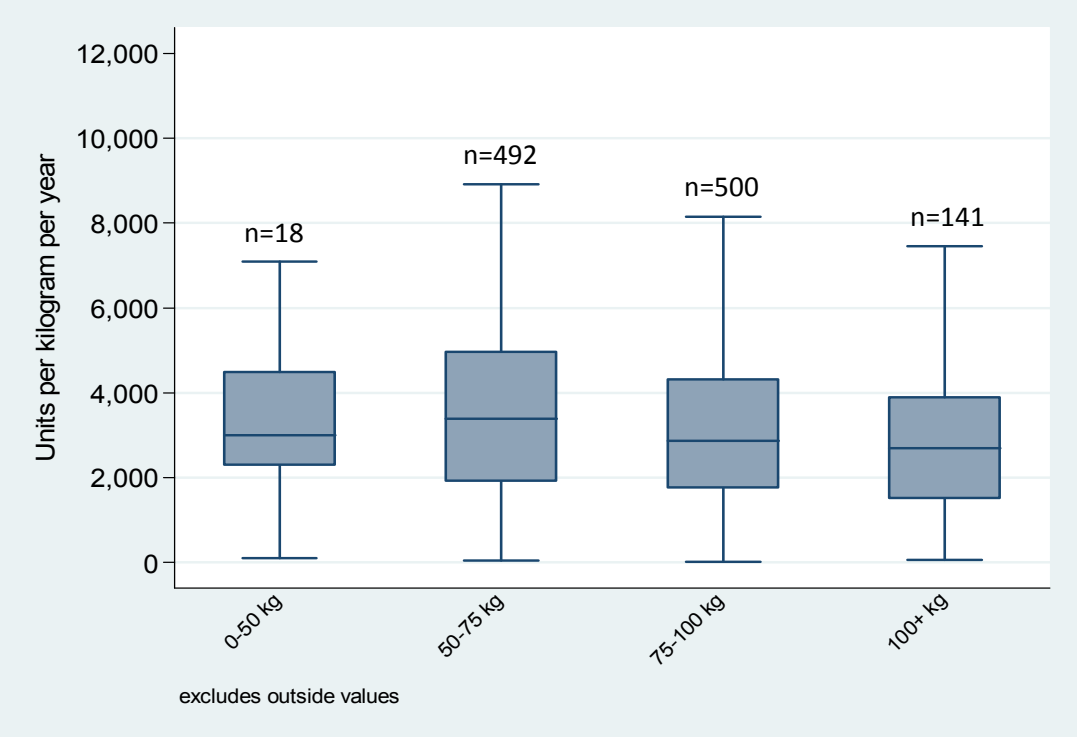
Weight data are missing for 49/1200 patients

Figures 14a & 14b: (overleaf) show box and whisker plots showing the median (central lines), IQR (box) and the arithmetic range (whiskers) of factor VIII usage per kg bodyweight per year in UK patients with severe haemophilia A, without inhibitors and broken down by age. Note that we have bodyweight data for 1151/1200 patients with severe haemophilia A over 16 years of age. Bodyweight data for children is less complete because it must be current and recent to be used for analysis

The most intensive general usage appears to be in the children (Figure 14a). This shows a dramatic increase in treatment intensity in the first two years of life, as prophylaxis is established, up to a median of 6737 iu/kg/year by the third year of life, as prophylaxis is established. Although half-life and recovery improve steadily until about age 6, treatment intensity (IU/Kg/Year) levels off and even declines after the third year of life.

Amongst adults over 16 years of age, treatment intensity was greatest in young adults levelling off at about 2500 IU/Kg/year in the mid-thirties. Most young adults are using prophylaxis. The median units per kilogram is in the prophylactic range 3,000-6,000 IU/kg/year for this group. Older patients have a median usage below the prophylactic range and their IQRs suggest that some of these patients use prophylaxis and some are on modest treatment on demand regimens.

Figure 15 **Median factor VIII units used per kilogram body weight per year in Severe Haemophilia A patients without inhibitors aged 16 and over, 2013/14**



Weight are missing for 49/1200 SHA patients known to be aged 16+

Figure 15: shows box and whisker plots (median, IQR and arithmetic range) of median units/kg/year used by all UK patients with severe haemophilia A over the age of 16 and without inhibitors, broken down by bodyweight. The total number of patients in each group is indicated by the number over each box and whisker. Note that we have bodyweight data for 1151/1200 patients with severe haemophilia A >16 years of age.

Since factor VIII recovery increases progressively as BMI increases, one would expect factor VIII consumption per kilogram to decline as bodyweight increases. This seems only marginally to be the case, suggesting that the dose may be largely scaled up by bodyweight without taking increased factor VIII recovery with increasing bodyweight into consideration (age effect on half-life and bodyweight effect on recovery), so that the obese may be over-treated.

Although Body Mass Index (BMI) would be a better reflection of obesity than bodyweight, it would have to be accepted that the >100 kg group illustrated will all be obese. Currently we do not collect height and so cannot calculate BMI.

Figure 16 **Median and interquartile range usage of factor VIII: UK patients with severe Haemophilia A lacking inhibitors broken down by age, 2008/09 – 2013/14**

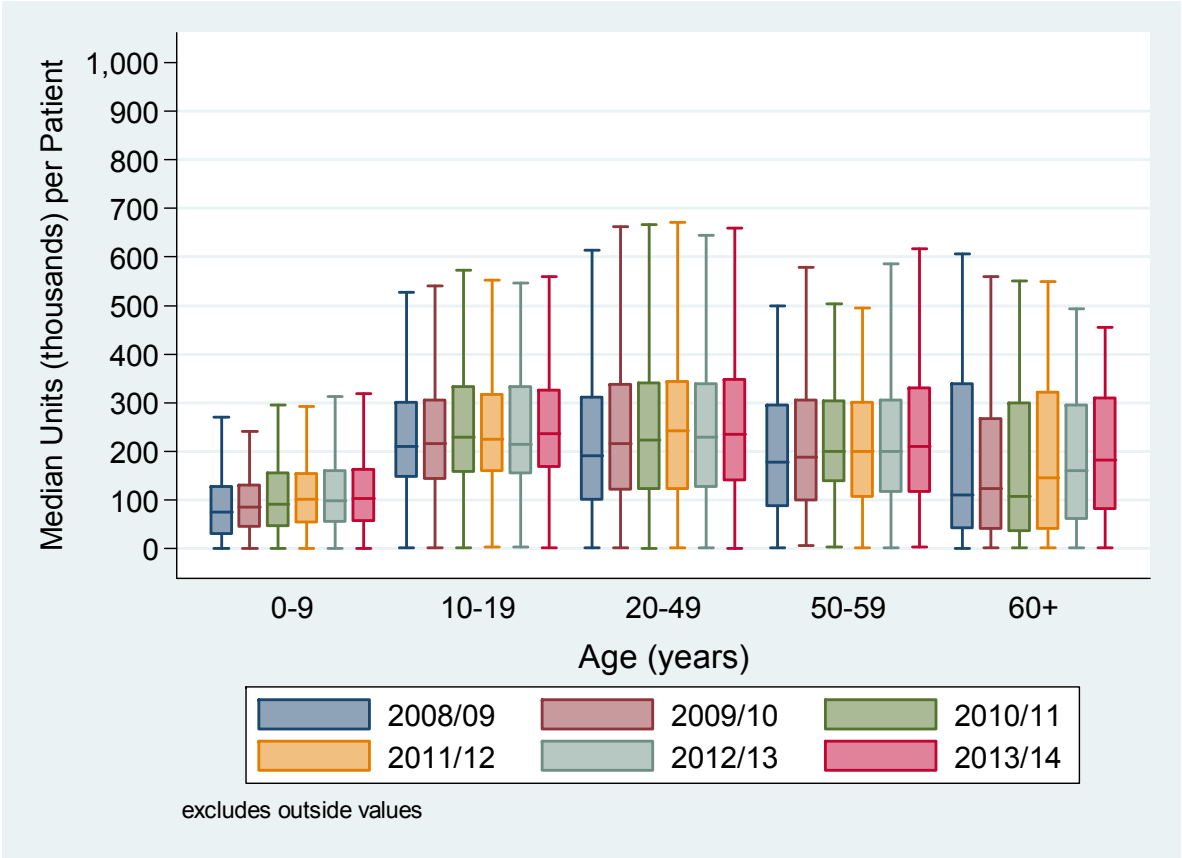


Figure 16: This shows box and whisker plots of median, IQR and arithmetic range of factor VIII usage by all UK patients with severe haemophilia A lacking inhibitors broken down by age and year. This shows a marked upward trend in the number of units issued per year in the under-10s, less marked upward trend in the 10-19 years age group in which patients appear to have reached adult treatment intensity. Since prophylaxis has been their standard of care since 1996, this implies greater intensity of prophylaxis in this group and probably reflects a general trend from 3-times a week to every second day prophylaxis.

Figure 17 **Severe Haemophilia A patients with no current inhibitor between April 2013 & March 2014: median usage by inhibitor history**

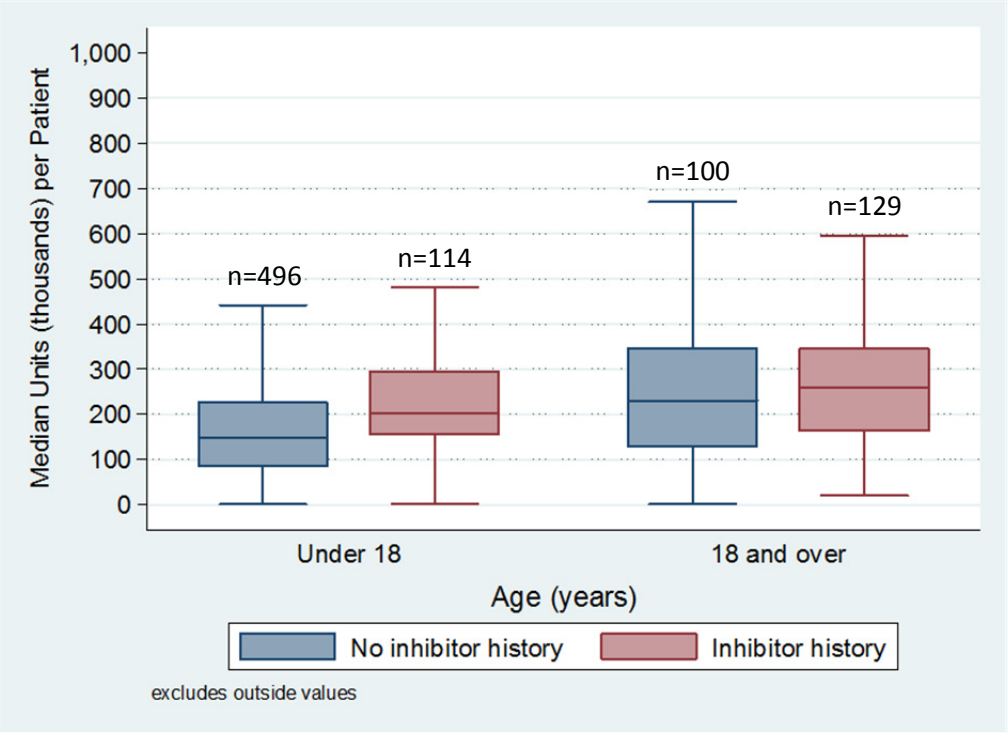
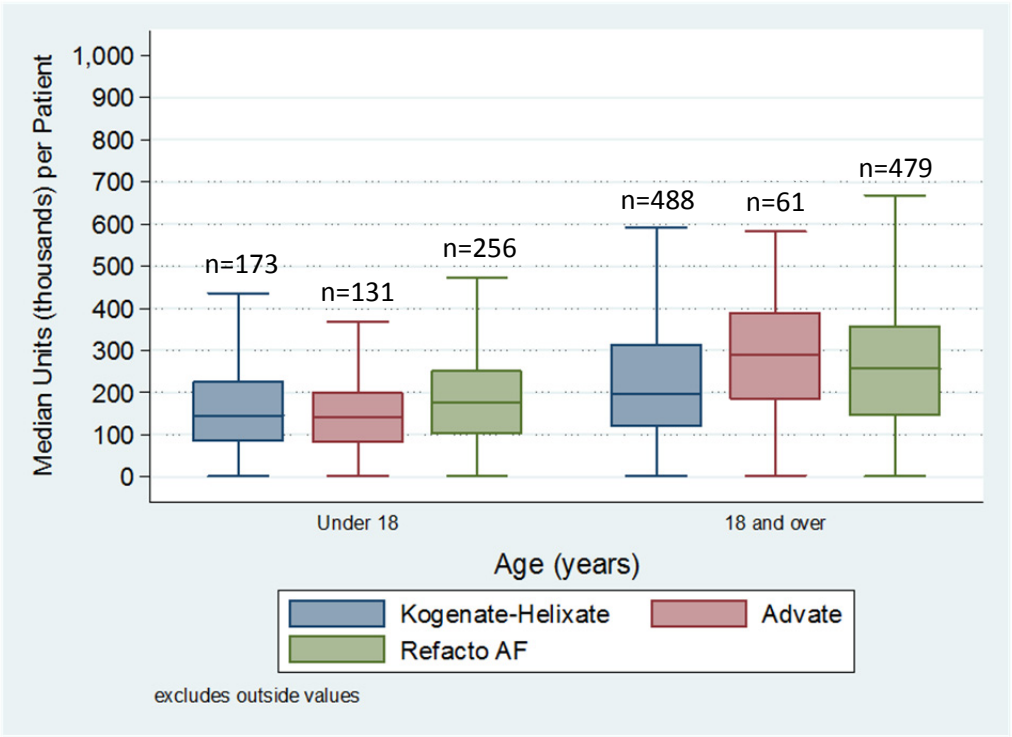
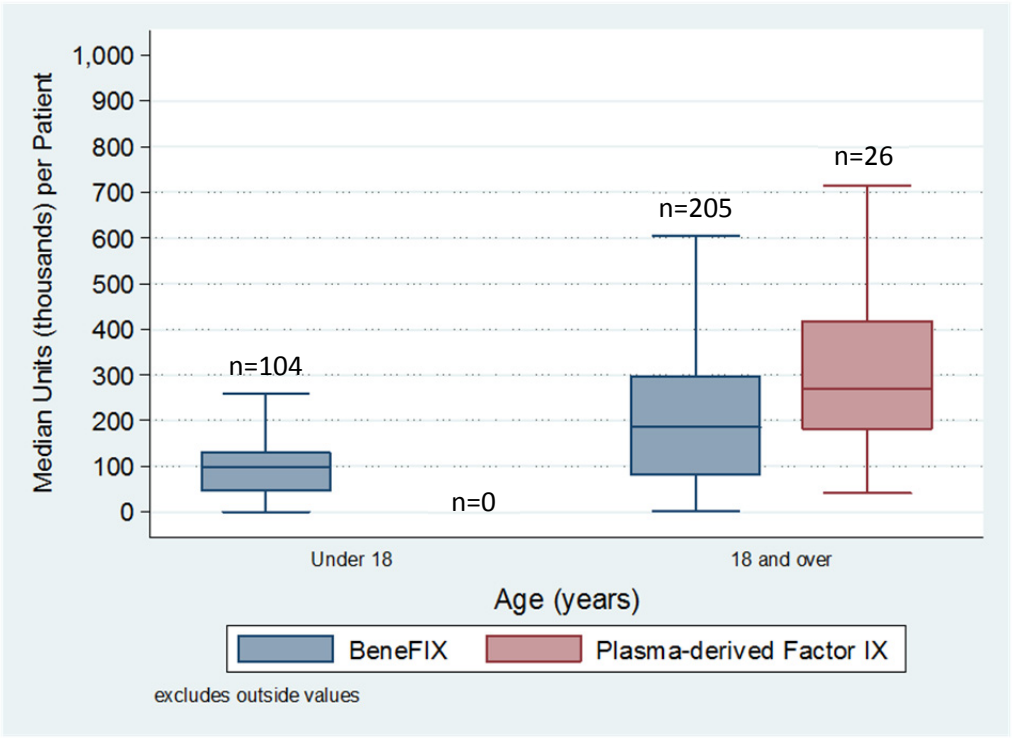


Figure 17: shows a box and whisker plot of median, IQR and arithmetic range of median usage of factor VIII for UK patients with severe haemophilia but lacking a current inhibitor. These data are broken down by age (less than 18 years, and 18 years and older) and by past history or no past history of factor VIII inhibitors. The number of subjects in each group is indicated by the number over each box.

This shows that children with a past history of factor VIII inhibitors use significantly more factor VIII than those lacking such a history (Mann-Whitney U test $p<0.005$) but this association is not currently seen in adults ($p=0.1$). Whilst there are a number of possible explanations for this, it raises the possibility that "tolerant" ex-inhibitor patients may still have a relatively reduced half-life and low-level circulating factor VIII inhibitors, below the limit of detection of the current Bethesda assay. This may gradually disappear through the use of prophylaxis, so that usage is not-associated with past inhibitor history amongst adult patients.

Figures 18a&b Severe Haemophilia A & B patients with no current inhibitor using only one product between April 2013 & March 2014: median usage





Figures 18 a & b: show box and whisker plots (Median, IQR and arithmetic range) comparing median annual factor VIII usage per patient with severe haemophilia A or B, lacking a current inhibitor and using only a single product during the course of that year.

This is further broken down by age and the brand of product used. The numbers of patients in each group are indicated by the numbers above each box.

Although there is no clear pattern of usage and the pattern of usage appears to differ between children and adults, the difference in volume of factor VIII used per patient did differ significantly between products. (Mann-Whitney U test: Kogenate/Helixate, ReFacto AF or Advate, under 18 years: $p=0.003$; 18 years and over: $p<0.005$).

There was also a statistically significant difference in usage of BeneFIX and plasma-derived factor IX for haemophilia B in adults aged 18 years and over, though the number using plasma derived factor IX was very small. Counter-intuitively, given the reduced recovery of BeneFIX, BeneFIX-users used significantly less factor IX than plasma-derived FIX users (18 years and over: $p=0.01$).

Table 11 Factor IX units used by UK Haemophilia Centres

Coagulation Defect	Patients Treated	Plasma FIX (IU)	Recombinant FIX (IU)	Investigational FIX (IU)	Total FIX (IU)
Haemophilia B	654	10,904,590	68,227,419	5,442,896	84,574,905
Haemophilia B Carrier	48	104,500	528,099	-	632,599
Combined Diagnoses	1	-	21,000	-	21,000
Total	**703**	**11,009,090**	**68,776,518**	**5,442,896**	**85,228,504**

Table 11: This shows UK factor IX usage for 2013/14, broken down by product type and diagnosis. Note that this includes the use of over 5,400,000 units (6.4%) of investigational recombinant factor IX. For reasons of study confidentiality, we are unable to break down this table into short and long-half-life products.

N.B:

Haemophilia B includes patients with FIX Leyden
Haemophilia B Carrier includes Females with FIX deficiency and FIX Leyden carriers

Table 12 Products used to treat Haemophilia B (including inhibitors)

Manufacturer	Product	Total Units	%
Baxter	FEIBA	1,556,500	1.81%
Biotest	Haemonine	204,000	0.24%
BPL	Replenine	4,602,590	5.36%
CSL Behring	Mononine	568,000	0.66%
Grifols	Alphanine	5,530,000	6.44%
Novo Nordisk	NovoSeven (mg)	6,984	0.01%
Pfizer	BeneFIX	67,986,919	79.15%
Various Manufacturers	Investigational Factor IX	5,442,896	6.34%
	Total	**85,897,889**	**100.00%**

Units in IU unless otherwise stated

Table 12: gives a breakdown of the products used to treat haemophilia B in the UK in 2013/14, organised by supplier. These figures have been cross-checked with sales figures provided by the suppliers. Whilst we would not expect a perfect match between manufacture's sales figures and NHD usage figures, there was a high level of correlation except for low-usage products. Sales figures are not reported for reasons of confidentiality.

Note that more than 5,400,000 million units of investigational factor IX were used in year. We have deliberately aggregated and anonymised these products to avoid any breach of individual centre's confidentiality agreements and to take account of commercial sensitivities. For reasons of confidentiality, we are unable to break down this table into short and long-half-life products. We would advise that data on trial products should be shared at a local level with commissioners so that they have a realistic estimate of product consumption and avoid any inadvertent reduction in future budget.

Figure 19 Market Share of Factor IX Concentrates known to have been used by UK Haemophilia Centres

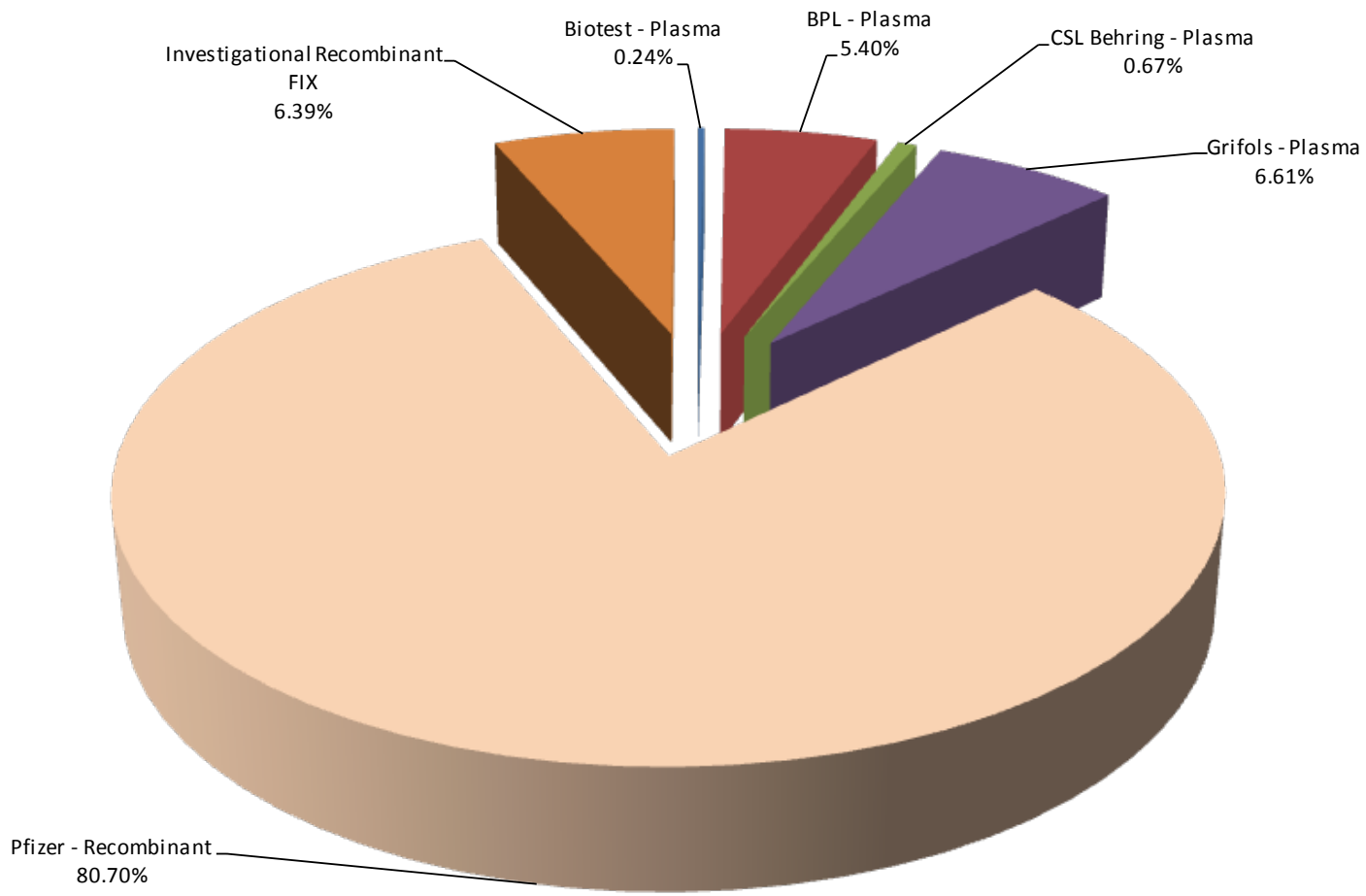


Figure 19: This pie-chart gives a breakdown of factor IX market share for 2013/14. Note that 6.39% of factor IX usage is accounted for by investigational products.

