Irish Haemophilia Society

Introduction to Haemophilia

Brian O'Mahony

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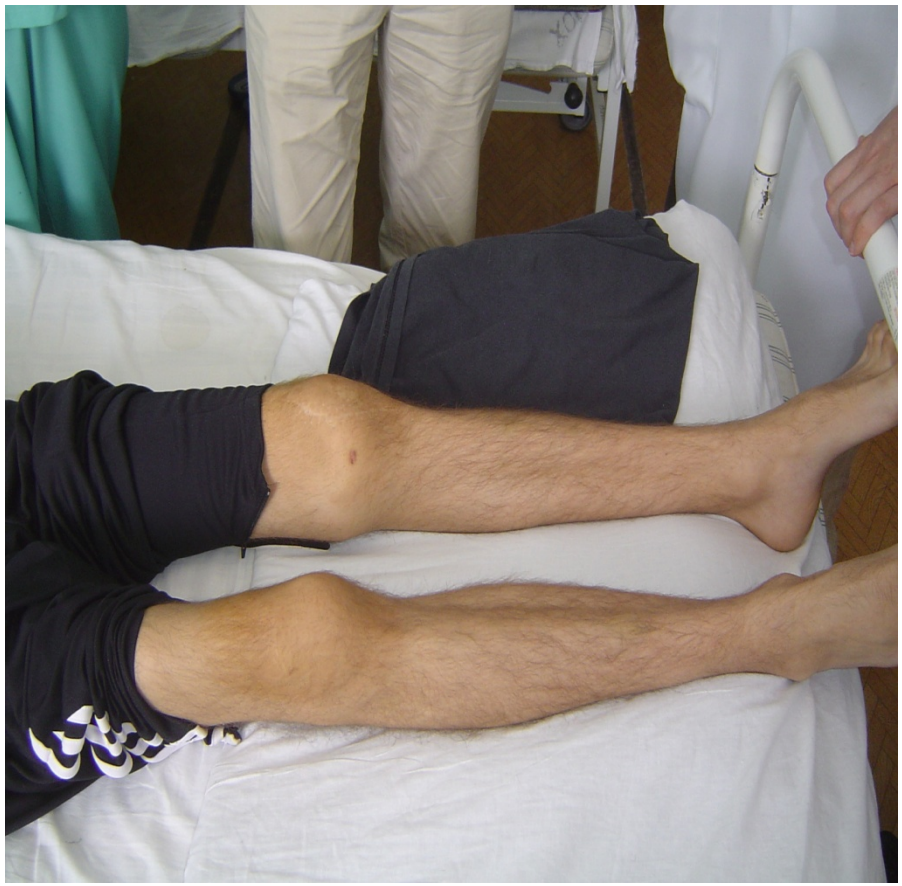
Content

- Introduction to Haemophilia
- Introduction to Von Willebrand's Disease
- Inheritance
- Bleeding patterns
- Introduction to Factor replacement therapy
  - Plasma derived and Recombinant products
  - Prophylaxis v On Demand
- Organisation of care
- HIV and Hepatitis C
- Current and future threats
- Risk Communication
- Future developments

Bleeding

- Aura
- Pain, Heat, Swelling
- Damage

- Early treatment



Haemophilia A

- FVIII deficiency
- 105 per million males
- 1.05 per 10,000 males
- 80% of Haemophilia

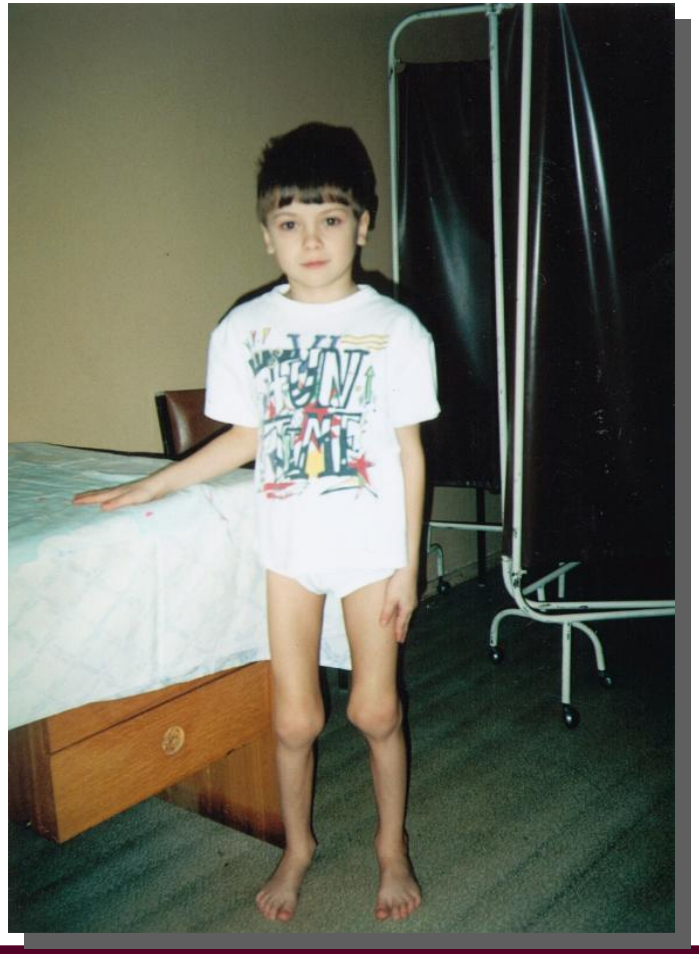
Haemophilia B

- FIX Deficiency
- 28 pre million males
- 0.28 per 10,000 males
- 20% of Haemophilia

Figure 8. Tsarevich Alexis.

