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Bleeding Disorder Statistics for April 2014 to March 2015

A report from the National Haemophilia Database

HAEMOPHILIA A

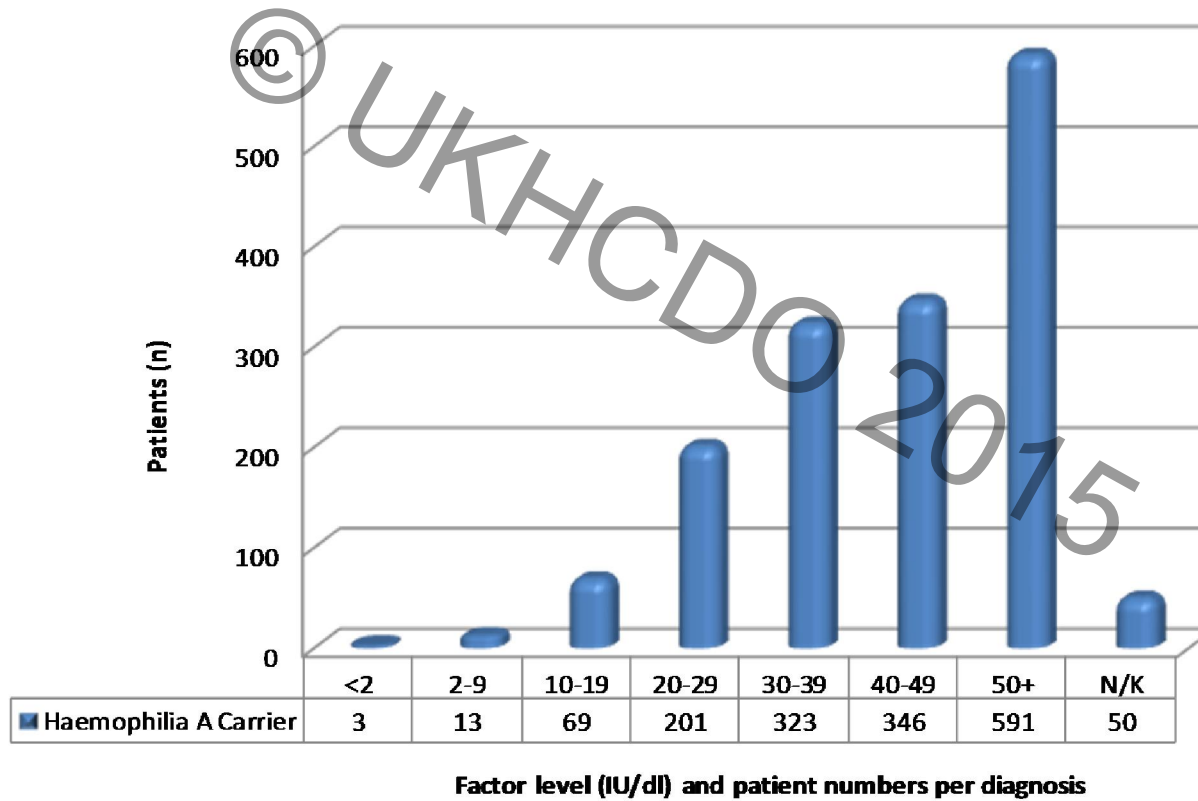
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Table 1 Patients with congenital Haemophilia A registered and treated April 2014 - March 2015

| Haemophilia A | Age Range | Factor VIII level (iu/dl) | | | | |
|---|--------------|---------------------------|------------|--------------|-----------|--------------|
| | | ≤ 1 | >1 & <5 | ≥ 5 & <50 | Unknown | Total |
| In Register (including low-level carriers) | <18 years | 702 | 145 | 773 | 7 | 1,627 |
| | ≥18 years | 1,333 | 392 | 3,413 | 47 | 5,185 |
| | Total | 2,035 | 537 | 4,186 | 54 | 6,812 |
| New Registrations * (including low-level carriers) | <18 years | 48 | 11 | 85 | 1 | 145 |
| | ≥18 years | 15 | 6 | 160 | 6 | 187 |
| | Total | 63 | 17 | 245 | 7 | 332 |
| Treated in year** (including low-level carriers) | <18 years | 681 | 111 | 205 | - | 997 |
| | ≥18 years | 1,259 | 229 | 715 | 1 | 2,204 |
| | Total | 1,940 | 340 | 920 | 1 | 3,201 |

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

Figure 1 Carriers of Haemophilia A currently registered, by baseline factor VIII level



Total number: 1596

Table 2 New Registrations of Haemophilia A between April 2014 & March 2015, by age at mid-year and severity

| Coagulation Defect | Age (years) | Number of Patients (Factor VIII level (iu/dl)) | | | |
|--------------------|-------------|--|-----------|------------|------------|
| | | ≤1 | >1 & <5 | ≥5 | Total |
| Haemophilia A | 0 : 4 | 41 | 10 | 30 | 81 |
| | 5 : 9 | 4 | 0 | 13 | 17 |
| | 10 : 19 | 2 | 1 | 12 | 15 |
| | 20 : 29 | 6 | 1 | 14 | 21 |
| | 30 : 39 | 6 | 2 | 9 | 17 |
| | 40 : 49 | 2 | 1 | 11 | 14 |
| | 50 : 59 | 0 | 2 | 10 | 12 |
| | 60 : 69 | 0 | 0 | 11 | 11 |
| | 70 + | 0 | 0 | 5 | 5 |
| Total | | 61 | 17 | 115 | 193 |

Figure 2 New Registrations of patients with Severe Haemophilia A over 5 years old at the time of registration – 2008/9-2014/15

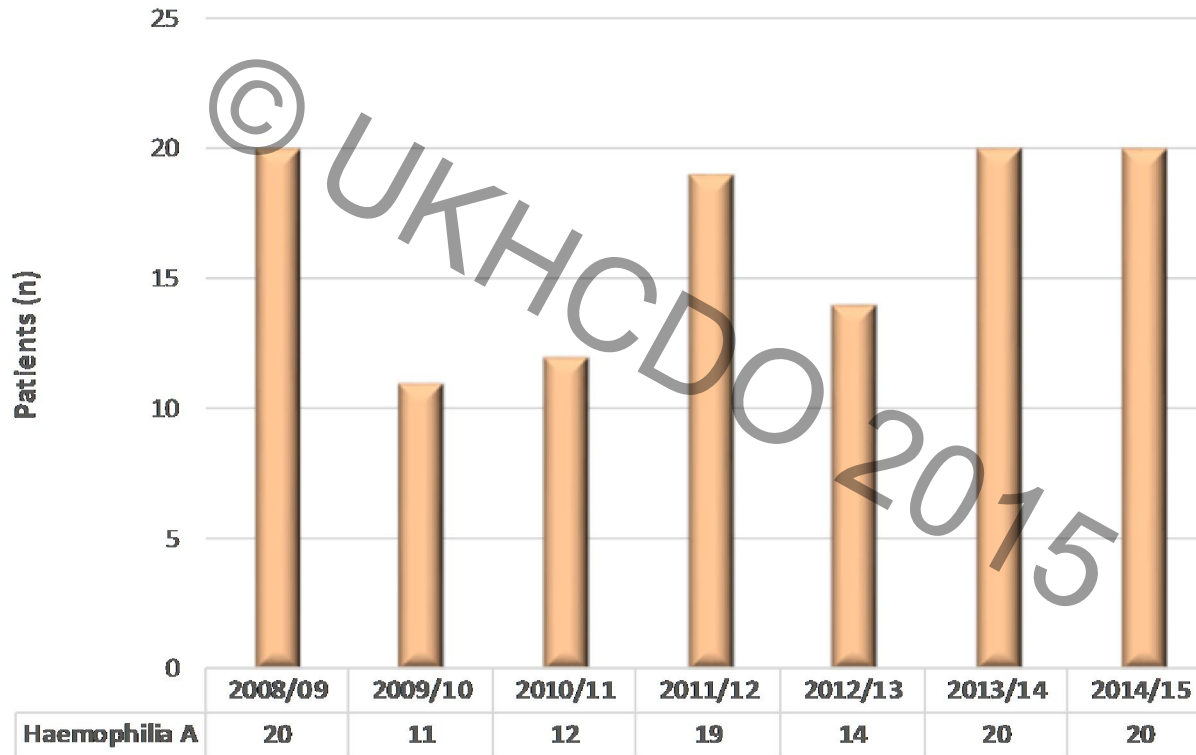
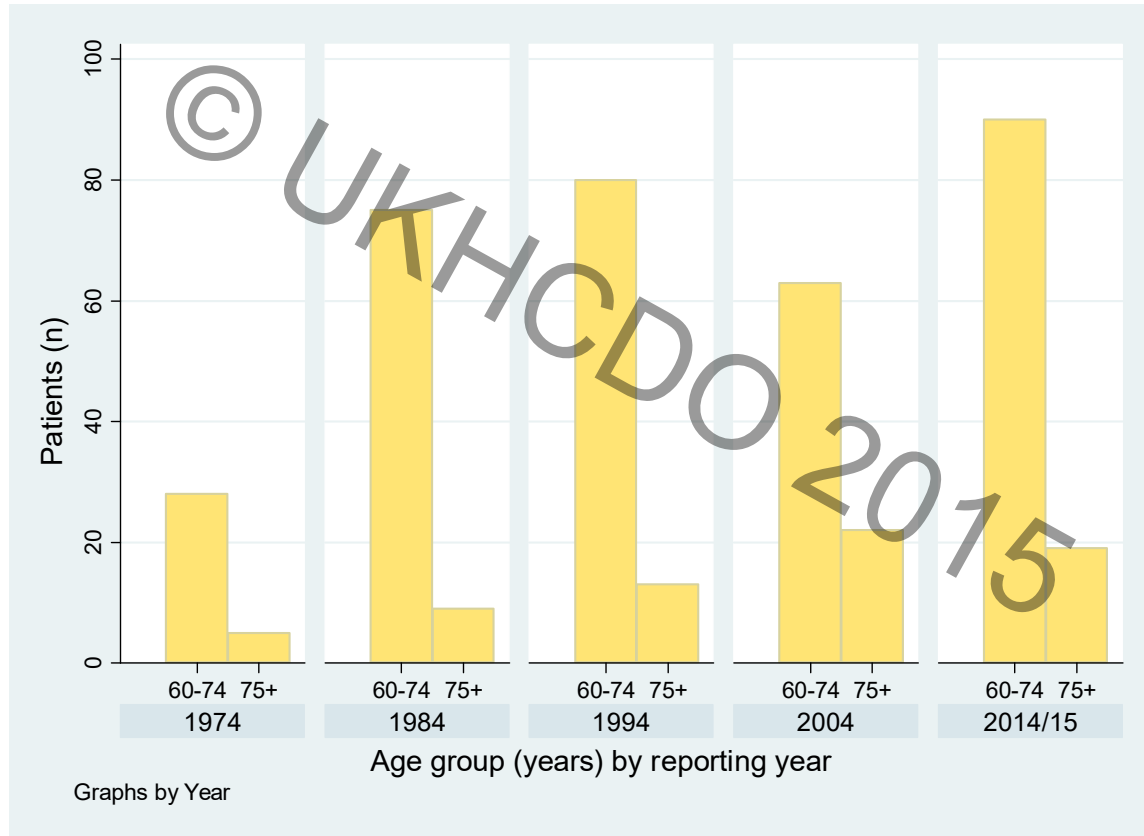


Figure 3 Trend in numbers of Severe Haemophilia A patients aged 60 years and above, 1974 – 2014/15 (including HIV +ve pts)



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Figure 4 Trend in numbers of non-Severe Haemophilia A patients aged 60 years and above, 1974 – 2014/15 (including HIV +ve pts)

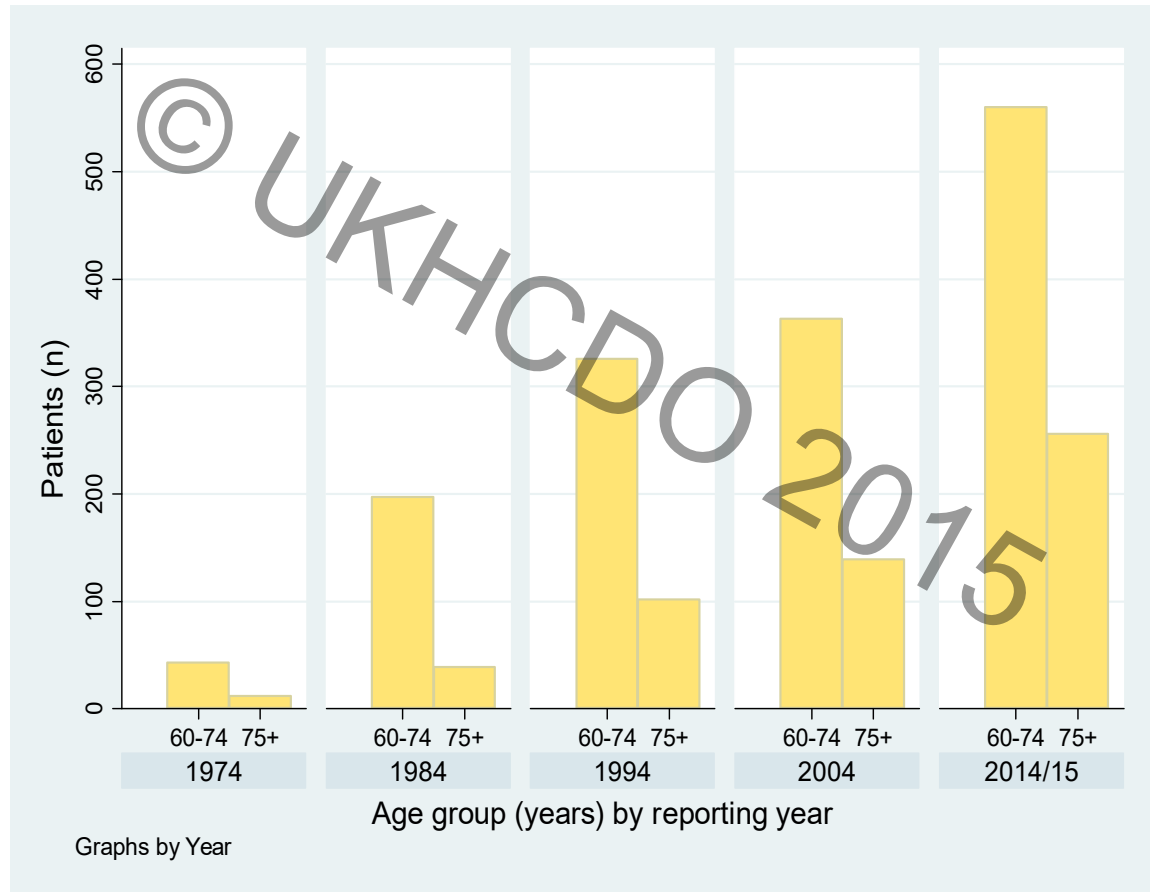
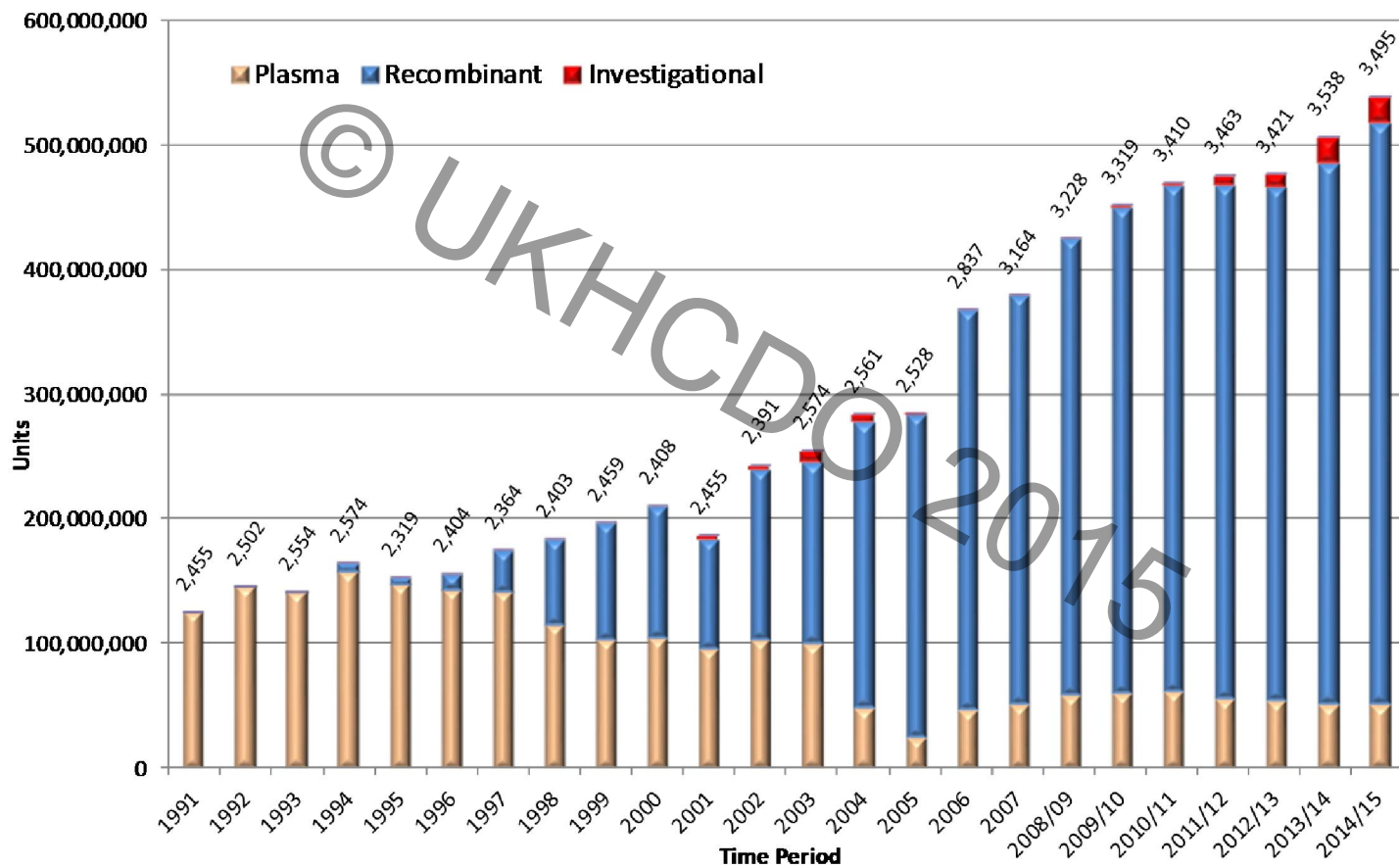


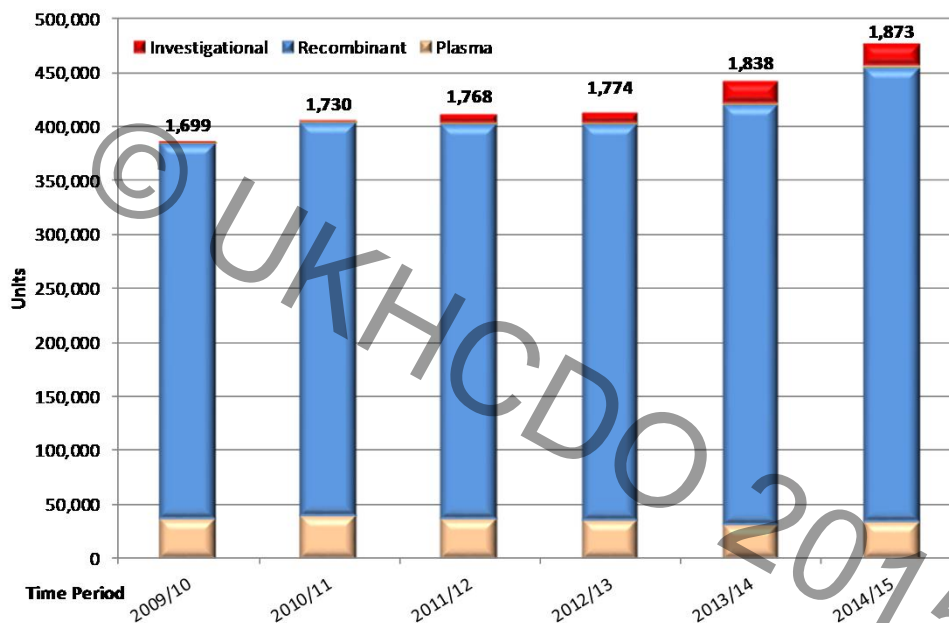
Figure 5 Factor VIII units used by UK Haemophilia Centres 1991-2014/15 all diagnoses



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

Figure 6 Factor VIII units used by UK Haemophilia Centres to treat Severe Haemophilia A – 2009/10 - 2014/15



