

Ageing and haemophilia

Dr. Michelle Lavin

Senior Clinical Research Fellow

NCC/RSCI



ST. JAMES'S
HOSPITAL



Ageing and haemophilia

- Joint damage
- Bleeding risk
- Operations
- Inhibitors
- Dentition
- Bone health

Ageing and general health

- General health
- Cardiovascular disease
- High blood pressure
- Poor kidney function
- Prostate issues

Arthropathy

- Physiotherapy and Exercise
- Maintain muscle strength, balance, bone health
- Orthotics
- Adaptation/Aids
- Radiosynovectomy
- Orthopaedic surgery

Bleeding

Variable bleeding patterns

- Less joint bleeding due to decreased activity, synovium burnt out
- BUT
- Any bleeding into damaged joints may be problematic
- Prophylaxis
 - Primary ?continue
 - Secondary

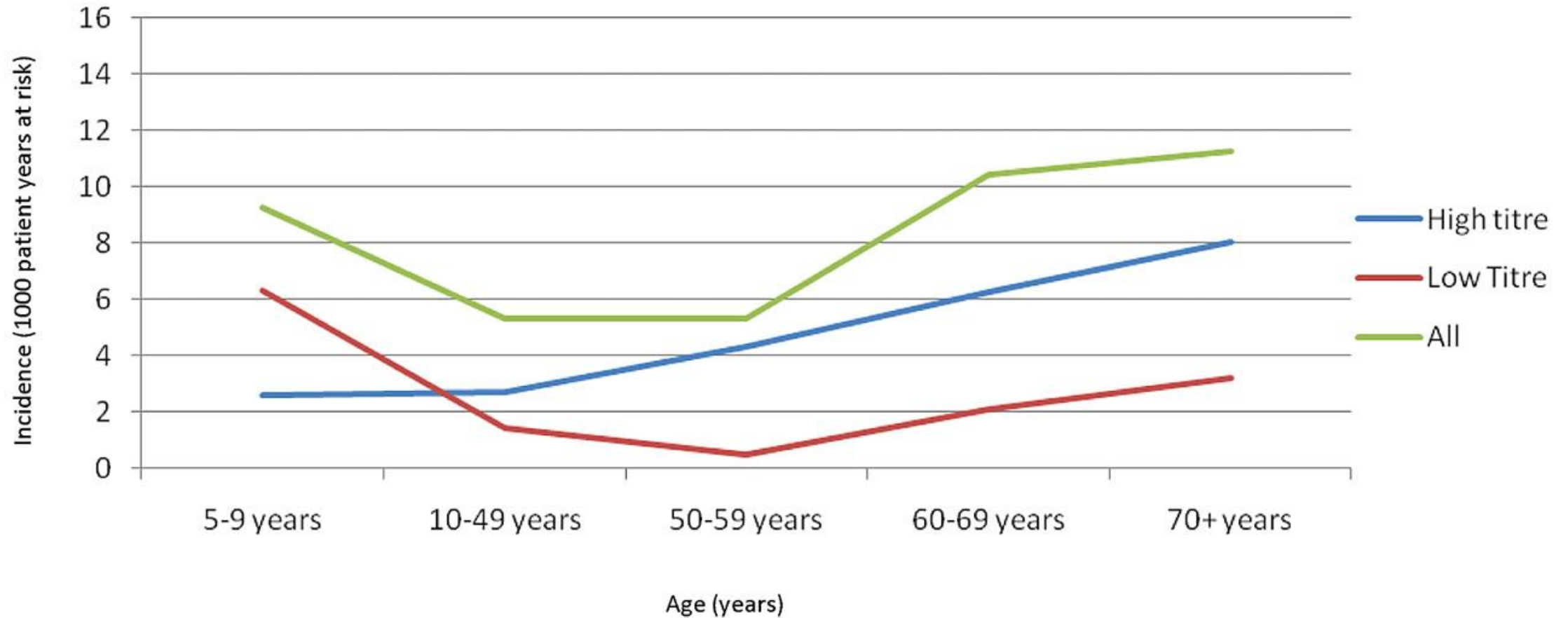
Pain management

- Paracetamol ± Codeine
 - Etoricoxib/Arcoxia – anti-inflammatory
 - Lignocaine patches
 - Opiates
-
- Non-medication techniques – exercise, sleep, meditation

Operations

- Surgical procedures increase with age
- Particular importance people with mild haemophilia

