EHC-ERN-EuroBloodNet Topic on Focus: Ageing well with rare bleeding disorders, for patients and their families

webinar

PATIENTS

HEALTH PROFESSIONALS

Bleeding Disorders and Ageing - Shall I bleed less with age?

Pr Sophie SUSEN & Pr Yesim DARGAUD
France

27 April 2026

Living Well, Ageing Well

EHC european haemophilia consortium

ebn ERN | EuroBloodNet

Disclosure for conflict of interest

Yesim Dargaud	Sophie Susen
• **Research Grants :** Bayer, Baxter, NovoNordisk, SOBI, Pfizer, CSL Behring, Octapharma, LFB • **Educational support**: NovoNordisk, Takeda, CSL Behring • **Advisory committee / Consultant** : Bayer, Baxter, NovoNordisk, SOBI, Pfizer, CSL Behring, Octapharma, LFB, Takeda, Biomarin, Roche • **Honorarium:** Institutional contracts established with the Lyon University Hospitals (HCL)	**Research Grants** : CorWave, CSL-Behring, Roche-Chugai, Stago LFB **Educational support:** Octapharma Takeda CSL Behring Advisory committee **Advisory board :** BioMarin, Bioverativ, CSL Behring, LFB, Pfizer, Sanofi, Shire/Takeda, Siemens Healthineers, NovoNordisk, Sobi **Consultant:** Advent, LFB, NovoNordisk, Sanofi, Sobi All fees go to Lille University

LEARNING OBJECTIVES

Modifications of the coagulation capacity with age

While risk of bleeding decrease with age in patients with VWD, the risk of GI bleeds may increase

Patients with hemophilia have several cardiovascular risk factors

Patients with severe hemophilia are naturally protected against thrombosis

This “protection” is lost with innovative therapies, but the same innovations open new perspectives for improved prevention and care of cardiovascular diseases

Pr Sophie SUSEN & Pr Yesim DARGAUD

01

How does blood coagulation change with age?

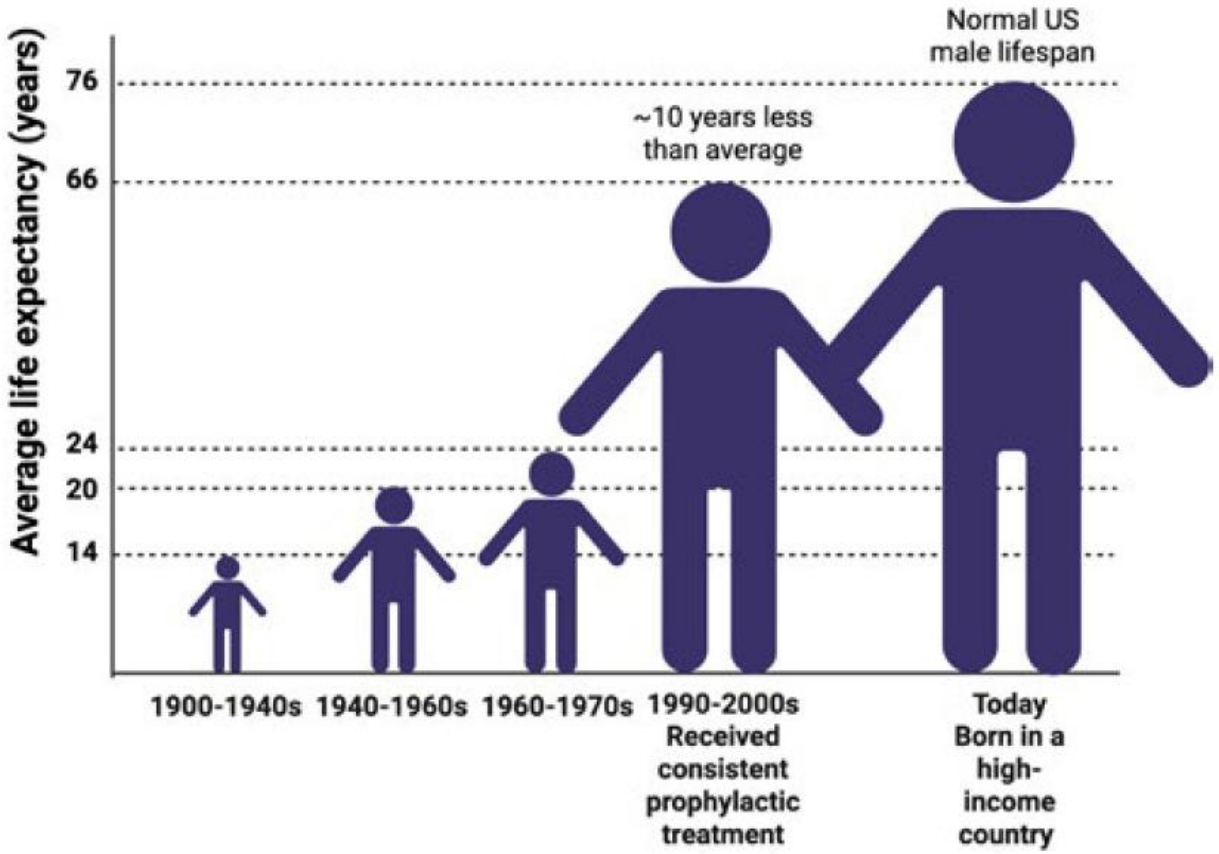
HAEMOPHILIA

RARE COAGULATION FACTOR DEFICIENCIES

VON WILLEBRAND DISEASE

Pr Sophie SUSEN & Pr Yesim DARGAUD

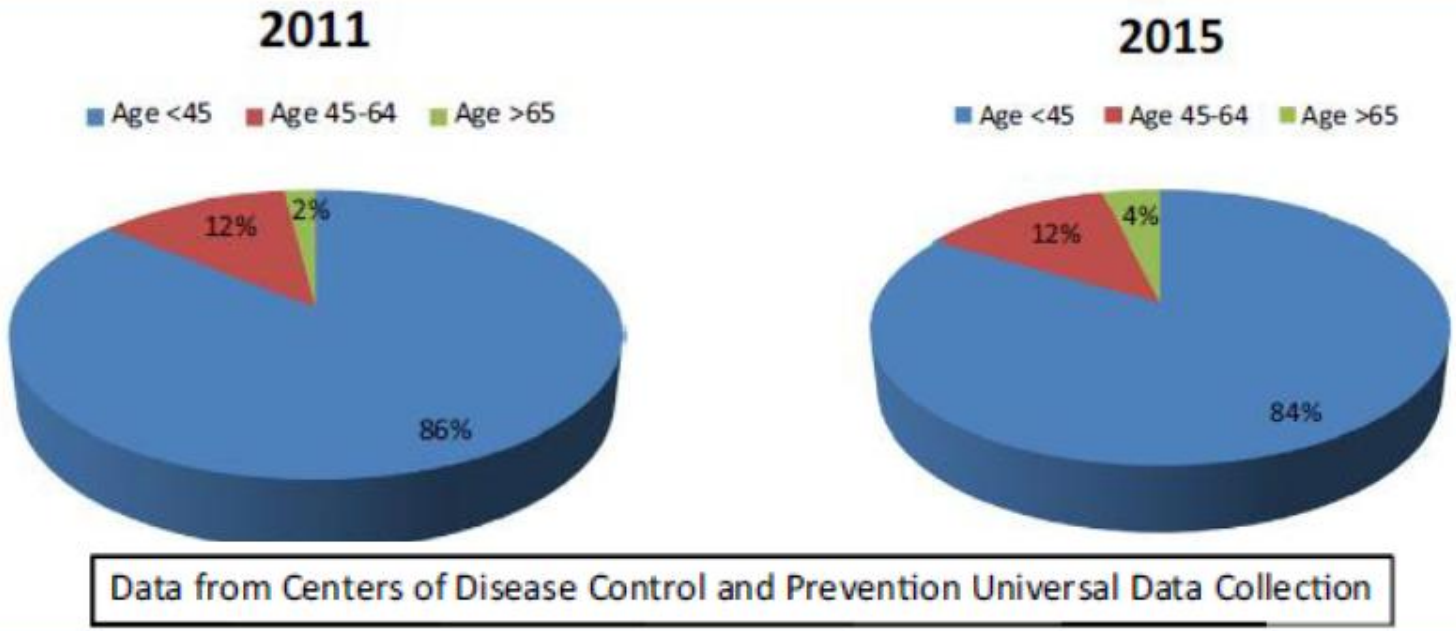
INCREASING LIFE EXPECTANCY OF PATIENTS WITH HEMOPHILIA



Lewandowska et al. Hematology 2025

Number of persons > 65 yrs with Haemophilia

PWH = ~ 400.000 worldwide

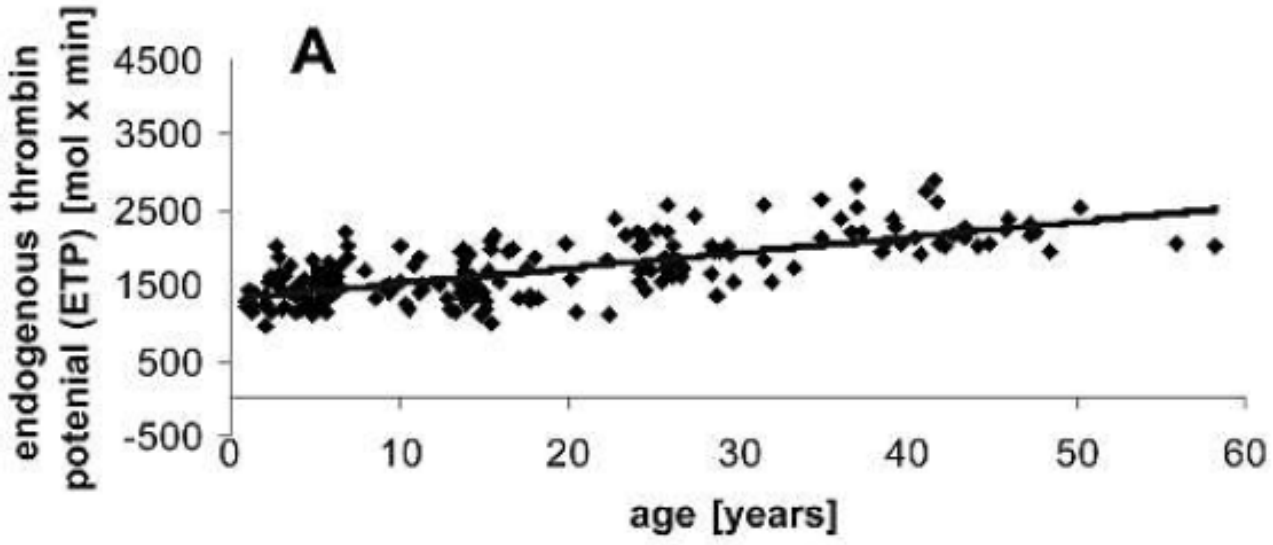


Data from Centers of Disease Control and Prevention Universal Data Collection

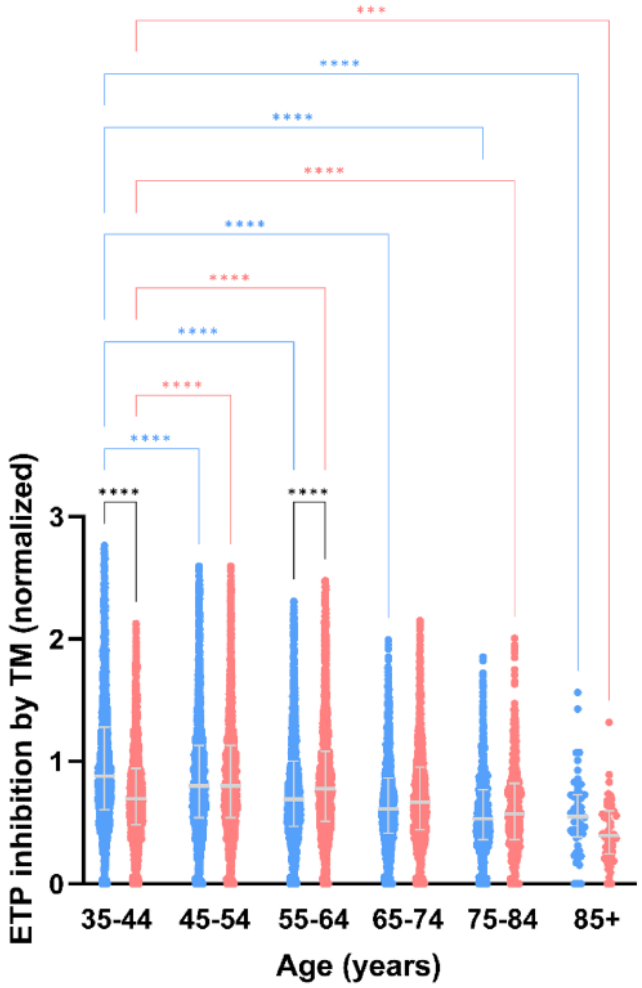
The population of elderly PWH is growing

