IMPROVING CARE FOR PEOPLE WITH VWD

Webinar on the recently published *ASH ISTH NHF WFH 2021 Guidelines on the Diagnosis and Management of von Willebrand Disease (VWD)*

May 18th at 9am EDT

Duration: 1h30min

Presentations will be given in English with live interpretations in Arabic, French, Russian and Spanish

WFH
WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
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www.wfh.org/VWDGuidelines

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توصيات دليل ASH ISTH NHF WFH بشأن تشخيص داء فون فليبراند (VWD)

محتوى الدليل

- يعرض هذا الدليل توجيهات مبنية على أدلة تهدف إلى تحسين دقة تشخيص داء فون فليبراند (VWD)، والحدّ من الاختبارات غير الملائمة، وتجنّب الأضرار الناجمة عن المبالغة في تشخيص المرض.

أهمية الدليل

- يُعدّ داء فون فليبراند أكثر اضطرابات نزف الدم الوراثي شيوعًا، لكنّ تشخيصه على نحو دقيق وفي الوقت المناسب لا يزال يمثل تحديًا.
- تشمل العوائق التي تحول دون إجراء تشخيص دقيق لهذا الداء حاليًا ما يلي:
  - محدودية أو انعدام الاختبارات المعملية المتخصصة والخبرات اللازمة لإجرائها.
  - عدم فهم الاختلافات بين أعراض نزف الدم الطبيعي وغير الطبيعي.
- من المُهمّ تحسين دقة تشخيص المرض لضمان حصول المرضى على الرعاية المناسبة والحدّ من الاختبارات غير الملائمة والأضرار الناجمة عن المبالغة في تشخيص المرض.

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Recomendaciones de las guías de ASH, ISTH, NHF, FMH para el tratamiento de la enfermedad de Von Willebrand (EVW)

Qué abarcan

- Recomendaciones basadas en pruebas científicas para el tratamiento de la EVW en el contexto de cirugías mayores y menores, pruebas durante procedimientos invasivos, uso de desmopresina, y uso profiláctico de concentrado de factor Von Willebrand (FVW).

Por qué son importantes

- La EVW es el trastorno de la coagulación hereditario más común.
- Actualmente hay una gran variabilidad en la práctica clínica aplicada al tratamiento de la EVW debido a la falta de pruebas científicas de certeza elevada para orientar la toma de decisiones.
- Hay múltiples subtipos de la EVW que requieren tratamiento individualizado con base en el diagnóstico específico, así como una gama de síntomas y múltiples terapias disponibles para su tratamiento. Lo más conveniente tanto para el médico como para el paciente es contar con orientación para correlacionar el trastorno con el tratamiento adecuado.

GLOBAL VWD CALL TO ACTION

Promoting **adequate care and treatment**
for people with von Willebrand Disease.

Each WFH national member organization (NMO) is invited to sign on to support VWD and other rare bleeding disorders recognition globally.

48 NMOs have already signed on!

For more information, visit: www.wfh.org/vwd

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WELCOME

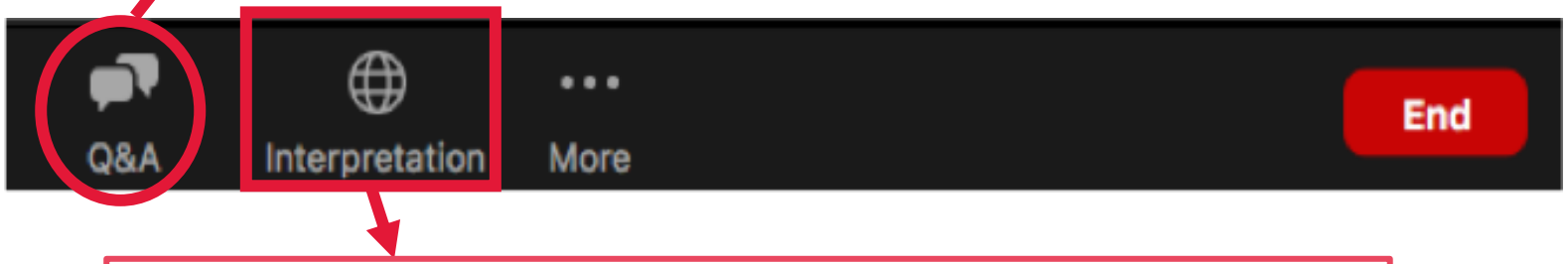
Nathan Connell, MD, MPH

Assistant Professor of Medicine, Harvard Medical School

QUESTIONS AND TRANSLATION

FOR COMPUTERS OR TABLETS

Please submit your questions in the Q&A box



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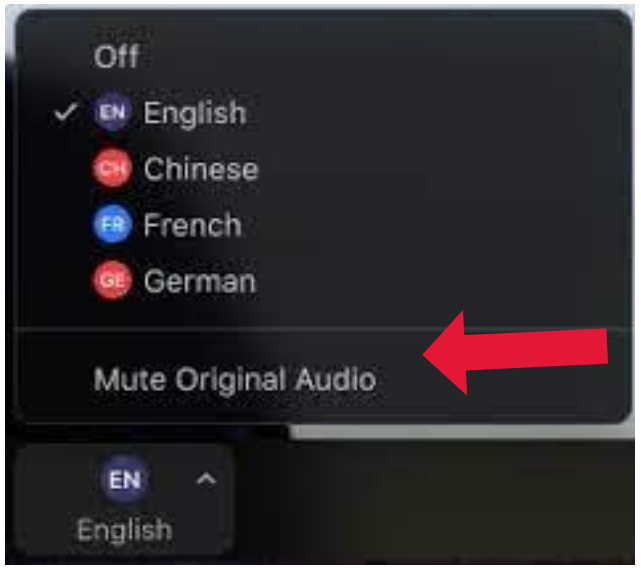

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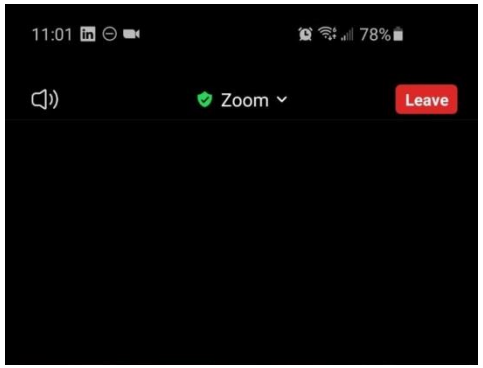
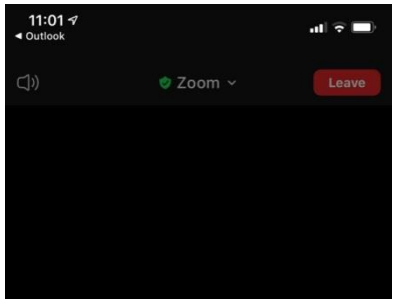
QUESTIONS AND TRANSLATION

FOR MOBILE PHONES





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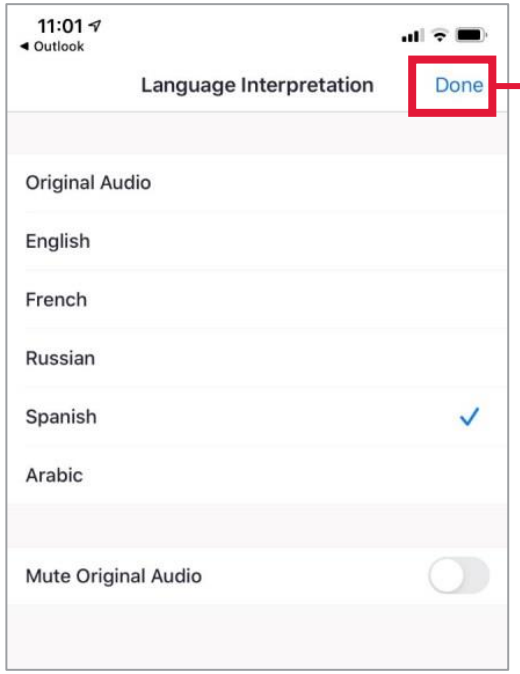

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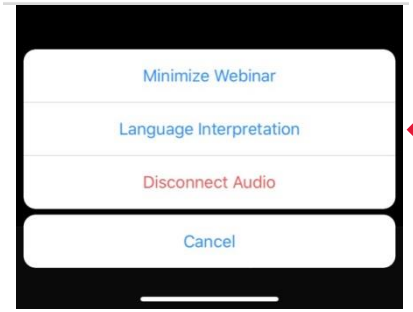

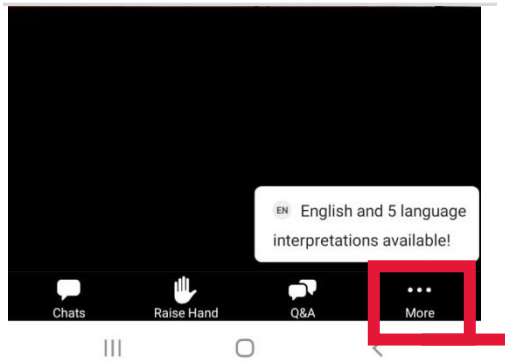

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AGENDA

1. Welcome
2. Update on Diagnosis of VWD
3. Update on Management of VWD
4. Patient Perspectives
5. Panel Discussion and Q&A

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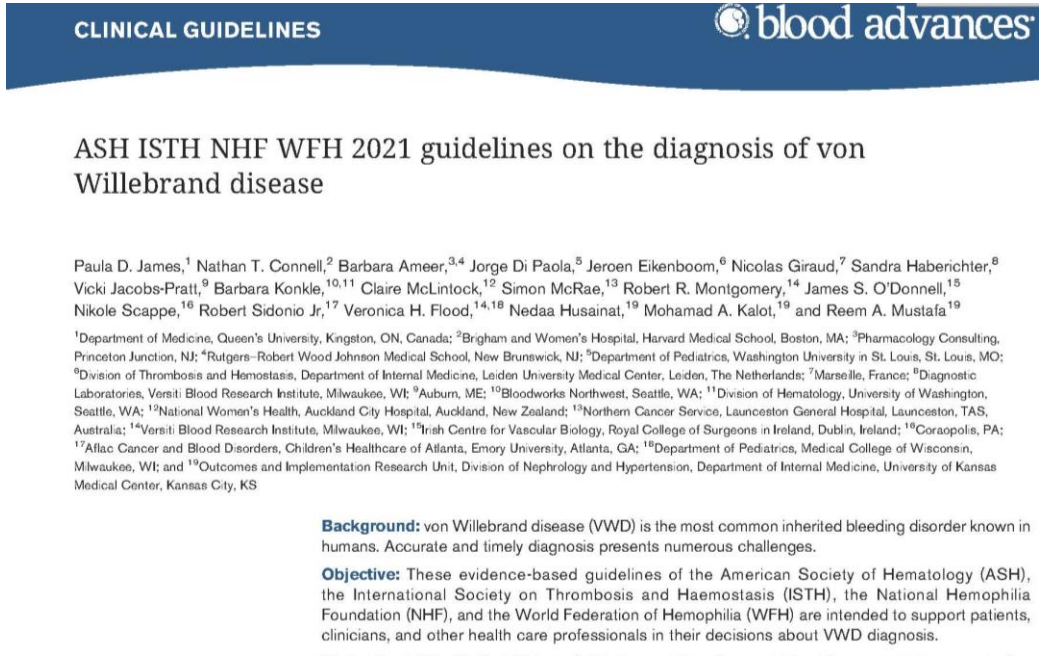

CLINICAL GUIDELINES

blood advances

ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease

Paula D. James,[1] Nathan T. Connell,[2] Barbara Ameer,[3,4] Jorge Di Paola,[5] Jeroen Eikenboom,[6] Nicolas Giraud,[7] Sandra Haberichter,[8] Vicki Jacobs-Pratt,[9] Barbara Konkle,[10,11] Claire McLintock,[12] Simon McRae,[13] Robert R. Montgomery,[14] James S. O'Donnell,[15] Nikole Scappe,[16] Robert Sidonio Jr,[17] Veronica H. Flood,[14,18] Nedaa Husainat,[19] Mohamad A. Kalot,[19] and Reem A. Mustafa[19]

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Background: von Willebrand disease (VWD) is the most common inherited bleeding disorder known in humans. Accurate and timely diagnosis presents numerous challenges.