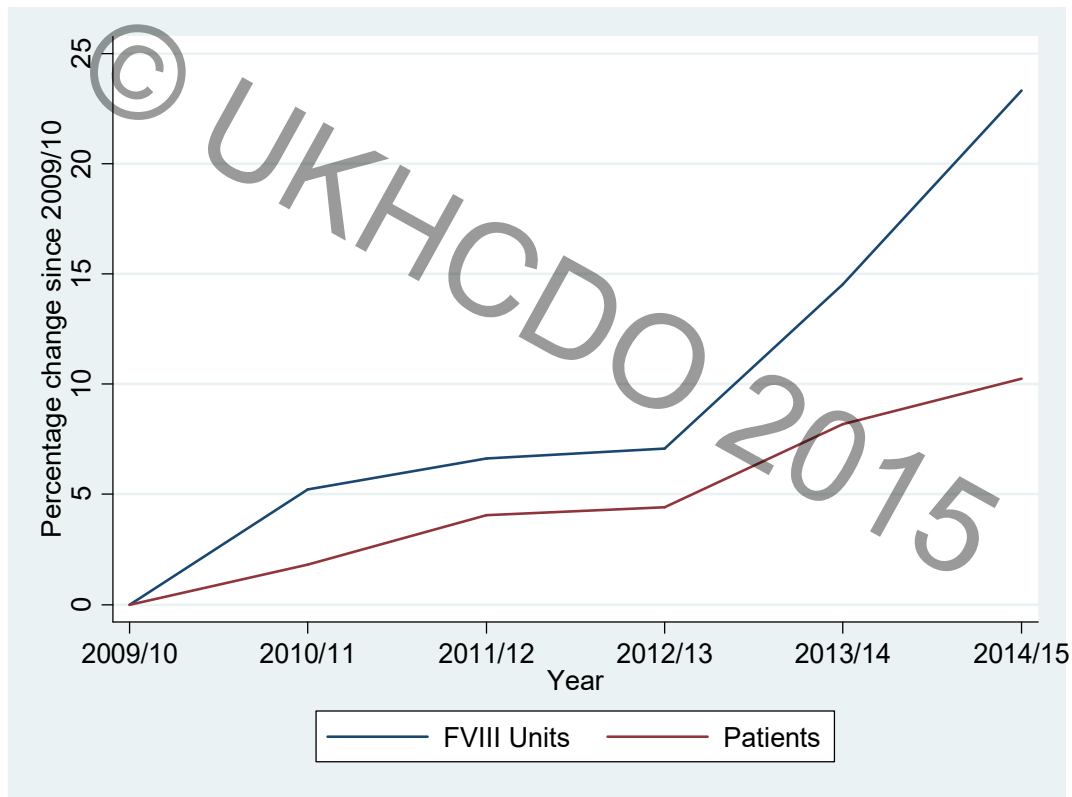
| Year | Plasma | | Recombinant (excluding investigational) | | Investigational rFVIII | | Total | | Patients | |
|---------|----------------|----------------------------|---|----------------------------|------------------------|----------------------------|----------------|----------------------------|----------|----------------------------|
| | IU (thousands) | % difference since 2009/10 | IU (thousands) | % difference since 2009/10 | IU (thousands) | % difference since 2009/10 | IU (thousands) | % difference since 2009/10 | n | % difference since 2009/10 |
| 2009/10 | 36,839 | 100.00% | 346,670 | 100.00% | 550 | 100.00% | 384,059 | 100.00% | 1,699 | 100.00% |
| 2010/11 | 39,346 | 106.81% | 363,507 | 104.86% | 1,224 | 222.77% | 404,078 | 105.21% | 1,730 | 101.82% |
| 2011/12 | 36,130 | 98.08% | 365,487 | 105.43% | 7,947 | 1445.90% | 409,564 | 106.64% | 1,768 | 104.06% |
| 2012/13 | 34,928 | 94.81% | 367,239 | 105.93% | 9,060 | 1648.34% | 411,227 | 107.07% | 1,774 | 104.41% |
| 2013/14 | 31,556 | 85.66% | 387,581 | 111.80% | 20,774 | 3779.65% | 439,911 | 114.54% | 1,838 | 108.18% |
| 2014/15 | 33,718 | 91.53% | 420,308 | 121.24% | 19,676 | 3579.94% | 473,702 | 123.34% | 1,873 | 110.24% |

Table 3 Treatment intensity of patients with Severe Haemophilia A – 2008/09 - 2014/15

| Treatment Period | FVIII Units | | Patients (n) | | Treatment Intensity (Units/Pt) | | Change in treatment intensity since 2008/09 (%) | |
|------------------|-------------|-------------|--------------|-----------|--------------------------------|-----------|---|-----------|
| | <18 Years | ≥18 years | <18 Years | ≥18 years | <18 Years | ≥18 years | <18 Years | ≥18 years |
| 2008/09 | 129,225,490 | 232,806,504 | 672 | 1,013 | 192,300 | 229,819 | 100.00 | 100.00 |
| 2009/10 | 130,103,228 | 253,073,724 | 664 | 1,035 | 195,939 | 244,516 | 101.89 | 106.39 |
| 2010/11 | 137,388,220 | 265,980,866 | 658 | 1,072 | 208,797 | 248,116 | 108.58 | 107.96 |
| 2011/12 | 134,306,611 | 274,447,846 | 650 | 1,118 | 206,626 | 245,481 | 107.45 | 106.82 |
| 2012/13 | 132,644,972 | 277,662,979 | 657 | 1,117 | 201,895 | 248,579 | 104.99 | 108.16 |
| 2013/14 | 139,607,617 | 299,352,773 | 677 | 1,161 | 206,215 | 257,840 | 107.24 | 112.19 |
| 2014/15 | 150,486,503 | 319,637,610 | 674 | 1,199 | 223,274 | 266,587 | 116.11 | 116.00 |

Treatment includes Plasma, Recombinant and Investigational factor VIII

Figure 7 Percentage change in total FVIII units and number of patients with Severe Haemophilia A since 2009/10



Figures 8a & 8b

Patients with Severe / Moderate Haemophilia A treated with FVIII by UK Haemophilia Centres – 1990 - 2014/15

Figure 8a

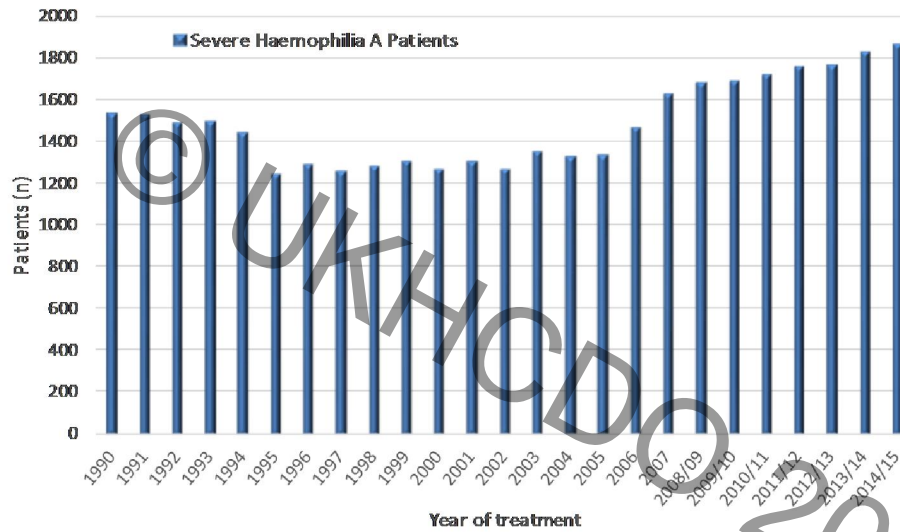
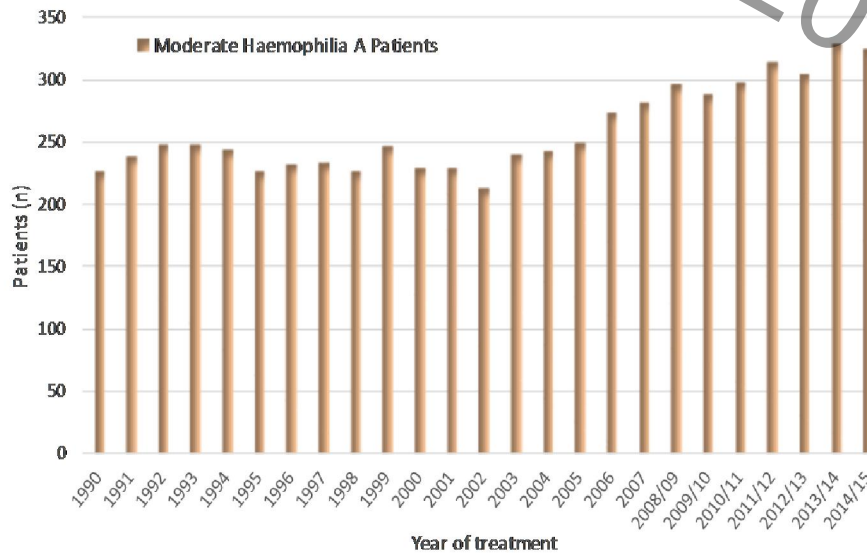


Figure 8b



Data table for Figures 8a & 8b

| Treatment Year | Severe Haemophilia A Patients | | Moderate Haemophilia A Patients | |
|----------------|-------------------------------|-------------------------|---------------------------------|-------------------------|
| | n | % difference since 1990 | n | % difference since 1990 |
| 1990 | 1546 | 100.0 | 227 | 100.0 |
| 1991 | 1537 | 99.4 | 238 | 104.8 |
| 1992 | 1493 | 96.6 | 248 | 109.3 |
| 1993 | 1507 | 97.5 | 248 | 109.3 |
| 1994 | 1453 | 94.0 | 244 | 107.5 |
| 1995 | 1252 | 81.0 | 226 | 99.6 |
| 1996 | 1296 | 83.8 | 232 | 102.2 |
| 1997 | 1268 | 82.0 | 233 | 102.6 |
| 1998 | 1289 | 83.4 | 226 | 99.6 |
| 1999 | 1310 | 84.7 | 246 | 108.4 |
| 2000 | 1278 | 82.7 | 229 | 100.9 |
| 2001 | 1316 | 85.1 | 229 | 100.9 |
| 2002 | 1276 | 82.5 | 213 | 93.8 |
| 2003 | 1356 | 87.7 | 240 | 105.7 |
| 2004 | 1332 | 86.2 | 243 | 107.0 |
| 2005 | 1343 | 86.9 | 249 | 109.7 |
| 2006 | 1474 | 95.3 | 274 | 120.7 |
| 2007 | 1638 | 106.0 | 282 | 124.2 |
| 2008/09 | 1685 | 109.0 | 296 | 130.4 |
| 2009/10 | 1699 | 109.9 | 288 | 126.9 |
| 2010/11 | 1730 | 111.9 | 297 | 130.8 |
| 2011/12 | 1768 | 114.4 | 314 | 138.3 |
| 2012/13 | 1774 | 114.7 | 304 | 133.9 |
| 2013/14 | 1838 | 118.9 | 329 | 144.9 |
| 2014/15 | 1873 | 121.2 | 325 | 143.2 |

Figure 9 Total Number of Severe Haemophilia A patients treated by commissioning region

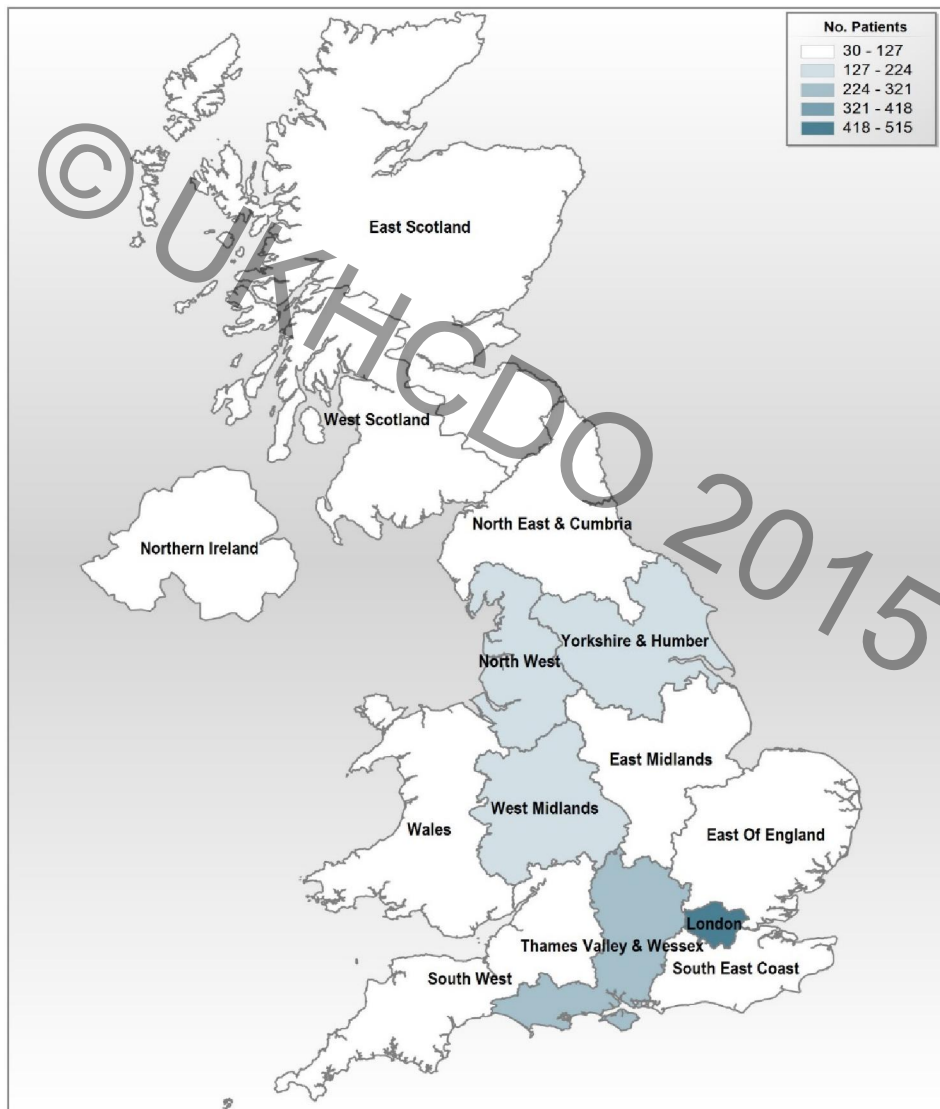


Figure 10 Total Factor VIII units issued to patients with Severe Haemophilia A (including Inhibitor) by commissioning region

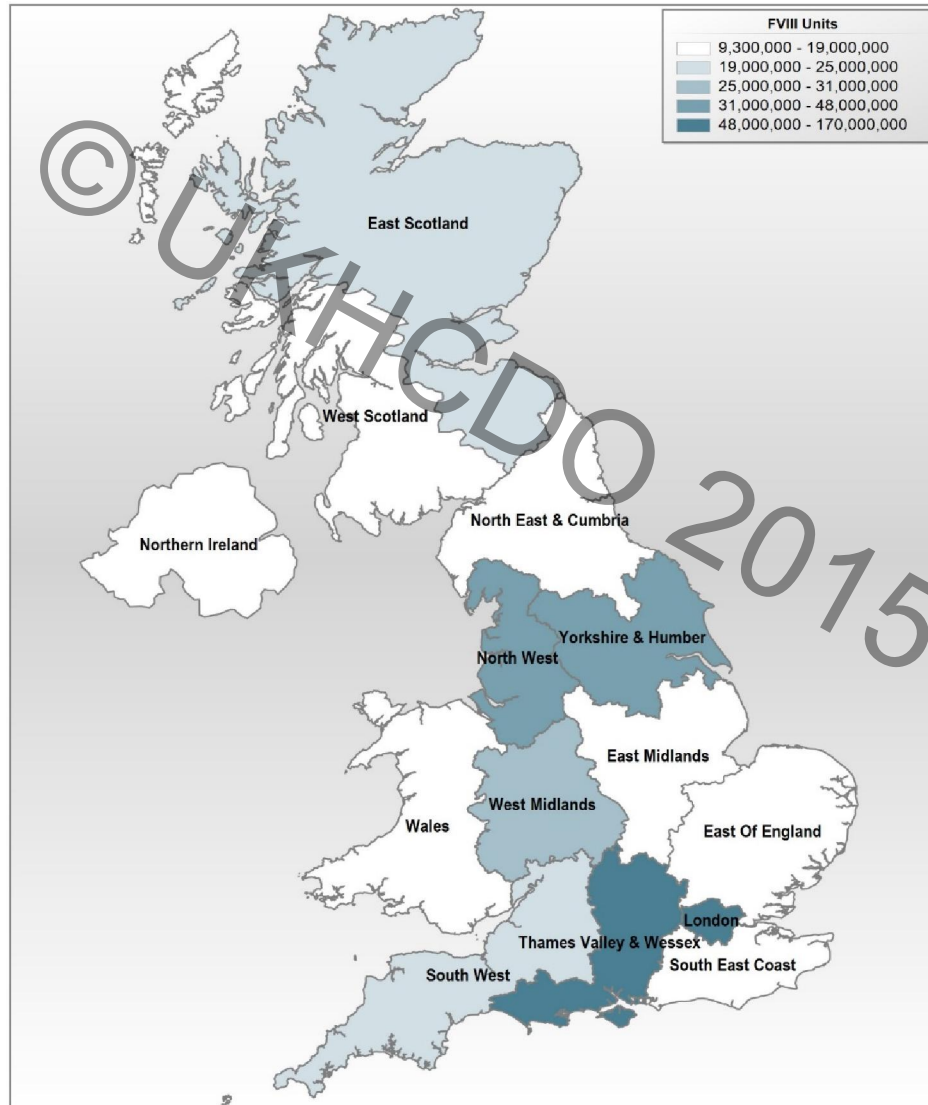


Figure 11 Factor VIII usage (including Inhibitor) divided by number of Severe Haemophilia A patients by commissioning region