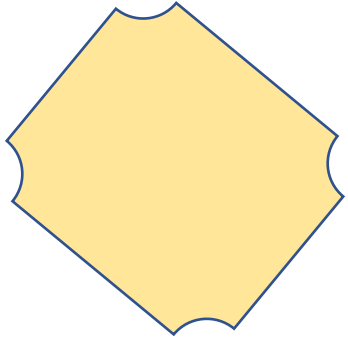
Inhibitor risk with age



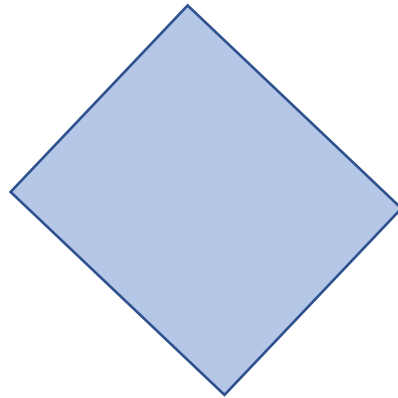
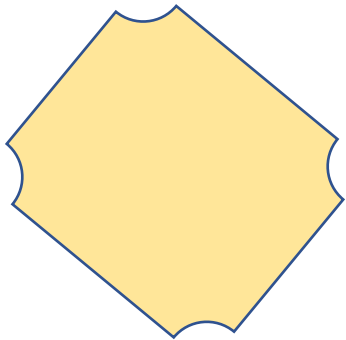
Your own Factor VIII

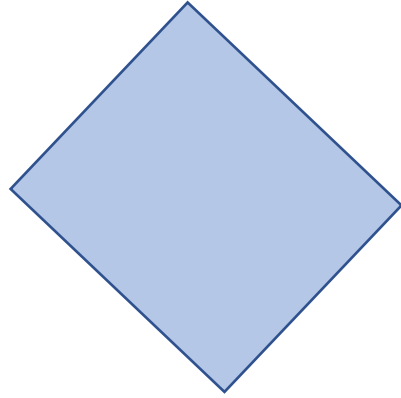
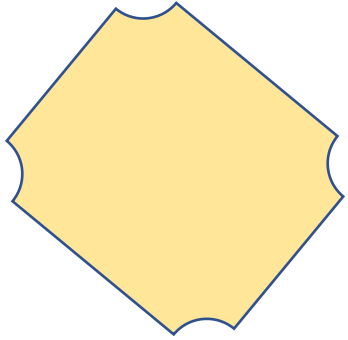
None

Your own Factor VIII

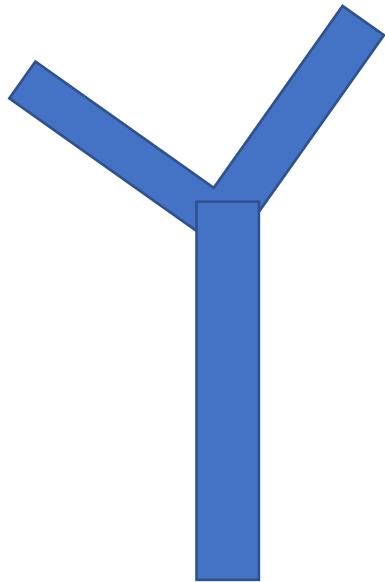


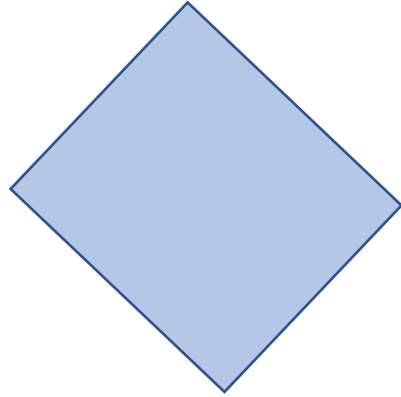
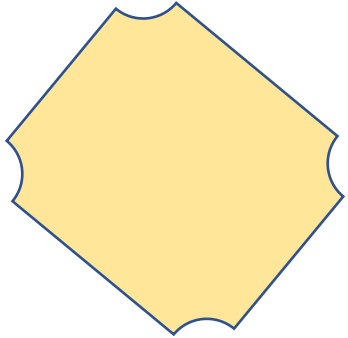
Administered
Factor VIII



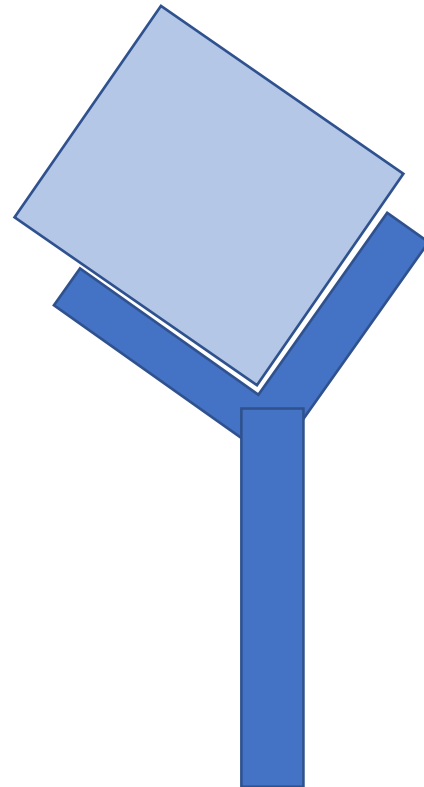
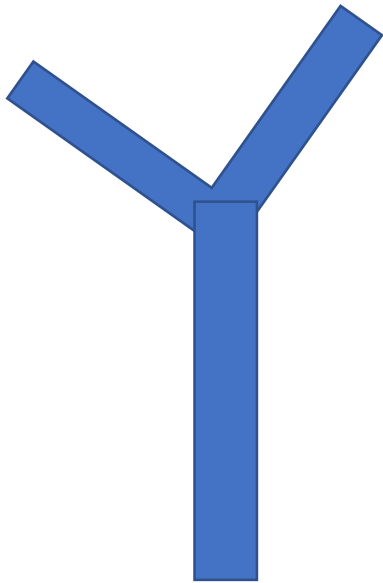