Objective: These evidence-based guidelines of the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) are intended to support patients, clinicians, and other health care professionals in their decisions about VWD diagnosis.

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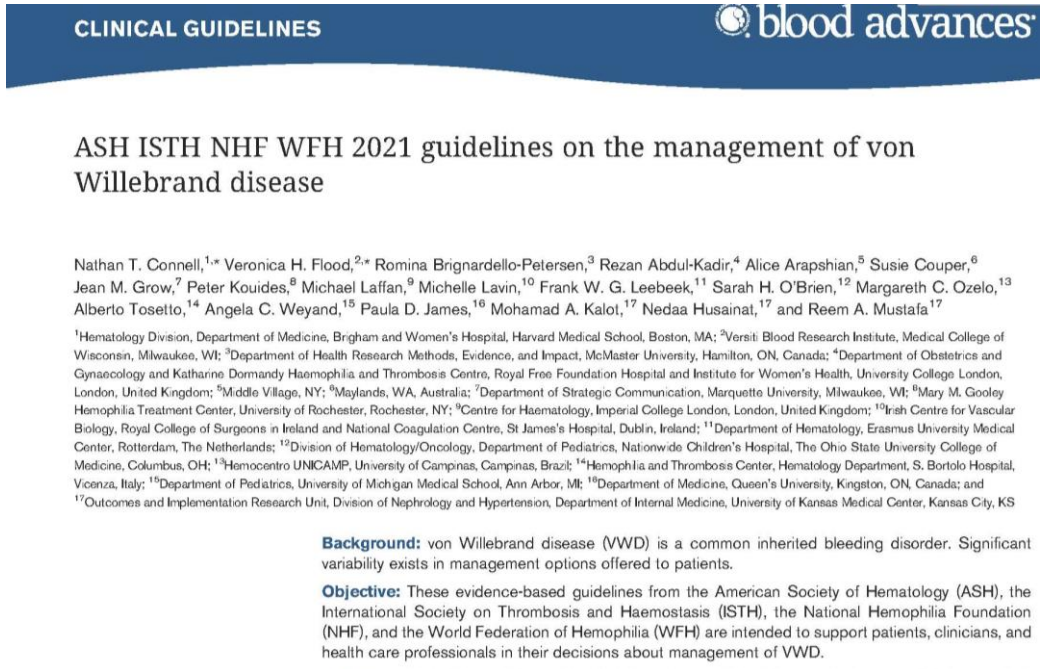

CLINICAL GUIDELINES

blood advances

ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease

Nathan T. Connell,[1,*] Veronica H. Flood,[2,*] Romina Brignardello-Petersen,[3] Rezan Abdul-Kadir,[4] Alice Arapshian,[5] Susie Couper,[6] Jean M. Grow,[7] Peter Kouides,[8] Michael Laffan,[9] Michelle Lavin,[10] Frank W. G. Leebeek,[11] Sarah H. O'Brien,[12] Margareth C. Ozelo,[13] Alberto Tosetto,[14] Angela C. Weyand,[15] Paula D. James,[16] Mohamad A. Kalot,[17] Nedaa Husainat,[17] and Reem A. Mustafa[17]

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Background: von Willebrand disease (VWD) is a common inherited bleeding disorder. Significant variability exists in management options offered to patients.

Objective: These evidence-based guidelines from the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) are intended to support patients, clinicians, and health care professionals in their decisions about management of VWD.

AMERICAN SOCIETY OF HEMATOLOGY

ISTH International Society on Thrombosis and Haemostasis

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SPEAKERS

Nathan Connell, MD, MPH
U.S.A.

Michelle Lavin, MB BCh BAO, PhD
Ireland

Nicolas Giraud
France

Baiba Ziemele
Latvia

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INTRODUCTION TO VWD

Nathan Connell, MD, MPH

Assistant Professor of Medicine, Harvard Medical School

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DISCLOSURES

No disclosures related to this talk.

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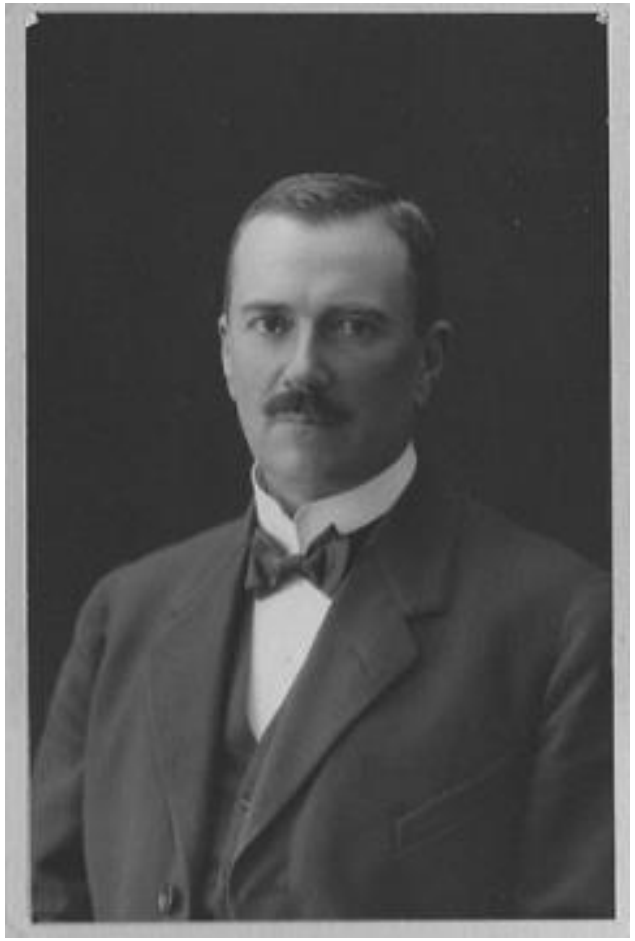
ERIK VON WILLEBRAND

Hereditär pseudohemofili



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PROF. RICHARD SIEVERS

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1926 FEBRUARI 1926

INNEHÅLL.

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ORIGINALARTIKLAR.

(Från Diakonissjukhusets i Helsingfors medicinska avdelning. Docent E. A. v. WILLEBRAND.)

Hereditär pseudohemofili.

Av

E. A. v. Willebrand.

(Med 3 figurer i texten.)

1. Sjukdomsbegrepp. Tidigare observerade fall.

I sitt nya stora arbete över de hemorragiska diatesernа framhåller E. FRANK (Breslau), att den klassiska hemofilien är en så exkvisit hereditär—familjär anomali, att det kan ifrågasättas, huruvida över huvud sporadiska fall av sjukdomen existera. Däremot är, säger han, den klassiska trombopenien så utpräglat sporadisk, att man kan diskutera, om en familjär form av densamma alls förekommer. Med trombopeni avses här den sjukdom, som sedan gammalt bär namnet morbus maculosus WERLHOFI eller purpura haemorrhagica och som på senaste tid av FRANK och en del andra forskare betecknats såsom essentiell trombopeni.

Hittills har man vetat betrakta ärftlig blodaresjukdom och hemofili såsom synonyma begrepp. Men om man genomögnar hithörande litteratur, skall man finna, om och i ett fåtal fall, beskrivningar över en familjär form av hemorragisk diates, som redan därigenom skiljer sig från äkta hemofili att den även förekommer bland kvinnor och, såsom det tycken, t. o. m. oftare än bland män. Men även i andra avseenden kan man draga en skarp gräns mellan ifrågavarande familjära lidande och hemofilien. Därom mera längre fram i kap. 6 om diagnosen.

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von Willebrand Disease

The most common inherited bleeding disorder

Affects men and women equally

Due to decreased amount, absence of, or decreased function of von Willebrand factor (VWF)

Bleeding is commonly mucocutaneous (easy bruising, gum bleeding, heavy menstrual bleeding, postpartum hemorrhage, bleeding after surgeries), but can involve joints and deep tissues

GUIDELINE DEVELOPMENT

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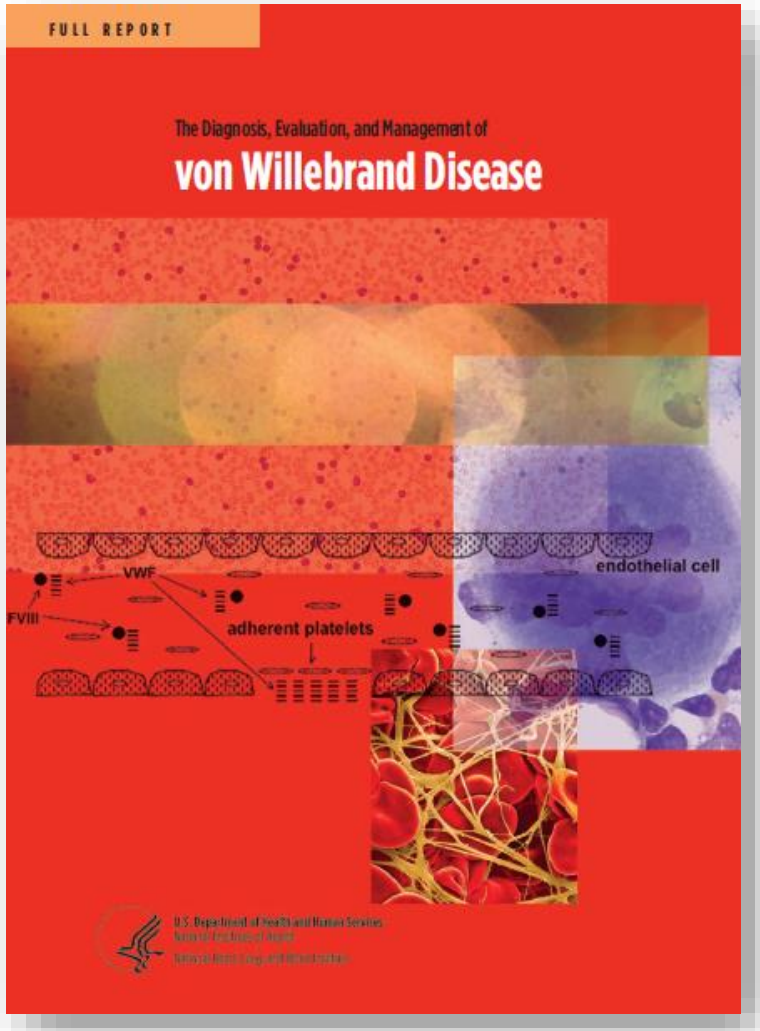
GUIDELINES FOR VWD



2007

- Expert panel convened by NHLBI in about 2004, in consultation with ASH and other stakeholders
- Literature searches ended in 2006
- Published in December 2007

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GUIDELINES FOR VWD

2015

"A well-qualified and authoritative organization, or a consortium of such organizations, should develop a new or updated evidence-based clinical practice guideline on VWD."

Report of November 2014 National Hemophilia Foundation Strategic Summit on VWD

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WHERE TO FIND THESE GUIDELINES

ASH ISTH NHF WFH 2021 Guidelines on the Diagnosis of von Willebrand Disease

James PD, Connell NT, Ameer B, et al. ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease. *Blood Adv.* 2021;5(1):280-300.

ASH ISTH NHF WFH 2021 Guidelines on the Management of von Willebrand Disease

Connell NT, Flood VH, Brignardello-Petersen R, et al. ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease. *Blood Adv.* 2021;5(1):301-325.

