Construction of a national database and its virtues

Professor Frank Hill

The Children's Hospital, Birmingham.

& UKHCDO

Databases to facilitate haemophilia care

- Local
- Regional
- National
- International

Warnings

- Collect data that is useful.
- Data that will stand the test of time.
- Data that can be annonymised.
- Confidentiality of data.
- Conform to legislation on data confidentiality.

What should be kept?

- Diagnostic data.
- Annual treatment data.
- Genetic data.
- Adverse events/complications of treatment.
- Causes of death.

History: 1968.

- The Ministry of Health designated 36 Haemophilia Diagnostic and Treatment Centres.
- The first meeting of UK Haemophilia Centre Directors in Oxford.
- UKHCDO was formed.
- It was agreed to form a national register of patients with bleeding disorders.
- First report was issued in 1969.

The History of the Database:

- UKHCDO established the Database in Oxford in 1969.
  - Paper based system.
    - New diagnoses, adverse events and annual treatment data.
    - Used the Oxford University mainframe computer for analysis.
  - Producing annual reports and research.
  - Transferred to small fileserver (Access) in 1990s
  - Programs written by Miss Spooner.
  - 2 staff (Rosemary Spooner and Pat Wallace).
  - Funded by Oxford Health Authority.

The History of the Database:

- 2000: further technical redevelopment of the database begins.
  - Collaboration between Oxford (R Spooner) and Manchester (R Hollingsworth).
  - Still a paper-based system,
- 2002: Miss Spooner retired.
- 2002: Database relocated to Manchester.
  - Hosted by Manchester Royal Infirmary.
  - 2002: Process 2-year backlog of data input.

Development of the Database 2000-2008

- a thumbnail sketch!

- HCIS System: -
  - Piloted at RFH, Manchester and Oxford.
  - Installed across the country.
- All centres networked and all reporting on-line.
- Database and HCIS rewritten and extensively redeveloped from ACCESS to SQL-Server: -
  - Registrations increase from 16,000 to 25,000 in 8 yrs.
  - Data capture in real-time and quarterly.
  - Reporting now within year for commissioning and DH planning Cycle.
- UKHCDO Website

Where are we now.....

- Enhanced credibility underpins funding.
  - DH, HPA, Regulators, Pharma etc.
- In-house research function and support for the Working Parties.
- Continual national data cleaning exercises
  - Factor levels, VWD, NSTS, deaths etc.
- Comprehensive IT Strategy in place.
- On a firm footing to address future challenges.

Function of the NHD and UKHCDO Secretariat

- To support the activities of UKHCDO.
- To collect national statistics to provide data to promote improved healthcare for patients with bleeding disorders. e.g. :-
  - Improved haemophilia centre admin.
  - Research.
  - DOH, healthcare planning e.g.Recombinant rollout. vCJD.

UKHCDO Database: What is Collected and Reported.

- All new diagnoses and deaths are reported.
- Treatment data are collected.
- All adverse events are reported
  - inhibitors,
  - hepatitis HIV and vCJD data
  - and other adverse events.
- Currently annual reports of treatment and outcome data from the whole UK.
- Additional specific studies from Working parties.
- Useful for family studies and diagnosis tracing.

UKHCDO Database:

- Collates national statistics of diagnosis, treatment and complications of bleeding disorders.
- Attempts to provide a complete record.
- Named data but anonymous aggregate reports.
- Managed by UKHCDO Data Management W.P.

Data Management Working Party

- The Governing Body of NHD for at least 18 years.
- Custom dictates that it is chaired by VC of UKHCDO
- Meets about 3 times/year.
- Membership includes: -
  - Chair and VC of UKHCDO.
  - All Working Party Chairs.
  - 2 Specialist Commissioners.
  - Head of MDSAS.
  - Reps from Data Managers Forum, HNA, NHD.
  - CEO Haemophilia Society.
  - A patient.

Reorganisation of the Database

Traditional Approach using Paper Reports

- Collating data was very time-consuming
- Data entry errors.
- Tracking data entry etc.
- Storage and security problems.
- Analysis was cumbersome.

A fully Integrated Software Approach

- Patient-held information systems.
  - Advoy.
  - Dialogue
- Haemophilia Centre Management Software:
- On-line Patient Registration Software:
- UKHCDO Integrated Database.
- UKHCDO Website.

Centre System

Problems developing a national system: -

- Each Centre had a different software system.
- Usually unsupported for future developments and errors
- Data held in different formats and different fields etc.
- Difficult to retrieve data
- Relatively inflexible

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

Centre System

Solution

- The goal was to achieve a single system.
- Equivalent data across all centres.
- Ease of remote support – PC Anywhere
  - (NHSnet)
- Ease of collating data for National Research.
- Reduced staff workload / National Training Program.
- Regular software upgrades.

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

Centre System

Carries out all Haemophilia Centre Functions: -

- Stock control/ ordering
- Hospital admissions
- Treatments, bleeds, prophylaxis, home treatments, viral and clinical data.
- Contracting information (DHA / PCT)
- Comprehensive reporting features
- Easy to use

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Web System

Features

- All haemophilia centres networked.
- Prospective online entry of data
- New patient Registrations
- Adverse Events
- Death Details
- Patient Amendments
- View your own Patients on the NHD
- Lookup N.H.D. Patients

Web System

Patient Registration

Centre enters new Registration

N.H.D. Holding Database

Checked

Transferred to N.H.D.

System emails new N.H.D. number to Centre

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

National Haemophilia Database

- Fileserver in Manchester.
- Written in Sequel server.
- Data goes into holding database.
- Named data.
- Then checked before going into main database.
- Centres may view their own data only.
- Very secure in server hotel. Daily backups, emergency power supply, backups in fireproof safe.

Conclusion:

- Over the past 8 years, the database has had to expand and increase in complexity.
  - To meet the requirements of UKHCDO.
  - To respond to the changing demands of the NHS.
    - Recombinant for all, National Procurement, Benchmarking.
  - To secure its funding base.
- The Database is now a world leader in the field.
- This development will have to continue
  - To support the research requirements of the UKHCDO Working Parties.
  - To help UKHCDO meet future challenges
    - PBR, Centre Designation, National Procurement.

Principal Causes of Death: Haemophilia A, B and VW 1981-96.

Total:	**1457**
HIV-related	564
Total HIV	734
Unknown	180
Cerebral bleed	159
Cancer	129
Respiratory	89
Liver disease	78

Post-op problems	16
Accidental Death	28
RTA	12
Head injury	9
Suicide	15
Para-suicide	7

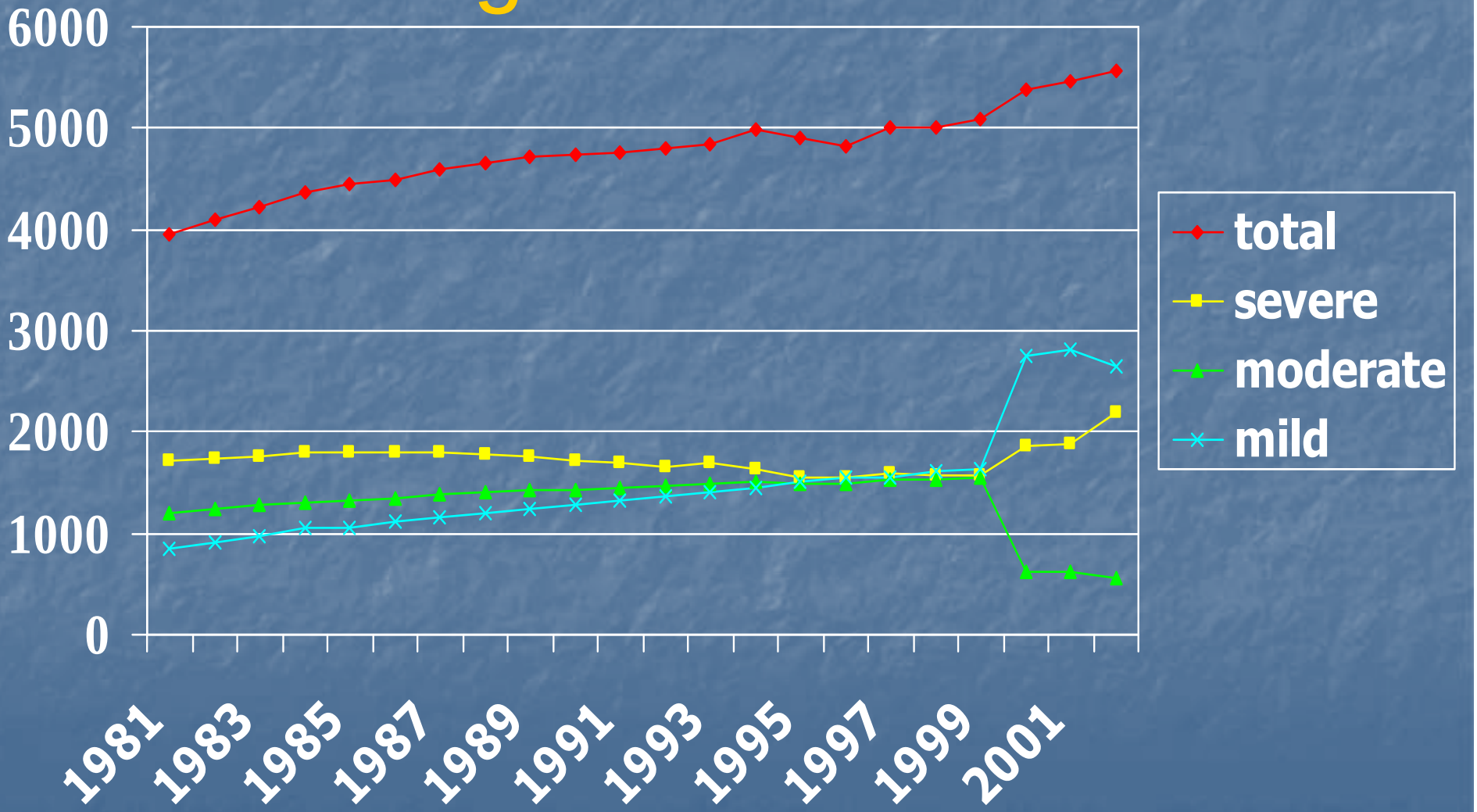
Major causes of death in Haemophilia A, B and VWD 1999-2002

Year	1999	2000	2001	2002
Cerebral Haemorrhage	7	17	8	12
Ischaemic Heart Disease	14	11	14	16
Cancer	12	14	15	17
Pneumonia	9	5	11	8
Liver Disease	5	16	6	9
HIV	8	5	4	4
Accident	4	5	3	4
Other	12	20	0	2

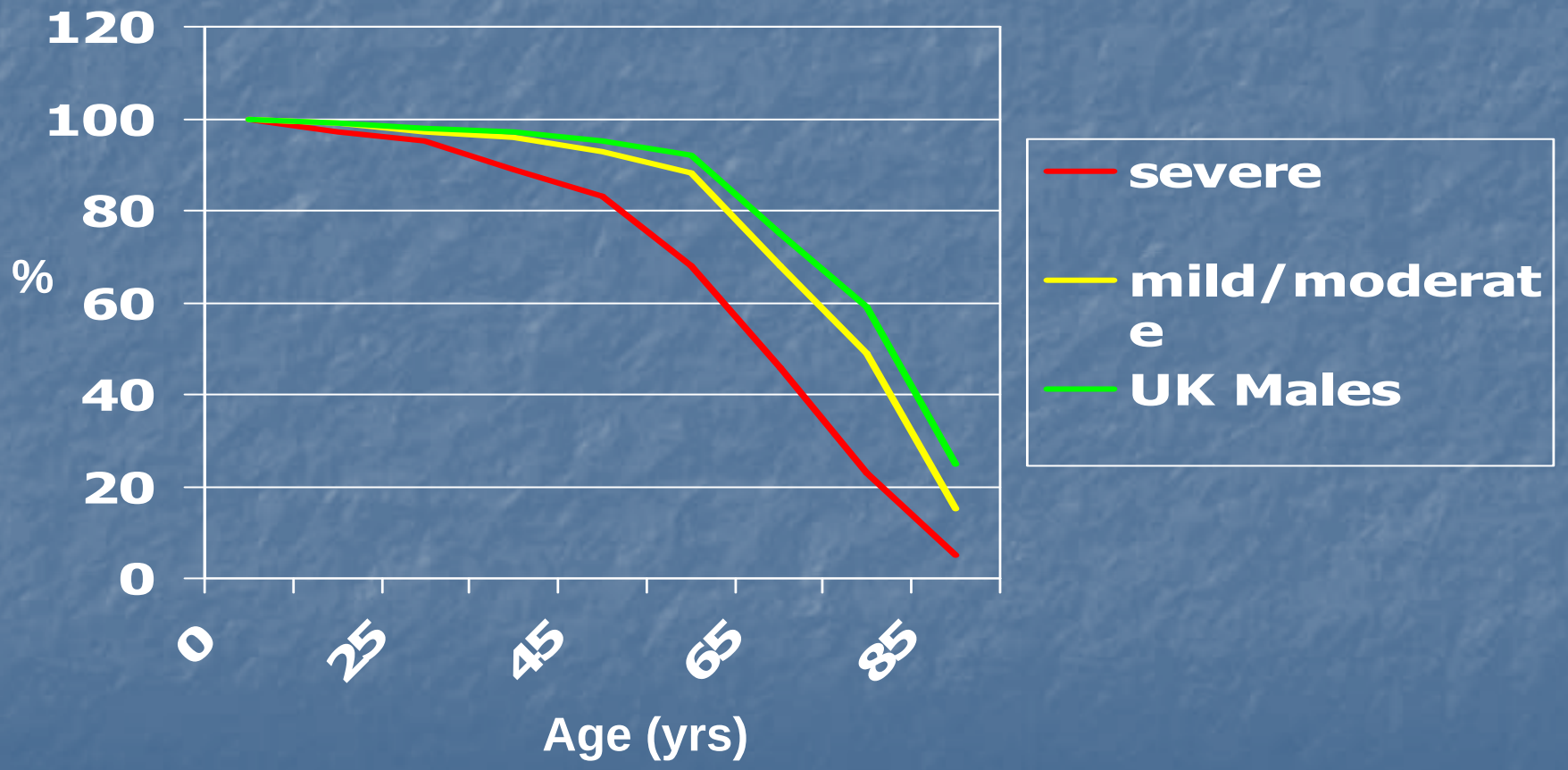
Adverse Events: 1999/2000

	1999	2000
New Inhibitors:	17	8
Recurrent Inhibitor	7	1
Transfusion reactions	3	8
Thrombosis/DIC	2	2
New Hepatitis	3	0