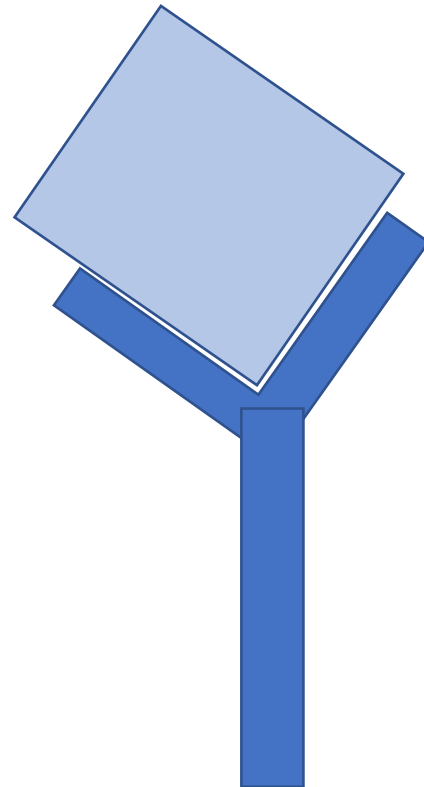
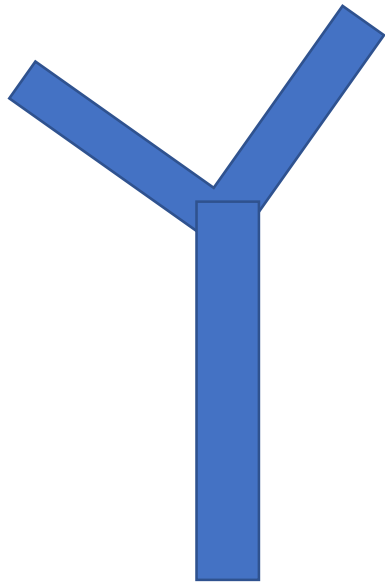
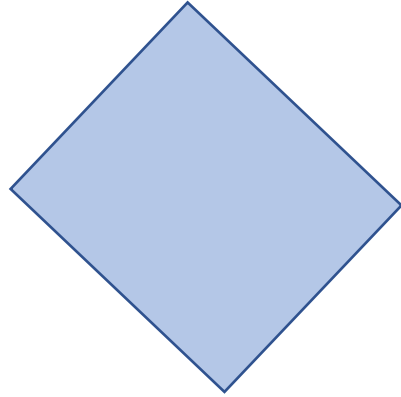
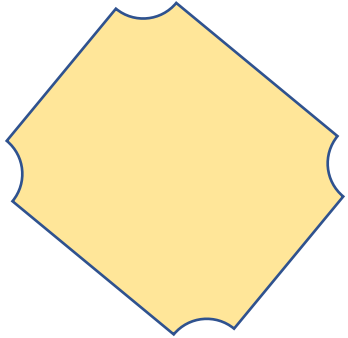
Body recognises as a foreign substance and makes an inhibitor