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VWD GUIDELINE COLLABORATION OBJECTIVES

- Facilitate clinical decision-making regarding the diagnosis and management of von Willebrand disease to contribute to ***better health outcomes, quality of life, and health equity***
- Increase ***access*** to appropriate diagnostic testing and therapeutic options
- Identify ***research priorities***
- Guide healthcare providers, patients, payers, and other stakeholders as to ***priority focus areas*** in VWD

AMERICAN SOCIETY OF HEMATOLOGY®

ISTH

NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

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KU MEDICAL CENTER
The University of Kansas

GUIDELINE DEVELOPMENT PROCESS

PANEL FORMATION

Each guideline panel was formed following these key criteria:

- Balance of expertise (including disciplines beyond hematology, and patients)
- Close attention to minimization and management of COI

CLINICAL QUESTIONS

10 to 20 **clinically-relevant questions** generated in **PICO format** (population, intervention, comparison, outcome)

Example: Clinical Question
"In a patients with VWD and history of severe and frequent bleeds, should routine prophylaxis with VWF concentrate or no routine prophylaxis be used?"

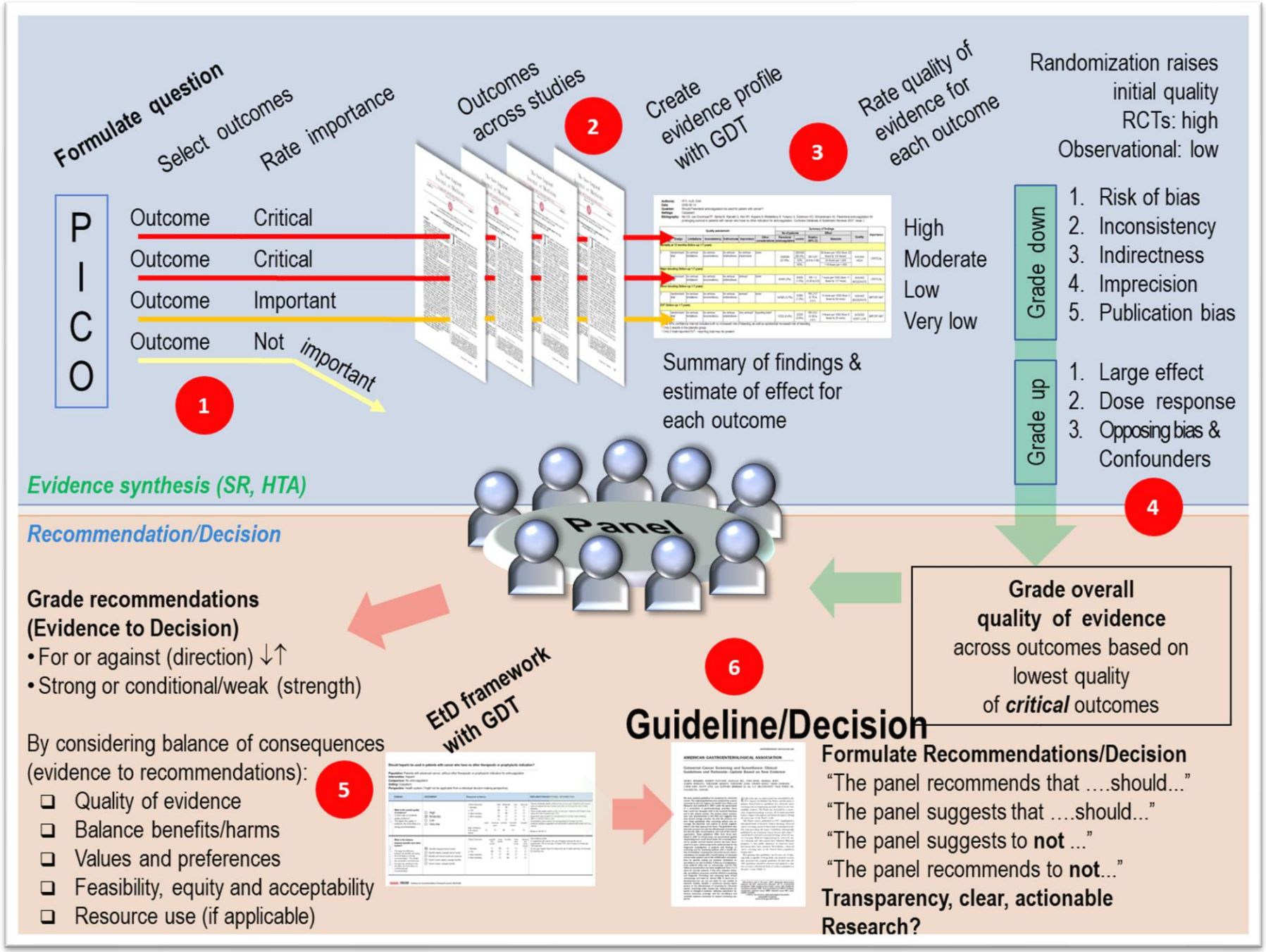
EVIDENCE SYNTHESIS

Evidence summary generated for each PICO question via systematic review of health effects plus:

- Resource use
- Feasibility
- Acceptability
- Equity
- Patient values and preferences

MAKING RECOMMENDATIONS

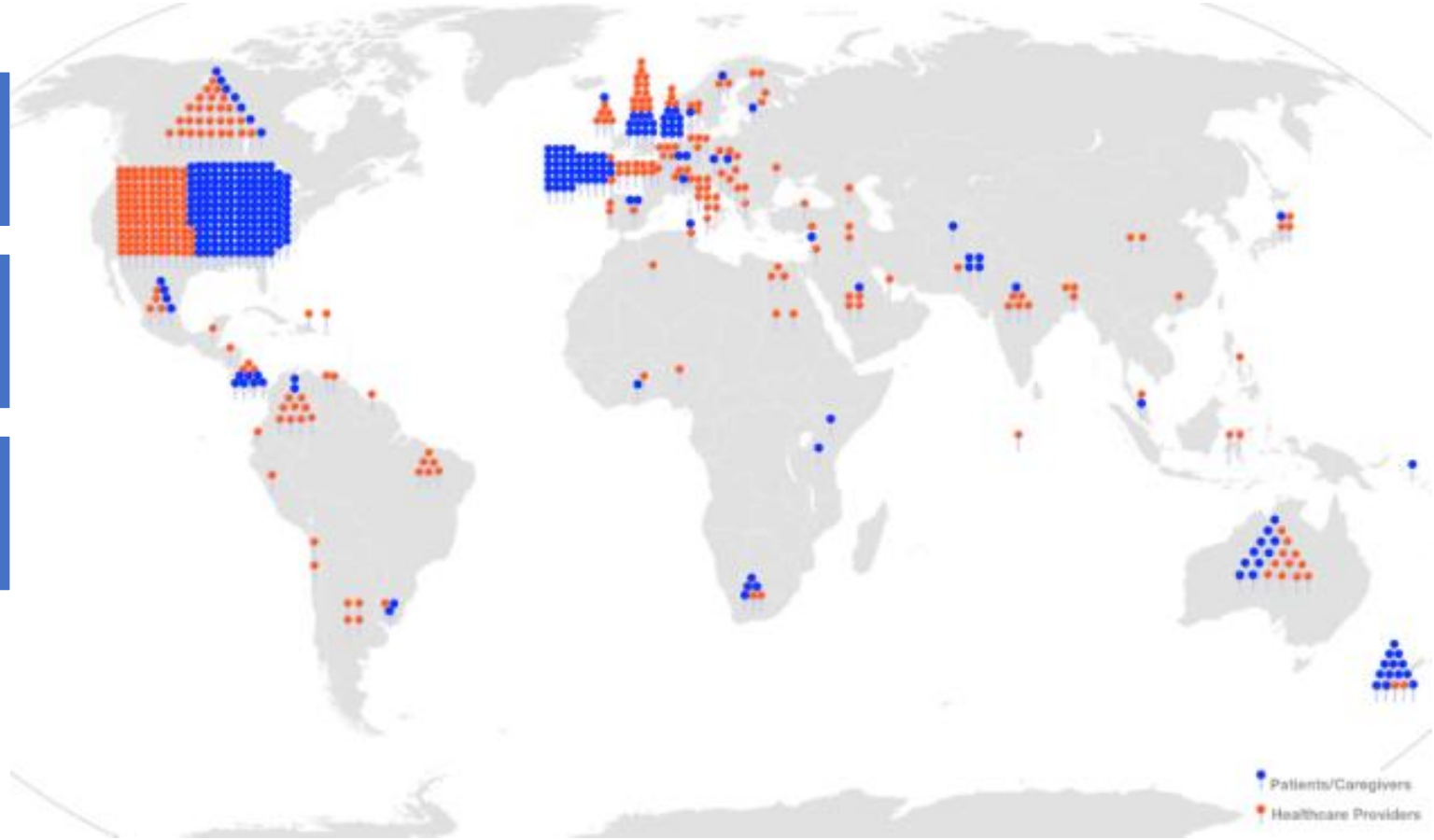
Recommendations made by guideline panel members based on evidence for all factors.



Slide Courtesy RA Mustafa

SCOPING SURVEY

71 countries	6 continents	601 participants
9,500 discrete comments	51% patients	49% healthcare providers
21% male	54% female	26% no gender identified
18% low / middle-income	82% high-income countries	

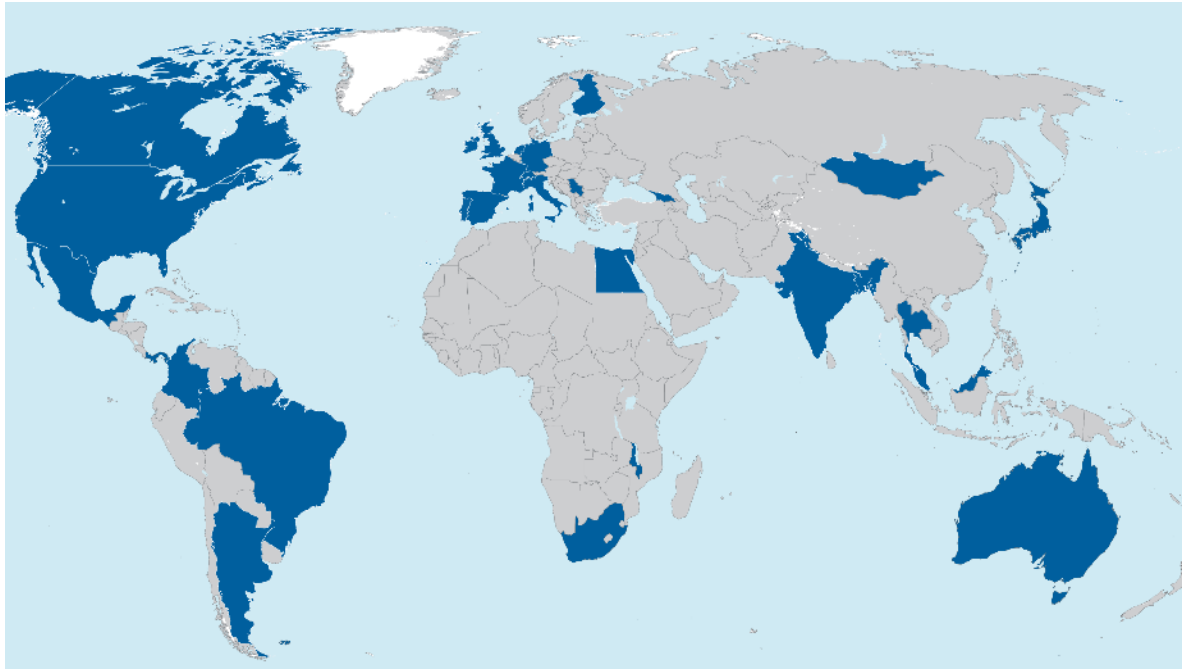


Kalot, MA, et al; An international survey to inform priorities for new guidelines on von Willebrand disease. *Haemophilia*. 2020; 26: 106– 116