Figure 20 **Factor FIX units by UK Haemophilia Centres 1990-2014 (by calendar year between 1990 and 2007 and by financial year from April 2008 onwards)**

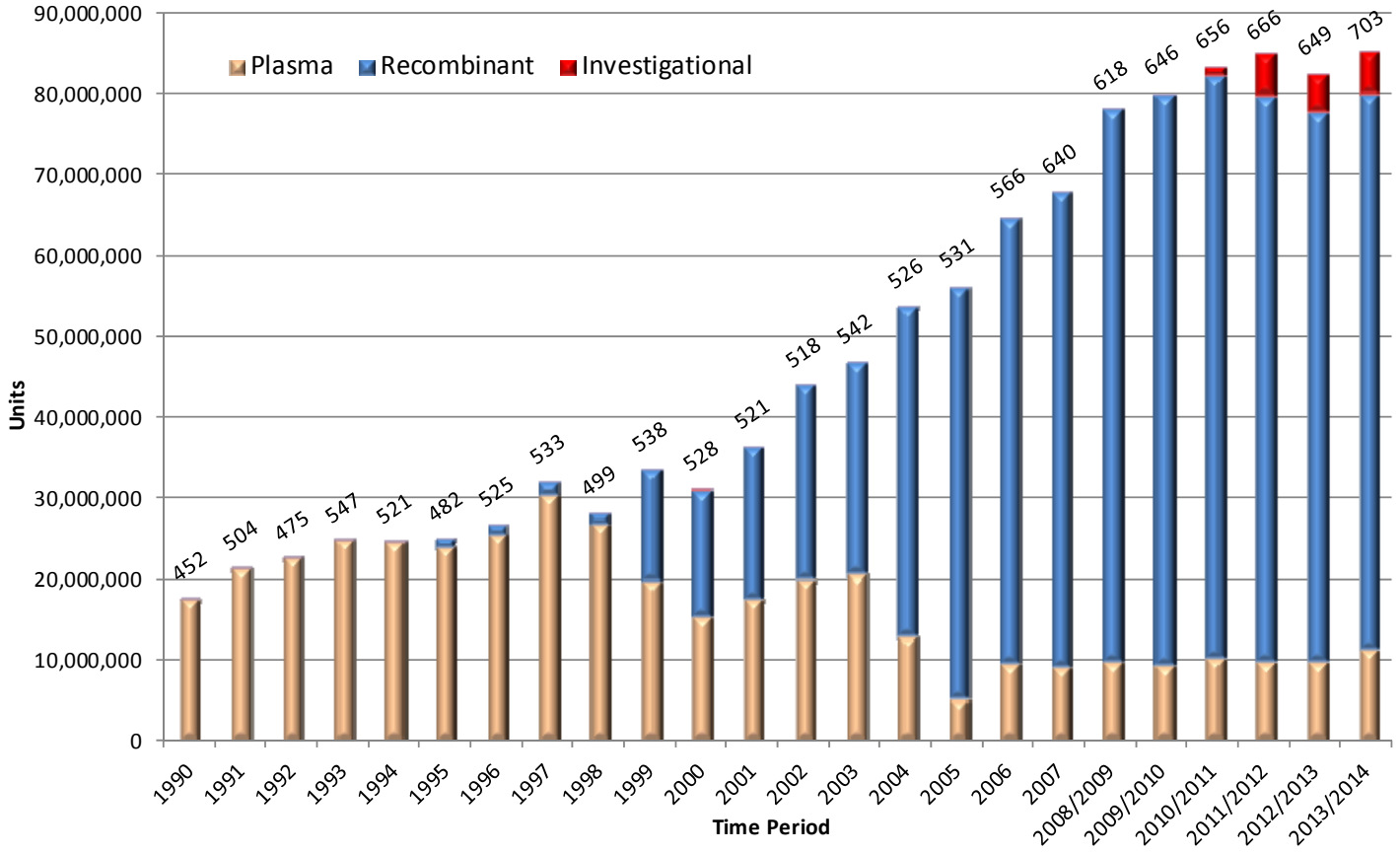


Figure 20 - shows UK factor IX use by year for all diagnoses broken down by product type from 1990 to 2013/14. The numbers over each column are the number of patients treated with factor IX (all diagnoses) during the year. These data were reported by calendar year until 2007 and by financial year thereafter. These data include over 5,400,000 million units of investigational factor IX used during 2013/14. This shows a steady, year on year increase in usage for most of this period, levelling off over the past four years with some fluctuation broadly in line with the number of patients treated.

Figure 21 **Factor IX Usage (including Inhibitor) divided by number of Severe Haemophilia B patients by commissioning region**

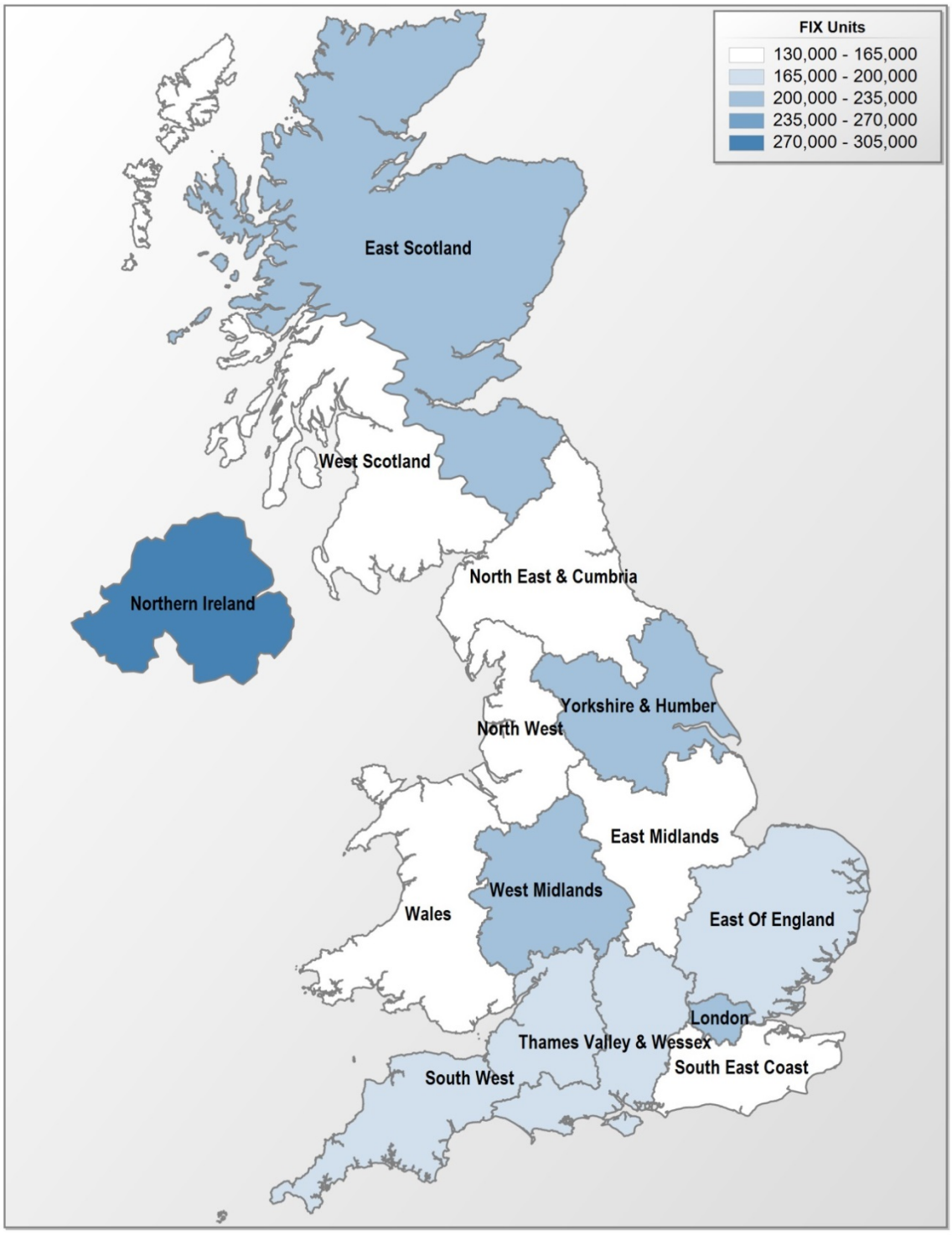


Figure 21: shows usage of factor IX per patient with severe Haemophilia B. This also gives a measure of the intensity of replacement therapy. Although there is, again, regional variation in usage, there is much less variation in the intensity of treatment than for haemophilia A. The reason for this difference is unknown.

Figure 22 Total number of Severe Haemophilia B patients by commissioning region

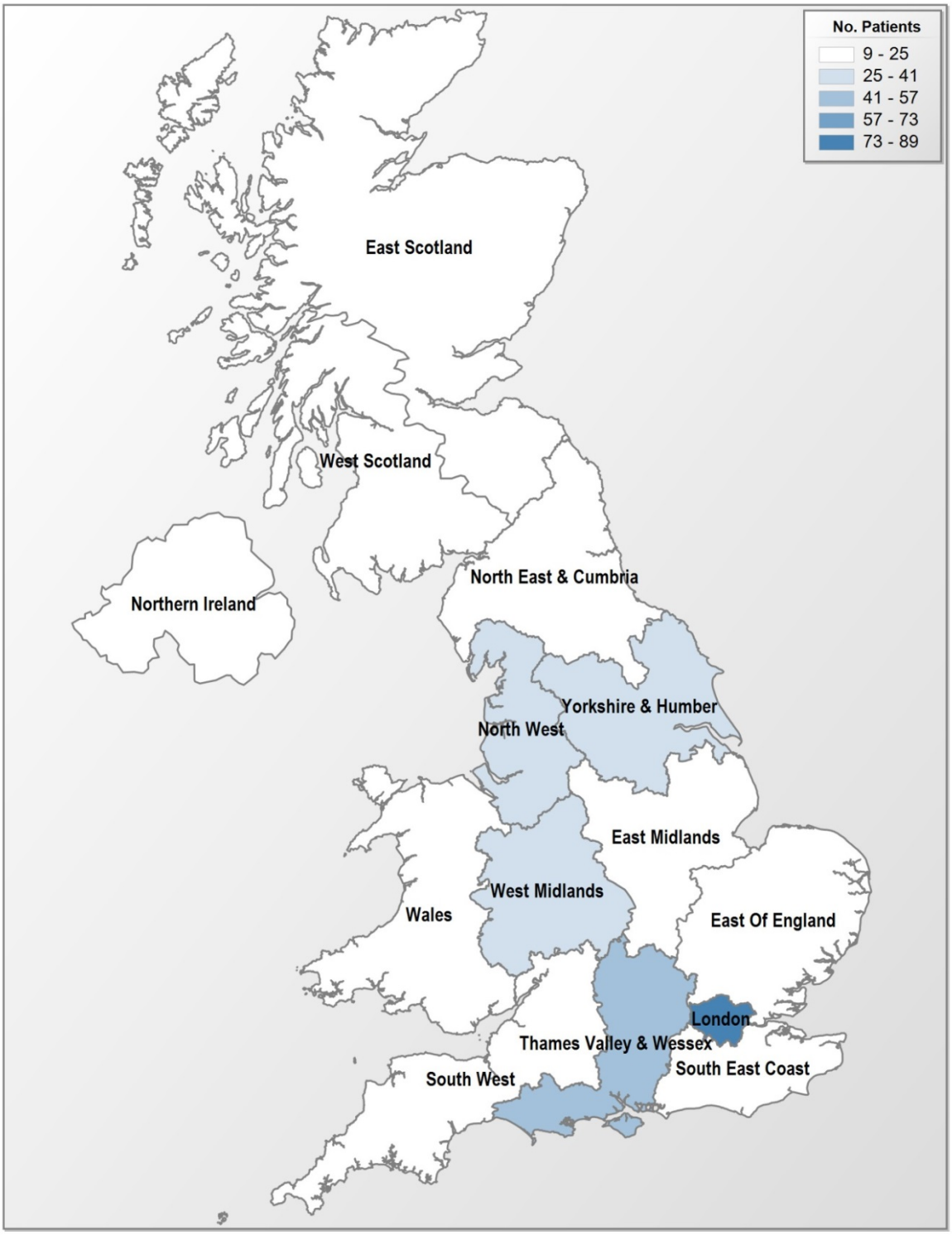


Figure 22: shows the number of patients with severe haemophilia B patients by commissioning region. As might be expected for a very low prevalence defect, there is wide regional variation in frequency.

Figure 23 FIX Units – usage per capita of general population by administration

Figure 23: shows factor IX usage per capita of population, correcting usage for population density. Variation in the apparent intensity of treatment from region to region may here be attributable to the low prevalence of the condition and very variable clinical phenotype. As for haemophilia A, we can no longer break down usage per capita by Specialist Commissioning region because this no longer corresponds with administrative region, which means that it is not possible to calculate population.

Table 13 Factor IX usage by region for Severe Haemophilia B patients only (incl. treatment for inhibitors)

Region	General Population *	Patients treated (n) Severe Haemophilia B	Total FIX Units (IU) Severe Haemophilia B	Mean Usage Severe Haemophilia B	FIX Units Per Capita Severe Haemophilia B
South Yorkshire & Bassetlaw		29	6,739,485	232,396	
London		88	18,608,133	211,456	
Birmingham & Black Country		25	5,147,750	205,910	
East Anglia		20	3,832,250	191,613	
Bristol, North Somerset & South Gloucestershire		14	2,348,040	167,717	
Wessex		41	6,873,440	167,645	
Cheshire, Warrington & Wirral		38	6,269,916	164,998	
Cumbria, Northumberland & Tyne and Wear		17	2,481,500	145,971	
Leicestershire & Lincolnshire		20	2,862,264	143,113	
Surrey & Sussex		14	1,906,500	136,179	
England	**53,493,729**	**298**	**57,069,278**	**191,508**	**1.07**
Northern Ireland	1,823,634	9	2,699,000	299,889	1.48
Scotland East	2,885,570	14	3,172,042	226,574	1.10
Scotland West	2,428,030	21	3,338,250	158,964	1.37
Wales	3,074,067	14	2,206,016	157,573	0.72
United Kingdom	**63,705,030**	**355**	**68,484,586**	**192,914**	**1.08**

English regions ranked by mean usage

* Source: ONS, Mid-2012 Population estimate based on the 2011 census: Adapted from data from the Office for National Statistics licensed under the Open Government Licence v.1.0.
Population data for Scotland supplied by National Records of Scotland © Crown Copyright 2012

Table 13: This shows usage by Commissioning area team ranked by units per year per patient with severe haemophilia B. This shows more variation in treatment intensity than with haemophilia A, although patient numbers for this diagnosis are very much smaller and so comparisons less reliable. Scottish and English usage per capita of population was very similar. Although usage in Northern Ireland appeared higher, no reasonable comparison can be made given that only nine patients with Haemophilia B are treated in the province and there is considerable interpersonal variation in clinical phenotype for this condition.

Figure 24 **Annual FIX usage 2013/14 in Severe Haemophilia B patients *aged under 18 years* with no current inhibitor, by centre, ranked by median usage**

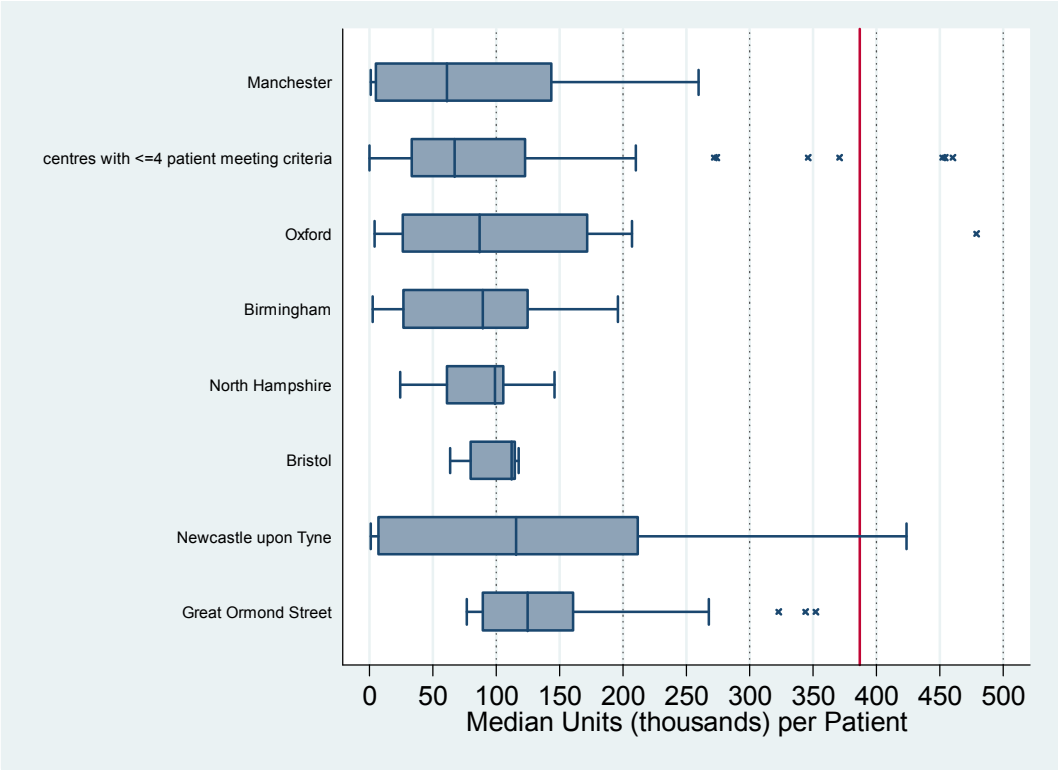


Figure 24:- Shows a box and whisker plot of median factor IX usage per patient with severe haemophilia B (median, IQR and arithmetic range) in UK children aged less than 18 years old lacking a current inhibitor during 2013/14, broken down by centre. Outliers are also shown. In previous years we showed all centres but since most had very few children with severe haemophilia B, this provided a meaningless comparison in which most of the variance was attributable to small numbers and variation in median age per centre. For that reason, we have aggregated centres with 1 - 4 patients and reported all other centres individually. The vertical red line indicates the 95th percentile of units, for the whole UK (386,956 IU/patient/year). Indicated outside values show where a patient's usage is more than 1.5 times the IQR from the nearest quartile at centre level.

Data Table for Figure 24

Haemophilia Centre	Patients treated	Patients treated with weight reported	Total Units	Median Units
Great Ormond Street	20	20	3,107,193	125,000
Newcastle upon Tyne	7	6	909,500	116,000
Bristol	6	6	602,250	112,500
North Hampshire	5	5	437,000	99,000
Birmingham	6	6	531,000	89,750
Oxford	8	8	1,055,000	87,000
Centres with <=4 patient meeting criteria	55	49	5,762,688	67,500
Manchester	11	10	927,500	61,500

Data Table for Figure 25

Haemophilia Centre	Patients treated	Patients treated with weight reported	Total Units	Median Units
Sheffield	11	10	3,763,720	390,000
Royal Free	29	29	7,407,970	273,000
Cambridge	13	13	3,281,000	258,000
St Thomas'	14	14	3,108,500	222,500
Manchester	22	21	5,007,666	185,500
Newcastle upon Tyne	10	10	1,572,000	182,500
Glasgow	21	21	3,786,250	174,500
Centres with <=4 patients meeting criteria	52	47	10,675,974	174,000
Cardiff	11	9	1,982,016	166,000
Oxford	18	18	3,656,440	159,950
Centres with 5-9 patients meeting criteria	53	49	10,631,919	152,000

Figure 25 **Annual FIX usage 2013/14 in Severe Haemophilia B patients *aged 18 years or more* with no current inhibitor, by centre, ranked by median usage**

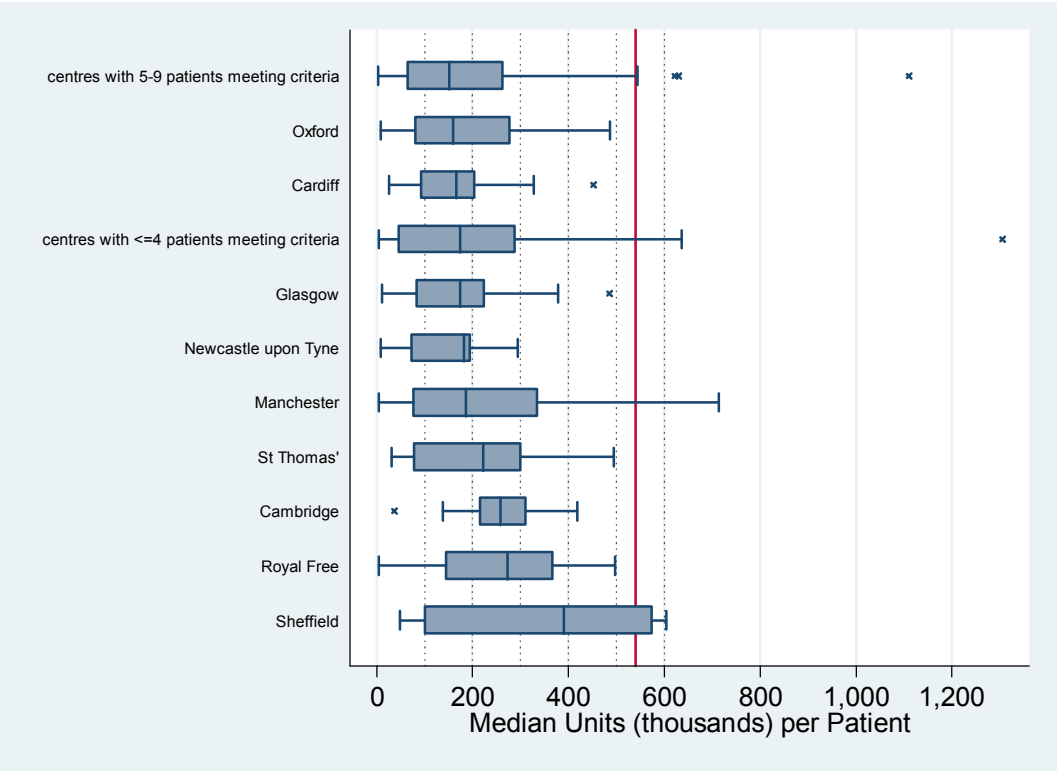


Figure 25: This shows box and whisker plots of median factor IX usage per patient with severe haemophilia B (median, IQR and arithmetic range) of UK patients aged 18 years or more, lacking a current inhibitor and broken down by centre. Statistical outliers are shown. These are defined as usage greater than 1.5 times the IQR from the nearest quartile at centre level, so a patient who may be an outlier in one centre would not be if they used the same amount of factor IX but were managed by other centres whose general usage was higher. Only those centres managing 10 or more patients with severe haemophilia B are identified and the remainder are aggregated according to centre size. The vertical red line indicates the 95th percentile of units for the whole UK (539,615 IU/patient/year).

Table 14 Concentrates used to treat von Willebrand Disease

Manufacturer	Product	Total Units
Baxter	Advate	3,000
Bayer	Kogenate	12,500
BPL	FVIII 8Y	49,320
	Optivate	87,000
CSL Behring	Beriplex	1,000
	Haemate P	14,642,600
Grifols	Alphanate	1,346,000
	Wilfactin	664,000
Novo Nordisk	NovoSeven (mg)	333
Octapharma	Wilate	6,218,150
Pfizer	ReFacto AF	39,500
Various Manufacturers	Investigational FVIIa (mg)	9
	Investigational rVWF	*

Units in IU unless otherwise stated
**Anonymised for confidentiality purposes*

Table 14: shows a breakdown of concentrates used to treat von Willebrand disease organised by supplier. NovoSeven has been used for von Willebrand Disease inhibitor patients. Kogenate was used in combination with other products including NovoSeven in a patient with type 3 von Willebrand Disease and inhibitors.

Potentially anomalous product use is accounted for as follows: -

Advate was given a patient in error.

Kogenate was given in error (instead of Haemate P)

Kogenate was given to cover cardiac surgery based on close laboratory monitoring.

NovoSeven and Kogenate were given in combination to a patient with type 3 VWD and an inhibitor.

Refacto was given in A&E in error. The patient was thought to have haemophilia A.

Refacto was given for surgery to a patient who was originally thought to have VWD but has now been shown to be a carrier of haemophilia A and heterozygous for type 2N von Willebrand disease.