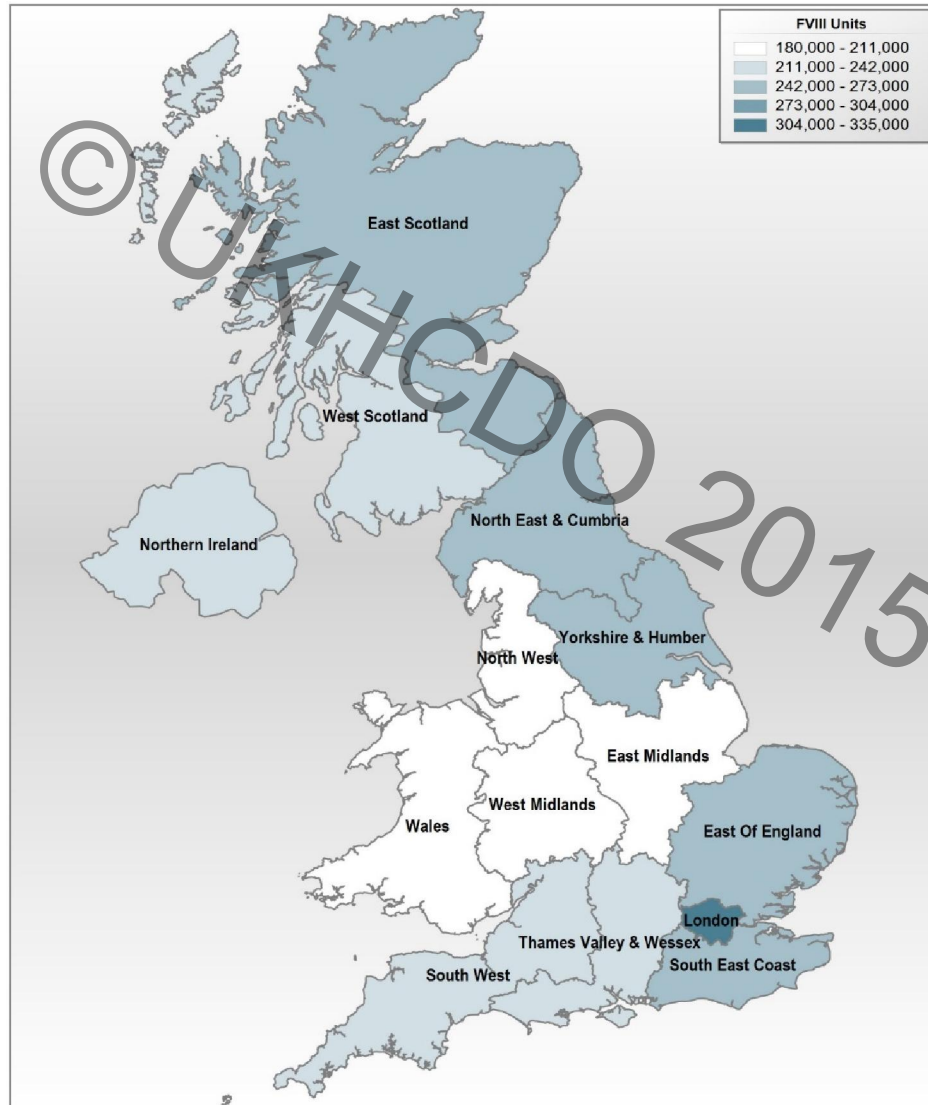


Figure 12 FVIII Units – usage per capita of general population by administration

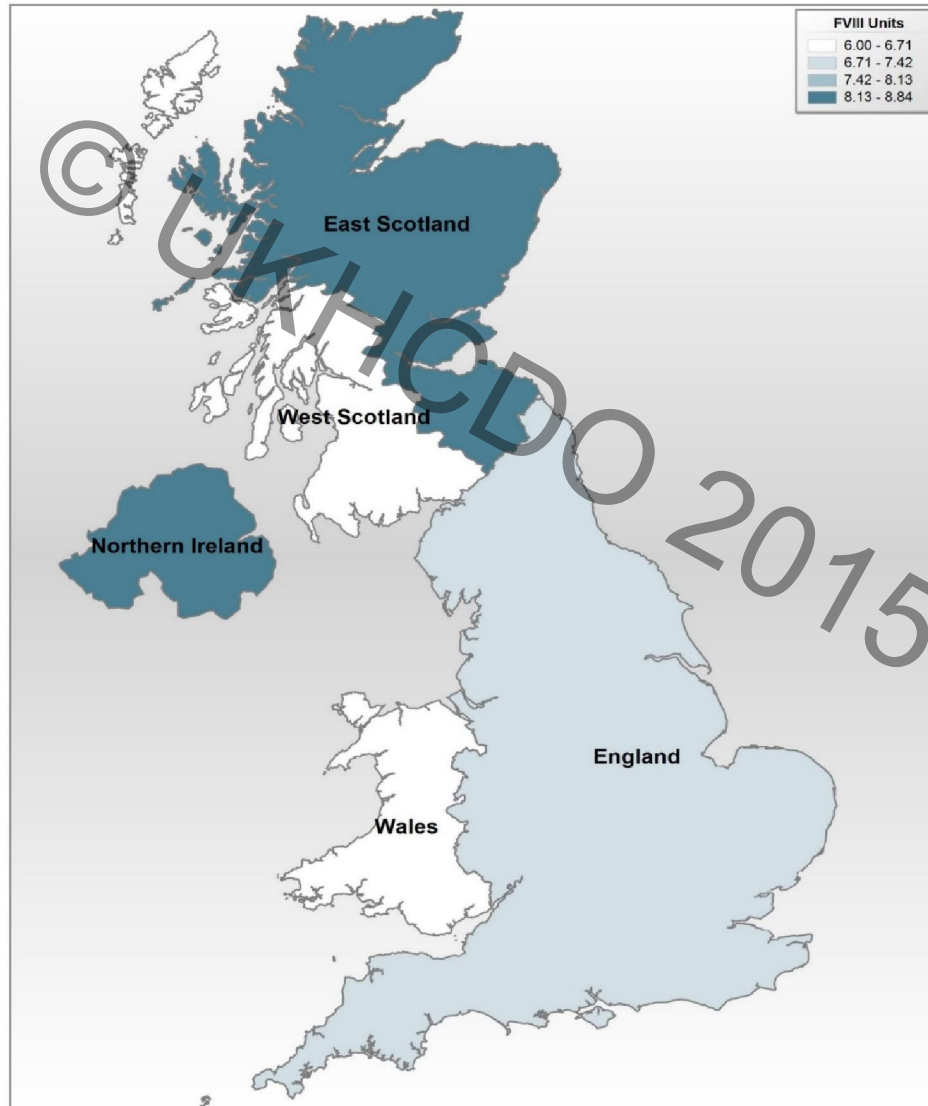


Table 4 Factor VIII usage by region for patients with Severe Haemophilia A (incl. treatment for inhibitors)

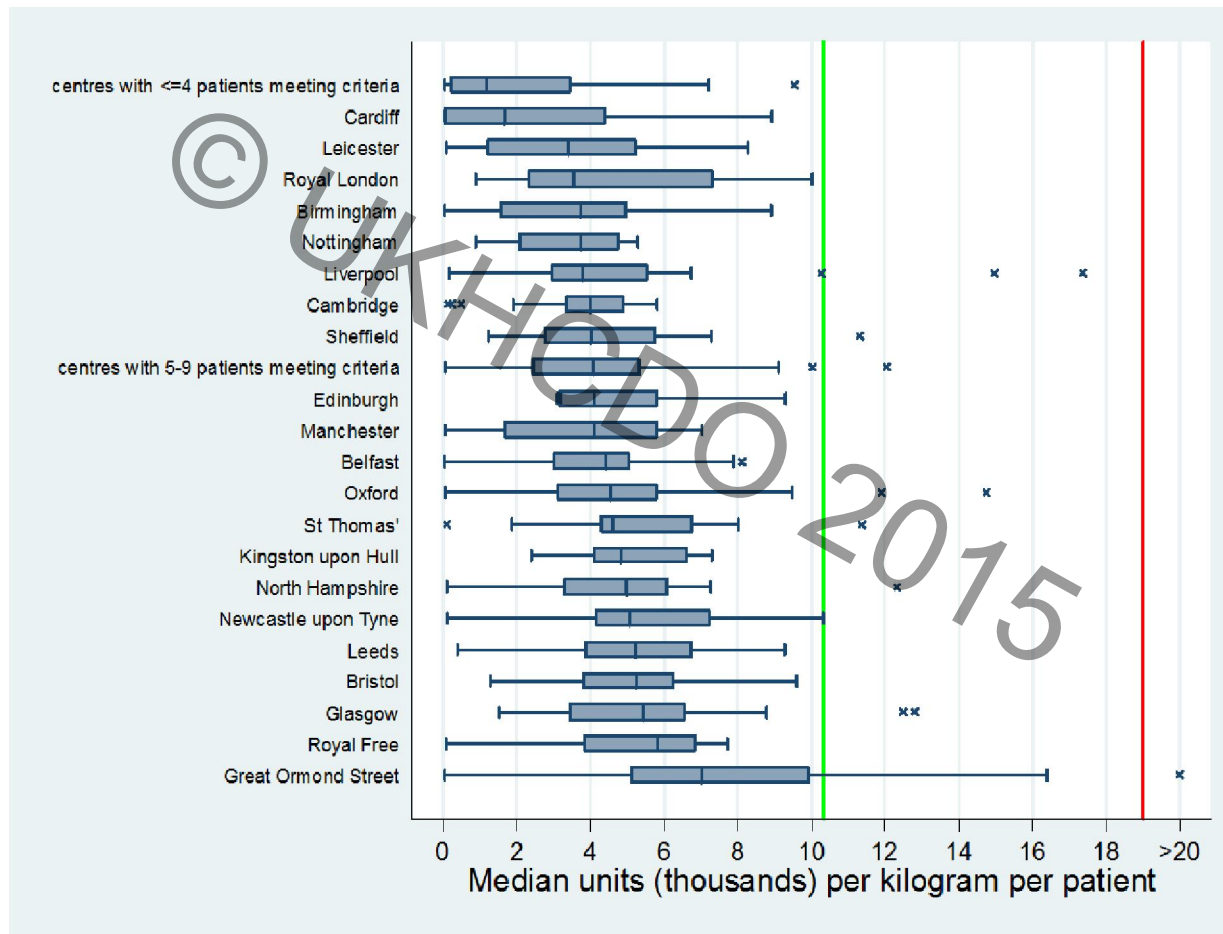
| Region | General Population | Patients treated (n) Severe Haemophilia A | Total FVIII Units (IU) Severe Haemophilia A | Mean Usage Severe Haemophilia A | FVIII Units Per Capita Severe Haemophilia A |
|---|--------------------|---|---|---------------------------------|---|
| London | | 505 | 162,794,644 | 322,366 | |
| Surrey & Sussex | | 35 | 9,332,250 | 266,636 | |
| Cumbria, Northumberland & Tyne and Wear | | 68 | 17,562,500 | 258,272 | |
| South Yorkshire & Bassetlaw | | 179 | 45,256,554 | 252,830 | |
| East Anglia | | 59 | 14,907,250 | 252,665 | |
| Wessex | | 233 | 51,006,000 | 218,910 | |
| Bristol, North Somerset & South Gloucestershire | | 88 | 19,164,250 | 217,776 | |
| Cheshire, Warrington & Wirral | | 183 | 35,229,545 | 192,511 | |
| Birmingham & Black Country | | 147 | 26,830,872 | 182,523 | |
| Leicestershire & Lincolnshire | | 93 | 16,838,067 | 181,054 | |
| England | 54,316,618 | 1,554 | 398,921,932 | 256,707 | 7.34 |
| Northern Ireland | 1,840,498 | 72 | 16,138,250 | 224,142 | 8.77 |
| Scotland East | 3,003,410 | 97 | 24,932,500 | 257,036 | 8.30 |
| Scotland West | 2,344,190 | 70 | 14,847,000 | 212,100 | 6.33 |
| Wales | 3,092,036 | 91 | 18,862,170 | 207,277 | 6.10 |
| United Kingdom | 64,596,752 | 1,873 | 473,701,852 | 252,911 | 7.33 |

English regions ranked by mean usage

Source accreditation:

England, Northern Ireland & Wales: Mid-2014 Population estimate: Office for National Statistics licensed under the Open Government Licence v.3.0.
Scotland: Mid-2014 Population Estimates supplied by National Records of Scotland © Crown Copyright 2015

Figure 13 Annual FVIII usage 2014/15 in Severe Haemophilia A patients aged under 18 years with no current inhibitor, by centre, ranked by median usage

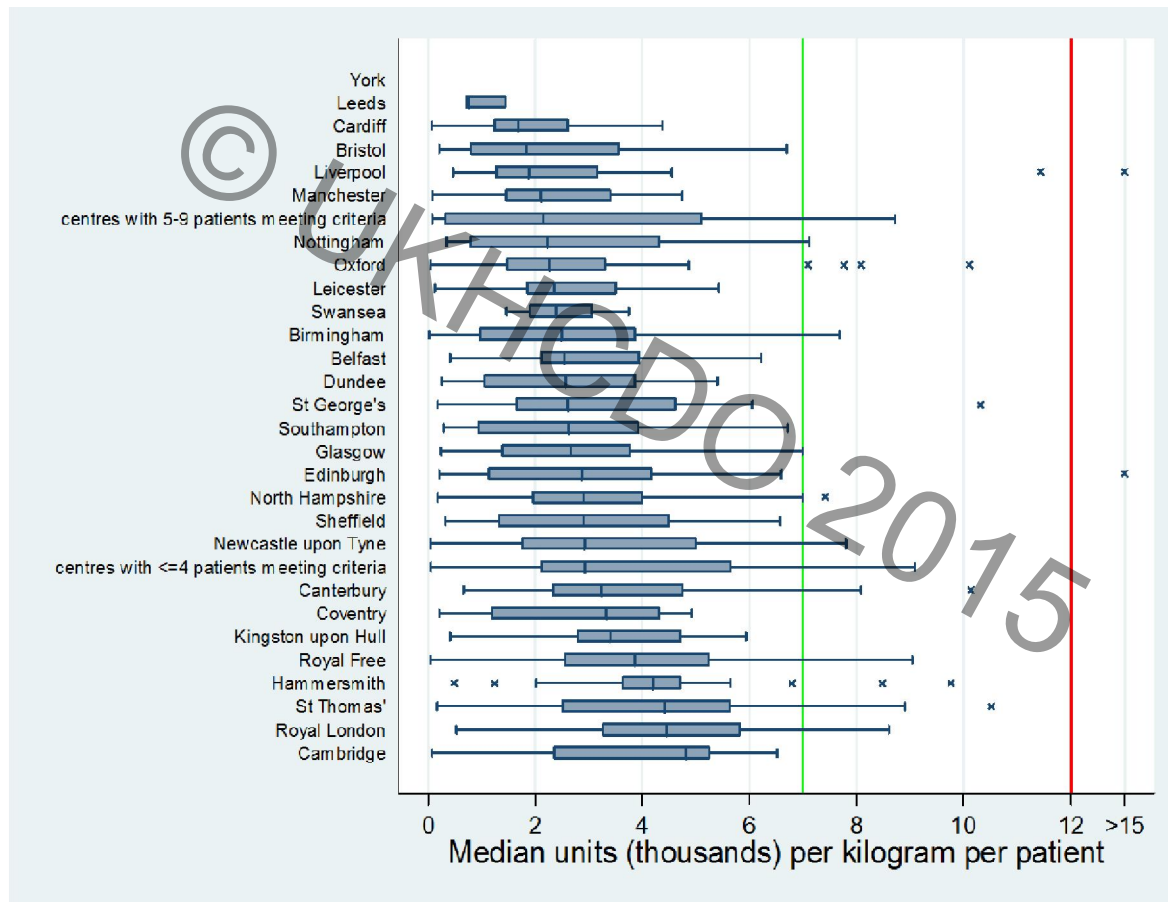


Indicated outside values show where a patient's usage is more than 1.5 times the interquartile range (iqr) from the nearest quartile at centre level
 The vertical green line indicates the 95th percentile of units, regardless of centre (10,341 IU/kg)
 The vertical red line indicates a break in the axis in order to illustrate extreme outliers

Data table for Figure 13

| Haemophilia Centre | Patients treated | Patients treated with weight reported | Total Units | Median Units | Median Units/Kg |
|--|------------------|---------------------------------------|-------------|--------------|-----------------|
| Belfast | 23 | 23 | 3,533,250 | 144,500 | 4,430 |
| Birmingham | 46 | 45 | 5,196,122 | 97,375 | 3,725 |
| Bristol | 24 | 23 | 4,381,500 | 141,250 | 5,248 |
| Cambridge | 23 | 23 | 3,179,500 | 125,000 | 4,000 |
| Cardiff | 16 | 11 | 2,121,750 | 155,250 | 1,671 |
| Edinburgh | 14 | 11 | 2,261,750 | 84,875 | 4,098 |
| Glasgow | 28 | 24 | 5,198,000 | 141,750 | 5,434 |
| Great Ormond Street | 79 | 79 | 19,406,831 | 240,500 | 7,015 |
| Kingston upon Hull | 11 | 8 | 3,272,250 | 251,000 | 4,821 |
| Leeds | 24 | 17 | 4,883,250 | 188,500 | 5,231 |
| Leicester | 11 | 11 | 931,450 | 82,500 | 3,415 |
| Liverpool | 22 | 18 | 2,820,000 | 129,000 | 3,788 |
| Manchester | 41 | 38 | 5,822,750 | 149,500 | 4,103 |
| Newcastle upon Tyne | 17 | 17 | 3,789,500 | 219,000 | 5,077 |
| North Hampshire | 21 | 21 | 2,949,500 | 145,250 | 4,994 |
| Nottingham | 16 | 13 | 1,892,000 | 100,250 | 3,754 |
| Oxford | 45 | 45 | 9,099,750 | 169,000 | 4,560 |
| Royal Free | 14 | 14 | 4,929,500 | 347,750 | 5,814 |
| Royal London | 17 | 15 | 2,819,250 | 127,500 | 3,557 |
| Sheffield | 24 | 23 | 4,191,500 | 135,375 | 4,010 |
| St Thomas' | 18 | 17 | 3,200,850 | 166,000 | 4,596 |
| Centres with <=4 patients meeting criteria | 34 | 27 | 4,260,500 | 97,000 | 1,181 |
| Centres with 5-9 patients meeting criteria | 59 | 52 | 11,193,500 | 166,000 | 4,068 |

Figure 14 Annual FVIII usage 2014/15 in Severe Haemophilia A patients aged 18 years or more with no current inhibitor, by centre, ranked by median usage



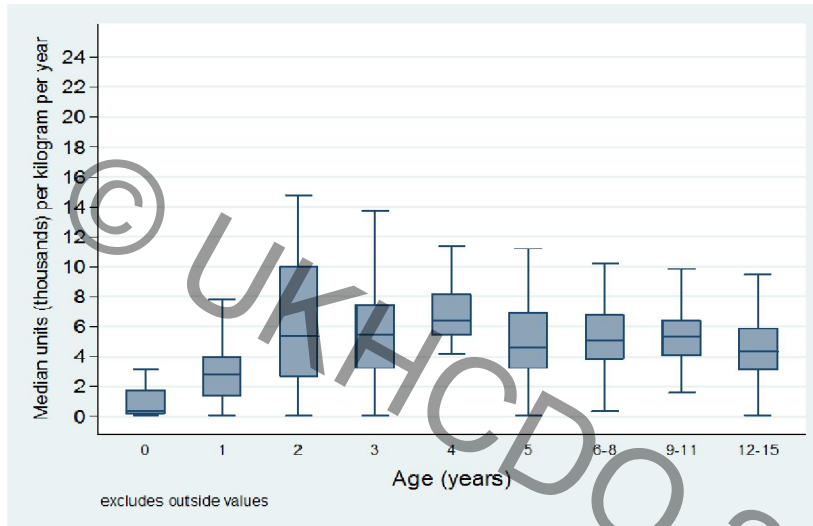
Indicated outside values show where a patient's usage is more than 1.5 times the iqr from the nearest quartile at centre level
 The vertical green line indicates the 95th percentile of units, regardless of centre (6,984 IU/kg)
 The vertical red line indicates a break in the axis in order to illustrate extreme outliers

Data table for Figure 14

| Haemophilia Centre | Patients treated | Patients treated with weight reported | Total Units | Median Units | Median Units/Kg |
|--|------------------|---------------------------------------|-------------|--------------|-----------------|
| Belfast | 43 | 29 | 10,030,500 | 210,000 | 2,545 |
| Birmingham | 69 | 44 | 14,040,500 | 188,000 | 2,488 |
| Bristol | 28 | 28 | 4,901,000 | 140,500 | 1,841 |
| Cambridge | 29 | 29 | 9,348,000 | 360,000 | 4,817 |
| Canterbury | 19 | 17 | 6,369,000 | 271,000 | 3,242 |
| Cardiff | 35 | 13 | 7,140,170 | 194,000 | 1,677 |
| Coventry | 10 | 10 | 2,434,000 | 264,000 | 3,329 |
| Dundee | 15 | 15 | 3,231,500 | 256,000 | 2,569 |
| Edinburgh | 27 | 27 | 7,443,500 | 210,000 | 2,860 |
| Glasgow | 50 | 50 | 11,390,500 | 222,250 | 2,660 |
| Hammersmith | 22 | 22 | 6,944,500 | 302,000 | 4,197 |
| Kingston upon Hull | 10 | 6 | 3,557,750 | 341,750 | 3,394 |
| Leeds | 31 | 3 | 9,052,002 | 285,000 | 760 |
| Leicester | 18 | 15 | 3,895,117 | 229,750 | 2,354 |
| Liverpool | 33 | 31 | 7,078,000 | 144,000 | 1,881 |
| Manchester | 89 | 53 | 18,029,295 | 194,000 | 2,104 |
| Newcastle upon Tyne | 46 | 40 | 12,794,000 | 236,000 | 2,929 |
| North Hampshire | 53 | 35 | 14,511,250 | 258,000 | 2,901 |
| Nottingham | 26 | 14 | 6,086,500 | 184,000 | 2,221 |
| Oxford | 88 | 86 | 17,924,750 | 183,500 | 2,261 |
| Royal Free | 118 | 112 | 37,101,850 | 319,500 | 3,867 |
| Royal London | 46 | 39 | 14,533,833 | 330,000 | 4,453 |
| Sheffield | 43 | 18 | 12,498,802 | 264,000 | 2,909 |
| Southampton | 14 | 11 | 2,912,000 | 151,000 | 2,621 |
| St George's | 29 | 26 | 7,030,750 | 213,000 | 2,611 |
| St Thomas' | 108 | 78 | 38,842,000 | 351,500 | 4,417 |
| Swansea | 10 | 4 | 1,621,500 | 158,000 | 2,380 |
| York | 10 | 0 | 2,279,000 | 217,000 | |
| Centres with <=4 patients meeting criteria | 26 | 15 | 6,950,500 | 232,000 | 2,932 |
| Centres with 5-9 patients meeting criteria | 64 | 11 | 14,322,000 | 183,250 | 2,148 |