Haemophilia -Severity

- Severe < 1%
- Moderate 1 to 5 %
- Mild 5 to 40%
- Severe - spontaneous bleeds



Von Willebrands

- Type 1 - Mild
- Type 2A - Moderate
- Type 2B
- Type 2N
- Type 3 - Severe

0.1% of Population

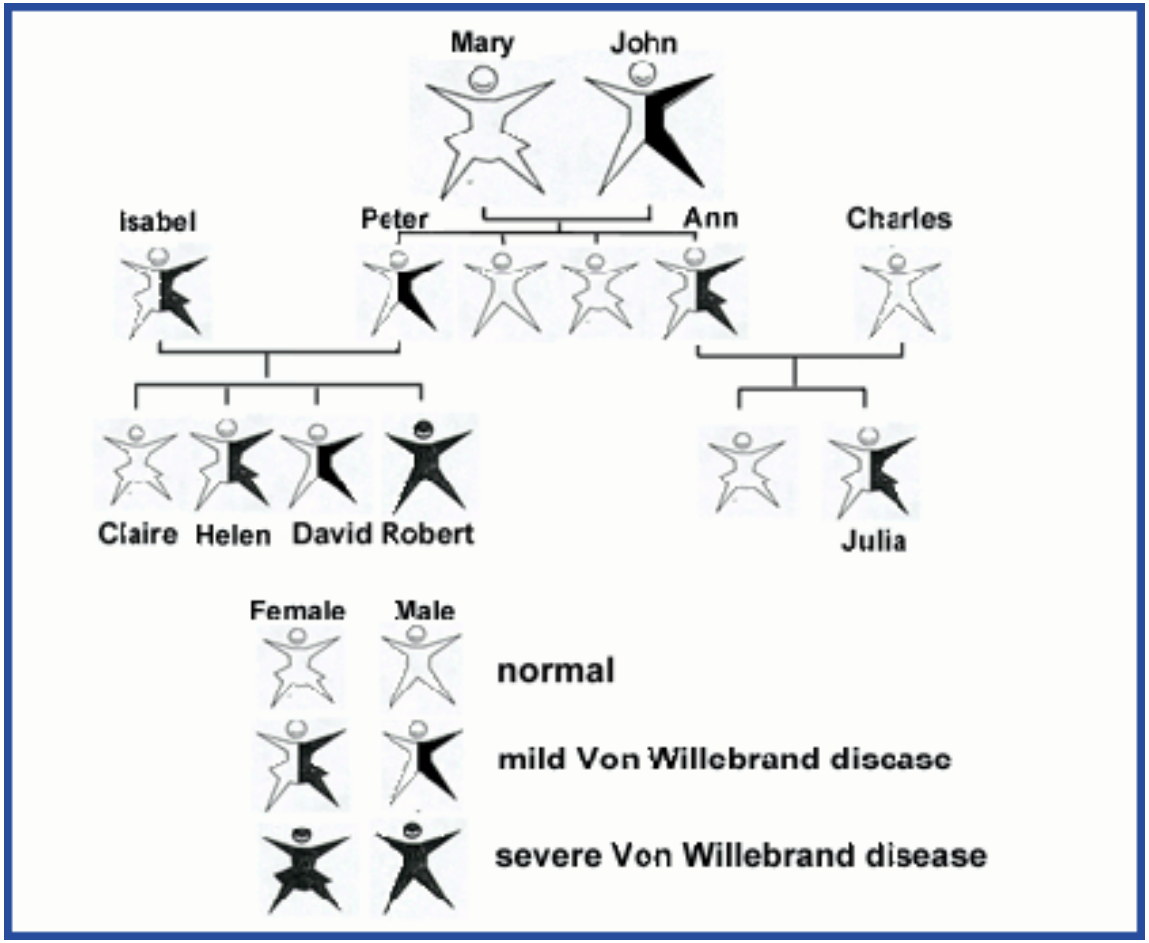
Ireland

- Haemophilia A 410
- Haemophilia B 203
- VWD 918
- Other 510

Inheritance of Haemophilia

- **Sex linked Inheritance**
  - X chromosome
- Carrier mother
  - Sons 50% chance, haemophilia
  - Daughters 50% chance, carriers
- Man with Haemophilia
  - Sons, no haemophilia
  - Daughters, obligatory carriers
- 30% Spontaneous Mutation