Table 15 Concentrates used to treat Rarer Bleeding Disorders

Manufacturer	Product	F.V deficiency	F.VII deficiency	F.IX Leyden	F.IX Leyden Carrier	F.X deficiency	F.XI Deficiency	F.XIII Deficiency
		Units	mg	Units	Units	Units	Units	Units
BPL	FX	-	-	-	-	40,400	-	-
	FXI	-	-	-	-	-	168,610	-
CSL Behring	Beriplex	-	-	-	-	738,750	-	-
	Fibrogammin P	-	-	-	-	-	-	585,750
	FXIII	-	-	-	-	-	-	18,273
Grifols	Hemoleven	-	-	-	-	-	7,860	-
Novo Nordisk	NovoSeven (mg)	11	2,614	-	-	-	59	-
Octapharma	Octaplas (units)	1,378	-	-	-	-	107	-
	Octaplex	-	-	-	-	710,000	-	-
Pfizer	BeneFIX	-	-	240,500	2,500	-	-	-
	ReFacto AF	-	-	-	-	-	10,000	-
Various Manufacturers	Investigational FVIIa (mg)	-	9	-	-	-	-	-
	Investigational FX	-	-	-	-	*	-	-
	Investigational FXIII (mg)	-	-	-	-	-	-	*

Units in IU unless otherwise stated

**Anonymised for confidentiality purposes*

Table 15: This gives a breakdown of product use during 2013/14 for UK patients with rarer bleeding disorders, broken down by diagnosis, product and supplier.

Table 16 Concentrates used to treat Acquired Defects

Manufacturer	Product	Acquired Haemophilia A	Acquired von Willebrands	Acquired FV deficiency	Acquired Other
		Units	Units	Units	Units
Baxter	Advate	163,000	-	-	-
	FEIBA	3,796,500	7,000	127,500	-
Bayer	Kogenate	13,000	-	-	-
BPL	FXI	-	-	-	2,550
CSL Behring	Beriplex	-	-	-	15,000
	Haemate P	-	93,000	-	-
	Helixate Nexgen	6,000	-	-	-
	Riastap (mg)	-	-	-	6
Grifols	Alphanate	-	39,000	-	-
	Fanhdi	14,000	-	-	-
Novo Nordisk	NovoSeven (mg)	1,468	-	21	1
Octapharma	Wilate	1,800	389,550	-	-
Pfizer	ReFacto AF	183,500	2,000	-	-

Units in IU unless otherwise stated

Table 16: Shows reported product use for UK patients with acquired disorders, broken down by diagnosis, product and supplier.

Table 17 Adverse Events

Adverse Event	Number of Events
Allergy Event	1
Infection Event	0
Inhibitor Event	23
Malignancy Event	4
Other Event	5
Poor Efficacy Event	1
Thrombotic Event	1
Total	**35**

Table 17: The NHD Adverse Event reporting system now mirrors the EUHASS report forms. Those centres who report to UKHCDO and EUHASS need only do so once, as the reports are submitted to both databases. For those centres who do not report to EUHASS, reports are submitted to the NHD only. The adverse even reporting system is currently being strengthened.

Adverse event reports which should be submitted to NHD / EUHASS are as follows:

Allergy Event
Death Event
Infection Event (replaced Hepatitis and HIV reports)
Inhibitor Event
Malignancy Event
Poor Efficacy Event (replaced Transfusion reaction)
Thrombotic Event
Other Event

Table 18 vCJD

Coagulation Defect	Patients 'at risk' for public health purposes 1980 - 2001 (old risk period)			Patients 'at risk' or no longer 'at risk' for public health purposes 1990 - 2001 (new risk period)		
	NHD Estimate (based on treatment records)	Confirmed by Centres to be 'at risk'	Patients who received an implicated batch(es)	NHD Estimate (based on treatment records)	Centre-list no longer at risk (NHD estimate)	Confirmed by Centres to be no longer 'at risk'
Haemophilia A (including carriers)	2,783	2,035	517	2,392	129	62
Haemophilia B (including carriers)	830	571	154	689	43	26
von Willebrand disease	757	518	34	663	38	17
F.XI Deficiency	142	99	0	134	3	2
F.VII deficiency	49	33	0	46	1	1
F.X deficiency	35	27	8	32	0	2
Other bleeding disorders	101	94	5	75	8	4
Total	**4,697**	**3,377**	**718**	**4,031**	**222**	**114**

Table 18: This shows the number of patients alive in March 2013 and considered to be "at-risk" of vCJD for public health purposes on the basis that they have been reported to us as having been treated with UK-sourced blood products during the risk period. This is broken down by exposure between 1980 and 2001 (the original risk-period) and exposure between 1990 and 2001 (the new risk-period in current use).

Unlike previous reports, we have reported the number of patients we estimate to have been exposed to UK blood products during the period of risk estimated from the contemporary factor VIII returns reported to NHD annually and then quarterly since 2008. Although this estimate may include inaccuracies in centre reports, we believe that this is the most complete estimate, since it was collected prospectively and includes some reports of treatment of which the current managing centre may be unaware.

According to this estimate, 4,697 patients, who are still alive, were thought to be at public health risk using the old risk period, of whom 4,031 are still considered at risk using the current (1990-2001) criteria.

In the original exercise only 3,377 of these patients were confirmed to be at risk by their Haemophilia Centre using the old criteria (Table 18). We believe that although centres expended considerable effort to check these data they remain incomplete because many patients attended several centres during the period and their present centre may have been unaware of treatment administered elsewhere. Furthermore treatment records, including some from 25-30 years ago may no longer exist. Where specific batches of product were traced, the use of only 52% to 90% of each batch could be accounted for, which illustrates this point perfectly. Since no new implicated batches have been identified in recent years, the risk that further batches will be identified is becoming remote. Inevitably, therefore, some patients who have received implicated batches cannot now be confirmed as having been so treated.

For reports of patients who received an implicated batch, we are entirely dependent on reports from Haemophilia Centres since NHD did not collect or record batch data during this period. Reports of patients treated with implicated batches are likely to be correct, as far as they go, but incomplete. Since we cannot account for the disposal of all of each implicated batches, some exposed patients may remain unidentified and unreported by centres.

Our data, derived from contemporary factor VIII returns suggest that 666 patients originally considered at public health risk based on NHD data alone and using the old criteria (1980-2001) are no longer at public health risk using the new criteria. Centres were notified of these patients and asked to cross-check with their records. We were anxious that if patients were to be told that they were no longer at risk, that this data should be correct.

Of the 222/3377 patients originally thought to be at risk but no longer considered at risk by NHD following the revision of the risk-period, centres have confirmed this "de-designation" in only 114 individuals. Repeated reminders to centres have yielded no further confirmatory data.

Table 19 Summary of patients 'at risk' of vCJD for public health purposes who received UK sourced plasma products as reported by Centres

Summary table of 'at risk' bleeding disorder patients who received UK sourced plasma products				
		Implicated batches	Non-implicated	Combined
Current status of 'at risk' patients	Alive	705	2647	3352
	Dead	104	521	625
	Total	809	3168	3977
Sex	M	769	2606	3375
	F	40	562	602
Current age band of living 'at risk' patients	0-19	6	55	61
	20-39	357	877	1234
	40-59	246	1064	1310
	60-79	91	534	625
	80+	5	115	120
	Not known	0	2	2

These data were last updated on 01/07/2014

Table 19: This table shows a breakdown of living patients considered to be 'at-risk' of vCJD for public health purposes using the original risk period (1980 – 2001).

Table 20 **Causes of death in patients with Haemophilia A, Haemophilia B and carriers of Haemophilia A & B**

Cause of Death	Severity (factor level iu/dl)			Total
	≤1	>1 and <5	≥5	
Accident	0	0	1	**1**
Bowel perforation	0	0	1	**1**
Carcinoma	3	2	8	**13**
Cerebral haemorrhage	3	1	2	**6**
COAD	2	0	1	**3**
Encephalopathy	0	0	1	**1**
Haemorrhage (Misc)	1	0	1	**2**
Hepatocellular Carcinoma	3	0	2	**5**
Infection (Bacterial)	2	0	5	**7**
Ischaemic Heart Disease	4	3	7	**14**
Liver Failure	0	0	3	**3**
Lymphoproliferative Malignancy	0	0	1	**1**
Renal Failure	0	0	1	**1**
Ruptured Aorta (Peripheral vascular disease)	0	0	1	**1**
Senility/Alzheimer's disease	0	0	2	**2**
Stroke (thrombotic)	0	0	1	**1**
Unknown	1	1	4	**6**
Total	**19**	**7**	**42**	**68**

Table 21 Causes of death in other coagulation defects

Coagulation Defect	Cause of Death	Total
Acquired Deficiency (other)	Infection (Bacterial)	1
	Lymphoproliferative Malignancy	1
Acquired F.V deficiency	Cerebral Oedema	1
Acquired Haemophilia A	AIDS	1
	Carcinoma	3
	Cerebral haemorrhage	3
	Cerebral palsy	1
	COAD	4
	Colitis	1
	Haemorrhage (Misc)	1
	Infection (Bacterial)	18
	Intestinal obstruction	1
	Ischaemic Heart Disease	7
	Leukaemia	1
	Liver Failure	1
	Malnutrition	1
	Parkinson's Disease	1
	Stroke (Unknown)	1
	Unknown	8
	Venous Thromboembolism	2
Acquired Haemophilia B	Ischaemic Heart Disease	1
Acquired von Willebrand Disease	Accident	1
	Haemorrhage (misc)	1
	Infection (Bacterial)	1
	Lymphoproliferative Malignancy	3
	Myelodysplasia	1
Combined diagnoses	Carcinoma	1
	Peripheral vascular disease	1
Dysfibrinogenaemia	Ischaemic Heart Disease	1
F.V deficiency	Infection (Bacterial)	2
	Senility/Alzheimer's disease	1
F.VII deficiency	Carcinoma	1
	Haemorrhage (Misc)	2
	Infection (Bacterial)	1
	Ischaemic Heart Disease	1
F.X deficiency	Carcinoma	1
	Ischaemic Heart Disease	1
	Peripheral vascular disease	1

Table 21 Causes of death in other coagulation defects (continued)

Coagulation Defect	Cause of Death	Total
F.XI Deficiency	ARDS	1
	Carcinoma	6
	Infection (Bacterial)	5
	Ischaemic Heart Disease	4
	Lymphoproliferative Malignancy	1
	Stroke (thrombotic)	1
	Unknown	1
Fibrinogen Deficiency	Carcinoma	1
Haemophilia A with Liver Transplant	COAD	1
	Encephalopathy	1
Haemophilia B with Liver Transplant	Hepatocellular Carcinoma	1
	Liver Failure	1
	Unknown	1
Miscellaneous	Carcinoma	1
Platelet defects	Carcinoma	2
	Cardiac tamponade	1
	Cerebral haemorrhage	1
	Haemorrhage (Misc)	1
	Infection (Bacterial)	3
	Ischaemic Heart Disease	1
	Renal Failure	1
	Unknown	1
Unclassified	Carcinoma	1
	Infection (Bacterial)	1
von Willebrand disease	Accident	1
	AIDS	1
	Carcinoma	6
	Cerebral haemorrhage	1
	Haemorrhage (Misc)	2
	Hepatocellular Carcinoma	3
	Infection (Bacterial)	19
	Ischaemic Heart Disease	5
	Liver Failure	1
	Renal Failure	1
	Stroke (Unknown)	2
	Suicide	1
	Unknown	4
	Venous Thromboembolism	1
	Total	**165**

Figure 26 Cumulative incidence chart of deaths from hepatocellular carcinoma or liver failure in UK patients with bleeding disorders 1969 - 2013

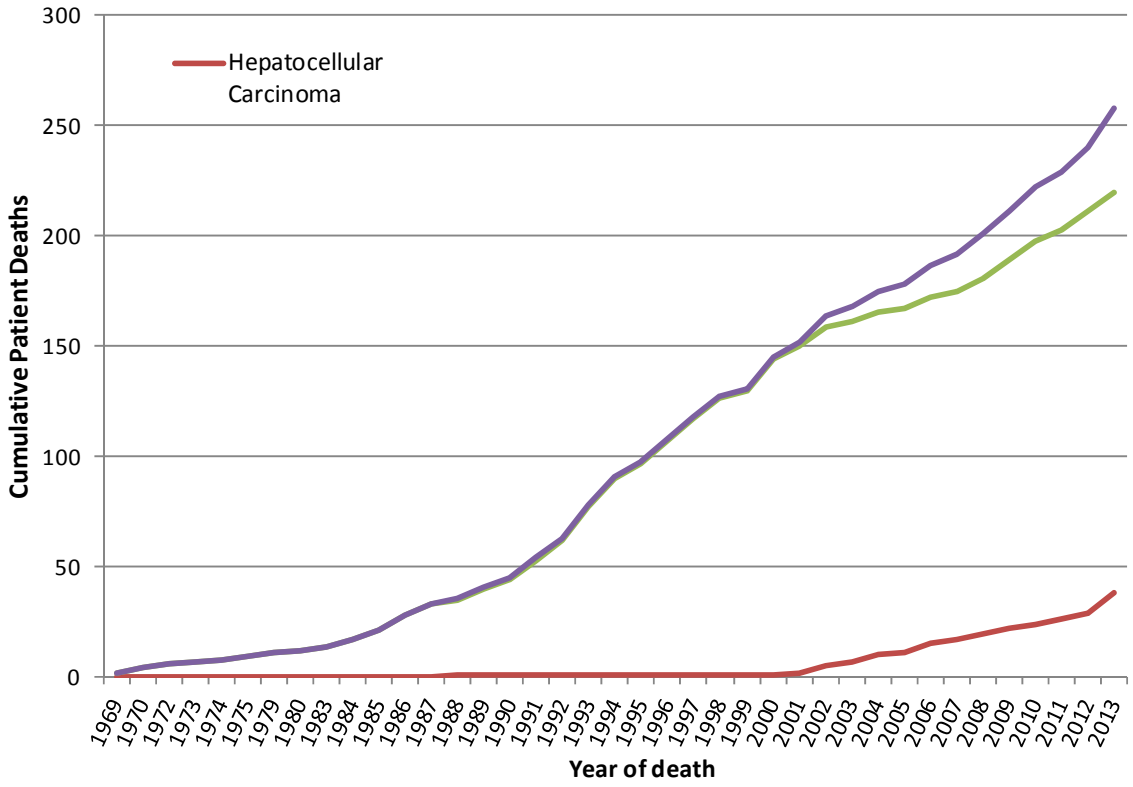


Figure 26: shows the cumulative incidence of deaths from liver disease by calendar year. This is based on reports from centres and from Health & Social Care Information Centre. Our data do not allow us to differentiate between different causes of severe liver disease such as alcohol and auto-immune disease. We therefore assume that these deaths, totalling 258 between1969 and 2013, are overwhelmingly caused by hepatitis C contracted from blood product therapy.

This shows an increased death rate from liver disease amongst HIV co-infected patients in the mid 1990's, settling to some extent with the advent of HAART. It also demonstrates the long latent period before cases of hepatocellular carcinoma were observed.

Figure 27 Total number of patients with Haemophilia A, Haemophilia B or von Willebrand Disease treated by UK Haemophilia Centres

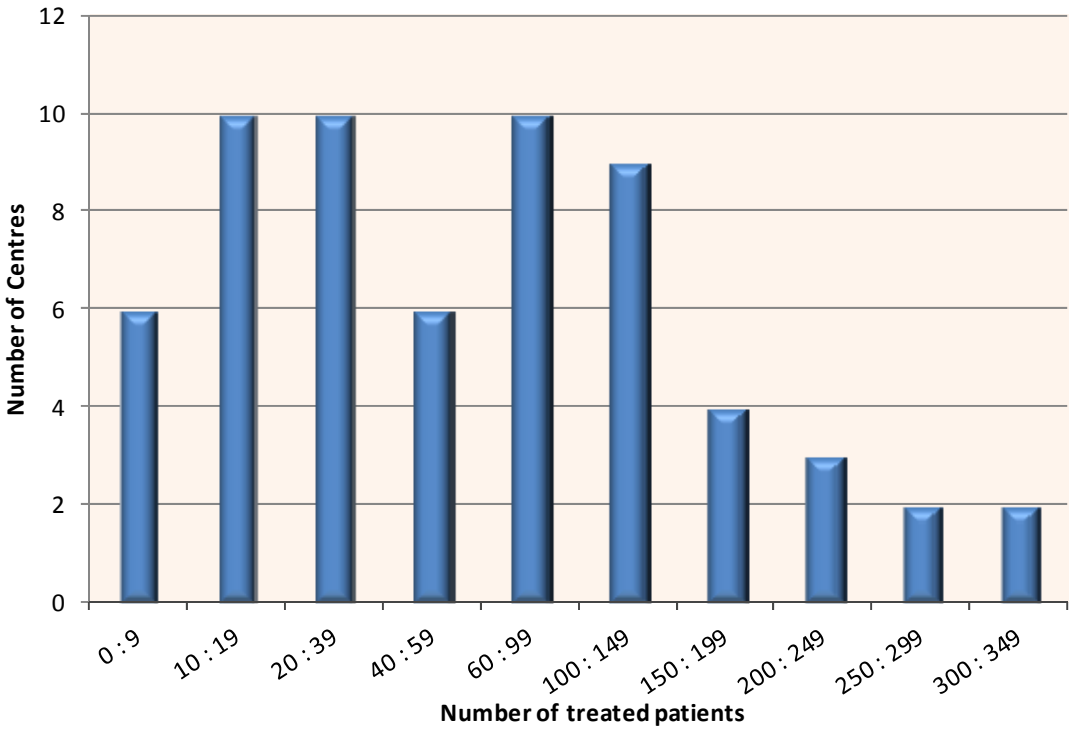
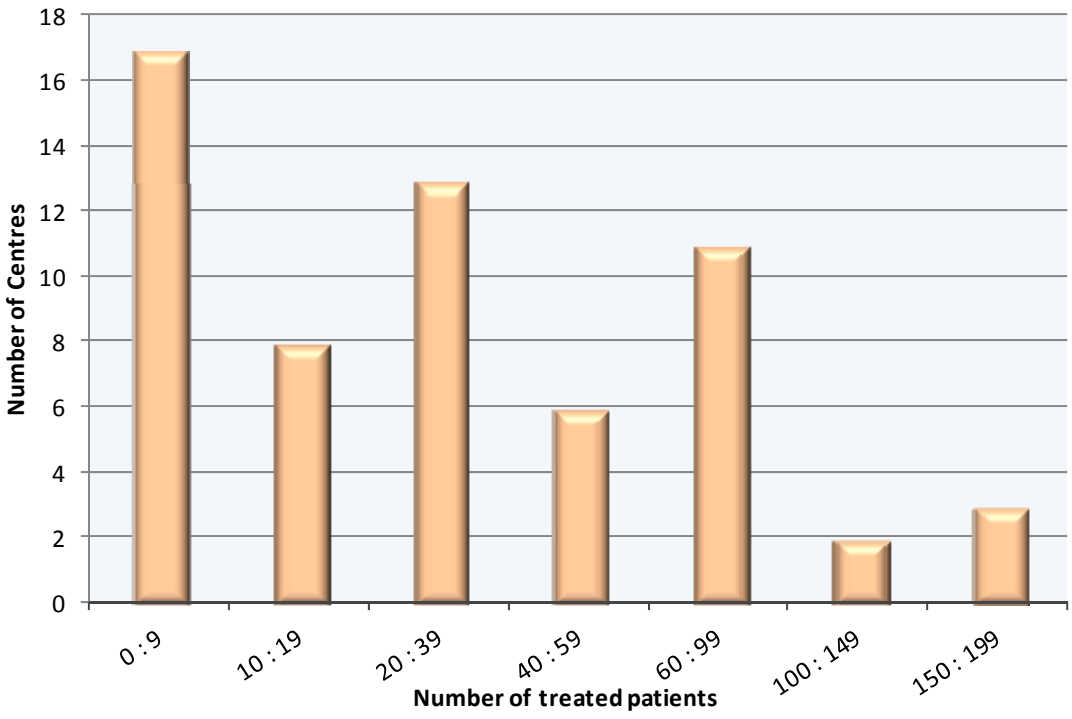


Figure 28 Total number of severely affected patients with Haemophilia A and Haemophilia B treated by UK Haemophilia Centres



Appendix 1 Quarterly Returns - Participating Centres

Centre Name	
Aberdeen	Leicester
Ashford & St. Peters	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

List of Abbreviations

IQR	Interquartile range
IU/dl	International units per decilitre
IU/kg	Units per kilogram
kg	Kilogram
NHD	National Haemophilia Database
UKHCDO	United Kingdom Haemophilia Centre Doctors' Organisation

3. Hepatitis C Look-back Report

This report is comprised partly of data imputed from the treatment records of NHD, collected over many years, and partly from data collected specifically in a HCV look-back exercise conducted from 2010. Centres found the look-back exercise burdensome and difficult and the data is consequently incomplete. Many patients were probably lost to follow-up.

Some extrapolations are possible, however.

Table 1 **Estimate of number of patients exposed to hepatitis C, based on historical clotting factor concentrate exposure during the period of risk**

Coagulation Defect	Alive	Dead	Total
Haemophilia A	2,632	1,828	4,460
Haemophilia A Carrier	114	30	144
Haemophilia A with Liver Transplant	7	13	20
Haemophilia B	698	240	938
Haemophilia B Carrier	61	6	67
Haemophilia B with Liver Transplant	2	3	5
von Willebrand disease	568	163	731
von Willebrand with Liver Transplant	0	1	1
F.V deficiency	2	0	2
F.VII deficiency	20	1	21
F.X deficiency	23	1	24
Factor X deficiency with Liver Transplant	0	1	1
F.XI Deficiency	46	14	60
F.XII (Hageman) defect	5	0	5
F.XIII Deficiency	17	2	19
Fibrinogen Deficiency	5	1	6
Prothrombin Deficiency	1	0	1
Combined V+VIII Deficiency	2	2	4
Other combined diagnoses	4	3	7
Acquired Haemophilia A	17	94	111
Acquired Haemophilia B	1	1	2
Acquired von Willebrands	2	11	13
Platelet defects	15	1	16
Miscellaneous	1	1	2
Unclassified bleeding disorder	16	2	18
Temporary coagulation defect, now normal	15	0	15
Total	**4,274**	**2,419**	**6,693**

Table 1 shows 6,693 patients considered at risk of HCV by virtue of concentrate use during the period of risk for HCV, broken down by diagnosis and whether they are alive/dead. This is based on concentrate use reported at the time to NHD. We think that this segment of the data is fairly complete and that 100% of these patients will have been exposed to HCV and that 25-30% of these will have cleared the virus spontaneously. Four thousand, two hundred and seventy four of these patients are still alive.

Table 2 **Estimate of number of patients *potentially* exposed to hepatitis C, based on historical exposure to blood components**

Coagulation Defect	Alive	Dead	Total
Haemophilia A	347	148	495
Haemophilia A Carrier	53	14	67
Haemophilia B	7	12	19
Haemophilia B Carrier	8	1	9
von Willebrand disease	469	126	595
F.V deficiency	3	3	6
F.VII deficiency	5	1	6
F.X deficiency	2	1	3
F.XI Deficiency	12	7	19
F.XII (Hageman) defect	5	3	8
F.XIII Deficiency	1	0	1
Fletcher factor	1	0	1
Fibrinogen Deficiency	7	2	9
Prothrombin Deficiency	1	0	1
Combined II+VII+IX+X Deficiency	1	0	1
Combined V+VIII Deficiency	5	0	5
Other combined diagnoses	2	0	2
Acquired Haemophilia A	0	3	3
Acquired von Willebrands	0	2	2
Platelet defects	5	2	7
Miscellaneous	0	1	1
Unclassified bleeding disorder	8	1	9
Temporary coagulation defect, now normal	4	1	5
Total	**946**	**328**	**1,274**

Table 2 shows a further 1,274 patients, considered *potentially* at risk of exposure to HCV by virtue of reported exposure to blood components during the period of risk for HCV (prior to the advent of HCV testing of donors in September 1992). This is also broken down by diagnosis and whether they are still alive or dead. This is based on treatment reports to NHD at the time. None of these patients is known to the database to have been treated with a clotting factor concentrate. The extent of their blood component exposure and hence the size of their risk will vary, but extrapolation of testing reports below implies that about 15% of these patients will have been exposed to HCV. Two thirds of these patients are reported to NHD as "*HCV status unknown*", either because they have not been tested or because documentation of their HCV status cannot easily be found. A significant proportion of these patients are probably lost to follow up at the reporting centre, have moved or are not reviewed regularly.

We strongly suspect that there was under-reporting of occasional treatment of mild bleeding disorders and so suspect that far more patients were treated than had been reported to NHD over the years. For that reason, we felt obliged to also consider all patients not included above but registered with a bleeding disorder during the period of risk (approx. 18,000 pts) to be potentially at risk of HCV exposure unless the centre could confirm that they had never been treated with blood products or concentrates.