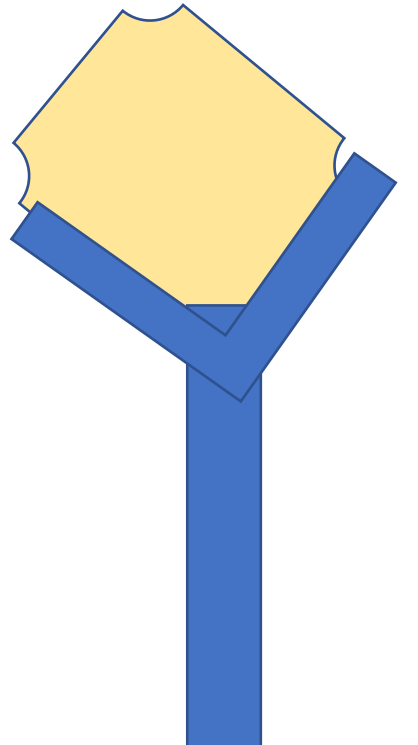


Binding of inhibitor to administered
Factor VIII stops it working as effectively



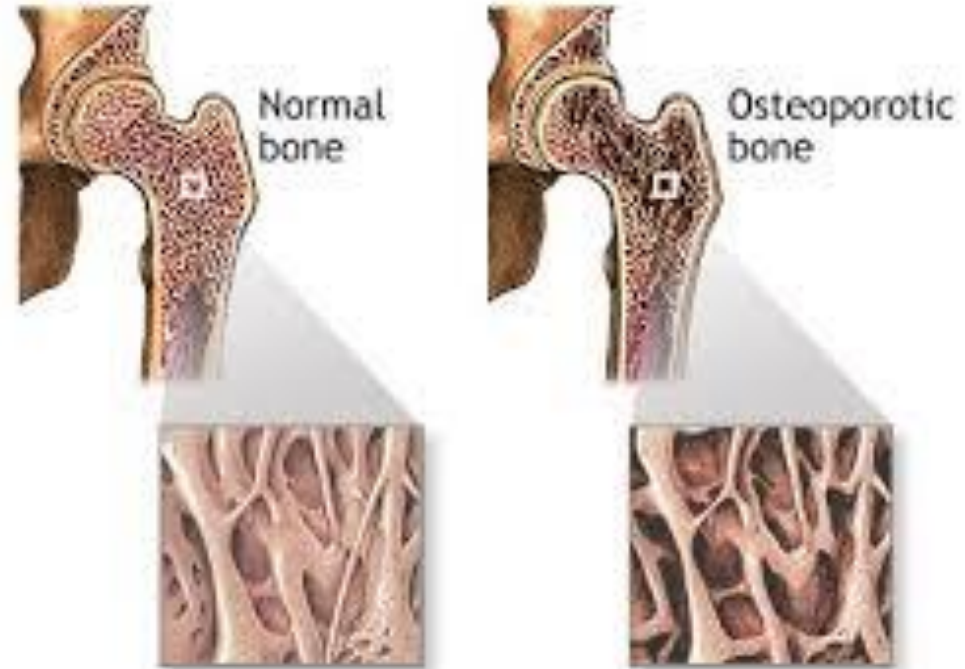


Binding of inhibitor to
your own Factor VIII
may reduce Factor VIII levels



- Risk of developing inhibitor with intense exposure to factor concentrate
- Mild haemophilia - may cross react with your own Factor VIII
 - Lower Factor VIII levels

Osteoporosis



Why does this matter in haemophilia

- UK, case control, n=37¹
- PWH =5% osteoporosis, 24% osteopenia; (controls= 0%, 3%)
- 91% vs 92% controls had low Vitamin D
- ? Peak BMD reached

- Low Vitamin D, reduced BMD
- Greece (n=104)² ; Italian study (n=78)³ ; Arizona (n=30)⁴

1. Wells et al. Haemophilia 2014
2. Anagnostis et al. Thromb Haemost 2012

3. Linari et al. Haemophilia 2013
4. Gerstner et al. Haemophilia 2009

- Meta-analysis, 13 studies
- Men with haemophilia -significant reduction in both lumbar spine and hip BMD
- Appears to begin in childhood

NCC Screening programme

- Bloods and DXA scan **all** patients with moderate and severe Haemophilia A & B
- Updated on results

Osteoporosis Prevention

Maximise and maintain bone mass – weight bearing or resistance exercise (adjust the factor treatment if needed)



Osteoporosis – More Prevention!

Vit D – Get out in the Sun (but not too much!)



67.3% of 153 patients admitted with hip fracture low Vita D levels

No excess alcohol, No Smoking

Calcium in your diet

SMART






Safe Sun Exposure NHS Advice






- Spend time in the shade between 11.00 am and 3.00 pm.
- **M**ake sure you never burn.
- **A**im to cover up with a T-shirt, hat and sunglasses.
- **R**emember to take extra care with children.
- **T**hen use factor 15+ sunscreen.

You should have >400 IU of Vitamin D per day.....

Cow's milk	3-40 IU/L
Fortified infant formula	400 IU/L
Butter	35 IU/100g
Egg yolk	20-25 IU/yolk
Cod liver oil	1360 IU/tsp
Fish	44-624 IU/100 g
Yoghurt	89 IU/100g
Cheese	12-44 IU/100g

Vitamin D – the top 10.....

	1	SUNLIGHT PROMOTES SYNTHESIS IN THE SKIN
COD LIVER OIL 440 IU (100% DV) 1 TSP	2	
	3	SALMON 400 IU (100% DV) 3 OZ
MACKEREL 400 IU (100% DV) 3 OZ	4	
	5	TUNA 228 IU (57% DV) 3 OZ

SARDINES 164 IU (41% DV) 3 OZ	6	
	7	RAW MILK 98 IU (24% DV) 1 CUP
EGGS 41 IU (10% DV) 1 LARGE	8	
	9	CAVIAR 33 IU (8% DV) 1 OZ
MUSHROOMS 2 IU (1% DV) 1 CUP	10	

Oral health

- Importance of dental health
- Bleeding is not normal
- Affect diet, nutrition
- Microbiome may be linked to cardiovascular disease risk



Oral health



Solution?