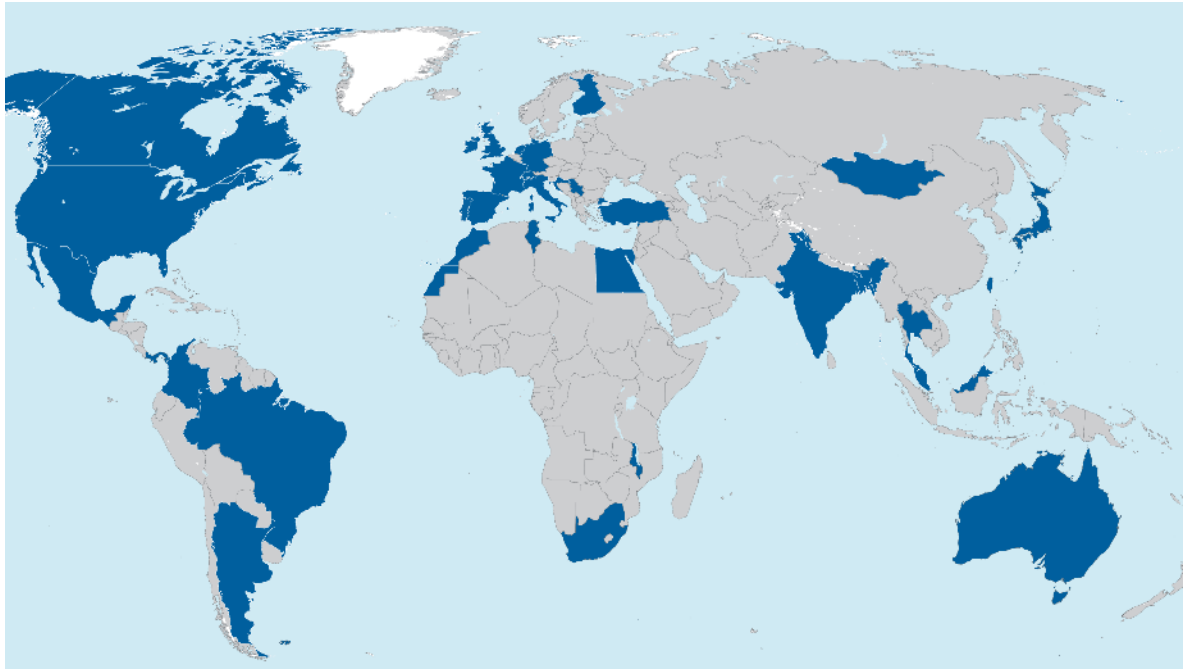
PUBLIC COMMENT RESPONSE

More than 100 people commented from 38 countries

~15% from patients!



Diagnosis



Management

How Patients and Clinicians Should Use These Recommendations

	STRONG Recommendation	CONDITIONAL Recommendation
For patients	Most individuals would want the intervention.	A majority would want the intervention, but many would not.
For clinicians	Most individuals should receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making.
For policy makers	The recommendation can be adapted as a policy in most situations	There is a need for substantial debate and involvement of stakeholders

Context

Panels took the perspective of a **high-resource setting**

- Important to understand what might be the goal of optimal care
- Advocacy efforts and policy work
- Adolopment (adaptation, adoption, *de novo* development)

Patient panelists were full voting members

VWD DIAGNOSIS PANEL

Paula D. James
Nathan T. Connell
Barbara Ameer
Jorge Di Paola
Jeroen Eikenboom
Nicolas Giraud
Sandra Haberichter
Vicki Jacobs-Pratt
Barbara Konkle
Claire McLintock
Simon McRae
Robert R. Montgomery
James S. O'Donnell
Nikole Scappe
Robert Sidonio
Veronica H. Flood
Nedaa Husainat
Mohamad A. Kalot
Reem A. Mustafa

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VWD MANAGEMENT PANEL

Nathan T. Connell
Veronica H. Flood
Romina Brignardello-Petersen
Rezan Abdul-Kadir
Alice Arapshian
Susie Couper
Jean M. Grow
Peter Kouides
Michael Laffan
Michelle Lavin
Frank W. G. Leebeek
Sarah H. O'Brien
Margareth C. Ozelo
Alberto Tosetto
Angela C. Weyand
Paula D. James
Mohamad A. Kalot
Nedaa Husainat
Reem A. Mustafa

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METHODOLOGY TEAM

- Mohamad Kalot
- Nedaa Husainat
- Omar Abughanimeh
- Yazan Aljabiri
- Alec Britt
- Osama Diab
- Ahmad Dimassi
- Abdallah El-Alayli
- Hussein El-Khechen
- Bader Madoukh
- Shahrzad Motaghi
- John Roller
- Shaneela Shahid
- Sammy Tayiem
- Hani Turkmani
- Aref Qureini
- Romina Brignardello-Petersen
- Reem A. Mustafa

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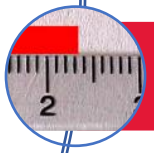
DIAGNOSIS OF VON WILLEBRAND DISEASE

Use of Bleeding Assessment Tools

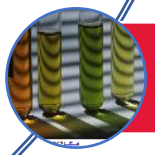
Assays of platelet-binding activity of VWF

VWF levels that normalize with age



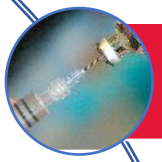
Diagnostic thresholds for type 1 VWD

Diagnosis of Type 1C VWD

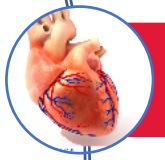


Assays and Diagnostic Thresholds for Type 2 VWD

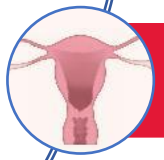
MANAGEMENT OF VON WILLEBRAND DISEASE


Prophylaxis


Desmopressin Challenge/Trial


Antithrombotic Therapy


Major and Minor Surgery


Gynecology: Heavy Menstrual Bleeding


Obstetric: Neuraxial Anesthesia and Postpartum Hemorrhage

UPDATE ON VWD DIAGNOSIS GUIDELINES

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DIAGNOSIS: DIAGNOSTIC THRESHOLDS

For patients with an abnormal initial VWD screen (low VWF:Ag and/or platelet-dependent VWF activity) suspected of type 1 VWD, should the diagnostic cutoff be at VWF:Ag and/or VWF platelet-dependent activity <0.30 IU/mL or <0.50 IU/mL?

Recommendation 6. The panel *recommends* a VWF level of <0.30 IU/mL regardless of bleeding, and for patients with abnormal bleeding, a VWF level of <0.50 IU/mL to confirm the diagnosis of type 1 VWD

Strong recommendation based on low certainty in the evidence of effects

James PD et al. Blood Adv. (2021)

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DIAGNOSIS: DIAGNOSTIC THRESHOLDS

Recommendation 6. The panel recommends a VWF level of <0.30 IU/mL regardless of bleeding, and for patients with abnormal bleeding, a VWF level of <0.50 IU/mL to confirm the diagnosis of type 1 VWD

Remarks:

- VWF level(s) refers to VWF:Ag and/or platelet-dependent VWF activity (eg, VWF:GPIbM).
- The lower limit of the normal range as determined by the local laboratory should be used if it is <0.50 IU/mL. ABO-specific reference ranges are not required.
- VWF is an acute-phase reactant that increases in response to a variety of stimuli (e.g., bleed, trauma, pregnancy). VWD diagnostic testing should be performed when patients are at a baseline state of health.

James PD et al. Blood Adv. (2021)

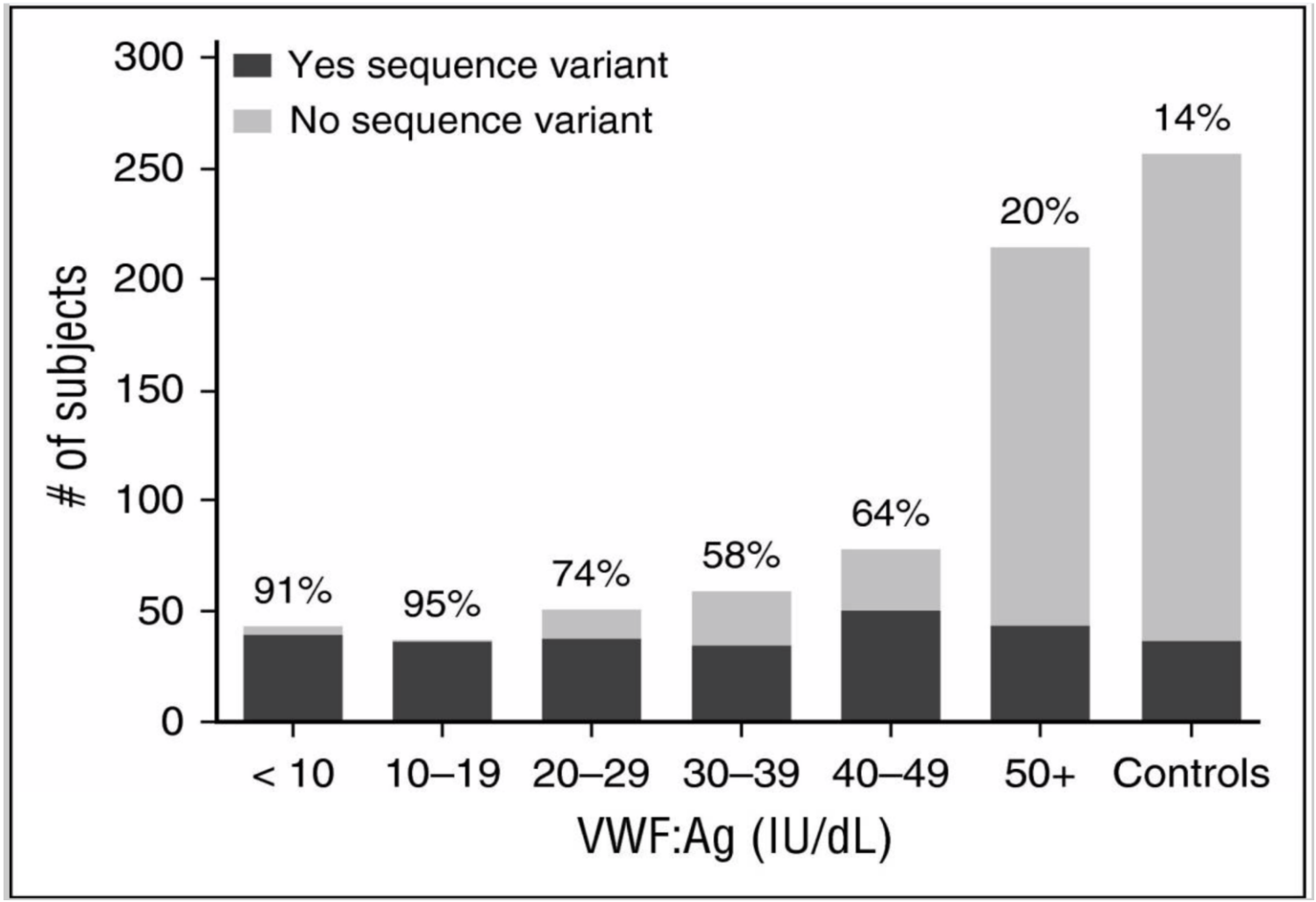
EVIDENCE TO DECISION (EtD)

Nine studies:

- 4 – mutation detection
- 2 – correlation between VWF levels and bleeding score
- 4 – likelihood ratios (2) & two odds ratios (2)
- 2 – prospective evaluation of patients (diagnostic accuracy)

James PD et al. Blood Adv. (2021)

SEQUENCE VARIANT FREQUENCY



Flood VH et al. Blood. (2016)