Angelini et al Semin. Hematol 2016; 53: 35

INCREASING COAGULATION CAPACITY WITH AGE



Haidl et al. Thromb Haemost 2006; 95: 772–5



Costanzo et al. Frontiers in Cardiovascular Medicine 2025

HEMOSTATIC CHANGES WITH AGING

	Change	Estimated magnitude per decade
Procoagulants		
Fibrinogen (FI)	↑	0.8–1 g/l↑
FV	↑	5–10%
FVIII	↑	5–10%
FX	(↑)–↑	0–5%
FXIII	(↑)–↑	0–5%
vWF	↑	10–15%
Anticoagulants		
Protein C/S	↑	NA
Antithrombin	↑ (women)/↓ (men)	+ 10% (women)/ – 10% (men)
Markers of thrombin generation		
D-dimer	↑↑	10–20%
Platelets		
Platelet count	↔	–
Aggregation to ADP or collagen	↑	NA

HEMOSTASIS MEASUREMENTS IN YOUNGER CONTROLS, OLDER CONTROLS AND CENTENARIANS

Measurements	Younger controls (1)	Older controls (2)	Centenarians (3)	*P*-values			Reference values
				1 vs 2	1 vs 3	2 vs 3	
Coagulation enzymes and activation peptides							
Factor VIIa (ng/ml)	3.18 (2.76–3.64)	3.24 (2.88–3.57)	4.46 (3.91–5.06)	NS	.002	.004	2.3–5.9
Factor IX activation peptide (pmol/L)	164 (144–185)	207 (187–229)	391 (351–435)	NS	<.001	<.001	131–284
Factor X activation peptide (pmol/L)	86 (81–92)	99 (85–115)	248 (228–272)	NS	<.001	<.001	35–112
Prothrombin fragment 1+2 (mmol/L)	0.56 (0.49–0.64)	0.69 (0.61–0.78)	1.15 (0.93–1.43)	NS	<.001	<.001	0.40–1.30
Thrombin/antithrombin complex (ng/mL)	2.0 (1.6–2.4)	2.4 (2.0–2.8)	5.9 (4.5–7.6)	NS	<.001	<.001	1.0–4.0
Fibrinopeptide A (mmol/L)	0.89 (0.74–1.06)	1.22 (1.0–1.50)	1.99 (1.72–2.31)	NS	<.001	<.001	0.50–2.0
Coagulation factors							
Fibrinogen (mg/dL)	253 (244–284)	312 (287–338)	347 (313–385)	NS	<.001	.005	193–365
Factor VIII (%)	97 (80–105)	134 (119–151)	165 (147–185)	<.001	<.001	.005	53–152
Plasmin–antiplasmin complex (ng/mL)	295 (262–332)	359 (316–408)	828 (738–927)	NS	<.001	<.001	80–280
D-dimer (ng/mL)	29 (24–36)	50 (38–64)	323 (255–408)	<.004	<.001	<.001	2.0–14.0

Mari et al. Experimental Gerontology 2008

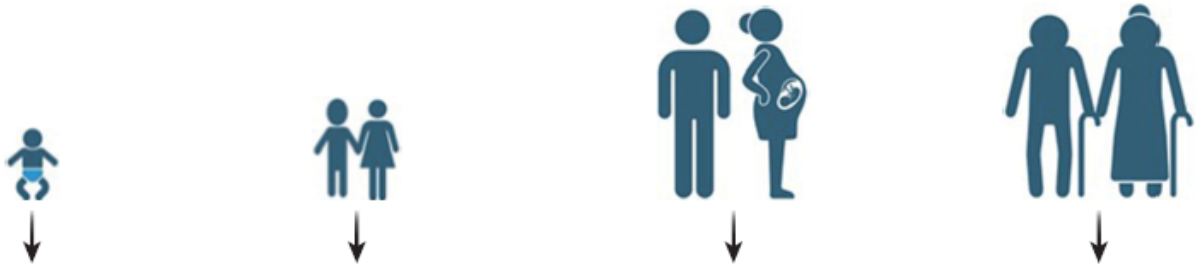
Factor IX

Age Group (yr)	N	IX:C (U/L)	IX:Ag (U/L)	Ratio IX:Ag/IX:C
0–15	58	800 ± 160	1000 ± 215	1.21 ± 0.3
16–44	43	994 ± 250	1349 ± 280	1.44 ± 0.4
45–67	19	1390 ± 480	1700 ± 330	1.32 ± 0.43

Sweeney et al. Am J Clin Pathol 1993; 99:687-688

Factor XI

Clinical Variation in FXI Deficiency: The Impact of Age and Sex



	Newborns	Children	Adults at reproductive age	Older Patients
FXI levels	Normal levels ~30%, reaching adult levels at 6 months	FXI levels reach adult levels at 6 months	Not affected by menstruation or pregnancy	Levels similar to younger adults
Surgeries and bleeding risk	Circumcision	Tonsillectomy Adenoidectomy Trauma related bleeds	Abnormal uterine bleeds Postpartum hemorrhage	Prostatectomy Urogenital surgery
Thrombosis	NA	NA	Thrombosis may rarely be associated with treatment by FXI/rFVIIa	Decreased incidence of VTE Protection from CHD (possible) [39,40]

Barg et al. Blood 2024

Mr John T… 87 y.o.

Patient Background: The patient was recently referred to our center prior to a planned mucosectomy due to a history of surgery-related bleeding and a tendency toward post-traumatic bruising.

Post–hepatitis C cirrhosis cured
Diabetes
Severe diabetic retinopathy
Obstructive sleep apnea
Moderate chronic kidney disease
Urinary incontinence
Smoking-related COPD

Bleeding History

•Tendency to develop ecchymoses after trauma, particularly in exposed areas
•History of ankle hematomas with delayed resolution
Episodes of rectal bleeding related to an anal fissure

Surgical History

•**Appendectomy (age 10):** performed at the stage of peritonitis, without hemorrhagic complications
•**Anal fissure surgery (age 44):** complicated by severe postoperative hemorrhage requiring repeated blood transfusions, leading to hepatitis C virus (HCV) infection
•**Left elbow post-traumatic hygroma (age 85):** surgically treated, complicated by a large postoperative hematoma Hemostasis

Factor IX activity: 27%
Genetic analysis confirmed the diagnosis of mild hemophilia B
Perioperative Management : The patient underwent mucosectomy using rFIX-FP (recombinant factor IX, extended half-life) administered before and after surgery
Outcome: no bleeding complications

Subsequent Clinical Course

•Six months later, the patient developed **atrial flutter**, for which catheter ablation was indicated

•The procedure was performed under **rFIX-FP coverage**, again without bleeding complications

Current Status

•The patient is now on anticoagulation therapy with **apixaban** (DOAC)

•Clinical course is favorable, with **no hemorrhagic complications reported**

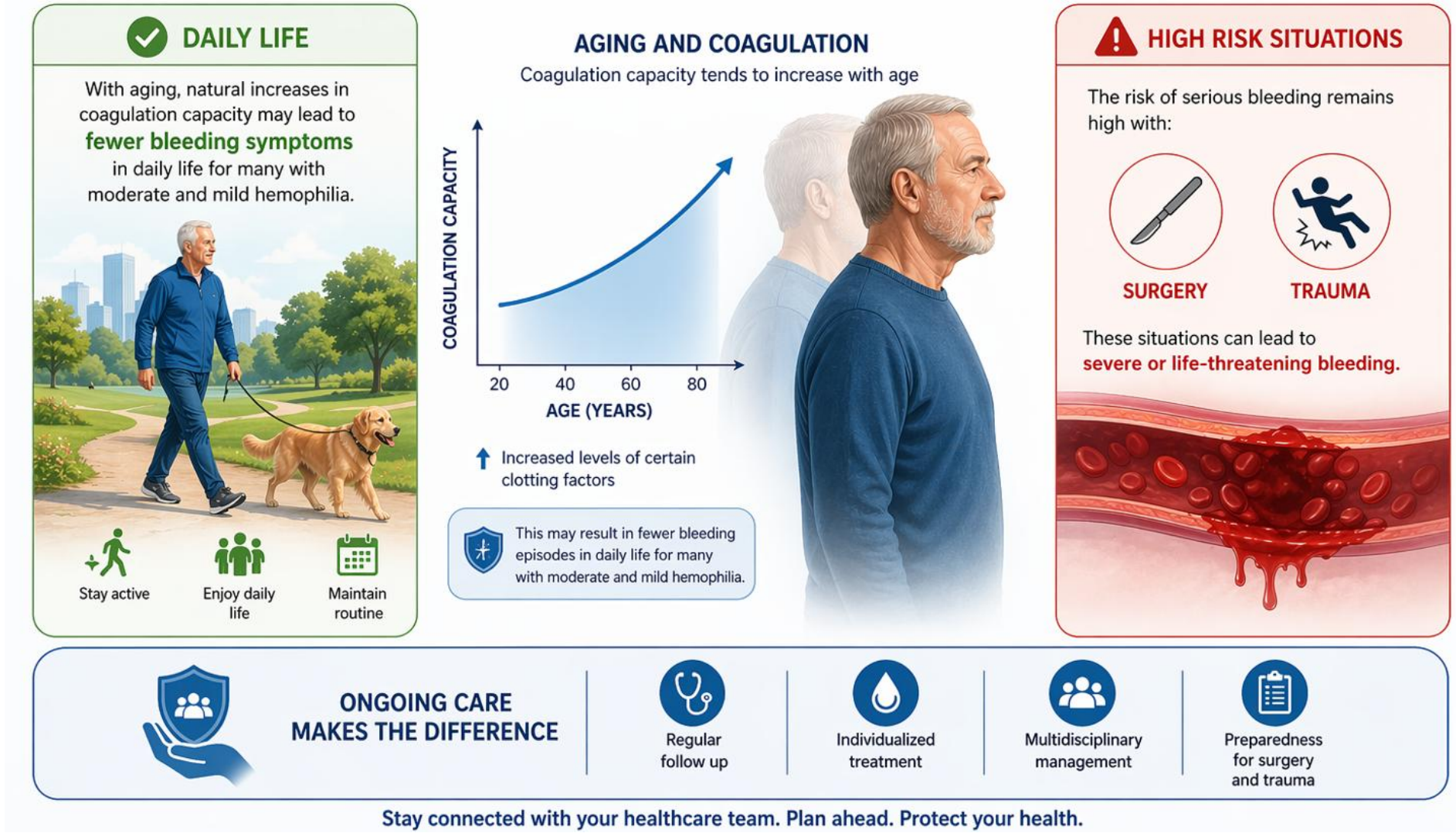
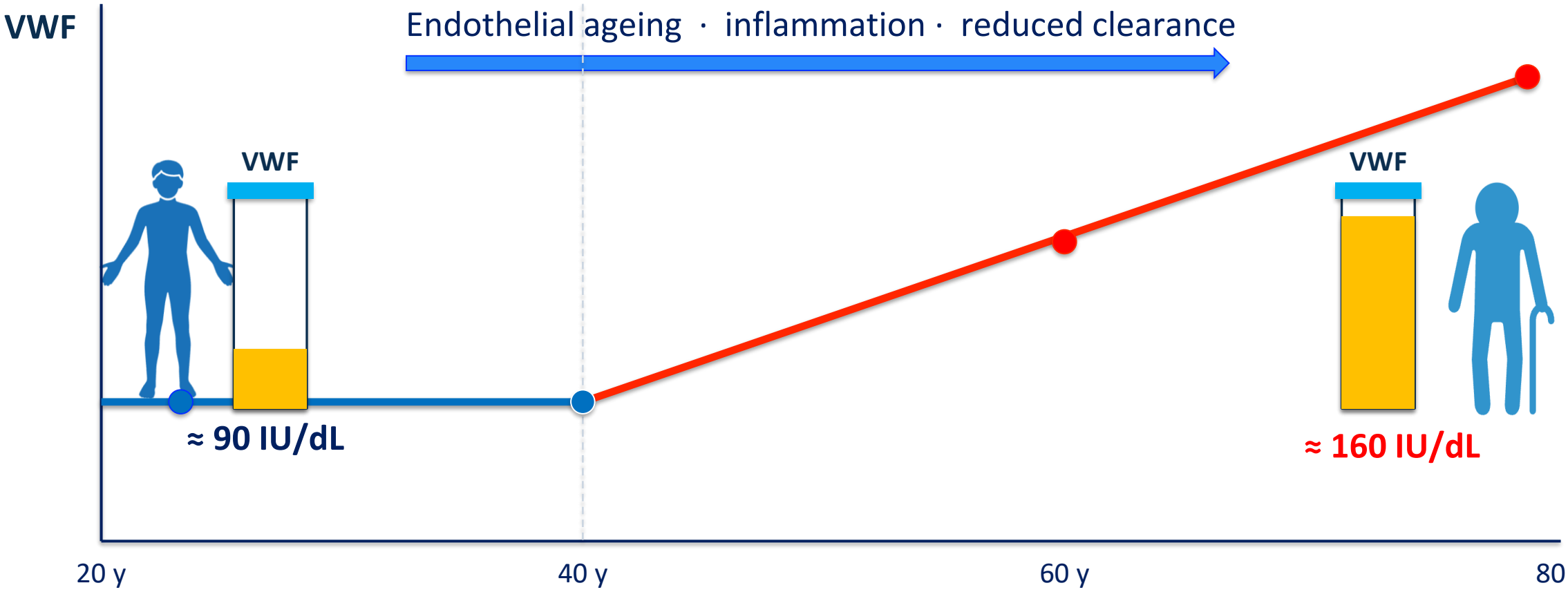