Haemophilia A Patients in-register 1981-2002

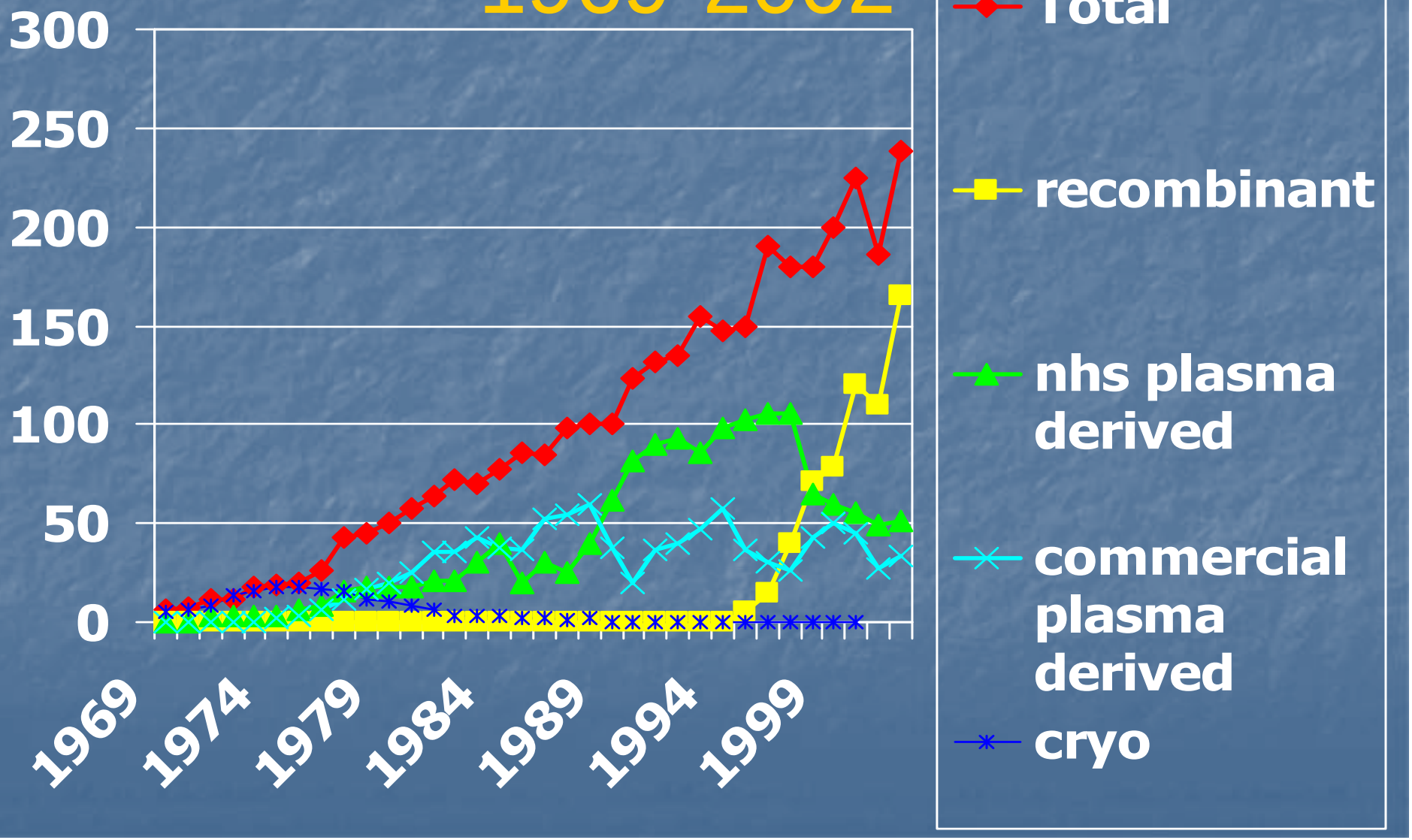


Survival in the UK Haemophilia population 1977-99

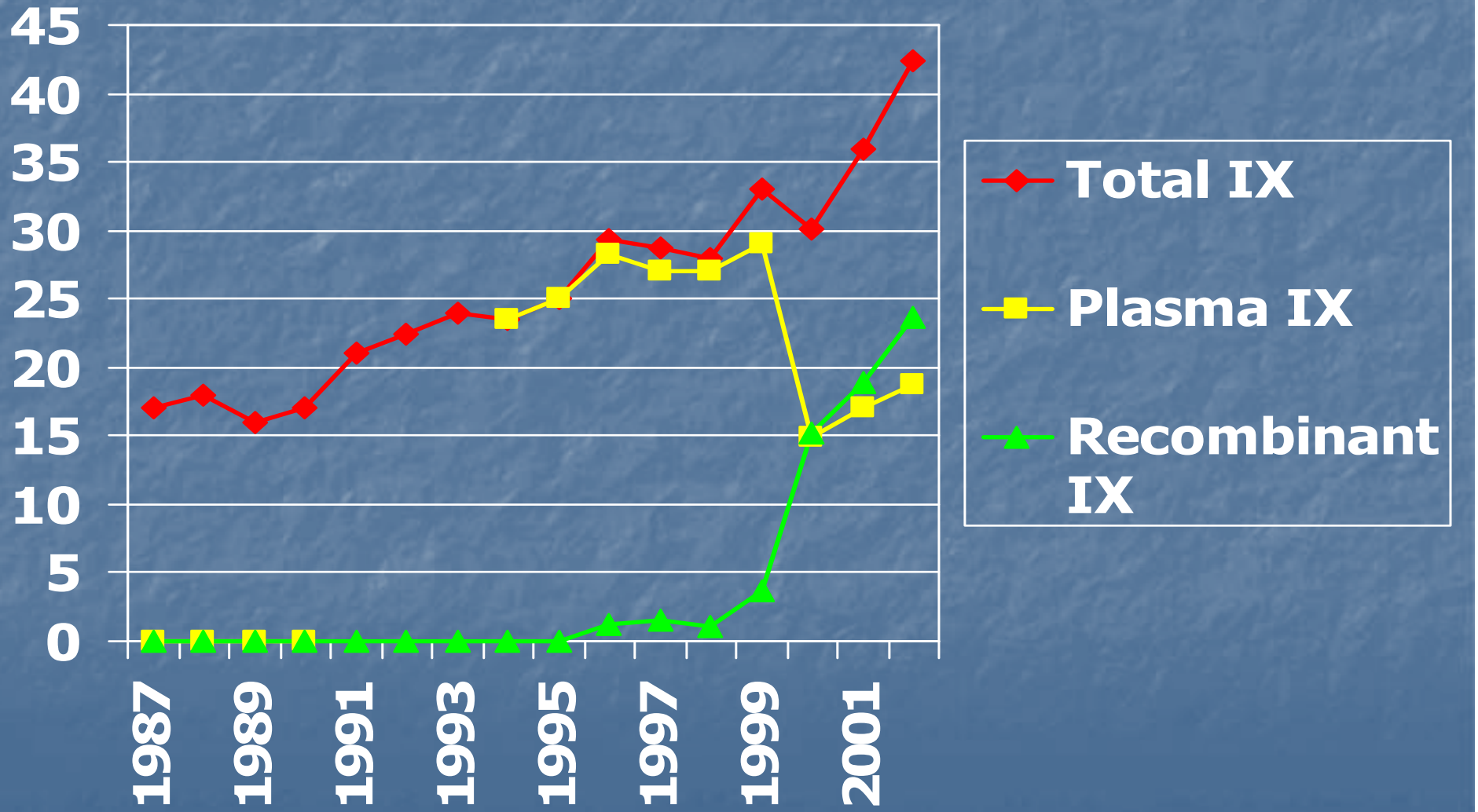


Darby et al 2003

UK Factor VIII Usage (MIU) 1969-2002



UK Factor IX usage (MIU) 1987-2002



Incidence of Inhibitors in the UK 1990-2003 by age of first detection: Severe Haemophilia A.

age	n	%*
0-9	76	22%
10-19	5	0.5%
20-29	3	0.4%
30-39	3	0.3%
40-49	4	0.6%
50-59	7	1.8%
60-69	5	3.0%
70+	1	1.2%

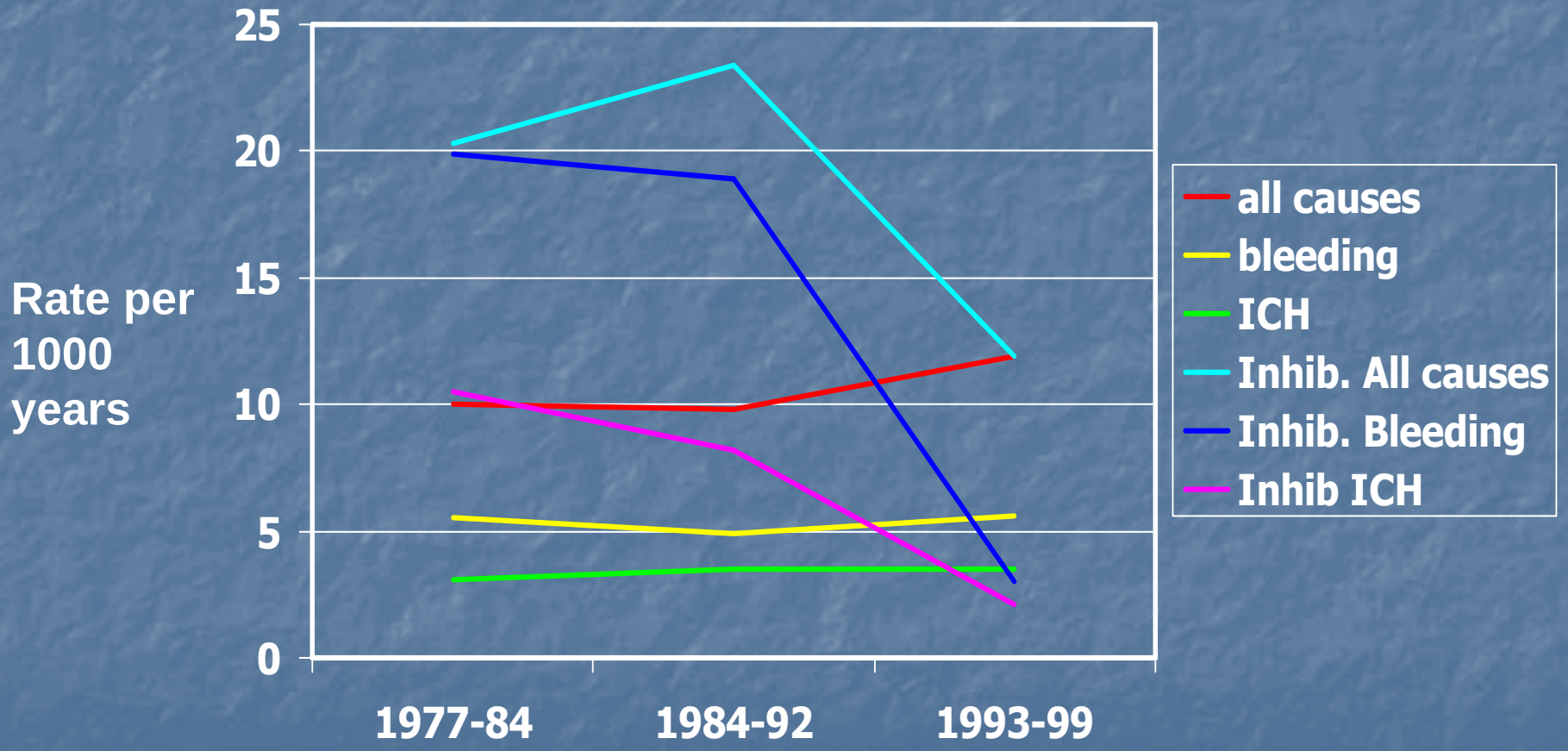
- The onset of inhibitors is bimodal.
- 27% of inhibitors arose *after* the second decade of life with a peak in the fifth and sixth decades.

* % of total age band.

