EHC Webinars

European von Willebrand Disease Community

Von Willebrand disease

Topic on focus

ERN-EuroBloodNet

Ageing

Prof Giancarlo Castaman (AOU Careggi, Florence, Italy), Nicolas Giraud (Association française des hémophiles) and Catherine Harrison (Haemophilia & Haemostasis Disorders at Sheffield Haemophilia & Thrombosis Centre)

European Reference Network for rare or low prevalence complex diseases

Co-funded by the Health Programme of the European Union

EHC european haemophilia consortium

European von Willebrand Disease Community

European von Willebrand Disease Community

EHC Webinars Von Willebrand disease Topic on focus ERN-EuroBloodNet

European Reference Network for rare or low prevalence complex diseases Network on Hematological Diseases (ERN EuroBloodNet)

Conflicts of interest

Disclosure conflict of interest: Cathy Harrison

Consultancy/speakers fees:	CSL, Novo Nordisk, Pfizer, Sobi, Roche-Chugai, Takeda
Event Sponsorship:	CSL, Roche-Chugai
Voluntary:	WFH Nurses Committee, EHC, Editorial Board Journal of Haemophilia Practice, The Haemophilia Society MASAG

Patients learning objectives

Age-Related Risks and Complications

- Increased Risk of Stroke and Cardiovascular Events
- Vascular Health Concerns Specific to Older Adults with VWD

Comprehensive Management Approaches

- Strategies for Managing Bleeding Episodes in Older Adults
- Preventative Care and Routine Monitoring for Complications

Joint Health and Mobility

- Impact of VWD on Joint Health Over Time
- Best Practices for Managing Joint Pain and Preventing Degeneration

Comorbid Conditions and Treatment Strategies

- Common Comorbidities in Aging VWD Patients (e.g., arthritis, osteoporosis)
- Tailored Treatment Plans to Address Multiple Health Conditions

Menopause

Changes in Factor Levels with Age

- Understanding the Rise in Factor Levels and Its Implications
- Re-Evaluating Diagnosis and Treatment in Older Patients

Revisiting Diagnosis and Long-Term Care Needs

- Considerations for Maintaining or Adjusting a VWD Diagnosis in Later Life
- Long-Term Monitoring and Care Recommendations

Learning objectives

Identify the role of MDT & the Specialist Nurse in ageing VWD care

Identify the most common presenting bleeding symptoms

Discuss how we can manage the most common presenting issues

Explore health promotion strategies for people ageing with VWD

Why Comprehensive Care?

To provide as much as possible on one site to meet all the patients' needs.

To bring together experts in all areas in partnership with affected individuals & families to avoid complications associated with the underlying bleeding disorder.

'to minimise disability & prolong life, to facilitate general, social & physical well-being, & to help each patient achieve full potential, whilst causing no harm'
World Federation of Hemophilia, 1989

Patient & public perspective

Consistently rate specialist nurses higher than any other health and social care professional:

- Understanding patient needs
- Designing and implementing care pathways
- Obtaining patient feedback
- Being transparent and honest
  - RCN, 2010; IPSOS, 2022 (specifically nurses)

Benefits of Specialist Nurses

- Reduced waiting times
- Prevent hospital admissions/readmissions
- Reduced post op hospital stay times
- Free up consultant appointments
- Provide services at the point of need
- Reduced patient treatment drop out rates
- Education of health and social care professionals
- Introduce innovative service delivery frameworks
- Direct specialist advice given to patients and families
- Deliver cost-effective, high-quality care with optimal patient outcomes
- Provide health promotion & maintenance through assessment, diagnosis & management of acute & chronic patient problems

RCN, 2008; National Association of Clinical Nurse Specialists, 2013

Most common reasons to call

- Epistaxis (Nose Bleeds)
- Heavy Menstrual Bleeding including relating to Menopause
- Gastrointestinal bleeding

Du et al (2023) VWD epidemiology, burden of illness and management: A systematic review. *Journal of Blood Medicine 14: 189-208*

VWD, bleeding and Quality of Life

Increased bleeding:

- Reduced Quality of life
- Reduced Social function
- Increased pain
- Reduced General health
- Reduced Physical function

De Wee et al (2010); Roberts et al (2021); Atik et al (2018); Du et al (2023)

Management of Heavy Menstrual Bleeding

- Monitoring with replacement iron therapy
- Tranexamic acid
- Hormonal therapy including Mirena coil
- DDAVP or Replacement Clotting Factor Therapy
- Pain relief/anti-inflammatory drugs
- Surgery
- Joint approach to management through collaboration of services

Curry et al (2022) Gynaecological management of women with inherited bleeding disorders: A UK Haemophilia Centre Doctors' Organisation Guideline. *Haemophilia 28(6): 917-937.*

Turan et al (2024) Review of interventions and effectiveness for heavy menstrual bleeding in women with moderate and severe von Willebrand disease. Haemophilia 30: 1177-1184

Du et al (2023) VWD epidemiology, burden of illness and management: A systematic review. *Journal of Blood Medicine 14: 189-208*

What about bleeding during perimenopause?

Abnormal uterine bleeding is common.

Causes are numerous, from decreasing/unstable ovarian function to premalignant & malignant conditions.

Benign findings e.g. endometrial polyps & myomas increase with age.

Cervical & vaginal causes of abnormal bleeding should be excluded by speculum examination.

Transvaginal ultrasound scans should be considered.

Endometrial biopsy or hysteroscopy may be necessary.

Treat resulting iron deficiency +/- anaemia.

Treat per Heavy menstrual bleeding management – mirena coil, endometrial ablation or surgery may be considered.

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium

European von Willebrand Disease Community

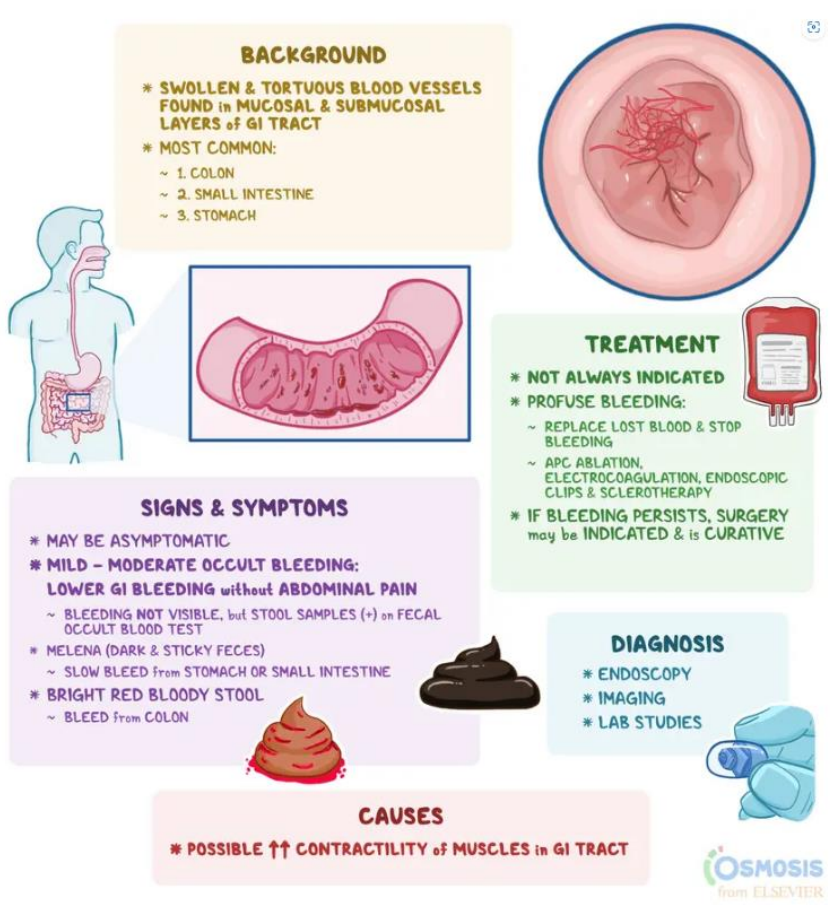
Dreisler et al (2021) Perimenopausal abnormal uterine bleeding *Maturitas 184: 107944*

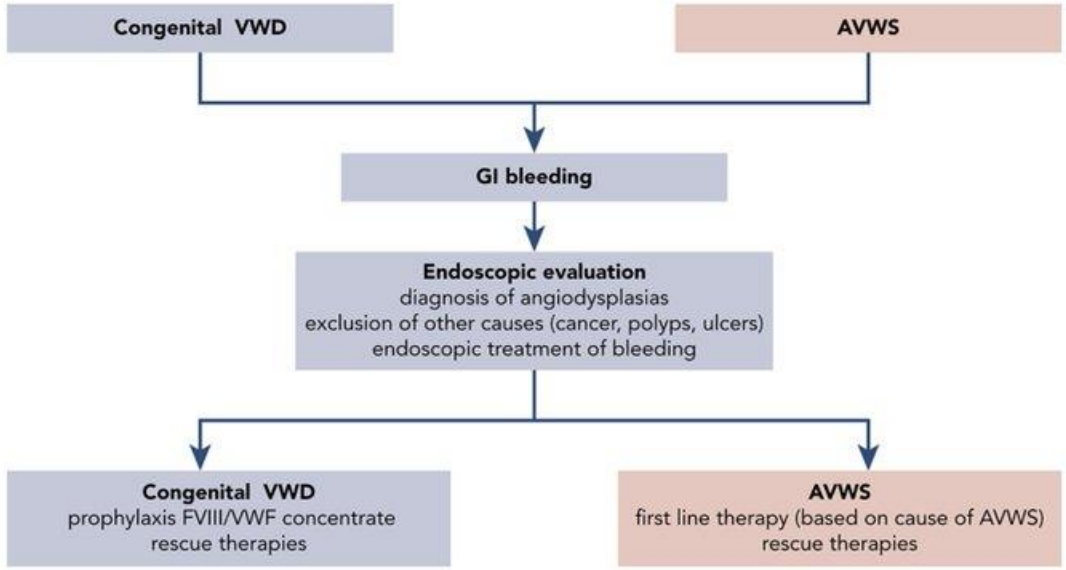
EHC Webinars Von Willebrand disease Topic on focus ERN-EuroBloodNet

What about peri-menopause & VWD?

- 58yo woman, T1 VWD Act 32 IU/dL
- Ehlers Danlos Syndrome
- Recurrent, heavy, prolonged PV bleeding
- HRT (Estradot & Utrogestan) caused significant increase i bleeding
- Investigated to rule out malignant causes
- Side effects with progesterone
- Consider mirena coil – possible risk of perforation with EDS
- Using tranexamic acid & on demand Veyvondi
- Consider GNRH analogues to induce full menopause

Gastrointestinal bleeding





Biguzzi et al (2020) How I treat gastrointestinal bleeding in congenital & acquired VWD *Blood 136 (10): 1125-1133*

Type 2 VWD

- 58yo, woman, 2A VWD Act 5-10 IU/dL
- Bleeding history:
  - Heavy menstrual bleeding
  - Nose bleeds
  - GI bleeding at 52yrs
  - Angiodysplasia diagnosed at 54yrs
- Treatment history:
  - DDAVP – peak 18IU/dL
  - Tranexamic acid
  - Mirena coil
  - Haemate P/Voncento on demand
  - Prophylaxis Voncento 25IU/kg once weekly at 54yrs for 9 months
  - APC & clipping of large angioectasia
  - On demand Voncento

- 59yo, woman, 2M VWD Act 5 IU/dL
- Bleeding history:
  - Heavy menstrual bleeding
  - Oral bleeding
  - GI bleeding at 47yrs
  - Nose bleeds
  - Severe widespread bruises
- Treatment history:
  - Tranexamic acid
  - On demand Haemate P/Voncento
  - APC for AVM in duodenum at 48yrs
  - Endometrial ablation at 40yrs
  - Tertiary prophylaxis Voncento 25IU/kg once 1-2 weekly *'feels like life is calm again, that they are back in control'*

Epistaxis

LOCAL CAUSES

LOCAL TRAUMA

ANATOMICAL IRREGULARITIES

INFLAMMATION

FACIAL TRAUMA

TOPICAL NASAL SPRAYS (incorrect/excessive use)

TUMORS (rare)

SYSTEMIC CAUSES

HIGH BLOOD PRESSURE

VASCULAR MALFORMATIONS

CARDIOVASCULAR DISEASES

BLEEDING DISORDERS

OSMOSIS.org

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium
Advocating for people with haemophilia and congenital bleeding disorders

European von Willebrand Disease Community

EHC Webinars
Von Willebrand disease
Topic on focus ERN-EuroBloodNet

Public perception of 'healthy ageing'

Theme 1: Healthy diet and lifestyle are components of healthy ageing	**Theme 2:** Maintaining normal bodily functions	**Theme 3:** Preventive care
Topic 1: Eating well (65.4%)	Topic 2: Mental cognition and brain health (4.3%)	Topic 3: Genetic contributions (1.3%)
Topic 4: Health benefits of yoga (1.3%)	Topic 8: Maintaining skin appearance (1.2%)	Topic 15: Immunization against flu and other respiratory viruses (0.5%)
Topic 5: Health supplements (1.2%)	Topic 10: Hearing impairment (0.7%)	Topic 16: Preventing falls (0.5%)
Topic 6: Arts and music (1.2%)	Topic 11: Maintaining sleep (0.7%)	
Topic 7: Healthy ageing month (1.2%)	Topic 12: Gut health (0.7%)	
Topic 9: Social integration (0.8%)	Topic 13: Bone health (0.7%)	
Topic 14: Healthy ageing events (0.6%)		

Ng et al (2023) Public perception on health ageing in the past decade: An unsupervised machine learning of 63,809 twitter posts *Heliyon 9(2): e13118*

Nurses' role to support navigation of healthcare systems

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium
Advocating for people with haemophilia and congenital bleeding disorders

European von Willebrand Disease Community

EHC Webinars
Von Willebrand disease
Topic on focus
ERN-EuroBloodNet

Take home messages

- Evidence of care management in ageing people with VWD is limited, we need to do more research and share experiences.
- Bleeding presentations vary significantly and may improve or deteriorate with age, but when occurring add a heavy burden on the individual affecting overall quality of life.
- Access to timely diagnosis & provision of specialist services is key.
- Listen to the impact of bleeding on the individual.
- Work to create an individualised care plan, including the consideration of prophylaxis.