Illustration created by ChatGPTPlus

VWF increases with age

≈ +10–15 IU/dL per decade after 40 years
(general population)

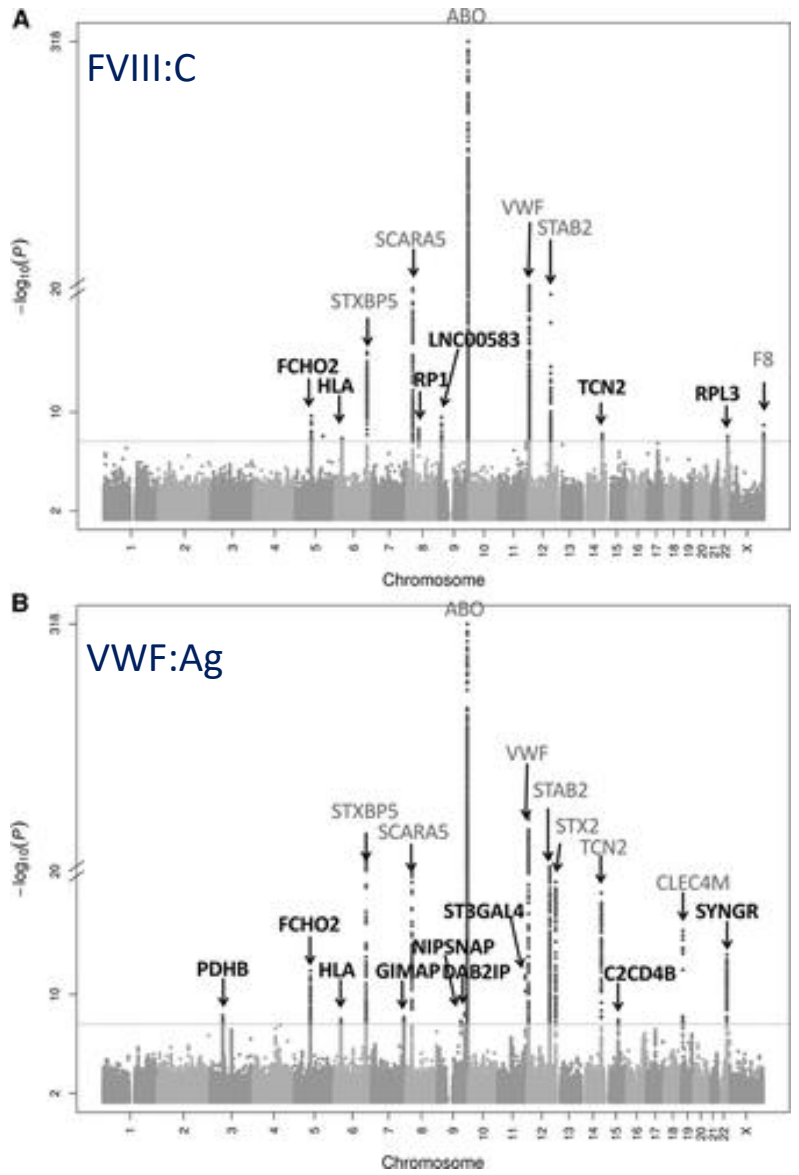


FVIII rises in parallel **ADAMTS13** activity declines **Thrombosis risk** increases

Review Seidizadeh et al. Lancet Haematol 2025

Causal role of VWF and FVIII in thrombotic events

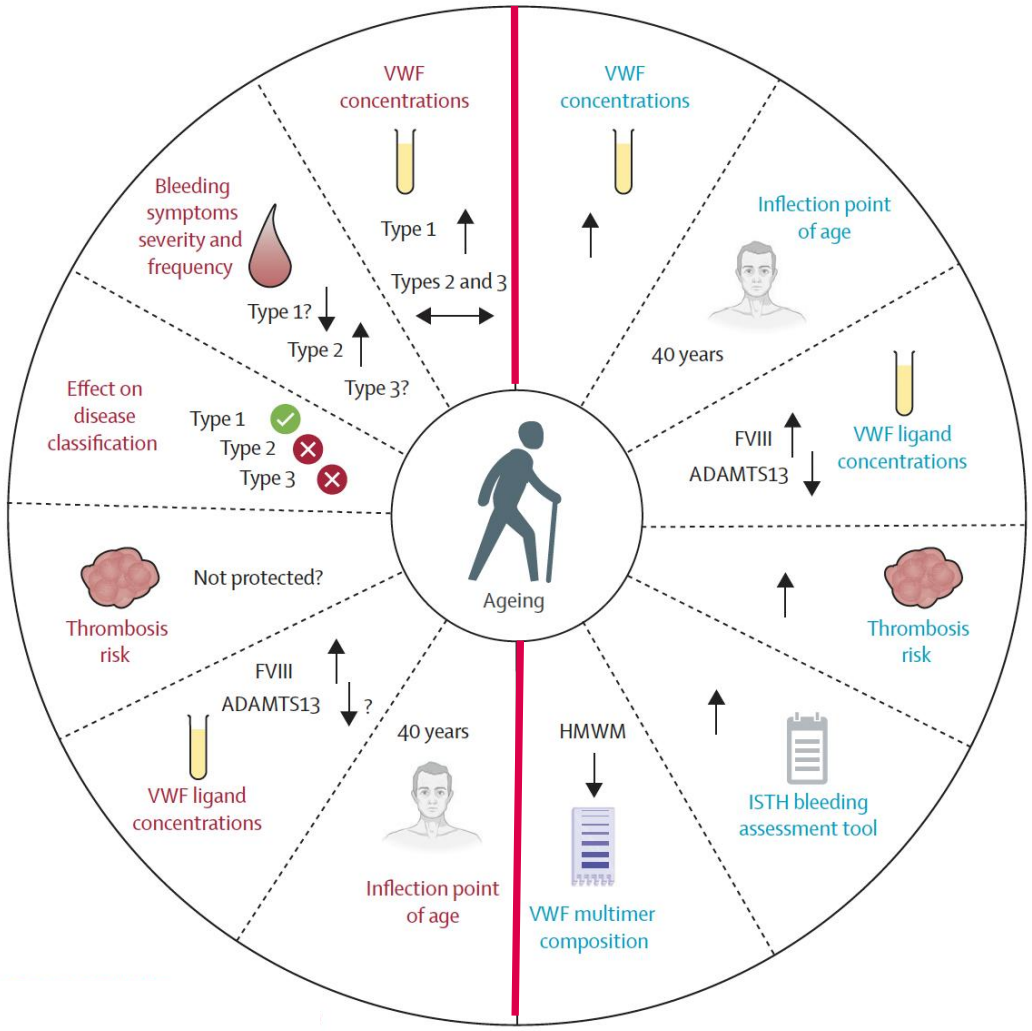
- Meta-analysis of genome-wide association results from 46 354 individuals of European, African, East Asian, and Hispanic ancestry
- 35 million variants
- In vitro gene silencing in endothelial cells for candidate genes
- 13 novel variants 7 with FVIII:C 11 with VWF
- Mendelian randomization suggest causal effects of
  - Plasma FVIII levels on VTE and coronary artery disease
  - Plasma VWF levels on ischemic stroke risk



Sabater-Lleal, Circulation 2019

VWF increases with age: In VWD?

Patients with VWD



General population

Van Loon et al, J Thromb 2012
Albanez et al, J Thromb Haemost 2016
Sanders et al, J Thromb Haemost 2014
Borghi et al, Haematologica 2017
Laffan et al, Haemophilia 2017
Seaman et al, Thromb. Hamost. 2020
Biguzzi et al, J Thromb Haemost 2021

Seidizadeh et al. Lancet Haematol 2025

Aging and VWD: evolution of VWF

“Can you grow out of von Willebrand disease?” => <u>NO</u> for type 2, type 3 and severe Type 1

ASH ISTH NHF WFH Guideline Recommendations for the Diagnosis of von Willebrand Disease (VWD)

The panel suggests reconsidering the diagnosis as opposed to removing the diagnosis for patients with previously confirmed type 1 VWD who now have VWF levels that have normalized with age

(conditional recommendation based on very low certainty in the evidence of effects).