UK Inhibitors 1991-2001: Age <10 yrs. Risk per Treatment-Year by Product

Product:	Treatment-yrs	Risk/Pt/Rx-Yr
ReFacto	261	0.031
Kogenate	1411	0.035
Recombinate	230	0.043
Method M	672	0.010
Monoclate	390	0.033
Alphanate	271	0.022
8Y	646	0.008
Other pdFVIII	218	0.046

Age-standardised death rates for severe haemophilia A with/without inhibitors: UK 1977-99.

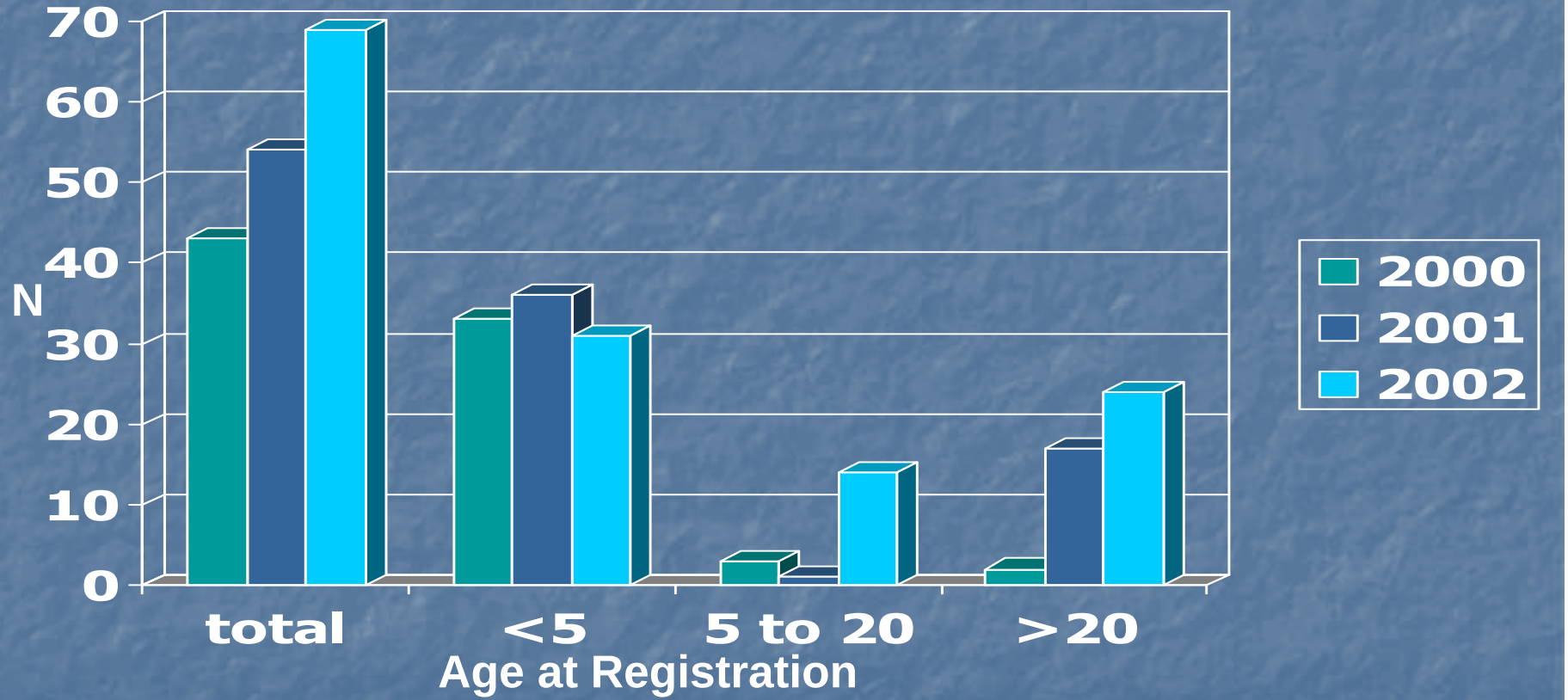


Darby et al, J of Thrombosis and Haemostasis 2004, 2, 1047-54

Registrations in NHD 11/10/04

Haemophilia A	5810
Haemophilia B	1240
VW Disease	7373
Factor XI	1,306
Fibrinogen	155
Factor VII	405
Factor X	155
Factor V	100
Total	**19,691**

Severe Haemophilia A: Age at Registration 2000-2002



Registration is often delayed but is improving

vCJD Database

HPA has asked us to collect: -

- Data on all UK bleeders (20,000 + pts).
- Treated or not treated with pooled UK blood products 1980-2001.
- Implicated and non-implicated batches.
- No of units used.
- Types of product used.
- Pts will be followed for development of vCJD.

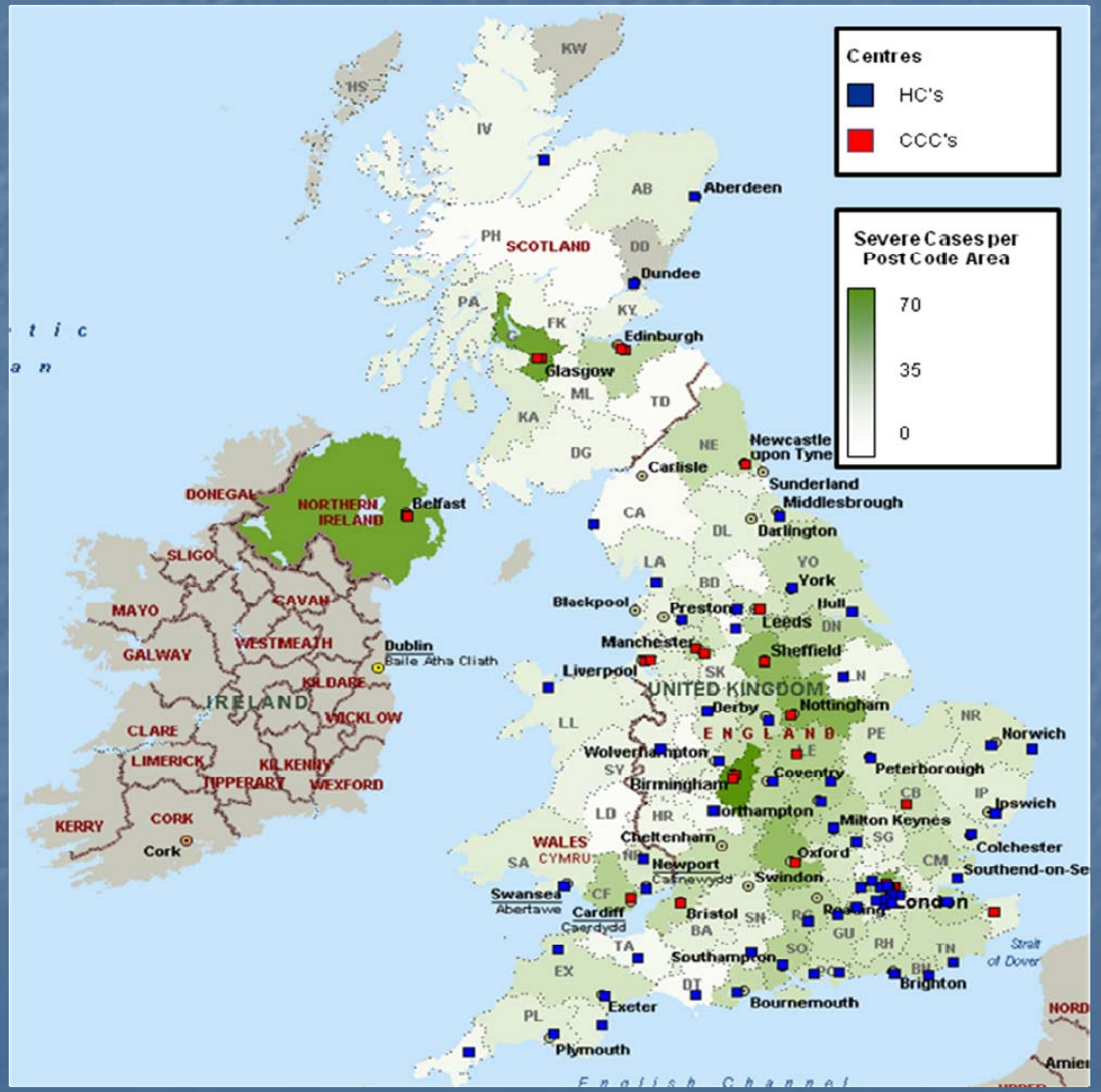
UK Bleeding Disorder Statistics for 2007

Dr CRM Hay

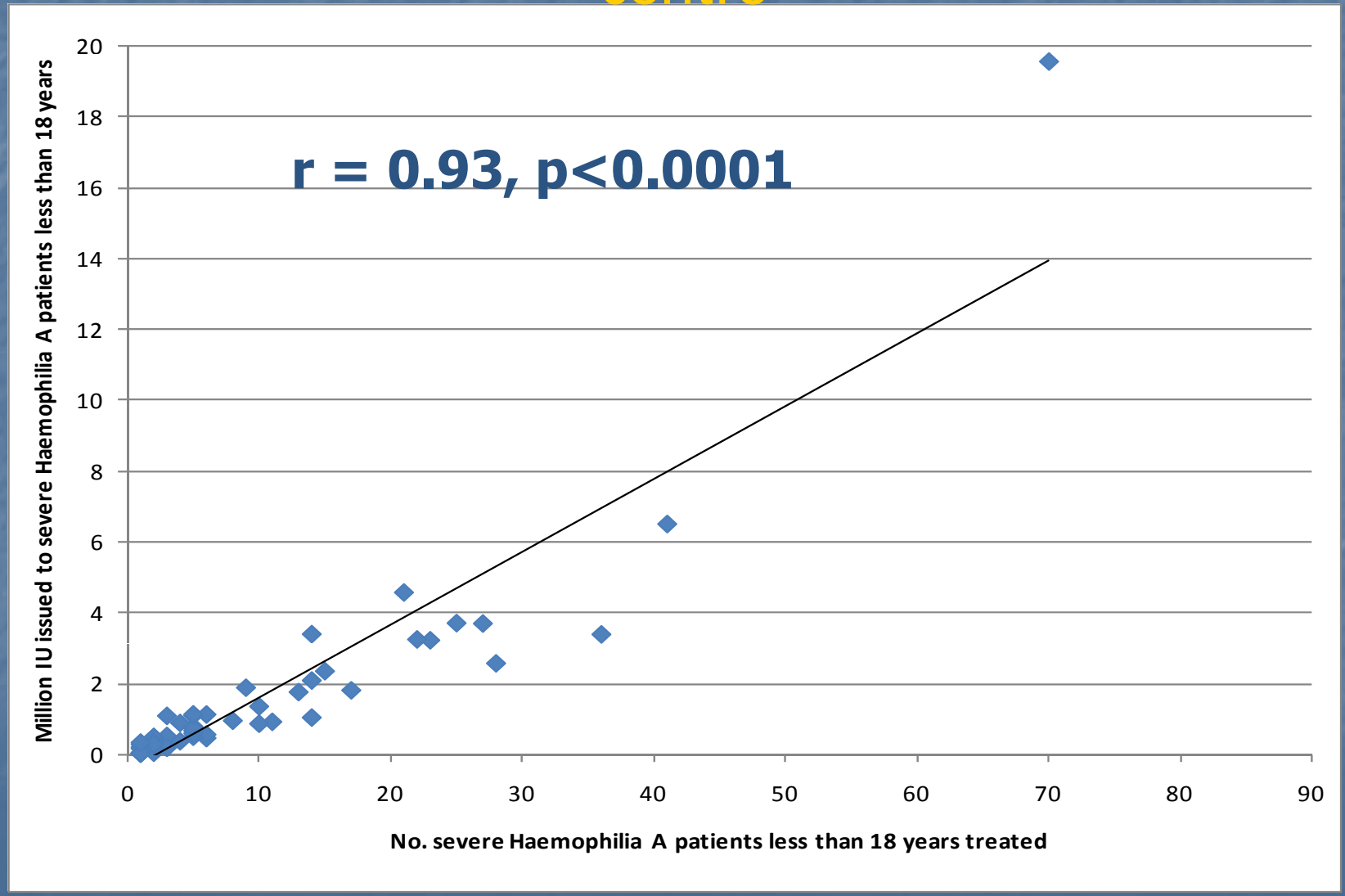
Registrations: -

		In 2007	Total in Register
Haem A	Severe	44	1,756
	Total	137	6,303
	De-registered	400+	
Haem B	Severe	13	363
	Total	34	1,340
VWD	male	126	8,610
	female	229	
Total all diagnoses		959	23,629