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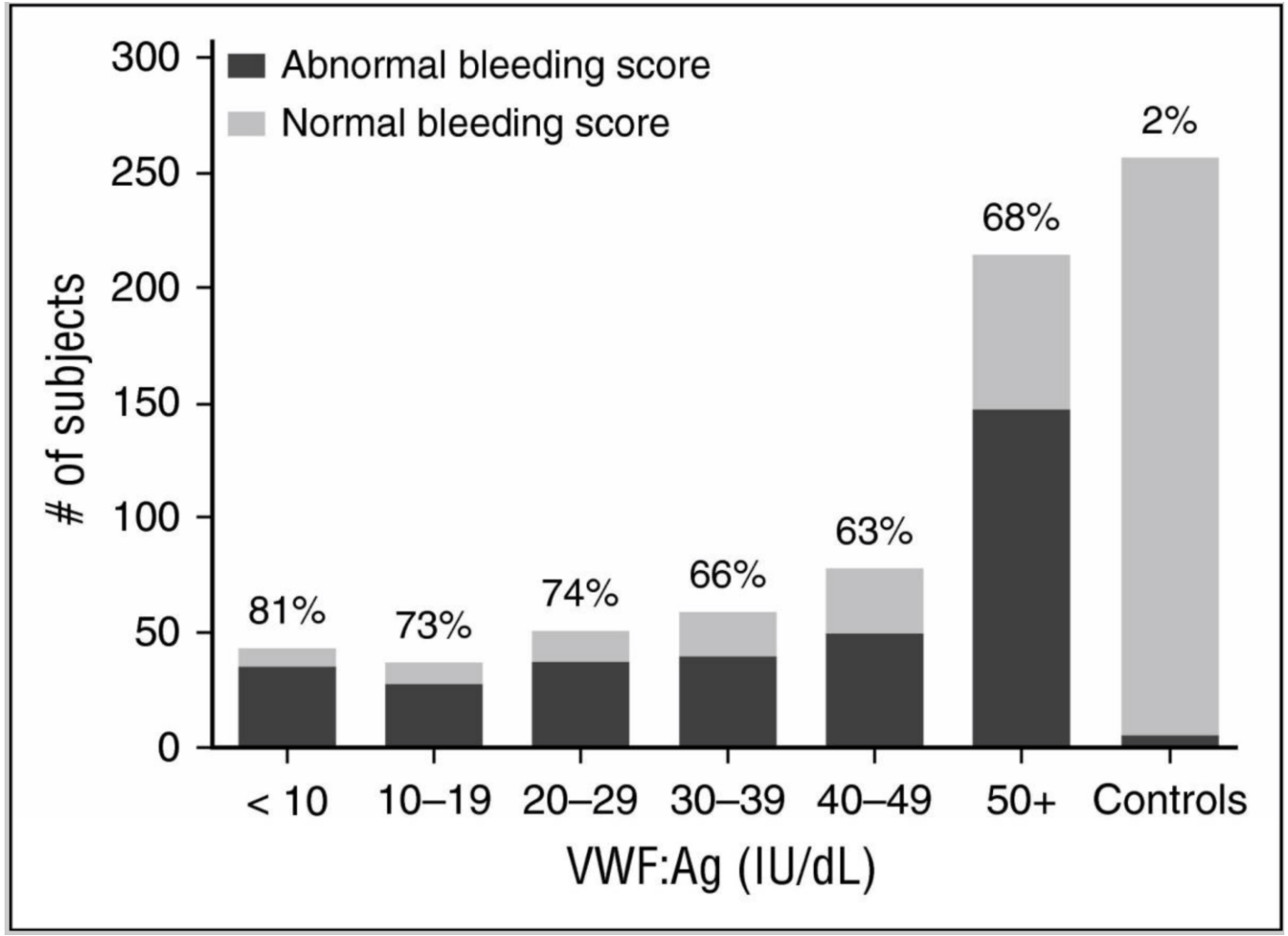
BLEEDING RATES AT VWF LEVELS



Flood VH et al. Blood. (2016)

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LIKELIHOOD RATIOS

	VWF < 20	VWF 20 - 30	VWF 30 - 40	VWF 41 - 50	VWF 51 - 60
Bucciarelli 2015			∞	**0.73**	**0.33**
	VWF < 20	**VWF 20 - 40**		**VWF 40 - 60**	
Tosetto 2007	**375**	**95**		**1.82**	

High LR
Low LR

The panel considered setting cut-off at 40

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KEY CONSIDERATIONS

- The panel is placing high value on:
  - not missing the diagnosis, especially in those patients who bleed
  - avoiding overdiagnosis in patients who do not bleed

- Despite the low certainty in the evidence, the panel decided on a strong recommendation for 2 reasons:
  - a high value was placed on an explicit diagnosis to ensure access to care for those with a bleeding phenotype, and
  - to ensure international uniformity in diagnostic criteria and the avoidance of center-specific thresholds based on a conditional recommendation

James PD et al. Blood Adv. (2021)

RESEARCH PRIORITIES

The panel identified the following research priorities:

- Detailed data for patients with VWF levels between 0.30 – 0.60 IU/mL, including:
  - Outcomes for bleeding with procedures
  - Prevalence of a concomitant bleeding disorder
- Correlation with bleeding symptoms and information about family members of patients with type 1 VWD

James PD et al. Blood Adv. (2021)

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OTHER KEY DIAGNOSTIC RECOMMENDATIONS

For patients with a low probability of VWD (e.g., seen in the primary care setting), the panel recommends using a validated bleeding-assessment tool (BAT) as an initial screening test to determine who needs specific blood testing over nonstandardized clinical assessment

Strong recommendation based on moderate certainty in the evidence from diagnostic accuracy studies ⨁⨁⨁◯

The panel suggests newer assays that measure the platelet-binding activity of VWF (eg, VWF:GPIbM, VWF:GPIbR) over the VWF ristocetin cofactor assay (VWF:RCo) (automated or nonautomated assay) for the diagnosis of VWD

Conditional recommendation based on low certainty in the evidence from diagnostic accuracy studies ⨁⨁◯◯

James PD et al. Blood Adv. (2021)

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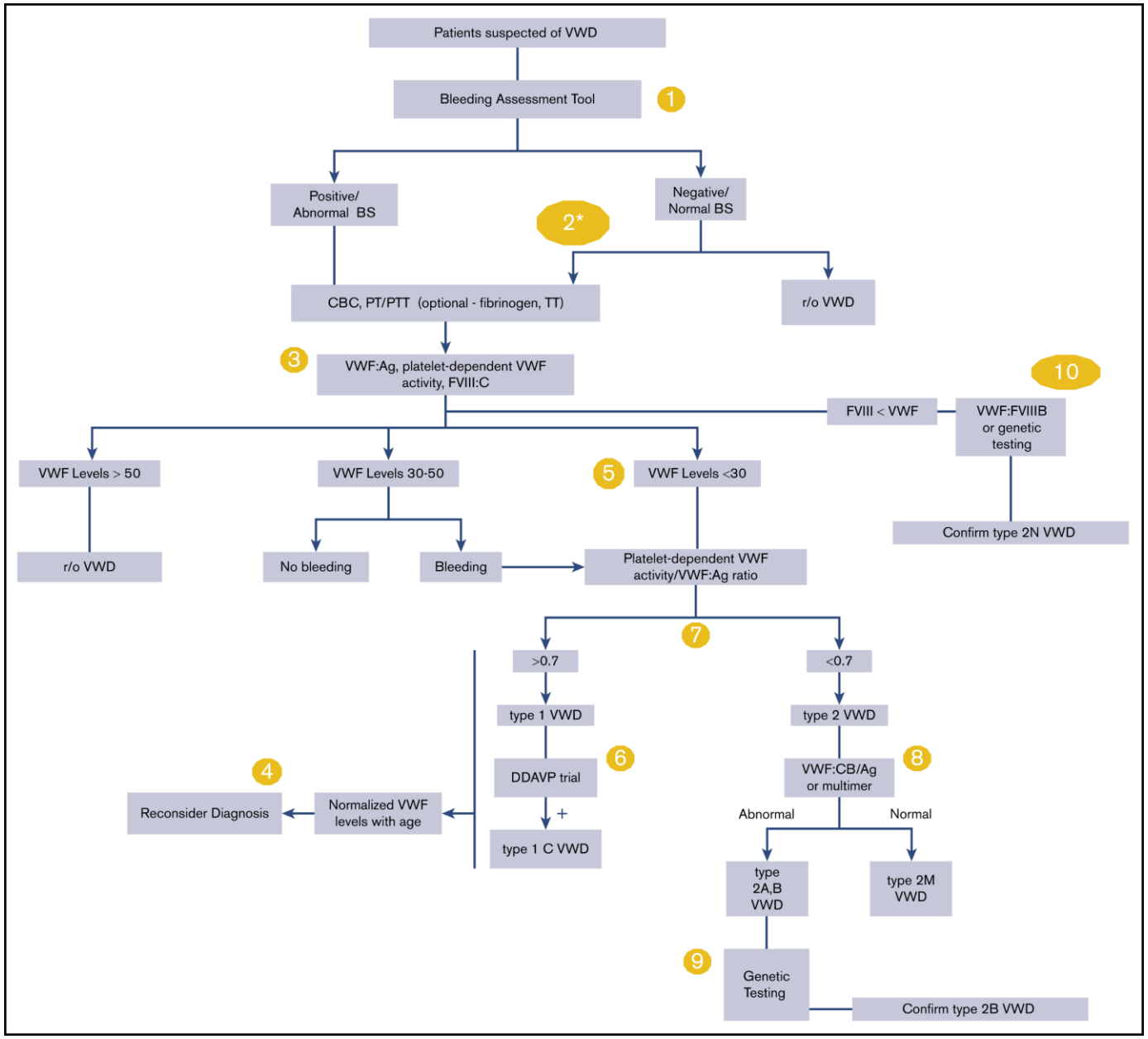
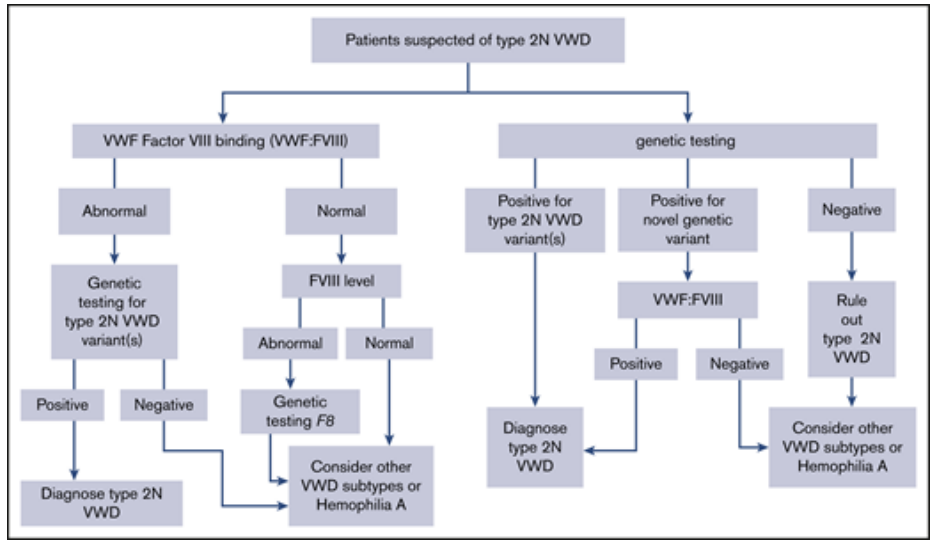
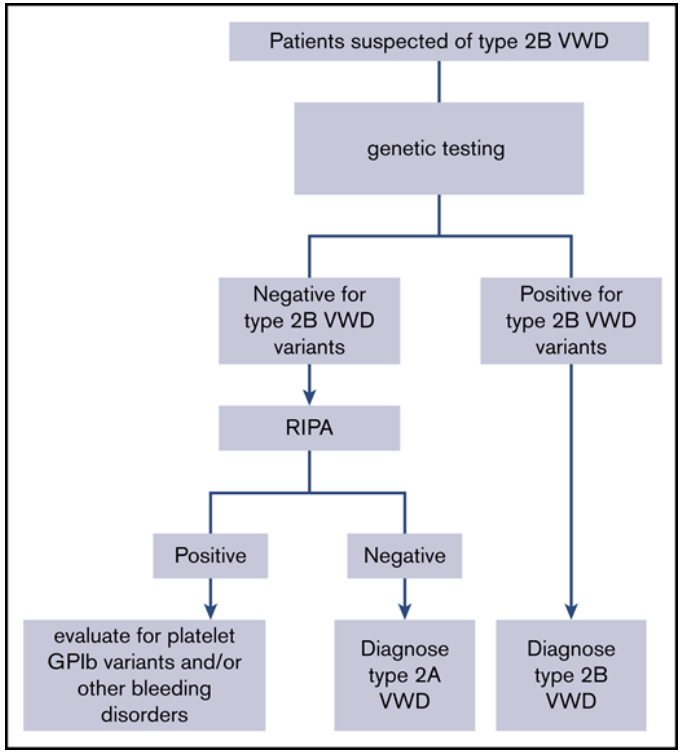