ISTH Bleeding Assessment Tool: Limitations

Saturable

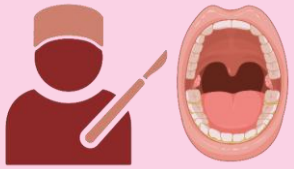
Nosebleed -cauterised once
BS=3

Multiple cauterisations
BS still 3

Time consuming

15-30 min
Need to be trained to exclude trivial bleedings
Learning curve

Assessment of challenges

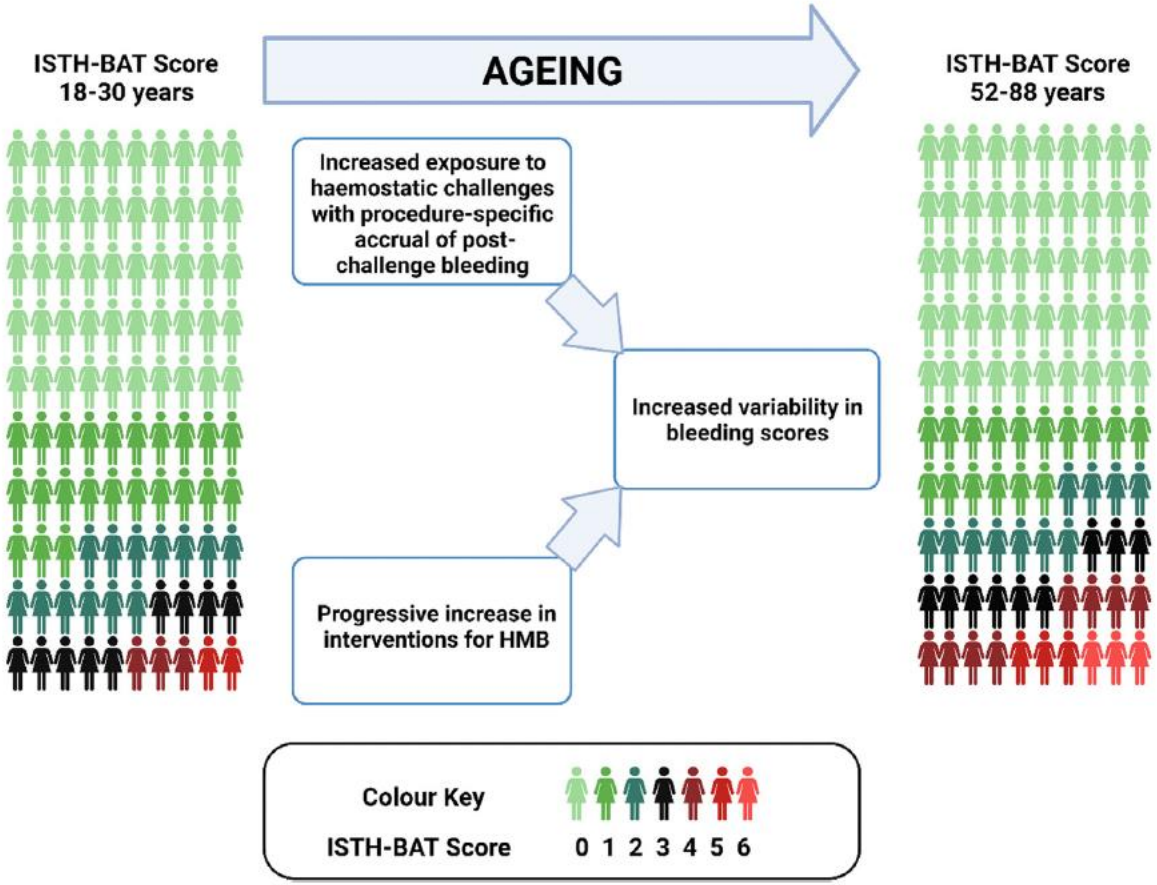


No negative score for haemostatic Challenges with no bleeding

Adapted from Michèle Lavin, EAHAD 2023

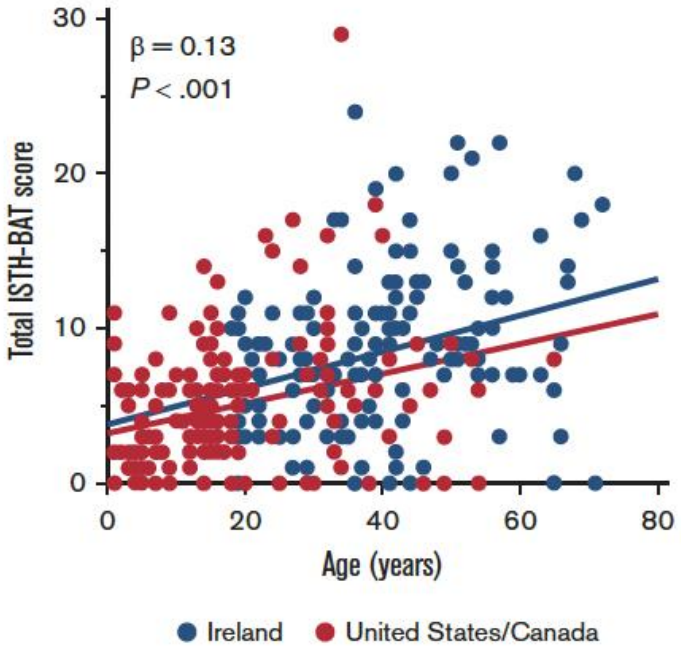
Rodeghiero F, J Thromb Haemost 2010

Aging and VWD: evolution of bleeding scores



*ISTH-BAT score with normal aging in **healthy females***

Doherty et al. J Thromb Haemost 2022

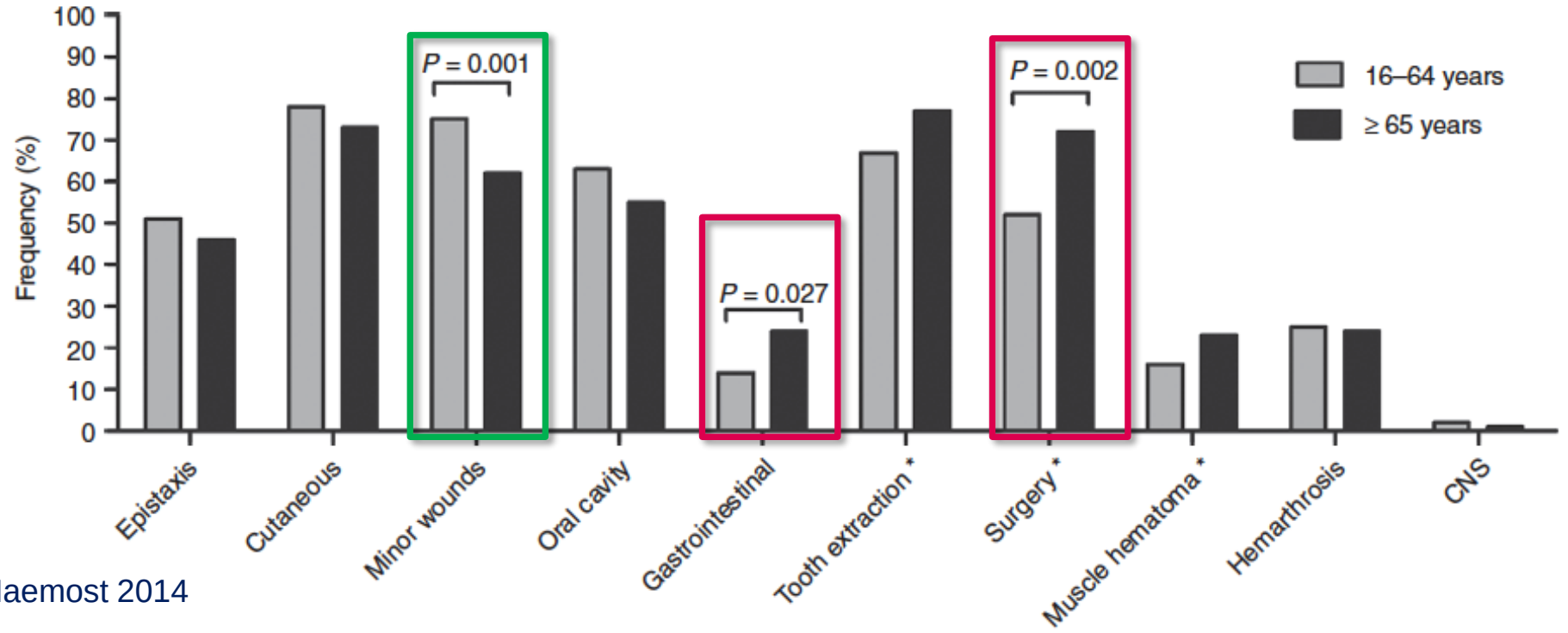


Low VWF

Atiq et al. Blood Advances 2025

Aging and VWD: evolution of bleeding phenotype

✓In the WiN study, **elderly (>65 years)** patients with VWD reported more bleeding episodes in the year preceding the study than **younger patients**: 42% vs 31%



Sanders, J Thromb Haemost 2014

02

Are there bleeding events that become more frequent with age?

VON WILLEBRAND DISEASE

Pr Sophie SUSEN & Pr Yesim DARGAUD

Gastrointestinal bleeding in VWD

A major unmet need in von Willebrand disease
significant morbidity and mortality, refractory to standard therapy

×2,5

Prevalence of gastrointestinal bleeding vs matched controls (Tsagianni et al. 2019)

30-80%

Rebleeding at 1–2 years despite endoscopic therapy (Rahmi G et al. 2014) (Rauch et al., 2021)

#1

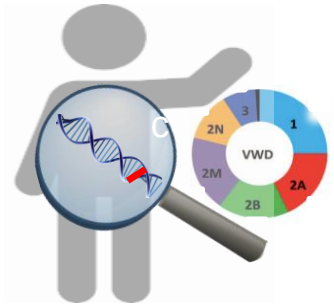
Cause of hospitalization in VWD (Tsagianni et al. 2019) (Holm et al., 2018)

×14 complications in Hereditary Hemorrhagic Telangectasia vs VWD (Zhang et al., 2024)

Angiodysplasia is the main independent predictor of GI bleeding in VWD

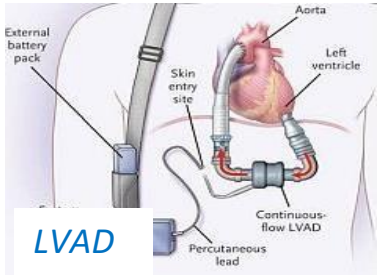
VWF and arteriovenous malformations

Congenital VWD

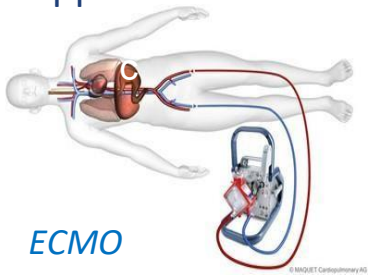


Acquired von Willebrand syndrome (AVWS)

Mechanical Circulatory Support devices

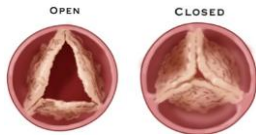


LVAD

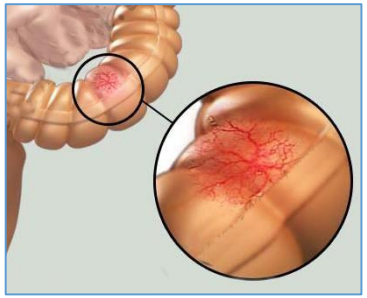


ECMO

Severe Aortic Stenosis



Vascular malformations



Gastrointestinal tract >85%
Non gastrointestinal 15%

Chornenki N et al. J Thromb Haemost 2021

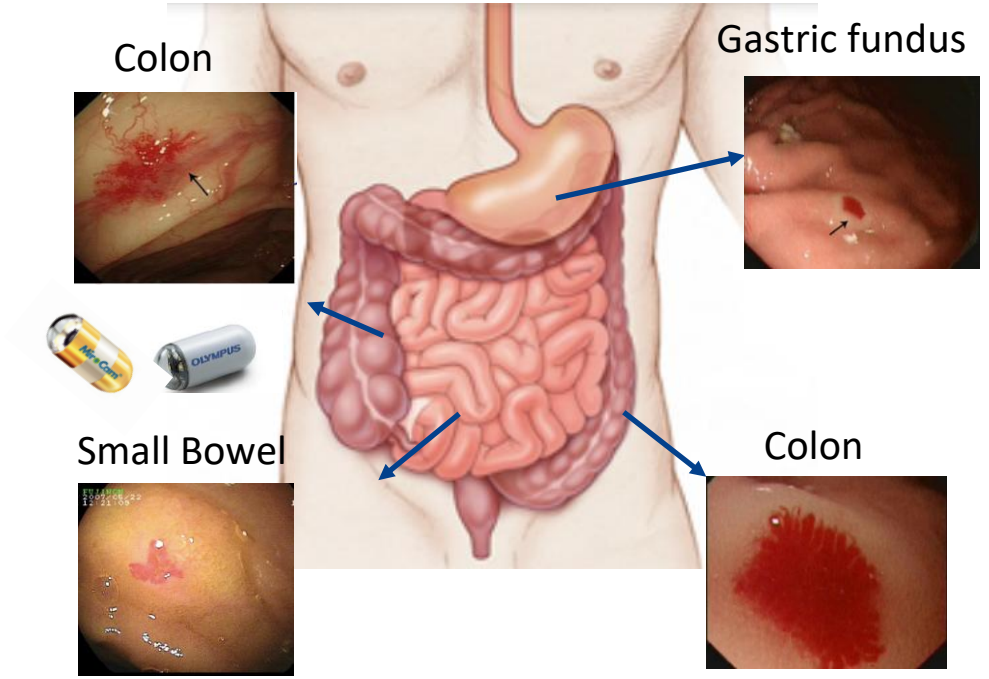
Arteriovenous malformation of gastrointestinal (GI) tract: GI Angiodysplasia