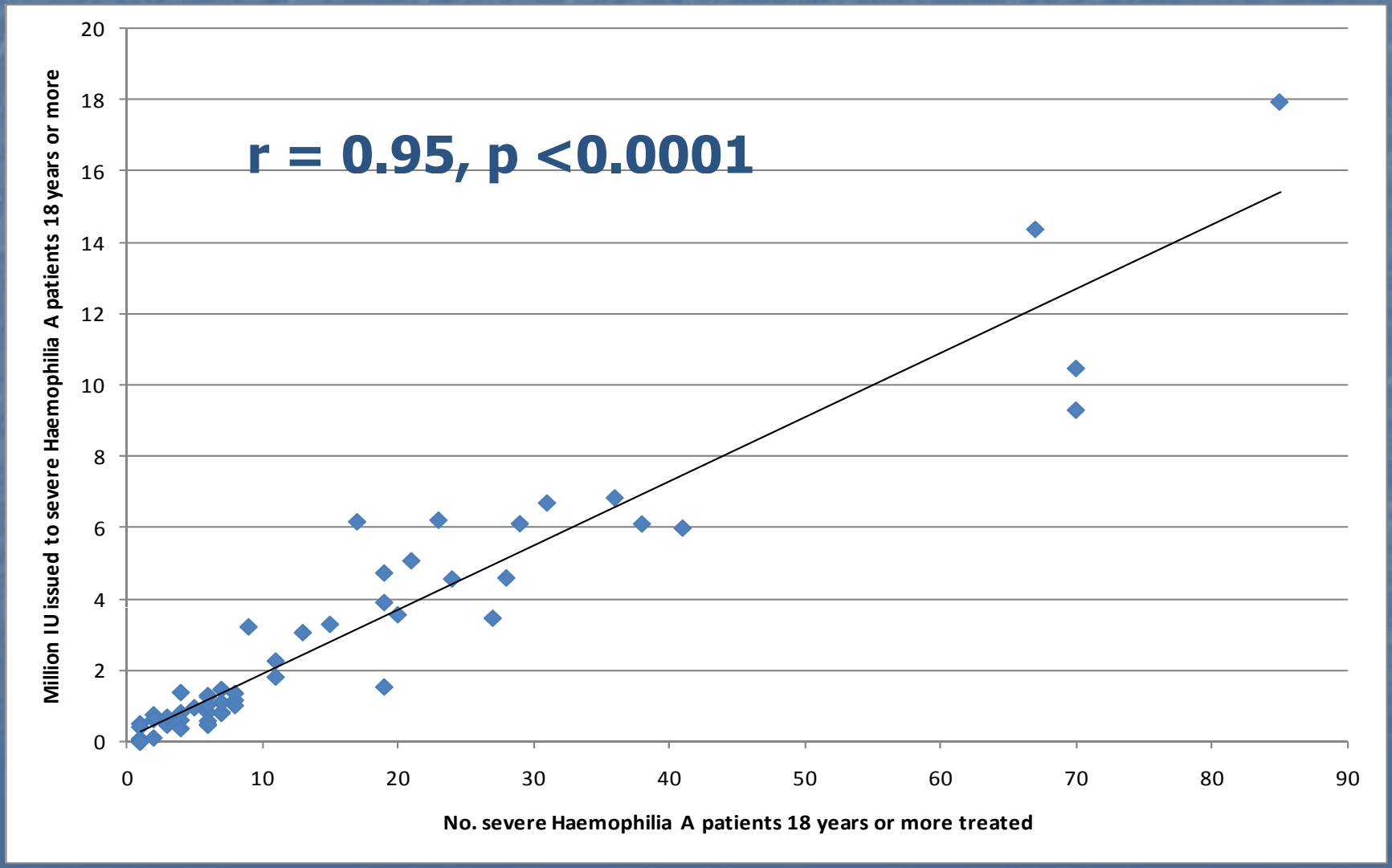
Density of Severe Haemophilia A & B population - by patient post code area



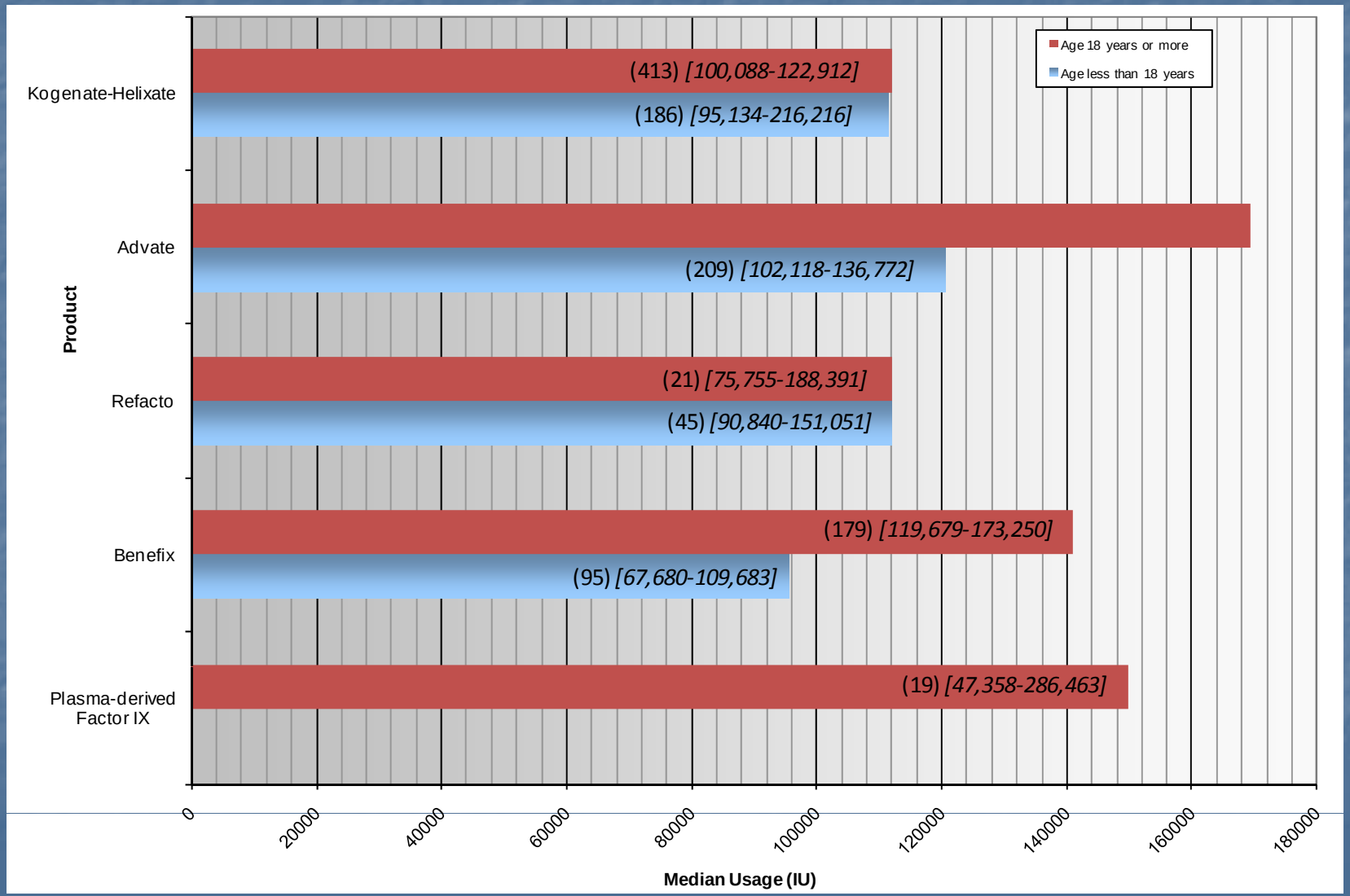
Severe Haemophilia A – No. pts without inhibitor **<18 years**, treated by factor VIII issued by each centre



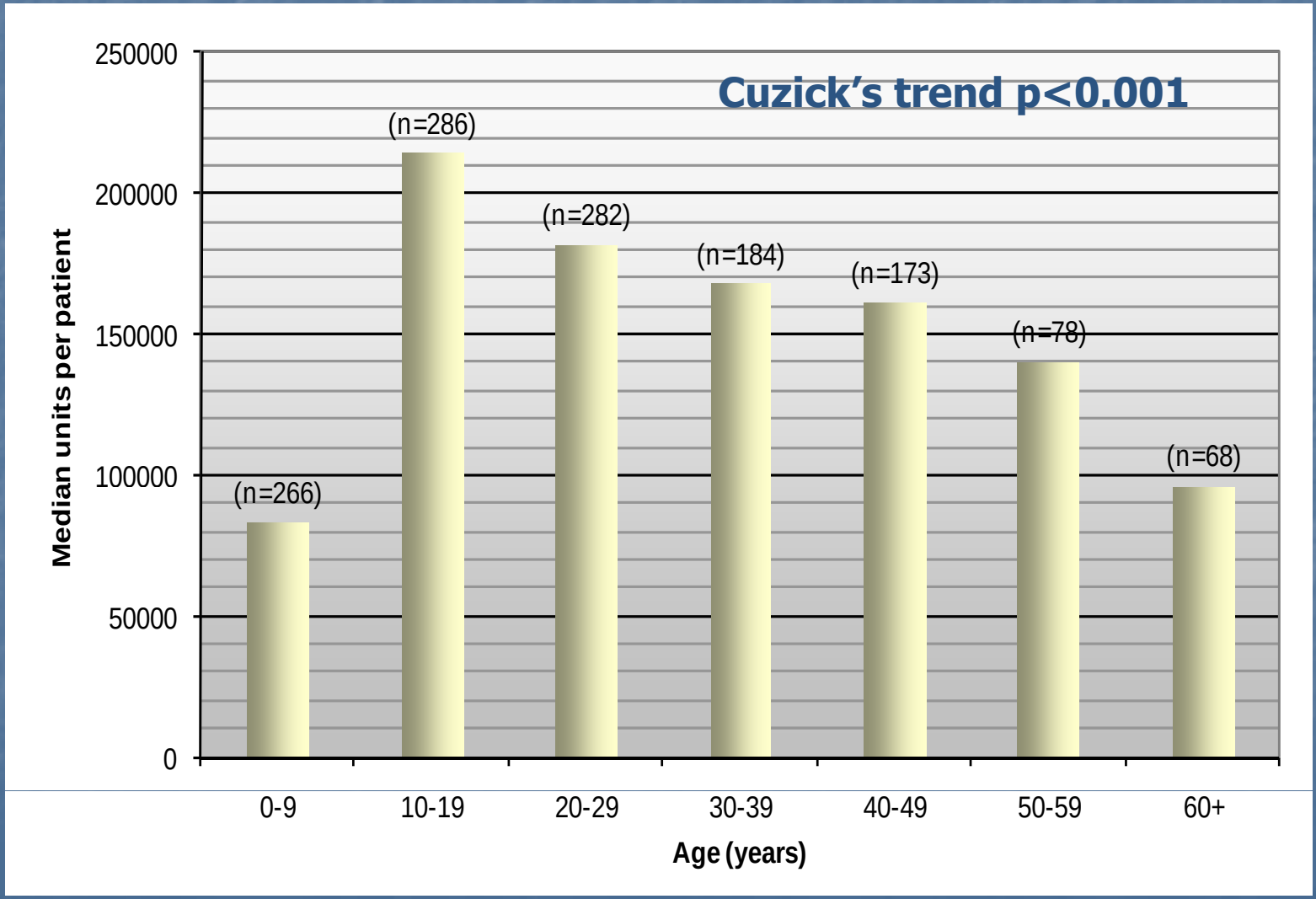
Severe Haemophilia A – No pts lacking inhibitor **≥ 18 yrs**, treated by factor VIII units issued by each centre



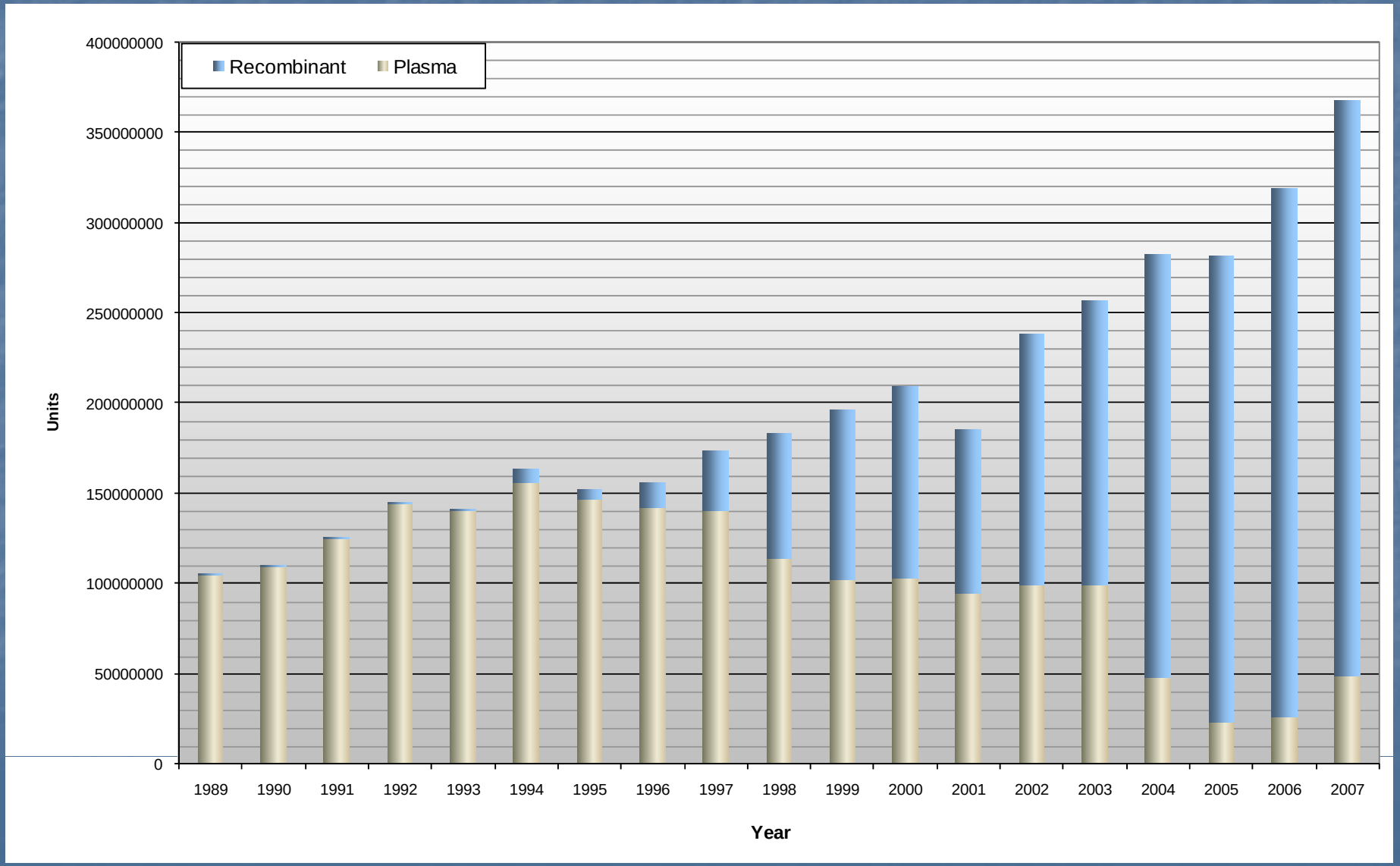
Severe haemophilia A and B lacking inhibitor using only one product during 2007: median usage