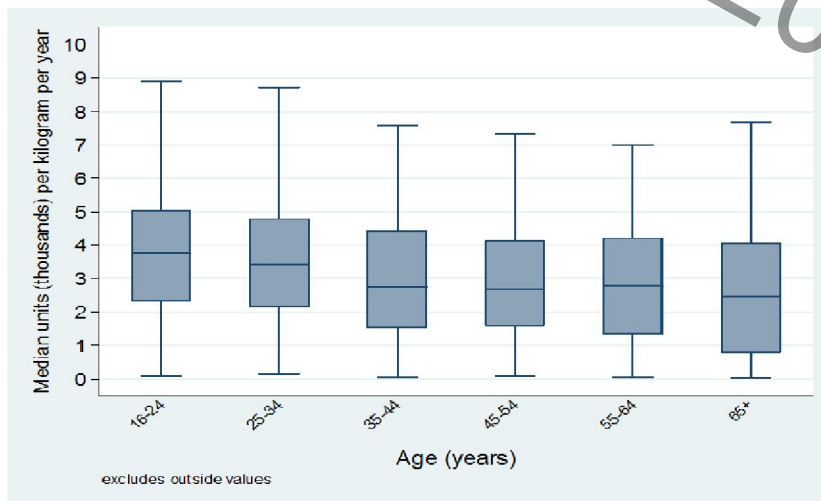
Figures 15a & b Median factor VIII units used per kilogram body weight per year in Severe Haemophilia A patients without inhibitors by age, 2014/15

15a. Paediatrics



Weight data are missing for 36/516, including, 5/31 aged <12m

15b. Adults



Weight data are missing for 338/1256

Figure 16 Median factor VIII units used per kilogram body weight per year in Severe Haemophilia A patients without inhibitors aged 16 and over, by bodyweight 2014/15

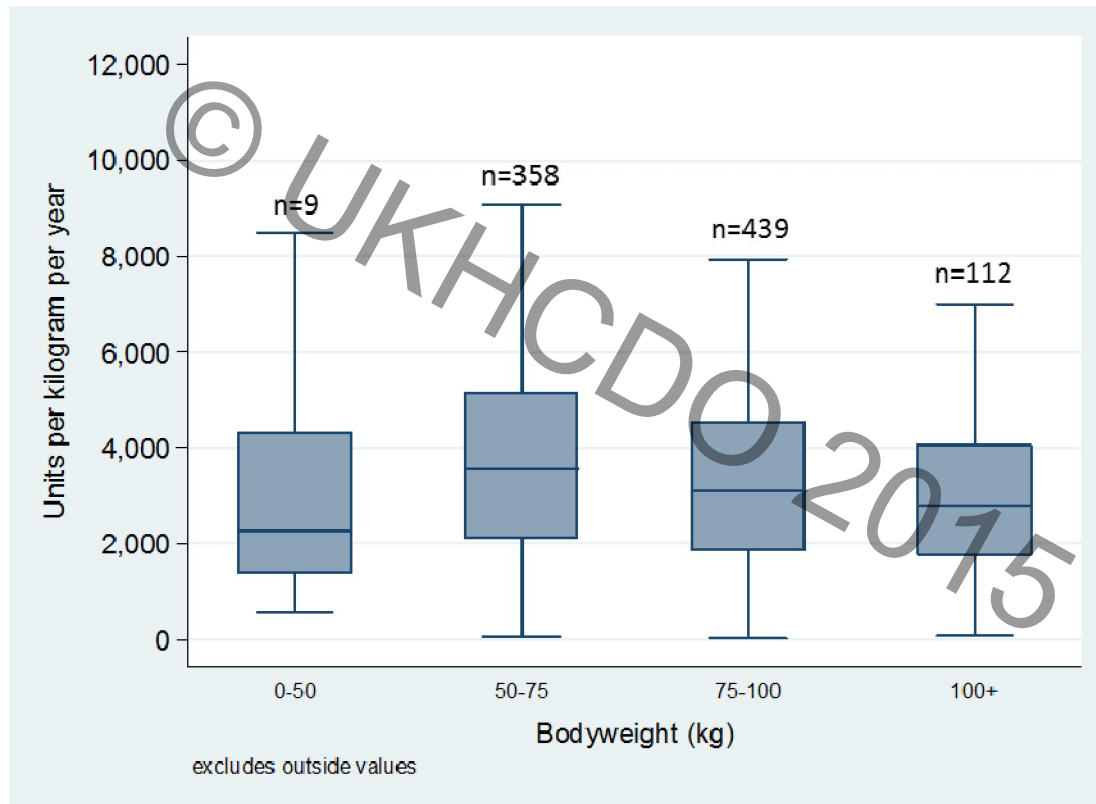


Figure 17 Median usage of factor VIII: UK patients with severe Haemophilia A without inhibitors broken down by age, 2009/10 – 2014/15

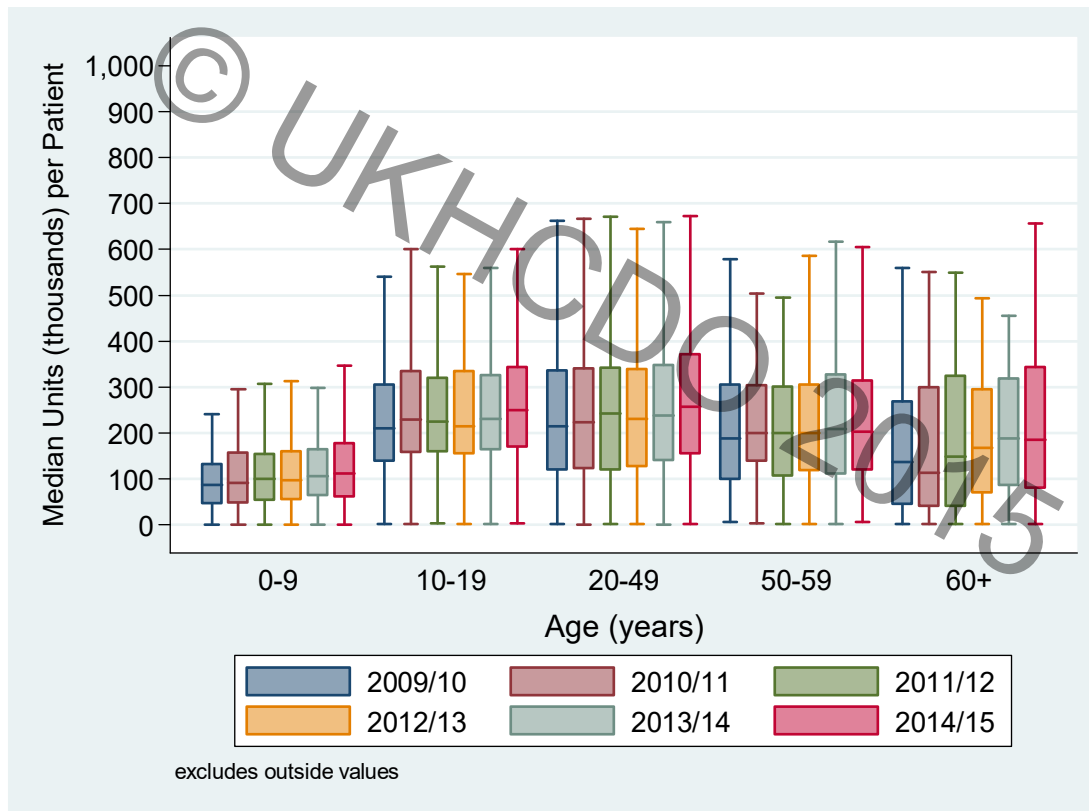
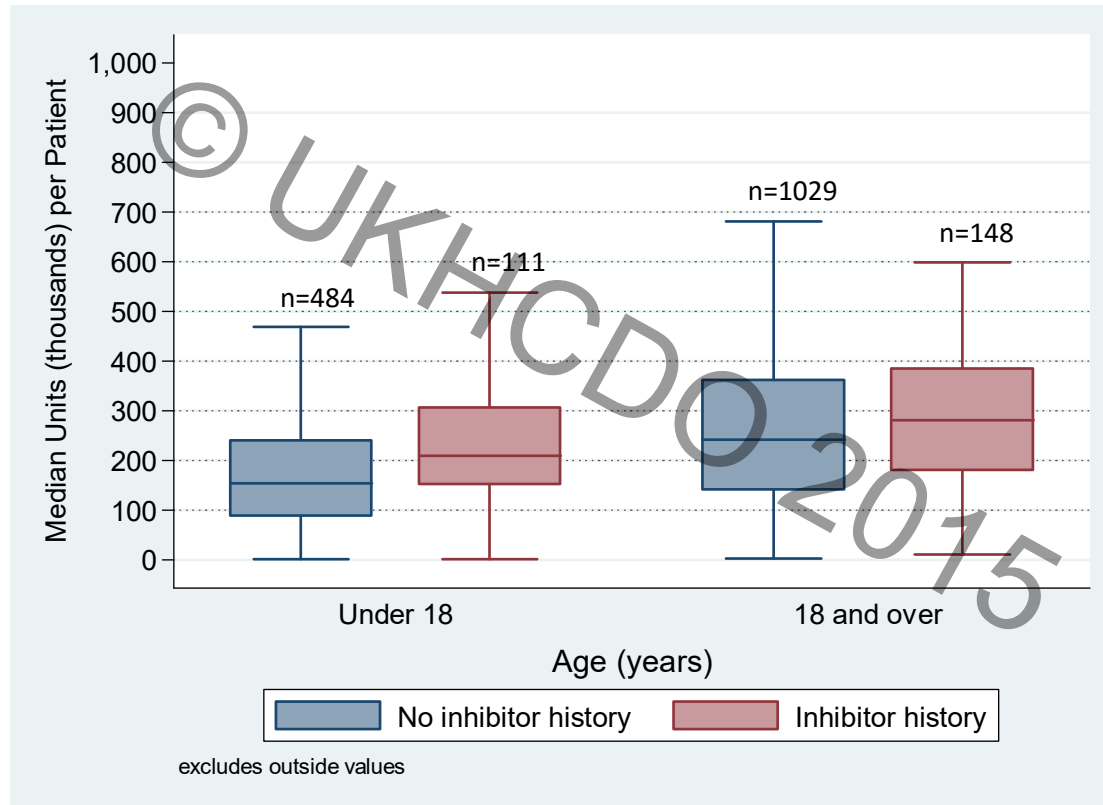
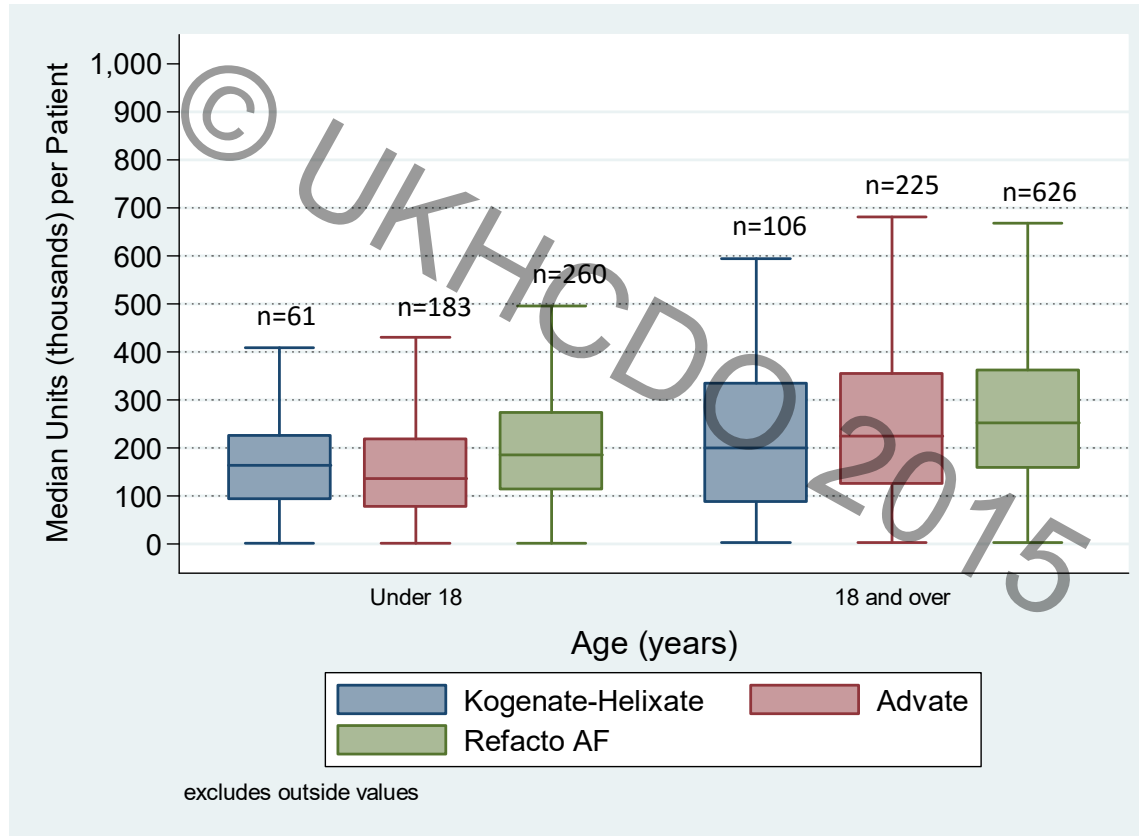


Figure 18 Severe Haemophilia A patients with no current inhibitor between April 2014 & March 2015: median usage by inhibitor history



(Mann-Whitney U test: Under 18 years: $p < 0.005$; 18 years and over: $p = 0.03$).

Figure 19 Severe Haemophilia A patients with no current inhibitor using only one product between April 2014 & March 2015: median usage



(Median test: Kogenate/Helixate, ReFacto AF or Advate, under 18 years: $p=0.003$; 18 years and over: $p=0.032$)

Table 5 Products used to treat Haemophilia A (including inhibitors) between April 2014 and March 2015

| Manufacturer | Product | Total Units |
|-----------------------|-----------------------------|-------------|
| Baxter | Advate | 143,473,602 |
| | FEIBA | 32,135,208 |
| Bayer | Kogenate | 26,351,700 |
| Biotest | Haemoctin | 370,000 |
| BPL | FVIII 8Y | 283,780 |
| | Optivate | 1,683,000 |
| CSL Behring | Haemate P | 170,000 |
| | Helixate Nexgen | 31,873,850 |
| | Riastap (g) | 22 |
| Grifols | Alphanate | 124,000 |
| | Fanhdi | 28,583,000 |
| Novo Nordisk | NovoSeven (mg) | 24,056.00 |
| Octapharma | Nuwiq | 1,479,750 |
| | Octanate | 4,079,500 |
| | Octaplex | 8,500 |
| Pfizer | BeneFIX | 2,500 |
| | ReFacto AF | 262,624,313 |
| Various Manufacturers | Investigational Factor VIII | 20,144,937 |

Units in IU unless otherwise stated

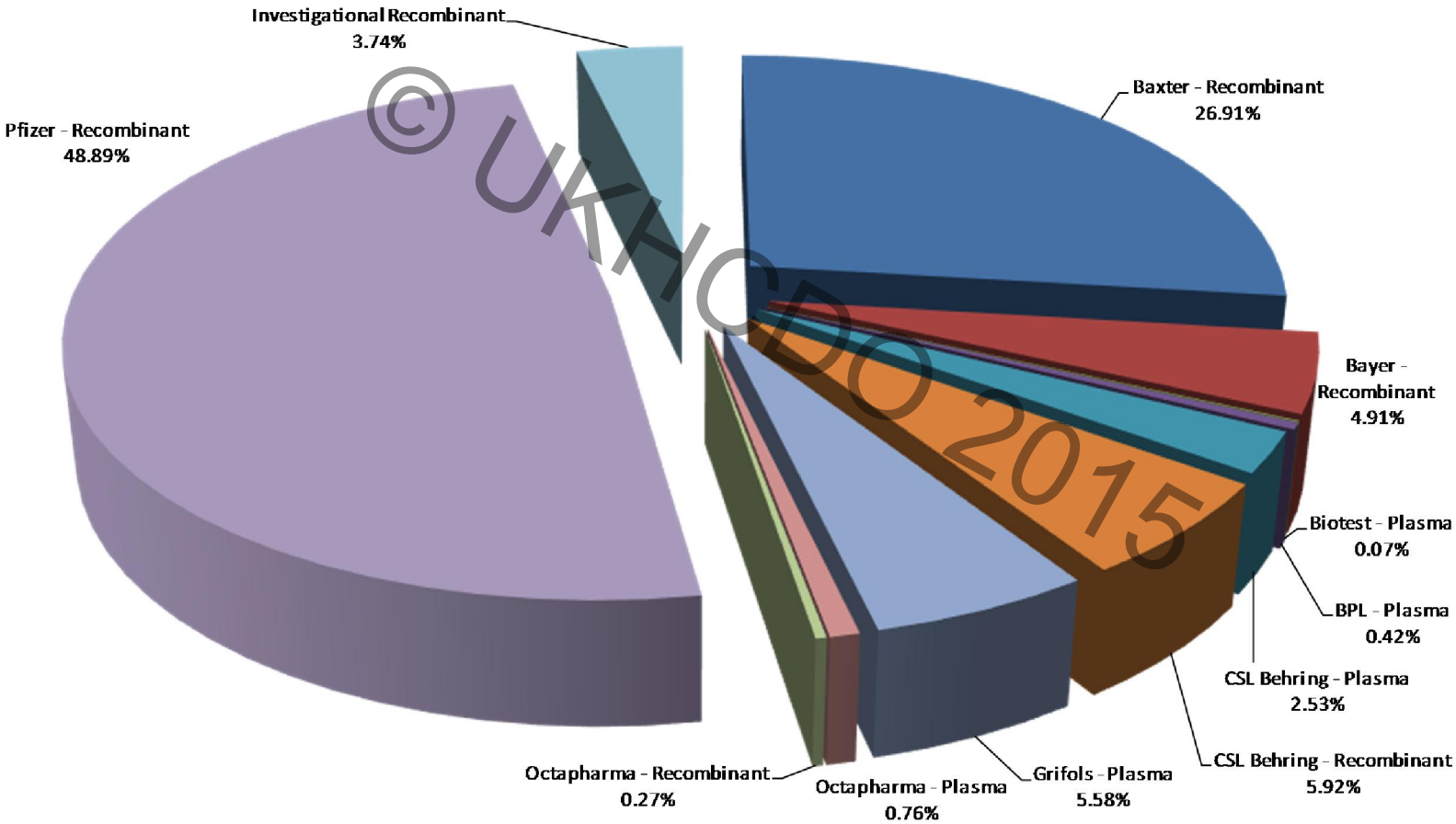
Table 6 Factor VIII units used by UK Haemophilia Centres between April 2014 and March 2015, broken down by diagnosis

| Coagulation Defect | Patients Treated | Plasma FVIII (IU) | Recombinant FVIII (IU) | Investigational FVIII (IU) | Total FVIII (IU) |
|---------------------------------|------------------|-------------------|------------------------|----------------------------|--------------------|
| Haemophilia A | 2,897 | 35,293,280 | 465,715,215 | 20,144,937 | 521,153,432 |
| Haemophilia A Carrier | 39 | 7,500 | 615,550 | - | 623,050 |
| Acquired Haemophilia A | 12 | 242,000 | 278,000 | - | 520,000 |
| von Willebrand disease | 716 | 22,007,050 | 5,250 | - | 22,012,300 |
| Acquired von Willebrand Disease | 27 | 682,511 | - | - | 682,511 |
| F.VII deficiency | 1 | 2,000 | - | - | 2,000 |
| Combined V+VIII Deficiency | 5 | - | 56,500 | - | 56,500 |
| Other combined diagnoses | 16 | 256,000 | 1,643,750 | - | 1,899,750 |
| Glanzmann's Thrombasthenia | 1 | 1,500 | - | - | 1,500 |
| Platelet defects* | 2 | 55,000 | - | - | 55,000 |
| Miscellaneous* | 5 | 26,500 | 2,000 | - | 28,500 |
| Unclassified* | 1 | 4,000 | - | - | 4,000 |
| Total | 3,722 | 58,577,341 | 468,316,265 | 20,144,937 | 547,038,543 |

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

Some products used to treat von Willebrand Disease will include VWF as well as FVIII

Figure 20 Market Share of factor VIII concentrates issued by UK Haemophilia Centres during 2014/15