TAKE HOME MESSAGES

Disclosures

(Last two years)

Employment	*NONE*
Research support	*NONE*
Scientific advisory board	*BAYER, BIOVIIIX, BIOMARIN, CSL-BEHRING, LFB, TAKEDA, NOVO NORDISK, PFIZER, ROCHE, SOBI*
Consultancy	*CSL BEHRING*
Speakers bureau	*BIOMARIN, BIOVIIIX, CSL-BEHRING, LFB, NOVO NORDISK, TAKEDA,ROCHE, SOBI*
Major stockholder	*NONE*
Patents	*NONE*
Honoraria	*NONE*
Travel support	*NONE*
Other	*NONE*

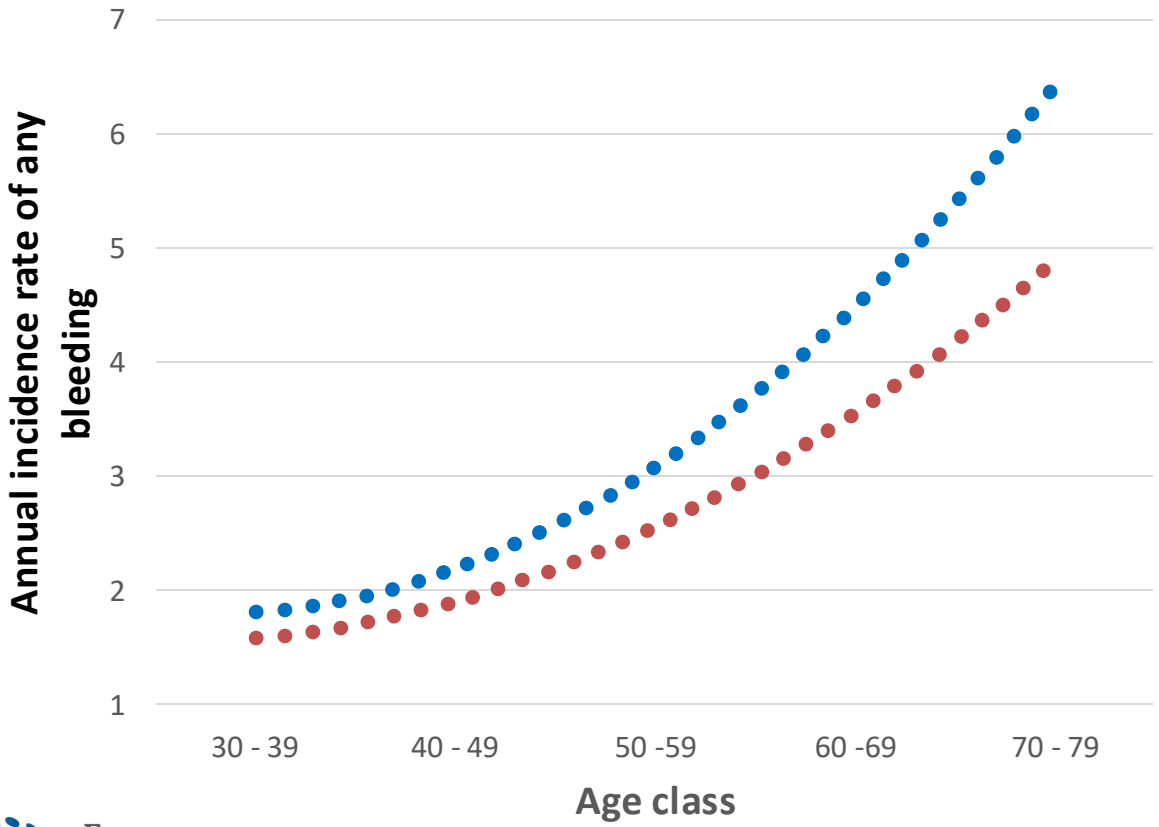
Risk of bleeding in general population and Von Willebrand Disease (VWD) and age

Does age influence the bleeding risk?

JAMA | Original Investigation

Annual Risk of Major Bleeding Among Persons Without Cardiovascular Disease Not Receiving Antiplatelet Therapy

Vanessa Selak, PhD; Andrew Kerr, MD; Katrina Poppe, PhD; Billy Wu, MPH; Matire Harwood, PhD;



3.0%

Median annualized incidence for any bleeding in males

2.8%

Median annualized incidence for any bleeding in females

Adapted from Selak et al. Jama, 2018; [1] sABR spontaneous Annual Bleeding Rate from Leebeek et al. Blood, 2022

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

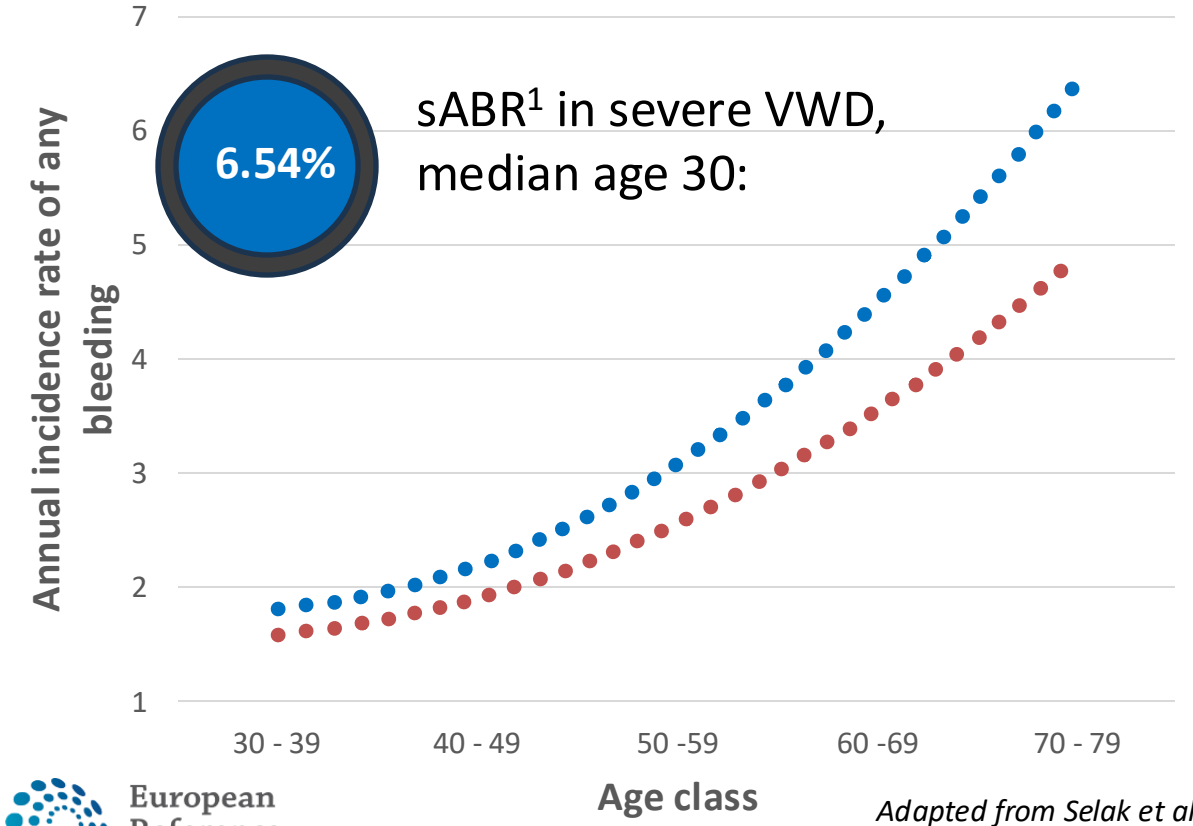
EHC european haemophilia consortium

European von Willebrand Disease Community

EHC Webinars Von Willebrand disease

Topic on focus ERN-EuroBloodNet

What about VWD?



6.54% sABR[1] in severe VWD, median age 30:

3.0% Median annualized incidence for any bleeding in males

2.8% Median annualized incidence for any bleeding in females

Adapted from Selak et al. Jama, 2018; [1] sABR spontaneous Annual Bleeding Rate from Leebeek et al. Blood, 2022

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium

European von Willebrand Disease Community

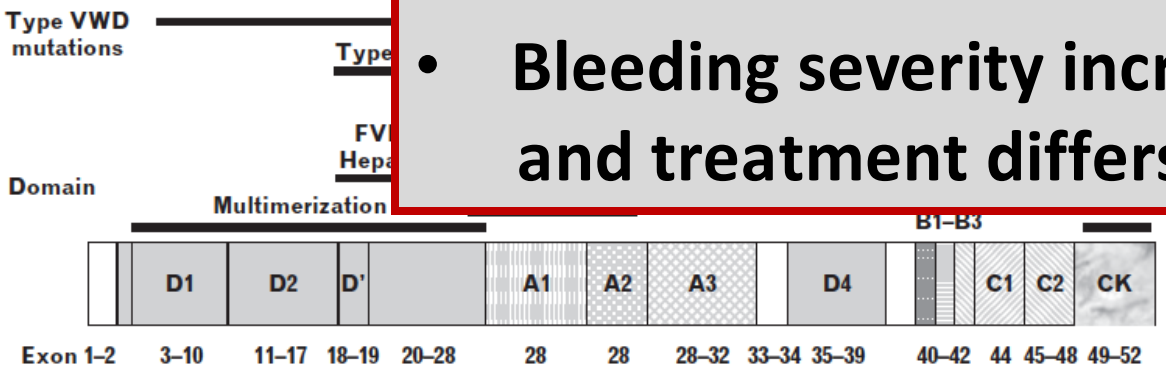
EHC Webinars Von Willebrand disease

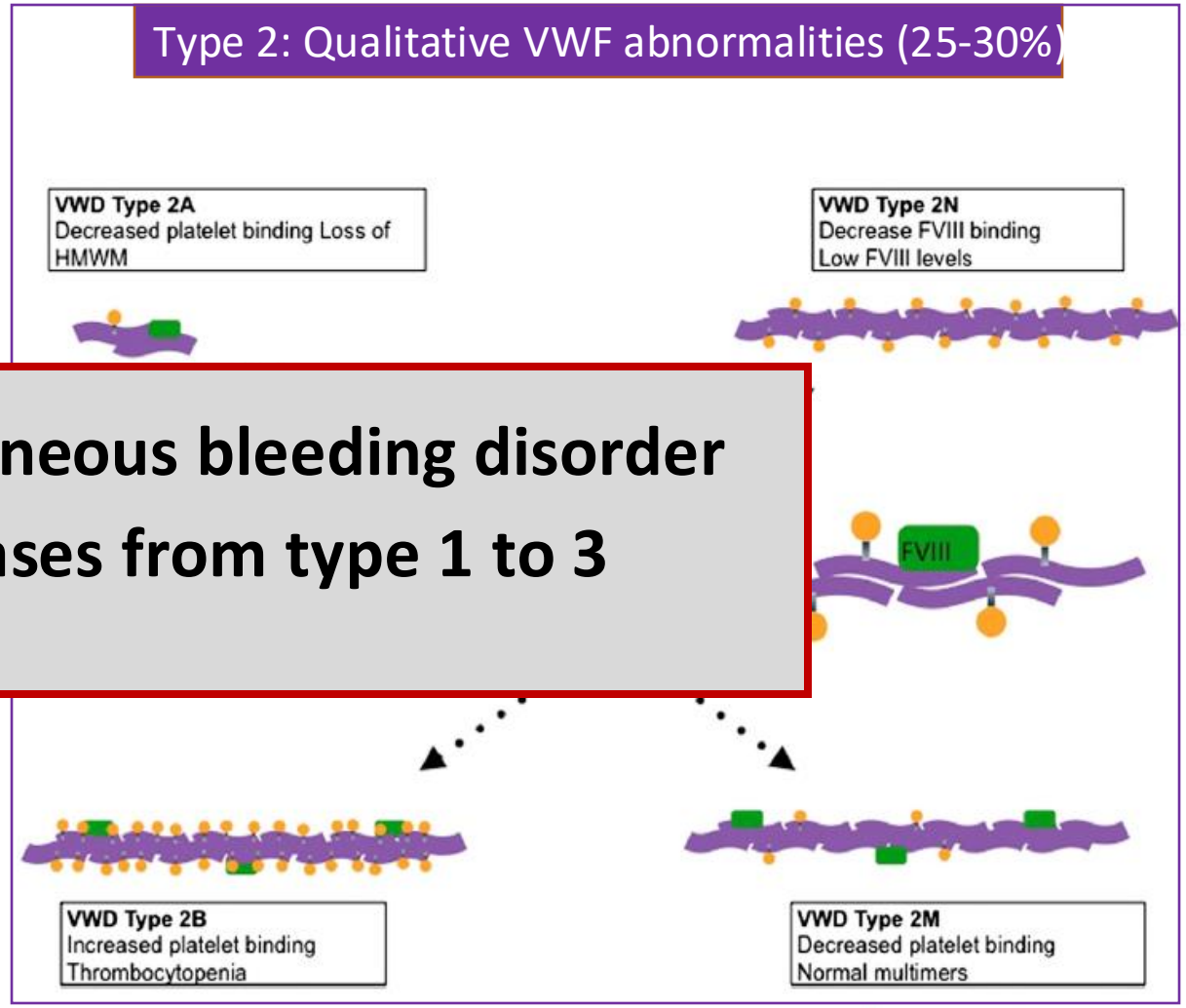
Topic on focus ERN-EuroBloodNet

CLASSIFICATION OF VON WILLEBRAND DISEASE

Quantitative deficiency of VWF	
Type 1	Partial quantitative deficiency (60-70%),including 1C
Type 3	Virtual absence of VWF (1-2%)

- **VWD is a very heterogeneous bleeding disorder**
- **Bleeding severity increases from type 1 to 3 and treatment differs**





European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium

European von Willebrand Disease Community

Castaman, Curr Opin Hematol 2013; Ng C. et al, Blood 2015

EHC Webinars Von Willebrand disease

Topic on focus ERN-EuroBloodNet

WiN (Willebrand in Netherlands)