Definition

- Unique or multiple acquired **superficial vascular lesions**
- Originating from the GI **mucosa and/or submucosa**

Most lesions are detected in patients older than 60 years

≃50% of patients have more than one lesion with different locations in the GI



Foutch PG et al. Am J Gastroenterol 1995
Junquera F et al. Gastroenterology. 1999
Sami SS et al. Aliment Pharmacol Ther. 2014
Becq A et al. Gastroenterol. Endoscopy. 2017

A case of Gastrointestinal bleeding

A 65-year-old woman with severe type 2B von Willebrand disease (diagnosed in 1987), receiving prophylaxis (introduced for epistaxis and history of menorrhagia)

- **August:** 1st episode of melena
  - Esophagogastroduodenoscopy and ileocolonoscopy: **normal**
  - Capsule endoscopy (performed externally): **normal**
  - Iron IV infusion
  - Daily treatment with VWF

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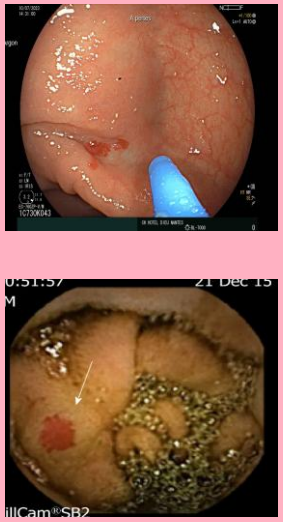
- **August:** 1st episode of melena
  - Esophagogastroduodenoscopy and ileocolonoscopy: **normal**
  - Capsule endoscopy (performed externally): **normal**
  - Iron IV infusion
  - Daily treatment with VWF
- **Late September:**
  - Recurrent melena
  - Hemoglobin drop of 5 g/dL → **Hb 7.6 g/dL**
  - Associated **hypotension**

A case of Gastrointestinal bleeding

Capsule endoscopy (VCE) performed within 48 hours of admission shows a proximal small-bowel angiodysplasia.



Endoscopic management of GI angiodysplasias

Devices

- EGD / Colonoscope
- Enteroscopes: **double-balloon (DBE)**

Techniques

- Argon plasma coagulation (APC)
- Mucosectomy
- Ligation
- Endoscopic submucosal dissection (ESD)

BUT lesions can be in inacessible site/high rebleeding rate

03

Are patients with bleeding disorders protected against cardiovascular risk as they age?

HAEMOPHILIA

RARE COAGULATION FACTOR DEFICIENCIES

VON WILLEBRAND DISEASE

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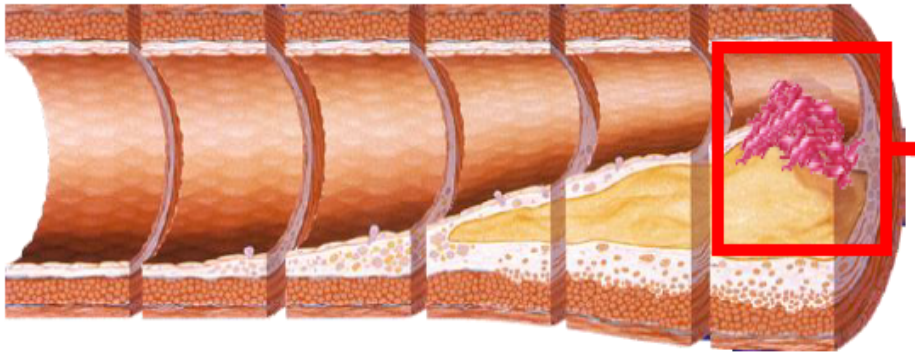
ATHEROMATOSIS & ATHEROTHROMBOSIS

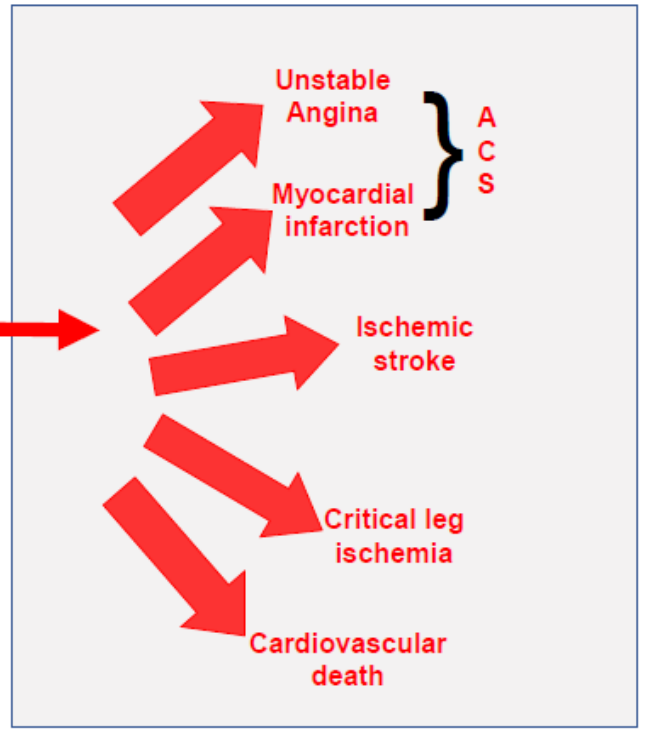


Atheromatosis

Influenced by cardio-vascular risk factors (Hypertension – Diabetes – Dyslipidemia – Family Risk Factors – Smoking – Sedentary Life-Style) Not different from non-haemophilia patients

Protection by FVIII/FIX deficiency :
1. Increased plaque stability
2. Reduced thrombin generation following plaque rupture

Loss of protection by prophylactic replacement or non-replacement therapies



Atherothrombosis

adapted from C. Hermans

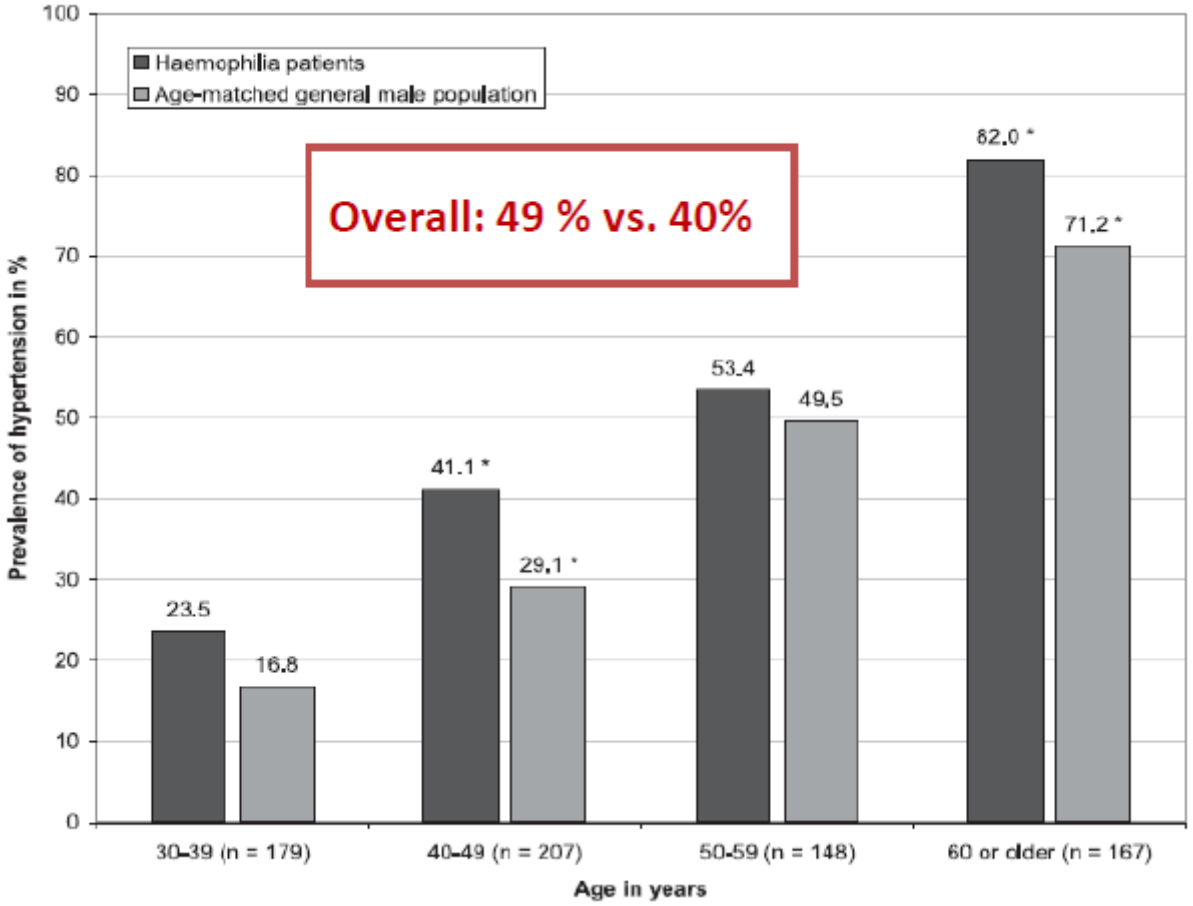
Br J Haematol. 2022 May; 197(4): 397–406.

CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH HEMOPHILIA

Risk factor	Diagnosis and monitoring	Intervention	Issues specific to PWH
Hypercholesterolemia	Check total cholesterol, HDL, LDL, and triglycerides	1. Lifestyle—exercise, diet, and weight loss 2. Statin—atorvastatin (20 mg) if 10-year CV risk is >10%. Aim for >40% reduction in non-HDL cholesterol at 3 mo	Exercise limited by pain and risk of bleeding due to joint disease. Statins—previous concern regarding theoretical increased risk of bleeding[a].
Hypertension	Yearly blood pressure, consider intervention if BP > 140/90 and 10-year CV risk is >10% (NICE, 2019)	1. Lifestyle—reduce salt, weight loss, and exercise 2. Medication: first line is ACEi, ARB, or calcium channel blocker	Exercise—as above
Smoking	Ask about smoking	1. Advise to stop 2. Refer to smoking cessation programs	Nil
Obesity	Check BMI and waist circumference yearly	1. Lifestyle (in consultation with specialist clinics/physicians/surgeons) 2. Pharmacologic therapies—including GLP-1 analogs (if BMI > 35 or >30 with comorbidities) 3. Bariatric surgery	Exercise—as above Managing risk of bleeding associated with major surgery
Type 2 diabetes	Check fasting glucose and HbA1c yearly	1. Lifestyle—weight loss 2. Pharmacologic—metformin ± SGLT2 inhibitor are first line	Nil
Alcohol	Ask about alcohol intake—maximum 100 g per week	1. Brief intervention 2. Referral to D&A programs if problematic use	Nil