James PD et al. Blood Adv. (2021)





THANK YOU

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UPDATE ON VWD MANAGEMENT GUIDELINES

Dr. Michelle Lavin
National Coagulation Centre, St. James's Hospital, Ireland
Irish Centre of Vascular Biology, RCSI

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DISCLOSURES

Conflict	Disclosure - if conflict of interest exists
Research Support	
Director, Officer, Employee	
Shareholder	
Honoraria	Indirect funding for educational support programs from Takeda
Advisory Committee	Tremeau Pharmaceuticals
Consultant	Sobi

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Management of VWD

General bleeding

Surgery

HMB & pregnancy

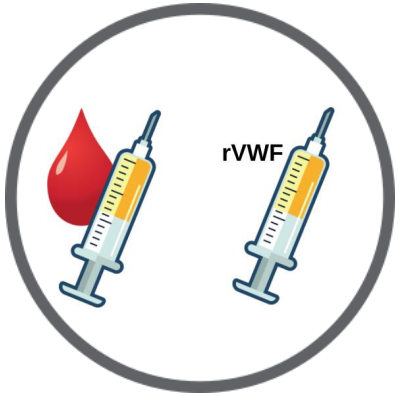
Aging

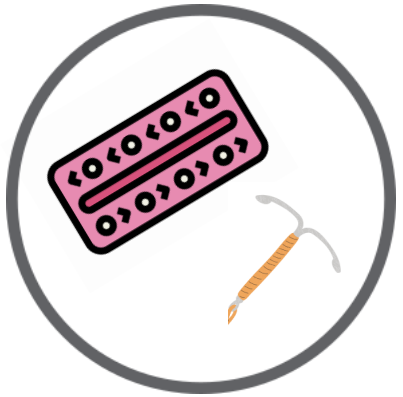
TREATMENT OPTIONS FOR VWD

TRANEXAMIC ACID

DESMOPRESSIN (DDAVP)

VWF REPLACEMENT THERAPY





IRON & HORMONAL THERAPIES

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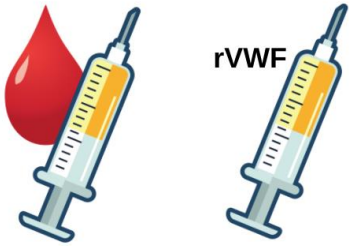
PROPHYLAXIS USE IN VWD



What is the role for prophylaxis in VWD?

- In patients with VWD with a history of severe and frequent bleeds, the guideline panel *suggests* using long-term prophylaxis rather than no prophylaxis.

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

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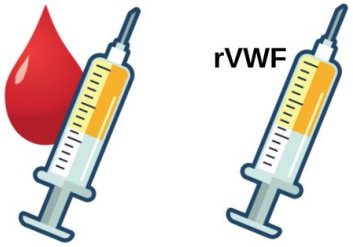
PROPHYLAXIS USE IN VWD



What is the role for prophylaxis in VWD?

- In patients with VWD with a history of severe and frequent bleeds, the guideline panel *suggests* using long-term prophylaxis rather than no prophylaxis.

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

- **More support for physicians and patients to access prophylaxis in VWD.**

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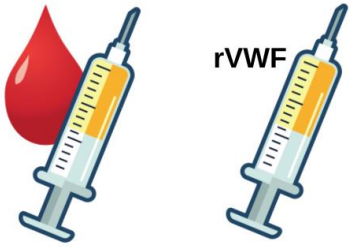
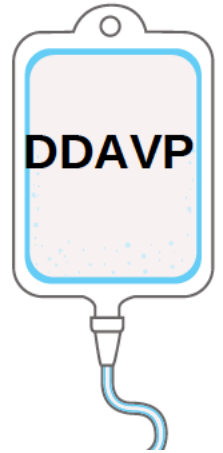
WHAT IS THE EVIDENCE?



- 1 randomized trial comparing prophylaxis with placebo.
- 5 studies with an explicit comparison between pre- and post-prophylaxis.
- 8 with an implicit comparison between pre- and post-prophylaxis.

https://guidelines.ash.gradepro.org/profile/JLMHIOqdI3E

DDAVP TRIAL



Who needs a DDAVP trial?

- In type 1 VWD patients with baseline VWF level of **<30 IU/dL**
- *Suggests* **performing a trial of desmopressin** and treating based on the results

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DDAVP TRIAL

Who needs a DDAVP trial?

- In type 1 VWD patients with baseline VWF level of 30 – 50 IU/dL

Can be presumed to be desmopressin responsive

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USE OF DDAVP IN VWD

VWD Subtype

TYPE 1		TYPE 2				TYPE 3
30-50 IU/dL	<30 IU/dL	2A	2M	2N	2B	
Adults will respond Children still need trial	Trial for all to assess response	May have a partial or shorter lived response			Avoid, may worsen low platelets	Will not respond
First line therapy if no contraindication	First line if responder + no contraindication to use	May be helpful for minor bleeding				

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THERAPEUTIC TARGETS

For minor surgery

	Post-op target	
	FVIII	**VWF:RCo**
Nichols et al. 2008	>30, preferable >50 for 3-5d	
Castaman et al. 2013	>30 for 2-4d	
Laffan et al. 2014	Not specified	
Windyga et al. 2016	>50 for 3-5d	>30 for 3-5d

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THERAPEUTIC TARGETS

For major surgery

	Post-op target	
	FVIII	**VWF:RCo**
Nichols et al. 2008	>50 for 7-10 days	
Castaman et al. 2013	80-100 for 36h then >50 for 5-10 days	
Laffan et al. 2014	>50	-
Windyga et al. 2016	D0 >80-100 D1-7 >50 D8-14 >30	D0>50 D1-14 >30

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SURGERY MANAGEMENT

How best to monitor surgery in people with VWD?

- Both FVIII and VWF activity levels of ≥0.50 IU/mL for at least 3 days after surgery.

- Minor procedures, the panel *suggests* increasing VWF activity levels to ≥0.50 IU/mL with desmopressin or factor concentrate **with the addition of tranexamic acid.**

- **Change from just FVIII alone, emphasis on TXA.**

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SURGERY MANAGEMENT

- The panel *suggests* **giving tranexamic acid alone** over increasing VWF activity levels to ≥0.50 IU/mL if
  - Type 1 VWD with baseline VWF activity levels of >0.30 IU/mL
  - **Mild bleeding phenotype**
  - **Minor mucosal procedures**

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SURGERY MANAGEMENT

- For patients at higher risk of thrombosis, it may be desirable to avoid the combination of extended increased VWF and FVIII levels (>1.50 IU/mL) and extended use of tranexamic acid.

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HEAVY MENSTRUAL BLEEDING

Planning to conceive?

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HEAVY MENSTRUAL BLEEDING

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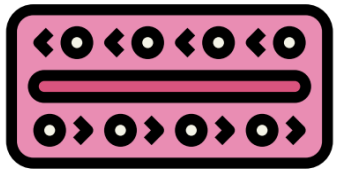

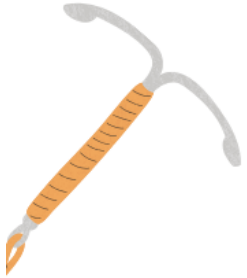

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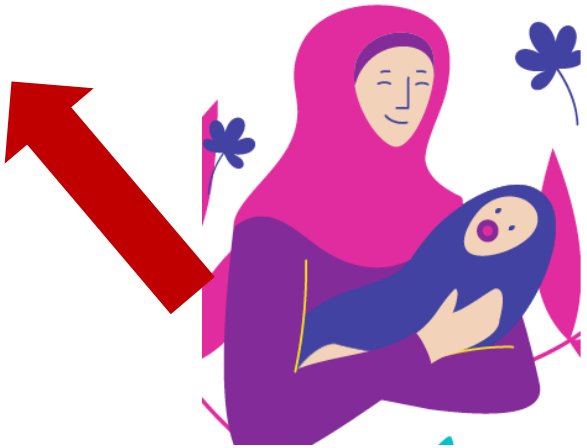

Planning to conceive?

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HEAVY MENSTRUAL BLEEDING

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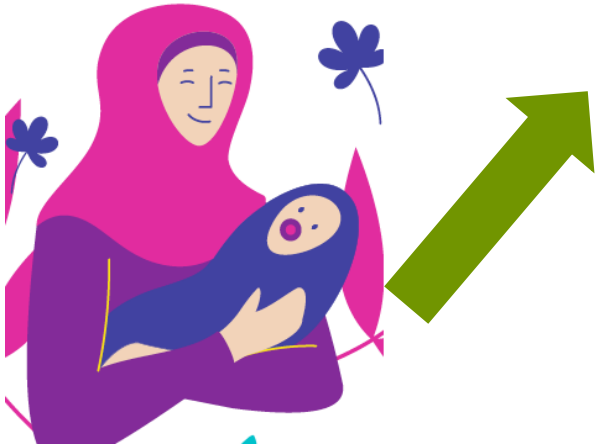

Planning to conceive?

over

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HEAVY MENSTRUAL BLEEDING

How to best manage HMB?

- The panel *suggests* using either hormonal therapy (combined hormonal contraception [CHC] or levonorgestrel-releasing intrauterine system) or tranexamic acid over desmopressin to treat women with VWD with heavy menstrual bleeding who do not wish to conceive.

- The panel *suggests* using tranexamic acid over desmopressin to treat women with VWD and heavy menstrual bleeding who wish to conceive.

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HEAVY MENSTRUAL BLEEDING

How to best manage HMB?

- Don’t forget possible role for prophylaxis!

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Management of VWD

General bleeding

Surgery

HMB & pregnancy

Aging

EPIDURAL ANAESTHESIA

What about spinal anaesthesia?

- In women with VWD for whom neuraxial anesthesia during labor is deemed suitable, the panel *suggests* targeting a VWF activity level of 0.50 to 1.50 IU/mL over targeting an activity level of >1.50 IU/mL to allow neuraxial anesthesia.

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TRANEXAMIC ACID AFTER DELIVERY

How to prevent Postpartum bleeding?

- The guideline panel *suggests* the use of tranexamic acid over not using it in women with type 1 VWD or low VWF levels (and this may also apply to types 2 and 3 VWD) during the postpartum period).

- (conditional recommendation based on low certainty in the evidence of effects ⨁⨁◯◯).

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Management of VWD

General bleeding

Surgery

HMB & pregnancy

Aging

AGING

Can you outgrow VWD? (diagnosis guideline)

- 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.

- Aging and comorbidities are known to increase VWF levels. However, the association between the increased VWF levels and bleeding symptoms is not established.