Bleeding score according to type of VWD

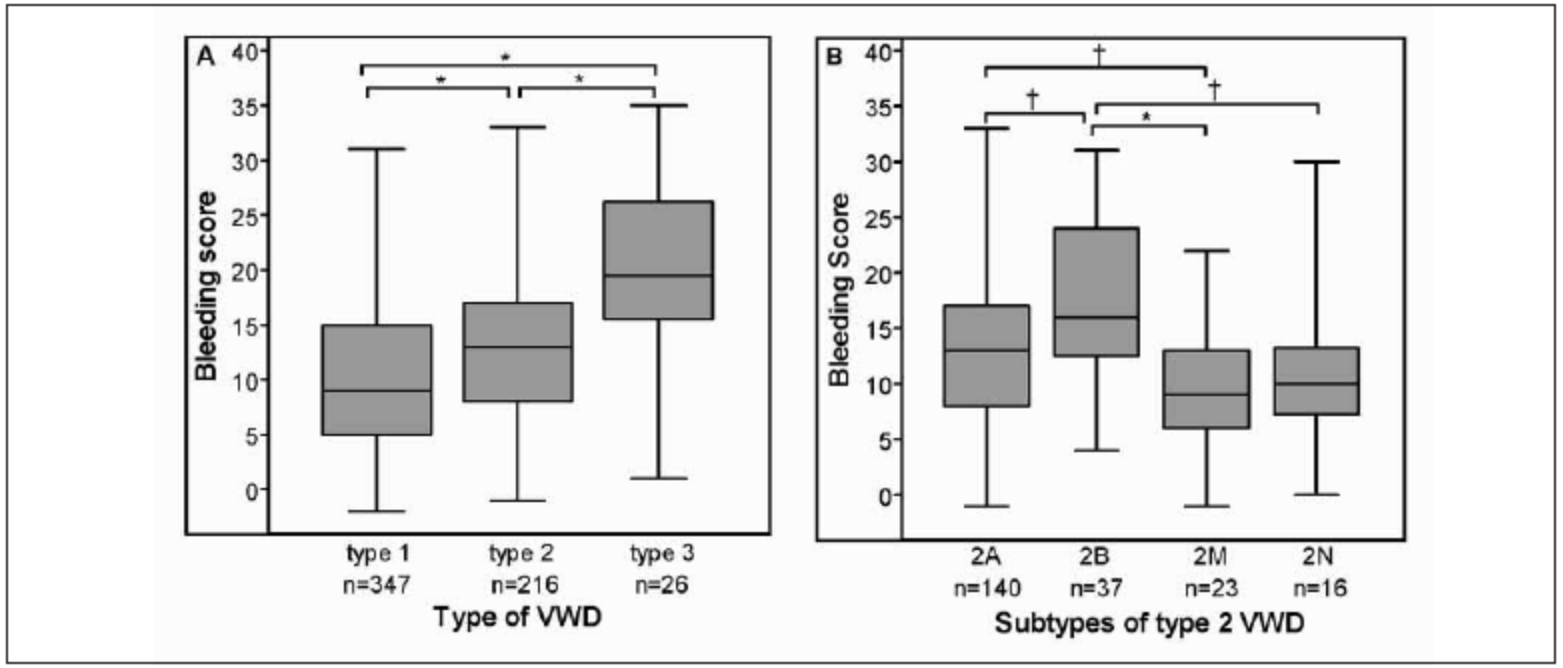


Figure 2: Bleeding score according to type of VWD. A) Bleeding score according to type of VWD. B) Bleeding score according to type 2 variants in patients with VWD. * p<0.001; † p<0.01.

De Wee et al, 2011

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

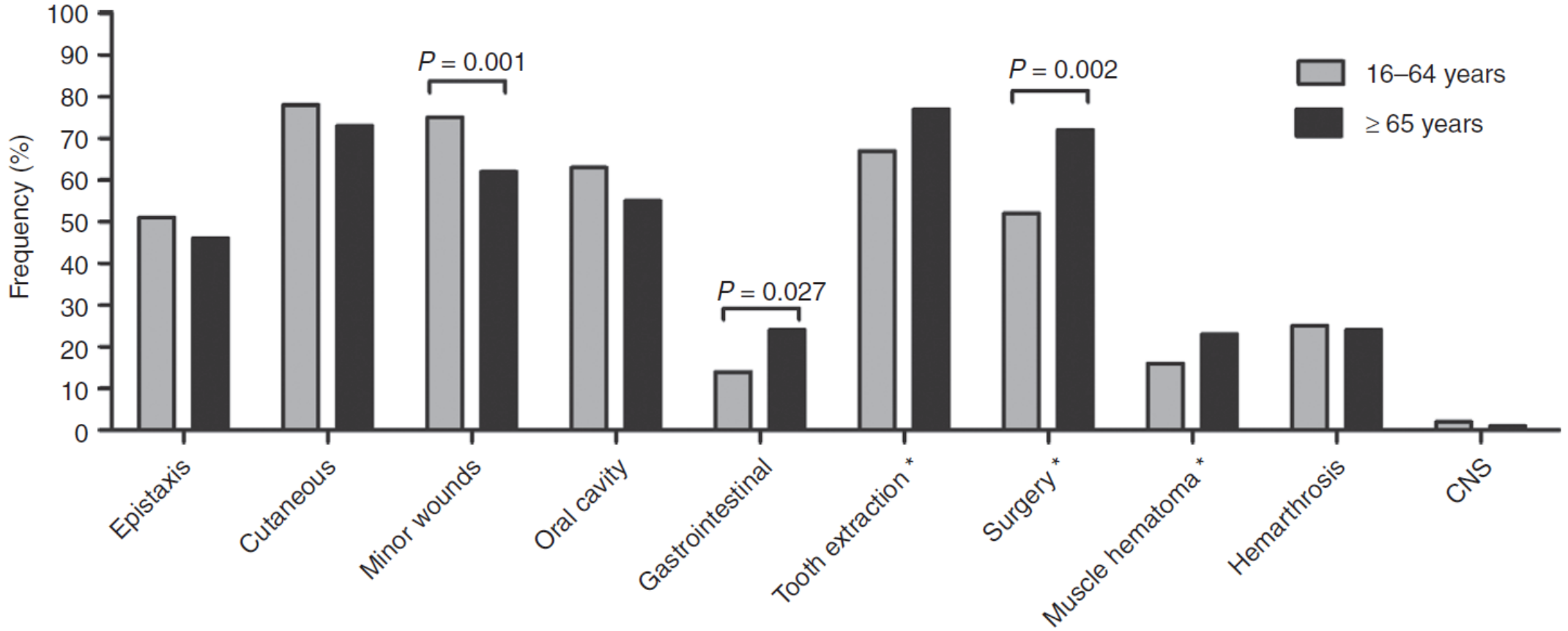
EHC european haemophilia consortium

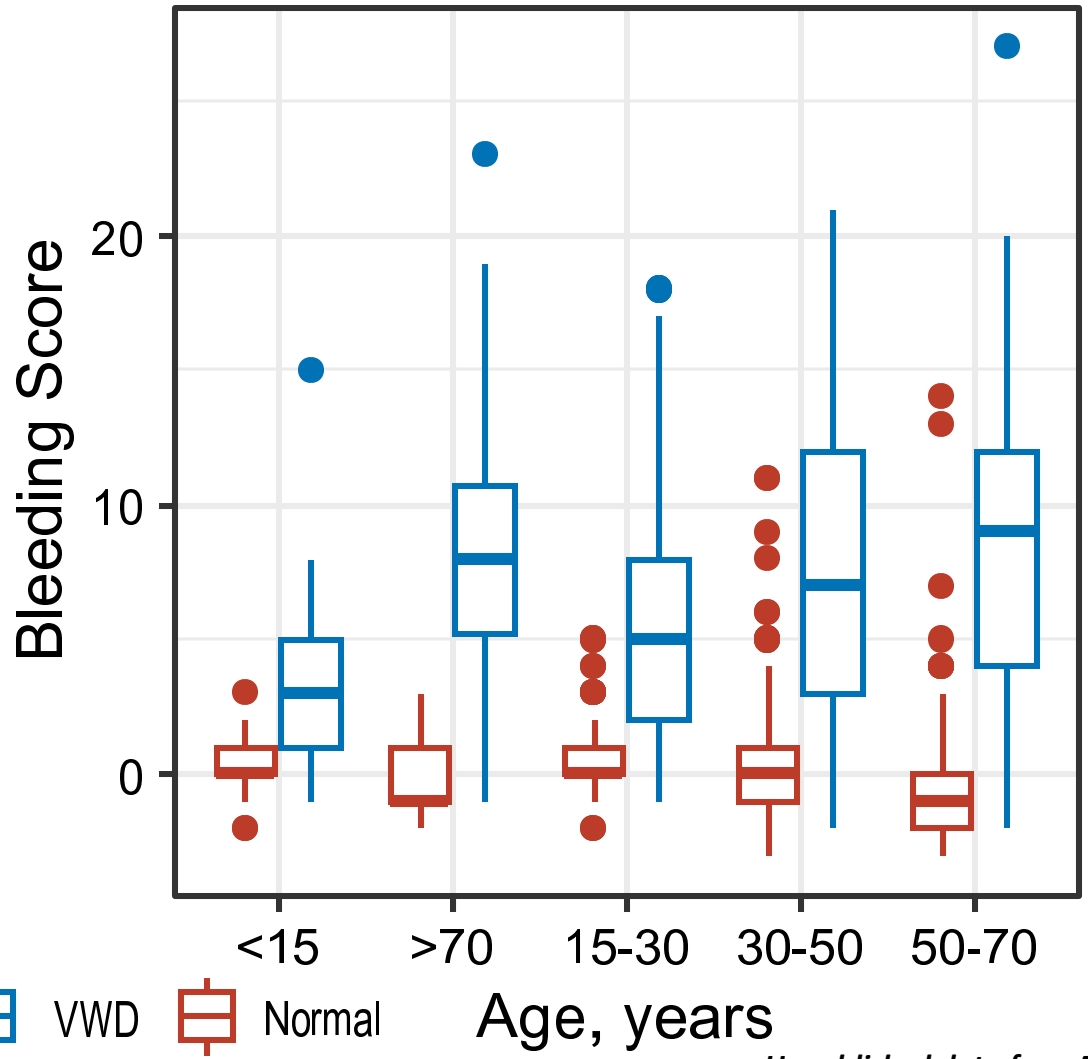
European von Willebrand Disease Community

EHC Webinars Von Willebrand disease

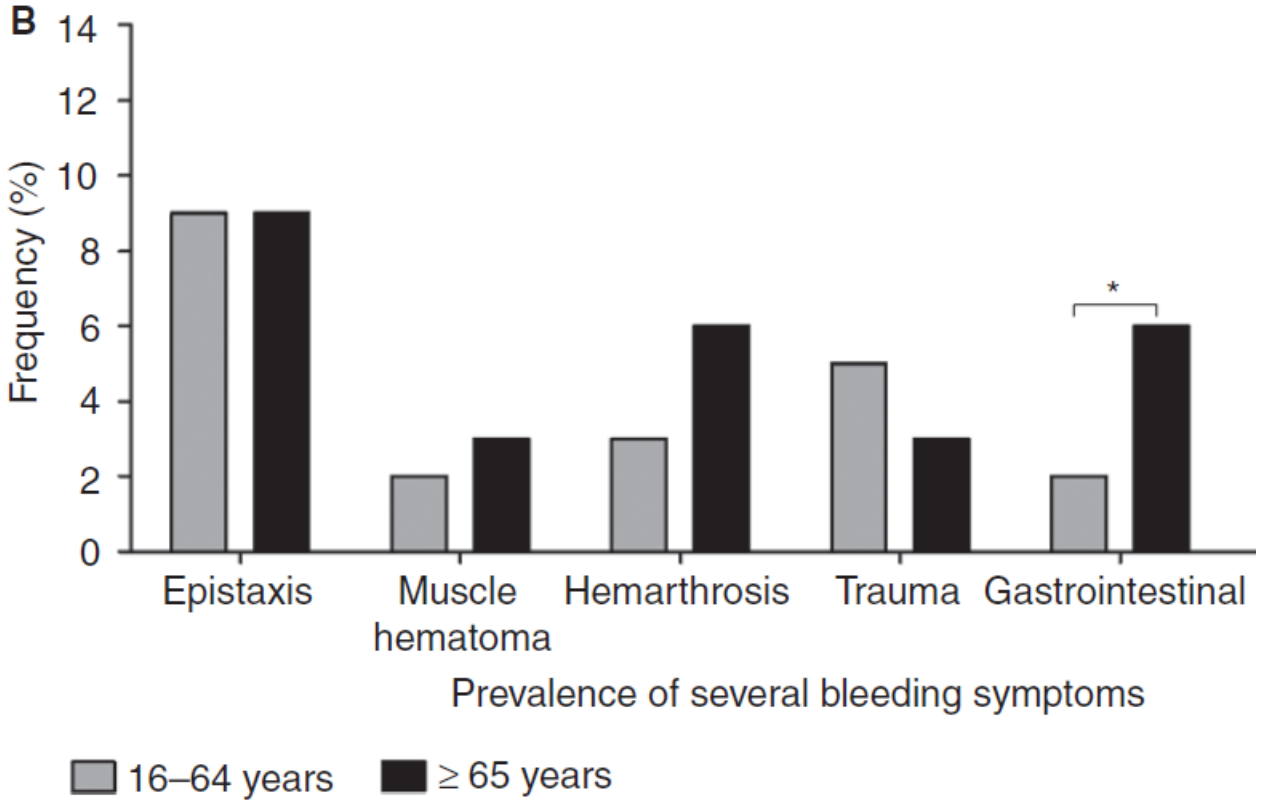
Topic on focus ERN-EuroBloodNet

In VWD, the impact of bleeding symptoms varies by age



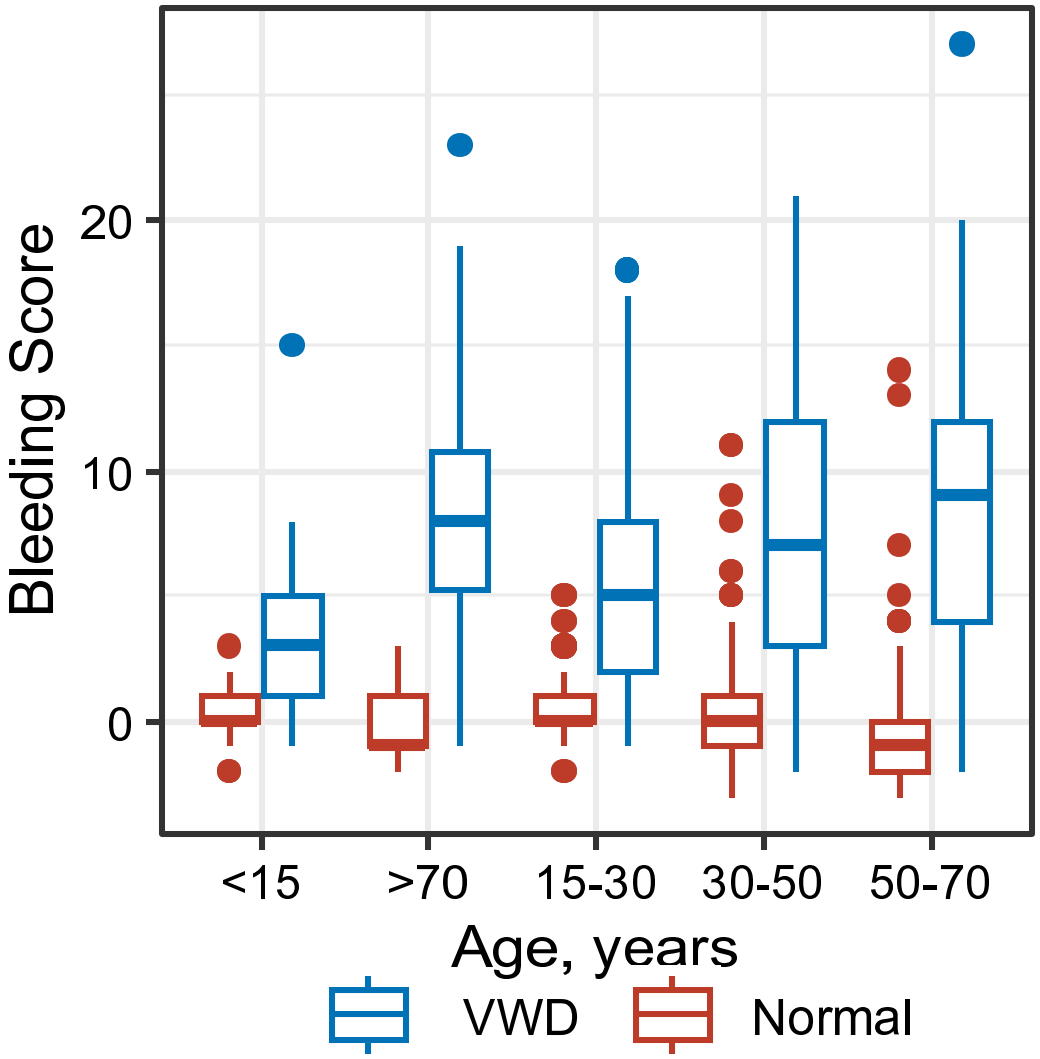


Prevalence of bleeding that required DDAVP or replacement therapy in the year preceding inclusion in the study [2]