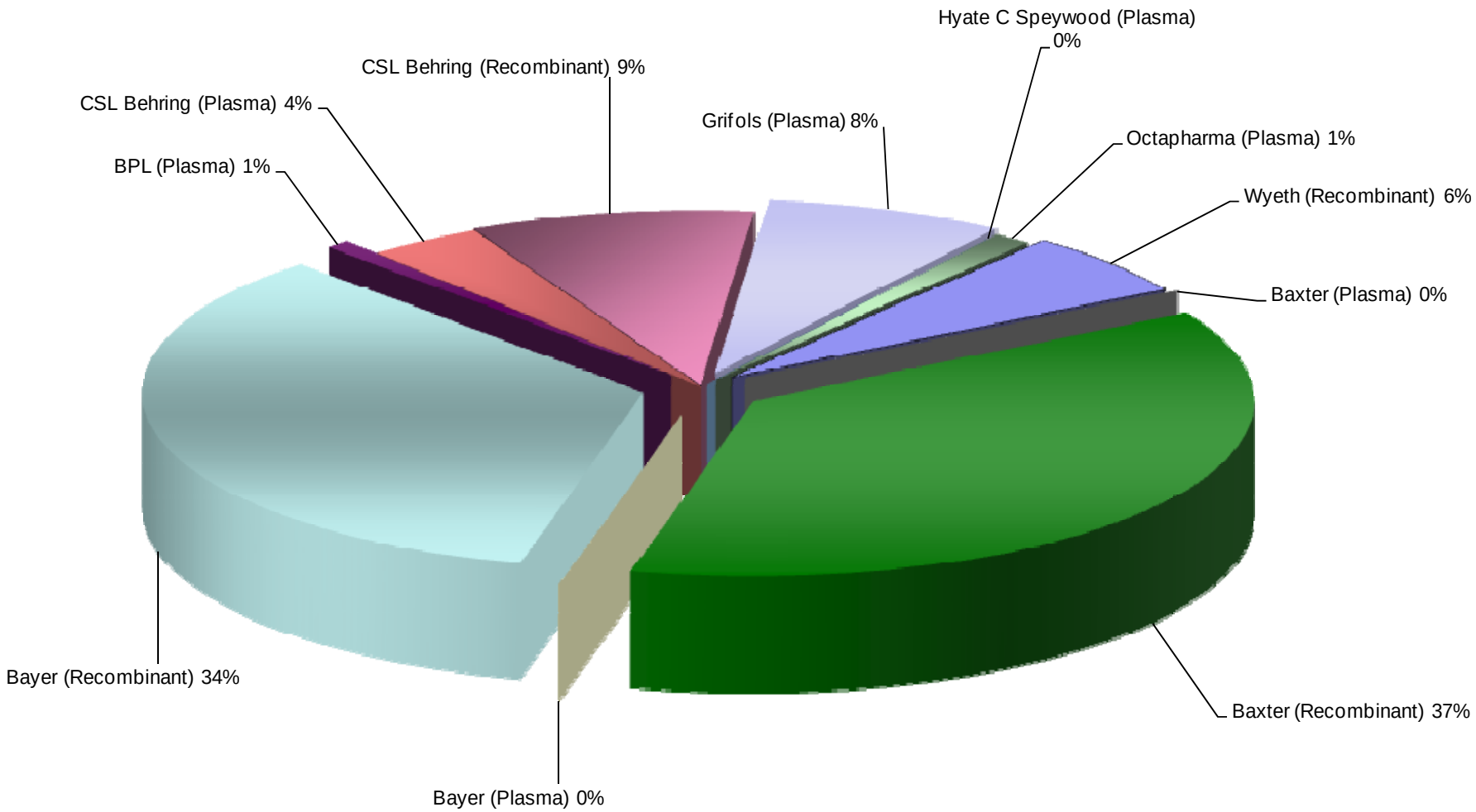
Severe Haemophilia A patients treated with FVIII products with no current inhibitor: median IU issued



Factor VIII usage by UK Haemophilia Centres: 1989-2007

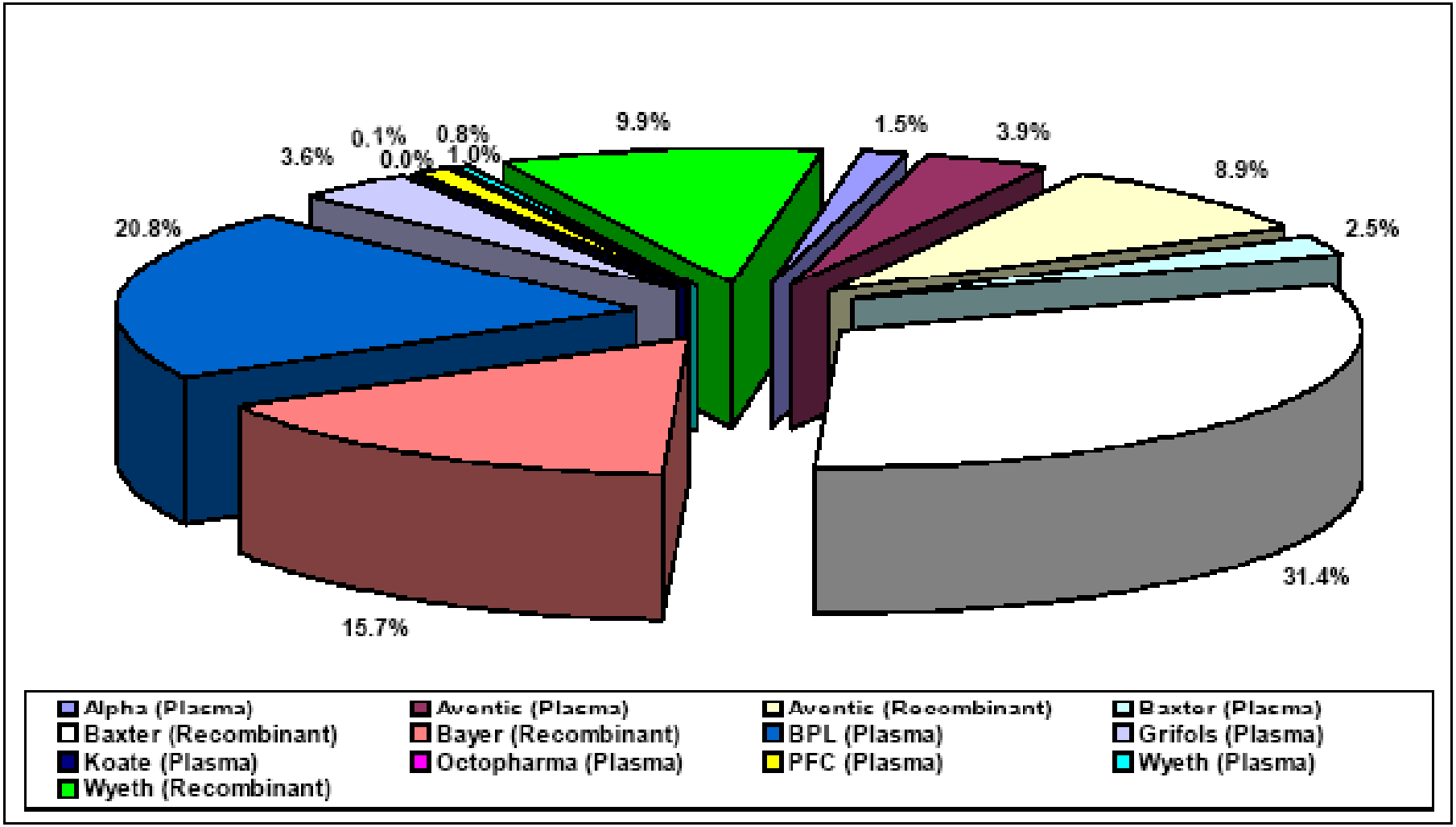


Market Share of factor VIII concentrates known to have been used by UK Haemophilia Centres