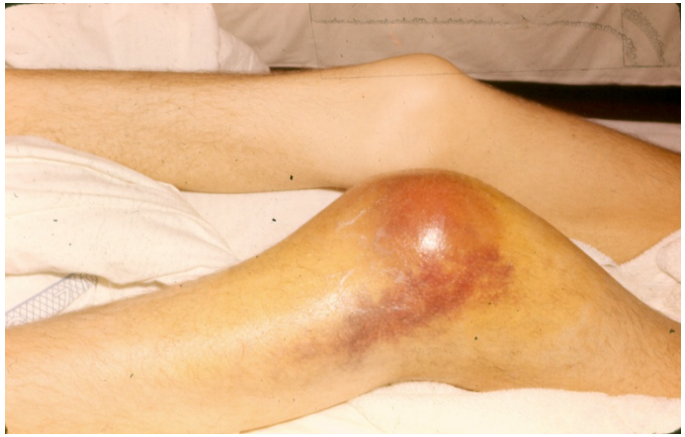
VWD Inheritance

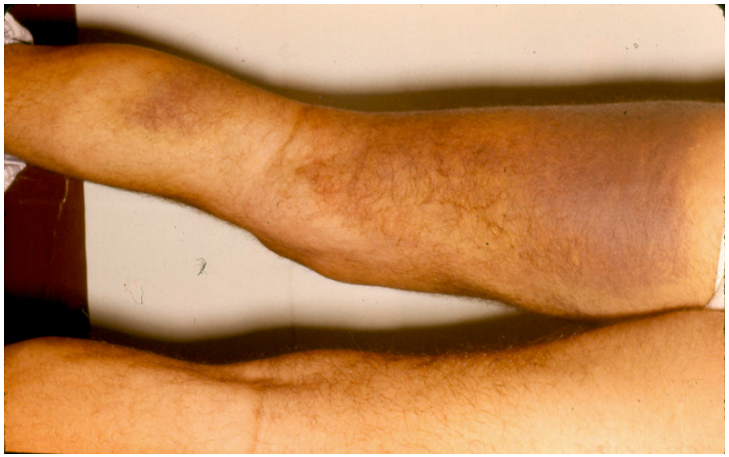


Bleeding

Serious

- Joints (haemarthrosis)
- Muscle/soft tissue
- Mouth/gums/nose
- Haematuria





Bleeding

Life Threatening

Central Nervous System

Gastrointestinal

Neck/Throat

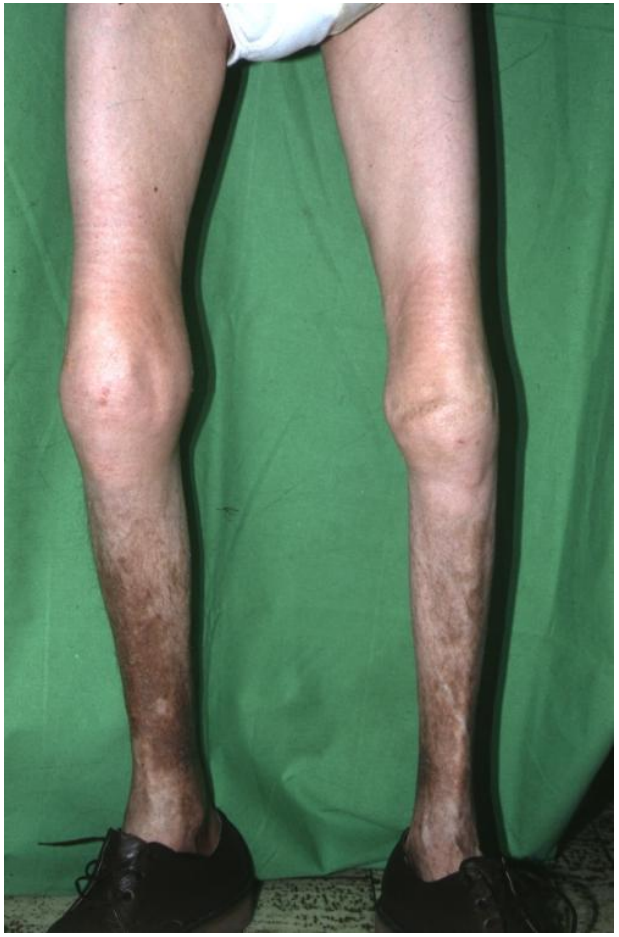
Severe Trauma

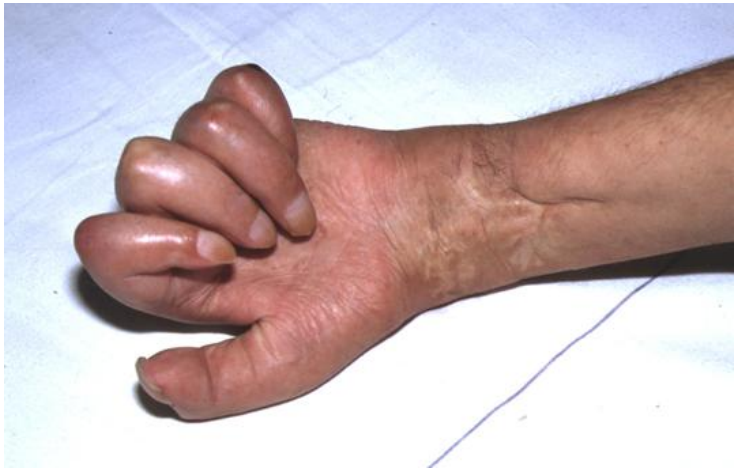
Incidence of bleeding into joints

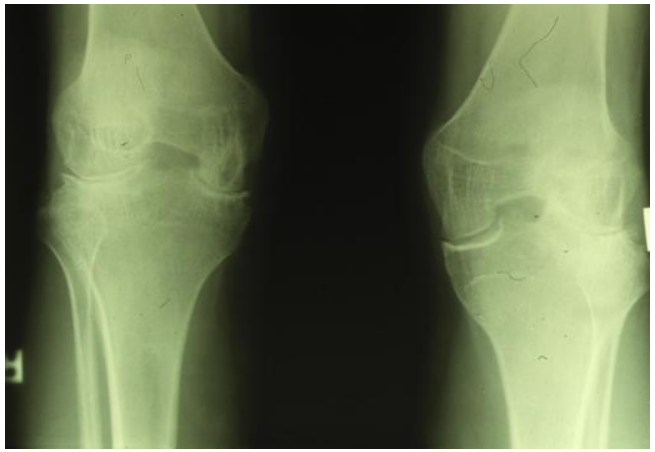
- Knee 45%
- Elbow 30%
- Ankle 15%
- Shoulder 3%
- Wrist 3%
- Hip 2%
- Other 2%