Unpublished data from MCMDM-1 study, 1146 normal subjects and 418 type 1 VWD; 2 Sanders et al. J Thromb Haemost, 2014

European Reference Network for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)
EHC european haemophilia consortium
European von Willebrand Disease Community
EHC Webinars Von Willebrand disease
Topic on focus ERN-EuroBloodNet

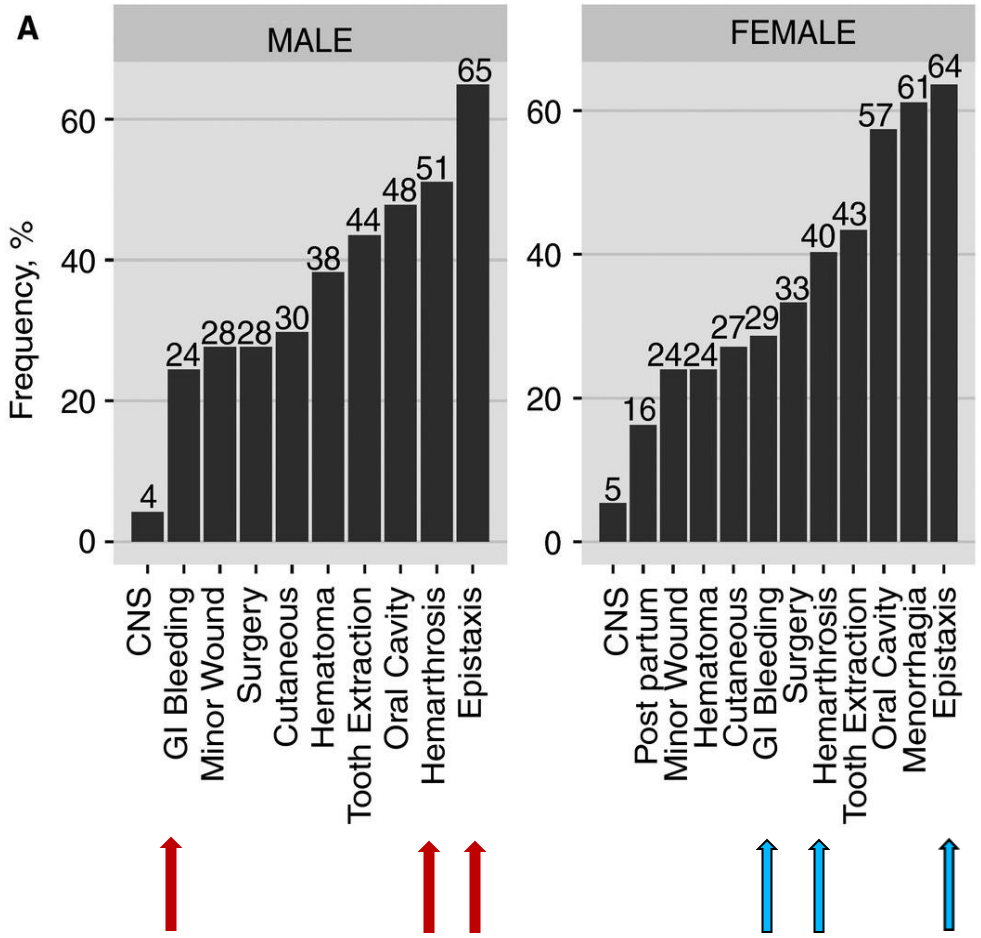


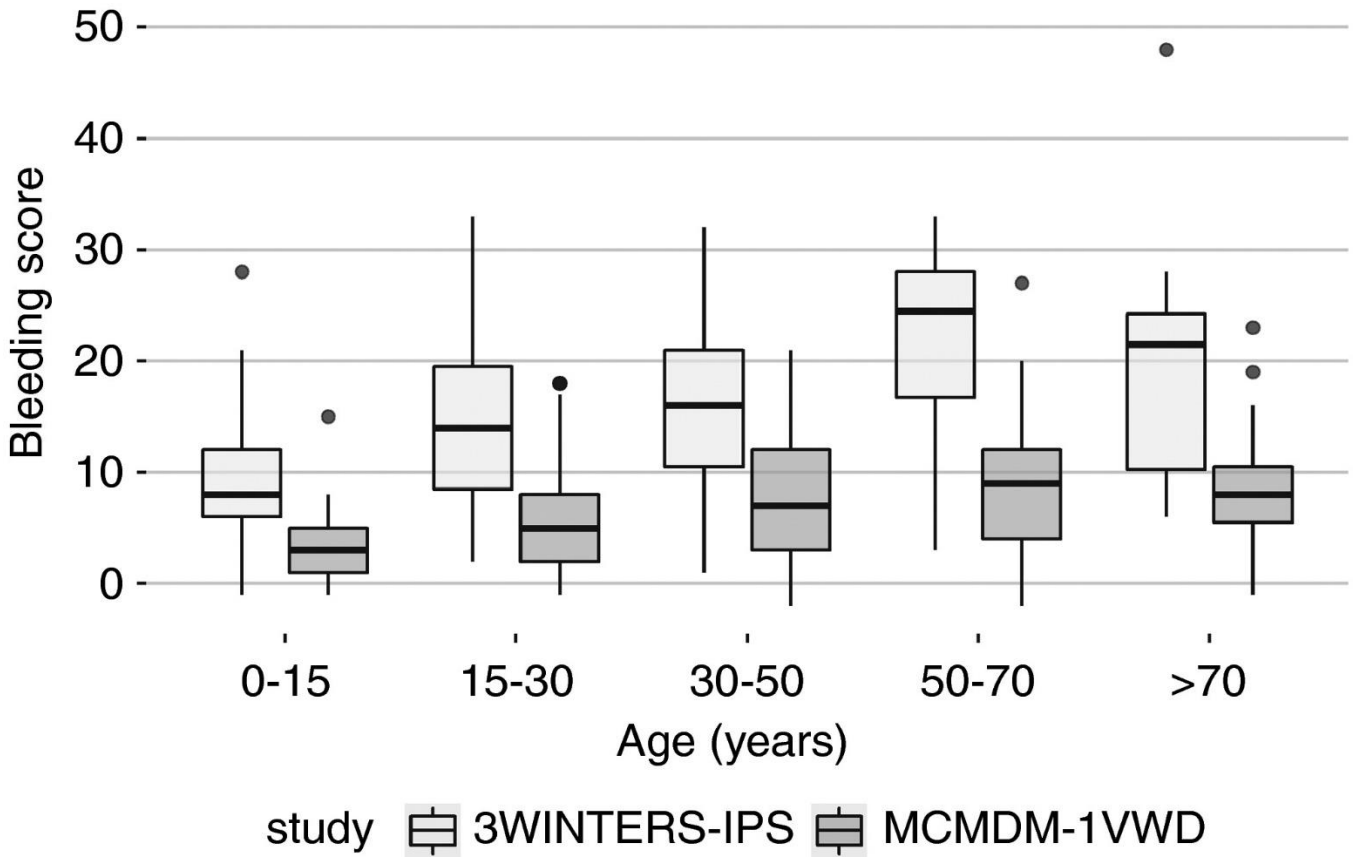
Conclusions:

- The incidence of bleeding symptoms is **two- to three-fold** increased in the elderly in the general population
- If the same increase applies to VWD patients, this means that elderly VWD patients may have an estimated **bleeding incidence of ≈ 10% pt-year**, making them a high-risk population

Unpublished data from MCMDM-1 study, 1146 normal subjects and 418 type 1 VWD; 2 Sanders et al. J Thromb Haemost, 2014

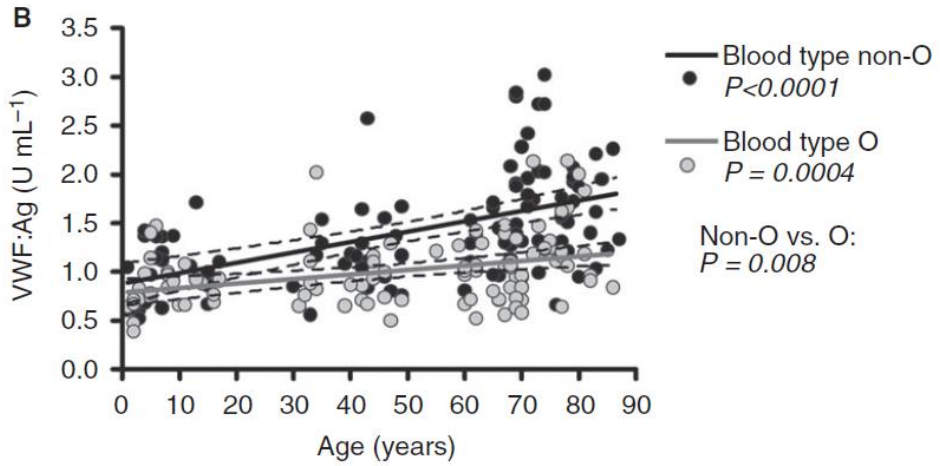
Bleeding symptoms in patients with type 3 von Willebrand disease: Results from 3WINTERS-IPS study compared to type 1

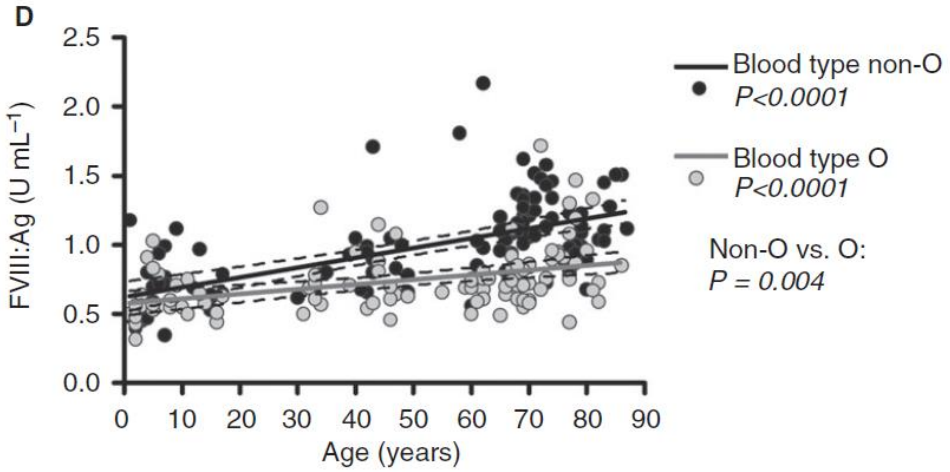


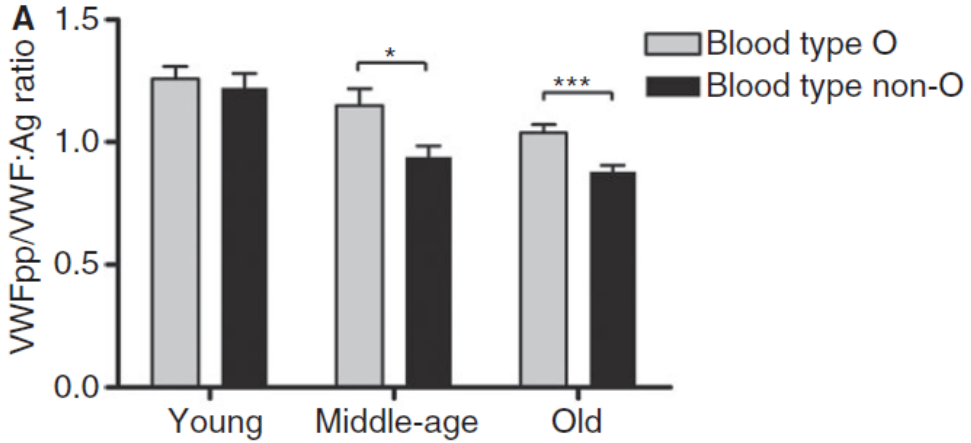


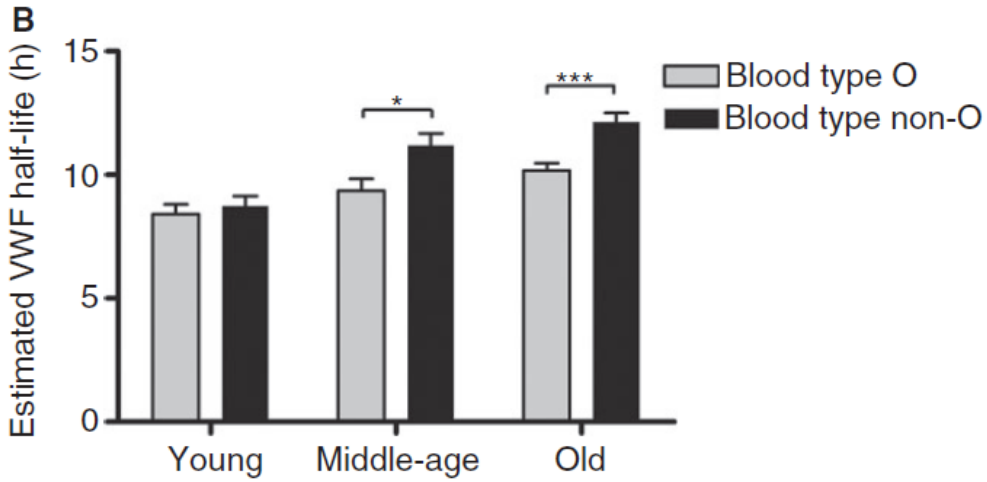
Tosetto A. et al, Journal of Thrombosis and Haemostasis, Volume: 18, Issue: 9, Pages: 2145-2154