Dix et al. J Thromb Haemost. 2024;22:1304–1312

HYPERTENSION IS MORE FREQUENT IN PATIENTS WITH HEMOPHILIA



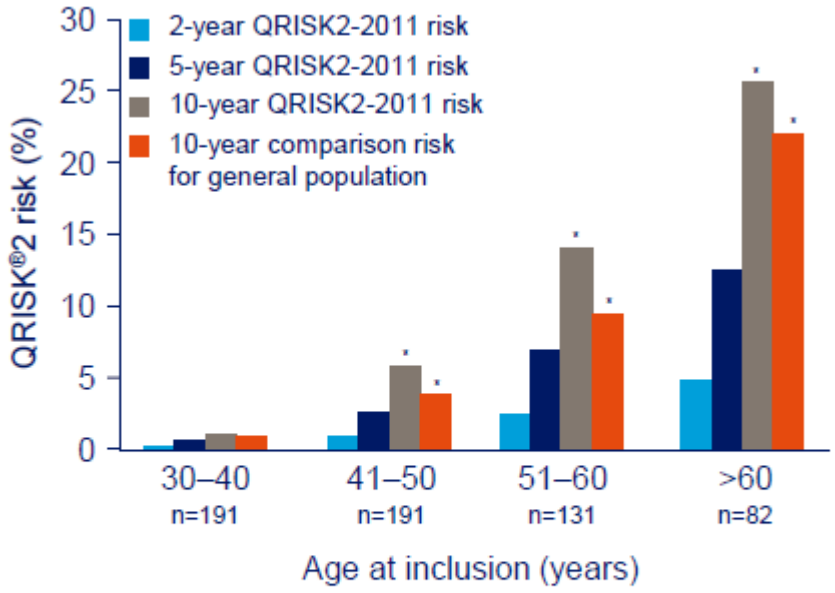
Van de Putte et al. Thromb Haemost 2012

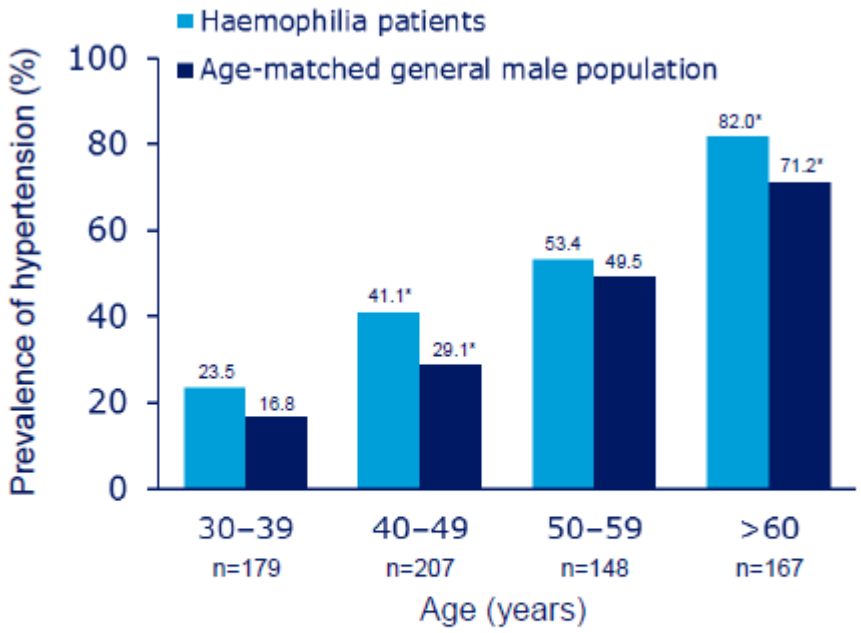
CARDIOVASCULAR DISEASE RISK IN PATIENTS WITH HEMOPHILIA

Author, Year	Country	Pts. n°	Main Results
Kulkarni, 2005	USA	3422	**CVD prevalence** 0.5% vs. GP 0.7%
Siboni, 2009	Italy	82	**CVD prevalence** 0.08% vs. GP 0.45% *p=0.009*
Biere-Rafi, 2011	Netherlands	300	RF prevalence = similar Predicted MR = similar
Ragni, 2011	USA	605	RF prevalence = similar In-hospital mortality = similar
Loevdahl, 2012	Sweden	8581	**Mortality from IHD 12.6%** vs. GP 28.9% *p<0.001*
Fransen vDP, 2012	Netherlands	408	MI 2.5% vs. GP 4.8%
Pocoski, 2014	USA	10024	**IHD 10.7%** vs. GP 5.8% *p<0.001* **MI 0.8%** vs. GP 0.3% *p<0.003*

GP = general population | MR = mortality risk | IHD = ischemic heart disease | MI = myocardial infarction

CARDIOVASCULAR DISEASE RISK IN PATIENTS WITH HEMOPHILIA





*Indicates a statistically significant difference between haemophilia patients and the general age-matched male population Fransen van den Putte DE, et al. Thromb Haemost 2013;109:16–23

Fransen van de Putte DE et al. Thromb Haemost 2012;108:750–755

RISK OF MYOCARDIAL INFARCTION IN PATIENTS WITH HEMOPHILIA

Cumulative incidence, % (95% CI)	MI	Angina pectoris	Non-fatal ischaemic stroke	Non-fatal intracranial bleeding
Overall population[a] (N=408)	2.5 (1.2–4.5)*	4.7 (2.8–7.2)	1.0 (0.3–2.5)	7.4 (5.0–10.3)*
Severe haemophilia (n=204)	0.5 (0.0–2.7)*	3.9 (1.7–7.6)	0.5 (0.0–2.7)	10.8 (6.9–15.9)*
Non-severe haemophilia (n=204)	4.4 (2.0–8.2)	5.4 (2.7–9.4)	1.5 (0.3–4.2)	3.9 (1.7–7.6)*
Age-matched male population	4.8 (4.6–4.9)	3.7 (3.6–3.8)	1.4 (1.3–1.4)	0.4 (0.3–0.4)

MI, myocardial infarction; [a]Dutch population
*Statistically significant between people with haemophilia versus age-matched males
Fransen van de Putte DE et al. Thromb Res 2012;130:157–162

IMPROVEMENT OF BLEEDING TENDENCY WITH TREATMENT INNOVATIONS FOR HAEMOPHILIA

Therapy	Trial	Population	Treated ABR (mean / estimated mean)	Reference (first author, journal, year)
Emicizumab	HAVEN 1	HA **with inhibitors**	**2.9**	Oldenburg, *NEJM*, 2017
Emicizumab	HAVEN 3	HA **without inhibitors**	**1.5 (weekly)** / **1.3 (Q2W)**	Mahlangu, *NEJM*, 2018
Concizumab	explorer7	HA/HB **with inhibitors**	**1.7** (estimated mean)	Shapiro, *NEJM*, 2023
Efanesoctocog alfa	XTEND-1	Severe HA **no inhibitors**	**0.69** (mean)	Pipe, *NEJM*, 2023
Fitusiran	ATLAS-INH	HA/HB **with inhibitors**	**1.67** (estimated mean)	Pasi, *NEJM*, 2023
Fitusiran	ATLAS-A/B	HA/HB **no inhibitors**	**3.1** (estimated mean)	Pasi, *Lancet Haematol*, 2021
Mim8	FRONTIER2	HA ± inhibitors	**0.45 (weekly)** / **0.20 (monthly)** *(on-demand subgroup)*	Young, *ISTH*, 2024*

USE OF ANTITHROMBOTIC AGENTS IN PATIENTS WITH HAEMOPHILIA

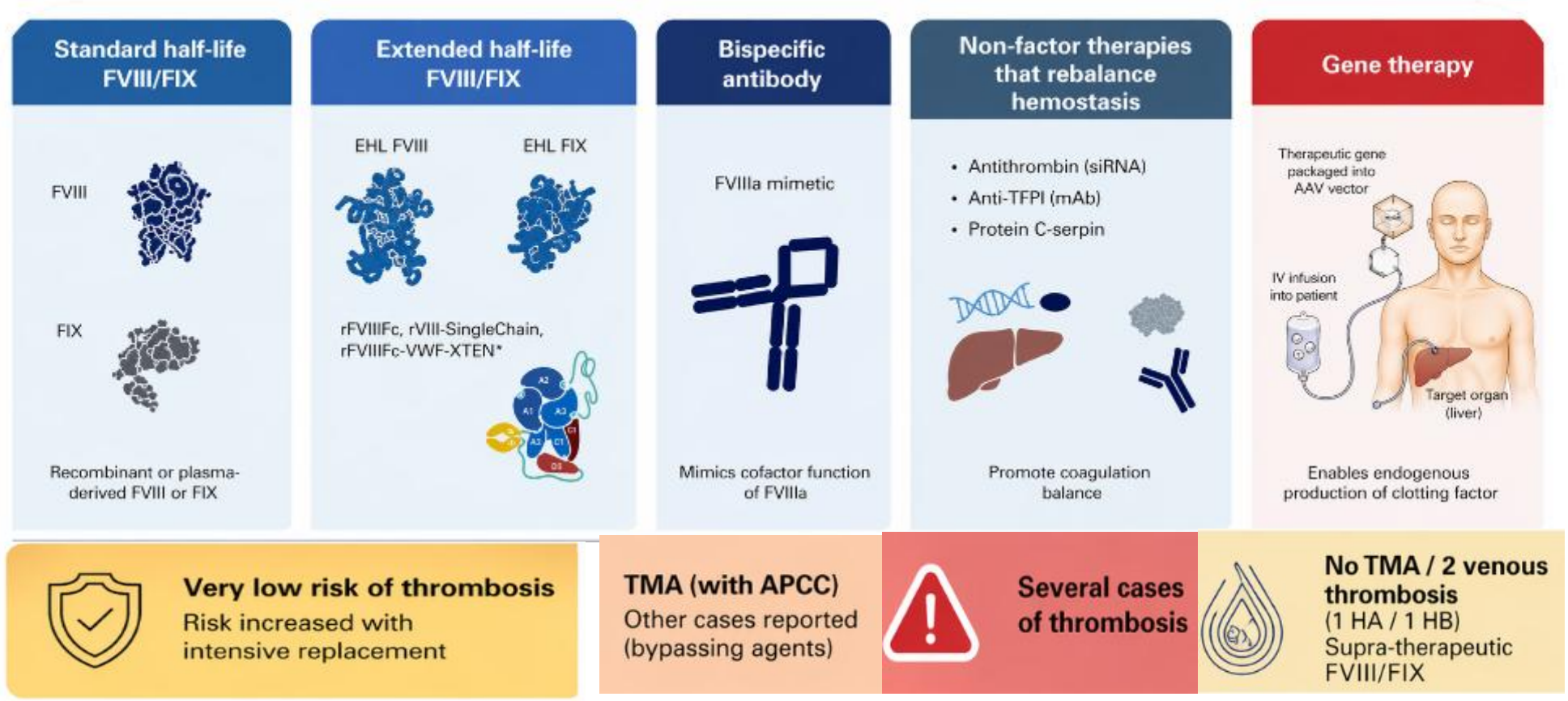
MAIN MODALITIES OF ANTITHROMBOTIC TREATMENTS IN PATIENTS WITH HEMOPHILIA ACCORDING TO EHA, ISTH, EAHAD, ESO GUIDANCE					
BASAL FACTOR VIII OR IX LEVELS	DURATION OF ANTITHROMBOTIC TREATMENT	SINGLE ANTI-PLATELET THERAPY (ASPIRIN – CLOPIDOGREL)	DUAL ANTI-PLATELET THERAPY	ANTICOAGULATION VKA DOAC (FULL DOSE)	TRIPLE THERAPY DUAL ANTIPLATELET THERAPY + VKA OR DOAC
< 20%*	Short and Long Term	Prophylaxis with FVIII or FIX Trough level : 1-5% Or emicizumab	Prophylaxis with FVIII or FIX Trough level > 20%	No anticoagulation Natural anticoagulation Avoid peak of FVIII/FIX > 25% during prophylaxis	Prophylaxis with FVIII or FIX Trough level > 80%
> 20%	Short and Long Term	Start	Start	Prefer DOAC	Prophylaxis with FVIII or FIX Trough level > 80%

DOAC : Direct Oral Anticoagulant / VKA : Vitamin K Antagonist
* Lowest factor level measured in case of discrepancy between one-stage or chromogenic assays

Experience from Israeli National HTC (600 patients with HA) Published in 2021	
Population	17 patients – Median age : 62 / 5 patients > 70 year
INH	2 INH +
CV risk factors	9 patients with multiple CV RF
HIV treatment	7
IHD	4 had cardiac revascularisation procedure
Antiplaletet treatment	4
Outcome	No death / no thrombosis
ABR	Higher in patients on antiplatelet therapy

Haemophilia. 2021;27:253–260.

RISK OF THROMBOSIS ASSOCIATED WITH HEMOPHILIA TREATMENTS



CAREFUL SCREENING OF PATIENTS IS REQUIRED FOR CARDIOVASCULAR RISK FACTORS

CAUTION

Risk factors for thrombosis: family or personal history, increasing age, obesity, hypertension, smoking habit, dyslipidemia, diabetes mellitus,
cardiovascular diseases, cancer, and inflammatory diseases. Inherited or acquired thrombophilia.
Multiple haemostatic treatments.