- Make friends with your Dentist
- Dental letters for Mild and Severe bleeding disorders available

General health

- Cardiovascular disease
- High blood pressure
- BMI
- Bowel screen
- Prostate cancer

Cardiovascular disease - (CVD)

- Systematic review - toward protection from CVD – not significant ¹
- Case control study ²
 - 100 hemophilia A and B patients; 200 unaffected controls
 - No significant difference in deaths from CVD over 10 years
 - Despite more diabetes and high blood pressure
 - ? protective effect of the hemophilia

1. Biere-Rafi S, Zwiers M, Peters M, et al. Neth J Med 2010;68:207–214.

2. Biere-Rafi S, Baarslag MA, Peters M, et al. Thromb Haemost 2011;105:274–278

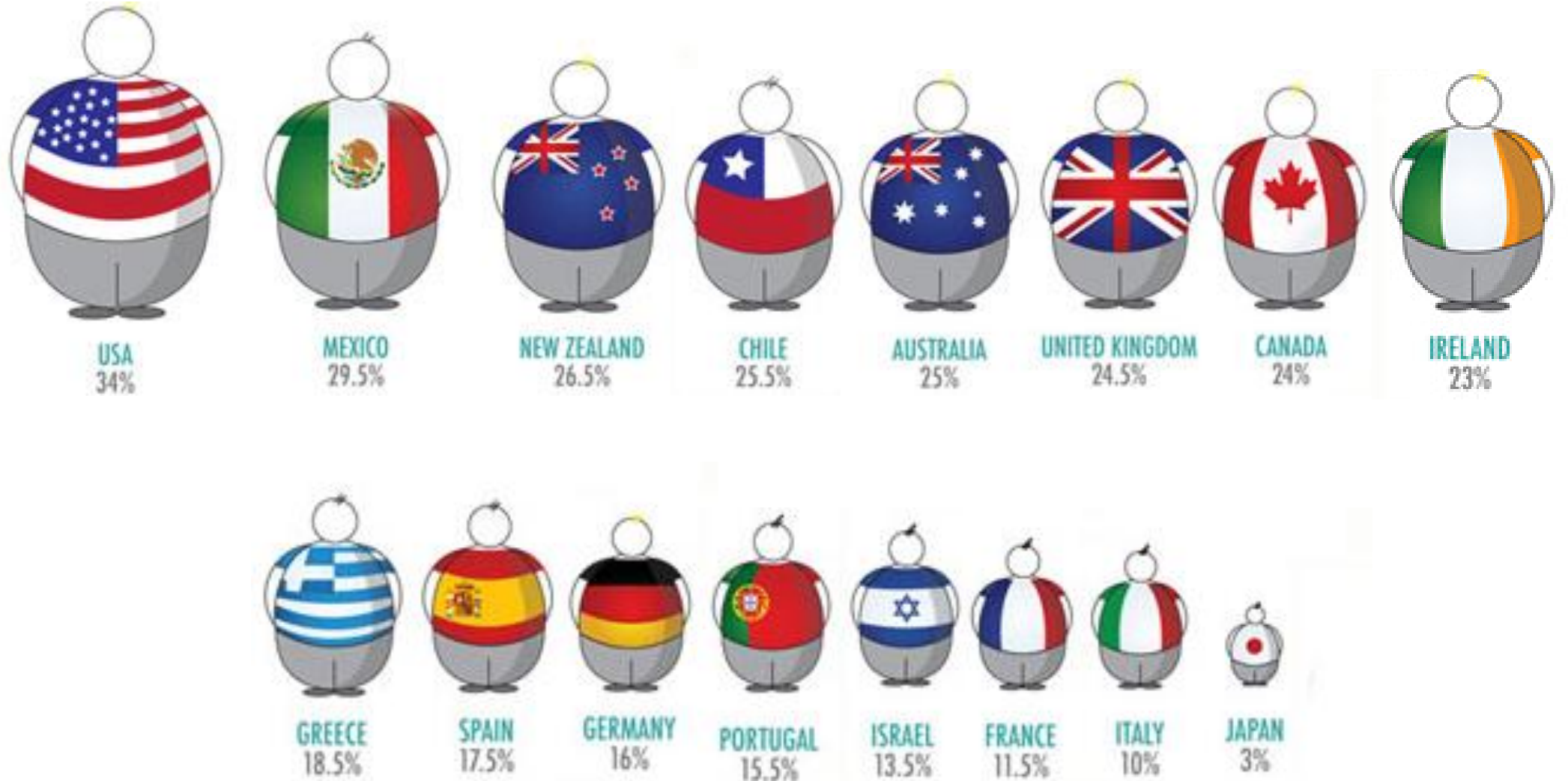
CVD

- Carotid intimal thickness - 69 PWH¹
 - not protected against the development of atherosclerosis
 - related to the traditional cardiovascular risk factors
- HIV - accelerated CVD²