HAEMOPHILIA B

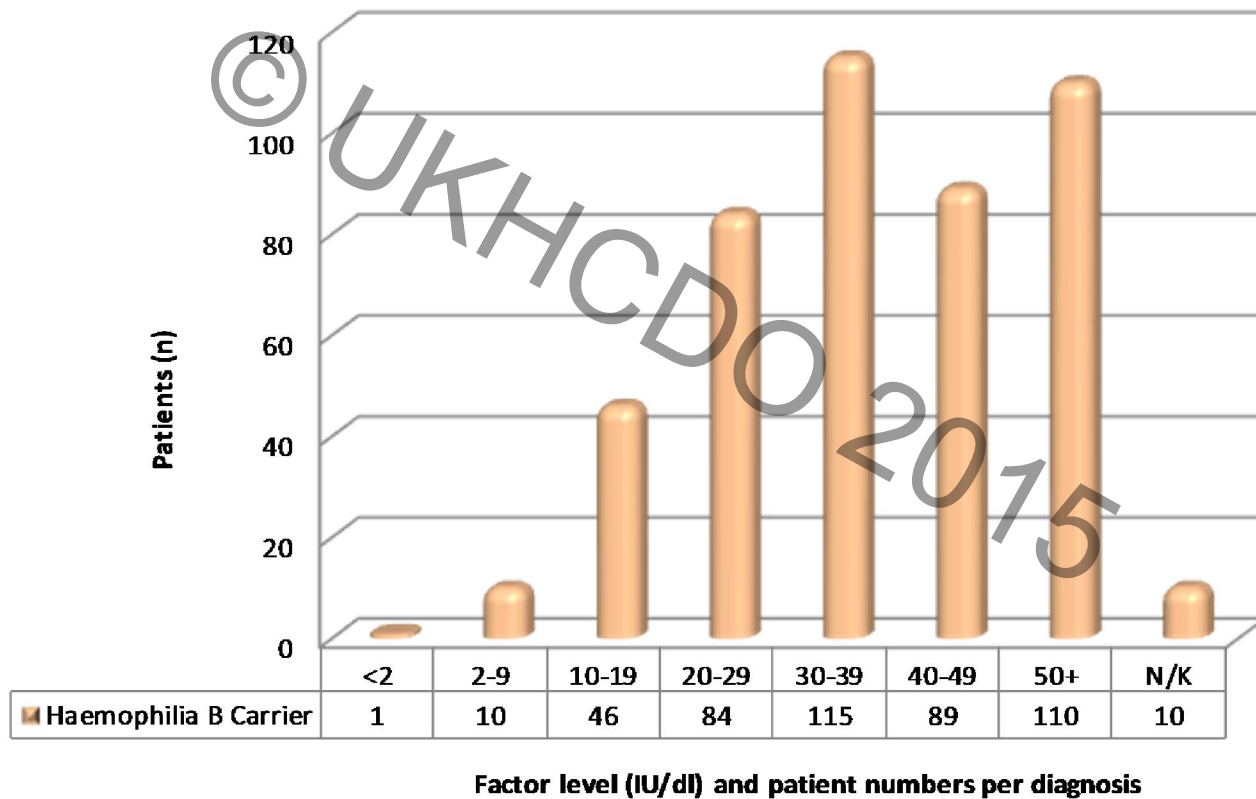
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Table 7 Patients with congenital Haemophilia B registered and treated April 2014 – March 2015

| Haemophilia B | Age Range | Factor IX level (iu/dl) | | | | |
|---|--------------|-------------------------|------------|------------|-----------|--------------|
| | | ≤ 1 | >1 & <5 | ≥ 5 & <50 | Unknown | Total |
| In Register (including low-level carriers) | <18 years | 127 | 56 | 171 | 1 | 355 |
| | ≥18 years | 284 | 190 | 719 | 10 | 1,203 |
| | Total | 411 | 246 | 890 | 11 | 1,558 |
| New Registrations * (including low-level carriers) | <18 years | 9 | 4 | 25 | - | 38 |
| | ≥18 years | 3 | 4 | 32 | - | 39 |
| | Total | 12 | 8 | 57 | - | 77 |
| Treated in year** (including low-level carriers) | <18 years | 119 | 36 | 37 | - | 192 |
| | ≥18 years | 253 | 80 | 142 | - | 475 |
| | Total | 372 | 116 | 179 | - | 667 |

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

Figure 21 Carriers of Haemophilia B currently registered, by baseline factor IX level



Total number 465

N.B:
 Haemophilia B Carrier includes:
 Females registered by their Haemophilia Centre as Females with IX deficiency
 Females registered by their Haemophilia Centre as Haemophilia B
 FIX Leyden carriers

Table 8 New Registrations of Haemophilia B between April 2014 & March 2015, by age at mid-year and disease severity

| Coagulation Defect | Age (years) | Number of Patients (Factor VIII level (iu/dl)) | | | |
|--------------------|-------------|--|----------|-----------|-----------|
| | | ≤1 | >1 & <5 | ≥5 | Total |
| Haemophilia B | 0:4 | 8 | 2 | 5 | 15 |
| | 5:9 | 1 | 1 | 2 | 4 |
| | 10:19 | 0 | 1 | 3 | 4 |
| | 20:29 | 0 | 3 | 3 | 6 |
| | 30:39 | 1 | 1 | 1 | 3 |
| | 40:49 | 1 | 0 | 1 | 2 |
| | 50:59 | 0 | 0 | 2 | 2 |
| | 60:69 | 0 | 0 | 1 | 1 |
| | 70+ | 0 | 0 | 1 | 1 |
| Total | | 11 | 8 | 19 | 38 |

N.B: Haemophilia B includes patients with FIX Leyden

Figure 22 Trend in numbers of Severe Haemophilia B patients aged 60 years and above, 1974 – 2014/15 (including HIV +ve pts)

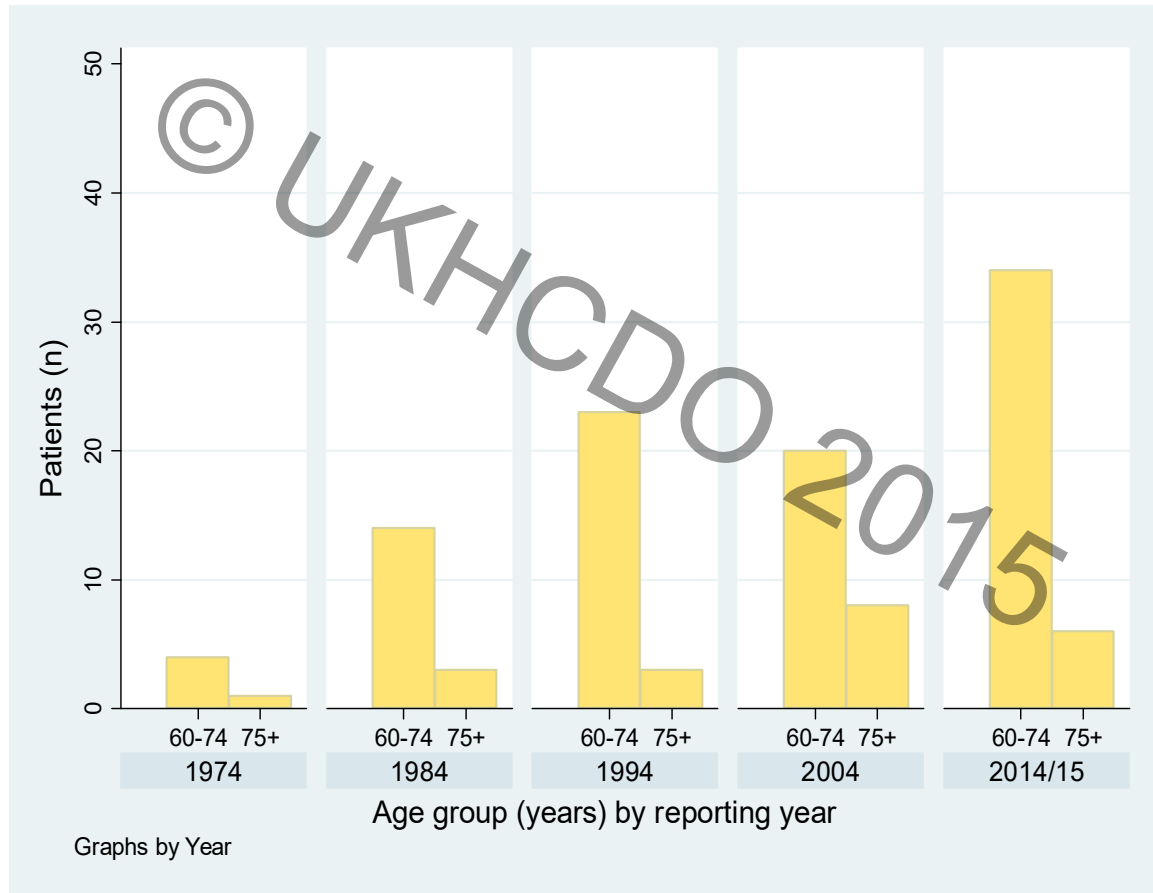


Figure 23 Trend in numbers of non-Severe Haemophilia B patients aged 60 years and above, 1974 – 2014/15 (including HIV +ve pts)

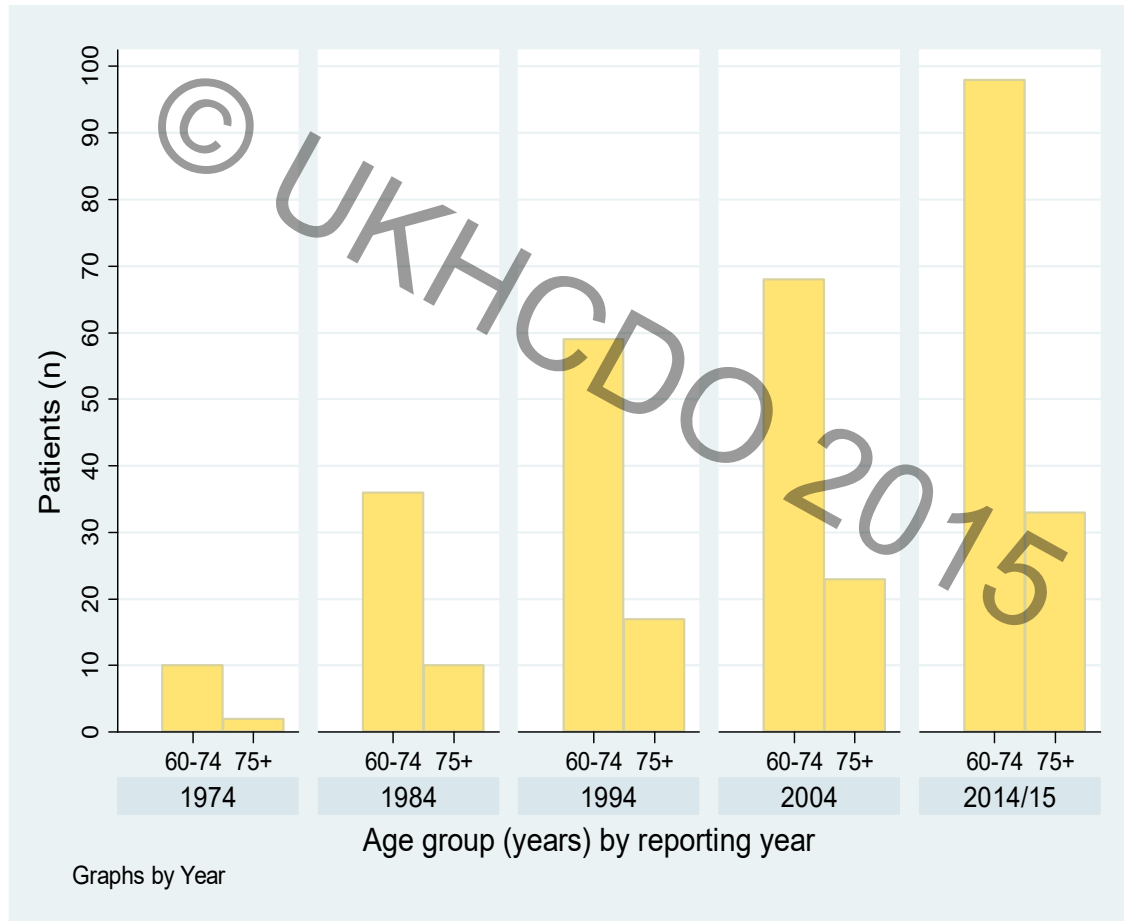
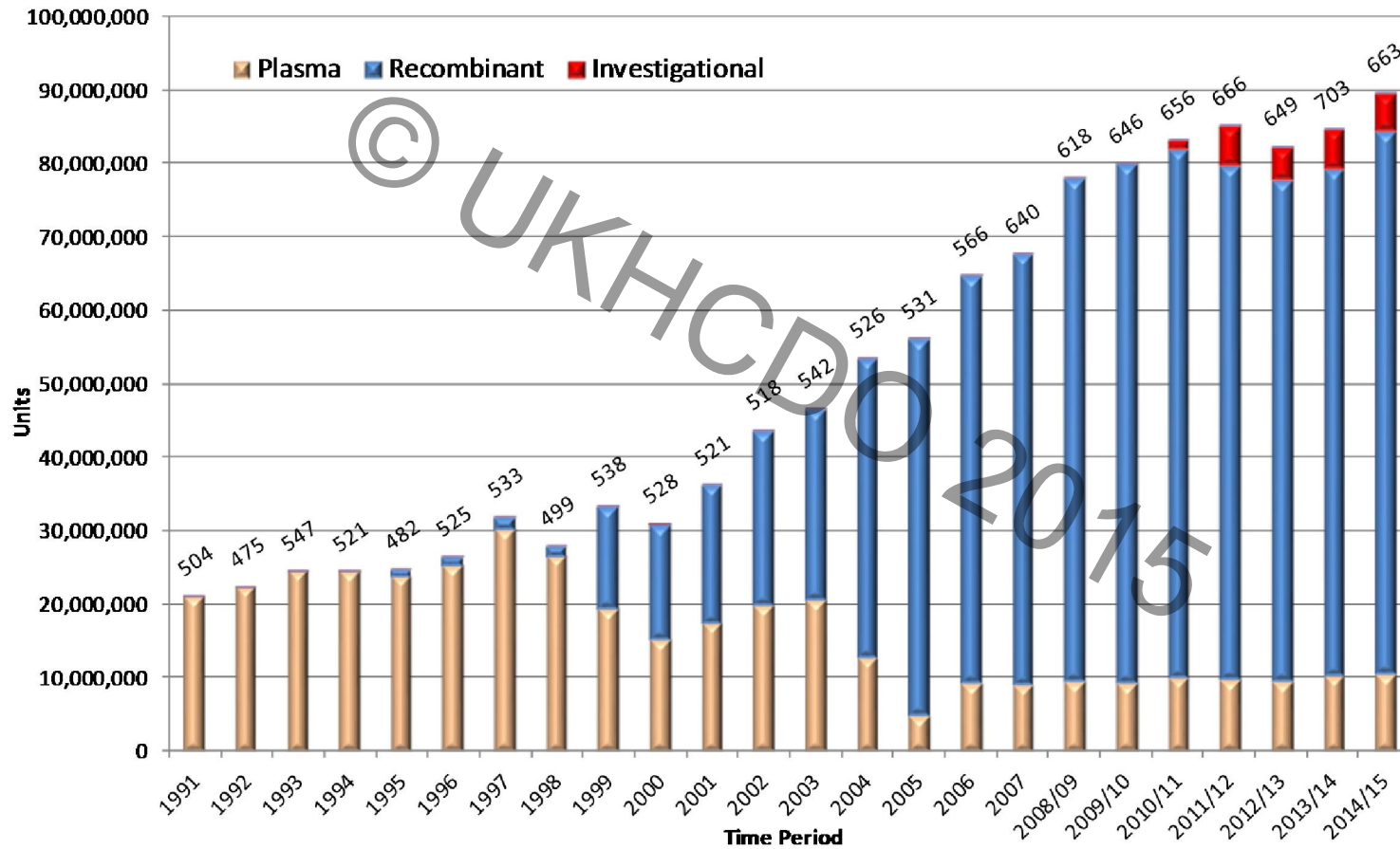


Figure 24 Factor FIX units used by UK Haemophilia Centres 1991-2014/15 all diagnoses



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

Figure 25 Total Number of Severe Haemophilia B patients treated by commissioning region

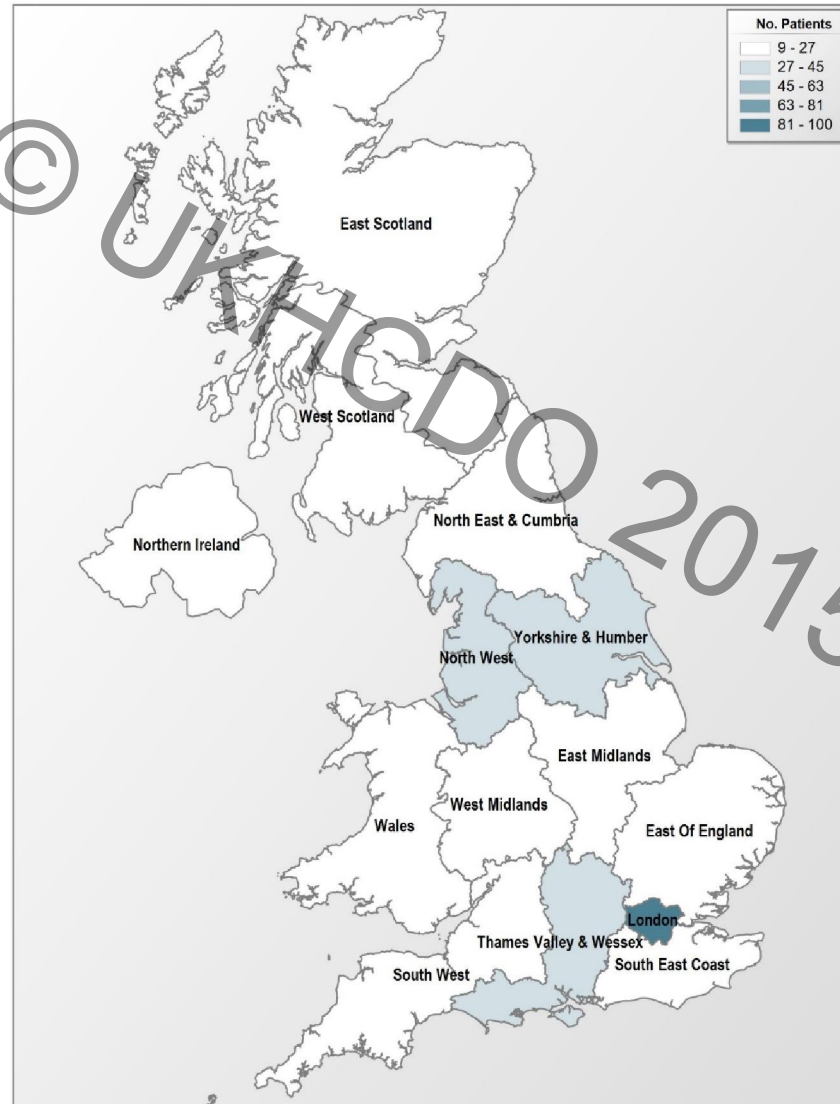


Figure 26 Total Factor IX units issued to patients with Severe Haemophilia B (including inhibitor) by commissioning region

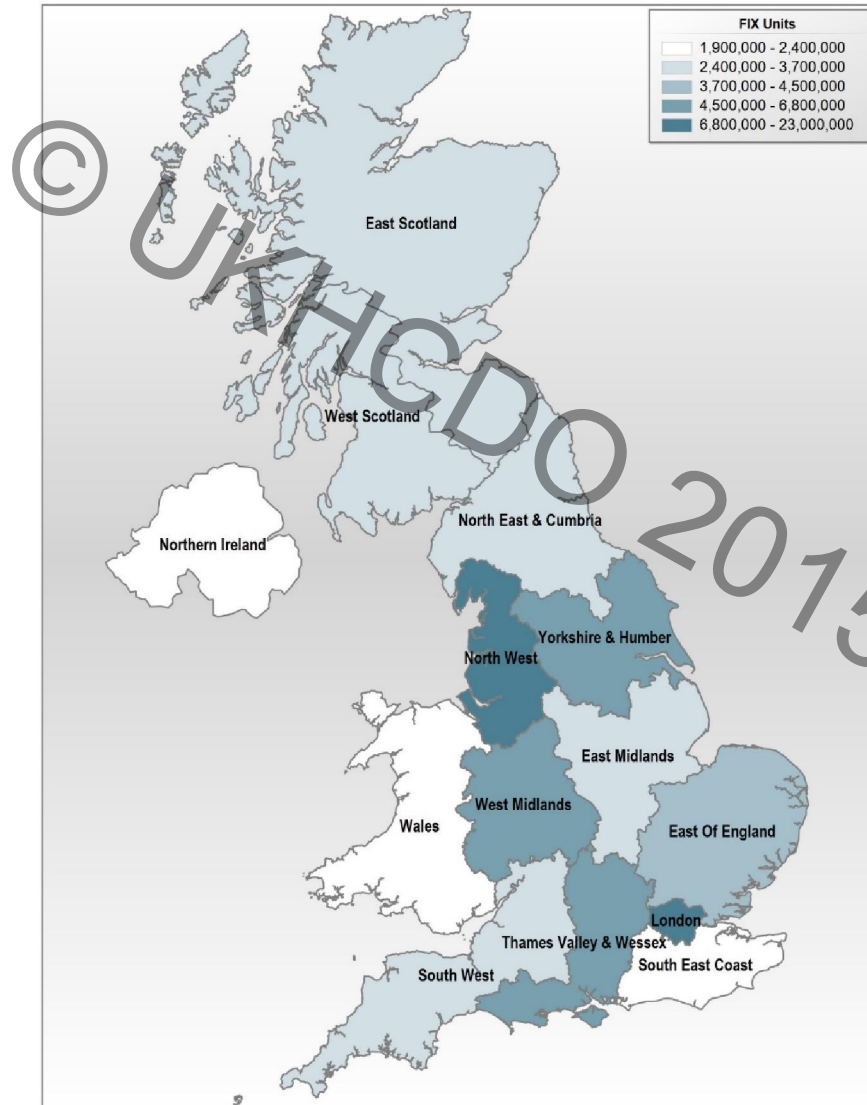


Figure 27 Factor IX Usage (including inhibitor) divided by number of Severe Haemophilia B patients by commissioning region