Von Willebrand Factor and age



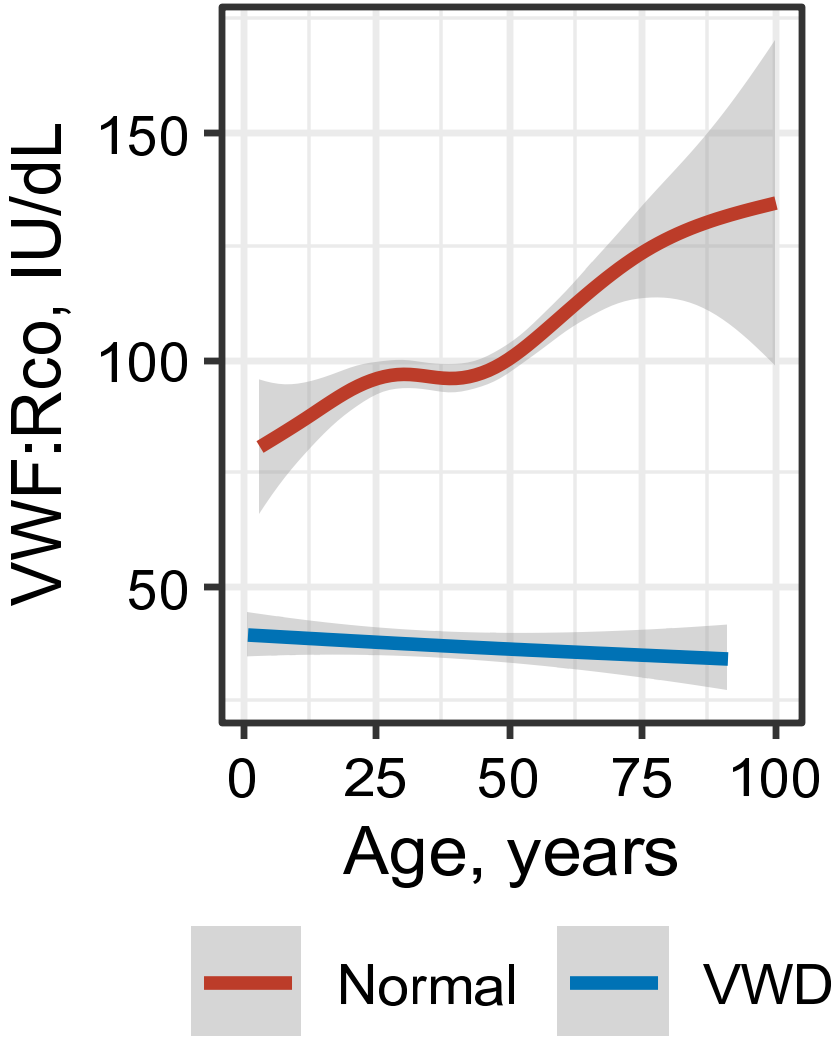


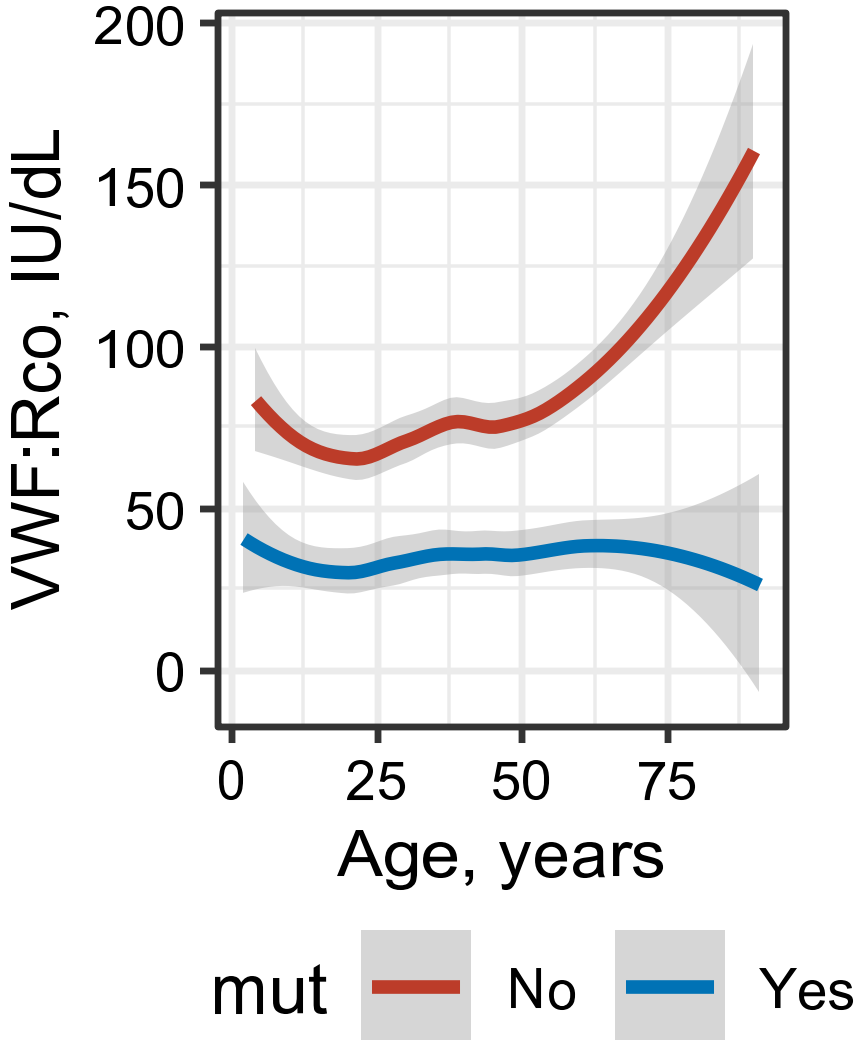




Elderly ABO non-O subjects show a more pronounced increase in VWF/FVIII, associated with prolonged VWF half-life

Albánez et al. J Thromb Haemost, 2016

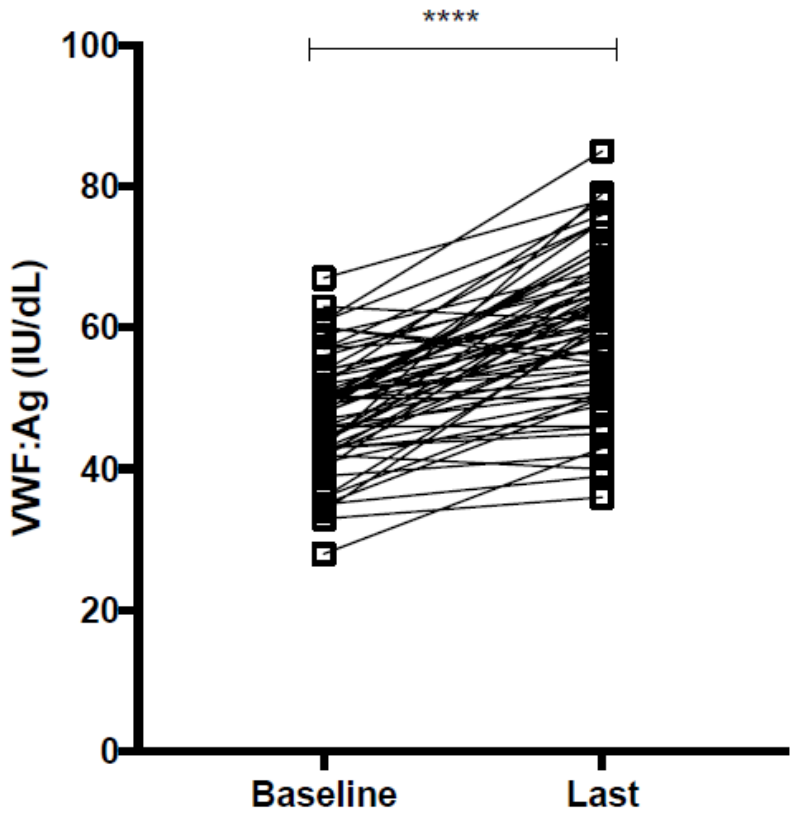




Unpublished data from MCMDM-1 study.; 1146 normal subjects and 418 type 1 VWD

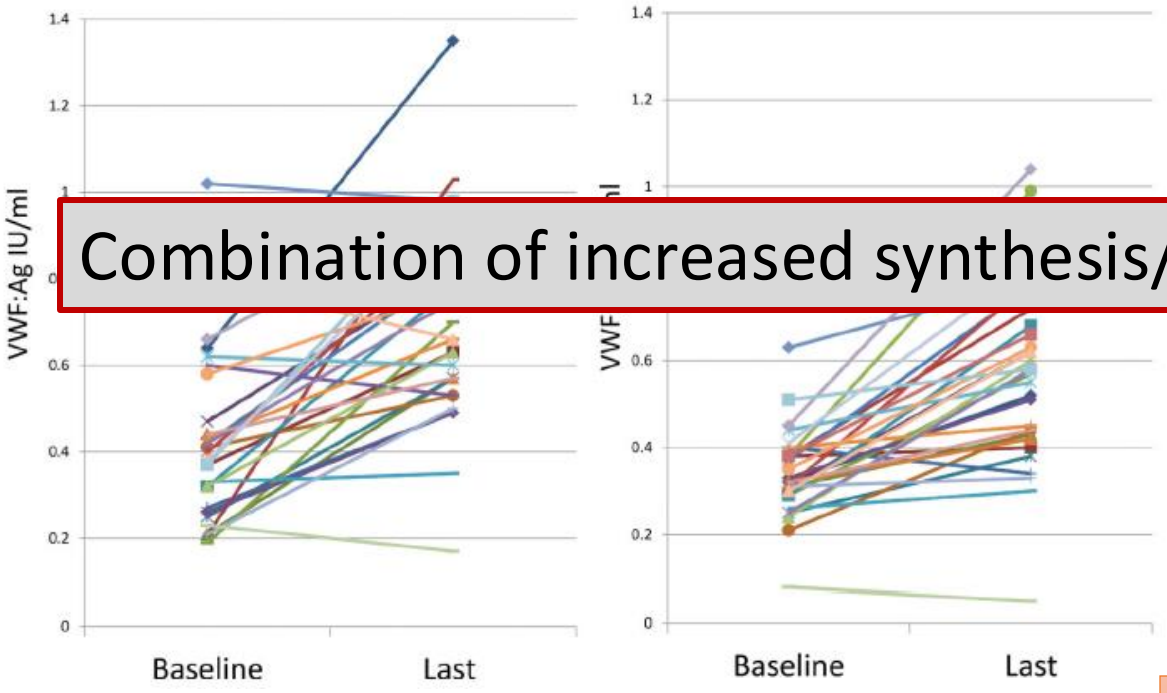
In patients with “low” VWF, normalization of VWF is possible

- An increase of VWF level is frequently observed
- Age-dependent effect
- Need for repeated testing to avoid over-diagnosis



Lavin et al. Blood, 2017.

Type 1 VWD/Low VWF: VWF:Ag and VWF:RCo changes with age



Mean observation period: 11 years (range 5-26)

Combination of increased synthesis/reduced clearance

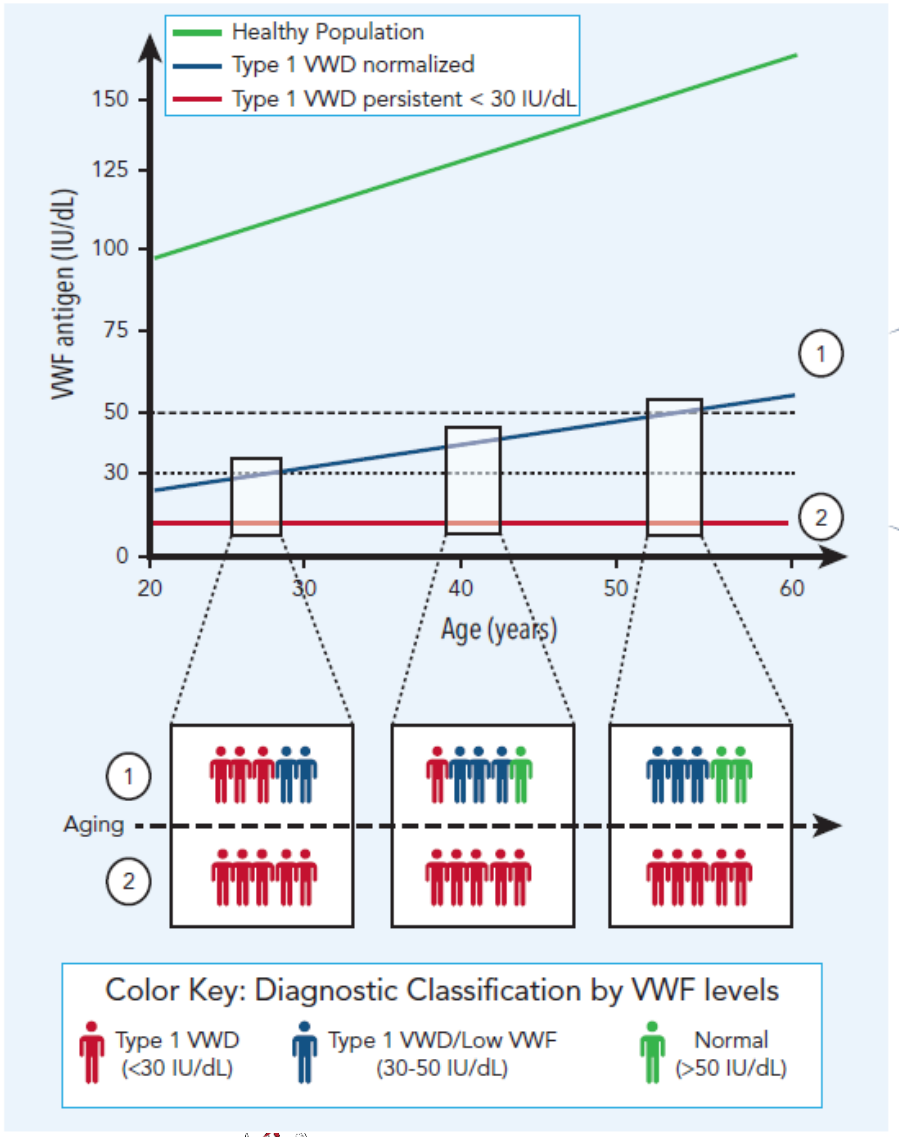
Comparison of Baseline and Last VWF levels