1. Zwiers et al. J Thromb Haemost 2012 Jan;10(1):23-9

2. Triant VA, et al. J Clin Endocrinol Metab 2007;92:2506–2512.

% Population obese



BMI and obesity

- 2011 figures
- Additional 34% Irish adults overweight

BMI

- Increased weight
 - Joints
 - Bleeds
 - How to dose prophylaxis/treatment
- Heart disease and stroke.
- High blood pressure.
- Diabetes.
- Some Cancers
- Breathing problems

Does haemophilia reduce CVD risk

- What to believe.....
- Screening risks
- Arcoxia
- No smoking

- If you develop cardiovascular disease – what next ?

The dreaded....



- Cardiovascular disease
 - Anticoagulation
 - Antiplatelet

Kidney disease

- ? more common in haemophilia population¹
- 6 US states - 1993-98²
 - x50 fold increased risk death from renal disease
- Cardiovascular risk factors
- Medications (Arcoxia)

1. CKD Prognosis consortium, Lancet 2010 Jun 12;375(9731):2073-81

2. Soucie JM, Nuss R, Evatt B, et al. Blood 2000;96:437-442

Blood pressure and bleeding

- Risk for CVD
- High blood pressure may increase bleeding risk
- Uncontrolled high BP – risk of brain haemorrhage

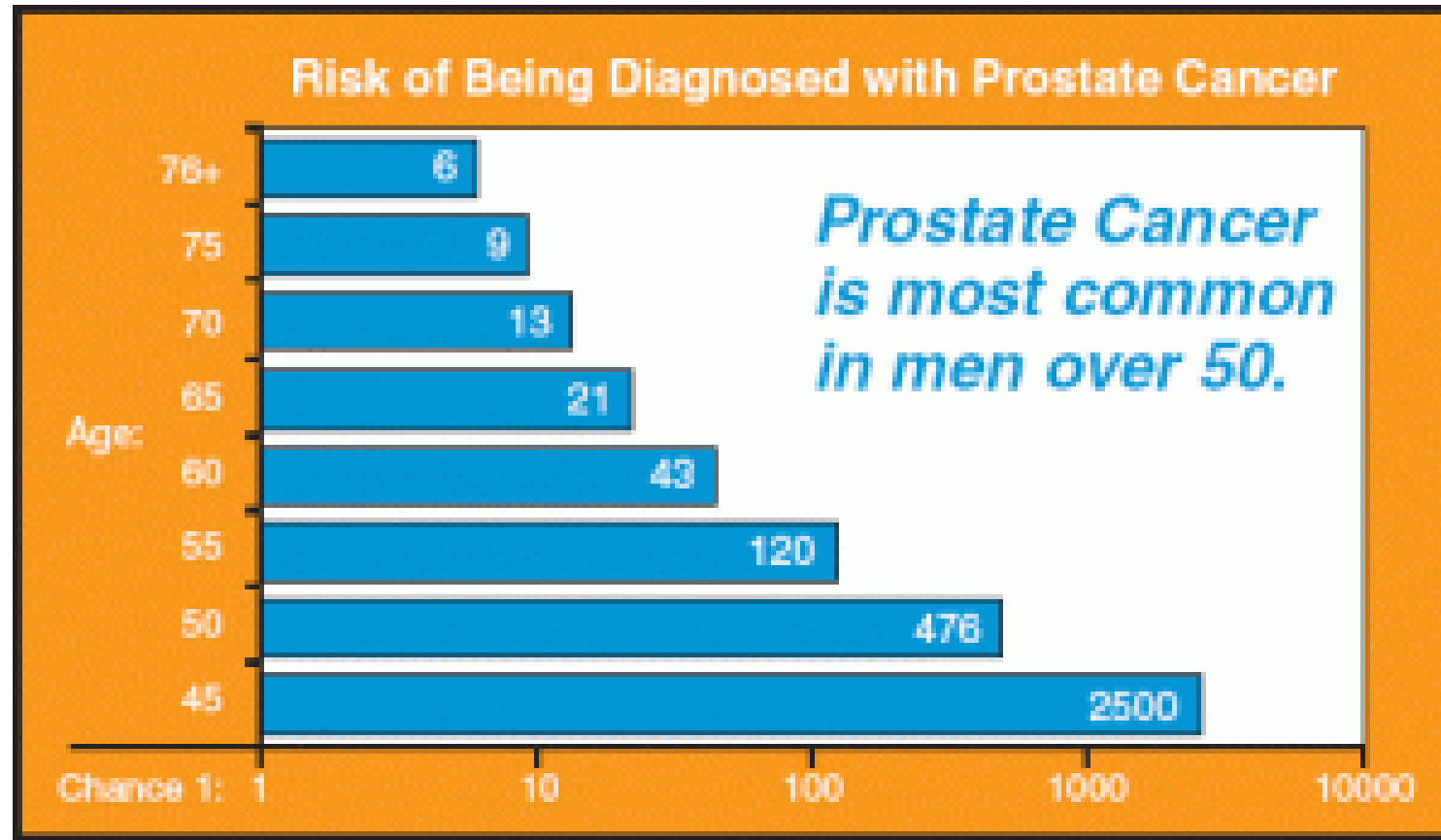
Take home message on cardiovascular disease

- GP checks
- Discussion
- Prevention is better!