- Target Joints

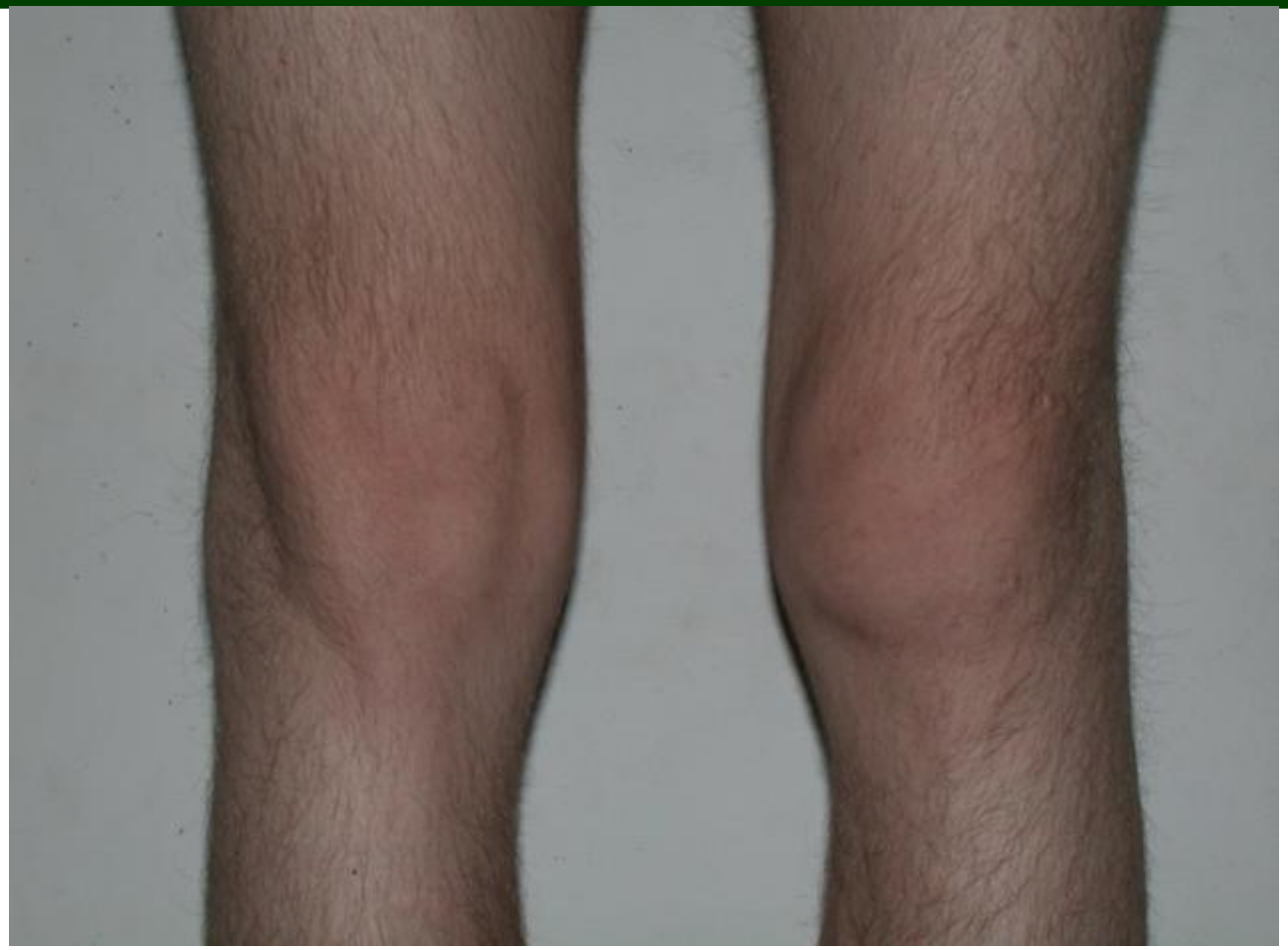
The musculoskeletal consequences of "undertreatment"