Of the 9,090 patients whose previous treatment history was reported as "unknown", HCV status was reported as also "unknown" in 7,567. Of the 1,523 patients whose treatment history was reported to us as "unknown" but who had been HCV tested, 398 had evidence of active HCV and 21 of past but cleared HCV. Thus 27.5% of those members of this group who were tested and had a test result reported to us had evidence of previous exposure to HCV.

Were this to be found in the whole of the 18,000 patients for whom we have no treatment reports, we would expect about 5,000 additional patients to have been exposed to HCV whose exposure to HCV is not documented or who have not been tested. It is likely that there is both testing and reporting bias, however, and that those treated are less likely to be lost to follow up and more likely to have been tested than those never treated. The true number of patients exposed is therefore likely to be significantly lower than this estimate. However, unless this group are tested and reported we cannot make an accurate estimate.

We would strongly recommend that all patients diagnosed with a bleeding disorder before September 1992 should be tested for HCV because centres (and the patients themselves) will frequently have no idea what their treatment history is

Table 3 Hepatitis C potentially eligible patients

Hepatitis C Potentially Eligible Patients	n	%
Number of eligible patients *	29,484	
Number of patients Alive ǂ	24,643	84%
Number of patients Deceased ǂ	4,841	16%

** Patients born before 01/01/1991*
ǂ Alive or dead after 31/03/2013

Table 3 shows the number of patients *potentially* exposed to HCV. That includes all patients known to have been treated at some time with clotting factor concentrates or blood components during the period of risk for hepatitis C and those patients who were registered during the period of risk whose treatment is uncertain but which *may* include blood or blood products. All patients exposed to clotting factor concentrates during the period of risk will have been exposed to HCV, whereas those exposed to blood components only will have a lower risk of exposure averaging 5-10%.

Our incomplete data shows that those whose treatment is uncertain to the database because no treatment has been reported to the database are mostly untested (approx. 7000 of 9000) but a significant proportion of those who have been tested (27.5%) have evidence of exposure to HCV.

Six of 2185 patients reported never to have had treatment were found to have evidence of exposure to HCV. This prevalence is in keeping with the background prevalence of HCV in the general population and probably does not represent infection from the use of blood products.

Table 4 Hepatitis C Look-back reports

Of those patients for whom a report has been submitted	n	% of submitted	% of eligible
Number of Reports Submitted	14,252		
Number of patients Alive	12,983	91%	44%
Number of patients Deceased	1,269	9%	4%

Table 4 shows that reports were received for 14,252 patients, 12,983 still alive, slightly less than 50% of the patients alive and eligible for the study.

Table 5 HCV Look-back: Exposure to Blood Components or Clotting Factor Concentrate and HCV status (live patients only)

Treament	Ab Neg	Ab Pos, Ag Neg	Ab Pos Ag Pos	Not known	Ab pos Ag N/K	Total
None	42	3	4	2,565	1	2,615
Blood Components	245	11	28	82	2	368
Clotting Factor Concentrate or both	291	239	444	140	26	1,140
Not known	1,035	332	382	4,784	22	6,555
Total	**1,613**	**585**	**858**	**7,571**	**51**	**10,678**

Table 5 shows the breakdown of reported blood component or concentrate use for the 12,983 patients reported to the HCV look-back. HCV status is reported as unknown for 79% of these patients and treatment history is reported as unknown for 70%.

For patients treated with concentrates during the period of risk 291/1,140 had no serological evidence of HCV exposure. Twenty five to thirty percent of patients clear the virus but clearance of antibody is thought to be less common and so this is a higher number of antibody negative patients than one might expect in a group of patients, all of whom are thought to have been exposed to concentrate at one time, albeit many years ago.

A further 849/1140 (74.5%) had evidence of exposure to HCV (Ab positive), of whom 444 (38.9%) are documented to have ongoing infection.

Three hundred and sixty-eight patients were reported to have been exposed to blood components (plasma, cryoprecipitate and platelets) of whom 41 (11.1%) had documented evidence of HCV exposure. This is a much lower prevalence than found in those patients whose treatment history is reported as unknown. However, HCV status was reported as unknown in 80 (22%) of this group.

Given that 27.5% of those with an unknown treatment history who had been tested have evidence of HCV exposure, all patients registered with a bleeding disorder whose treatment history is uncertain should be tested for HCV. Many of these patients may have been treated with concentrates at some time.

Table 6 Diagnostic breakdown for patients reported to be HCV antibody positive

Coagulation Defect	Severe	Moderate	Mild	Unknown	Total
Haemophilia A	421	120	327	1	**869**
Haemophilia B	111	50	66	0	**227**
Females with VIII deficiency	0	0	22	1	**23**
Females with IX deficiency	0	2	13	0	**15**
von Willebrand disease					**128**
F.VII deficiency					**4**
F.X deficiency					**3**
F.XI Deficiency					**3**
Fibrinogen Deficiency					**5**
Combined von Willebrands + IX deficiency					**1**
Combined V+VIII Deficiency					**1**
Acquired Haemophilia A	2	0	1	1	**4**
Glanzmanns Thrombasthenia					**1**
Other platelet defects					**3**
Haemophilia A with Liver Transplant	1	0	3	1	**5**
Haemophilia B with Liver Transplant	0	0	0	2	**2**
Unclassified					**3**
Temporary coagulation defect, now normal					**1**
Total	**553**	**183**	**547**	**15**	**1,298**

Additional data was requested on a randomly selected cohort making up 20% of the live and eligible patients. It was intended to extrapolate from this randomly selected sub-set. The response to this was disappointing in general but the data is presented below.

Table 7 Number of patients alive with severe liver disease

Disease	Number of patients
Cirrhosis	67
Hepatocellular Carcinoma	7
Liver Failure	9
Liver Transplant	12

Figure 1 Genotypes

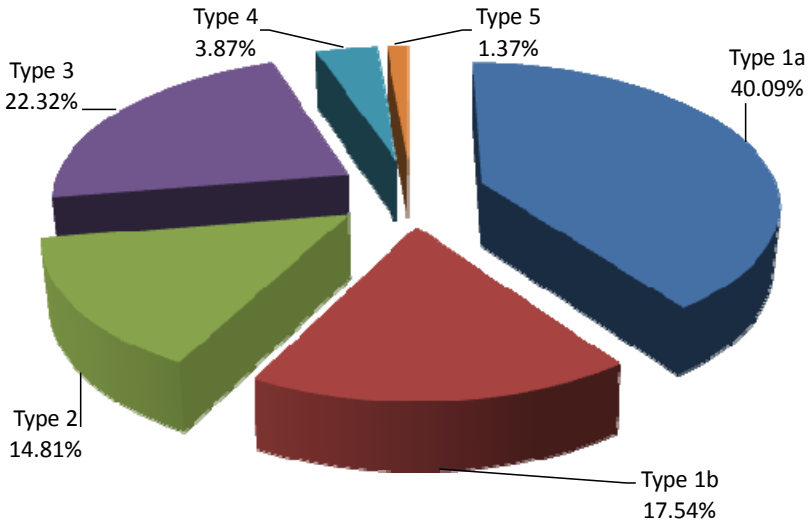


Figure 1 shows the known distribution of HCV genotypes at the time of reporting. Soime patients were treated successfully before genotyping became available and so it is now not known with which HCV genotype they were infected.

The distribution of genotypes differes from that found in the UK population in having a relative excess of type 1a and in having genotypes 4 and 5, not normally found outside sub-saharan Africa. Both these differences reflect the US and African sources of much of the plasma used to manufacture clotting factor concentrates in the late nineteen seventies and early eighties.

Figure 2 Treatment outcomes

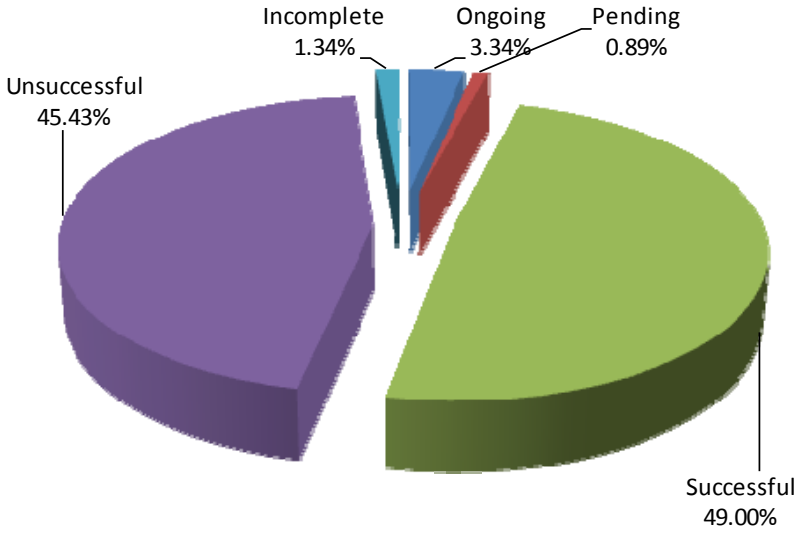


Figure 2 illustrates the proportion of patients with HCV treated successfully or unsuccessfuly or awaiting or undergoing antiviral treatment for HCV. This shows a response rate (almost exclusively to interferon-based regimens somewhat less than 50%, reflecting the high prebvalence of type 1 genotypes.

Figure 3 Genotypes of patients whose treatment was successful

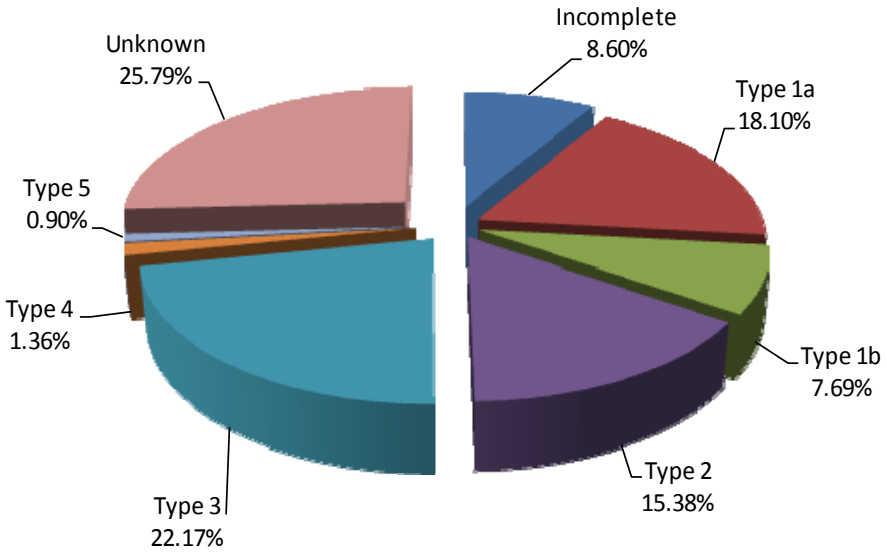


Figure 3 shows the genotypic breakdown of patients in whome antiviral therapy has successfully eradicated HCV. In 25.8% of cases, the genotype is unknown since treatment antedated genotyping. Type 2 and 3 predominate, because of the much lower response-rate associated with Type 1 using more traditional interferon and Ribivarin regimens.

Figure 4 Genotypes of patients whose treatment was unsuccessful

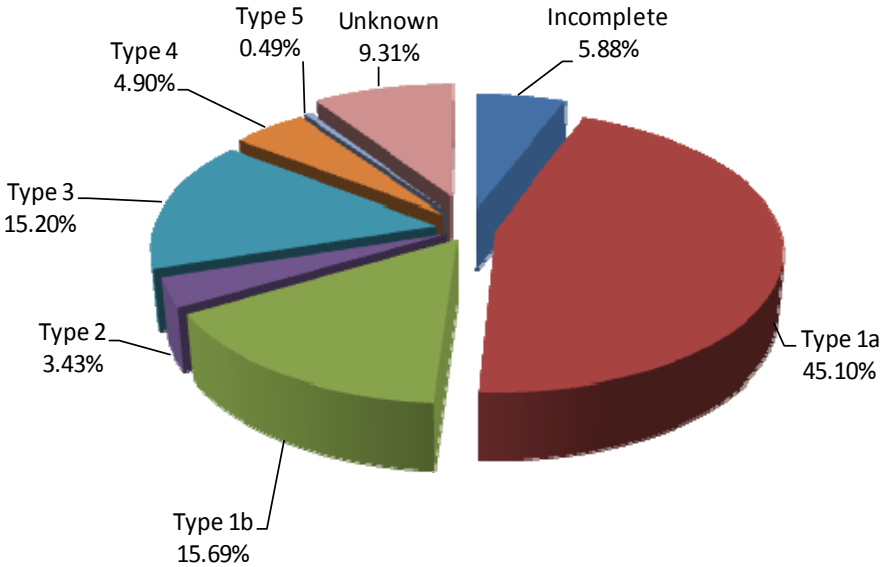


Figure 4 shows that genotype 1 predominated amongst patients in whom HCV eradication was unsuccessful. This is in keeping with the known poorer response rate of type 1 HCV to treatments current during that period.

4. Haemtrack Report

Introduction

Haemtrack is being adopted by an increasing number of patients and currently has more than 2,200 registrants on home therapy for a bleeding disorder. It is used for all diagnoses requiring home therapy and has even been used by some centres to monitor home therapy for thrombotic disorders, though clearly not designed for this purpose.

The introduction of the android smartphone app has been a step forward. An increasing proportion of patients report their data to us using a phone app - our preferred option. We get the data more quickly and suspect that data quality is better if the phone app is used because it is very easy to use and people always have their phone with them

Ensuring that patients are entering their data conscientiously and accurately requires on-going reinforcement from both medical and nursing staff, but those centres who have used the reports in clinic and for patient management have found them extremely useful. In general there has not only been an increase in the proportion of patients in each centre using the system, but there has also been a progressive improvement in the quality of the data. This is reflected in the proportion for whom Haemtrack usage figures closely match centre issues, as reported back to NHD, and also by the progressive reduction in the interval between a treatment being given and being reported to the centre. Centres have been able to check and amend the data before it is sent on to the central database over the past year and this may also have resulted in an improvement in data quality. Steps that have and which are going to be taken are described in greater detail in the Haemtrack Group Report.

Centres vary in the quality of data submitted and so for some this is clearly a work in progress. Perhaps not surprisingly, the system is used far more in Comprehensive Care Centres (CCC's) than in Haemophilia Centres (HC's).

The report which follows shows a basic analysis of this increasingly enormous body of data. A Haemtrack Management Group has been formed and PhD in data mining appointed to analyse these data and they have recently started work.

Prof Charles RM Hay
Lynne Dewhurst
Dr Hua Xiang
Manchester October 2014

Haemtrack Basic Demographics

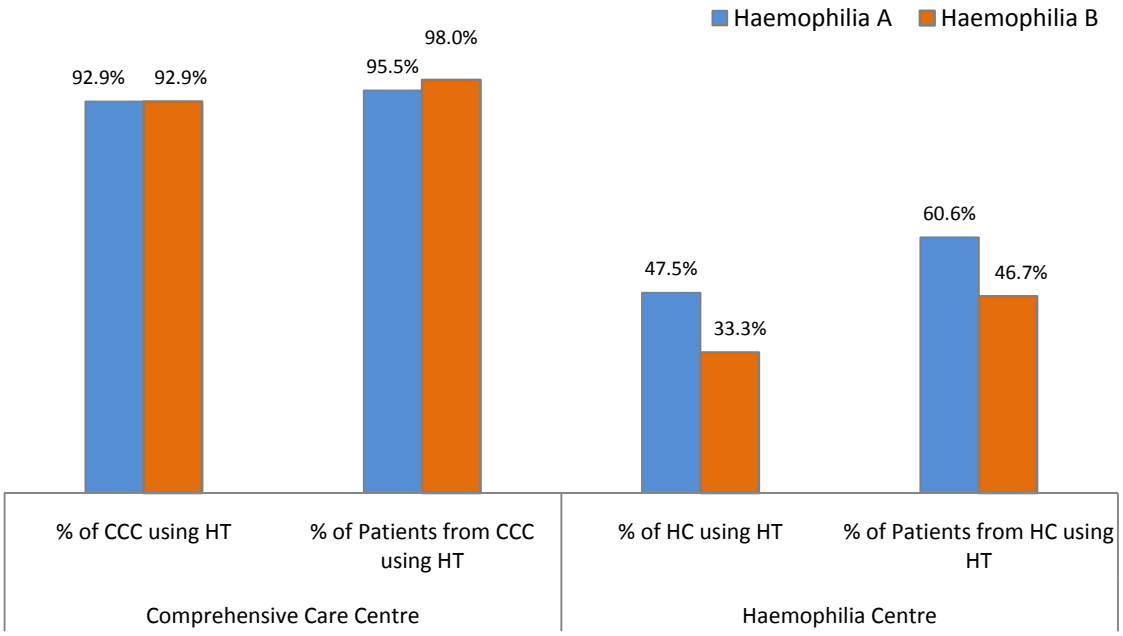
Tables 1 and 2 and Figures 1 - 4 illustrate the basic demographics of the system, which centres are using it and which patients and how many reports they are downloading.

The only qualification for use is that the patients are on home-therapy for a bleeding disorder. Consequently, although the system is mainly used for patients with Haemophilia A and B, it is also used for a wide variety of other bleeding disorders including Factor XIII deficiency, and various other rare disorders. The age-range of users reflects the age range of our patients so that advancing age does not appear to be a barrier to use! Clearly, the system has caught on to a far greater extent amongst CCC's (92.9% of which use the system and which have registered more than 95% of their patients) than HC's. We will have to campaign to recruit more of the Haemophilia Centres to use the system.

Given that this is a home care system, it is perhaps surprising how many mildly affected patients are registered to use it. A significant minority of patients with moderate severity haemophilia A and B patients use the system but this probably reflects the significant overlap in bleeding phenotype between severe and moderate haemophilia.

Usage of Haemtrack has clearly increased at a rapid rate in recent years and further increases in use already appear to be slowing down. Most CCC patients are already recruited. Every centre will have a small proportion of non-compliant patients who may never be recruited. Further recruitment goes more slowly in the smaller centres (see Figure 1, Table 1). This also appears to be reflected in the number of treatments reported, which has levelled out at about 12,000 per month; equivalent to an average of one treatment per patient every three days (Figure 4).

Figure 1 Comprehensive Care Centre Vs Haemophilia Centre: Use of Haemtrack



April 2013 – March 2014

***Figure 1*:** This shows a comparison of the proportion of eligible centres and the proportion using Haemtrack broken down according to centre type. Whilst almost all Comprehensive Care Centres (CCC's) and a very high proportion of the patients from participating centres are using Haemtrack, less than half of Haemophilia Centres (HC's) and a little over half their patients are using the system.

Figure 2 Haemtrack users - age breakdown – Severe Haemophilia A & B

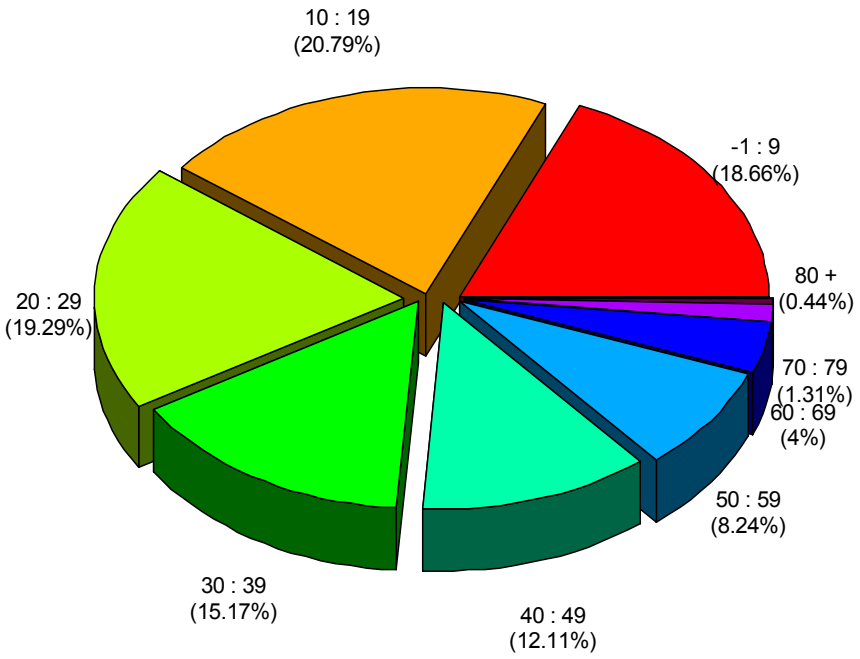


Figure 2: This age distribution shows the frequency of each age band.

Table 1 Patients registered to use Haemtrack per centre – up to May 2014

Centre Name	Patients Registered (n)
Guy's & St Thomas' Haemophilia Reference Centre	190
Oxford Haemophilia Centre	176
Manchester Royal Infirmary	142
Royal Free Haemophilia Centre and Thrombosis unit	137
Great Ormond Street Hospital	118
Barts Health NHS Trust	108
Newcastle	105
Cambridge Comprehensive Haemophilia Centre	103
Sheffield (Adults)	72
Bristol Haemophilia Centre	71
Basingstoke Haemophilia Comprehensive Care Centre	65
St Georges Healthcare NHS Trust	55
West Midlands Adult Comprehensive Care Centre	54
Royal Manchester Childrens Hospital	51
Arthur Bloom Centre - Cardiff	50
Liverpool - Alder Hey	50
St James' Hospital - Leeds	48
Kent Haemophilia Centre	46
Leicester Royal Infirmary Haemophilia Centre	46
Nottingham Haemophilia Centre	46
Birmingham Children's Hospital CCC	42
Edinburgh Haemophilia & Thrombosis Centre	42
Glasgow Royal Infirmary	40
Bradford Haemophila Centre	34
Southampton Haemophilia Care Centre	34
The Roald Dahl Centre - Liverpool Adult's	34
Sheffield Children's NHS Foundation Trust	30
Hull Royal Infirmary	29
Hammersmith Hospital, Imperial College ACHT	28
Royal Hospital for Sick Children, Glasgow	26
Dundee Haemophilia Centre	24
Truro Haemophilia Centre	22
United Lincolnshire Hospitals NHS Trust	19
Swansea Haemophilia Centre	17
Derby Haemophilia Centre	14
Torbay Hospital	9
Aberdeen	7
North Staffordshire	7
Shrewsbury and Telford NHS Trust	7
Plymouth Haemophilia Centre	6
Bangor Haemophilia Centre	5
Lewisham	5
Norwich & Norfolk University Hospital	4
York Teaching Hospital NHS Foundation Trust	4
Royal Devon and Exeter Hospital	3
Inverness Haemophilia Centre	2
Royal Bournemouth and Poole	2
Royal Wolverhampton Hospital Trust	1
Taunton	1
Total	**2231**

Figure 3 **Patients regularly using Haemtrack – Haemophilia A and B between 2008 and 2013**