Bowel screen

- Postal samples for FOB as part of the national screening programme
 - 60-69 years old every 2 years
- If positive for blood – colonoscopy scheduled
- Advise to contact screening programme and SJH

Risk of prostate cancer

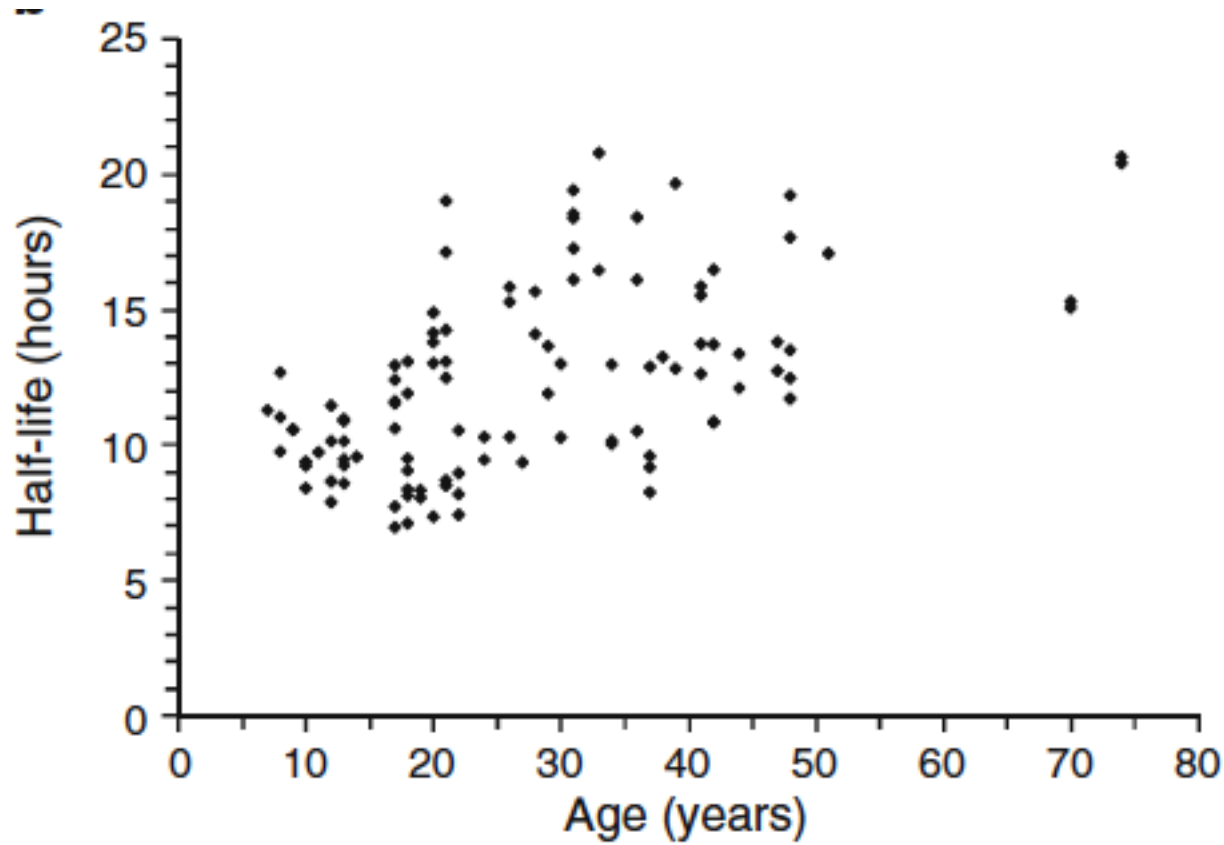


- American Cancer Society

Prostate check

- Annual check 45 -70 years of age
- PSA alone is **not** a prostate screen

All doom and gloom?



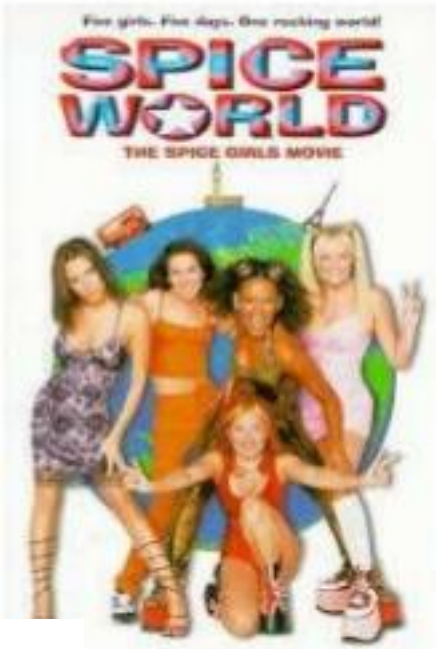
Factor VIII PK may increase with age,
not Factor IX



DANGER

Ahead

A lot changes in 20 years.....