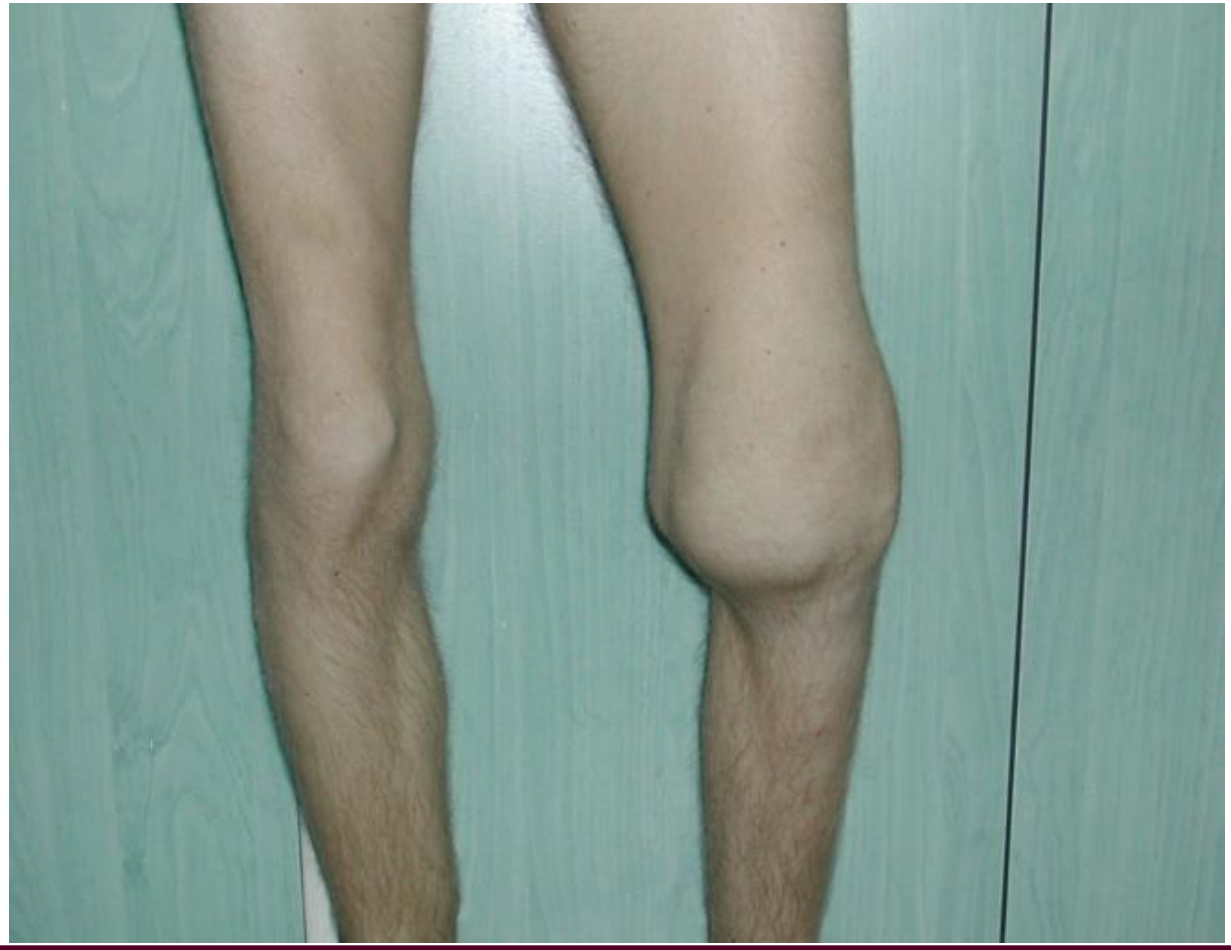




“Target” joint, Chronic Synovitis



Advanced state of haemophilic arthropathy



Treatment Principles

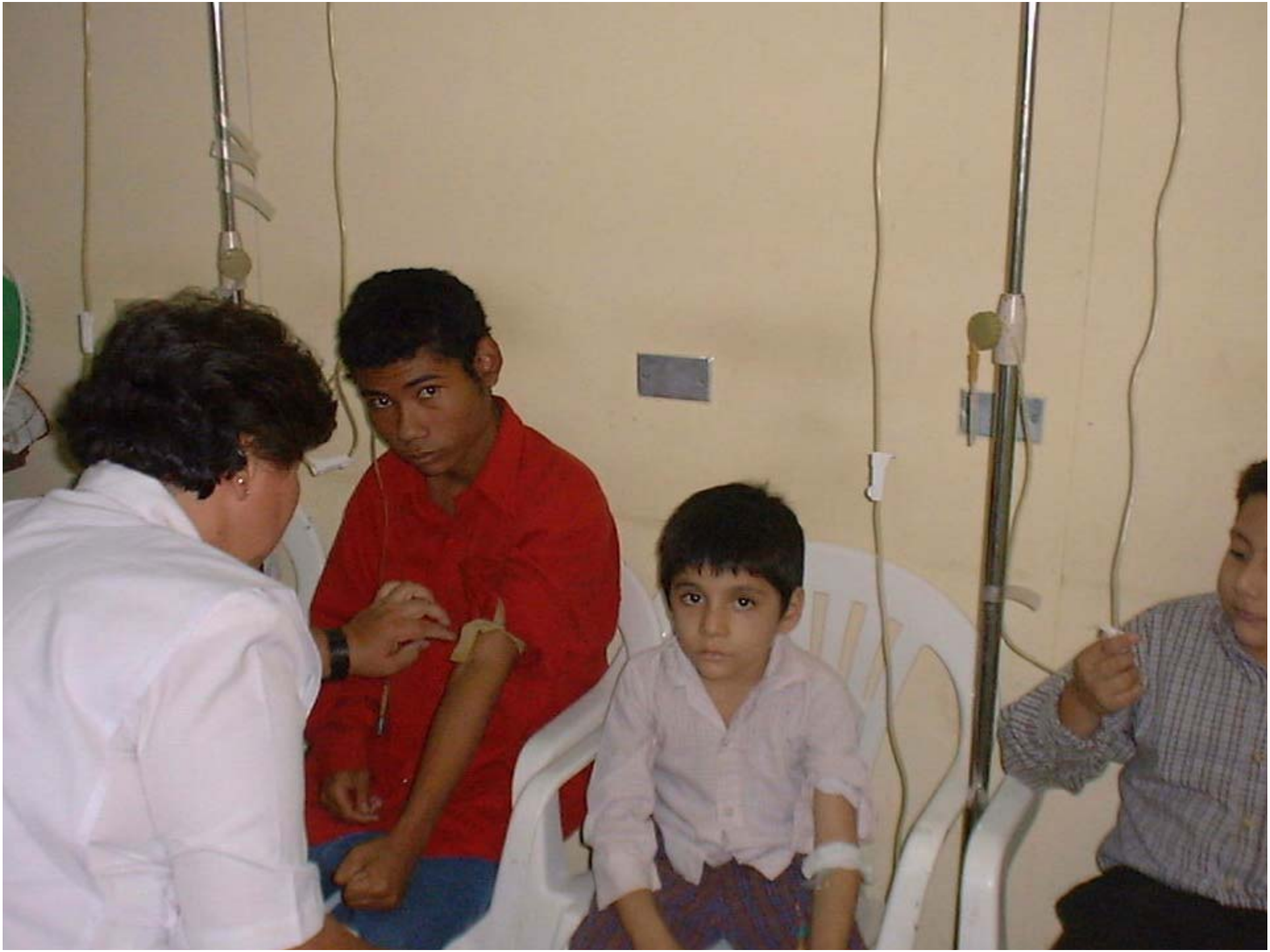
- Prevention of bleeding should be the goal - Prophylaxis
- Treat acute bleeds early
- Home therapy – early treatment
- Severe bleeds – hospital
- Avoid aspirin, Intramuscular injections, non steroidal anti-inflammatory agents
- Treat with Factor Concentrates

Development of Replacement Therapy

1960's
- Plasma
- Cryoprecipitate

1970's
- Cryoprecipitate
- Factor Concentrates
- Prothrombin Complex Concentrates

1980's
- Concentrates
- Virally inactivated concentrates



Development of Replacement Therapy

1990's
- High Purity Concentrates
- Recombinant concentrates
- DDAVP

2000's
- 2nd Generation Recombinant
- 3rd Generation recombinant

Plasma-derived Concentrate

- Manufactured from plasma
- Virally inactivated
- Excellent safety record since 1991
- Donor selection
- Donor screening (tests)
- Good manufacturing practice
- Viral inactivation
- Post use surveillance

Recombinant Concentrates

- Manufactured from cell bank with recombined gene
- Viral inactivation
- No viral transmissions since use in 1994

- 1st Generation
- 2nd Generation
- 3rd Generation

On Demand Therapy

- Treat bleeding episodes
- Treat early
- Home treatment
  - Clinical management

Prophylaxis

- **Prevention**

  Maintain level > 1%

  FVIII - 3 times weekly

  FIX - 2 times weekly

  CVAD devices

  Secondary prophylaxis

  - Target joint
  - Life event

Factor replacement therapy

Outcome at different doses

	France ('on demand')	The Netherlands (intermediate-dose prophylaxis)	Sweden (high-dose prophylaxis)
Numbers	116	21	19
Age at study analysis	23	21	16–22
Age at start of home treatment	8.9	9.1	NA
Age at start of prophylaxis	NA	4.6	2.6
Annual number of joint bleeds	**16.3**	**5.3**	**3**
Pettersson score	18.8	6.0	6.5
Orthopaedic joint score	7.7	2.0	2.4
Clotting consumption (IU/kg/year)	1634	1828	3713

van den Berg HM, *et al.* Haemophilia 2003;9(suppl):27–31

Manco Johnson Study - Prophylaxis New England Journal of Medicine 2007

- Data on 65 children with Haemophilia collected over 5 years
- On –demand v Prophylaxis
- 93% on Prophylaxis had normal joints
- 55% On- Demand had normal joints
- **Prophylaxis associated with 83% reduction in joint damage**

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Manco Johnson Study - Prophylaxis New England Journal of Medicine 2007

- 18 abnormal joints in 15 Children
- 13/15 were on demand
- 2/15 were on Prophylaxis

Study demonstrates conclusively that Prophylaxis is effective at preventing joint bleeds and preserving joint function and structure in young boys with Haemophilia A.