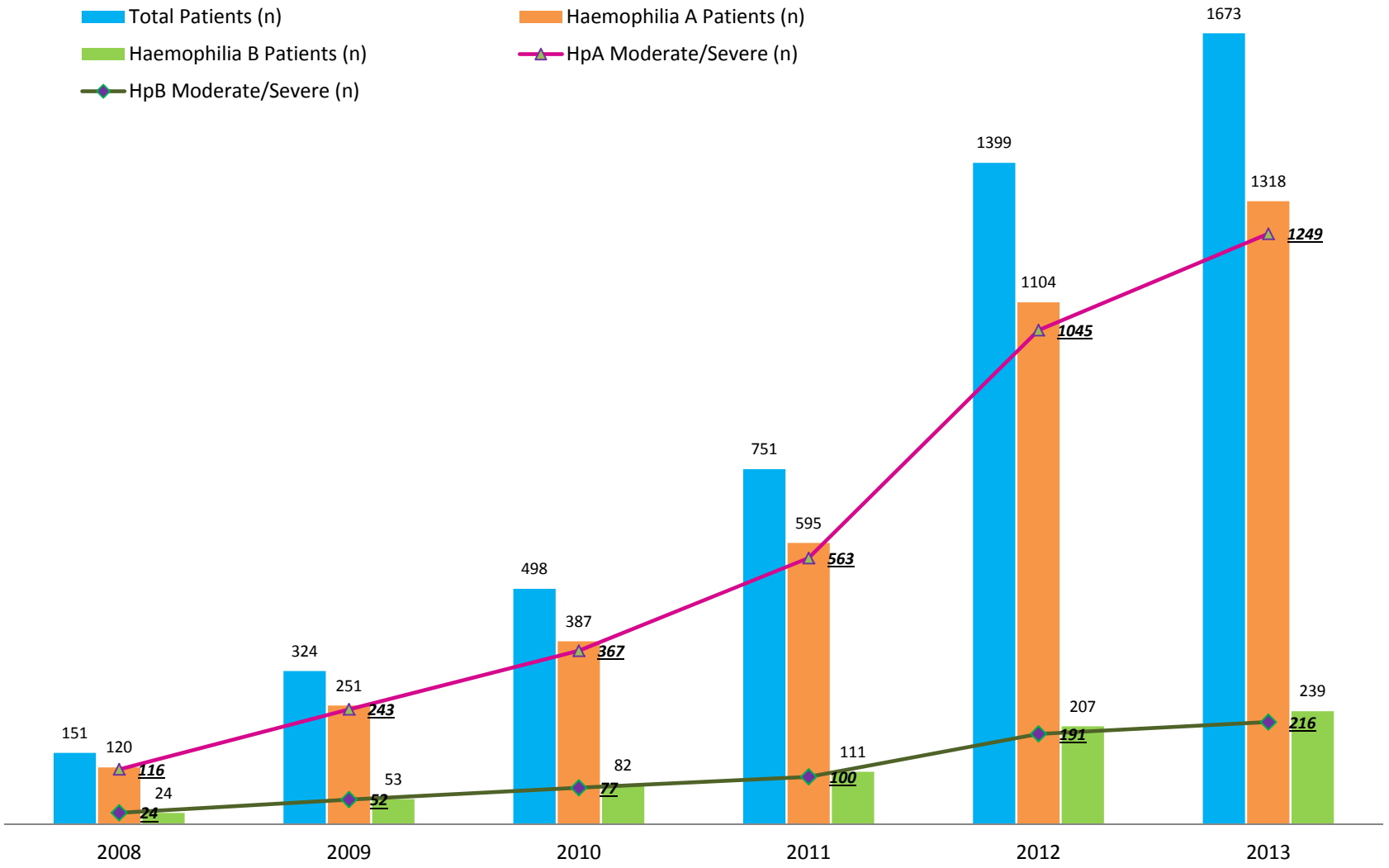


Figure 4 **Total treatments reported on Haemtrack per month, broken down by the reason for treatment - April 2011-March 2014**

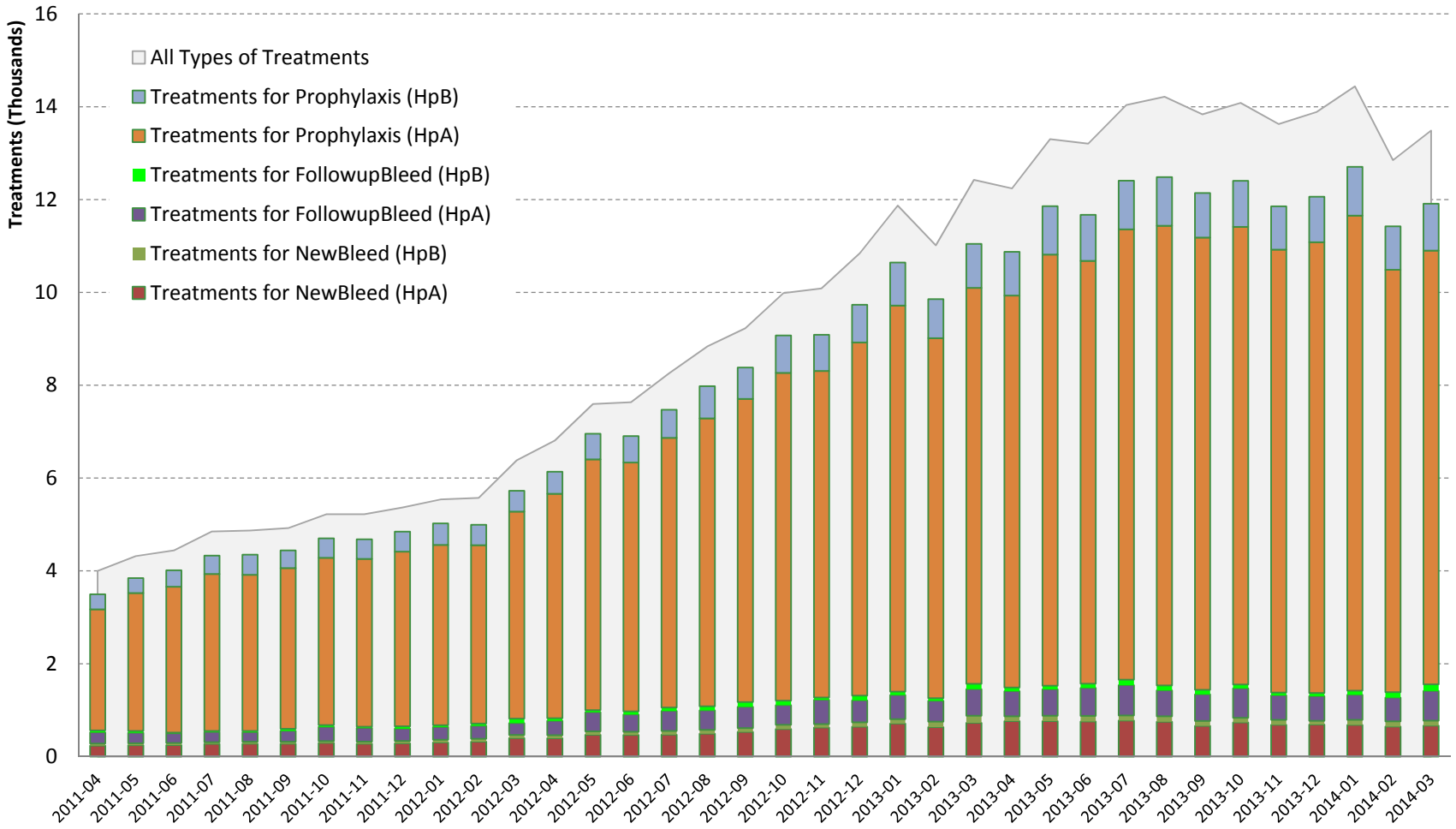


Table 2 Diagnosis of Haemtrack users by disorder and severity

Coagulation Defect	Patients (n)					Patients (% of total)			
	Severe	Moderate	Mild	Unknown	Total	Severe	Moderate	Mild	Unknown
Haemophilia A	1,486	140	43	71	**1,740**	85.40%	8.05%	2.47%	4.08%
Haemophilia B	273	32	7	23	**335**	81.49%	9.55%	2.09%	6.87%
von Willebrands	7	1	-	1	**9**	77.78%	11.11%	0.00%	11.11%
Females with FVIII deficiency	1	-	-	1	**2**				
Females with FIX deficiency	-	-	-	1	**1**				
FIX Leyden	40	9	5	40	**94**				
Factor VII Deficiency	1	-	-	1	**2**				
Factor X Deficiency	5	-	1	2	**8**				
Factor XI Deficiency	-	-	-	1	**1**				
Factor XIII Deficiency	9	-	-	2	**11**				
Fibrinogen Deficiency	4	-	-	7	**11**				
Prothrombin Deficiency	-	-	-	1	**1**				
Dysfibrinogenaemia	-	-	-	2	**2**				
Combined Haemophilia A & B	-	-	-	1	**1**				
Combined Haemophilia A + von Willebrands	1	1	1	-	**3**				
Acquired Haemophilia A	-	-	-	1	**1**				
Platelet defects (misc)	-	-	-	1	**1**				
Severe Platelet Disorder	-	-	-	1	**1**				
Miscelaneous	1	-	-	2	**3**				
Unclassified	-	-	-	1	**1**				
Multiple Diagnoses	2	-	-	1	**3**				
Total	**1,830**	**183**	**57**	**161**	**2231**				

Table 2: Shows the diagnosis and severity of registrants. Given that this is a home therapy register, it is perhaps surprising that so many mildly affected patients are on home therapy.

Data Quality

Steps taken to keep improving the quality and completeness of the Haemtrack data are described in more detail in the Haemtrack Group report. However, it is clear from our data that considerable progress has already been made in improving the completeness and quality of the data. Data quality should be tested locally for credibility by centre staff before data is uploaded and can also be tested centrally in various ways, by comparing patient-reported usage with centre–reported issues (Figure 5) and at a national level by comparing product issues reported to NHD with usage reported to Haemtrack. We can also look at the interval between treatment and reporting (Figures 6 and 7). This shows quite clearly that patients using the smartphone apps report their data far more quickly (Figure 7). We are quite sure that the improvement seen in data quality is attributable in large measure to considerable efforts by Haemophilia Centres.

Using those measures, it is clear that the interval between treatment and reporting has reduced continuously and dramatically over the past 3 years, from an average of two months down to a week (Figure 6). Intuitively, one would expect that data reported in a timely manner are likely to be more accurate and complete. We suspect that this reduction may reflect patient education by centres and the widespread adoption of the smartphone apps. We would encourage all patients to enter all treatments on the day of administration.

Whilst there is always room for improvement, there is also a high correlation between Centre-reported issues and patient-reported usage, which appears to be improving year on year. This is shown in Figure 5 which shows the percentage of issues reported to have been used by 1276 patients with severe haemophilia A or B during 2013/14. This shows that 76% have >50% compliance and 55% have 75-125% compliance.

Figure 5 Percentage of product issued reported through Haemtrack

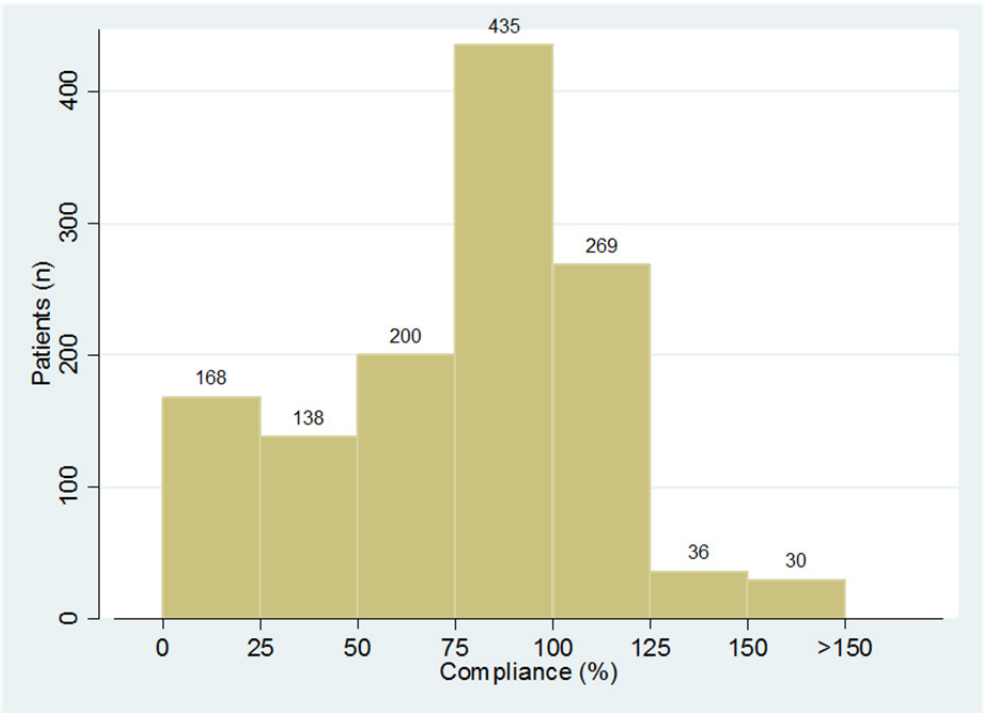


Table 3 Product Usage – comparison between Haemtrack and NHD

Treatment Period: 1st April 2013 - 31st March 2014		NHD reported issued (IU)	Haemtrack reported used (IU)	% Match
Haemophilia A	Advate	14,538,874	14,131,400	97.20%
	Fanhdi	9,911,000	9,680,000	97.67%
	FEIBA	7,338,500	7,355,535	100.23%
	FVIII 8Y	468,030	443,260	94.71%
	Helixate NexGen	15,762,298	15,239,800	96.69%
	Kogenate	41,199,000	41,084,769	99.72%
	NovoSeven (mg)	1,833	1,571	85.71%
	Octanate	2,148,500	2,155,000	100.30%
	Refacto AF	58,755,730	58,295,938	99.22%
	Investigational	311,160	354,524	113.94%
Haemophilia B	Alphanine	770,500	702,000	91.11%
	BenefIX	20,472,628	20,569,179	100.47%
	FEIBA	1,230,000	1,207,000	98.13%
	Mononine	294,000	323,000	109.86%
	NovoSeven (mg)	3,535	3,257	92.14%
	Replenine	2,282,950	2,164,442	94.81%
von Willebrand Disease	Alphanate	475,000	525,000	110.53%
	Haemate P	2,890,000	2,736,000	94.67%
	Wiloctin	1,649,000	1,517,300	92.01%
Factor VII Deficiency	NovoSeven (mg)	238	252	105.88%
Factor X Deficiency	Beriplex	12,000	13,000	108.33%
	Octaplex	75,000	90,000	120.00%
Factor XI Deficiency	FXI	31,395	34,795	110.83%
Factor XIII Deficiency	Fibrogammin P	15,000	12,500	83.33%
Fibrinogen Deficiency	Riastap (mg)	483	475	98.34%
Combined diagnoses	FEIBA	867,000	818,500	94.41%
	Helixate Nexgen	586,000	518,000	88.40%
	Kogenate	480,000	501,000	104.38%
Unclassified bleeding disorder	NovoSeven (mg)	30	33	110.00%

Includes:

- Patients using a Haemtrack account during the first month of the reporting year
- Patients within 0.75 – 1.25 ratio of compliance
- Patients with an inhibitor or a history of inhibitors

Figure 6 **Interval between treatment and reporting on Haemtrack. A dramatic and progressive reduction is shown**

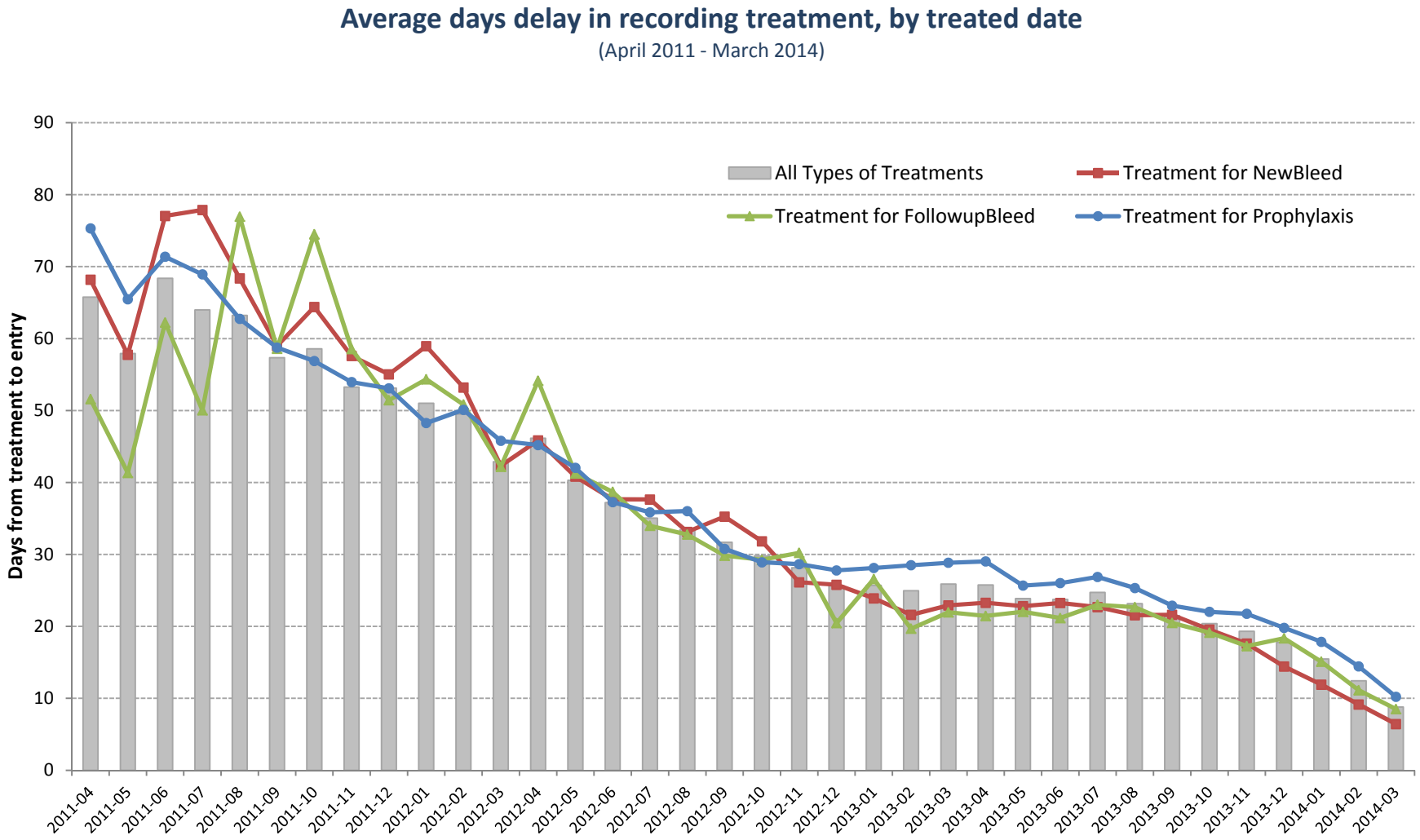
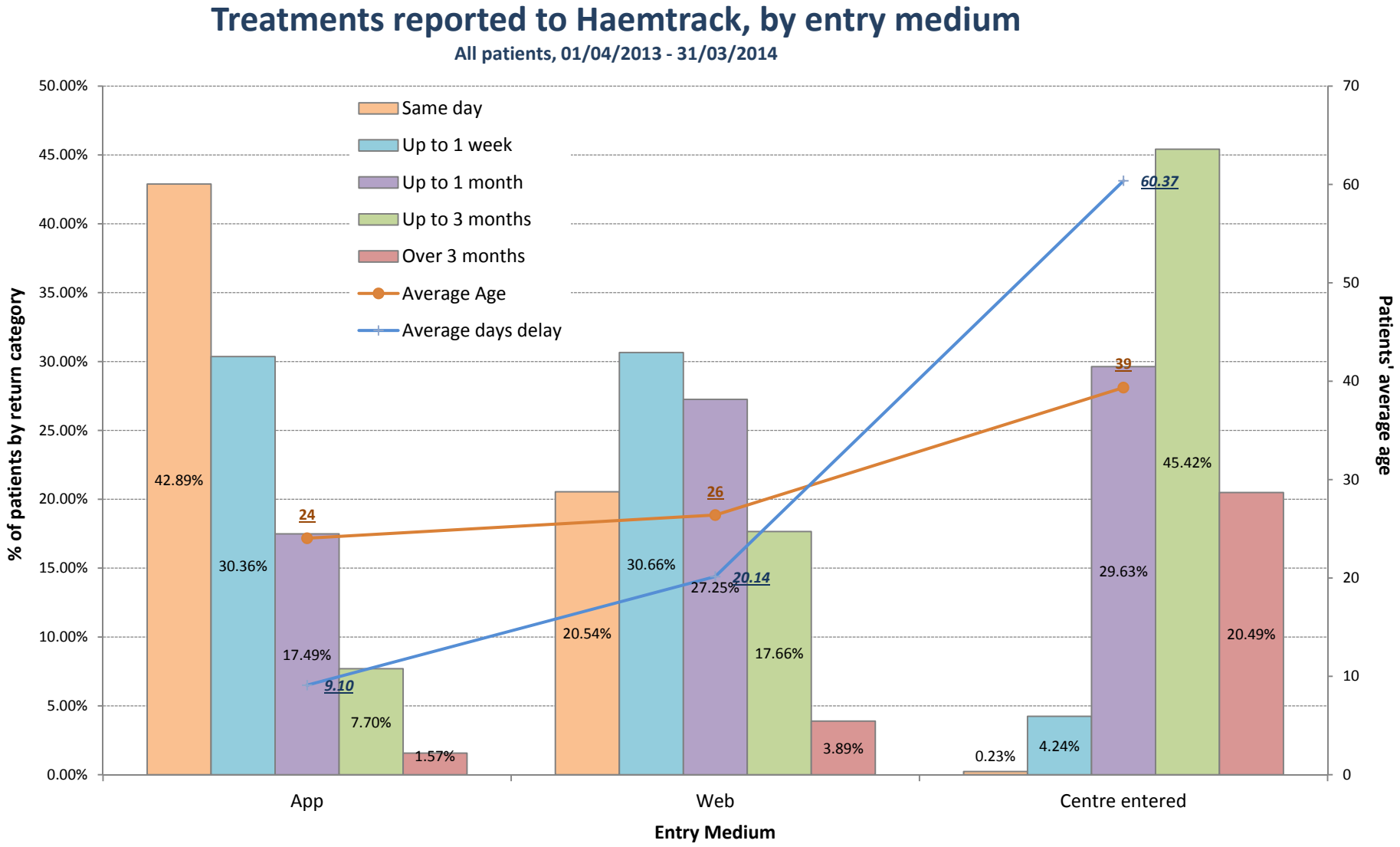


Figure 7 **Influence of reporting method on time to report treatment**



Bleed Data and Treatment Regimen

The following sections describe in more detail the types of treatment regimen used, distribution of bleeds and details of their treatment.