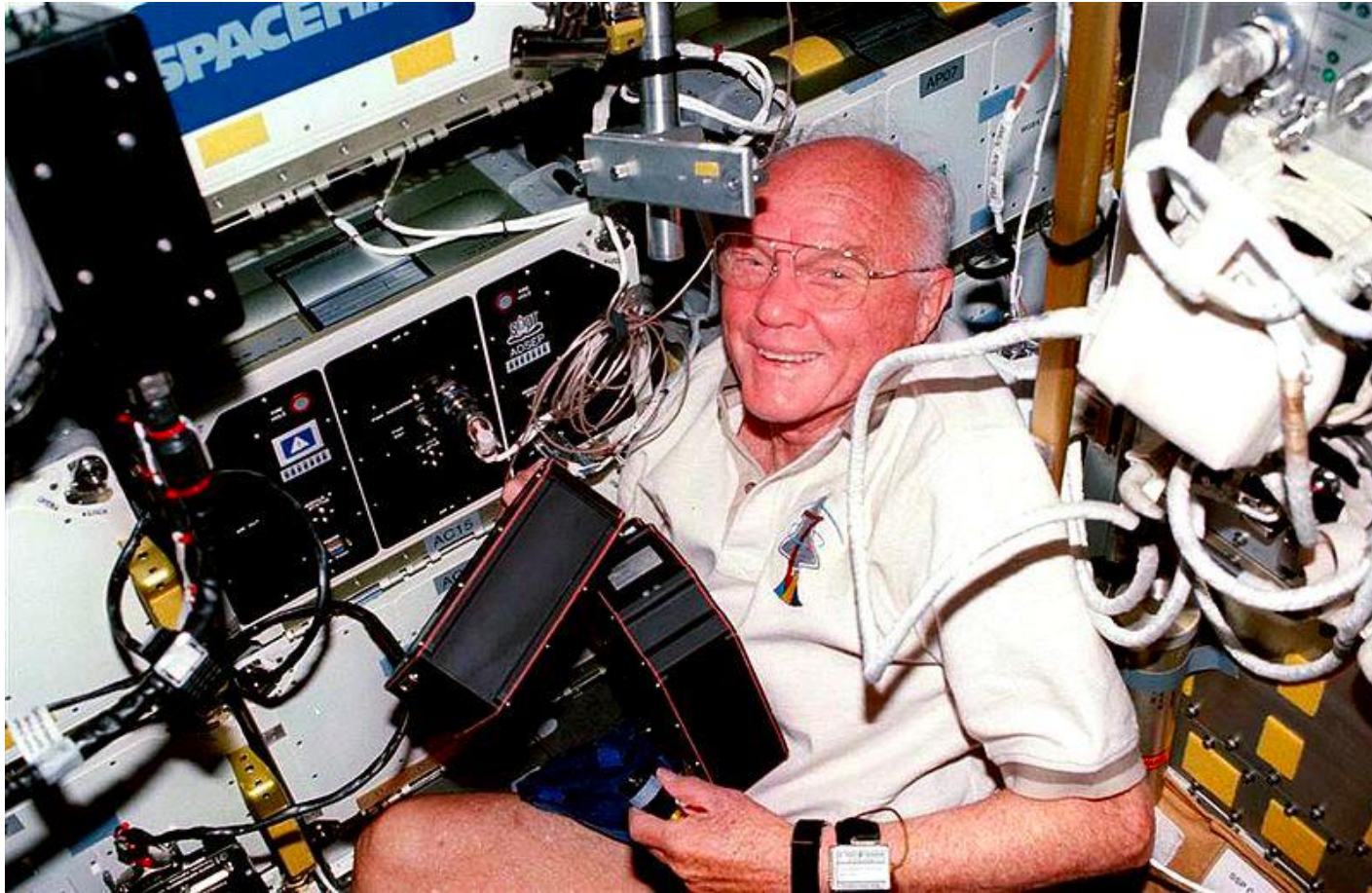


Future of haemophilia

- Personalised programmes
 - Improved understanding
- Novel treatment
 - Long acting agents
 - Emicizumab
 - Gene therapy



NO
AGE
LIMIT



John Glenn, 77
Oldest man in space



- Michael Caine, 84
- 9 films since 2010



- Harriette Thompson, 92
- Completing her 15th marathon (started running in her 70s)



Dr. Frank Schearer, 101
Oldest known water skier

- Age is an issue of mind over matter. If you don't mind, it doesn't matter
 - Mark Twain