Cardiovascular disease in VWD: Prevalence of arterial thrombosis in the Dutch cohort

VWD patients – WiN study

n=635 included after completed a questionnaire

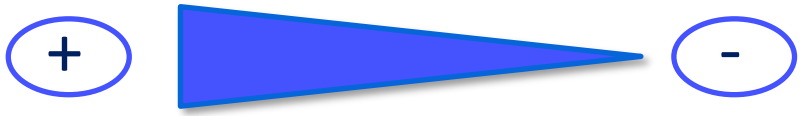
VWD **with arterial thrombosis**
N= 21
Age : 64 (42–81)

VWD **without arterial thrombosis**
N=614
Age : 45 (16–85)

5 acute MI
3 ischemic stroke

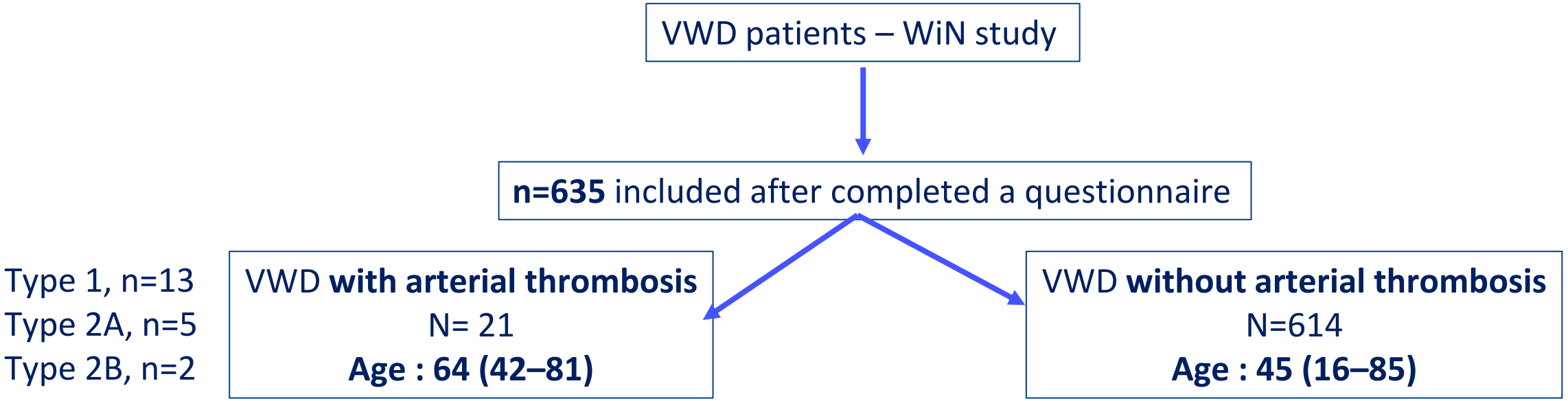
12 unstable angina pectoris
9 Transient ischemic attack

Smoking
Hypertension
Hypercholesterolemia
Family history of CVD



Sanders YV, J Thromb Haemost 2013

Cardiovascular disease in VWD: Prevalence of arterial thrombosis in the Dutch cohort



VWF:Ag (IU/dL)	36 (22-59)	30 (19-45)	0.28
VWF:Act (IU/dL)	22 (15-78)	24 (8-53)	0.22
FVIII:C	68 (42-93)	52 (34-73)	0.06

Sanders YV, J Thromb Haemost 2013

Cardiovascular disease in VWD: Prevalence of arterial thrombosis in the Dutch cohort

VWD patients – WiN study

Arterial thrombosis 21/614
3.3%

General population

2 ≠ reference populations

Expected numbers in age and sex matched in the general population

Overall reduction in arterial thrombotic morbidity

- 63% (SMR 0.37; 95%CI, 0.16-0.67) – source Central Bureau of Statistics
- 39% (SMR 0.61; 95%CI, 0.35-0.95) – source National public Health Compass

Sanders YV, J Thromb Haemost 2013

Cardiovascular disease in VWD: Prevalence of arterial thrombosis in the Dutch cohort

VWD patients – WiN study

Arterial thrombosis 21/614
3.3%

Hemorrhagic stroke 12/614
2%

General population

2 ≠ reference populations

Expected numbers in age and sex matched in the general population

Overall reduction in arterial thrombotic morbidity

5 to 10 times increase in risk of hemorrhagic stroke

Sanders YV, J Thromb Haemost 2013

THE CLOSING MESSAGES

Living with a rare bleeding disorder today goes beyond bleeding alone.

With age, new health challenges arise.

Managing elderly patients means balancing bleeding and clotting risks—through personalized, coordinated, multidisciplinary care.

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EHC-ERN-EuroBloodNet Topic on Focus: Ageing well with rare bleeding disorders, for patients and their families

webinar

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Session 3: Bleeding Disorders and Ageing - Shall I bleed less with age?

Dr William McKeown

Person with Severe Haemophilia A
EHC SC Member
EUHASS SC Member
Consultant Geriatrician and Stroke Physician – Antrim Area Hospital
Lead for Undergraduate Ageing and Health – Queen's University Belfast

27th April 2026

Living Well, Ageing Well

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Disclosures

Consultancy	Name of Institutes/Companies
Advisory Commitee member	N/A
Speaking Honoraria	SOBI, Pfizer, Biomarin
Consultancy Fees	CSL-Behring, Regeneron

Key Points

- A quick refresher on frailty
- The bleeding-thrombosis paradox of frailty
- Atypical bleeding presentations
- Challenging Moments
- Preventing bleeding – beyond haemostasis

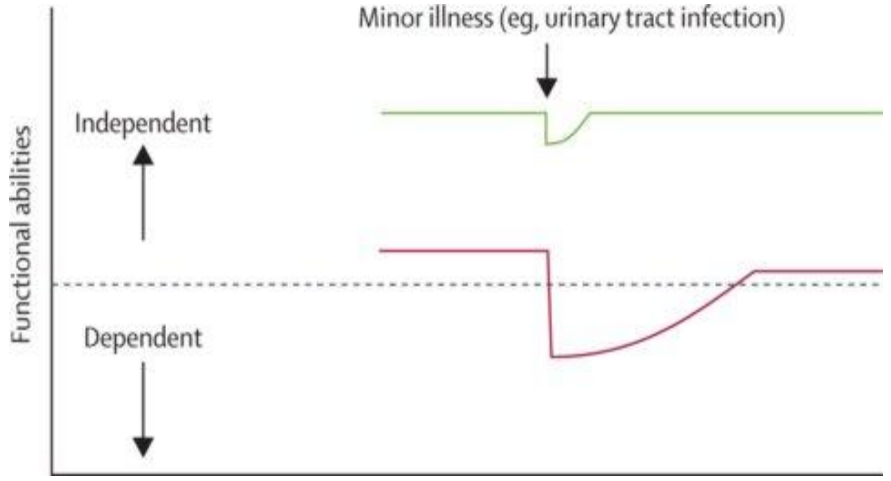
01

A Quick Refresher on Frailty

Frailty – A Definition

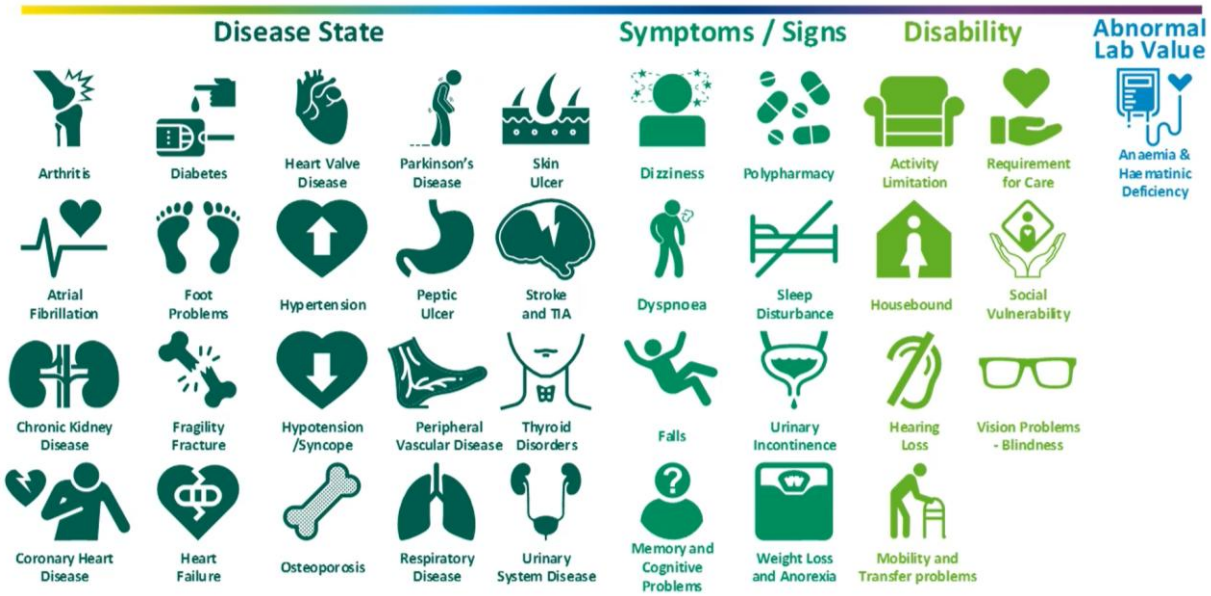
- **Definition:** A state of increased vulnerability due to a cumulation of deficits which leads poor resolution of homoeostasis after a stressor event

- In short – **a loss of resiliance**



Why do people with bleeding disorders get frailty?