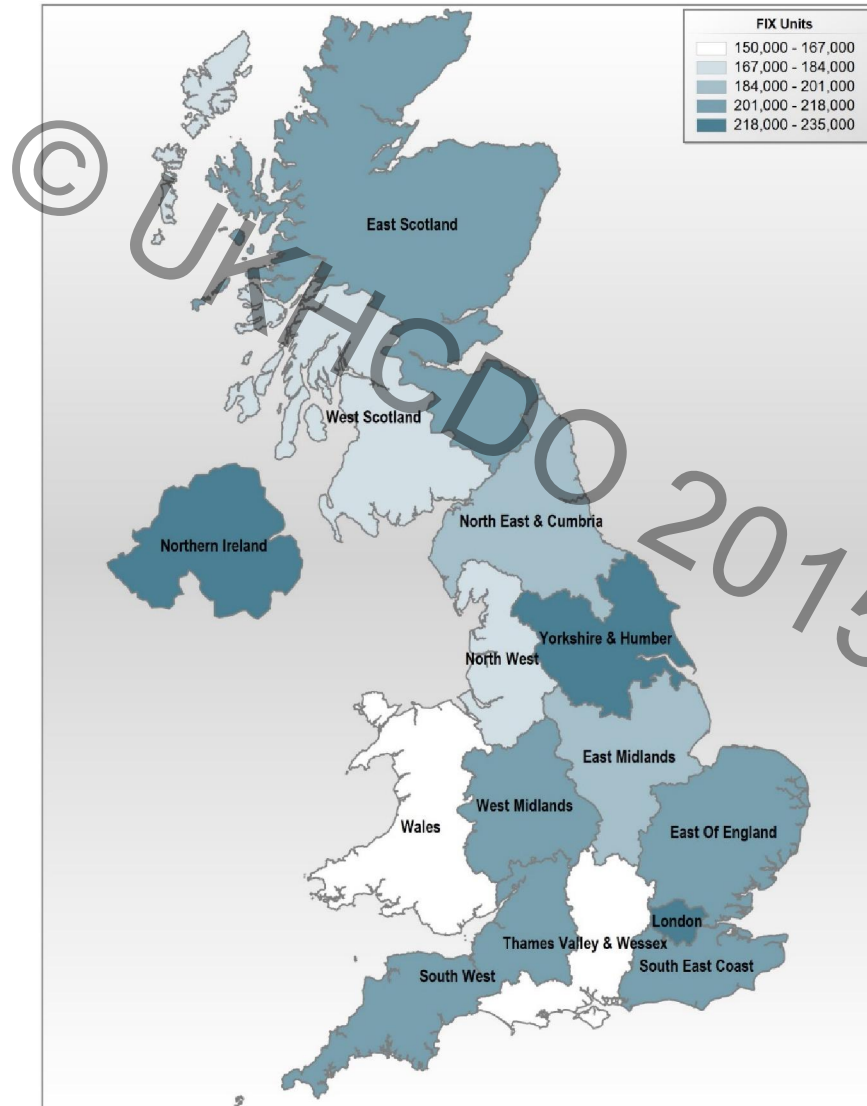


Figure 28 FIX Units – usage per capita of general population by administration

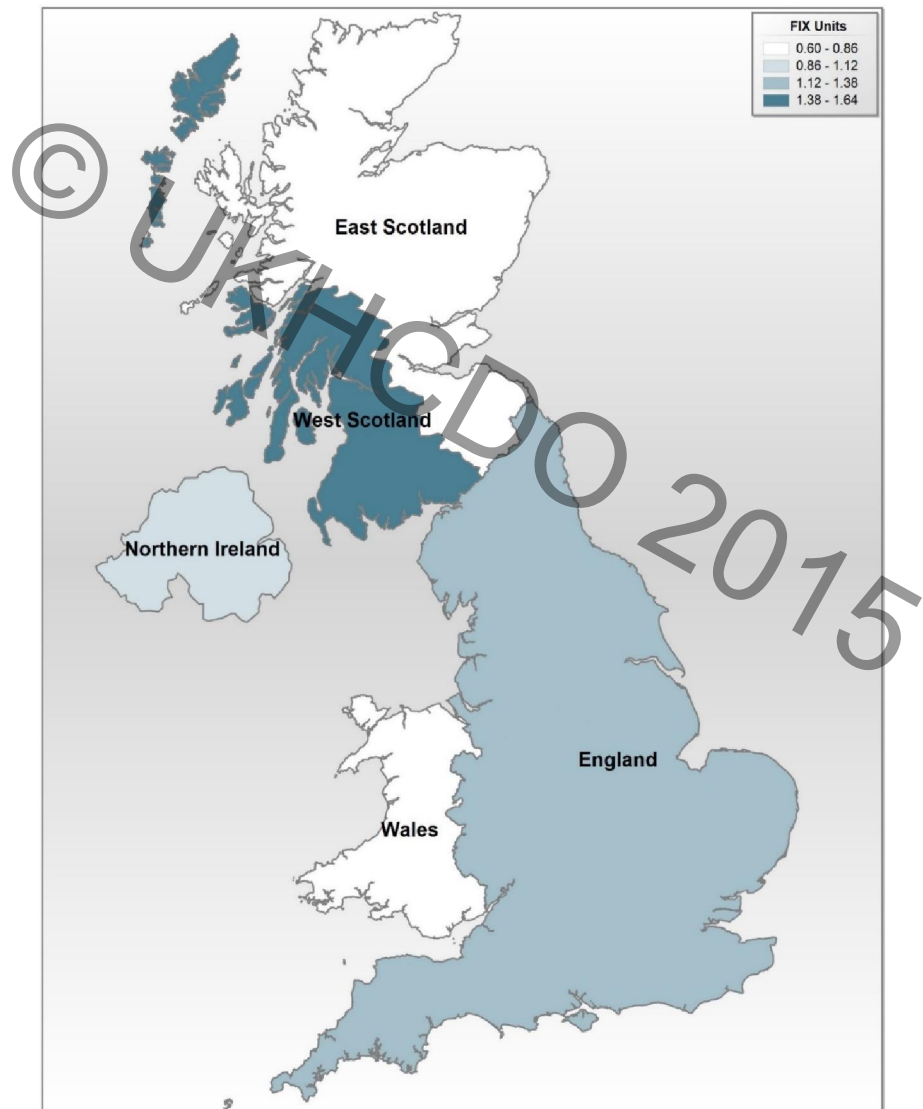


Table 9 Factor IX usage by region for patients with Severe Haemophilia B (incl. treatment for inhibitors)

| 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 | | 28 | 6,389,389 | 228,192 | |
| London | | 99 | 22,535,421 | 227,631 | |
| Surrey & Sussex | | 11 | 2,387,000 | 217,000 | |
| Birmingham & Black Country | | 25 | 5,313,250 | 212,530 | |
| Bristol, North Somerset & South Gloucestershire | | 14 | 2,926,000 | 209,000 | |
| East Anglia | | 19 | 3,836,250 | 201,908 | |
| Cumbria, Northumberland & Tyne and Wear | | 17 | 3,319,000 | 195,235 | |
| Leicestershire & Lincolnshire | | 18 | 3,317,904 | 184,328 | |
| Cheshire, Warrington & Wirral | | 41 | 7,097,424 | 173,108 | |
| Wessex | | 40 | 6,672,385 | 166,810 | |
| England | 54,316,618 | 305 | 63,794,023 | 209,161 | 1.17 |
| Northern Ireland | 1,840,498 | 9 | 1,986,500 | 220,722 | 1.08 |
| Scotland East | 3,003,410 | 12 | 2,488,500 | 207,375 | 0.83 |
| Scotland West | 2,344,190 | 22 | 3,680,750 | 167,307 | 1.57 |
| Wales | 3,092,036 | 13 | 2,053,447 | 157,957 | 0.66 |
| United Kingdom | 64,596,752 | 361 | 74,003,220 | 204,995 | 1.15 |

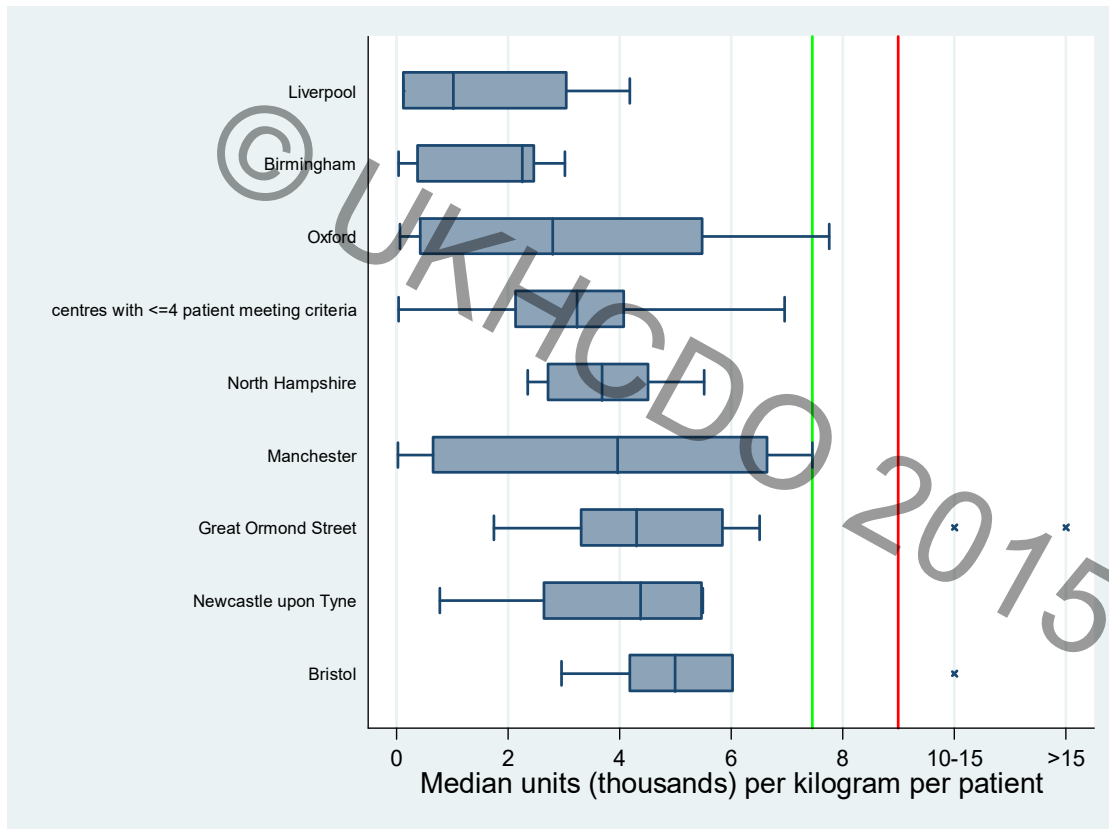
© UKHCDO 2015

English regions ranked by mean usage

Source accreditation:

England, Northern Ireland & Wales: Mid-2014 Population estimate: Office for National Statistics licensed under the Open Government Licence v.3.0.
 Scotland: Mid-2014 Population Estimates supplied by National Records of Scotland © Crown Copyright 2015

Figure 29 Annual FIX usage 2014/15 in Severe Haemophilia B patients *aged under 18 years* with no current inhibitor, by centre, ranked by median usage



Indicated outside values show where a patient's usage is more than 1.5 times the iqr from the nearest quartile at centre level
 The vertical green line indicates the 95th percentile of units, regardless of centre (7,461 IU/kg)
 The vertical red line indicates a break in the axis in order to illustrate extreme outliers

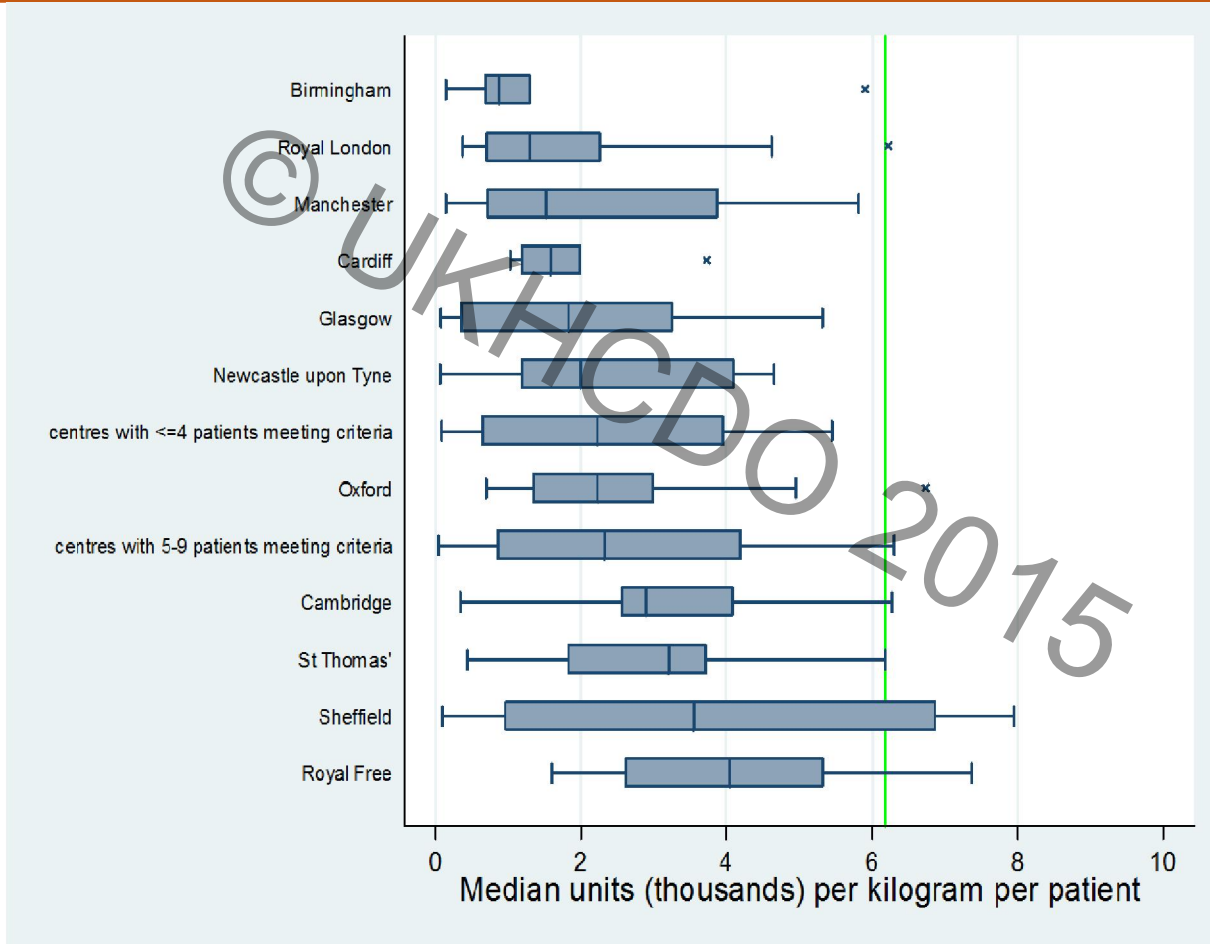
Data table for Figure 29

| Haemophilia Centre | Patients treated | Patients treated with weight reported | Total Units | Median Units | Median Units/Kg |
|--|------------------|---------------------------------------|-------------|--------------|-----------------|
| Oxford | 9 | 9 | 1,248,500 | 73,500 | 2,805 |
| Bristol | 5 | 5 | 742,500 | 107,000 | 5,000 |
| Birmingham | 6 | 6 | 477,750 | 76,625 | 2,259 |
| North Hampshire | 5 | 5 | 513,250 | 111,000 | 3,688 |
| Manchester | 11 | 11 | 1,363,000 | 108,000 | 3,972 |
| Liverpool | 5 | 4 | 300,500 | 8,000 | 1,028 |
| Great Ormond Street | 24 | 22 | 3,462,477 | 132,500 | 4,313 |
| Newcastle upon Tyne | 7 | 7 | 1,173,000 | 168,000 | 4,382 |
| Centres with <=4 patients meeting criteria | 47 | 34 | 6,088,404 | 107,000 | 3,239 |

Data table for Figure 30

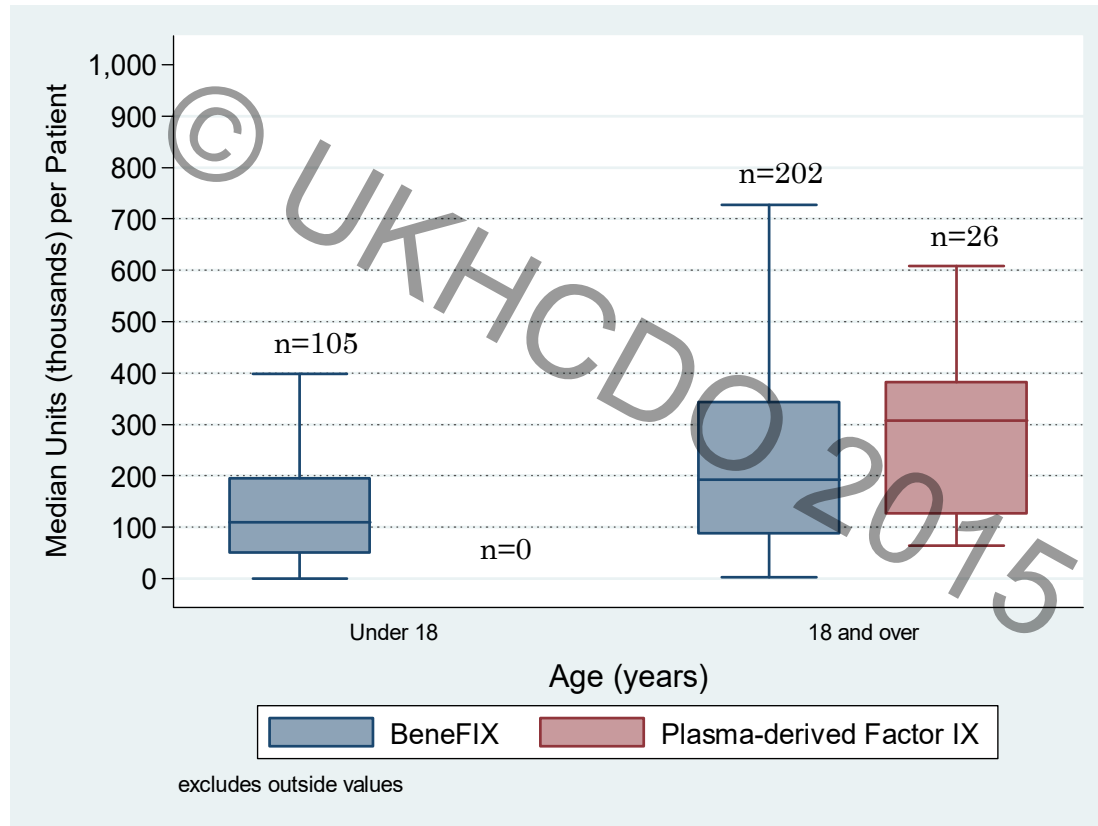
| Haemophilia Centre | Patients treated | Patients treated with weight reported | Total Units | Median Units | Median Units/Kg |
|--|------------------|---------------------------------------|-------------|--------------|-----------------|
| Birmingham | 10 | 6 | 2,358,000 | 167,500 | 869 |
| Cambridge | 13 | 12 | 3,242,750 | 257,000 | 2,892 |
| Cardiff | 10 | 5 | 1,626,447 | 120,366 | 1,580 |
| Glasgow | 22 | 21 | 4,087,000 | 160,000 | 1,834 |
| Manchester | 22 | 10 | 5,060,924 | 160,220 | 1,516 |
| Newcastle upon Tyne | 10 | 9 | 2,146,000 | 155,000 | 1,996 |
| Oxford | 16 | 16 | 3,563,135 | 189,000 | 2,227 |
| Royal Free | 28 | 27 | 8,883,424 | 285,000 | 4,053 |
| Royal London | 13 | 10 | 2,356,520 | 120,000 | 1,295 |
| Sheffield | 12 | 7 | 3,975,589 | 373,640 | 3,551 |
| St Thomas' | 17 | 14 | 4,291,000 | 256,000 | 3,201 |
| Centres with ≤4 patients meeting criteria | 49 | 31 | 9,225,550 | 160,500 | 2,222 |
| Centres with 5-9 patients meeting criteria | 34 | 21 | 7,451,500 | 189,500 | 2,321 |

Figure 30 Annual FIX usage 2014/15 in Severe Haemophilia B patients aged 18 years or more with no current inhibitor, by centre, ranked by median usage



Indicated outside values show where a patient's usage is more than 1.5 times the iqr from the nearest quartile at centre level
 The vertical green line indicates the 95th percentile of units, regardless of centre 6,181 IU/kg

Figure 31 Severe Haemophilia B patients with no current inhibitor using only one product between April 2014 & March 2015: median usage



(Mann-Whitney U test: 18 years and over: $p=0.02$).