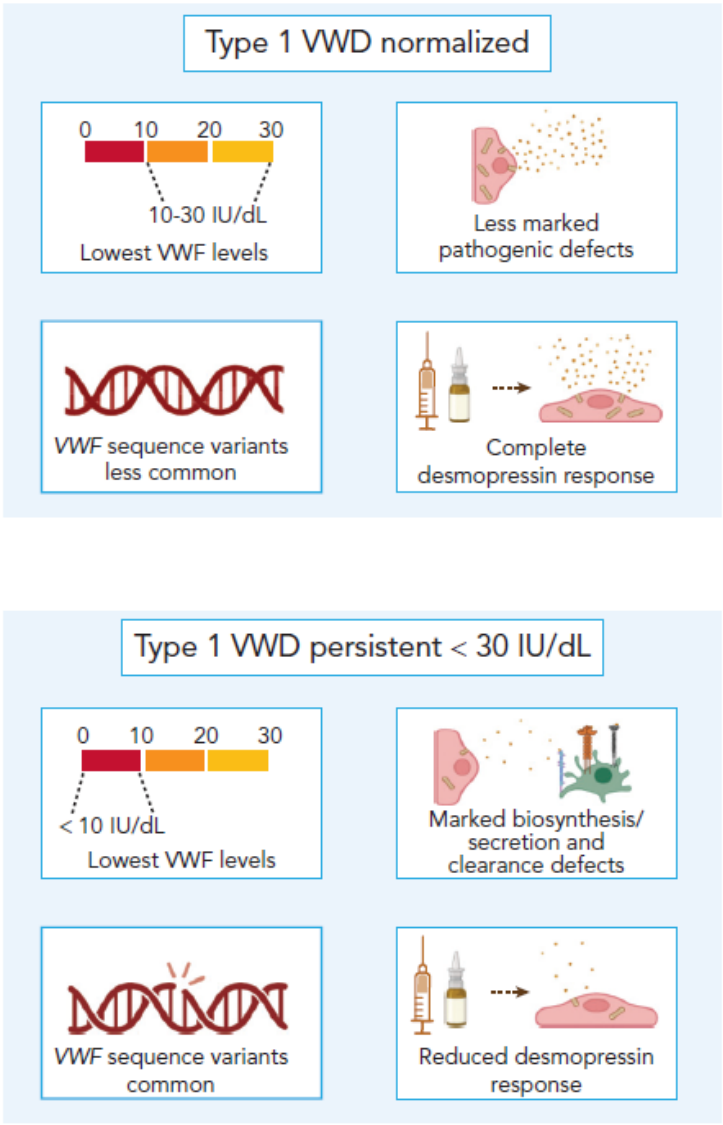
	Baseline, IU/ml Mean (range)	Last, IU/ml Mean (range)	*P*
A. All patients (n=31)			
			<0.0001
			<0.0001
FVIII:C	0.75 (0.24-1.55)	0.90 (0.22-1.41)	0.0081
B. Patients with VWF:Ag <0.30 IU/ml (n=8)			
VWF:Ag	0.23 (0.19-0.27)	0.57 (0.17-1.03)	0.0071
VWF:RCo	0.29 (0.08-0.4)	0.42 (0.05-0.72)	0.046
FVIII:C	0.60 (0.24-0.81)	0.80 (0.26-1.37)	0.0.21

58% of patients normalized VWF:Ag and VWF:RCOF

VWF level does not change in patients with severe type 1, type 2 and 3

Rydz N. et al, Haemophilia 2015





European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium
Advocating for people with haemophilia and congenital bleeding disorders

European von Willebrand Disease Community

EHC Webinars
Von Willebrand disease
Topic on focus ERN-EuroBloodNet

VWD, VWF, AGE AND TYPE 1 DIAGNOSIS

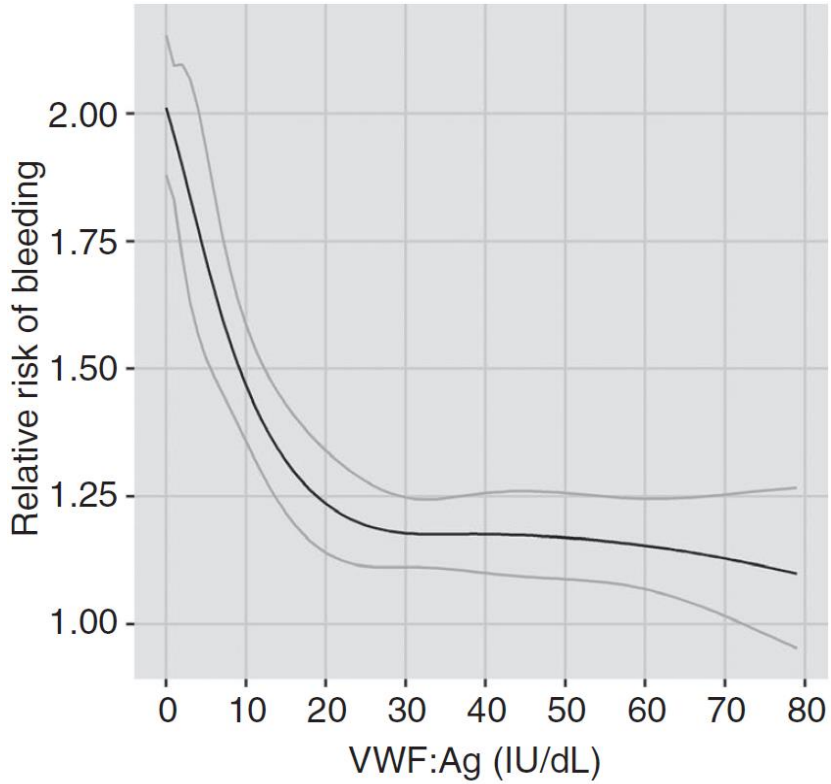
VWF levels that normalize with age. RECOMMENDATION 5. The panel *suggests* reconsidering the diagnosis as opposed to removing the diagnosis for patients with previously confirmed type 1 VWD who now have VWF levels that have normalized with age (conditional recommendation based on very low certainty in the evidence of effects ⊕◯◯◯).

Remarks:

- With this recommendation, the panel worked under the assumption that the original diagnosis of type 1 VWD was accurate.
- Aging and comorbidities are known to increase VWF levels. However, the association between the increased VWF levels and bleeding symptoms is not established.
- Decisions about reconsidering or removing the diagnosis should consider the patient's values and preferences and be informed by a shared decision-making process.

What are the minimal VWF/FVIII levels required for safe hemostasis?

- We don't know – no evidence that elderly people have different hemostatic requirements
- Bleeding symptoms are associated with VWF levels < 20 IU/dL [1]
- Guidelines suggest VWF levels above 50 IU/dL for at least three days after surgery [2-4]

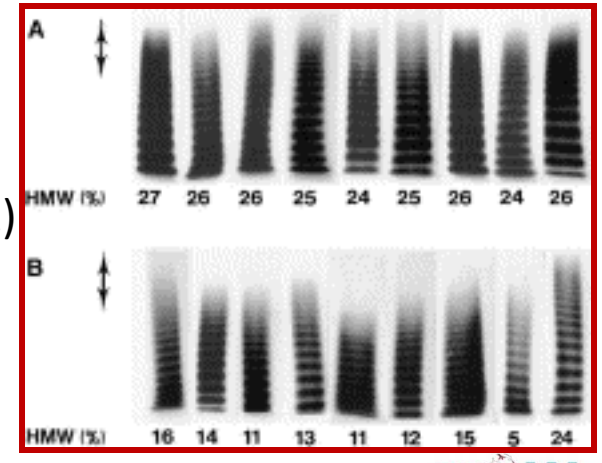


1. Tosetto et al. J Thromb Haemost, 2020; 2. Connell et al. Blood Adv, 2021; 3. Castaman et al. Haematologica, 2013

Most critical bleeds in elderly VWD patients

Gastrointestinal bleeding and angiodysplasia

- Mostly acquired as a degenerative aging process
- Fortuitous endoscopic findings in ~ 3 % of nonbleeding individuals > 65 years (Meyer et al, 1981)
- GI bleeding due to angiodysplasia major cause of digestive tract bleeding in the general population and commonly observed in elderly people, with incidences ranging from 2.6% to 6.2% in endoscopies for bleeding (Danesh et al, 1987; Sharma & Gorbien, 1995)
- A proportion of patients with GI bleeding and angiodysplasia have a deficiency of the largest HMW VWF multimers, mainly associated with aortic valve stenosis (Veyradier et al, 2001)



NON-BLEEDING

BLEEDING

European Reference Network for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium
Advocating for people with haemophilia and congenital bleeding disorders

European von Willebrand Disease Community

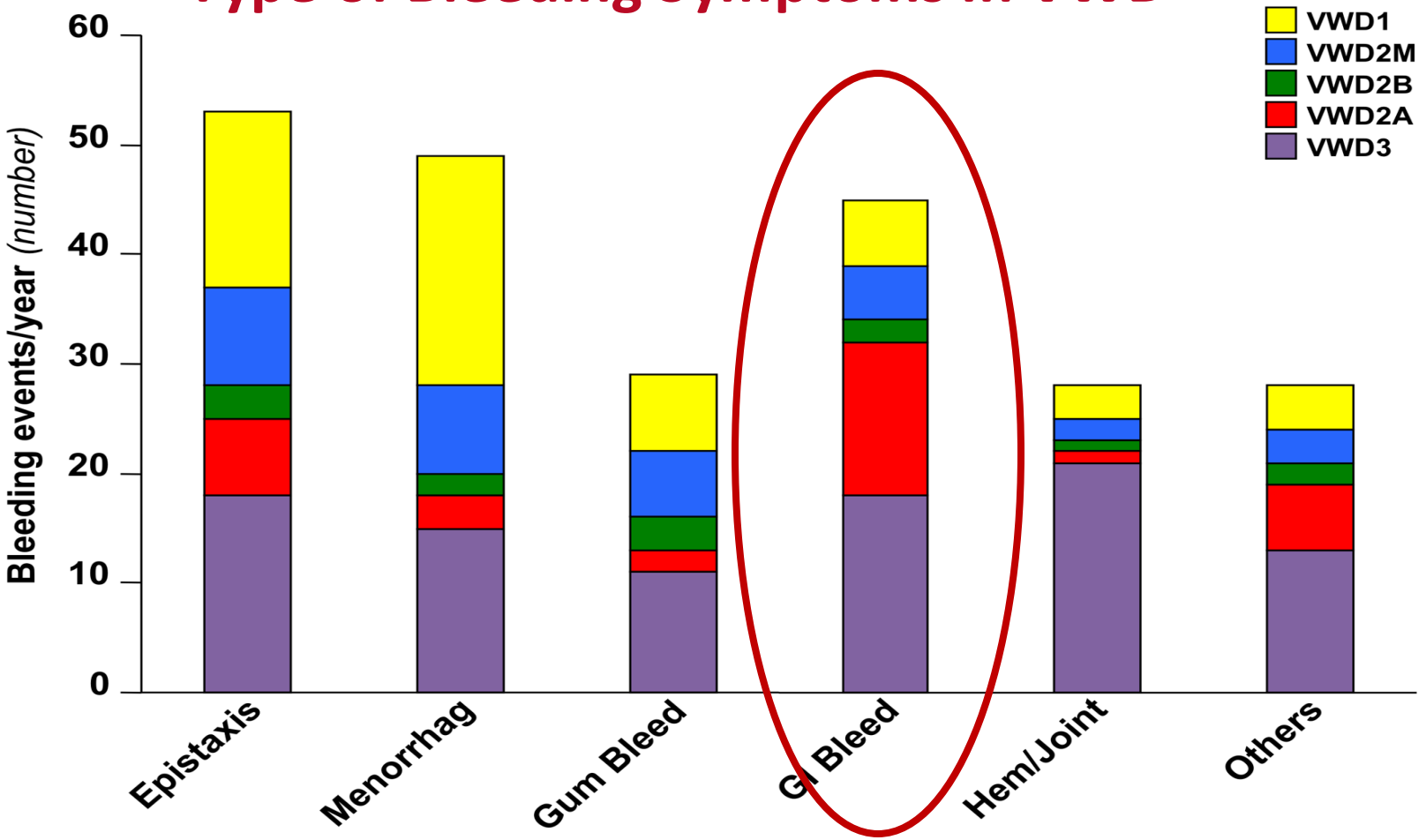
EHC Webinars
Von Willebrand disease
Topic on focus ERN-EuroBloodNet

blood
Prepublished online April 30, 2014;
doi:10.1182/blood-2014-02-557264

The bleeding score predicts clinical outcomes and replacement therapy in adults with von Willebrand disease: a prospective cohort study of 796 cases

Augusto B. Federici, Paolo Bucciarelli, Giancarlo Castaman, Maria G. Mazzucconi, Massimo Morfini, Angiola Rocino, Mario Schiavoni, Flora Peyvandi, Francesco Rodeghiero and Pier Mannuccio Mannucci