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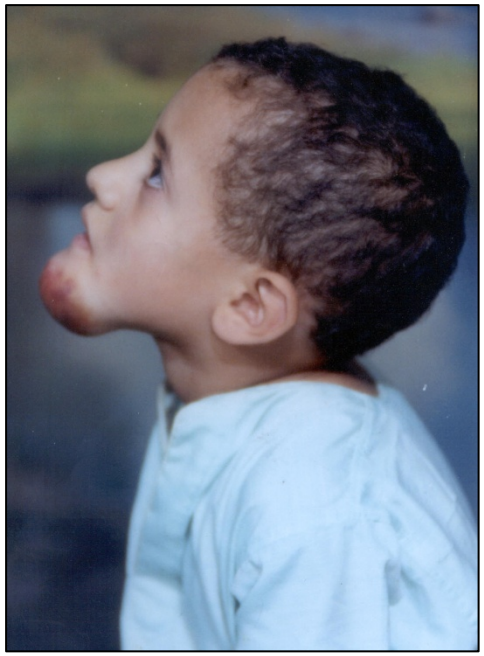
Minimum “Survival” standard

- Treatment in a care centre
- Safe and efficacious replacement therapy
- Factor concentrates for:
  - Life / Limb threatening bleeding episodes
  - Surgery
  - Major bleeding episodes



Good Standard of Care

- Treatment in a comprehensive care centre
- Provision of safe and efficacious replacement therapy
- Home treatment
- ‘On Demand’ therapy

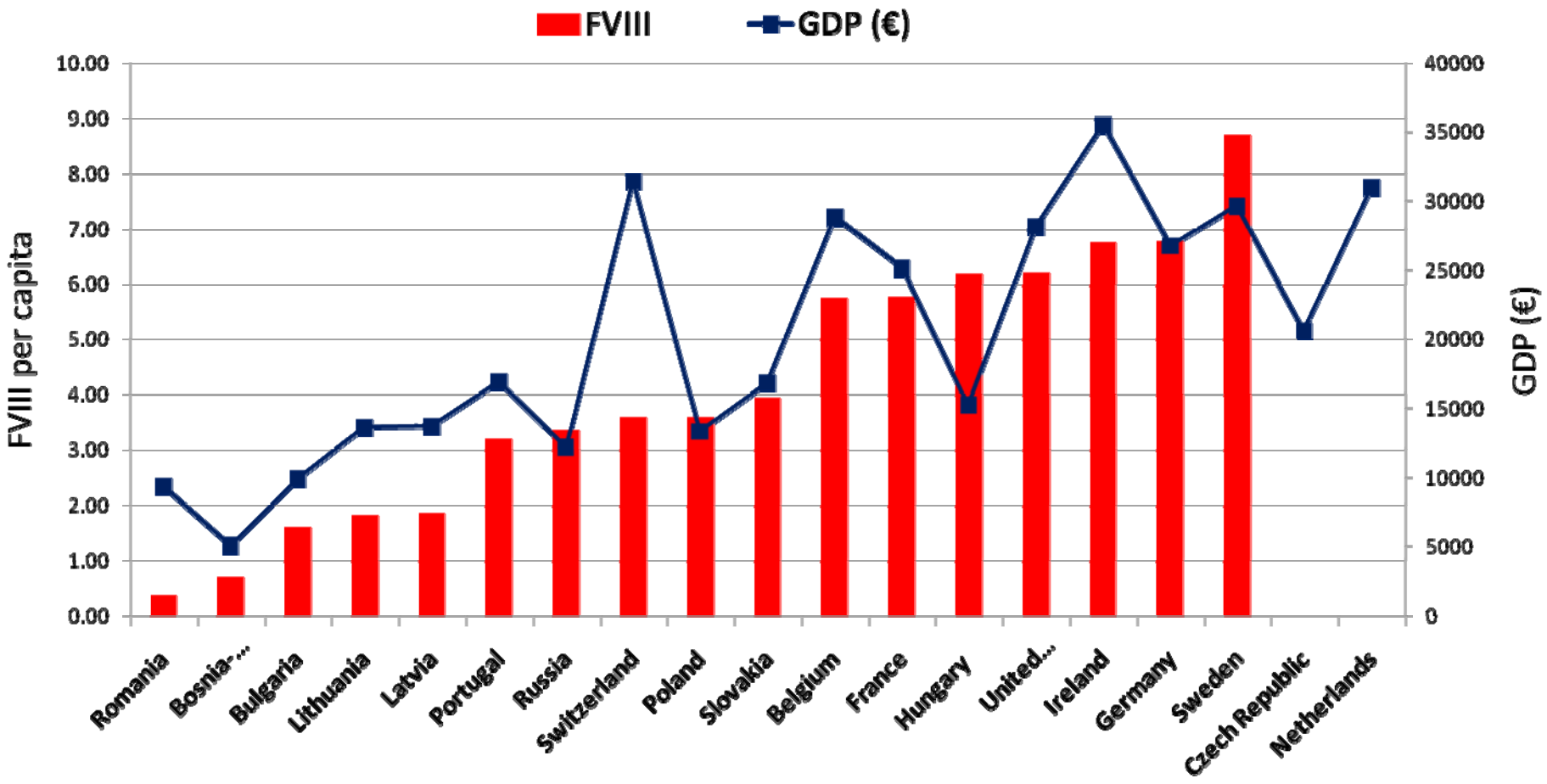
Optimum Haemophilia Care

- Treatment in a comprehensive care centre
- Provision of safe and efficacious replacement therapy
- Home treatment
- Prophylaxis
- Educated and involved patients / Parents

Objectives of Treatment-
As Access to replacement Therapy increases:

Objective	Per Capita FVIII use
Survival	0 – 1
Functional Independence	1 – 3
Joint Integrity	3 – 6
Full integration into Society	5 – 7

Concentrate Use per capita



Different Reality and perception – Optimum Care

Child :

- Normal life expectancy
- Avoid joint damage
- Normal education, career prospects
- Prophylaxis

Different Reality and perception – Optimum Care

Young Adult :

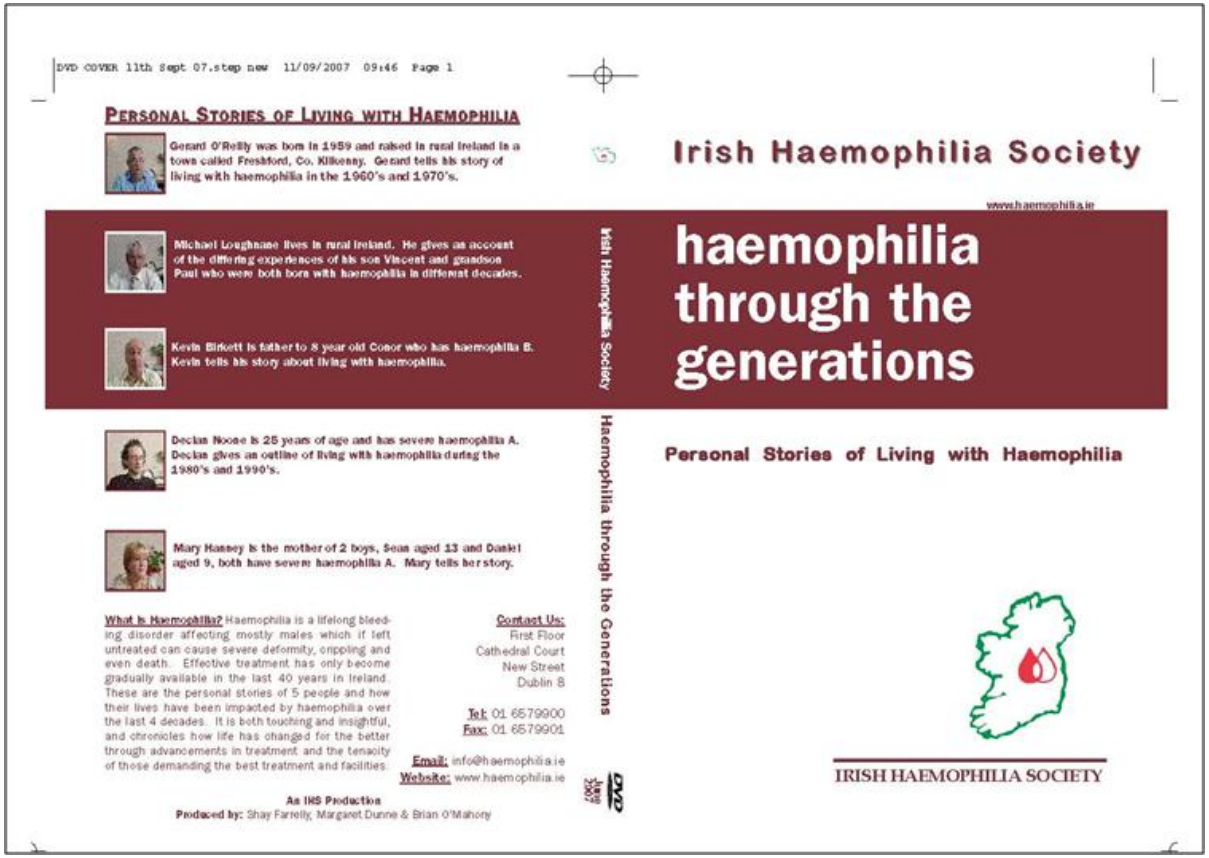
- No further joint damage
- Education, career prospects better
- Hepatitis C
  - Better treatment in 10 years
  - Relationships, lifestyle
  - Engage with peers, community

Different Reality and perception – Optimum Care

Older Adults (+ 45 yrs)

- Joint surgery, replacement
- Careers defined by past
- Better HIV therapy, survival
- More aggressive HCV therapy
- First generation who have to consider disease of old age: heart disease, cancer
- First generation to have grandchildren with haemophilia

I.H.S. Educational DVD



National Haemophilia Program…Organisation

- National Haemophilia program with Government support
- Integrated within healthcare system
- National Register
- National treatment protocols
- Organised network of treatment centre’s
- National purchase of replacement therapy

Organisation

- National Register at NCHCD
- IT system (Clintech) linking 3 comprehensive care centre's
- National Treatment protocols –NHC- endorsed by Irish Haematology Society
- 3 Comprehensive care centres- NCHCD /OLCH / CUH
- Secondary centres- Waterford /Galway / Limerick / Letterkenny / Sligo

NCHCD Ireland

Organisation

- National centre's offer 24 hour advice to other hospitals
- Patients self treat at home and attend centres for review /major bleeds / surgery/ HIV, Hepatitis C / Specialist care
- Statutory National Haemophilia Council
- Haemophilia Product Selection and Monitoring

Haemophilia Legislation- Ireland

Number 15 *of* 1996

HEALTH (AMENDMENT) ACT, 1996

ARRANGEMENT OF SECTIONS

Section

1. Short title, collective citation, construction and commencement.
2. Provision of health services without charge to certain persons who have contracted hepatitis C.

Number 34 *of* 1997

HEPATITIS C COMPENSATION TRIBUNAL ACT, 1997

ARRANGEMENT OF SECTIONS

Section

1. Interpretation.
2. Establishment day.
3. The Tribunal.
4. Claims before Tribunal.
5. Awards of Tribunal.
6. Dissolution of and claims before non-statutory scheme Tribunal.
7. Regulations to give effect to Act.
8. Settlements.
9. Extension by regulations of persons who may make a claim before Tribunal.
10. Special account.
11. Reparation Fund.
12. Report of Tribunal.
13. Power to remove difficulties.