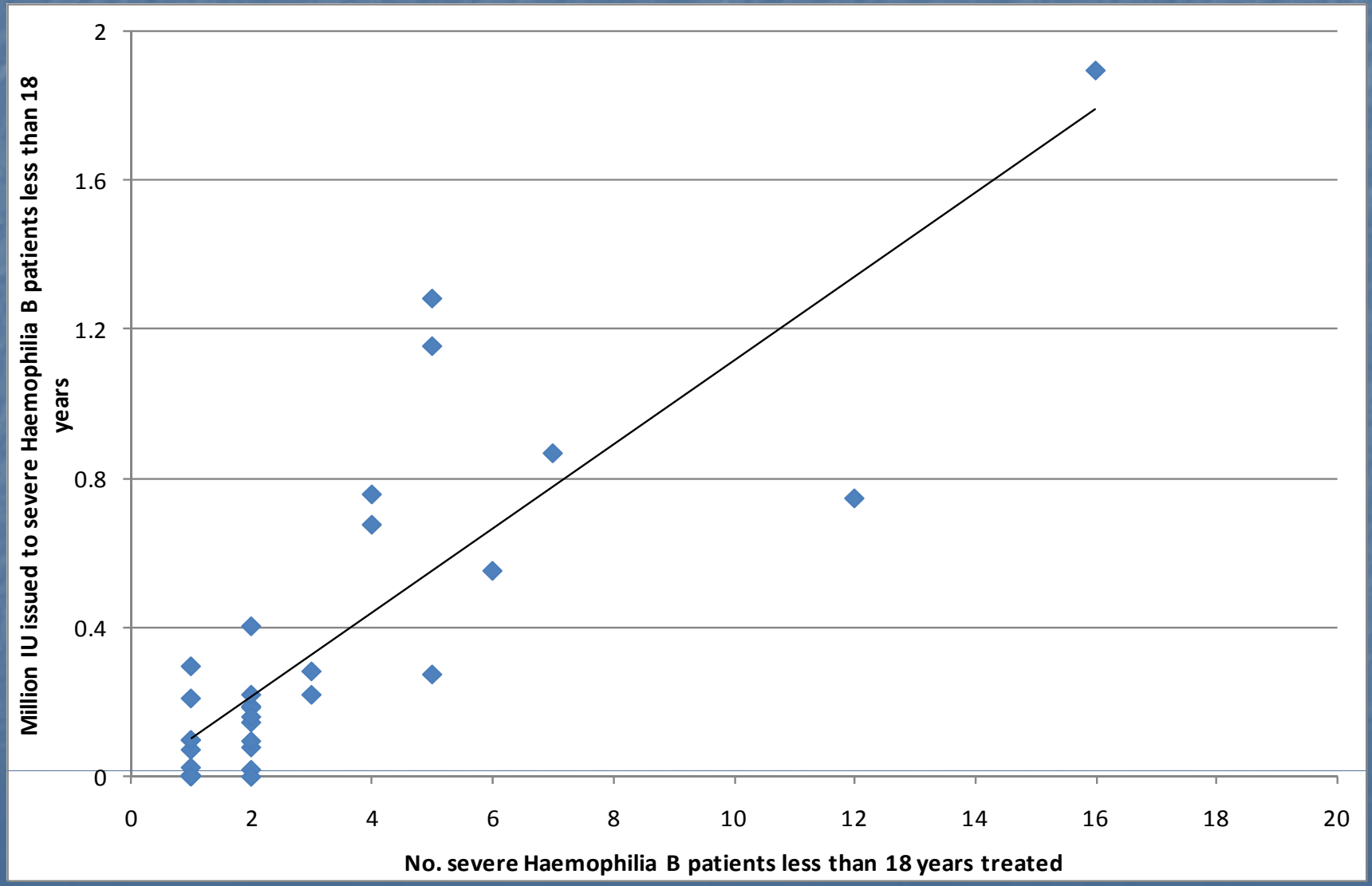


Factor VIII Market-Share 2002

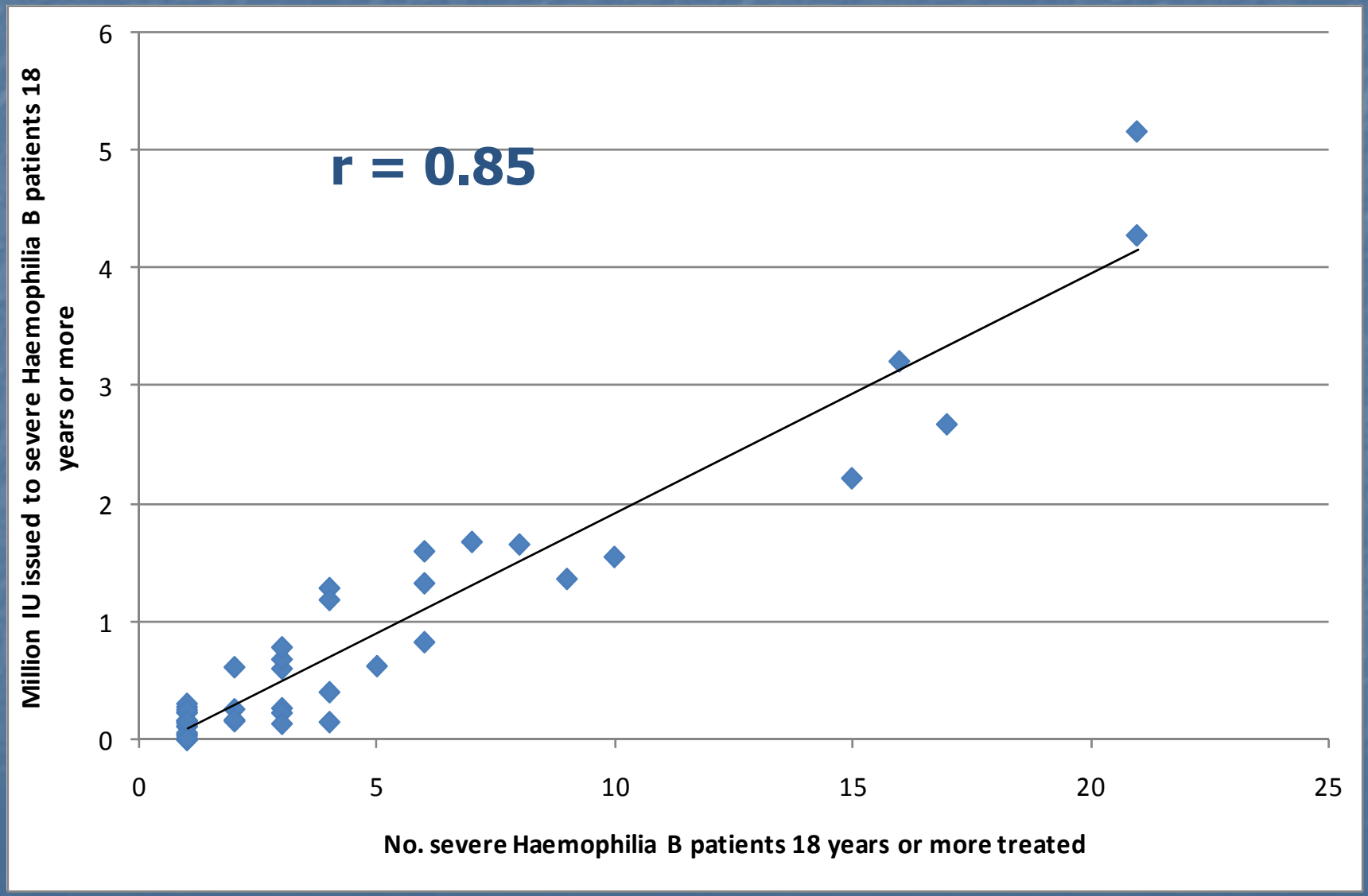
Market share of factor VIII concentrates known to have been used by UK Haemophilia Centres in 2002



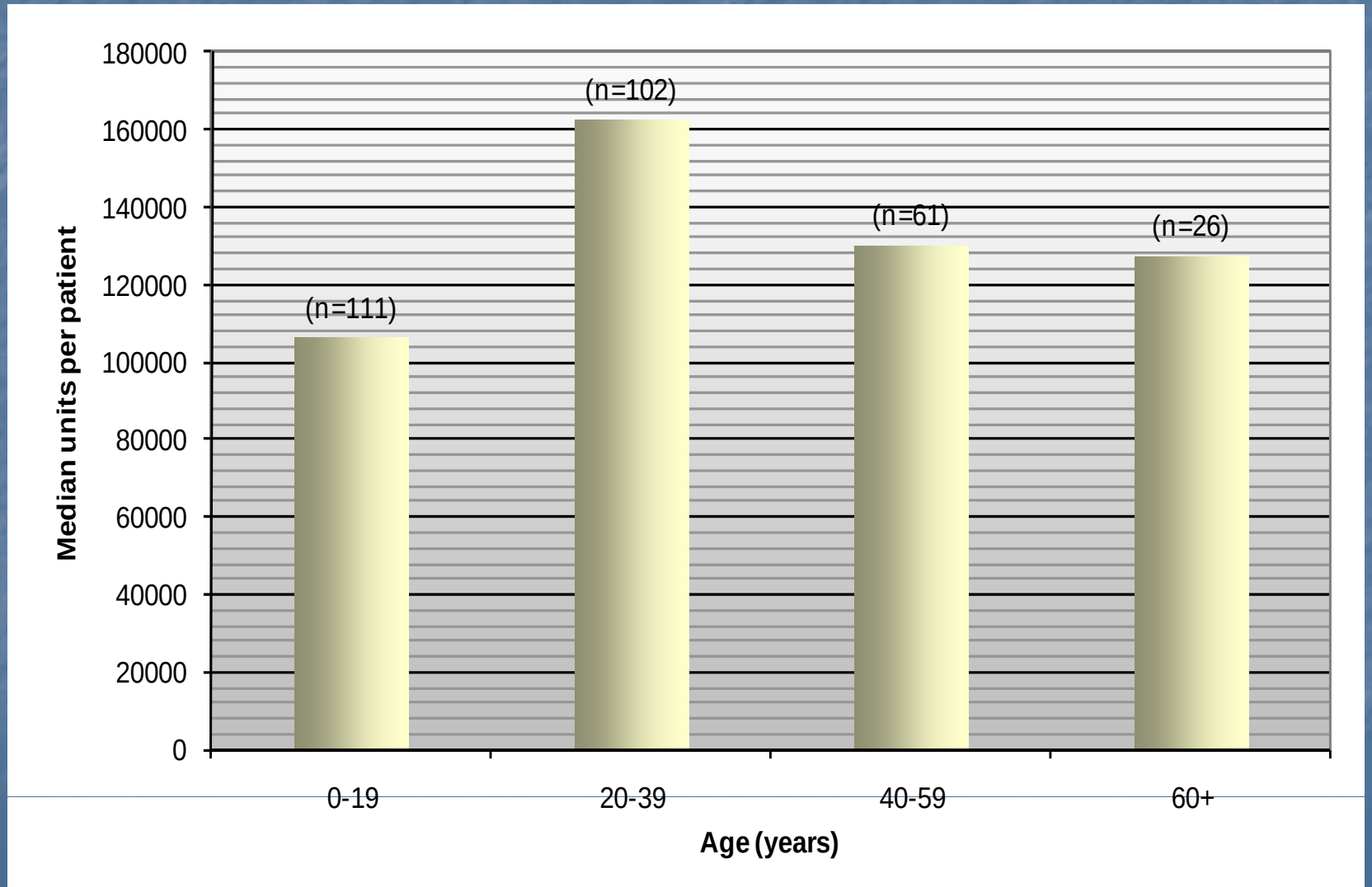
Severe Haemophilia B: Pts lacking inhibitor **< 18 yrs**, compared to number of units issued



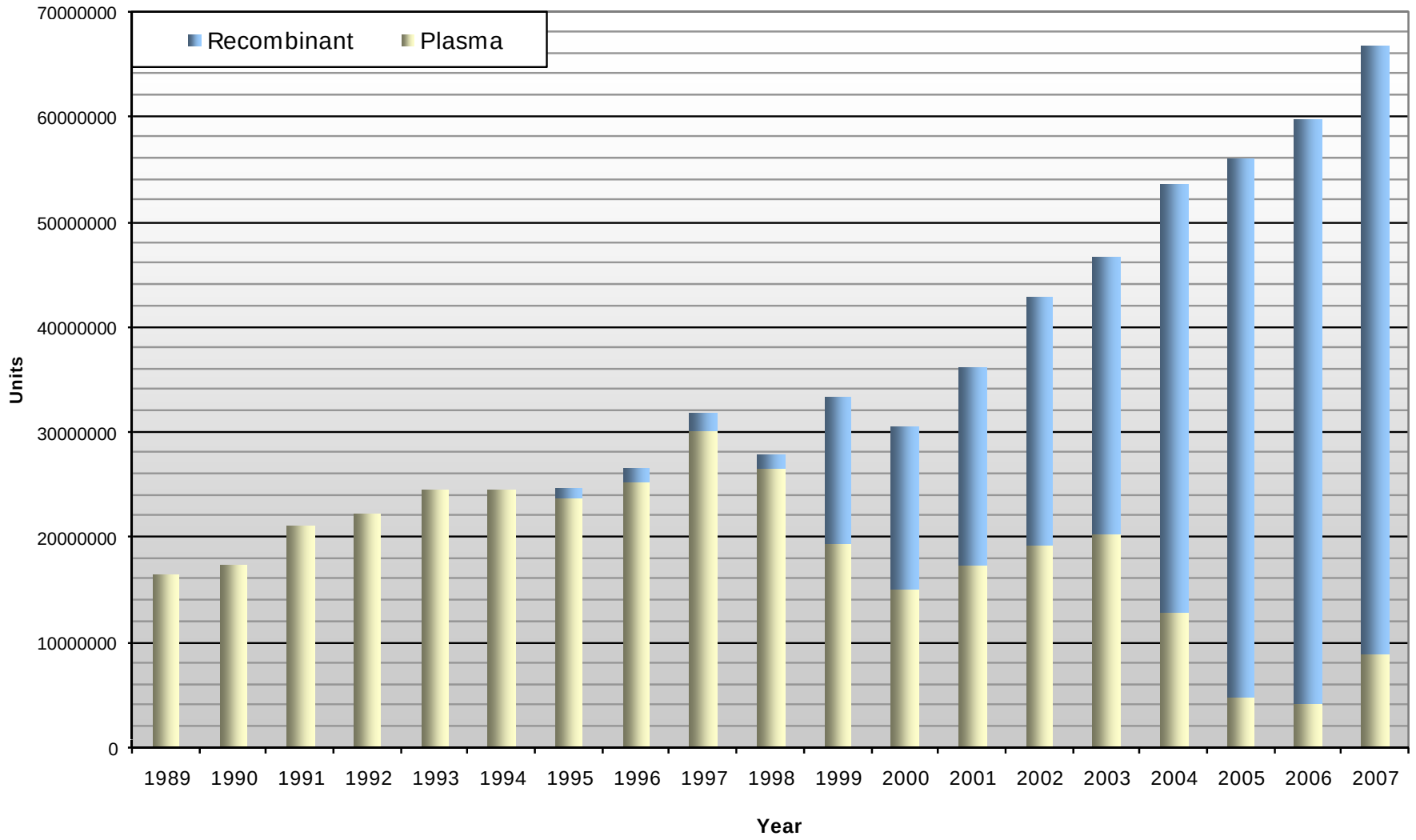
Severe Haemophilia B: Pts lacking inhibitor **≥18 yrs** compared to number of units issued