Table 4 Treatment regime (all registered patients)

Treatment Regime	Patients (n)	% of Patients *
Prophylaxis	1157	55.60%
On Demand	493	23.69%
Immune Tolerance	16	0.77%
Not Recorded	415	19.94%
	2,081	

Table 5 Number of treatments reported by treatment type

Treatment Type	Treatments Entered (n)	% of Total
Routine Prophylaxis	129,174	81.07%
New Bleed	10,298	6.46%
Follow Up Bleed	8,470	5.32%
Prescribed Treatment	5,124	3.22%
Activity	2,206	1.38%
Other	1,791	1.12%
Immune Tolerance	1,039	0.65%
Surgery	981	0.62%
Physiotherapy	255	0.16%
Total	**159,338**	

Bleeds reported between 01/04/2013 and 31/03/2014

Table 6 Bleed type

Bleed Location	Bleeds (n)	% of Total
Joint	6,782	62.55%
Muscle / Soft Tissue	2,968	27.37%
Mouth	749	6.91%
Other	344	3.17%
Total	**10,843**	

Bleeds reported between 01/04/2013 and 31/03/2014

Table 7 Bleed position ranked by frequency

Bleeds reported between 01/04/2013 and 31/03/2014

Bleed Position	Bleeds (n)	% of Total
Ankle - Right	1,098	10.12%
Ankle - Left	1,072	9.88%
Elbow - Left	964	8.89%
Elbow - Right	774	7.13%
Knee - Right	714	6.58%
Knee - Left	693	6.39%
Back	263	2.42%
Shoulder - Right	258	2.38%
Head	228	2.10%
Thigh - Right	220	2.03%
Hand - Left	209	1.93%
Hand - Right	200	1.84%
Foot - Right	186	1.71%
Nosebleed	182	1.68%
Thigh - Left	179	1.65%
Shoulder - Left	178	1.64%
Lower Arm - Right	177	1.63%
Not listed	*160*	*1.47%*
Foot - Left	*155*	*1.43%*
Gums	154	1.42%
Wrist - Right	151	1.39%
Other Tissue	150	1.38%
Lower Arm - Left	145	1.34%
Nose	143	1.32%
Toe - Right Foot	137	1.26%
Finger - Right Hand	135	1.24%
Wrist - Left	130	1.20%
Hip - Left	126	1.16%
Hip - Right	118	1.09%
Finger - Left Hand	112	1.03%
Calf - Left	110	1.01%
Lower Leg - Right	106	0.98%

Bleed Position	Bleeds (n)	% of Total
Upper Arm - Left	105	0.97%
Upper Arm - Right	103	0.95%
Lower Leg - Left	94	0.87%
Toe - Left Foot	91	0.84%
Calf - Right	82	0.76%
Blood in stool	65	0.60%
Groin - Right	54	0.50%
Groin - Left	52	0.48%
Blood in urine	52	0.48%
Neck	50	0.46%
Mouth	49	0.45%
Stomach	46	0.42%
Buttock - Left	40	0.37%
Lips	37	0.34%
Tongue	37	0.34%
Buttock - Right	37	0.34%
Shin - Left	35	0.32%
Shin - Right	30	0.28%
Cheek - Right	23	0.21%
Other Joint	22	0.20%
Cheek - Left	22	0.20%
Groin	20	0.18%
Dental Treatment	16	0.15%
Shoulder	14	0.13%
Buttock	12	0.11%
Psoas - Left	10	0.09%
Cheek	6	0.06%
Blood in vomit	5	0.05%
Psoas - Right	5	0.05%
Testes	4	0.04%
Blood in semen	3	0.03%
Total	**10,848**	

Most Common		
Bleed Position	**Bleeds (n)**	**% of Total**
Ankle	2,170	20.00%
Elbow	1,738	16.02%
Knee	1,407	12.97%

Figure 8 Self-reported location of bleeds broken down by cause

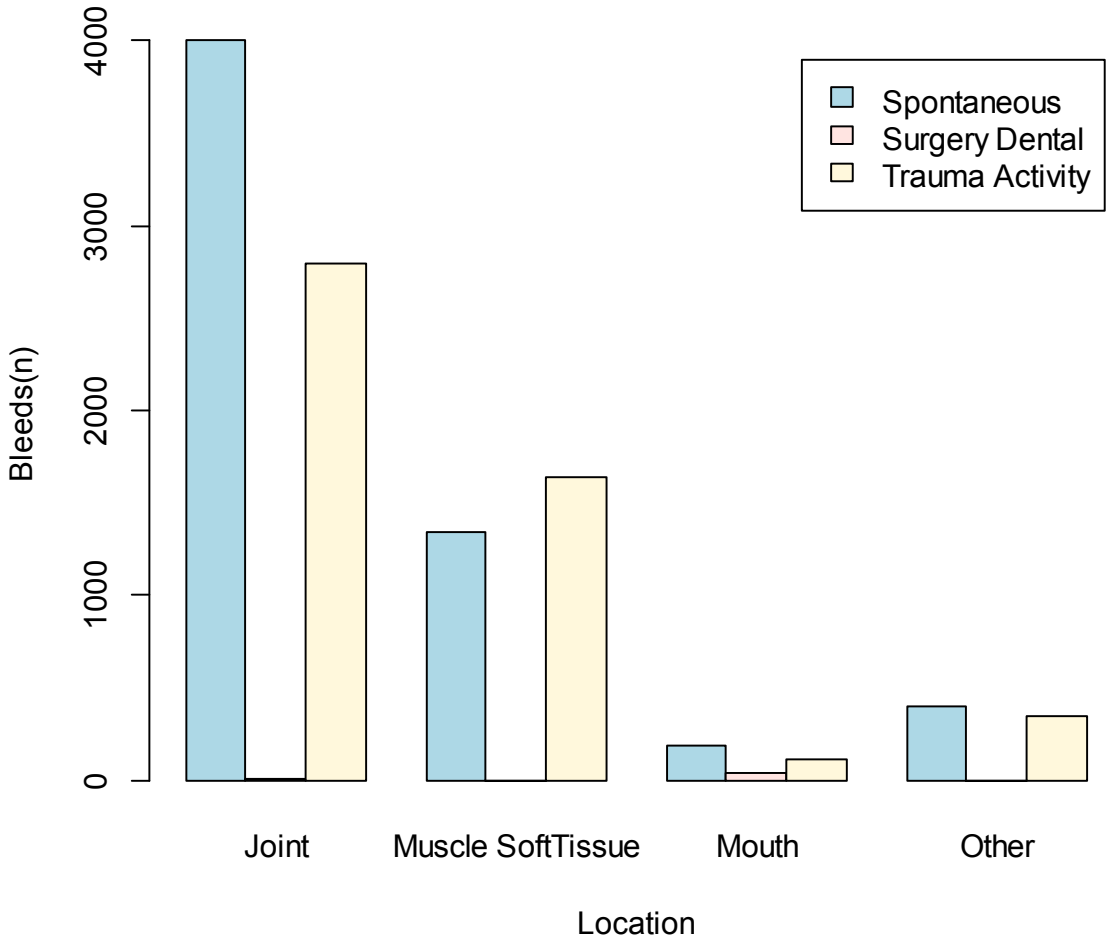
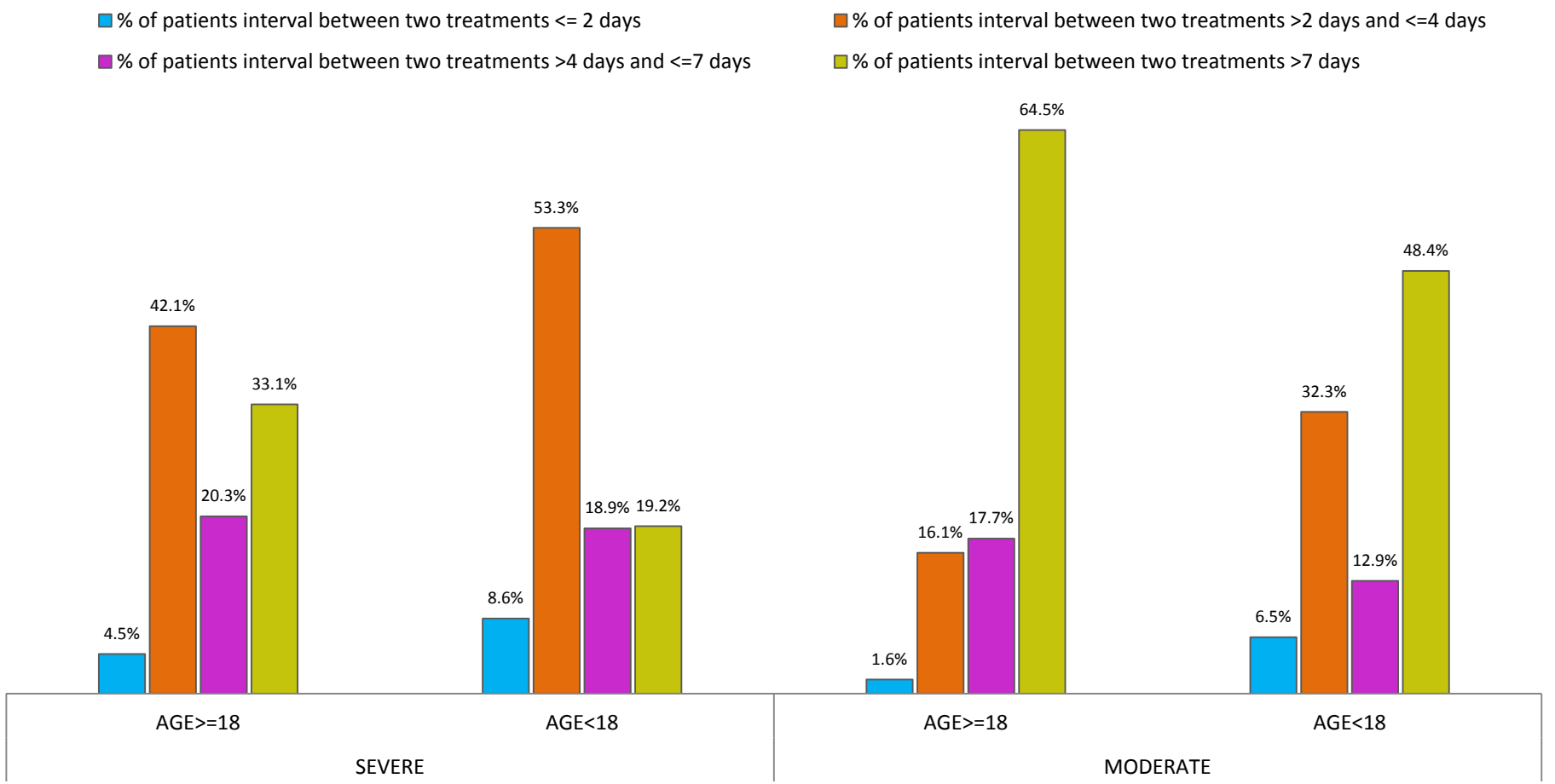


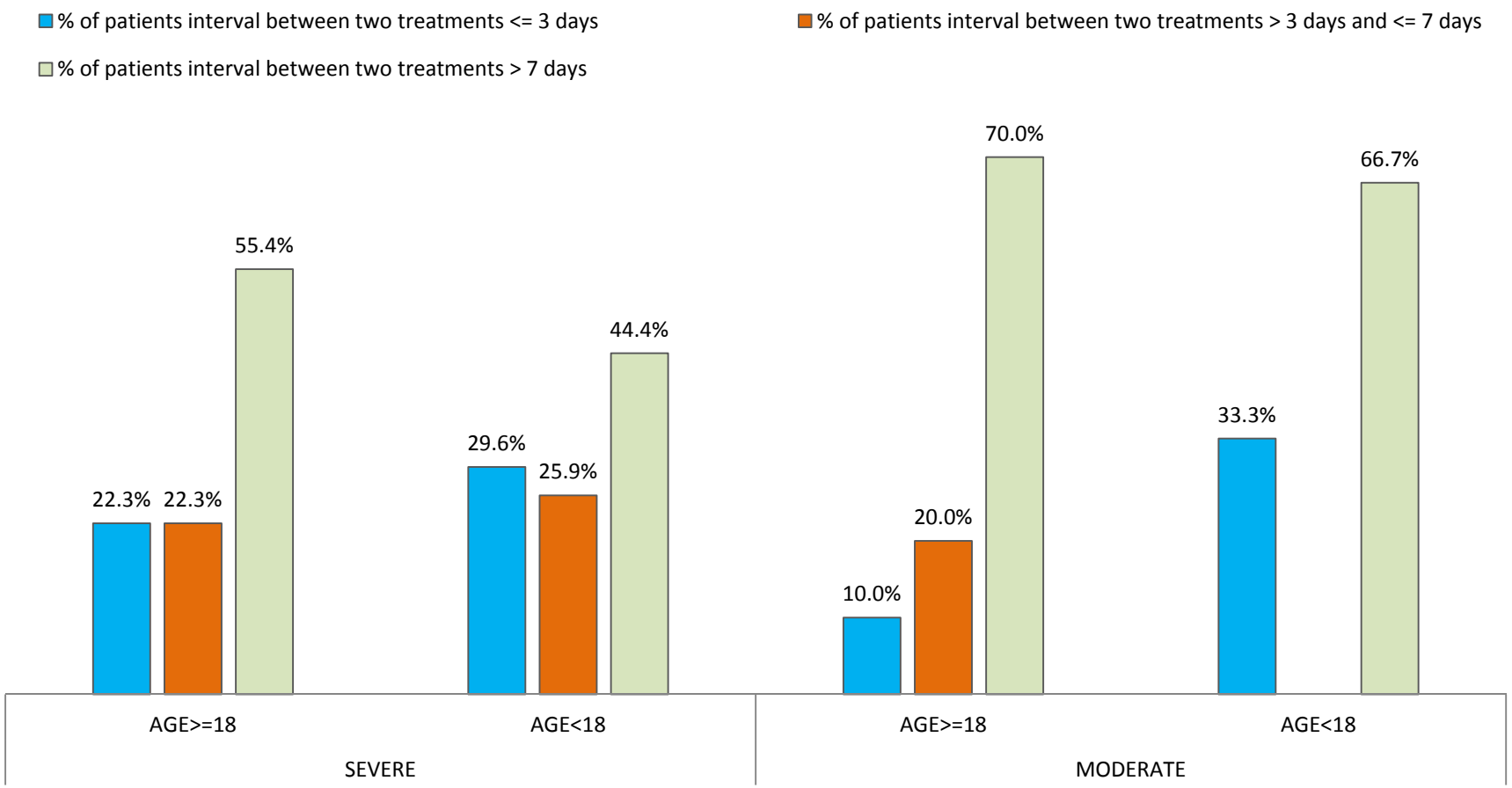
Figure 9 Frequency of treatment amongst regular users of Haemtrack with Haemophilia A



April 2013 – March 2014

Figure 9: This suggests that only 47% of adults and 62% of children with severe haemophilia A are complying with or recording a prophylactic regimen and that the remainder are treating on demand or using prophylaxis intermittently. This method of estimating who is using prophylaxis corresponds closely with the patient's self-reported treatment reason, from which an estimate of 55% of patients using prophylaxis is derived.

Figure 10 Frequency of treatment amongst regular users of Haemtrack with Haemophilia B



April 2013 – March 2014

Figure 10: This bar chart suggests that 45% of adults and 56% of children with severe haemophilia B use factor IX prophylactically. This corresponds with the treatment reason given by the patient but may be a lower proportion than reported by centres.

Figure 11 Heat map of treatment type, treatment intensity and bleeding disorder severity

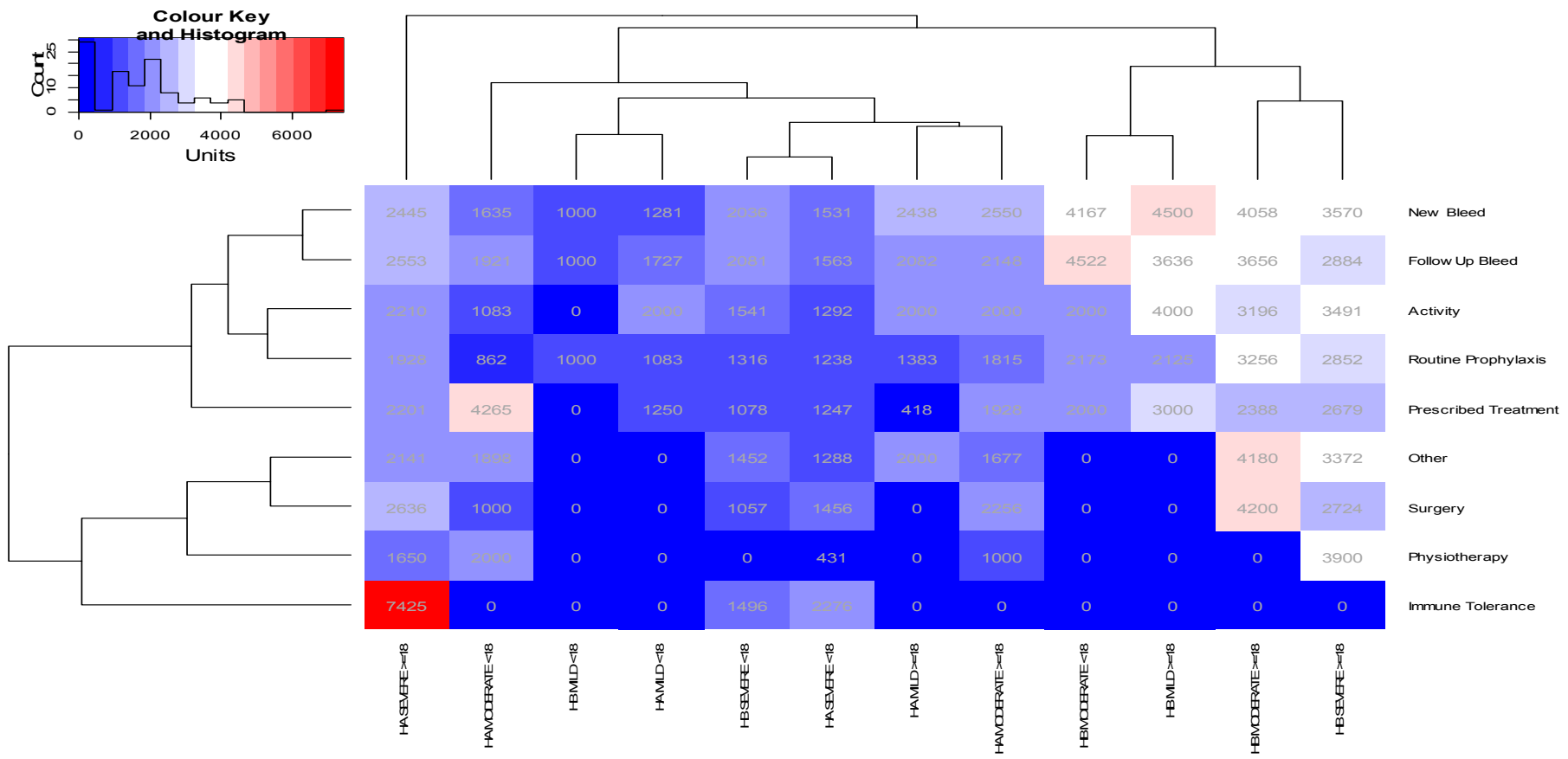


Figure 11: illustrates the hierarchical structures of clusters by patient group (diagnosis severity and age break down) and treatment type based on the mean value of the units reported for each single treatment. The intersection of a column and a row represents the mean units of treatment in a corresponding patient group and for a corresponding treatment type. All cells are coloured from blue to red to indicate the mean units from low to high (the colour keys are shown in the left corner scale). For example, the first cell (intersection of the first column and the first row) indicates the mean units for new bleed treatments on Haemophilia A severe adults patients. All patient groups and treatment types were clustered and were linked at increasing levels of dissimilarity, as shown by the dendrograms in the top and the left side of the heat

map. For example, for the patient groups, the clustering process starts out with all examples in 12 patient group clusters of size 1 each, and each patient group consists of nine elements (the treatment type). Then the pairs (group) of patient group that yield the smallest error sum of squares will form a new cluster. This process stops when all patient groups are combined into a single large cluster of size 12. The heat map clearly shows that the patient groups and the treatment types are grouped in terms of the mean units.

Table 8 Bleed location and cause: comparison by treatment regime – by bleed rate incidence – Haemophilia A

Joint Bleeds								
Cause of bleed	Patients under the age of 18 years				Patients 18 years and over			
	Prophylaxis n = 294 pts		On-Demand n = 30 pts		Prophylaxis n = 353 pts		On-Demand n = 169 pts	
	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient
Spontaneous	208	0.71	44	1.47	839	2.38	1,112	6.58
Trauma / Activity	278	0.95	24	0.80	547	1.55	618	3.66
Total	**486**	**1.65**	**68**	**2.27**	**1,386**	**3.93**	**1,730**	**10.24**

Muscle / Soft Tissue Bleeds								
Cause of bleed	Patients under the age of 18 years				Patients 18 years and over			
	Prophylaxis n = 294 pts		On-Demand n = 30 pts		Prophylaxis n = 353 pts		On-Demand n = 169 pts	
	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient	Bleeds (n)	Incidence per patient
Spontaneous	157	0.53	12	0.40	249	0.71	314	1.86
Trauma / Activity	301	1.02	17	0.57	231	0.65	368	2.18
Total	**458**	**1.56**	**29**	**0.97**	**480**	**1.36**	**682**	**4.04**

Age at 30/09/2013
Treatments entered between 01/04/2013 and 31/03/2014

Table 9 Bleed severity

Bleeds reported between 01/04/2013 and 31/03/2014

Bleed Severity	Bleeds (n)	% of Total
Life or Limb Threatening	11	0.11%
Major (very bad)	1,704	16.56%
Minor (not so bad)	8,575	83.33%
Total	**10,290**	

Table 10 Bleeds impacting on regular activity

Bleeds reported between 01/04/2013 and 31/03/2014

Cause of Bleed	Bleeds (n)	% of Total
Spontaneous	2,488	52.79%
Trauma / Activity	2,211	46.91%
Surgery / Dental	14	0.30%
Total	**4,713**	

Table 11 Pain scale of reported bleeds

Bleeds reported between 01/04/2013 and 31/03/2014

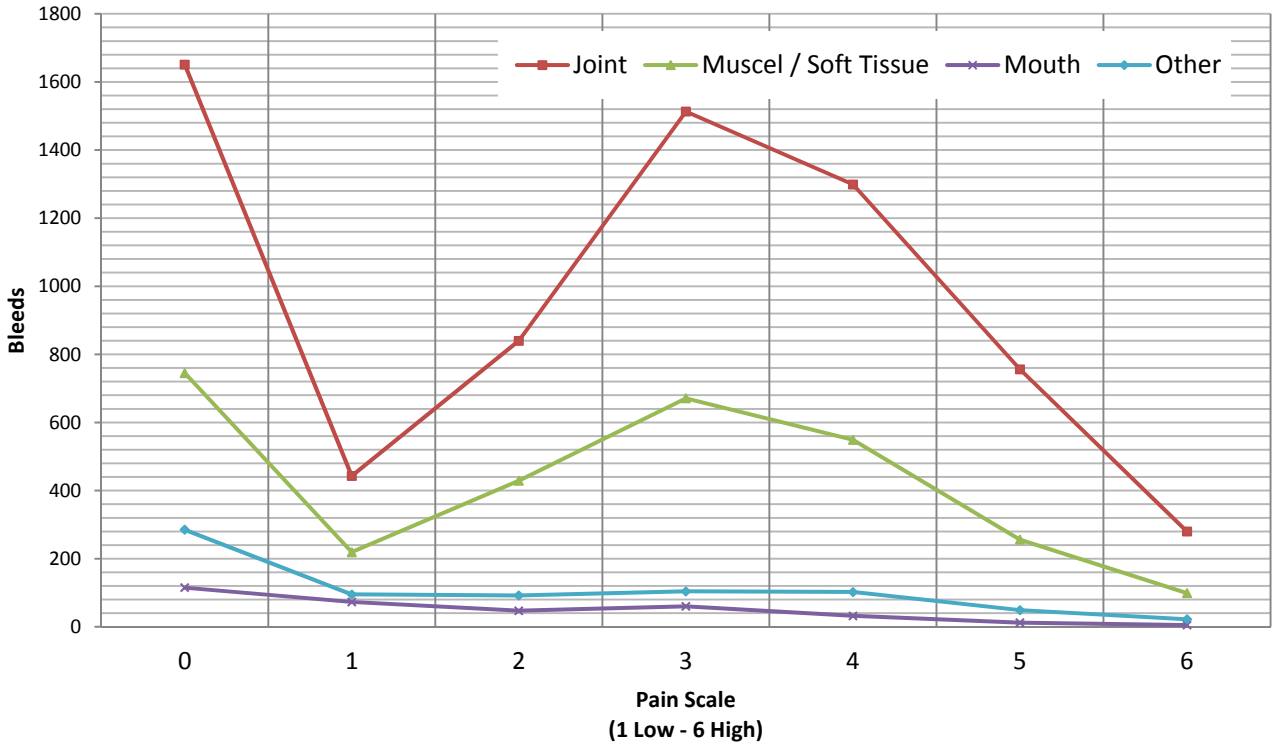
Pain Scale (1 low – 6 high)	Bleeds (n)	% of Total
Not reported	2,796	25.79%
1	830	7.65%
2	1,408	12.99%
3	2,348	21.65%
4	1,982	18.28%
5	1,073	9.90%
6	406	3.74%
Total	**10,843**	

Table 12 Pain scale comparing joint and muscle/sort tissue bleeds

Bleeds reported between 01/04/2013 and 31/03/2014

Pain Scale (1 low – 6 high)	Joint		Muscle / Soft Tissue	
	Bleeds (n)	% of Total	Bleeds (n)	% of Total
Not reported	1,323	24.60%	549	23.94%
1	349	6.49%	172	7.50%
2	656	12.20%	286	12.47%
3	1,154	21.46%	556	24.25%
4	1,109	20.62%	474	20.67%
5	609	11.33%	201	8.77%
6	177	3.29%	55	2.40%
Total	**5,377**		**2,293**	

Figure 12 Pain scale distribution by bleed type (all patients)