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AGING

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- Aging and comorbidities are known to increase VWF levels. However, the association between the increased VWF levels and bleeding symptoms is not established.

- **Uncertain if bleeding in older adults abates with increased levels**

Antiplatelets or anticoagulation use

If someone has heart disease and needs anti-platelets/Aspirin, what is the advice?

- 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.

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

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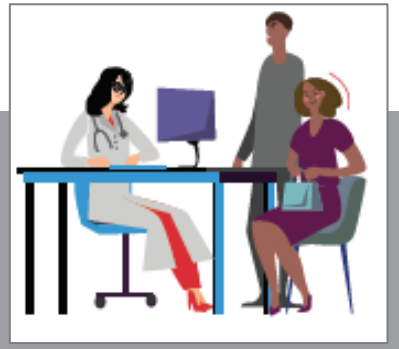
GOOD PRACTICE STATEMENTS

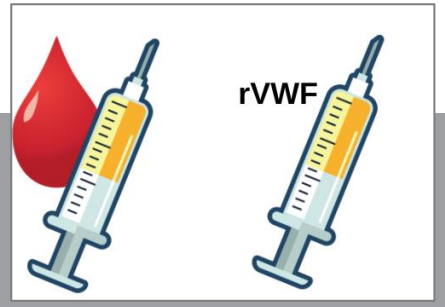
Multidisciplinary team input prior with the patient



Patient education

Risks/benefits

Informed, shared decision making



? Prophylaxis

DDAVP not suitable

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How do these guidelines change practice for people with VWD?

- New diagnostic thresholds, type 1 and type 2
- No DDAVP trials for “Low VWF” patients
- Clarifies post-op monitoring
- Support for prophylaxis
- Cardiovascular disease – individualized approach for antiplt use
- Postpartum TXA

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LIMITATIONS OF GUIDELINES

- Trying to cover 7 subtypes of VWD in 10 management and diagnostic questions
- Hugely limited by lack of research
- No strong recommendations

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BENEFITS

- People with VWD, basic scientists, clinicians, research methodologists
- Identified gaps in research and understanding
- Can help people with VWD where access to care determined by payers
- Independent of pharma involvement; CoI clearly stated
- Multiple organisations, differing interest, similar goals

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Where to find these guidelines:

ASH ISTH NHF WFH 2021 Guidelines on the Diagnosis of von Willebrand Disease

Paula D. James, Nathan T. Connell, Barbara Ameer, Jorge Di Paola, Jeroen Elkenboom, Nicolas Giraud, Sandra Haberichter, Vicki Jacobs-Pratt, Barbara Konkle, Claire McKlintock, Simon McRae, Robert Montgomery, James S. O'Donnell, Nikole Scappe, Robert Sidonio, Jr., Veronica H. Flood, Nedaa Husainat, Mohamad A. Kalot, and Reem A. Mustafa

James PD, Connell NT, Ameer B, et al. ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease. *Blood Adv.* 2021;5(1):280-300.

ASH ISTH NHF WFH 2021 Guidelines on the Management of von Willebrand Disease

Nathan T. Connell, Veronica H. Flood, Romina Brignardello-Petersen, Rezan Abdul-Kadir, Alice Arapshian, Susie Cooper, Jean M. Grow, Peter Kouides, Michael Laffan, Michelle Lavin, Frank W. G. Leebeek, Sarah H. O'Brien, Margareth C. Ozelo, Alberto Tosetto, Angela C. Weyand, Paula D. James, Mohamad Kalot, Nedaa Husainat, and Reem A. Mustafa

Connell NT, Flood VH, Brignardello-Petersen R, et al. ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease. *Blood Adv.* 2021;5(1):301-325.

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PATIENT PERSPECTIVES

Nicolas Giraud

President of the French Hemophilia Society

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Is this an innovative process to include the voice of the patients?

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Is this an innovative process to include the voice of the patients?

Are the VWD guidelines long overdue?

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Is this an innovative process to include the voice of the patients?

Are the VWD guidelines long overdue?

Can these guidelines be applicable everywhere in the world?

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THE NEW VWD GUIDELINES: SO WHAT?

Baiba Ziemele
WFH Board member
President of the Latvia Hemophilia Society

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BATs

Evaluation of symptoms irrespective of VWF levels

EVIDENCE

Extensive analysis of published literature and experience to support recommendations and unmet needs

DEFINITIONS

Clear description of types and how to diagnose them

TIPS

What is what?

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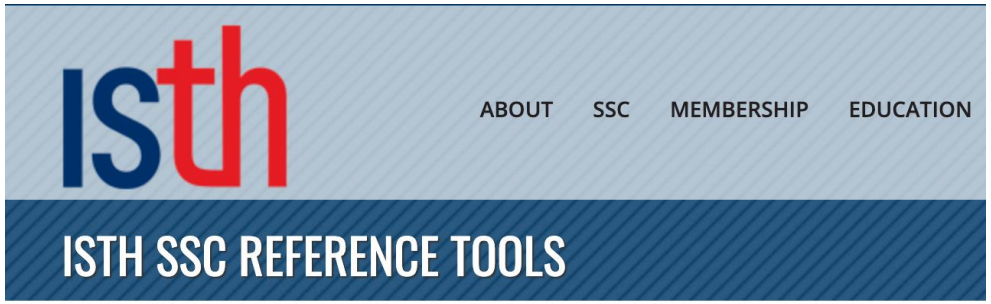
BLEEDING ASSESMMENT TOOLS

The increased value of phenotype over just factor levels to provide adequate treatment

Scoring Key

Symptom	Score -1	0	1	2	3	4
Epistaxis	--	No or trivial (less than 5)	> 5 or more than 10'	Consultation only	Packing or cauterization or antifibrinolytic	Blood transfusion or replacement therapy or desmopressin
Cutaneous	--	No or trivial (< 1cm)	> 1 cm and no trauma	Consultation only	--	--
Bleeding from minor wounds	--	No or trivial (less than 5)	> 5 or more than 5'	Consultation only	Surgical hemostasis	Blood transfusion or replacement therapy or desmopressin
Oral cavity	--	No	Referred at least one	Consultation only	Surgical hemostasis or antifibrinolytic	Blood transfusion or replacement therapy or desmopressin
Gastrointestinal bleeding	--	No	Associated with ulcer, portal hypertension, hemorrhoids, angiodysplasia	Spontaneous	Surgical hemostasis, blood transfusion, replacement therapy, desmopressin, antifibrinolytic	--
Tooth extraction	No bleeding in at least 2 extractions	None done or no bleeding in 1 extraction	Reported, no consultation	Consultation only	Resuturing or packing	Blood transfusion or replacement therapy or desmopressin
Surgery	No bleeding in at least 2 surgeries	None done or no bleeding in 1 surgery	Reported, no consultation	Consultation only	Surgical hemostasis or antifibrinolytic	Blood transfusion or replacement therapy or desmopressin
Menorrhagia	--	No	Consultation only	Antifibrinolytics, pill use	Dilation & curettage, iron therapy, ablation	Blood transfusion or replacement therapy or desmopressin or hysterectomy Hysterectomy
Postpartum hemorrhage	No bleeding in at least 2 deliveries	None done or no bleeding in 1 surgery	Consultation only	Dilation & curettage, iron therapy, antifibrinolytics	Blood transfusion or replacement therapy or desmopressin	
Muscle hematomas	--	Never	Post trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring desmopressin or replacement therapy	Spontaneous or traumatic, requiring surgical intervention or blood transfusion
Hemarthrosis	--	Never	Post trauma, no therapy	Spontaneous, no therapy	Spontaneous or traumatic, requiring desmopressin or replacement therapy	Spontaneous or traumatic, requiring surgical intervention or blood transfusion
Central nervous system bleeding	--	Never	--	--	Subdural, any intervention	Intracerebral, any intervention



Share |

The below resources were developed by the SSC Subcommittees as reference tools:

- ISTH-SSC Bleeding Assessment Tool
  (BAT translated in additional languages see here under "supporting information")
- Scoring system for Disseminated Intravascular Coagulation (DIC)
- Bleeding Score and Questionnaire for Type 1 Von Willebrand Disease

https://elearning.wfh.org/resource/compendium-of-assessment-tools/#bleeding_assessment_tools1a42-60ce78a1-2573f205-9a34

https://www.isth.org/page/reference_tools

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CLEAR DEFINITIONS

- Less confusion between low VWF and VWD
- Clear descriptions of types and diagnostic pathway

NORMAL VWF LEVELS		
LOW VWF LEVEL 30-50%		
VWD TYPE 1	VWD TYPE 2	VWD TYPE 3
1, 1C	2A, 2B, 2N, 2M	3

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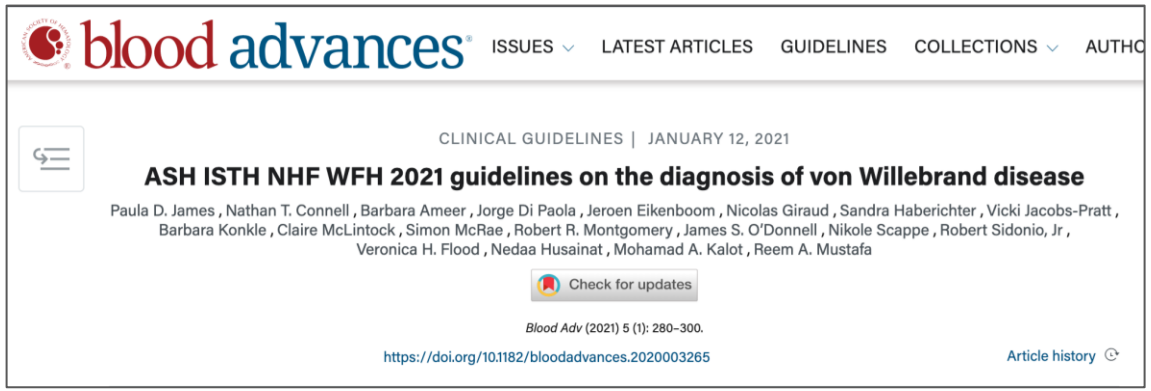
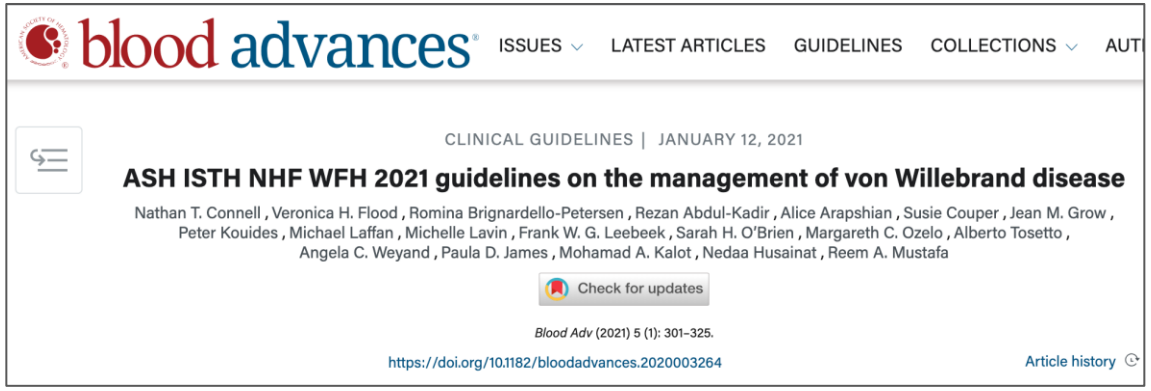
ADVOCACY WORK FOR NMOs

Condensed review of all published evidence in short and clear recommendations allow patients and patient advocates to support their requests to HCPs and governments





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TIPS

The most practical part of recommendations: obvious and well known for some, raised questions and misunderstandings in others

Frequent bleeds were defined as

- **≥5 bleeding episodes in the last 12 months**, or
- **≥3 episodes of hemarthrosis at the same joint** or
- **≥2 episodes of gastrointestinal hemorrhage** either unexplained or in association with underlying gastrointestinal angiodysplasia with requirement of [VWF concentrate] therapy.