Table 10 Products used to treat Haemophilia B (including inhibitors) between April 2014 and March 2015

| Manufacturer | Product | Total Units |
|-----------------------|---------------------------|-------------------|
| Baxter | FEIBA | 2,079,000 |
| Biotest | Haemonine | 210,000 |
| BPL | Replenine | 4,340,305 |
| CSL Behring | Beriplex | 31,000 |
| | Mononine | 566,000 |
| Grifols | Alphanine | 5,174,500 |
| Novo Nordisk | NovoSeven (mg) | 7,079 |
| Pfizer | BeneFIX | 73,542,235 |
| Various Manufacturers | Investigational Factor IX | 5,194,750 |
| Total | | 91,144,869 |

Table 11 Factor IX units used by UK Haemophilia Centres

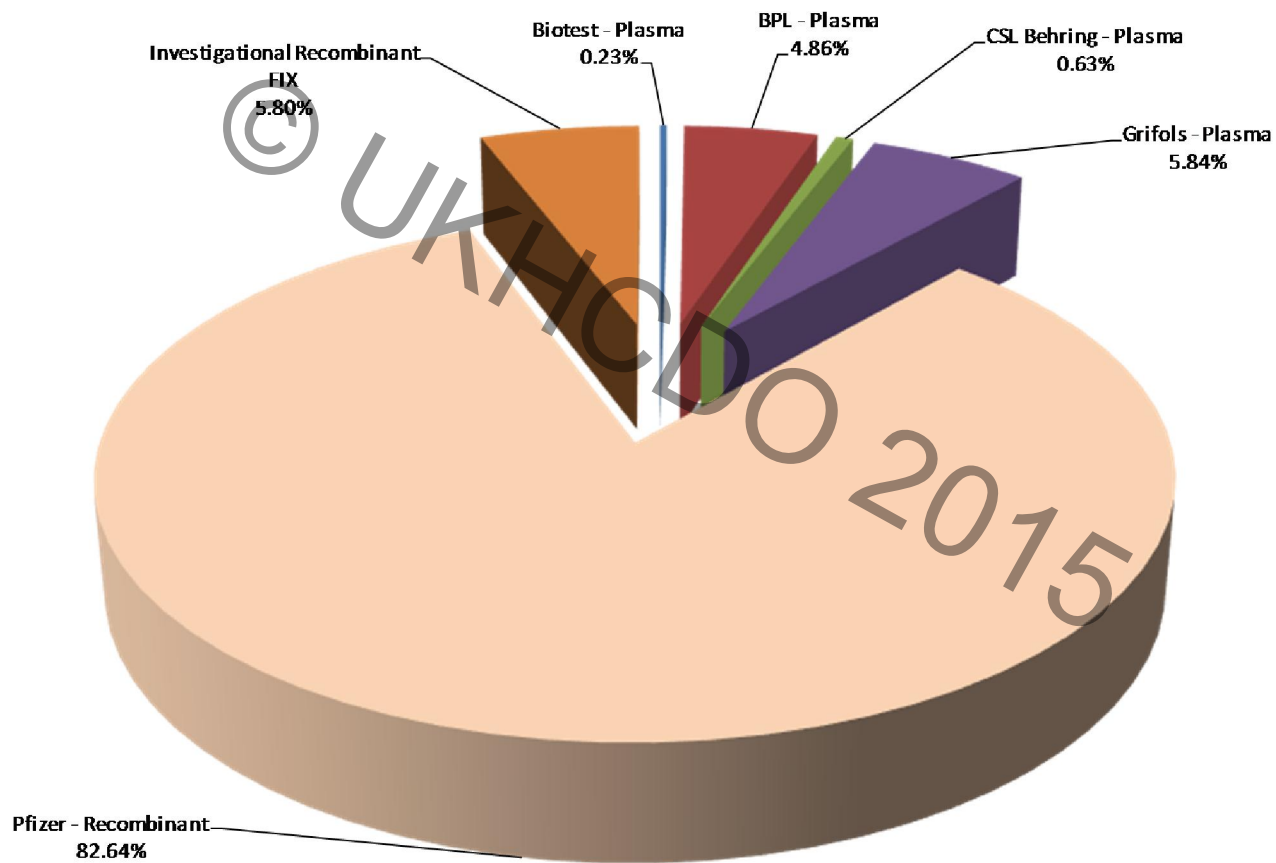
| Coagulation Defect | Patients Treated | Plasma FIX (IU) | Recombinant FIX (IU) | Investigational FIX (IU) | Total FIX (IU) |
|-----------------------|------------------|-------------------|----------------------|--------------------------|-------------------|
| Haemophilia A | 1 | - | 2,500 | - | |
| Haemophilia B | 626 | 10,290,805 | 73,737,235 | 5,194,750 | 89,222,790 |
| Haemophilia B Carrier | 34 | 69,050 | 227,000 | - | 296,050 |
| Combined Diagnoses | 2 | - | 63,000 | - | 63,000 |
| Total | 663 | 10,359,855 | 74,029,735 | 5,194,750 | 89,581,840 |

N.B:

Haemophilia B includes patients with FIX Leyden

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

Figure 32 Market Share of factor IX concentrates issued by UK Haemophilia Centres during 2014/15



VON WILLEBRAND DISEASE

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Table 12 Patients with Von Willebrand Disease currently registered, by severity, age group and gender

| von Willebrand disease | <18 years (VWD Activity iu/dl) | | | | ≥18 years (VWD Activity iu/dl) | | | | Total | Treated |
|--|-----------------------------------|-----|-----|-----------|-----------------------------------|-------|-----|-----------|---------------|------------|
| | <30 | ≥30 | N/K | Sub Total | <30 | ≥30 | N/K | Sub Total | | |
| Males | | | | | | | | | | |
| Type 1 | 168 | 301 | 40 | 509 | 392 | 622 | 130 | 1,144 | 1,653 | 66 |
| Type 2A | 53 | 15 | 5 | 73 | 145 | 40 | 11 | 196 | 269 | 53 |
| Type 2B | 15 | 5 | 0 | 20 | 36 | 19 | 2 | 57 | 77 | 19 |
| Type 2M | 18 | 6 | 2 | 26 | 54 | 11 | 3 | 68 | 94 | 27 |
| Type 2N | 0 | 3 | 0 | 3 | 5 | 17 | 5 | 27 | 30 | 0 |
| Type 2 Unspecified | 10 | 9 | 0 | 19 | 20 | 7 | 3 | 30 | 49 | 8 |
| Type 3 | 34 | | | 34 | 55 | | | 55 | 89 | 61 |
| Type Unreported | 141 | 230 | 21 | 392 | 457 | 614 | 86 | 1,157 | 1,549 | 84 |
| Sub Total Males | | | | | | | | | 3,810 | 318 |
| Females | | | | | | | | | | |
| Type 1 | 122 | 256 | 30 | 408 | 596 | 1,684 | 273 | 2,553 | 2,961 | 96 |
| Type 2A | 43 | 11 | 3 | 57 | 194 | 70 | 13 | 277 | 334 | 69 |
| Type 2B | 8 | 10 | 2 | 20 | 57 | 35 | 2 | 94 | 114 | 18 |
| Type 2M | 21 | 9 | 1 | 31 | 89 | 25 | 8 | 122 | 153 | 21 |
| Type 2N | 1 | 1 | 0 | 2 | 15 | 41 | 7 | 63 | 65 | 7 |
| Type 2 Unspecified | 5 | 0 | 0 | 5 | 34 | 19 | 5 | 58 | 63 | 5 |
| Type 3 | 19 | | | 19 | 47 | | | 47 | 66 | 44 |
| Type Unreported | 160 | 217 | 17 | 394 | 729 | 1,507 | 236 | 2,472 | 2,866 | 147 |
| Sub Total Females | | | | | | | | | 6,622 | 407 |
| Grand Total - Males and Females | | | | | | | | | 10,432 | 725 |

Table 13 New Registrations of Von Willebrand Disease between April 2014 & March 2015, by age at mid-year, 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 | 20 | 37 | 0 | 57 | 8 | 7 | 0 | 15 | 72 |
| Type 2A | 0 | 1 | 0 | 1 | 6 | 0 | 1 | 7 | 8 |
| Type 2B | 2 | 0 | 0 | 2 | 2 | 0 | 0 | 2 | 4 |
| Type 2M | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 2 |
| Type 2N | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 2 | 3 |
| Type 2 Unspecified | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 2 |
| Type 3 | 4 | | | 4 | 0 | | | 0 | 4 |
| Type Unreported | 20 | 19 | 2 | 41 | 11 | 10 | 0 | 21 | 62 |
| Sub Total Males | | | | | | | | | 157 |
| Females | | | | | | | | | |
| Type 1 | 10 | 26 | 0 | 36 | 21 | 49 | 1 | 71 | 107 |
| Type 2A | 6 | 1 | 0 | 7 | 6 | 2 | 0 | 8 | 15 |
| Type 2B | 0 | 1 | 0 | 1 | 2 | 4 | 0 | 6 | 7 |
| Type 2M | 5 | 2 | 0 | 7 | 3 | 0 | 0 | 3 | 10 |
| Type 2N | 0 | 1 | 0 | 1 | 0 | 3 | 0 | 3 | 4 |
| Type 2 Unspecified | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Type 3 | 2 | | | 2 | 1 | | | 1 | 3 |
| Type Unreported | 14 | 31 | 0 | 45 | 22 | 53 | 1 | 76 | 121 |
| Sub Total Females | | | | | | | | | 267 |
| Grand Total - Males and Females | | | | | | | | | 424 |

Table 14 Von Willebrand types updated since 2013/14

| VW Old Type | Total | VW New Type | | | | | | |
|--------------------|--------------|--------------|--------------------|------------|-----------|-----------|-----------|-----------|
| | | Type 1 | Type 2 Unspecified | Type 2A | Type 2B | Type 2M | Type 2N | Type 3 |
| Type 1 | 45 | - | 1 | 16 | 7 | 17 | 2 | 2 |
| Type 2 Unspecified | 35 | 5 | - | 22 | 5 | 3 | - | - |
| Type 2A | 12 | 8 | - | - | 4 | - | - | - |
| Type 2B | 6 | 2 | - | 4 | - | - | - | - |
| Type 2M | 8 | 7 | - | 1 | - | - | - | - |
| Type 2N | 2 | 2 | - | - | - | - | - | - |
| Type 3 | 5 | 4 | - | 1 | - | - | - | - |
| Type Unreported | 2,190 | 1,613 | 28 | 299 | 78 | 69 | 32 | 71 |
| Grand Total | 2,303 | 1,641 | 29 | 343 | 94 | 89 | 34 | 73 |

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Table 15 Concentrates used to treat von Willebrand Disease (including inhibitors) between April 2014 and March 2015

| Manufacturer | Product | Total Units |
|--------------------|----------------|-------------|
| Bayer | Kogenate | 1,250 |
| BPL | FVIII 8Y | 27,000 |
| | Optivate | 210,000 |
| CSL Behring | Haemate P | 12,720,500 |
| | Voncento | 1,336,400 |
| Grifols | Alphanate | 1,143,000 |
| LFB Biomedicaments | Wilfactin | 25,000 |
| | Willfact | 458,000 |
| Novo Nordisk | NovoSeven (mg) | 137 |
| Octapharma | Wilate | 6,571,150 |
| Pfizer | ReFacto AF | 4,000 |

Units in IU unless otherwise stated

INHIBITORS: CONGENITAL AND ACQUIRED
HAEMOPHILIA A, HAEMOPHILIA B AND VON
WILLEBRAND DISEASE

Table 16 Inhibitors by Disease Severity – Haemophilia A, Haemophilia B & von Willebrand Disease

| Coagulation Defect | Severity / Subtype | In Register * | Inhibitors | | |
|------------------------|--------------------|---------------|----------------------|------------------|------------------|
| | | | Newly Reported n (%) | Ongoing n (%) | Historical n (%) |
| Haemophilia A | ≤1 iu/dl | 2,034 | 22 (1.1) | 169 (8.3) | 435 (21.4) |
| | >1 and <5 iu/dl | 531 | 8 (1.5) | 24 (4.5) | 49 (9.2) |
| | ≥5 iu/dl | 3,256 | 4 (0.1) | 24 (0.7) | 71 (2.2) |
| | Unknown | 1 | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Total | 5,822 | 34 (0.6) | 217 (3.7) | 555 (9.5) |
| Haemophilia B | ≤1 iu/dl | 410 | 0 (0.0) | 9 (2.2) | 15 (3.7) |
| | >1 and <5 iu/dl | 240 | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | ≥5 iu/dl | 564 | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Total | 1,214 | 0 (0.0) | 9 (0.7) | 15 (1.2) |
| von Willebrand disease | Type 1 | 4,614 | 0 (0.0) | 0 (0.0) | 1 (0.0) |
| | Type 3 | 155 | 1 (0.6) | 7 (4.5) | 7 (4.5) |
| | Others | 5,663 | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| | Total | 10,432 | 1 (0.0) | 7 (0.1) | 8 (0.1) |

N.B: Haemophilia B includes patients with FIX Leyden

* Including patients not regularly treated

Table 17 Concentrates used to treat Inhibitors in *Congenital* bleeding disorders

| Manufacturer | Product | Haemophilia A | Haemophilia B | von Willebrand Disease | F.VII deficiency | Combined Diagnoses |
|-----------------------|-----------------------------|---------------|---------------|------------------------|------------------|--------------------|
| Baxter | Advate | 14,278,750 | - | - | - | 5,000 |
| | FEIBA | 32,104,208 | 2,079,000 | - | - | 805,500 |
| Bayer | Kogenate | 3,568,500 | - | 1,250 | - | - |
| BPL | FVIII 8Y | 283,780 | - | - | - | - |
| | Optivate | 1,668,000 | - | - | - | - |
| CSL Behring | Haemate P | 121,000 | - | 227,000 | - | - |
| | Helixate Nexgen | 4,365,750 | - | - | - | - |
| | Voncento | - | - | 26,000 | - | - |
| Grifols | Fanhdi | 16,220,000 | - | - | - | - |
| Novo Nordisk | NovoSeven (mg) | 24,018 | 7,069 | 135 | 555 | 241 |
| Octapharma | Nuwiq | 107,000 | - | - | - | - |
| | Octanate | 2,877,000 | - | - | - | - |
| Pfizer | Benefix | - | 284,000 | - | - | - |
| | ReFacto AF | 6,429,000 | - | - | - | - |
| Various Manufacturers | Investigational Factor VIII | 377,750 | - | - | - | - |

Table 18 Concentrates used to treat Acquired Inhibitors

| Manufacturer | Product | Acquired Haemophilia A | Acquired von Willebrands | Acquired Other |
|----------------------|-----------------|------------------------|--------------------------|----------------|
| Baxter | Advate | 168,500 | - | - |
| | FEIBA | 4,584,000 | - | - |
| Bayer | Kogenate | 92,000 | - | - |
| CSL Behring | Haemate P | - | 455,500 | - |
| | Helixate Nexgen | 2,000 | - | - |
| | Voncento | - | 24,000 | - |
| Grifols | Alphanate | 6,000 | - | - |
| | Fanhdi | 236,000 | - | - |
| IDEC Pharmaceuticals | Rituximab | 13,274 | - | - |
| Novo Nordisk | NovoSeven (mg) | 1,759 | 1 | 50 |
| Octapharma | Octaplex | 2,500 | - | - |
| | Wilate | - | 203,011 | - |

Units in IU unless otherwise stated

Table 19 FEIBA usage: breakdown by diagnosis

| Coagulation Defect | Total (iu) |
|---------------------------|-------------------|
| Haemophilia A | 32,135,208 |
| Haemophilia B | 2,079,000 |
| F.XI Deficiency | 5,000 |
| Acquired Haemophilia A | 4,584,000 |
| Combined Diagnoses | 805,500 |
| | 39,608,708 |

Table 20 NovoSeven usage: breakdown by diagnosis

| Coagulation Defect | Total (mg) |
|---------------------------------|---------------|
| Haemophilia A | 24,056 |
| Haemophilia B | 7,079 |
| von Willebrand disease | 138 |
| Acquired Deficiency (other) | 50 |
| Acquired Haemophilia A | 1,759 |
| Acquired von Willebrand Disease | 1 |
| Bernard Soulier | 99 |
| F.V deficiency | 36 |
| F.VII deficiency | 2,564 |
| F.X deficiency | 2 |
| F.XI Deficiency | 35 |
| Glanzmann's Thrombasthenia | 1,562 |
| Other combined diagnoses | 243 |
| Platelet defects | 446 |
| Unclassified | 7 |
| | 38,077 |

RARER BLEEDING DISORDERS

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Table 21 Patients with rarer types of bleeding disorders registered and treated April 2014 – March 2015

| Coagulation Defect | Number of Patients in Register | | | Treated | % Treated |
|---|--------------------------------|--------------|--------------|------------|--------------|
| | Total | Males | Females | | |
| Probable von Willebrand disease | 163 | 42 | 121 | 17 | 10.43% |
| Platelet-type Pseudo von Willebrand Disease | 14 | 6 | 8 | 0 | 0.00% |
| F.V deficiency | 197 | 81 | 116 | 16 | 8.12% |
| F.VII deficiency | 1,044 | 508 | 536 | 53 | 5.08% |
| F.X deficiency | 231 | 99 | 132 | 37 | 16.02% |
| F.XI Deficiency | 2,666 | 1,135 | 1,531 | 66 | 2.48% |
| F.XIII Deficiency | 65 | 37 | 28 | 54 | 83.08% |
| Prothrombin Deficiency | 12 | 5 | 7 | 4 | 33.33% |
| Afibrinogenemia | 9 | 7 | 2 | 9 | 100.00% |
| Dysfibrinogenemia | 349 | 142 | 207 | 13 | 3.72% |
| Hypofibrinogenemia | 63 | 23 | 40 | 4 | 6.35% |
| Fibrinogen Deficiency | 135 | 61 | 74 | 16 | 11.85% |
| Combined II+VII+IX+X Deficiency | 4 | 1 | 3 | 0 | 0.00% |
| Combined V+VIII Deficiency | 27 | 13 | 14 | 9 | 33.33% |
| Other combined diagnoses | 299 | 131 | 168 | 36 | 12.04% |
| Acquired Haemophilia A | 421 | 209 | 212 | 96 | 22.80% |
| Acquired Haemophilia B | 2 | 2 | 0 | 0 | 0.00% |
| Acquired von Willebrands | 106 | 54 | 52 | 28 | 26.42% |
| Acquired Prothrombin Deficiency | 3 | 2 | 1 | 0 | 0.00% |
| Acquired F.XIII Deficiency | 2 | 1 | 1 | 0 | 0.00% |
| Acquired F.V Deficiency | 3 | 0 | 3 | 1 | 33.33% |
| Acquired Deficiency (other) | 8 | 7 | 1 | 1 | 12.50% |
| Glanzmann's Thrombasthenia | 118 | 49 | 69 | 37 | 31.36% |
| Bernard Soulier | 80 | 40 | 40 | 10 | 12.50% |
| Other platelet defects | 1,975 | 627 | 1,348 | 84 | 4.25% |
| Miscellaneous | 217 | 62 | 155 | 11 | 5.07% |
| Unclassified bleeding disorder | 271 | 40 | 231 | 20 | 7.38% |
| Haemophilia A with Liver Transplant | 8 | 8 | 0 | 0 | 0.00% |
| Haemophilia B with Liver Transplant | 3 | 3 | 0 | 0 | 0.00% |
| von Willebrand with Liver Transplant | 1 | 1 | 0 | 0 | 0.00% |
| Total | 8,496 | 3,396 | 5,100 | 622 | 7.32% |