Type of Bleeding Symptoms in VWD



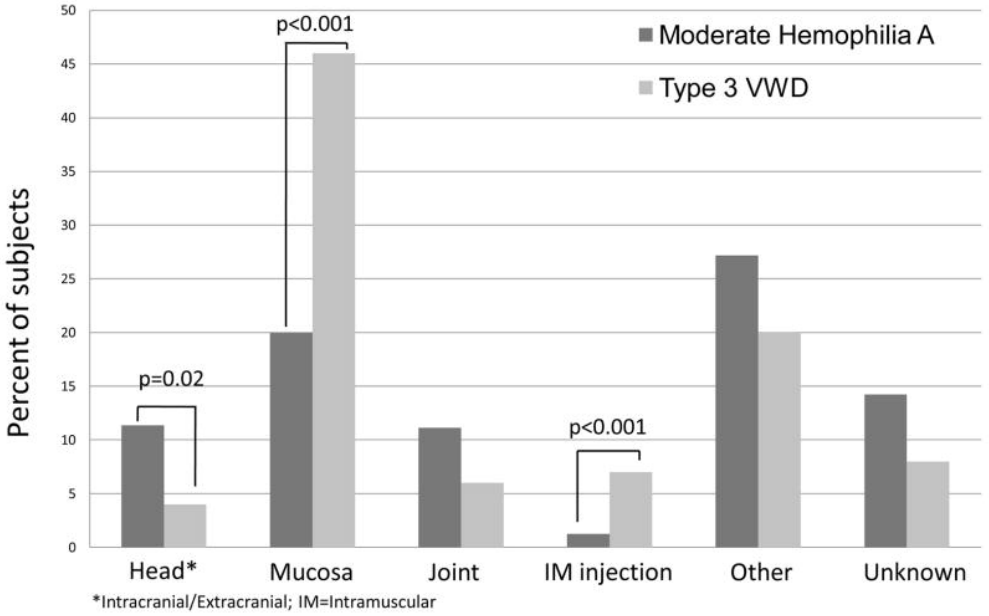
Joint bleeding

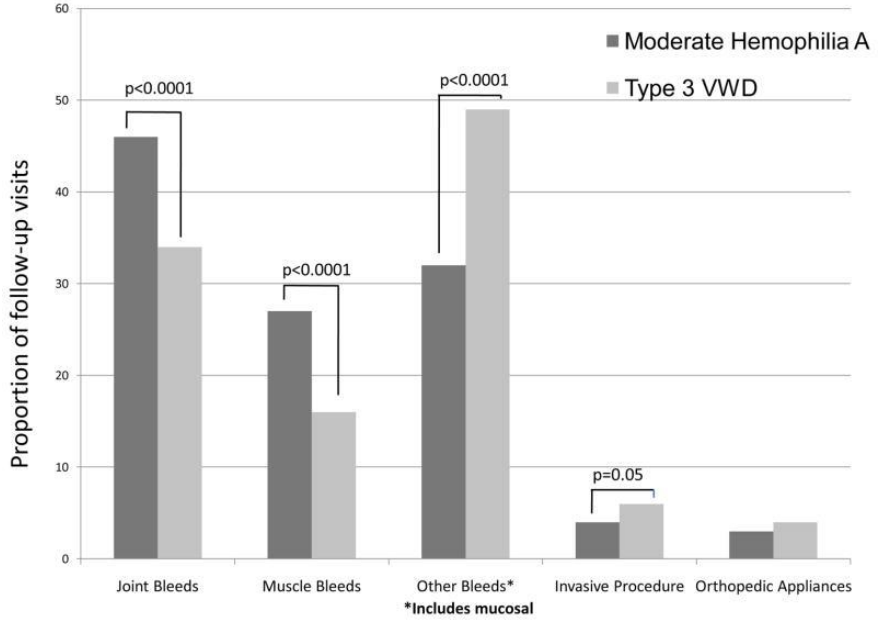
- Joint bleeds are reported by almost a quarter of patients with moderate and severe VWD, start mostly before the age of 16 years and occur in all three types of moderate to severe VWD (Van Galen et al, 2015)

- JB in VWD are associated with more severe VWD, male sex, more CFC consumption, more self-reported and X-ray recorded joint damage and lower HR-QoL

- Prophylaxis reduces joint bleed frequency and is likely to prevent joint damage when more than five JB occur

Similar rates of joint function limitation between Type 3 VWD and moderate HA





- No difference in joint ROM loss over time between individuals with VWD and moderate HA.
- Higher FVIII level was associated with preserved joint ROM ($p < 0.001$).
- Lower FVIII level correlated with a higher rate of joint ($p< 0.001$) and muscle ($p< 0.001$), but not mucosal bleeding ($p=0.10$).

[haematologica reports]
2005;1(4):30-31

Long-term prophylaxis in von Willebrand disease. Experience from Sweden

- 35 patients (28 type 3, 3 2B, 2 2A, 1 type 1 on prophylaxis for 11 yr (2 - 45)
- Once-thrice weekly infusions (25 U/Kg FVIII)
- 17 patients on prophylaxis for hemarthrosis had **1-4 episodes/year**
- **Most developed chronic arthropathy by clinical-radiologic evidences**
- Improved QoL, no thrombosis

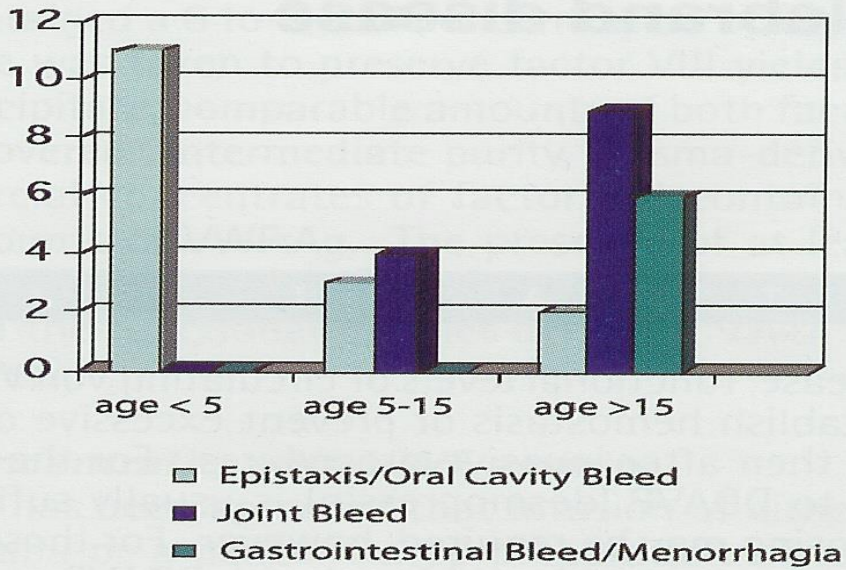


Figure 1. Clinical indication for prophylaxis by age at commencement of therapy.

Long-term prophylaxis in VWD with a VWF concentrate

ORIGINAL ARTICLE

jth

Management of von Willebrand disease with a factor VIII-poor von Willebrand factor concentrate: Results from a prospective observational post-marketing study

Jenny Goudemand[1] | Françoise Bridey[2] | Ségolène Claeyssens[3] | Nathalie Itzhar-Baïkian[4] | Annie Harroche[5] | Dominique Desprez[6] | Claude Négrier[7] | Pierre Chamouni[8] | Hervé Chambost[9] | Céline Henriet[2] | Sophie Susen[1,10] | Annie Borel-Derlon[11]

	GI bleeds (13 patients)	Joint bleeds (14 patients)
Infusions for prophylaxis	4,036	3,341
VWF infusion dose (IU/kg)	45.2 (22 – 55)	42.2 (26 – 76)
N. Infusions per week	2.5 (1 – 3)	1.9 (1.2 – 3.3)
ABR	1.1 (0.0 – 11)	0.8 (0.0 – 5.4)
Breakthrough bleeds	56/4,036 (1.4 %)	51/3,069 (1.7 %)

Goudemand et al. *J Thromb Haemost.* 2020;18:1922–1933

VWD, age and comorbidities: Cardiovascular risk and management

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium

Advocating for people with haemophilia and congenital bleeding disorders

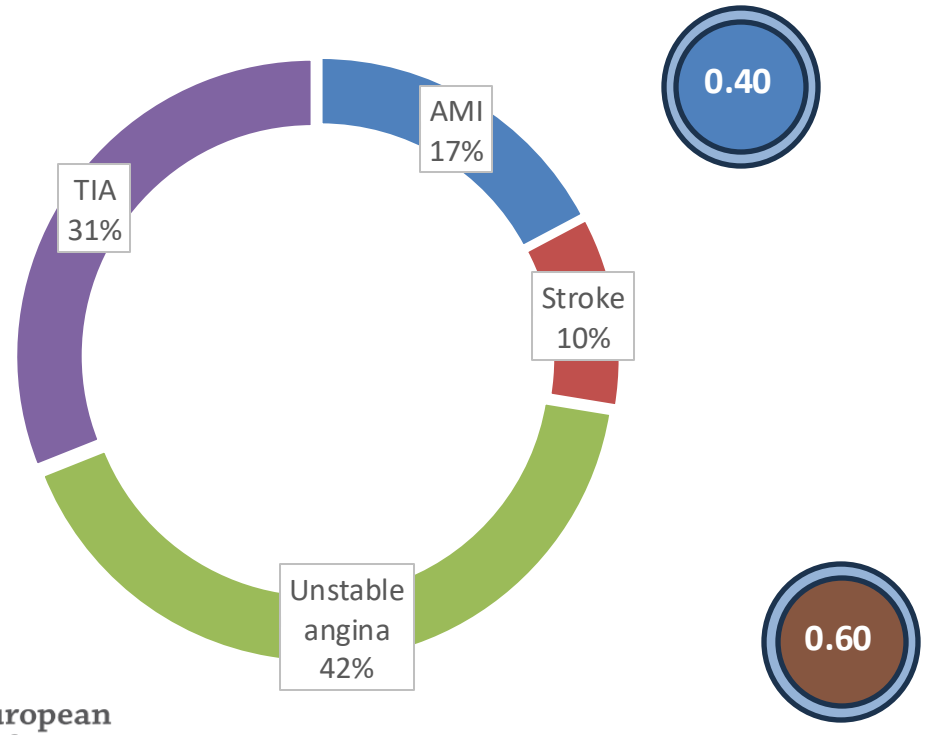
European von Willebrand Disease Community

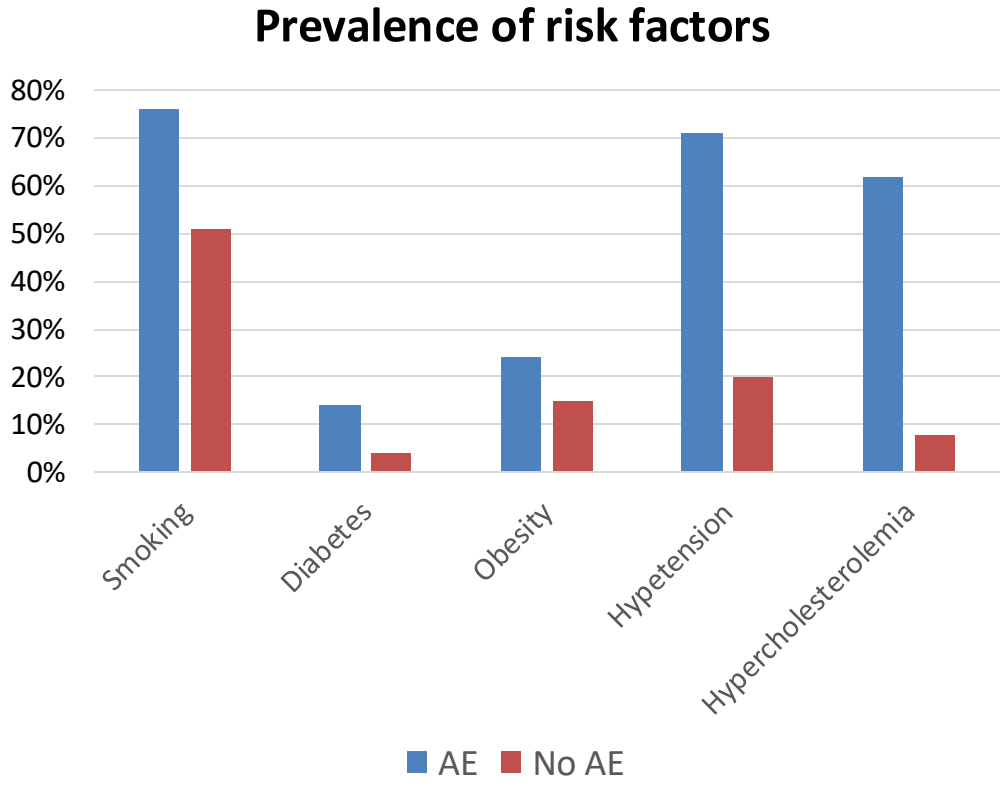
EHC Webinars

Von Willebrand disease

Topic on focus ERN-EuroBloodNet

Prevalence of arterial thrombosis in VWD, WiN cohort





Sanders et al. Journal of Thrombosis and Haemostasis, 2013

European Reference Network for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

EHC european haemophilia consortium

European von Willebrand Disease Community

EHC Webinars Von Willebrand disease Topic on focus ERN-EuroBloodNet

ORIGINAL ARTICLE

Does deficiency of von Willebrand factor protect against cardiovascular disease? Analysis of a national discharge register

C. D. SEAMAN,*† J. YABES,‡ D. M. COMER‡ and M. V. RAGNI*†

The prevalence of CVD in VWD patients was less than the prevalence of CVD in non-VWD patients (15.0% versus 26.0%).

Table 4 Baseline characteristics of von Willebrand disease (VWD) patients with and without cardiovascular disease (CVD)

	VWD patients with CVD	VWD patients without CVD	*P*-value
Admissions	1138	6418	
Age (years)			
Mean (SE)	68.20 (0.41)	46.40 (0.24)	< 0.001
Gender (%)			
Male	39.62	21.90	< 0.001
Female	60.38	79.10	< 0.001
Length of stay (days)			
Mean (SE)	5.85 (0.2)	4.38 (0.07)	< 0.001
Inpatient mortality (%)	3.13	1.02	< 0.001
CVD risk factors (%)			
Hypertension	70.00	31.59	< 0.001
Hyperlipidemia	44.97	12.84	< 0.001
Diabetes mellitus	30.96	10.66	< 0.001
Obesity	10.55	8.99	< 0.001
Smoking	11.53	12.20	< 0.001

SE, standard error.

Recommendation for antithrombotic treatment in PWH

- FVIII 1–5 IU/dL for SAPT (aspirin or clopidogrel)
- FVIII ≈ 20 IU/dL for DAPT or oral anticoagulation
- FVIII ≈ 80 IU/dL for triple therapy (oral anticoagulation and DAPT)
- Clotting factor concentrates should be given to reach peak levels of FVIIII 80-100 before PCI and maintain >50 IU/dL for 24–48 h
- Prevention programs for PWH are key

Schutgens & Castaman, 2023

Prophylaxis

Recommendation 1

In patients with VWD with a history of severe and frequent bleeds, the guideline panel *suggests* using long-term prophylaxis rather than no prophylaxis (conditional recommendation based on low certainty in the evidence of effects ⊕⊕◯◯).