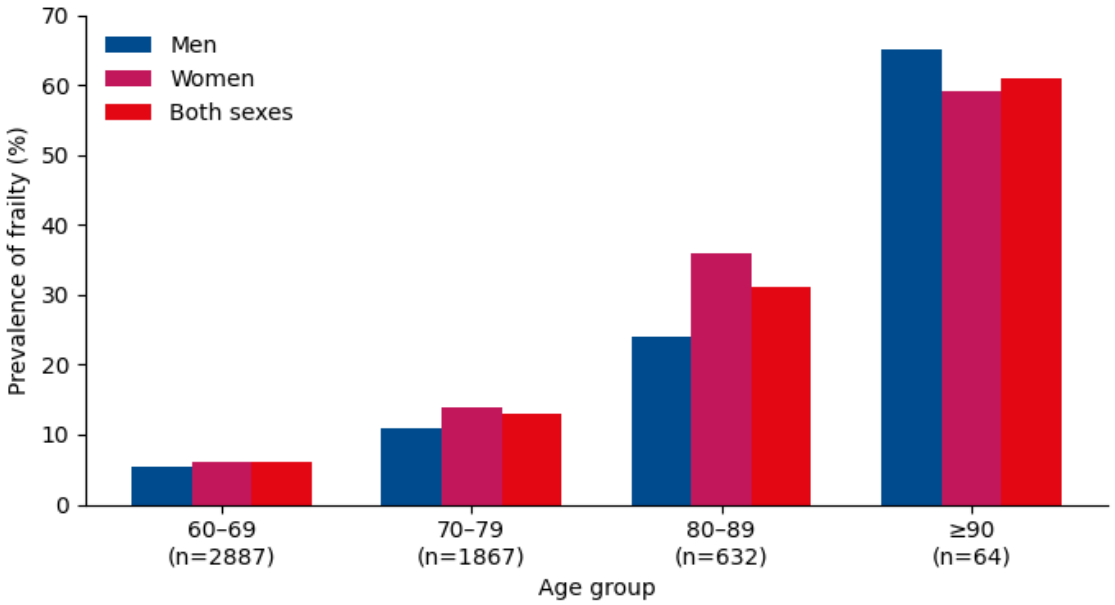
Bleeding disorder +

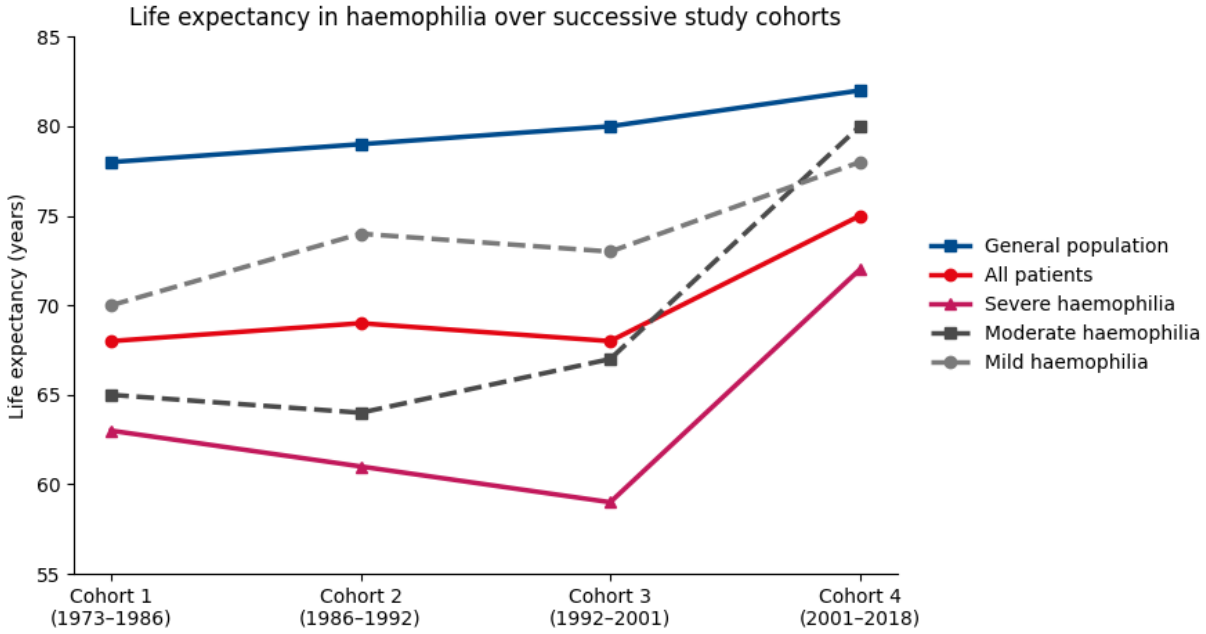


= Frailty

Accumulated Health Deficits (Rockwood, Song et al. 2005)

Demographics of Frailty



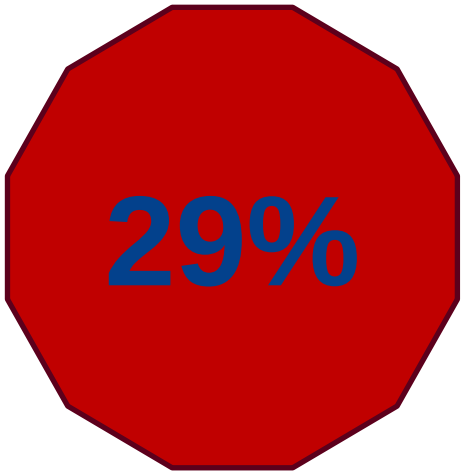


Prevalence of Frailty Increases with Age

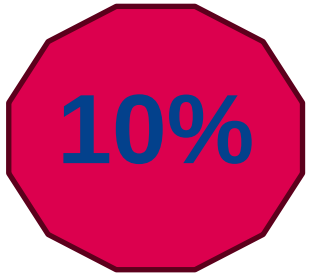
The Haemophilia Population is Ageing

Frailty in PWH vs General Population

>65 years



PWH



General Population

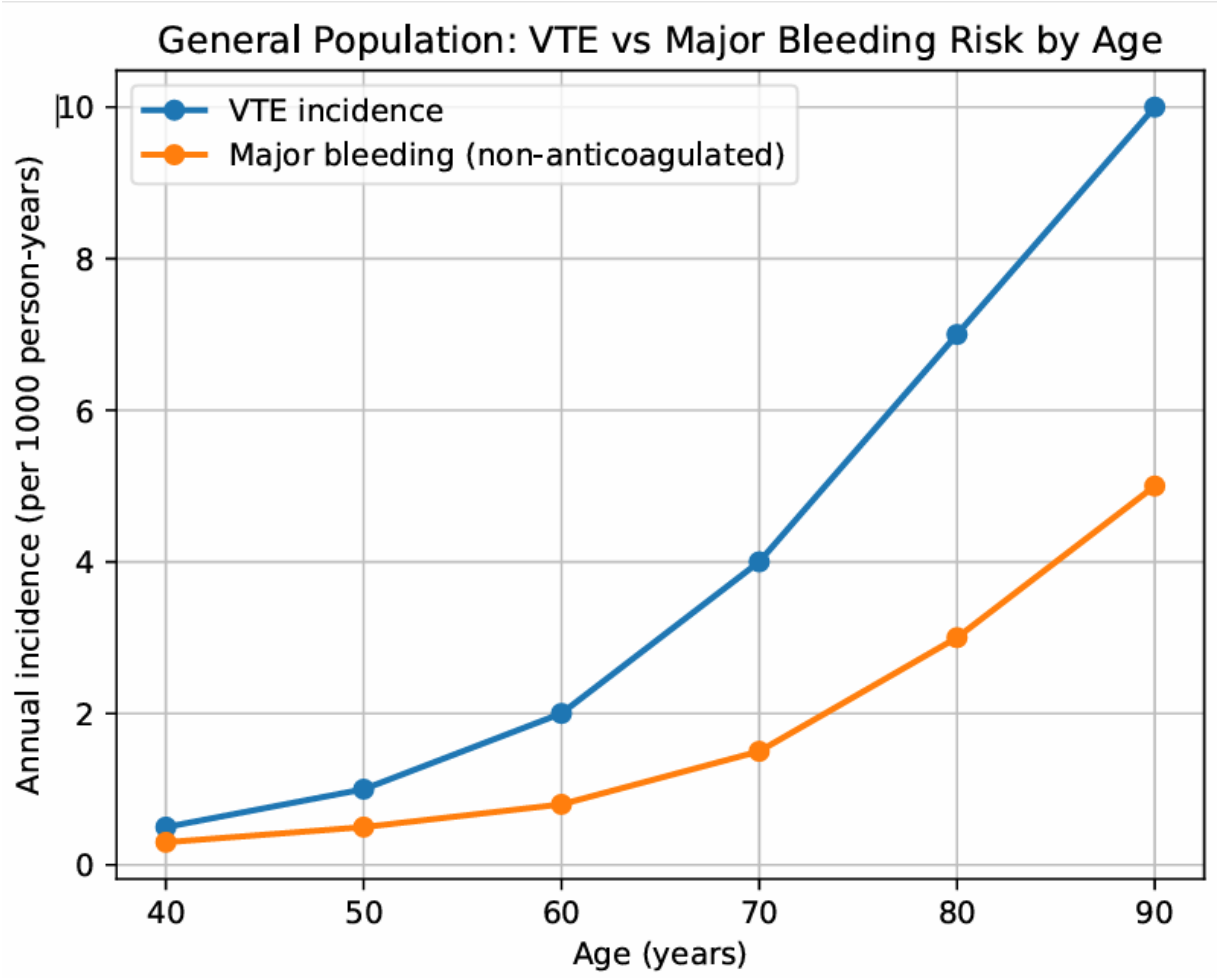
(Sangha, Obeidalla et al. 2023)

02

The Bleeding-Thrombosis Paradox of Frailty

The Bleeding-Thrombosis Paradox of Frailty

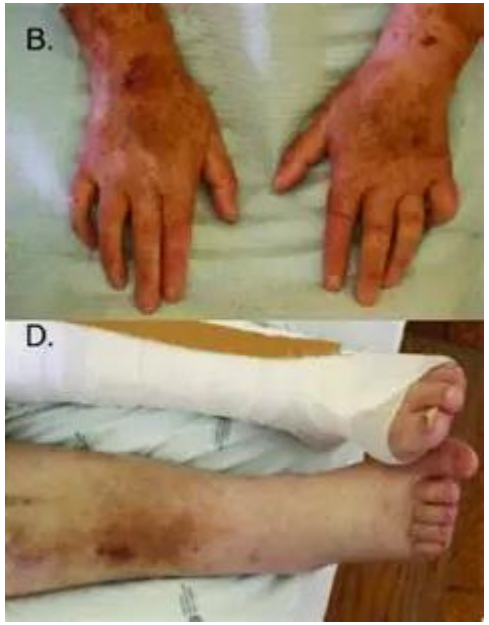
- Increased age associated with:
  - Increased clot/thrombosis risk ⬆
  - Increased bleeding risk ⬆
- Means that anti-platelets/anti-coagulants have higher bleed risk **but** also higher benefit

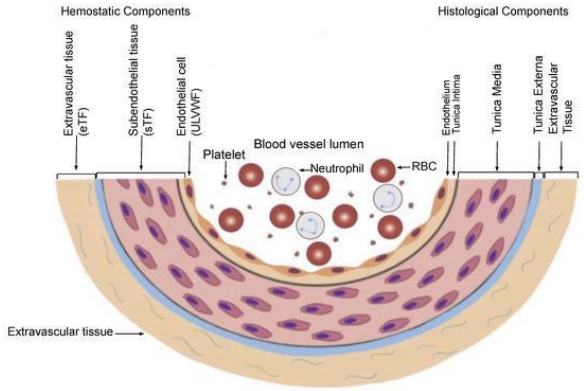


(Heit 2012), (Li, Geraghty et al. 2017)

Why does frailty increase bleeding?

Biological	Clinical/Co-Morbidities	Iatrogenic
• Vascular Fragility • Sarcopenia • Malnutrition	• Falls and trauma • Chronic kidney disease • Low Hb/Anaemia • Hypertension • Liver Disease	Polypharmacy: • Anti-coagulants • Anti-platelets • SSRIs





03

Atypical Bleeding Presentations

Typical Joint Bleed Presentation

Typical Presentation

- Pain
- Hot swollen joint
- Reduced ROM
- Patient can localise pain
- Describe recent injury

Atypical Joint Bleed in Cognitive Impairment/Frailty

Atypical Presentation

- Increased confusion/delirium
  - Agitated
  - Withdrawn
- Reduced mobility
- Grimacing on movement
- Groaning
- Resisting care
- No clear history/timeline

Consequences of Atypical Presentations

- Infection → presents as delirium or decline
- Fracture → presents as immobility/behavioural change
- Heart disease → atypical or silent presentations
- Stroke/TIA → subtle focal signs missed
- Constipation/urinary retention → agitation/delirium
- Pain syndromes → behavioural disturbance

Delay in recognising bleeding likely will lead to prolonged bleeding, delay in treatment and slower recover

04

Challenging moments in frailty

Challenging Moments 1 – High Risk Bleeding Moments in Frailty

High risk moments for bleeding

Bleeding risk is *episodic* not static

Challenging Moments 2 – Advanced Frailty and Nursing Homes

Skills and Training	Care coordination challenges	End-of-life and goals of care
Staff may lack confidence in: • Recognising bleeding complications • Administering clotting factor (if required) • Understanding urgency of symptoms	Fragmentation between: • Primary care • Haematology services • Nursing home staff Lack of clear individualised care plans	Balancing: • Burden of hospital transfer • Invasive treatments • Bleeding control Advance care planning often **not aligned with bleeding risk**

05

Preventing bleeding – beyond haemostasis

Lots can be done to prevent bleeding!

- Comprehensive Falls Assessment
- Medication optimization
- Proactive monitoring in high-risk periods
- Education of patients/carers

Comprehensive Falls Assessment

- Medical
  - **Screen for osteoporosis (FRAX)**
  - Review Medication
  - Review Comorbidities
  - Review Pain
- Nursing
  - **Assess lying standing blood pressures**
  - Assess vision
- Physiotherapy
  - Strength and balance training
  - Appropriate walking aid
  - Falls prevention
  - Second stair- rail
  - **Environmental Assessment**

Impact of a Multifactorial Falls Assessment

Multifactorial falls interventions reduce falls risk by **34%** (Lee and Yu 2020)

Medication Review

- Structured medication review
- Review patient understanding
- Reduced or stop potentially inappropriate medications
- Consider non-pharmacological options

Impact of Superpolypharmacy (10+ medications)

Double mortality

Triple Falls Risk

1) Be vigilant for bleeding in the older person

2) Bleeding risk does not just come from bleeding disorders

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