Pain Scale: 0 = not reported
April 2013 – March 2014

Figure 13 Time interval between bleed-onset and treatment

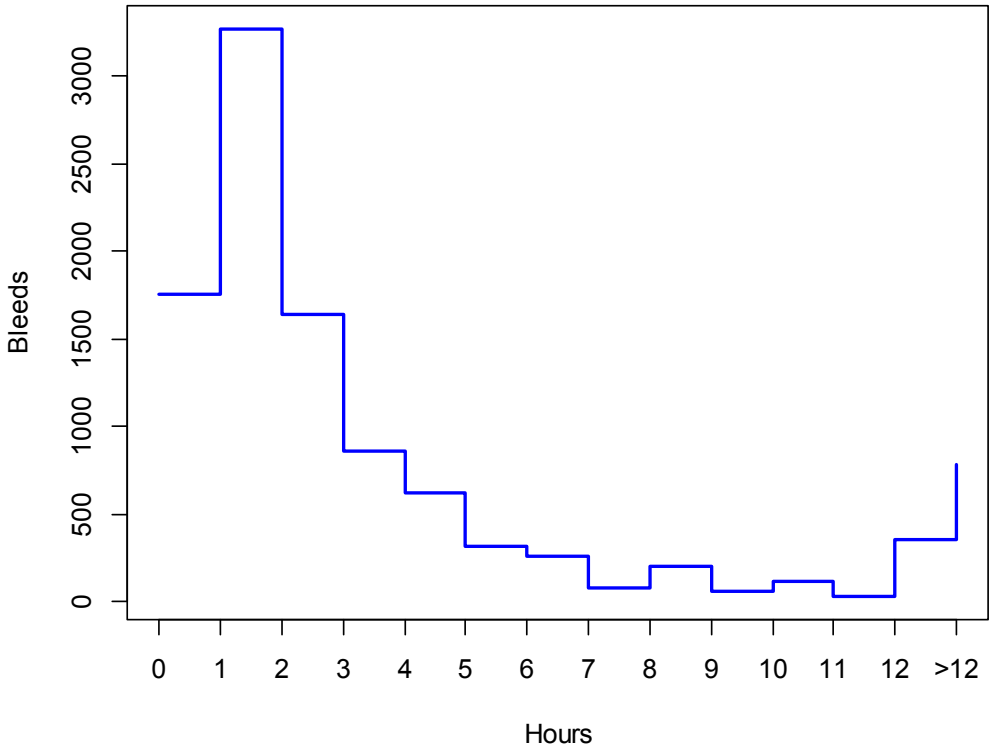
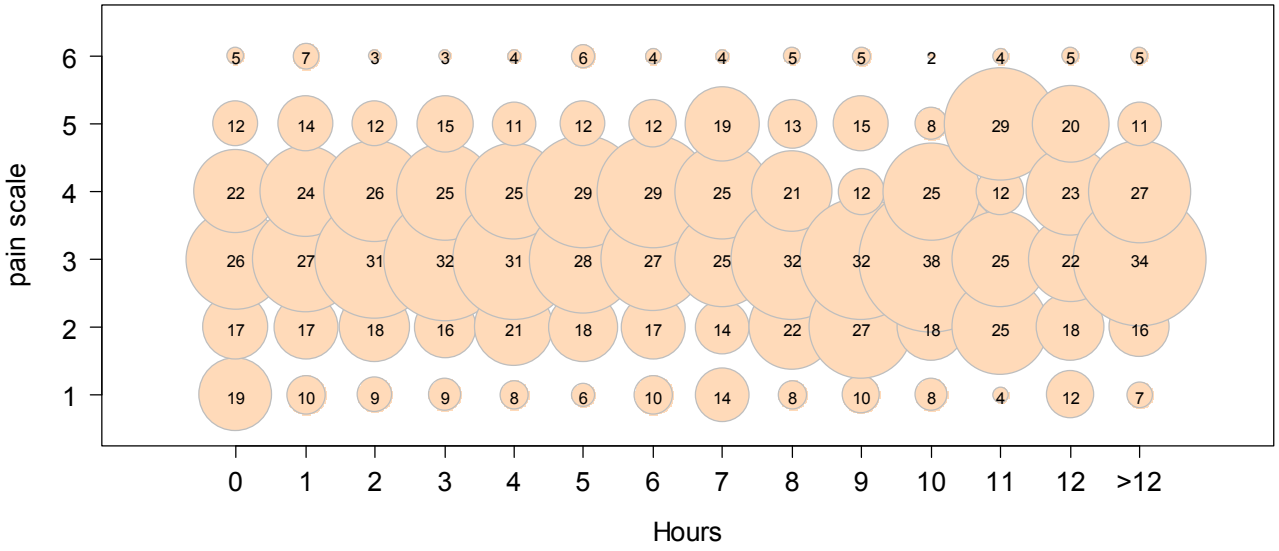


Figure 14 Bubble diagram showing the relationship between reported pain scale and reported interval between bleed onset and treatment



1-low, 6 = high
April 2013 – March 2014

Figure 14: Circles represent the percentage of total number of treatments at each pain level in the time interval indicated by the bubble position. This shows that although most bleeds are treated promptly and cause little pain, there are a substantial proportion of bleeds for which treatment is delayed and these tend to be more painful by the time they are treated. In fact most bleeds treated early have low pain scores and most treated after a delay have a moderate to severe pain score. One can only speculate on the cause of this delay in starting treatment. Patients are advised to treat all bleeds early. However, patients with significant arthropathy encounter increasing difficulty distinguishing between the symptoms of arthropathy and an early bleed. We had considered the possibility that older patients with significant arthropathy may have increased difficulty distinguishing between the pain of a new bleed and the discomfort from arthropathy and might delay treatment until they were sure it was a bleed. However, the age breakdown in Table 13 shows that the greatest delays in treating were actually observed most frequently in the 0-19 year age group, suggesting that this may be a training issue or else non-verbal presentation in very young children.

Table 13 Time interval between joint bleed-onset and treatment, by age - Severe Haemophilia A

Time After Bleed (hours)	Percentage of total bleeds in each age group							
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79
1	39.11%	34.42%	30.80%	32.81%	33.68%	37.51%	24.38%	6.74%
2	17.34%	9.18%	15.68%	19.12%	19.07%	19.77%	19.01%	21.35%
3	7.66%	5.16%	9.20%	11.93%	8.25%	10.62%	9.50%	3.37%
4	4.03%	3.82%	6.82%	6.67%	7.30%	4.29%	6.61%	5.62%
5	4.44%	3.44%	6.36%	3.33%	2.06%	2.15%	1.24%	-
6	2.02%	2.29%	2.61%	3.33%	1.46%	1.24%	2.89%	-
7	1.61%	0.96%	0.68%	0.61%	0.43%	0.34%	2.89%	-
8	1.21%	1.91%	2.16%	1.75%	0.95%	1.13%	2.48%	-
9	1.21%	0.57%	0.80%	0.44%	0.34%	0.45%	0.41%	-
10	0.81%	2.29%	1.14%	0.61%	0.60%	-	0.83%	-
11	0.81%	0.38%	0.45%	0.18%	0.26%	0.34%	-	-
12	6.45%	5.54%	3.86%	1.75%	1.98%	1.81%	2.89%	3.37%
>12	8.47%	13.38%	7.61%	3.95%	3.52%	2.49%	2.48%	2.25%
Not Reported	4.84%	16.63%	11.82%	13.51%	20.10%	17.85%	24.38%	57.30%

5. Data Management Working Party

Membership	Representing
Dr Gerry Dolan	Co-Chair
Dr David Keeling	Co-Chair
Nancy Brodie	UK Haemophilia Data Managers Forum
Christina Burgess	The Haemophilia Society
Liz Carrol	The Haemophilia Society
Prof Peter Collins	Representing Wales
Lynne Dewhurst	National Haemophilia Database
Claire Foreman	NHS England
Emma Franklin	Haemophilia Nurses Association
Prof Charles Hay	UKHCDO Ltd & National Haemophilia Database
Dr Rob Hollingsworth	Medical Data Solutions and Services
Dr Ri Liesner	Invited Guest
Ben Palmer	Medical Statistician
Jon Currington	NHS England
Vacant post	Patient Representative

UKHCDO Working Party Chairs

Dr Liz Chalmers	Paediatric Working Party
Dr John Hanley	Musculoskeletal Working Party
Dr Dan Hart	Inhibitor Working Party
Prof Mike Laffan	Von Willebrand Working Party
Dr Andrew Mumford	Rare Disorders Working Party

The UKHCDO Data Management Working Party has a key role in the organisation. The major part of the work of the NHD is the collection and analysis of data from the Haemophilia Centres in the United Kingdom and this is overseen by the working party. The aggregated national data are particularly important for national procurement and managing the subsequent contract. As well as phenotypic data, genotype data is being accrued at an impressive rate and will be particularly valuable in patient management and research. The NHD is undertaking a thorough review of the patient information leaflets so that patients remain fully informed about the NHD and the (anonymous) use of their data. We have to be careful when we debate what additional information would improve patient care and the Data Management Working Party remains committed to ensuring that outcome measures are relevant and manageable.

We recognise the demands for increased quality and volume of data and recognise the need for regular meetings for data managers to support and help them with the range of issues involved in collecting accurate data.

More detailed, patient generated, data is becoming available in greater quantity through Haemtrack which is now accessible on Android as well as iPhone. The Data Management

Working Party has set up a dedicated group (The Haemtrack Management Group) to explore these data.

The research and development activities of UKHCDO working parties requires close collaboration with NHD and the Data Management Working Party. An excellent example of this is the paper "Factor VIII brand and the incidence of factor VIII inhibitors in previously untreated UK children with severe haemophilia A, 2000-2011" published in Blood this year.

We would like to take the opportunity again to thank Professor Hay for managing the National Haemophilia Database on behalf of the UKHCDO and to Rob Hollingsworth and MDSAS for their continued support and maintenance of our national information systems. Lynne Dewhurst, Ben Palmer, Helen Brown, Rachel Lockwood, Sarah Rooney, Tom Sharpe, Jess Smith and Amy Tidmarsh and Hua Xiang of the National Haemophilia Database have been invaluable in their very high quality work on our behalf.

Finally, last but not least, we wish to acknowledge all the important work done at the Centre level and acknowledge work by individual patients and the Haemophilia Centre staff and we thank them for their tireless work in providing data for this very important resource.

Dr Gerry Dolan & Dr David Keeling
Chairs & Secretary, UKHCDO Data Management Working Party

6. Haemtrack Group

Membership

Dr Gerry Dolan	Chairman
Ben Palmer	Secretary
Nancy Brodie	
Dr Elizabeth Chalmers	
Dr Pratima Chowdary	
Lynne Dewhurst	
Prof Charles Hay	
Dr Rob Hollingsworth	
Dr Lishel Horn	
Clare Ibbs	
Dr Ri Liesner	
Prof John Pasi	
Debra Pollard	
Antony Woolcomb	
Dr Hua Xiang	
Patient Representative (position currently vacant)	

Mission

To optimise the quality of the Haemtrack data and to direct the development and rollout of the system and the analysis of the data

Meetings

The full group met for the first time on 1st August 2014 though there had been earlier more limited meetings and conference calls to set the group up and start the ball rolling. The group is made up principally of centre directors with an interest in this area, Haemophilia Nurse Specialists, Physiotherapists and statisticians (Ben Palmer and Hua Xiang). This is a sub-group of the Data Management Working Party.

In the first meeting and previous conference calls, the group was principally concerned with reviewing the Haemtrack system as it currently exists, to review the questions asked by the software and to identify any ambiguity which may give rise to inconsistency in the way that patient enter data. This has been extensively discussed and two questionnaires have been devised and were reviewed, one for the patients and one for the centres. These will be sent out shortly.

Previously, it had been impossible for centres to review and amend incorrect data sent in by patients (usually batch or brand data). Recently, the software had been amended to permit centres to do this and it was necessary for centres to validate the data before it was uploaded. This seemed to be working well in pilot sites. There will be a two-phased approach, with non-HCIS centres getting it first, and HCIS centres getting it with the new version of HCIS.

Questionnaire

Debra Pollard, Lishel Horne, Ri Liesner and Antony Woolcomb drafted two questionnaires (one for patients and one for centre staff), which have been reviewed by the whole group. It was thought that the staff questionnaire would be purely electronic, whereas the patient questionnaire would have both electronic and paper versions. Not all questions would be relevant to both electronic and paper versions of the patient questionnaire. The electronic version could be attached to the Haemtrack website, although attaching it to the smartphone apps would be more complicated. Electronically, there are several things that can be done to capture patients. The aim of the questionnaires is to identify how the patients and centres use Haemtrack as a guide to its future management and modification.

Information Leaflets

Nancy Brodie, Charles Hay and Rob Hollingsworth have written a patient information leaflet, which will help patients understand the purpose of Haemtrack and how to use it. This is currently being reviewed by patients to ensure that is written at the right level and is understandable.

A similar leaflet is being written for centres but this will be finalised once we have analysed the results of the Centre Questionnaire. Almost all Comprehensive Care Centres (93%) are now using Haemtrack and almost 98% of eligible patients in those centres are registered. Uptake by patients registered to use Haemtrack by Haemophilia Centres is far lower, about half. Clearly many of these centres are not convinced of the value of the system or may not be staffed adequately to introduce it.

Consent

All patients give consent when they register with Haemtrack for the first time. This is done on-line. The consent and information leaflet in current use is heavily based on the Advoy leaflet, which went before. This is a rather legalistic document which is no longer considered fit for purpose and so it is being rewritten, to replace the current document within three months.

Data analysis

Hua Xiang PhD has been appointed as a data miner. She has been identifying a subset of Haemtrack data of good quality for further more detailed analysis. Some of this analysis is presented in the Haemtrack Report. The group is actively reviewing the possibilities for future analysis of this dataset.

Software Updates –Progress Implementation review

A barcoding app project is underway. Apple iOS has a built-in barcode reader for the iPhone, with free support. The android equivalent will follow.

Data validation has been implemented for all non-HCIS centres, and will follow for HCIS centres when they get the new version of HCIS (currently being piloted at RFH).

Data management skills education was discussed. A rolling step-by-step training and accreditation programme is required due to staff turnover.

The next meeting is planned for November.

Prof CRM Hay
October 2014
Manchester

7. Inhibitor Working Party

Membership

P Collins	Chairman
D Hart	Secretary
E Chalmers	
C Hay	
R Liesner	
B Palmer	
S Rangarajan	
K Talks	
M Williams	

The working party reformed in March 2011

There have been two face to face meetings this year and eight teleconferences.

Activities

National immune tolerance induction protocol

A protocol for first line ITI for minimally treated severe patients has been developed by the working party in collaboration with the paediatric working party and this has been ratified by the advisory committee. This protocol is based on the recently published inhibitor guidelines.

The protocol has been adopted by the English Clinical Reference Group and all first line ITI for children with severe haemophilia A are expected to be treated according to this protocol and outcomes reported to the NHD.

Analysis of data held by NHD

Inhibitor surveillance in previously treated patients

A paper describing the outcomes of switching product following the previous tender has been submitted to Haemophilia and is undergoing peer review. The results do not suggest any increase in inhibitor formation related to switching although, even with the large number of patients available for UKHCDO to analyse, the study is underpowered.

Inhibitor rates associated with brands of recombinant factor VIII

A recent study has suggested that the risk of a PUP developing an inhibitor varies with the brand of recombinant factor VIII (NEJM 368:231-9, 2013). It is important that this finding is investigated in other cohorts of patients. The NHD has identified all PUPs first treated in the UK between 2000 and 2011 and is investigating the rate of inhibitor development associated with each product. This exercise has being extended so that a multivariate analysis can be

performed to include the main known risk factors for inhibitor development (mutation, family history, ethnicity and intensive treatment).

Centres have been asked to clarify important data points and to ensure that the cohort investigated is appropriate and the response to data requests has been very positive. This work has been the main focus of the working party and a major exercise of data collection and cleaning has been performed in collaboration with the NHD. The data analysis has been performed in consultation with the executive committee and the advisory committee.

The results will be an important contribution to patient safety and will be reported soon.

Acquired haemophilia survey

A survey of UK treaters regarding immunosuppressive treatment of acquired haemophilia A has been completed and accepted for publication as a letter in Haemophilia. The study was led by Dr Batty from the Royal London Hospital.

Future of the working party

The inhibitor working completed its three year term in March 2014 and has been reconstituted under the chair of Dr Hart. The composition of the new working party was not known at the time of writing.

Dr Peter Collins
Chairman, Inhibitor Working Party
September 2014

8. Musculoskeletal Working Party

Membership

John Hanley	Chairman
Pratima Chowdary	Secretary
Peter Briggs	
Stephen Classey	
Desmond Creagh	
Simon Frostick	
Nick Goddard	
Paul McLaughlin	
Jecko Thachil	
Jonathan Wilde	
Mark Wood	

Meetings

The Musculoskeletal Working Party was convened in late 2011 (due for review in late 2014). This year the group met on 28th March 2014 at St Thomas's Hospital, London. In addition there has been regular communication by email to progress the current projects.

Objectives

The remit of the working party is to review recent literature and current practice with a view to drawing up guidelines on the management of musculoskeletal problems in patients with haemophilia.

Activities and progress

Survey of Current Practice

A survey of current practice was circulated to all Haemophilia Comprehensive Care Centres and Haemophilia Centres in the UK. The results of the survey have revealed significant variation in practice particular in the use of intra-articular steroid injections and radioactive synovectomy in the management of synovitic joints. The results of the survey have been submitted for presentation at the joint UKHCDO/BSHT meeting in Edinburgh, October 2014.

Work with the National Haemophilia Clinical Reference Group

Members of the working party (led by Jonathan Wilde) produced and submitted a Clinical Commissioning Policy on radiosynovectomy which has been approved by the Haemophilia CRG. This has clarified the role of radiosynovectomy and outlined the commissioning process.

Guidance documents in preparation

There has been slow progress with this over the past 12 months. The first guideline is now almost complete and will be circulated for wider comments in the near future. The second guideline will be worked on over the next 6 months with an aim to complete in 2015.

1. Guidance on management of acute joint/muscle bleeds and chronic joint/muscle problems. This document is now near completion and will be circulated for wider discussion in the near future.
2. Guidance on the peri-operative management of patients with bleeding disorders undergoing orthopaedic procedures.

Educational event

The Musculoskeletal Working Party was planning to organise a multidisciplinary educational event in 2014 to provide a forum for discussion and an opportunity to share best practice. However, the World Federation of Haemophilia International Musculoskeletal Congress will be held in Belfast from the 7th to 10th May 2015. Members of the Musculoskeletal Working Party are involved in the organisation of the meeting and several are also presenting. The working party is promoting the WFH meeting to encourage a good attendance from the UK.

Outputs in 2014

A SURVEY OF THE MUSCULOSKELETAL MANAGEMENT OF HAEMOPHILIA IN THE UK. A McKernan[1], J Hanley[2], P Chowdary[3], S Classey[4], S Frostick[5] on behalf of the Musculoskeletal Working Party, UKHCDO. [1]Department of Haematology, Derby Hospitals NHS Foundation Trust, Derby; [2]Haemophilia Centre, Newcastle Hospitals NHS Trust, Newcastle upon Tyne; [3]Haemophilia Centre, Royal Free London NHS Foundation Trust; [4]Guys and St. Thomas's NHS Foundation Trust, London; [5]Institute of Translational Medicine, University of Liverpool, Liverpool. Presented at Joint British Society for Haemostasis & Thrombosis, UK Platelet Group & United Kingdom Haemophilia Centre Directors' Organisation meeting Edinburgh, October 2014

John Hanley
Chairman, Musculoskeletal Working Party
September 2014

9. Paediatric Working Party

Membership

Elizabeth Chalmers	Chair
Jeanette Payne	Secretary
Jayanthi Alamelu	
Peter Collins	
Mary Mathias	
Mike Richards	
Oliver Tunstall	
Mike Williams	

Meetings

Meetings 2013 – two face to face meetings, one combined with the Inhibitor Working Party. One additional teleconference.

Meetings 2014 – 2 face to face meetings

Summary of current activities

Guideline issues

This working party is responsible for two current BCSH/UKHCDO guidelines -

Management of haemophilia in the fetus and newborn. Published 2011

Prophylaxis in children with haemophilia A. Published 2010

These guidelines are reviewed at each working party meeting and are considered up to date at this time. Aspects of guideline (1) are likely to be revisited in the UKHCDO/RCOG guideline on obstetric management of inherited bleeding disorders which is currently being written.

The working party has contributed a paediatric section on dental care in haemophilia patients and has commented on the recently published VWD guideline.

The working party regularly reviews new guidelines in order to discuss their impact on paediatric practice.

Current - audits/projects

1. Audit of prophylaxis in haemophilia against current BCSH/UKHCDO Guideline
    a. Data collection is complete and the data is currently being analysed
2. Intracranial haemorrhage in inherited bleeding disorders
    a. Retrospective data collection has been completed and the data is being analysed
    b. Prospectively data collection on ICH will be added to UKHCDO adverse event reporting
3. Follow up of Immune Tolerance Therapy in the UK
    a. Retrospective data has been collected and is currently being analysed

4. Management of Immune tolerance - ongoing in collaboration with Inhibitor Working Party
5. Use of subcutaneous DDAVP in children – ongoing

Dr Elizabeth Chalmers
Chair, Paediatric Working Party
September 2014

10. Rare Disorders Working Party

Membership

Andrew Mumford	Chairman
Sam Ackroyd	
Raza Alikhan	
Louise Bowles	
Pratima Chowdary	
John Grainger	
Jason Mainwaring	
Mary Mathias	
Niamh O'Connell	

Meetings

The group met face to face on 14th November 2013 (Mumford, Mathias, Mainwaring, Alikhan, Bowles, Ackroyd, O'Connell)

In addition there were 6 teleconferences in 2103 in two sub-groups

Remit

The main activity of the working party has been completion of the 2014 Rare Coagulation Disorders Guideline. This has now progressed through consultation, sounding, submission, peer-review and editorial processing at the British Journal of Haematology. The guideline is now available as an Epub ahead of print.

Activities

The working party has collaborated with the Paediatric Working Party to design a UK survey of intracranial haemorrhage in haemophilia and rare coagulation and platelet disorders and has contributed to a UKHCDO consultation on adoption of recombinant FXIII concentrate for prophylaxis in FXIII deficiency. The working party has facilitated launch of the EU Prospective registry of FXIII and fibrinogen deficiency at UK centres within the EUPHANET consortium framework. On-going projects include a retrospective survey of UK prescribing practice for rare coagulation disorders (with Data Management Working Party).

Publications

Guideline for the diagnosis and management of the rare coagulation disorders: A United Kingdom Haemophilia Centre Doctors' Organization guideline on behalf of the British Committee for Standards in Haematology.

Mumford AD[1], Ackroyd S, Alikhan R, Bowles L, Chowdary P, Grainger J, Mainwaring J, Mathias M, O'Connell N; the BCSH Committee

Br J Haematol. 2014 Aug 6. doi: 10.1111/bjh.13058. [Epub ahead of print]

Dr Andrew Mumford
Chairman, Rare Disorders Working Party
September 2014

11. von Willebrand Disease Working Party

Membership

Mike Laffan	Chairman
David Keeling	
James O'Donnell	
Will Lester	
Andrew Will	
Campbell Tait	
Anne Goodeve	
Carolyn Millar	

Meetings

The working party has met once since last year's report (Sept 2013) and communicated extensively by email.

Activities

Revise diagnostic and treatment guidelines of 2004

The dual guidelines on diagnosis and management have been revised and condensed into a single guideline. This has been through internal review and sounding board and has been submitted for publication in the BJH. All the above members contributed extensively to this document.

National Haemophilia Database

The working party will now review the way in which VWD is entered on the database and to review the problems with existing registration data. A request for access to existing database details has been submitted to the DMWP and access to the data agreed.

VWF concentrate

The working party has been asked to consider the criteria that should be applied in choosing a VWF-containing concentrate for treatment of VWD in different circumstances.

Professor Mike Laffan
Chairman, von Willebrand Disease Working Party
September 2014

12. Obstetric Task Force

Membership (multidisciplinary)

Dr Charlie Hay	Chairman
Dr Sue Pavord	Secretary
Dr Liz Chalmers	
Dr Will Lester	
Dr Bella Madan	
Dr Rachel Rayment	
Dr Tony Cumming	Clinical Scientist
Dr Gabriella Gray	Obstetrician
Dr Rezan Kadir	Obstetrician
Dr Nuala Lucas	Anaesthetist
Dr Helena Maybury	Obstetrician
Dr Claire Tower	Obstetrician
Juliette Webster	Specialist midwife

Remit

The task force has been established to revise and update the 2006 UKHCDO guidelines on management of pregnancy in women with congenital bleeding disorders, or carriers thereof

The guidelines are being developed in conjunction with the Royal College of Obstetricians and Gynaecologists; the scoping and literature search has been conducted in accordance with their usual procedures.

The aim is to produce a green topped guideline, targeted at haematologists, obstetricians, neonatologists and anaesthetists.

Related UKHCDO guidelines include the management of haemophilia in the fetus and neonate and genetic diagnosis. Membership of the group has been selected to reflect the overlap

Meetings

There have been two meetings held to date and a third in 4 weeks' time.

Activities

Two sections have been written so far.

The main addition to the 2006 guideline is the management of platelet function disorders. The section on prenatal diagnosis and management of rare factor deficiencies will be expanded.

The most controversial issue is the optimal mode and timing of delivery. It is recognised that there is little evidence to help inform the guideline and recommendations will mainly be based on expert opinion.

Dr Sue Pavord
Secretary, Obstetric Task Force
September 2014

13. Genetic Laboratory Network

Background

The UKHCDO GLN (formerly GTN) was formed in 2002, arising out of the UKHCDO Genetic Working Party, 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 related inherited bleeding disorders (many of the laboratories are also involved in other areas as well).

Representatives of the Network sit on the UKHCDO GWP, attend meetings of the UKGTN and attended those Haemophilia Alliance meetings that took place during 2014.

Meetings

The UKHCDO GTN holds bi-annual meetings and met on 21st November 2013 in London and 27th May 2014 in Manchester. The next meeting is scheduled for late October or November in Cardiff.