Table 22 Patients with selected rarer bleeding disorders registered and treated April 2014 – March 2015, 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 | 47 | 13 | 150 | 3 | 0 | 0 | 197 | 16 |
| F.VII deficiency | 118 | 22 | 926 | 31 | 0 | 0 | 1044 | 53 |
| F.X deficiency | 38 | 28 | 193 | 9 | 0 | 0 | 231 | 37 |
| F.XI Deficiency | 221 | 18 | 2442 | 48 | 2 | 0 | 2665 | 66 |
| Total | 424 | 81 | 3,711 | 91 | 2 | - | 4,137 | 172 |

| Coagulation Defect | <2 | | ≥2 | | N/K | | Total | |
|--------------------|-----------|-----------|-----------|-----------|----------|----------|-----------|-----------|
| | In Reg | Treated | In Reg | Treated | In Reg | Treated | In Reg | Treated |
| F.XIII Deficiency | 38 | 35 | 27 | 19 | 0 | 0 | 65 | 54 |
| Total | 38 | 35 | 27 | 19 | - | - | 65 | 54 |

| F.XIII Deficiency IU/dl | In Reg | Treated | Treated % |
|-------------------------|-----------|-----------|-----------|
| <2 | 38 | 35 | 92.1 |
| 2 - <5 | 7 | 7 | 100.0 |
| 5 - <10 | 12 | 10 | 83.3 |
| 10 - <15 | 2 | 2 | 100.0 |
| 15 - <25 | 1 | 0 | 0.0 |
| ≥25 | 5 | 0 | 0.0 |
| Total | 65 | 54 | |

64.8% <2 IU/dl treated
29.2% of patients with ≥2 IU/dl treated

Table 23 New registrations of rarer bleeding disorders between April 2014 & March 2015 showing their coagulation defect and gender

| Coagulation Defect | Male | Female | Total | ↑ / ↓ from 2013/14 |
|---|------------|------------|--------------|--------------------------|
| Platelet-type Pseudo von Willebrand Disease | 3 | 3 | 6 | ↑ |
| Probable von Willebrand disease | 8 | 18 | 26 | ↓ |
| F.V deficiency | 16 | 21 | 37 | ↑ |
| F.VII deficiency | 56 | 39 | 95 | ↓ |
| F.X deficiency | 12 | 9 | 21 | ↑ |
| F.XI Deficiency | 99 | 141 | 240 | ↓ |
| F.XIII Deficiency | 2 | 0 | 2 | ↓ |
| Afibrinogenemia | 4 | 1 | 5 | N/A |
| Dysfibrinogenemia | 27 | 37 | 64 | ↓ |
| Hypofibrinogenemia | 16 | 24 | 40 | ↑ |
| Fibrinogen Deficiency | 1 | 2 | 3 | N/A |
| Prothrombin Deficiency | 0 | 1 | 1 | N/A |
| Acquired Haemophilia A | 58 | 37 | 95 | ↑ |
| Acquired Haemophilia B | 1 | 0 | 1 | N/A |
| Acquired Prothrombin Deficiency | 1 | 1 | 2 | N/A |
| Acquired von Willebrands | 9 | 10 | 19 | ↑ |
| Acquired Deficiency (other) | 1 | 0 | 1 | ↓ |
| Glanzmann's Thrombasthenia | 2 | 2 | 4 | ↓ |
| Bernard Soulier | 6 | 2 | 8 | ↑ |
| Other platelet defects | 75 | 173 | 248 | ↑ |
| Other combined diagnoses | 16 | 19 | 35 | ↑ |
| Miscellaneous | 5 | 11 | 16 | ↓ |
| Unclassified bleeding disorder | 11 | 59 | 70 | ↑ |
| Total | 429 | 610 | 1,039 | ↑ |

Table 24 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 |
|-----------------------|-----------------------|----------------|------------------|-------------|---------------------|----------------|-----------------|-------------------|
| Baxter | FEIBA | - | - | - | - | - | 5,000 | - |
| | FVII | - | 42,000 | - | - | - | - | - |
| BPL | FX | - | - | - | - | 347,300 | - | - |
| | FXI | - | - | - | - | - | 200,715 | - |
| CSL Behring | Beriplex | - | - | - | - | 671,750 | - | - |
| | Fibrogammin P | - | - | - | - | - | - | 649,668 |
| | Haemate P | - | 2,000 | - | - | - | - | - |
| Novo Nordisk | NovoSeven (mg) | 36 | 2,564 | - | - | 2 | 35 | - |
| | NovoThirteen | - | - | - | - | - | - | 22,500 |
| Octapharma | Octaplas (units) | 940 | - | - | - | 15,000 | 5,069 | - |
| | Octaplex | 1,500 | - | - | - | 642,375 | - | - |
| Pfizer | BeneFIX | - | - | 195,000 | 4,500 | - | - | - |
| Various Manufacturers | Investigational FX | - | - | - | - | * | - | - |
| | Investigational FXIII | - | - | - | - | - | - | * |

Units in IU unless otherwise stated
*Anonymised for confidentiality purposes

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ADVERSE EVENTS

Table 25 Adverse Events reported between April 2014 & March 2015

| Adverse Event | Number of Patients | Number of Events |
|---------------------|--------------------|------------------|
| Allergy Event | 4 | 5 |
| Infection Event | 0 | 0 |
| Inhibitor Event | 35 | 35 |
| Malignancy Event | 1 | 1 |
| Other Event | 0 | 0 |
| Poor Efficacy Event | 0 | 0 |
| Thrombotic Event | 1 | 2 |
| Total | 41 | 43 |

See table 16 for breakdown of inhibitors by disease severity in Haemophilia A, B and von Willebrand disease

Table 27 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 batches | Combined |
| Current status of ‘at risk’ patients | Alive | 699 | 2638 | 3337 |
| | Dead | 110 | 574 | 684 |
| | Total | 809 | 3212 | 4021 |
| Sex | M | 769 | 2636 | 3405 |
| | F | 40 | 576 | 616 |
| Current age band of living ‘at risk’ patients | 0-19 | 2 | 43 | 45 |
| | 20-39 | 346 | 852 | 1198 |
| | 40-59 | 258 | 1073 | 1331 |
| | 60-79 | 87 | 558 | 645 |
| | 80+ | 6 | 110 | 116 |
| | Not known | 0 | 2 | 2 |

These data were last updated on 30/06/2015

MORBIDITY AND MORTALITY

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Table 28 Causes of death in patients with Haemophilia A, Haemophilia B and all Carriers of Haemophilia A & B

| Cause of Death | Severity (factor level iu/dl) | | | | Total |
|--------------------------|-------------------------------|-----------|-----------|----------|-----------|
| | ≤1 | >1 and <5 | ≥5 | N/K | |
| Accident | 0 | 1 | 0 | 0 | 1 |
| ARDS | 2 | 0 | 0 | 0 | 2 |
| Carcinoma | 1 | 2 | 4 | 0 | 7 |
| Cerebral haemorrhage | 3 | 2 | 2 | 0 | 7 |
| COAD | 0 | 0 | 2 | 0 | 2 |
| Hepatocellular Carcinoma | 1 | 0 | 0 | 0 | 1 |
| Infection (Bacterial) | 0 | 1 | 3 | 0 | 4 |
| Ischaemic Heart Disease | 0 | 0 | 5 | 0 | 5 |
| Liver Failure | 0 | 0 | 1 | 0 | 1 |
| Stroke (Unknown) | 1 | 0 | 0 | 0 | 1 |
| Unknown | 10 | 2 | 28 | 1 | 41 |
| Total | 18 | 8 | 45 | 1 | 72 |

N.B: Includes FIX Leyden and FIX Leyden carriers

Table 29 Causes of death in other coagulation defects

| Coagulation Defect | Cause of Death | Total |
|-------------------------------------|--------------------------------|------------|
| Acquired Deficiency (other) | Unknown | 2 |
| | AIDS | 1 |
| Acquired Haemophilia A | Carcinoma | 2 |
| | Haemorrhage (Misc) | 1 |
| | Infection (Bacterial) | 4 |
| | Unknown | 32 |
| | Lymphoproliferative Malignancy | 3 |
| Acquired von Willebrand Disease | Unknown | 5 |
| | Liver Failure | 1 |
| Afibrinogenemia | Carcinoma | 1 |
| | Infection (Bacterial) | 1 |
| Dysfibrinogenemia | Ischaemic Heart Disease | 1 |
| | Liver Failure | 1 |
| | Unknown | 1 |
| | Infection (Bacterial) | 1 |
| F.V deficiency | Unknown | 1 |
| | Unknown | 1 |
| F.VII deficiency | Unknown | 6 |
| | Unknown | 2 |
| F.X deficiency | Carcinoma | 2 |
| | Infection (Bacterial) | 2 |
| | Peripheral vascular disease | 1 |
| | Unknown | 15 |
| | Ischaemic Heart Disease | 1 |
| Fibrinogen Deficiency | Unknown | 5 |
| | Unknown | 1 |
| Haemophilia A with Liver Transplant | Unknown | 1 |
| Haemophilia B with Liver Transplant | Unknown | 1 |
| Hypofibrinogenemia | Unknown | 1 |
| Miscellaneous | Unknown | 2 |
| Platelet defects | Infection (Bacterial) | 1 |
| | Unknown | 8 |
| Unclassified | Infection (Bacterial) | 1 |
| von Willebrand disease | Carcinoma | 5 |
| | Cardiomyopathy | 1 |
| | COAD | 2 |
| | Haemorrhage (Misc) | 1 |
| | Infection (Bacterial) | 4 |
| | Unknown | 32 |
| Total | | 152 |

Figure 33 Cumulative incidence chart of deaths from hepatocellular carcinoma or liver failure in UK patients with bleeding disorders 1969 - 2014

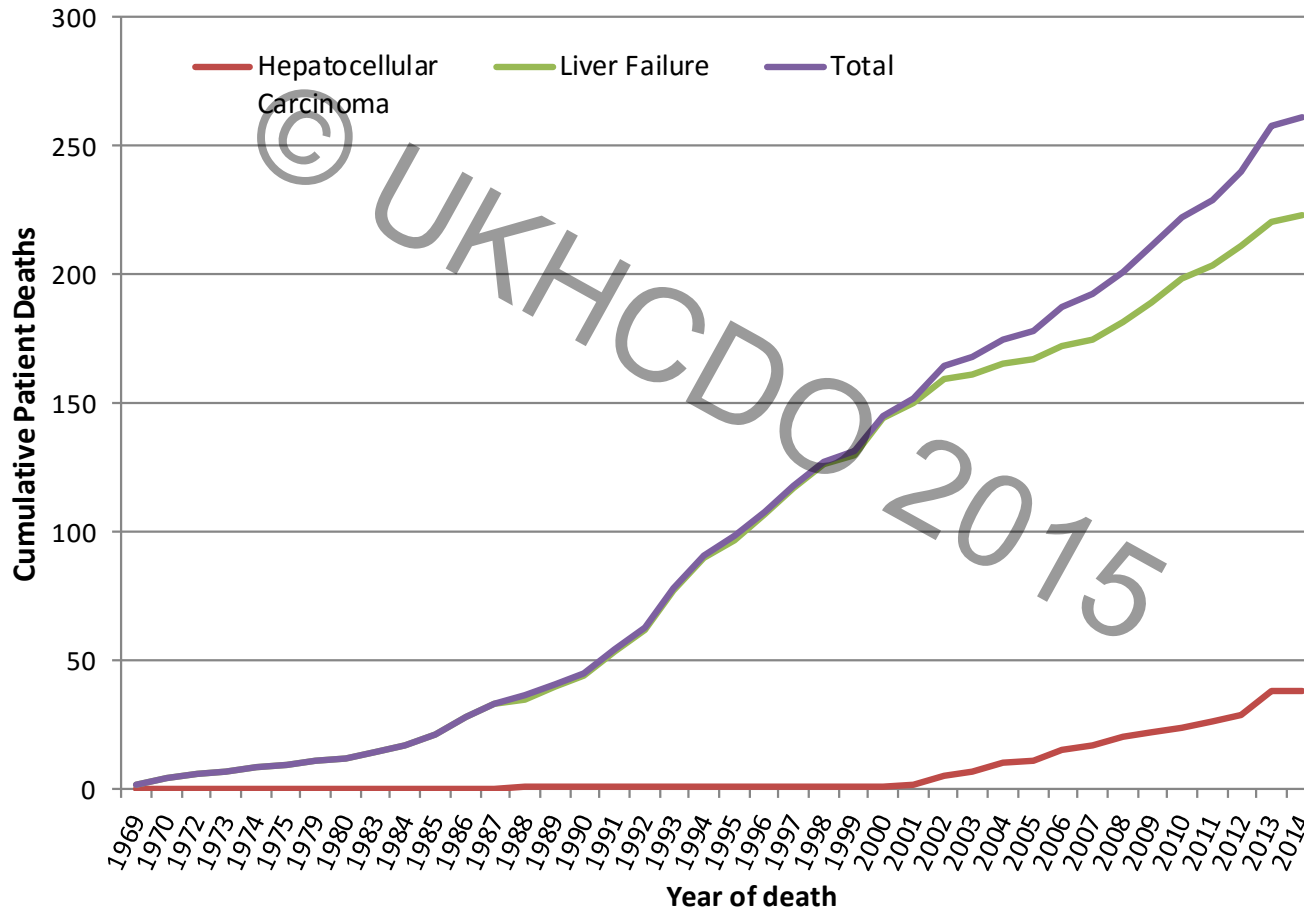


Figure 34 Total number of patients with Haemophilia A, Haemophilia B or von Willebrand Disease treated by UK Haemophilia Centres

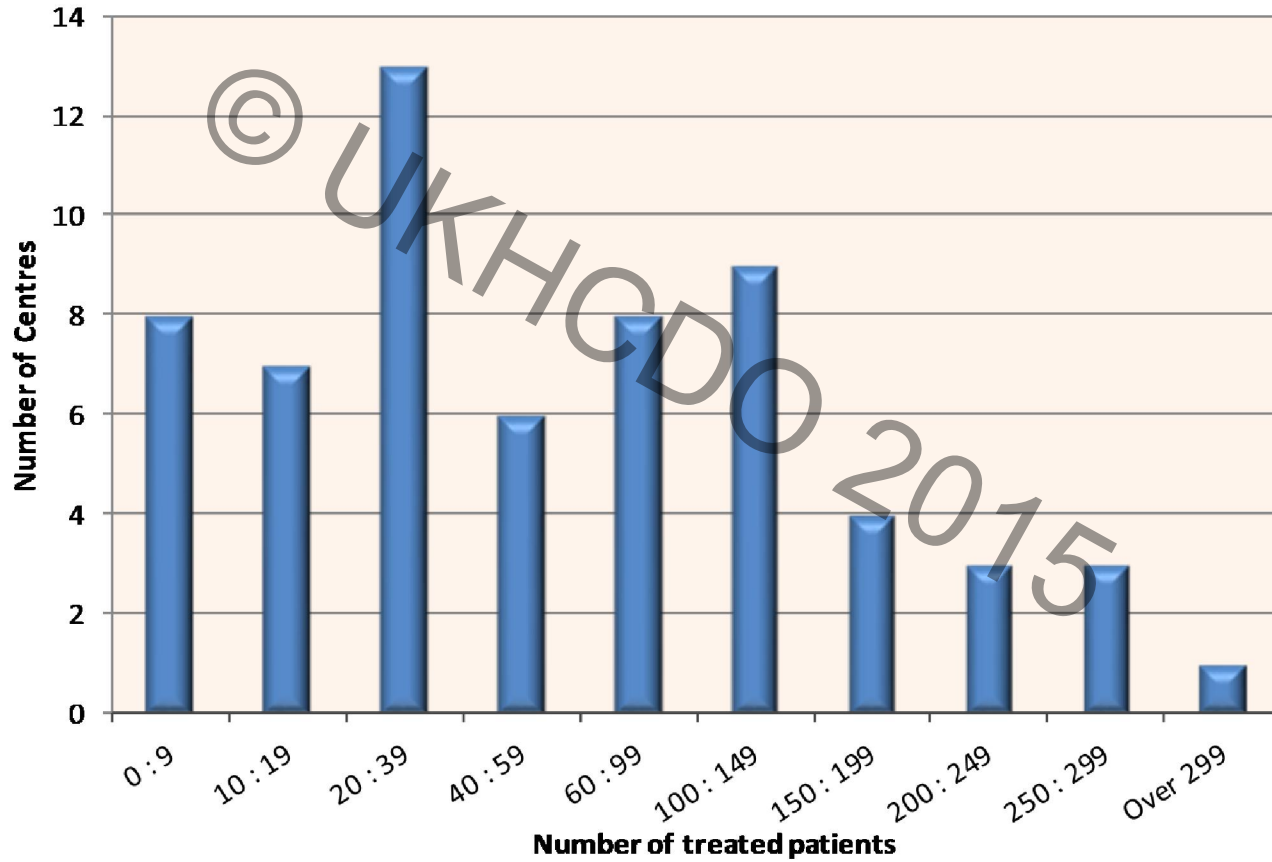
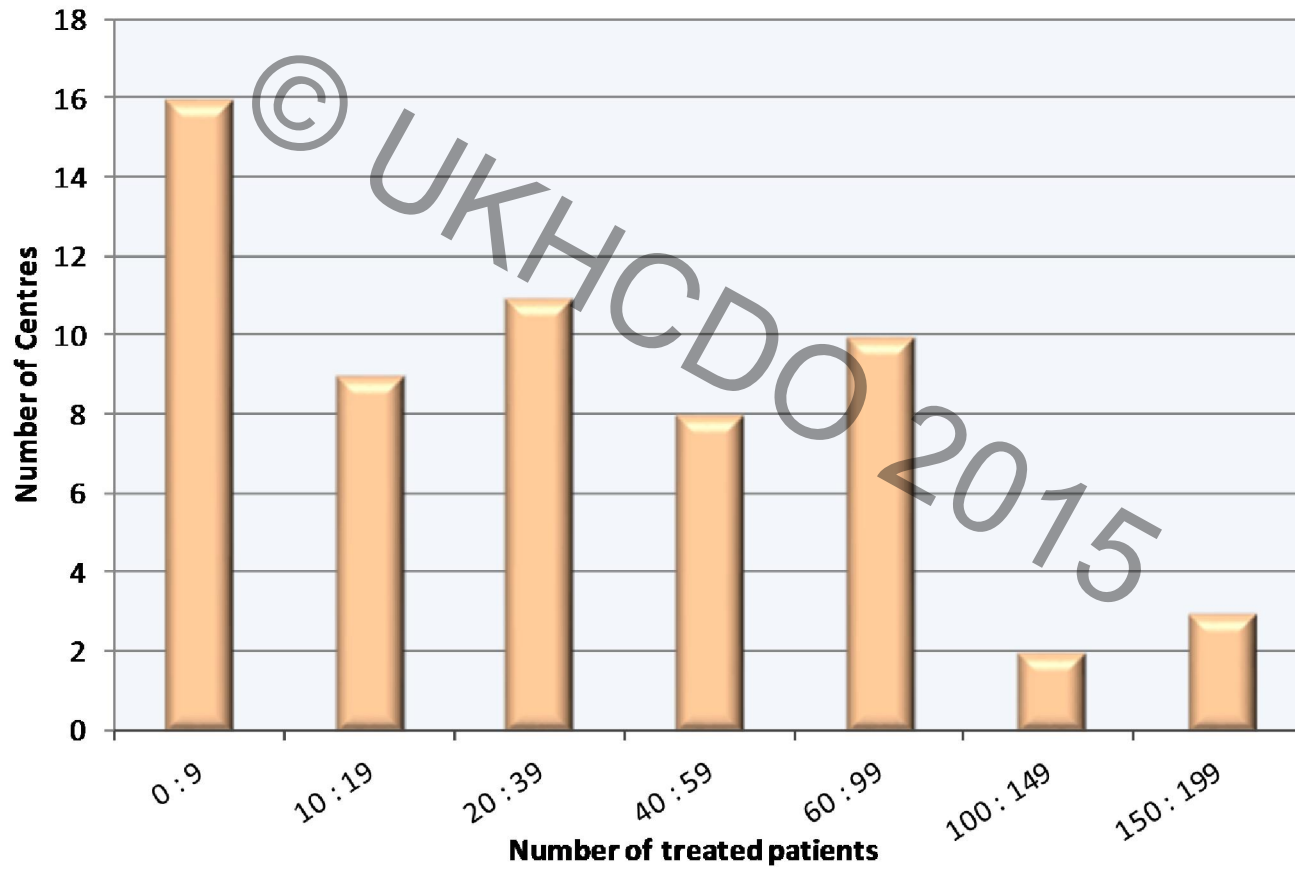


Figure 35 Total number of patients with severe Haemophilia A and Haemophilia B treated by UK Haemophilia Centres



Appendix 1 Quarterly Returns - Participating Centres

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