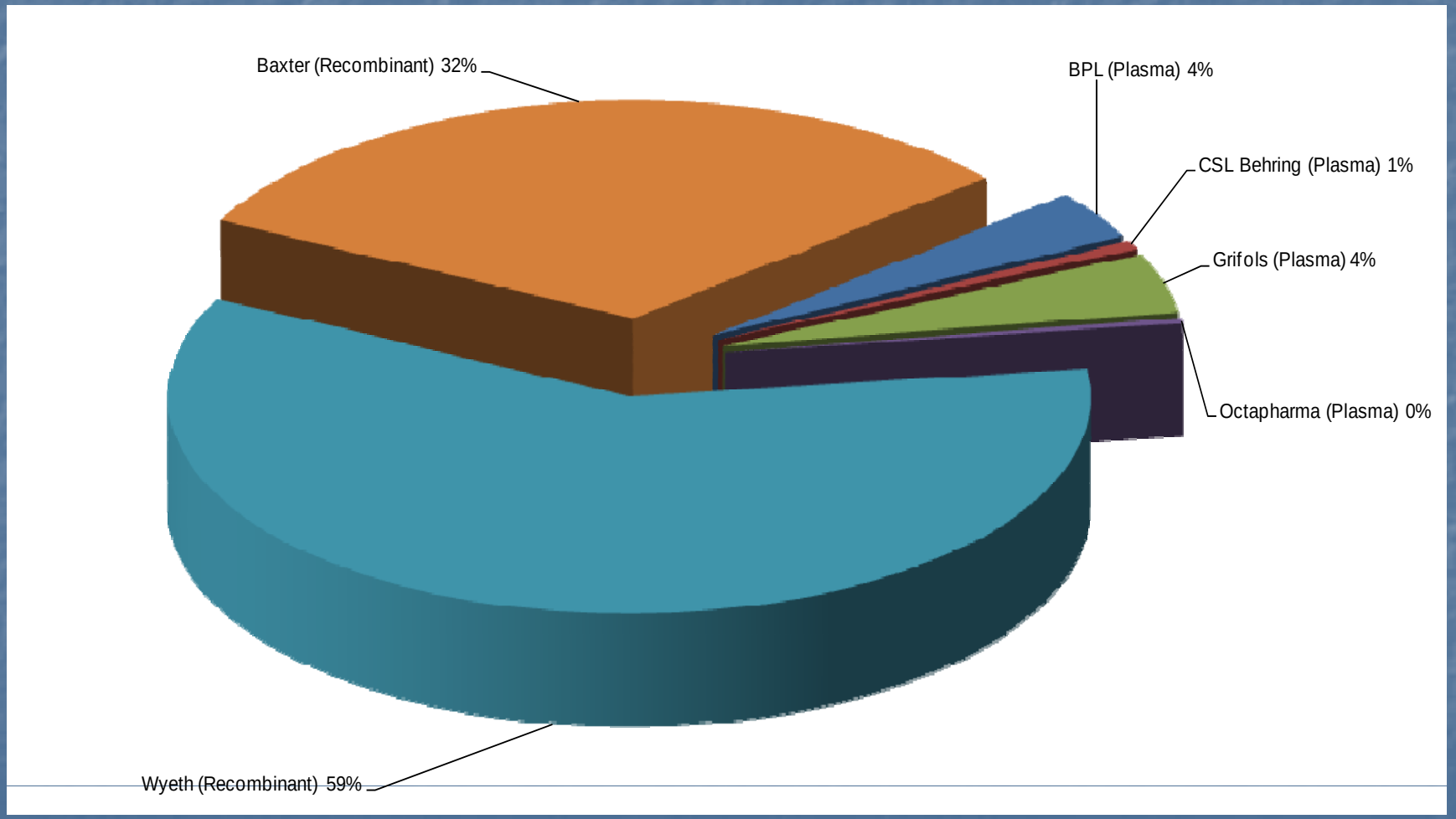
Severe Haemophilia B patients with no current inhibitor: median IU issued



Total factor IX units used by UK Haemophilia Centres 1989-2007

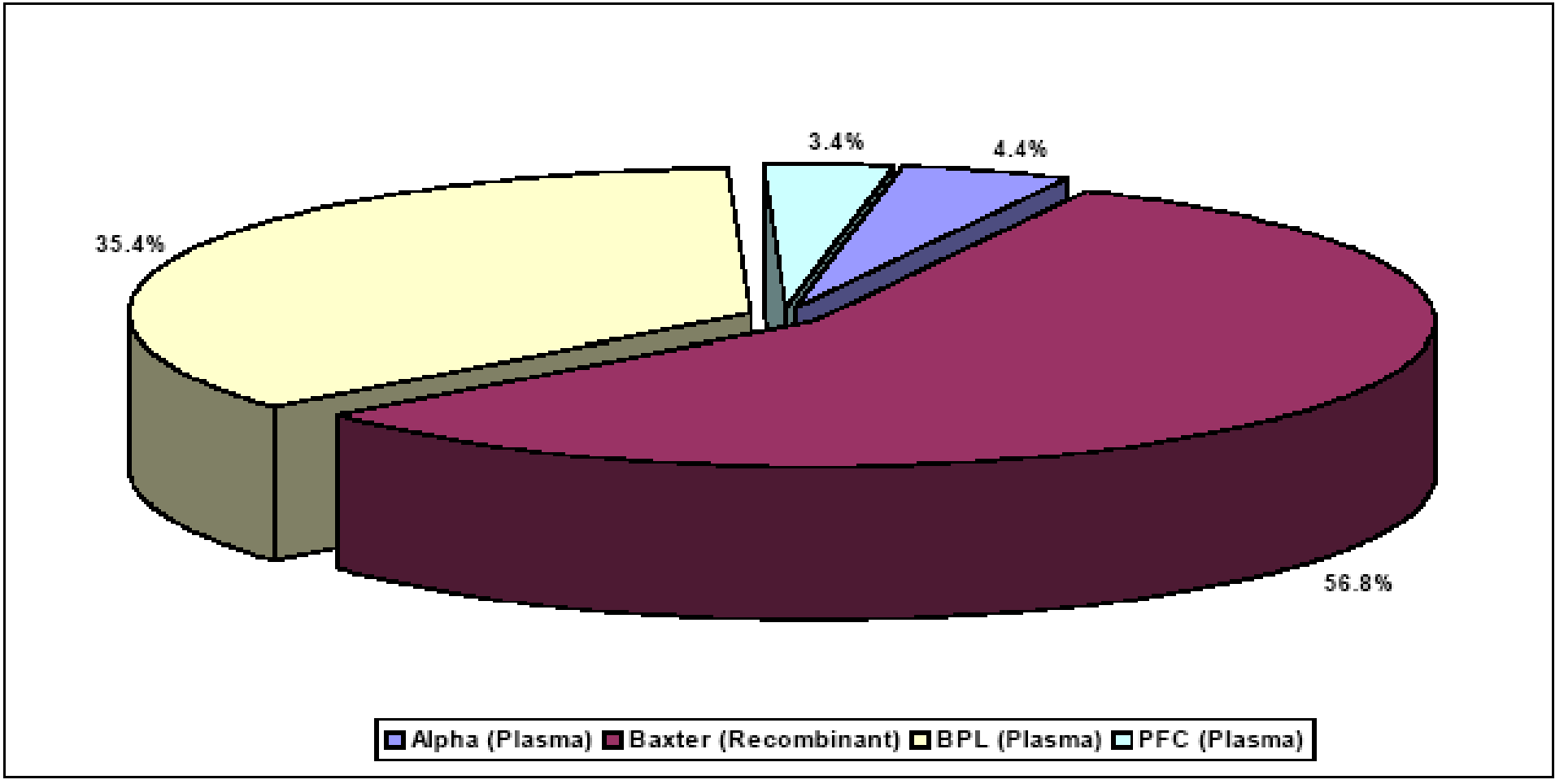


Market share of Factor IX concentrates known to have been used by UK Haemophilia Centres



Factor IX Market-Share 2002

Market share of factor IX concentrates known to have been used by UK Haemophilia Centres in 2002



Von Willebrand's Disease

Total registered	
Male	
Female	

Products used: -

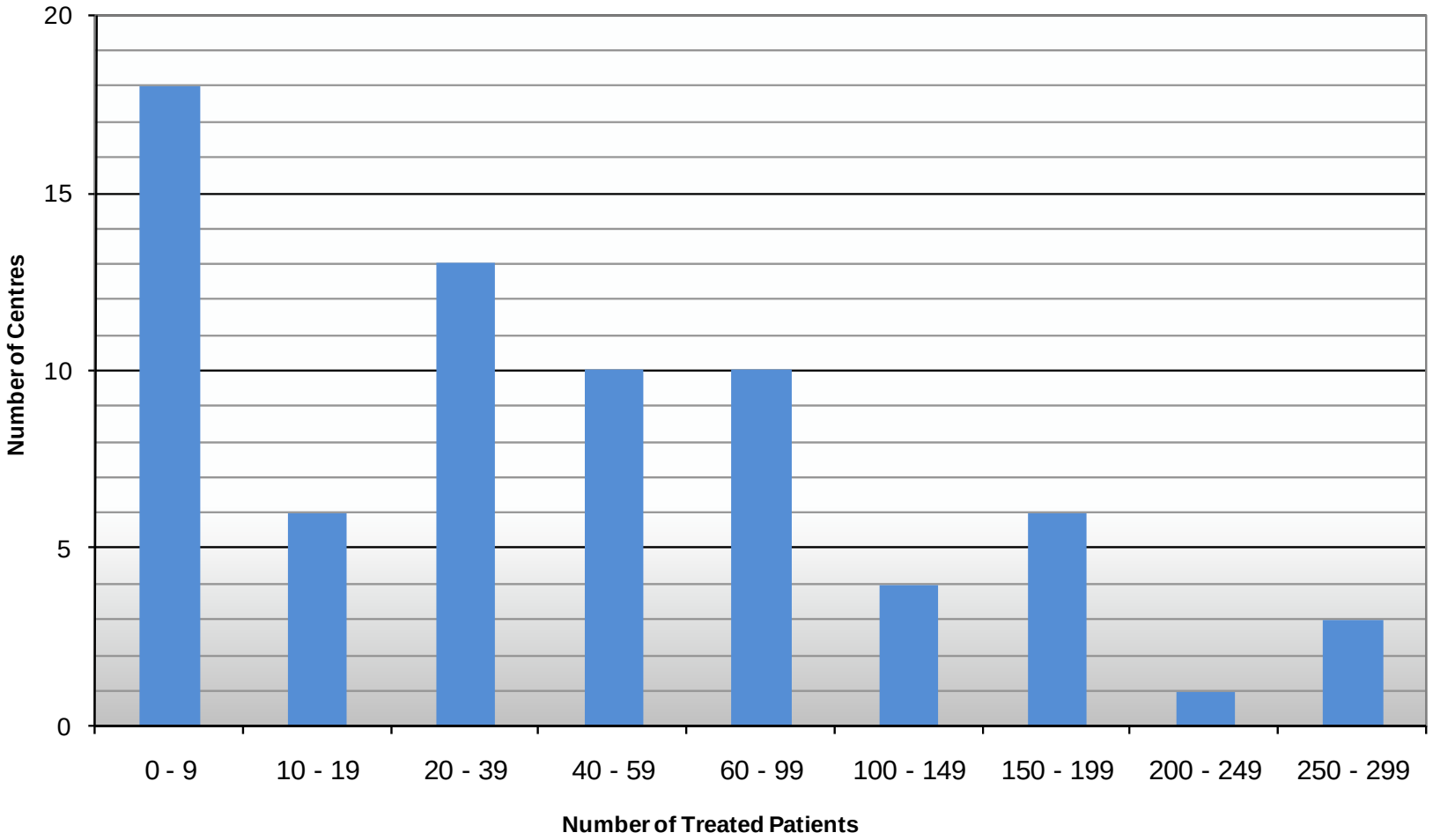
DDAVP	+++
Haemate P	13.03M IU
Alphanate	1.89M IU
Wilfactin	1.04M IU
8Y/Optivate	0.75M IU

Type 1	2,223
Type 1A/B	7
Type 2	95
Type 2A	169
Type 2B	76
Type 2D	1
Type 2M	88
Type 2N	43
Type 3	69
Subtotal Typed	2,795
Un-typed	5,992

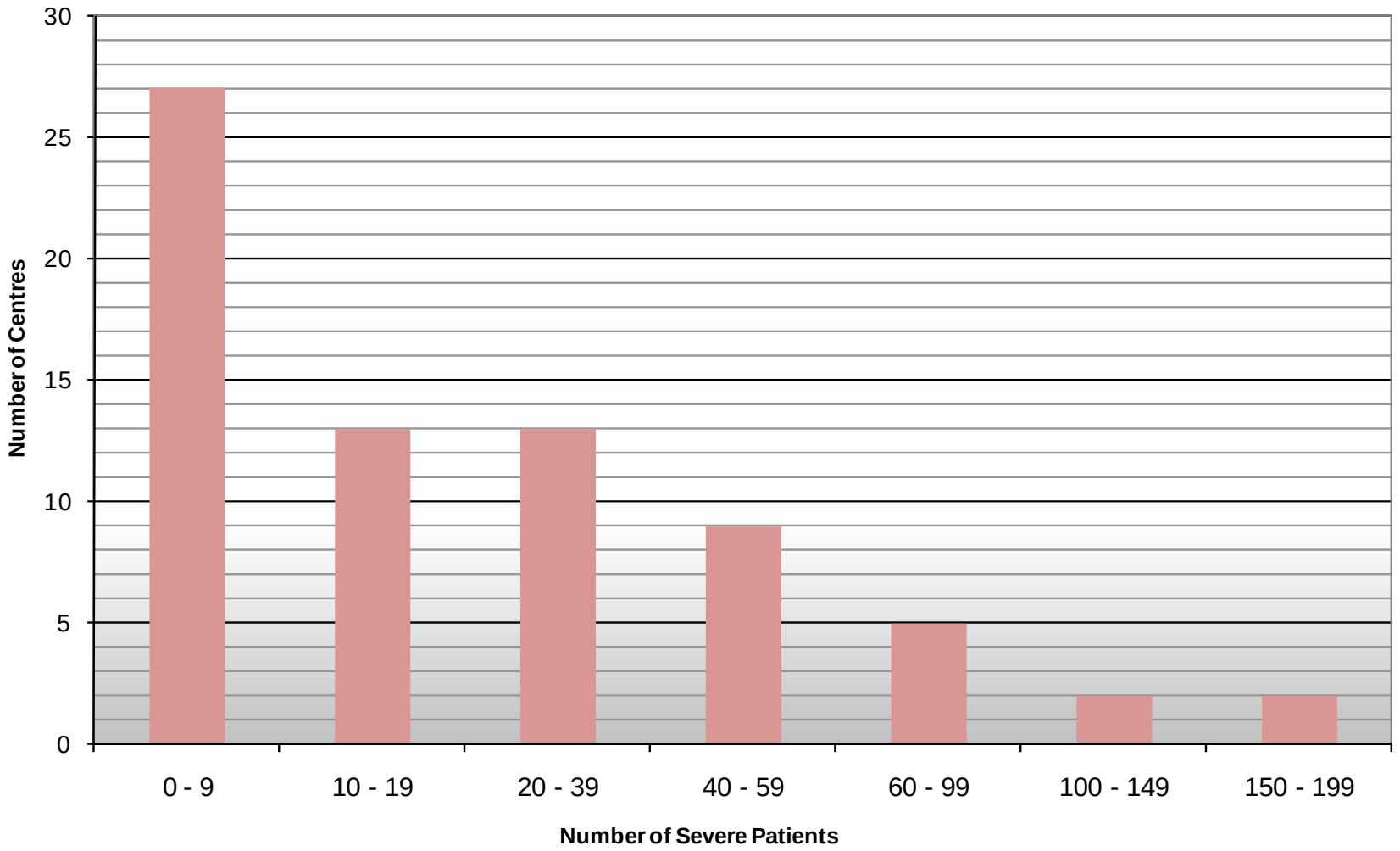
Principal causes of death 2007 (Haemophilia A, B and VWD).