Chair & Secretary

Steve Keeney (Chair) and Vince Jenkins (Secretary) continue in these positions.

Current activities

1. UK Genetic Testing Network (UKGTN) revised remit – UKHCDO response:

The UKGTN have revised their remit to include *"Any genetic test provided by a UKGTN member laboratory for NHS service provision for rare disorders that usually affects fewer than 1 in 2000 as described in the UK Rare Disease Strategy"*. Steve Keeney has coordinated the overall opinion of the UKHCDO via the GLN and GWP on this proposal and has fed back to the UKGTN that there are no objections to this process. This was fed back formally at the UKGTN CSAG meeting on 16th of September. Individual GLN labs that are not registered with the UKGTN have been advised that they may wish to consider applying for membership if they perceive it is in their interest.

2. Laboratory Audit:

The latest round of the Haemophilia Centre Triennial audit programme was the first where the genetic lab audit was incorporated to form an integrated audit process. The success of the merged audit programme will be reviewed, with Marian Hill representing the UKHCDO-GLN.

3. National Haemophilia Database Genetics Portal

The inclusion of a portal to the National Haemophilia Database for the upload of genetic mutation data is now in routine use across the GLN. At the last check (August 2014) there were 1324 mutation entries across F8, F9 and VWF mutation data entries from the 12 labs registered.

4. Locus Reference Genomic (LRG) development

Steve Keeney has input to the development of LRG reference sequences for the main bleeding disorder genes. The F9 LRG is now live, F8 is in final stages of preparation, and VWF is in development.

5 Bleeding Disorder Genetic Analysis Best Practice Guidelines

The BPGs for Haemophilia A and Haemophilia B are still considered current, although nearing a review. The VWD genetic analysis guideline update is underway.

6 Haemophilia Genetics NEQAS scheme

The Haemophilia Genetics EQA scheme, run by UK NEQAS in Sheffield, continues with bi-annual distributions. The results for each round of the scheme are reviewed and discussed at the following network meetings and any relevant comments fed back to the steering group. The scheme currently includes F8, F9 and VWF gene analysis.

7. Participation in other groups

A representative from the network attends the:

- Clinical and Scientific Advisory Group UK Genetics Testing Network (see item 1 above)
- The Haemophilia Alliance meeting, attended by Bim Theophilus on behalf of the GLN, has now been replaced by the Clinical Reference Group for Haemophilia. No role for a scientific or laboratory member has been created in the new group.
- Various members sit on relevant UKHCDO working parties - Two members of the network sit on the UKHCDO GWP and have had input to the draft updated 'Clinical Genetic Services for Haemophilia' document, now submitted.

Dr Steve Keeney
Chairman, UKHCDO Genetic Laboratory Network
September 2014

14. Triennial Audit

Membership

David Perry Chairman
Helen Brown
Gerry Dolan
Charles Hay
Marian Hill
Catherine Harrison [to replace Chris Harrington]
Tim Nokes
Vicky Vidler

Left this year

Jonathan Wilde
Chris Harrington
Georgie Robinson [Haemophilia Society]

The number of times it has met (even by conference call) in the last year

Zero: A planned meeting in May 2014 was cancelled as it proved impossible to coordinate a time that was convenient to the majority of members. The Audit group will plan to meet in early 2015.

Remit

The remit of the Audit working party is to plan, coordinate and review the triennial audit programme.

Activities

The last audit was undertaken in 2012-13 and included, in addition to the audit of Comprehensive Care Centres (CCC), a pilot study of Haemophilia Centres with which each CCC interacted. In addition the Audit merged the historically separate genetics audit programme.

The on-going activities of the Audit WP will include:

1. To discuss integration with the CRG for Haemophilia and other Bleeding Disorders.
2. A more efficient audit of the regional Haemophilia Centres [and non-Haemophilia Centres] with which each CCC interacts.
3. The generation of a final Audit report for the last round of triennial audits including Best Practise and how this might be disseminated.
4. Recruiting additional members to represent the Haemophilia Society and the Commissioners.

Dr David J Perry
November 2014

15. UK Haemophilia Data Managers Forum Group

Membership

The group currently has a membership of 89

Mission

The United Kingdom Haemophilia Data Managers Forum Group is a national group which strives to share information, whilst encouraging and supporting personnel involved in the collation and analysis of Haemophilia Data throughout the UK.

The UK Haemophilia Data Managers Forum Group has continued to support this mission statement throughout this year. Late 2013 saw a change in Office Bearers of this Group as voted by its members, Nancy Brodie returned as Chair and Lynne Dewhurst as Secretary.

Meetings

A meeting held in November 2013 identified a need to review and update our Terms of Reference within which the above mission statement is held and to which as a Group we continually strive to work. These updates were made and accepted in agreement with members of the Group and include:

- The term for elected Office Bearers simulates that adopted recently by UKHCDO. This has also been endorsed by UKHCDO via the UKHCDO Data Management Working Party.
- All finances shall be managed through UKHCDO Ltd in order to maintain transparency of the Group.
- All members should show mutual respect without bias to other members at all times.

Three meetings of this Group have been held over the past year. Consistent topics include but are not limited to:

- Updates on all current systems (NHD, Haemtrack and HCIS)
- Updates from relevant working parties
- Data Protection
- Home Delivery
- Haemnet

Attendance at these meetings has been very good with an average of 20+ members in attendance at each. This is especially encouraging in a year which has been yet again, very busy for data managers, not least with the recent tendering process for rFVIII concentrates and the requirements of information prior to and after the award of contract on 1st April.

Many interesting and pertinent presentations have been given at these meetings. Professor C Hay took time to give presentations at 2 meetings, discussing the NHD and updating the Group on some important work undertaken from this system. He also gave an update on the highlights from the UKHCDO Bleeding Disorder Statistics for 2012/13. Professor Hay was

very cognisant that little of this work could be produced without the input and hard work of the Haemophilia Data Managers.

Another informative presentation of note was given to the Group by Alison Greenwood from the Commercial Medicines Unit (CMU) updating on the national tender for clotting factor concentrates. This gave everyone a better understanding of why it was important to supply accurate figures in a timely manner.

In the year ahead this Group will continue to be all inclusive and support new and old members at all times. An education need has been identified and it is planned to initiate and take forward a grassroots training programme which will be for existing and new data managers; educating on all systems (NHD, Haemtrack and HCIS), as well as initiating a much needed mentoring programme for new Data Managers. This should create a better understanding of the role of the Data Manager on the relevance and necessity for accurate technical capability of the systems and data entry but equally important, create a better understanding of Haemophilia which, combining these areas, should assist in facilitating even better data collation and information transfer.

As always, the Group would like to extend thanks to sponsors whose funding has enabled the meetings to take place and Sarah Rooney for her very efficient organisation of these meetings on our behalf. Also, thanks to Dr Dolan and UKHCDO who continue to support this group (particularly Prof C Hay for the time he has spent presenting at our meetings), the Data Management Working Party for continued endorsement and guidance and finally Dr R Liesner for ensuring the Group complies with proper financial procedures.

Nancy Brodie – Chair
Lynne Dewhurst – Secretary
UK Haemophilia Data Managers Forum
September 2014

16. Haemophilia Nurses Association

Committee

Elected 2012

Kate Khair	Chair
Anna Farrell	Vice-chair
Emma Franklin	Secretary
Cathy Mumby	Treasurer
Martin Bedford	
Helen Greensmith	
Jayne Keaney	
Anica Phillott	

The Haemophilia Nursing Association (HNA) is the specialist group representing nurses involved in the care of people with bleeding disorders in the UK. The HNA held a very successful AGM in February 2014, at which the first HNA research bursary winners were announced. Two members are now undertaking short projects investigating why patients participate in CTIMPs when they already have access to recombinant products and the patient/parent benefits of participating in long acting factor trials.

The HNA continues to use Haemnet (www.haemnet.com) as our main means of communication and as a platform for national research. SO-FIT, the first ever nursing and physiotherapy collaborative research project, across 16 haemophilia centres which started in 2014 has recruited nearly 100 young people with haemophilia to assess self-reported functional assessment and quality of life vs. physiotherapy joint health care assessment

Haemnet has supported individual nurses with research grant applications and execution of research projects including development of an educational film scripted with patients that is to be launched at EHC in October 2014. We are also working with an academic GP group at the University of Birmingham to examine the diagnostic pathways of women with bleeding disorders. We are working with the University to deliver a CPD-based training course for GPs in November 2104 on bleeding disorders in women.

We heard from nurses and allied health professionals that they learnt from discussing case studies to enhance patient care though best practice, but that publishing in the main stream journals was becoming more difficult especially for individual cases or small series. Conversely publishing long qualitative research was also complicated due to limits on word numbers and so on. This prompted us to develop and launch *The Journal of Haemophilia Practice* (JHP), an international, on-line journal freely available at www.haemjournal.com. The third edition is about to be published. We have published case studies, reviews, qualitative research, outcomes studies and opinion pieces, where leaders in the field of haemophilia give opinions of past, present and future haemophilia care. Although it developed as a nurse initiative, this journal is not limited to nurses/allied health providers; every edition so far has had a medical author paper published too!

Three members will step down from the HNA committee this year, and the new committee will be announced at our AGM in March 2015. We continue to encourage applications for a growing number of research bursaries and to encourage nurses to publish their work.

Kate Khair
Chair, Haemophilia Nurses Association
September 2014

17. Haemophilia Chartered Physiotherapists Association

The HCPA consists of chartered specialist physiotherapists with an interest in the physiotherapy management of people with Haemophilia and other bleeding disorders. This group was initially established to provide support and networking opportunities for individuals in the field and to help others new to the specialty. Over the years it has developed to become an exciting forum for new ideas and ways of working, enabling research and promotion of physiotherapy as key component in the MDT management of Haemophilia.

HCPA Education/ Continuing Professional Development

The annual Physiotherapy educational meeting and HCPA AGM, funded by an educational grant from Bayer Healthcare, were held in Birmingham in February 2014. In its eighth year, it continues to be a full and productive programme, with upwards of 40 physios attending the 2014 meeting.

In keeping with the aim of education and promoting clinical excellence, this year's meeting focused on a 'Back to Basics' education programme. The emphasis was a review of haemostasis and laboratory investigations, and the day-to-day clinical applications of such. The topics generated questions and deliberations around how this may affect what we do as therapists, as well as thought provoking issues concerning exercise, sport, injury and the future with long acting products.

As well as the lectures, Dr David Stephenson and Steven Classey facilitated a practical review of real time Ultrasound (USS) for joint assessment. This has been prompted by the ongoing discussions in general Haemophilia care about how practicable the use of ultrasound may be, as well as concerns from some physios about training, time to assess and implications for scope of practice. In the next few years it is anticipated that some therapists will initiate pilot projects in their centres into the use of ultrasound, and we await these results with interest.

A new addition to the meeting format this year was to include a 'free paper' session. This was primarily to encourage and support individuals to write an abstract, submit it for review and be then offered the opportunity to present their work to the group. The presentations were judged independently and the winner received a CPD bursary award (to attend an MSK/Haemophilia related course/conference). This year's winner was PhD student Luke Suckling who used the award to attend the WFH world conference in Melbourne. Out of the 5 presentations, 2 have gone on to be accepted for publication in Haemophilia journal. The session proved to be resounding success and the same format will be planned for next year's meeting – with the aim of encouraging abstracts to be submitted for the WFH MSK conference in Belfast.

Paul McLaughlin
Chairman, Haemophilia Chartered Physiotherapist's Association
September 2014

18. BCSH Haemostasis and Thrombosis Task Force

Membership

Dr D Keeling	Chairman
Dr H Watson	Secretary
Dr I Jennings	
Dr E Gray	NIBSC representative
Dr E Chalmers	
Prof M Laffan	
Dr A Mumford	
Dr C Tait	BSHT representative
Prof I Walker	NEQAS Representative
Prof M Makris	UKHCDO Representative - Up to April 2013
Dr Keith Gomez	UKHCDO Representative - Since May 2013

UKHCDO guidelines published in association with the BCSH

Laffan M, Lester W, O'Donnell JS, Will A, Tait RC, Goodeve A, Millar CM, Keeling D. The diagnosis and management of von Willebrand disease: a guideline from the UK Haemophilia Centre Doctors Organisation. British Journal of Haematology 2014 (in press)

Collins PW et al. Diagnosis and treatment of factor VIII and IX inhibitors in congenital haemophilia. British Journal of Haematology 2013; 160:153-170

Collins PW et al. Diagnosis and management of acquired coagulation inhibitors: a guideline from UKHCDO. British Journal of Haematology 2013; 162: 758-773

BCSH guidelines in development

Clinical genetics services for haemophilia

The treatment and prevention of bleeding in heritable platelet disorders

Patient based point of care testing for patients on vitamin K antagonists

Cancer and thrombosis

UKHCDO relationship with BCSH Task Force

There is a well-defined pathway for guidelines of UKHCDO working parties to be published in collaboration with the BCSH. There are significant advantages in getting guidelines through the BCSH, not least of which is publication in a Wiley Blackwell journal – usually British Journal of Haematology or Haemophilia.

If any working party is intending to publish a guideline, they should contact Keith Gomez (the UKHCDO representative on the Task Force) at an early stage to get the production of the guideline approved under the BSCH methodology.

Professor Mike Makris
July 2014

19. Haemophilia Society

2013/14 was very much a year of change for the Haemophilia Society with the departure and replacement of the CEO and the reorganisation of the staff structure to give effective support for implementation of the Society's strategy. We believe that our necessary investment of time in these internal matters has put the charity in a much stronger position to meet our members' needs going forward.

Chris James resigned from his post as Chief Executive in July 2013; the post was filled for six months by an interim CEO, Rachel Youngman. During her period as CEO, the Board finalised the charity's new Vision and Mission statements and agreed the review of the Strategy and of staff requirements, which Rachel developed. This led to a restructuring and to the departure of many of the existing staff.

After a formal recruitment process, Liz Carroll was appointed as the new Chief Executive in November 2013 and joined in January 2014. Liz had previously worked in senior roles in a major cancer patients' charity after starting her career as a nurse; this included experience in haematology. She gradually recruited staff to fill the new posts and began work on delivering the new strategy. The immediate priorities were to stabilise the Society after all the change and to ensure it was effective, efficient and sustainable for the future.

A particular issue has been funding. Our £100,000 annual grant from the Department of Health ended in March 2013 and we also saw significant reductions in other income, particularly grants from pharmaceutical companies. As result, we needed to make major savings and to develop new sources of income. The new staffing is at a lower cost and we are working to reduce premises costs by finding cheaper accommodation for when our lease ends in December 2014.

The updated Vision and Mission statement allowed us to improve our communication with members and other stakeholders and to improve the alignment of our activities with our Mission. For example, we reinforced our commitment to working for all bleeding disorders and we are improving our focus on measuring outcomes from activities so as to be able to prove value for money to funders and members.

Vision

Wellbeing for everyone with a bleeding disorder.

Mission

For all those affected by bleeding disorders, to:

- Provide information and services;
- Build community and mutual support;
- Influence government health and welfare policies, including advocating for those impacted by contaminated blood;
- Involve people in making decisions about their own care.

The prolonged period of change has had an impact on our ability to deliver as much as we would hope during the year, but we were nevertheless able to continue services and to initiate new activities. We held our first event for women with bleeding disorders and ran improved weekend events for new families. We put considerable effort into rebuilding our website to make it accessible and user friendly and to provide a more powerful resource for those seeking information; this work is ongoing at the year end. We also made progress in strengthening our structure of Local Groups.

As well as developing our website, we have continued to provide information and support via the phone, email and via social media. Activity on our three Facebook pages and on Twitter has significantly increased with these becoming a major source of information and peer support for the community. We also reviewed several of our information publications. We continued to get positive feedback from members on our membership magazine, HQ, and we have worked to extend the range of articles included. We also agreed to develop our first public awareness campaign for women with bleeding disorders to be delivered in June 2014.

We held successful children's activity weekends and ran a very well evaluated pilot service for families with a newly diagnosed child. The service ran over a residential weekend where parents could hear from medical and nursing experts about bleeding disorders, treatments and developments, as well as having facilitated small group sessions to discuss and share thoughts and feelings about the psychosocial aspects of coping with a child with a bleeding disorder. The positive feedback from this pilot will be written up and presented and will inform the planning of future weekends for newly diagnosed families.

We continue to grow and develop our Local Groups, with several new groups opening and long standing groups becoming reinvigorated. Several new groups have already run activities, supported families and raised funds for the charity. Other groups continue to focus on campaigning on contaminated blood issues. It remains a strategic goal to have active Local Groups throughout the UK.

Following the restructure of NHS England, the Department of Health (DH) has lost all its direct authority over the NHS. This has complicated our advocacy, as instead of having one central contact we have to network widely with and within the four Nations. The meetings between the DH and the Haemophilia Alliance have stopped and we have been looking at how we can best work with the different structures within the NHS

We have developed positive working relationships with NHS England and with the Specialist Clinical Commissioning Group. For example, we have representation on the Clinical Reference Group which sets standards for care and we were involved in the national tender for Factor 8. Through our trustee, Lynne Kelly, we worked closely with NHS Wales but the need to engage with four devolved health services continues to put a strain on the reduced resources of the Society and we are considering how we manage this challenge, particularly in Northern Ireland and Scotland where we are looking to find local people who could assist. We continue to cooperate across many areas with the UK Haemophilia Centre Doctors' Association (UKHCDO) and with the Haemophilia Nurses Association (HNA). We also maintain relationships with the DH.

During the year we put considerable effort into finding funding and academic support for a "Burden of Illness" study on severe haemophilia. The background is that the National Institute for Health and Care Excellence (NICE) decides which treatments the NHS will fund

on an analysis of costs versus directly observable benefits to health. However, for a chronic condition such as haemophilia, there can be wider benefits to people who would otherwise suffer additional problems such as missing work or school or necessitating carers to miss work to look after them. A "Burden of Illness" study creates a more comprehensive economic analysis incorporating such factors, and in principle could justify new treatments which a standard NICE analysis would reject as too expensive. At the March year end we had achieved the appropriate promises of funding but were still working on reaching agreement with an academic partner which would carry out the actual research. We are hopeful that we will finalise our negotiations and be able to go ahead in the third quarter of 2014.

We supported the work of the Penrose Enquiry and await its delayed publication. In Westminster, the Society acts as the Secretary to the All Party Parliamentary Group on Haemophilia and Contaminate Blood (APPG), and we have been working with the APPG to set up an inquiry through YouGov into the experiences of the beneficiaries of the Trusts and Foundations set up to support those affected by contaminated blood. We have also been supporting the important initiative led by Alistair Burt MP to bring full and final compensation following the contaminated blood tragedy.

We have begun initial planning for the 2018 Congress of the World Federation of Haemophilia in Glasgow, which The Haemophilia Society will host. This is a major international conference held every 2 years which is expected to attract over 6,000 clinicians, researchers, people affected by bleeding disorders, and other interested parties. The more focussed planning will begin in 2016 and we will need to attract capable volunteers to lead workstreams and to help on the ground. We will work with the UKHCDO and HNA in our planning for the event. We have also been involved in planning the Conference of the European Haemophilia Consortium which we will host in Belfast in October 2014.

Through our work, we encourage and advocate for everyone affected by a bleeding disorder to lead fulfilling lives, make informed choices and, through the Society and otherwise, to support and inspire others. We do this by providing accessible knowledge and support so that people can make their own informed decisions. We work to influence policy and practice so that the management, care and treatment for bleeding disorders is consistent, effective and accessible; and we enable the voices of those with bleeding disorders to be heard through our membership in NHS and other forums, and in the wider community.

We look forward to continuing and expanding this work, and to improving our communication with our members and stakeholders so that we can encourage greater participation in the Society's activities.

Liz Carroll
Chief Executive, The Haemophilia Society
August 2014

20. The Macfarlane Trust

During 2013 and early 2014, the Trust experienced a number of changes of personnel – both Trustees and staff. Two long-standing Trustees, Elizabeth Boyd and Russell Mishcon, retired when their periods of office expired after more than 13 years and 7 years respectively. Kate Evans, a Trustee appointed on the recommendation of the Haemophilia Society, also resigned due to work and personal commitments. Three new Trustees were appointed: Jamie O'Hara was appointed by the Haemophilia Society to succeed Kate Evans, and the Trust also appointed Paul Biddle and Alasdair Murray, who bring experience in finance and policy to the board.

Following a Board-approved restructuring, Roz Riley, who had worked for the Trust since 2000, latterly as Support Services Manager, left in October 2013. Linda Haigh, Finance Manager, also left in January 2014 after 10 years in the organisation. The Trust has subsequently been pleased to welcome Victoria Prouse and Joyce Materego as the new Director of Operations and Director of Finance respectively.

In 2013/14 the majority of the Trust's annual budget continued to be used to make regular discretionary top-up payments to primary beneficiaries and regular payments to widows. The Board also agreed a cost of living increase to regular payments to primary beneficiaries of 2.7% for 2014/15. A winter fuel payment was made to primary beneficiary households in 2013/14, and a similar payment will be made in 2014/15.

In July 2013 the Board decided to commit funds from its reserves to support beneficiaries by funding improvements to their properties which were related to health and mobility needs. After inviting applications, the Trust allocated funds to 110 beneficiaries, totalling £811,000. This was a one-off exercise; we do not foresee monies being available in the future to do so again. We are confident that we have been able to make a significant positive impact on the lives of those beneficiaries who were awarded grants through this exercise. Many have expressed their appreciation through letters and emails to the Chief Executive and her team.

The Trust had partial success in 2013 regarding its negotiations with the Department of Health (DH) over its financial allocation for 2014/15. The Trust submitted a strong case for increasing its allocation from £2.2 million for 2013/14 to £3.2 million for 2014/15. This was always presenting a major challenge, given the state of the economy and general reductions in public spending. The DH agreed a figure which is, effectively, the same as the previous year. Bearing in mind the reductions being made elsewhere in public spending budgets, this was the best outcome we could have expected in the circumstances. The Board has agreed to continue supplementing the annual DH allocation from the reserve funds; this means that in 2014/15 we will be operating at a similar level to last year. However, the level of reserve funds is now reducing year on year and we are already having, reluctantly, to be discerning when deciding which grants we can fund. Unless the DH and government are able to increase the annual allocation to us, before long we will have no alternative but to review the feasibility of our current funding policies. It cannot be assumed that they will increase our budget. The Trust will, nevertheless, continue to press strongly for an increase in annual funding.

The Board is encouraged that the level of interest and awareness of national politicians has risen tremendously over the last year or so. This is in no small way attributable to a number of beneficiaries lobbying their MPs. There is, sometimes, a misunderstanding as to the responsibilities of MFT. These are confined to allocating regular funding to the beneficiary community and negotiating the best possible financial allocation from the DH to do so. Our responsibilities do not extend to lobbying for the wider interests and needs of the beneficiary community, even if sometimes we would like to do so. This is for others to do and the efforts of the beneficiary community, as recognised above, are invaluable in that respect.

Jan Barlow
Chief Executive, Macfarlane Trust
September 2014

21. Royal College of Physicians Clinical Effectiveness Forum

The Royal College of Physicians clinical Effectiveness forum meets semi-annually. During the last year, the main areas of discussion were around the following topics:

- The current status of the Future Hospital Programme
- Review of the national quality agenda, individual clinical outcome publication and open data & data sharing
- The role of guideline development and quality improvement
- The role of Health Quality Improvement Programme and quality improvement
- Evidence and quality improvement and the global concept of setting higher standards.
- Rationale and policy background to shared decision making and support for self-management as an approach to partnership working with patients and carers
- The key elements of shared decision making are patients and clinicians working together to select tests, treatments, management or support packages based on clinical evidence and patient preference
- Patients bring experience, personal values, knowledge and preferences, whereas clinicians bring best evidence presented clearly and skilfully
- Improved outcomes are the result of interaction between proactive prepared health team and informed activated patient
- A care plan is at the heart of a partnership approach to care and a central part of effective care management. The process of agreeing a care plan offers people active involvement in deciding, agreeing and owning how their condition is to be managed'
- The hours spent with healthcare professionals is a fraction of the time that patients with long term conditions spend in self-management
- Shared Decision Making (SDM) and Support for Self- Management (SSM) refer to a set of attitudes, roles, and skills, supported by tools and organisational systems, which put patients and carers into a full partnership relationship with clinicians in all clinical interactions. It was recognised that that patients and carers expect this to be the usual / default experience in their clinical interactions with Physicians and will work towards making this part of normal practice
- There was discussion that this practice and skills set needs to be woven into physician training and assessment, both undergraduate and post graduate as well as Consultant Physician training

Dr Bella Madan
September 2014