Remarks:

- Bleeding symptoms and the need for prophylaxis should be periodically assessed.

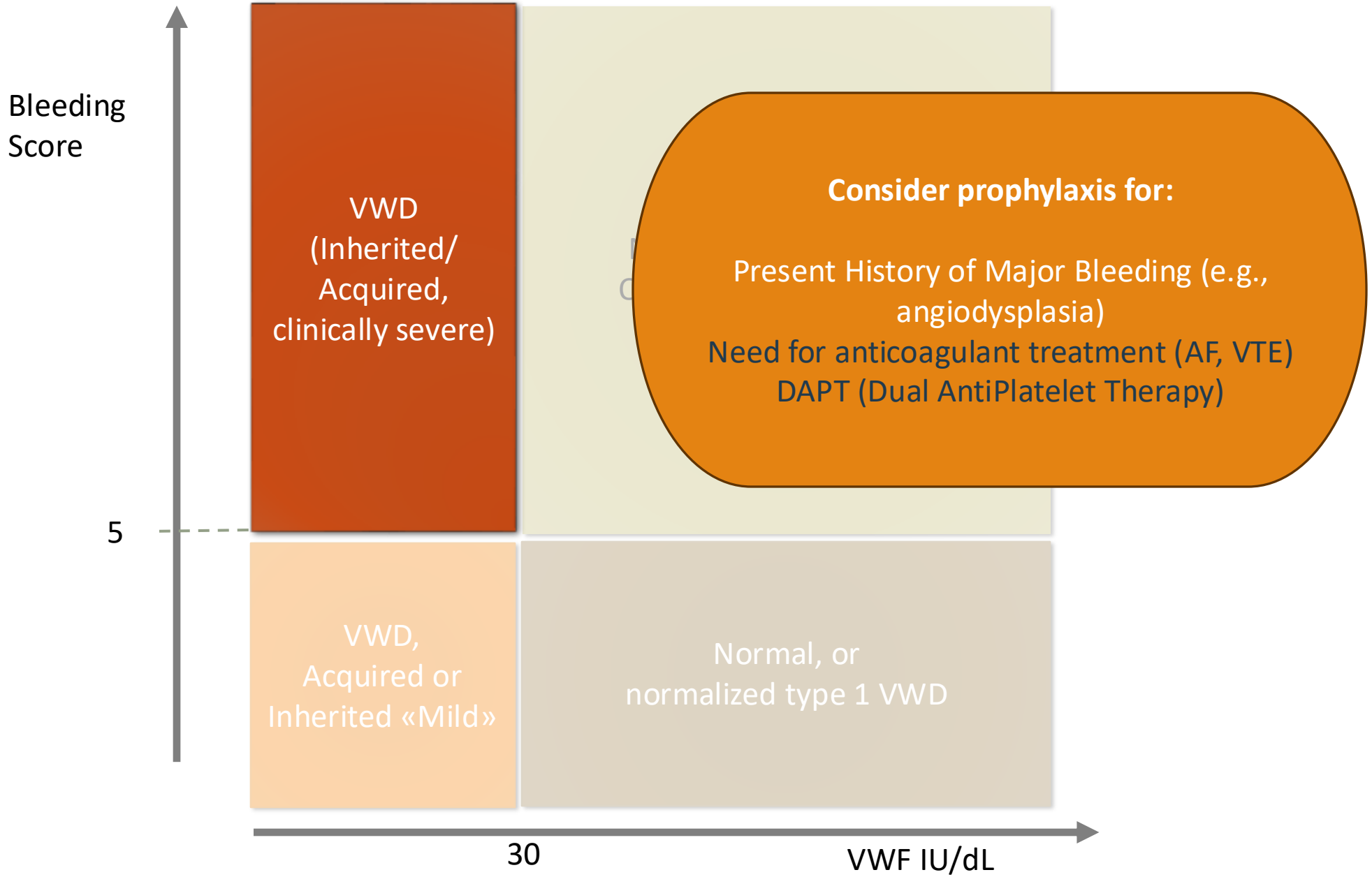
Managing cardiovascular events

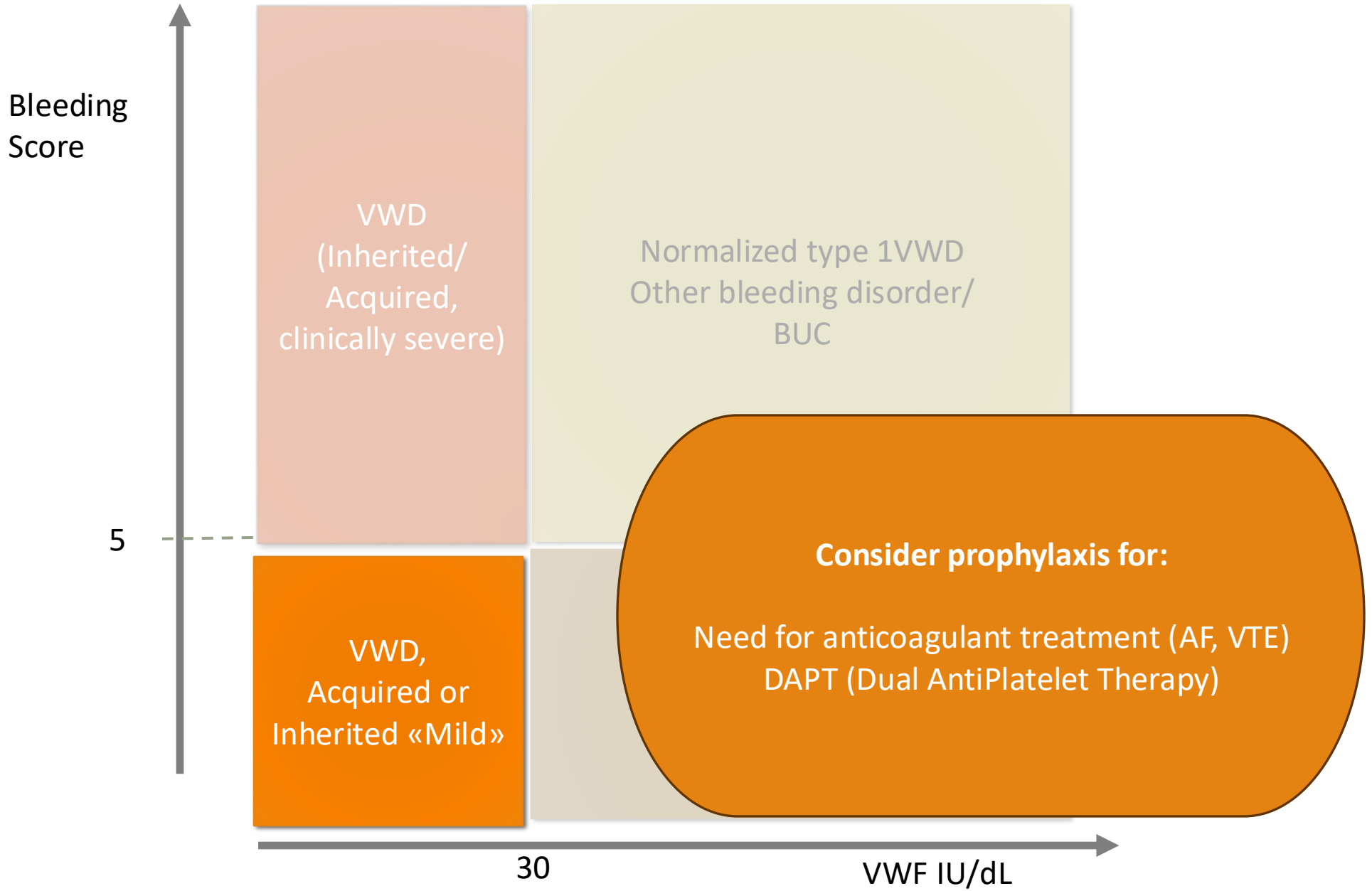
Recommendation 3

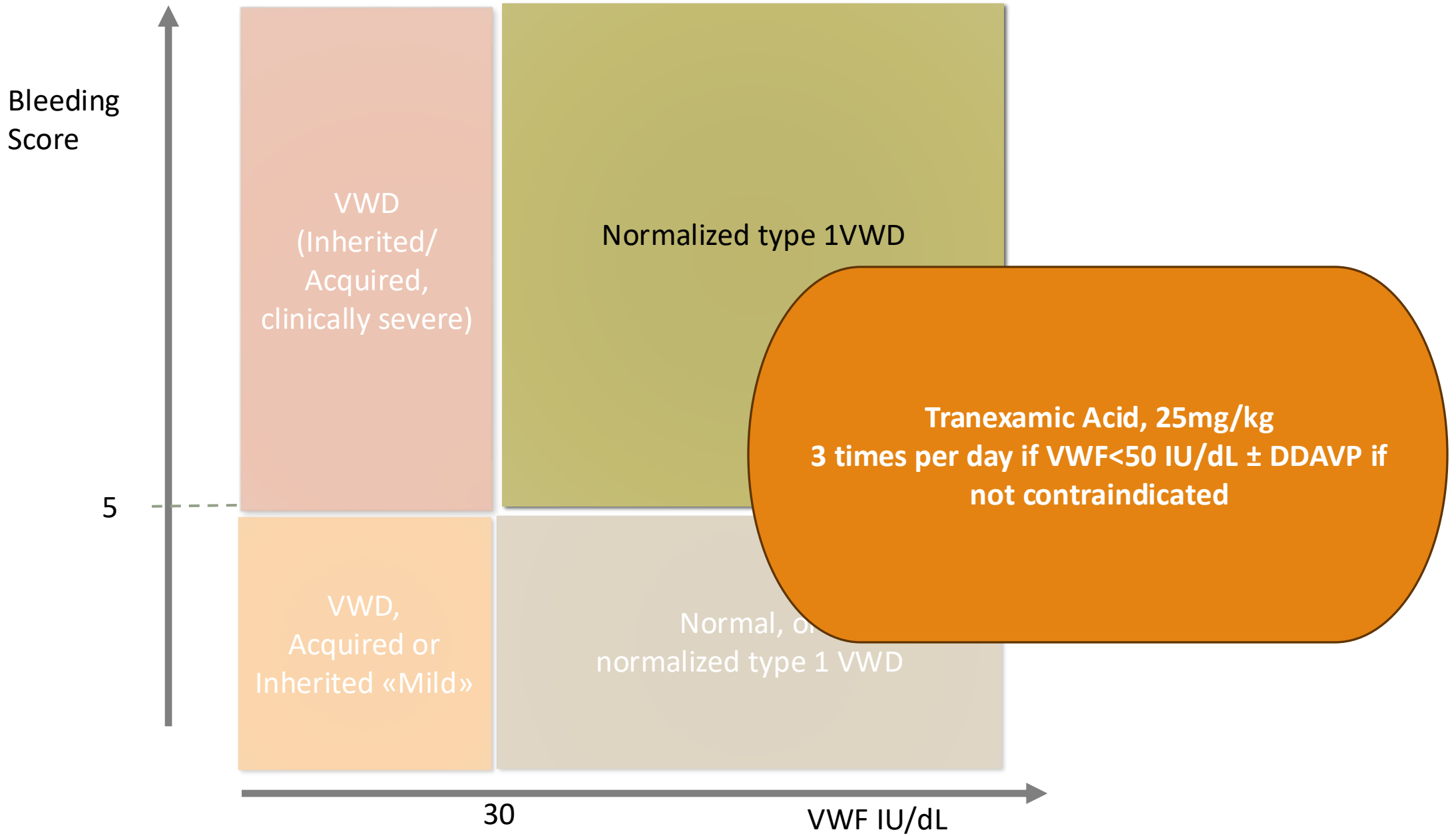
In patients with VWD and cardiovascular disease who require treatment with antiplatelet agents or anticoagulant therapy, the panel *suggests* giving the necessary antiplatelet or anticoagulant therapy over no treatment (conditional recommendation based on low certainty in the evidence of effects ⊕⊕◯◯).

Remark:

It is important to reassess the bleeding risk throughout the course of treatment.


Bleeding Score
VWD (Inherited/ Acquired, clinically severe)
Consider prophylaxis for:
Present History of Major Bleeding (e.g., angiodysplasia)
Need for anticoagulant treatment (AF, VTE)
DAPT (Dual AntiPlatelet Therapy)
5
VWD, Acquired or Inherited «Mild»
Normal, or normalized type 1 VWD
30
VWF IU/dL


Bleeding Score
VWD (Inherited/ Acquired, clinically severe)
Normalized type 1VWD Other bleeding disorder/ BUC
5
VWD, Acquired or Inherited «Mild»
Consider prophylaxis for:
Need for anticoagulant treatment (AF, VTE)
DAPT (Dual AntiPlatelet Therapy)
30
VWF IU/dL


Bleeding Score
VWD (Inherited/ Acquired, clinically severe)
Normalized type 1VWD
Tranexamic Acid, 25mg/kg
3 times per day if VWF<50 IU/dL ± DDAVP if not contraindicated
5
VWD, Acquired or Inherited «Mild»
Normal, or normalized type 1 VWD
30
VWF IU/dL

TAKE HOME MESSAGES

- Patients with VWD type 1 and VWF ≥ 30 U/dL at diagnosis tend to normalize with age
- Bleeding phenotype over age risk should guide need for treatment
- Patients with VWD type 1 and VWF< 30 U/dL, type 2 and 3 do not show significant changes with age
- Bleeding risk remain substantially unchanged, little is known on normalized cases
- Co-morbidities may influence VWF levels and could influence bleeding risk
- Prophylaxis for recurrent bleeding/joint bleeding if not already ongoing
- Antithrombotic treatment should not be avoided if considered indicated

www.ehc.eu

vwd@ehc.eu

@EHC_Haemophilia

EHC - European Haemophilia Consortium

European Haemophilia Consortium

@EHCTVChannel EHC Youtube channel

www.eurobloodnet.eu

@ERNEuroBloodNet

eurobloodnet-european-reference-network-on-rare-hematological-diseases

Eurobloodnet - European Reference Network on Rare Hematological Diseases

ERN-EuroBloodNet's EDUcational Youtube channel

This project is carried out within the framework of European Reference Network on Rare Haematological Diseases (ERN-EuroBloodNet)-Project ID No 101085717. ERN-EuroBloodNet is partly co-funded by the European Union within the framework of the Fourth EU Health Programme.

Co-funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or European Health and Digital Executive Agency (HaDEA). Neither the European Union nor the granting authority can be held responsible for them.