- Carcinoma 17 (2 Liver)
- Ischaemic Heart Disease 13
- Haemorrhage 16
  - Cerebral Haemorrhage 9
- Liver failure 4
- Infection 8
- AIDS 2

Haemophilia A, B and von Willebrand's Disease Pts (all severities) treated by UK Haemophilia Centres



Severe Haemophilia A, B and von Willebrand's Disease pts treated by UK Haemophilia Centres



Data Quality

- Commissioners consider that centres have a contractual obligation to submit data to NHD.
- DoH requires return of data.
- They are increasingly looking to NHD for data to support healthcare planning, benchmarking and reviews of service configuration.
- We therefore all have a duty to ensure the data is therefore as accurate as possible.
- In the last year we have made great strides in improving data quality.
- In the next year we intend to improve data further.

Data Quality

- Internal cross-checks: -
  - Demographics checked with CNST.
  - Automatic reconciliation with HCIS system.
  - Centre data compared with previous 2 years.
  - No coding data (grossly unreliable) used.
  - Deaths cross-checked with ONC.
  - Data queries raised.
  - Centres should check data annually.
- Data cleaning campaigns.
  - VWD, inhibitors, registrations of untreated Haem A/B.
- 2 data chasers and the appointment of a data quality officer.
  - Will visit centres for training purposes and audit.

Conclusion

- The database continues to evolve and improve.
- The database is incomplete, particularly for mild bleeding disorders.
- It is an invaluable research tool.
- It is becoming increasingly useful clinically.
- It is invaluable for healthcare planning and is increasingly used by DoH

UKHCDO Website

- Constitution and mission statement.
- Contacts for every Haemophilia Centre.
- Diary: Meetings and scientific meetings.
- Guidelines.
- Working parties (inc photos of Chairs).
- Contacts and photos for Executive and WP Chairs.
- Bulletin board and newsletter.

Publications from the NHD

Darby, Keeling, Spoone, Giangrande, Collins and Hay, the Incidence of factor VIII and factor IX inhibitors in the haemophilia population of the UK and their effect on subsequent mortality, 1977-99 J T&H 2004, 2, 1047-54.

Darby, Kan, Spooner, Giangrande, Lee, Makris. The impact of HIV on mortality rates in the complete UK haemophilia population. AIDS 2004, 20, 525-33.

Wilde, Lee, Darby, et al. the incidence of lymphoma in the UK Haemophilia population between 1979 and 1999. AIDS 2002, 16, 1803-7

Immune status in HIV-1 infected men and boys with haemophilia in the UK. UKHCDO. Aids 1998, 12, 956-8

Ludlam CA. New varant CJD and the treatment of haemophiliaLancet 1997, 350, 1425-31

Hay, Ollier, Pepper, Cumming, Keeney et al. HLA class II profile: a weak determinant of factor VIII inhibitor development in severe haemophilia

Darby, Ewart, Giangrande, Spooner and Rizza, Importance of age at infection with HIV for survival and development of AIDS in the UK Haemophilia population. UKHCDO. Lancet 1996, 8, 1573-9.

Darby, Ewart, et al. Mortality before and after HIV infection in the complete UK population of haemophiliacs. UKHCDO. Nature, 1995, 7, 79-82.

Many guidelines

and a National Service Specification.

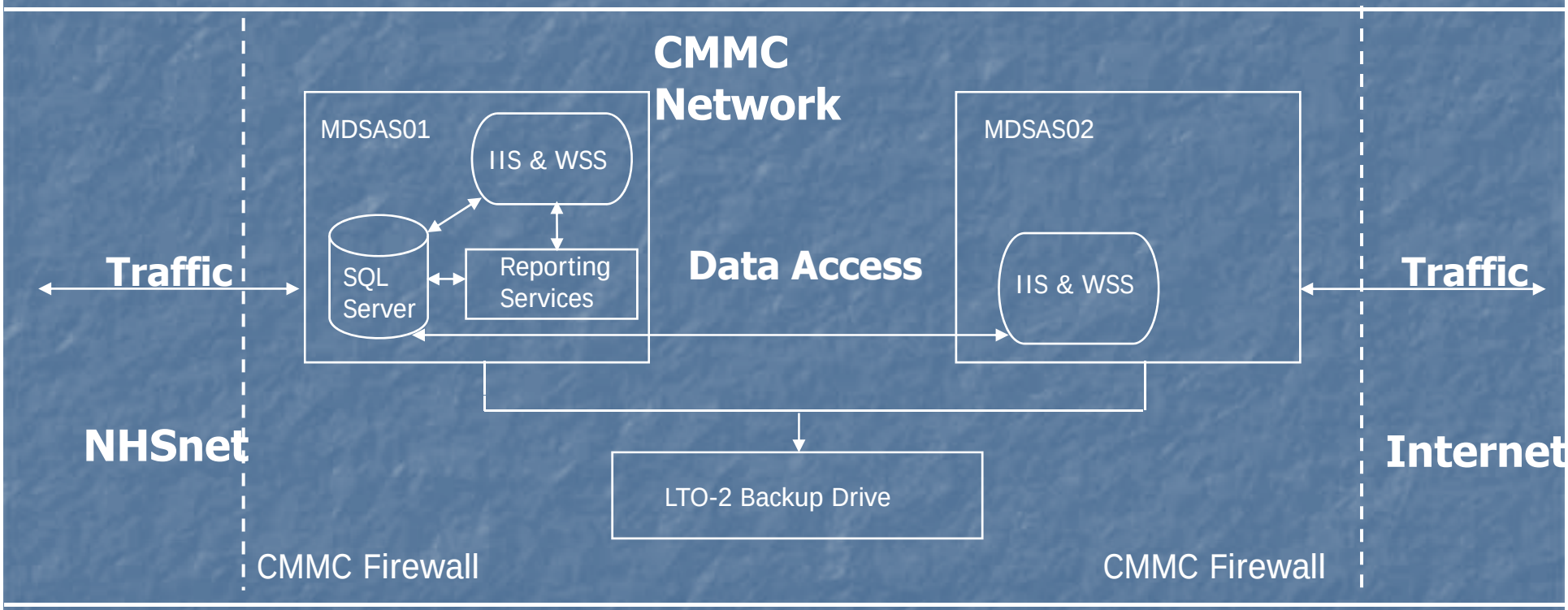
Contact

Website;

http://nhd.cmmc.nhs.uk/ukhcdo/

Hardware Infrastructure

•MDSAS 01 – Virtual Servers : Data store, NHSnet applications, SharePoint and NHSnet Websites
•MDSAS 02 – Virtual Servers : Internet applications, SharePoint and Websites



Backup Strategy:

• Rotational tape backup with father / grandfather using LTO-2 backup drive inc. Livestate virtual server backup SQL Server agent backup service with nightly backups

NHSnet

Haemophilia Centre

Clinicians

Register new pts / events via web

Lookup patients on NHD

Email National Registration Numbers

PAS

Patient Data

HCIS

Monthly Data Export

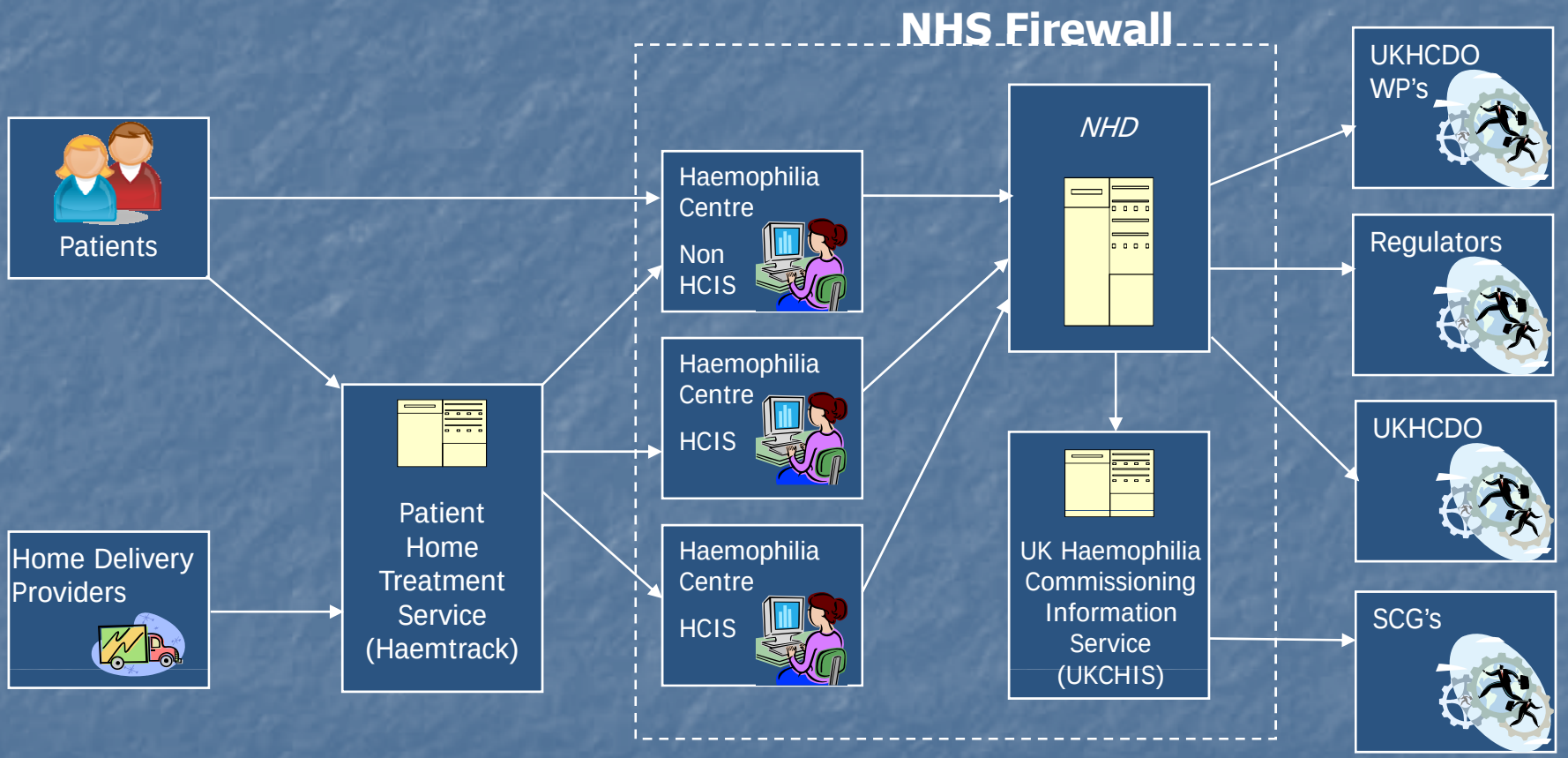
Stock Controllers

Contracting

NHD Fileserver

All data sent between Centre and NHD is encrypted with 128 bit SSL Security

NHD IT Structure



The UK National Haemophilia Database.

Dr CRM Hay

Manchester Royal Infirmary

Where are we now.....

- Much enhanced up to date annual report.
- Able to support national and international projects requiring rapid data accrual and analysis:
  - Recombinant Rollout,
  - National Procurement,
  - EUHASS,
  - vCJD Surveillance,
  - Pharmaco-vigilance and adverse event surveillance

Data Protection Act (1998)

- **Written informed consent for all named data *or data that can be traced back to the individual by any identifier whatsoever.***
- **The consensus within UKHCDO was to continue collecting named data.**
- **Informed consent was required.**
- **Where consent is withheld, data must be censored.**
- **Subsequent modifying acts require us to *inform* the patients as the opportunity presents rather than obtain written consent. Consent is implied unless with held.**
- **Patient information leaflet (30,000 copies).**

Redevelopment

Adoption of electronic reporting has been very successful!

- Time to registration of new patients dramatically faster.
- Data quality has improved
- More secure than postage
- Data entry errors have been reduced
- Storage and security problems

NHD
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