Number 21 *of* 2002

HEPATITIS C COMPENSATION TRIBUNAL (AMENDMENT) ACT, 2002

ARRANGEMENT OF SECTIONS

Section

SI No. of 2007

HAEMOPHILIA PRODUCT SELECTION and MONITORING ADVISORY BOARD (ESTABLISHMENT) ORDER, 2007

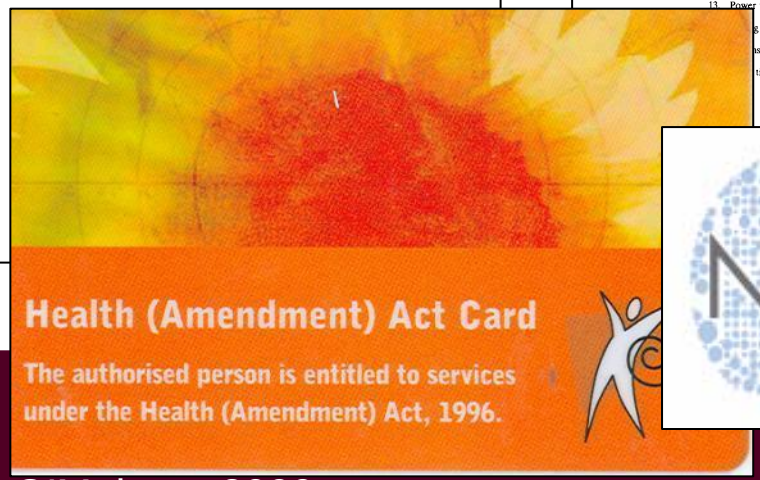
I, Mary Harney, Minister for Health and Children, (herein referred to as "the Minister") in exercise of the powers conferred on me by Section 3 of the Health (Corporate Bodies) Act, 1961 (No. 27 of 1961) as amended by Section 22 of the Health (Amendment) (No. 3) Act, 1996 (No. 32 of 1996) and adapted by the Health (Alteration of Name of Department and Title of Minister) Order 1997 (S.I. No. 308 of 1997) hereby order as follows:

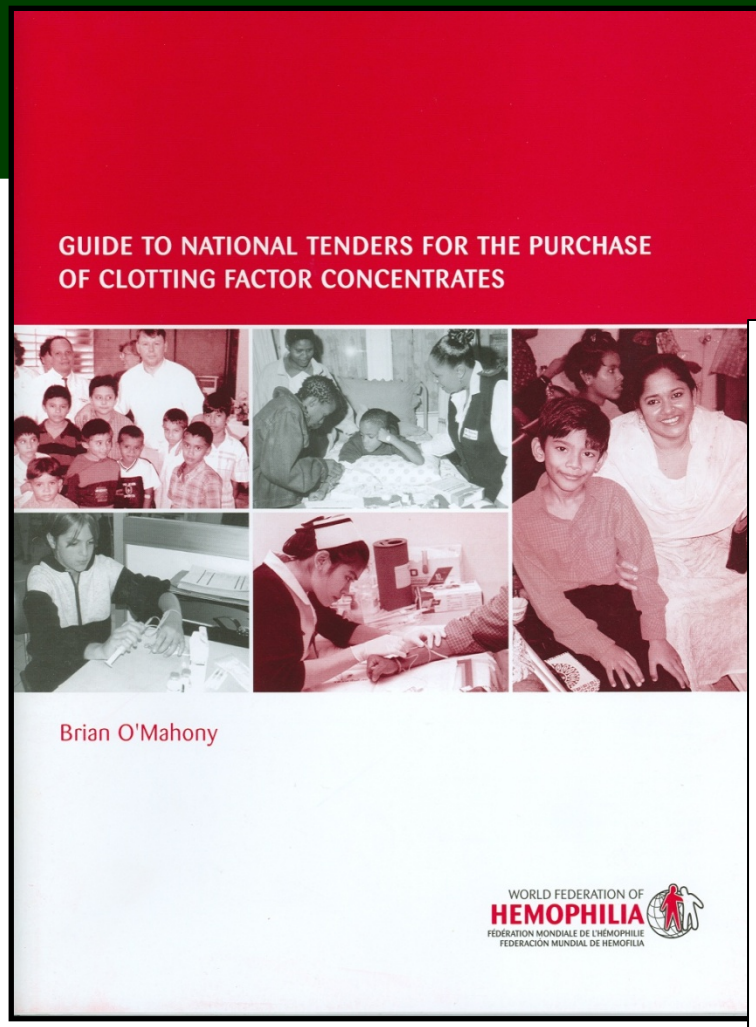
1. This Order may be cited as the Haemophilia Product Selection and Monitoring Advisory Board (Establishment) Order 2007.
2. In this Order:

"Board" means the Haemophilia Product Selection and Monitoring Advisory Board established by this Order;

"Chairperson" means the Chairperson for the time being of the Board;

3. (1) A body to be known as the Haemophilia Product Selection and Monitoring Advisory Board is hereby established to perform the functions conferred upon it by this Order.





Score Sheet: Product Selection & Monitoring Advisory Group FACTOR VIII (July 2008)							
SCORING CRITERIA		Total Marks Available	SCORES AWARDED				
Phase 1							
Safety	Human albumin in culture medium	10					
	Additional human or animal protein (eg monoclonal antibodies)	5					
	Viral inactivation	10					
	Inhibitors	30					
	Prion Removal	10					
	Excipients (presence or absence of albumin as a stabiliser)	20					
	Others	10					
	Total for Safety	95					
Efficacy	Recovery/Half Life (adult/paediatric)	12					
	Clinical Response (adult/paediatric)	18					
	Total for Efficacy	30					
Quality	Stability	5					
	Volume of Administration	3					
	Instructions for Use & Handling	3					
	Ease of Administration	4					
	Application of Unique Bar-Code	3					
	Total for Quality	18					
Security of Supply / Availability	Number of Manufacturing Plants	6					
	Security of Supply	10					
	Total for Supply/ Availability	16					
Scientific Support	Clinical Opinion	3					
	Consumer Opinion	3					
	Tender	3					
	Total for Scientific Support	9					
Total Scores Awarded: Phase 1		168					
Phase 2							
Cost	Total For Cost	30					
Total Scores Awarded: Phase 2							