Major surgery was considered to include:

- procedures requiring surgical opening into the large body cavities,
- procedures where severe hemorrhage was possible,
- interventions involving joints,
- third-molar extractions, and
- interventions where the patient's life was at risk.

Minor surgery was considered to include:

- procedures involving simple dental extractions and
- other outpatient procedures not otherwise specified under major surgery.

https://ashpublications.org/bloodadvances/article/5/1/301/474884

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www.wfh.org/VWDGuidelines

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توصيات دليل ASH ISTH NHF WFH بشأن تشخيص داء فون فليبراند (VWD)

محتوى الدليل

- يعرض هذا الدليل توجيهات مبنية على أدلة تهدف إلى تحسين دقة تشخيص داء فون فليبراند (VWD)، والحدّ من الاختبارات غير الملائمة، وتجنّب الأضرار الناجمة عن المبالغة في تشخيص المرض.

أهمية الدليل

- يُعدّ داء فون فليبراند أكثر اضطرابات نزف الدم الوراثي شيوعًا، لكنّ تشخيصه على نحو دقيق وفي الوقت المناسب لا يزال يمثل تحديًا.
- تشمل العوائق التي تحول دون إجراء تشخيص دقيق لهذا الداء حاليًا ما يلي:
  - محدودية أو انعدام الاختبارات المعملية المتخصصة والخبرات اللازمة لإجرائها.
  - عدم فهم الاختلافات بين أعراض نزف الدم الطبيعي وغير الطبيعي.
- من المُهمّ تحسين دقة تشخيص المرض لضمان حصول المرضى على الرعاية المناسبة والحدّ من الاختبارات غير الملائمة والأضرار الناجمة عن المبالغة في تشخيص المرض.

ISTH International Society on Thrombosis and Haemostasis | NATIONAL HEMOPHILIA FOUNDATION for all bleeding disorders | FMH FEDERACIÓN MUNDIAL DE HEMOFILIA / FÉDÉRATION MONDIALE DE L'HÉMOPHILIE / WORLD FEDERATION OF HEMOPHILIA

Recomendaciones de las guías de ASH, ISTH, NHF, FMH para el tratamiento de la enfermedad de Von Willebrand (EVW)

Qué abarcan

- Recomendaciones basadas en pruebas científicas para el tratamiento de la EVW en el contexto de cirugías mayores y menores, pruebas durante procedimientos invasivos, uso de desmopresina, y uso profiláctico de concentrado de factor Von Willebrand (FVW).

Por qué son importantes

- La EVW es el trastorno de la coagulación hereditario más común.
- Actualmente hay una gran variabilidad en la práctica clínica aplicada al tratamiento de la EVW debido a la falta de pruebas científicas de certeza elevada para orientar la toma de decisiones.
- Hay múltiples subtipos de la EVW que requieren tratamiento individualizado con base en el diagnóstico específico, así como una gama de síntomas y múltiples terapias disponibles para su tratamiento. Lo más conveniente tanto para el médico como para el paciente es contar con orientación para correlacionar el trastorno con el tratamiento adecuado.

GLOBAL VWD CALL TO ACTION

Promoting **adequate care and treatment**
for people with von Willebrand Disease.

Each WFH national member organization (NMO) is invited to sign on to support VWD and other rare bleeding disorders recognition globally.

48 NMOs have already signed on!

For more information, visit: www.wfh.org/vwd

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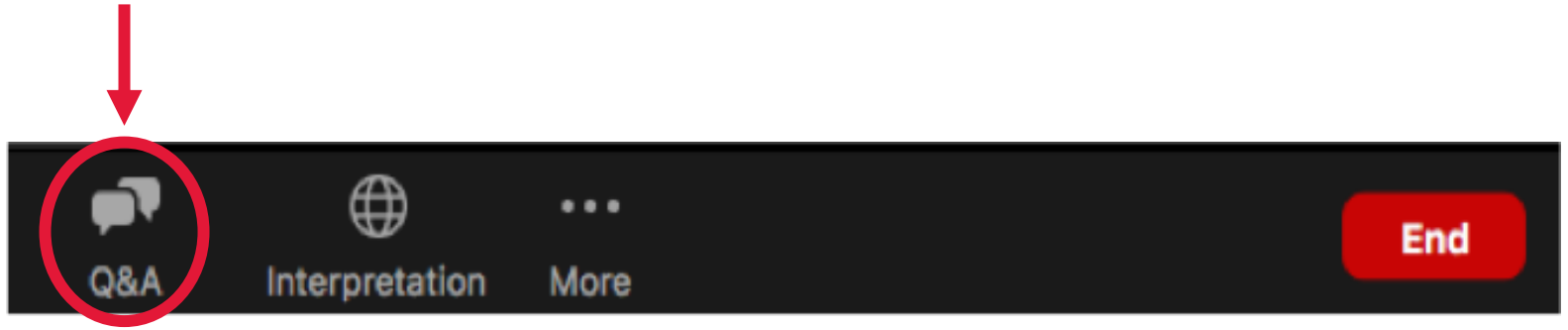
QUESTION & ANSWER

Please submit your questions in the Q&A box



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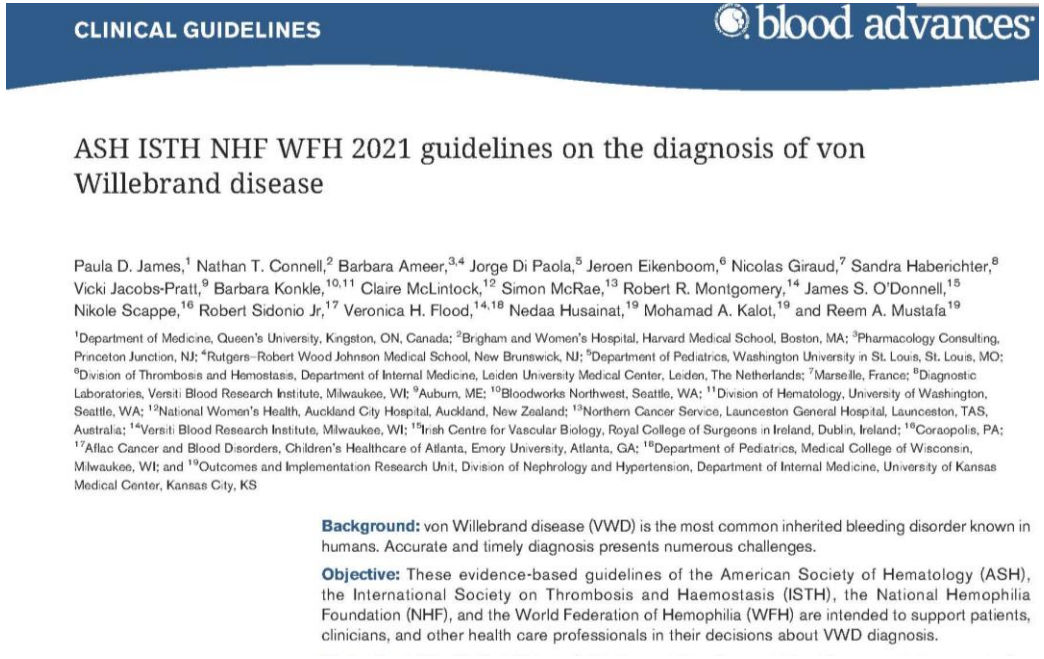
ASH ISTH NHF WFH 2021 Guidelines on the Diagnosis and Management of VWD



CLINICAL GUIDELINES

blood advances

ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease

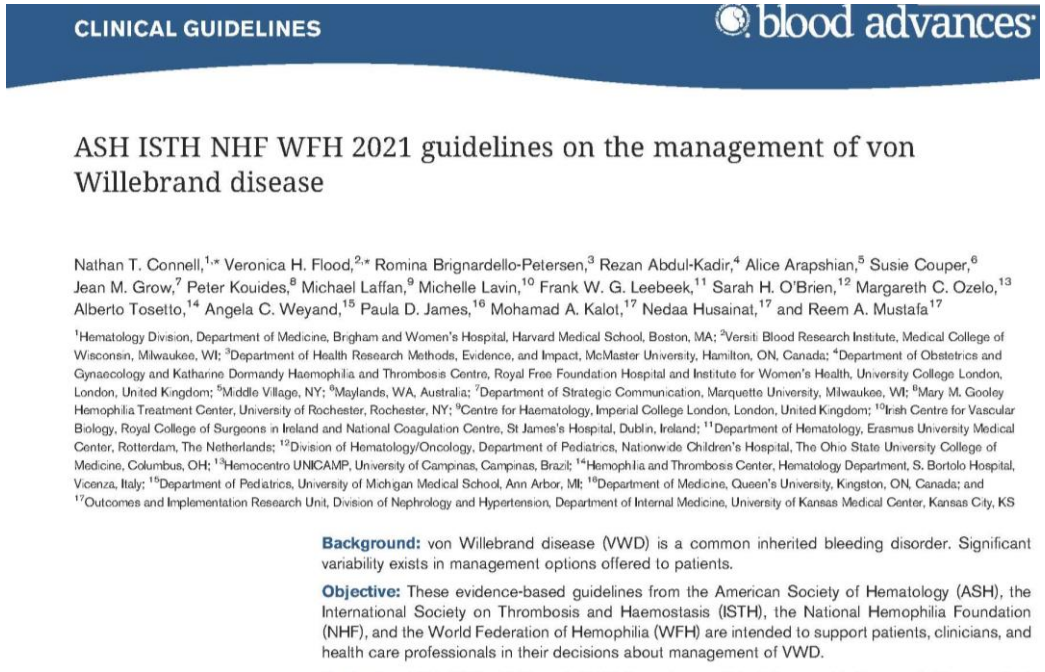
Paula D. James,[1] Nathan T. Connell,[2] Barbara Ameer,[3,4] Jorge Di Paola,[5] Jeroen Eikenboom,[6] Nicolas Giraud,[7] Sandra Haberichter,[8] Vicki Jacobs-Pratt,[9] Barbara Konkle,[10,11] Claire McLintock,[12] Simon McRae,[13] Robert R. Montgomery,[14] James S. O'Donnell,[15] Nikole Scappe,[16] Robert Sidonio Jr,[17] Veronica H. Flood,[14,18] Nedaa Husainat,[19] Mohamad A. Kalot,[19] and Reem A. Mustafa[19]

[1]Department of Medicine, Queen's University, Kingston, ON, Canada; [2]Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [3]Pharmacology Consulting, Princeton Junction, NJ; [4]Rutgers–Robert Wood Johnson Medical School, New Brunswick, NJ; [5]Department of Pediatrics, Washington University in St. Louis, St. Louis, MO; [6]Division of Thrombosis and Hemostasis, Department of Internal Medicine, Leiden University Medical Center, Leiden, The Netherlands; [7]Marseille, France; [8]Diagnostic Laboratories, Versiti Blood Research Institute, Milwaukee, WI; [9]Auburn, ME; [10]Bloodworks Northwest, Seattle, WA; [11]Division of Hematology, University of Washington, Seattle, WA; [12]National Women's Health, Auckland City Hospital, Auckland, New Zealand; [13]Northern Cancer Service, Launceston General Hospital, Launceston, TAS, Australia; [14]Versiti Blood Research Institute, Milwaukee, WI; [15]Irish Centre for Vascular Biology, Royal College of Surgeons in Ireland, Dublin, Ireland; [16]Coraopolis, PA; [17]Aflac Cancer and Blood Disorders, Children's Healthcare of Atlanta, Emory University, Atlanta, GA; [18]Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI; and [19]Outcomes and Implementation Research Unit, Division of Nephrology and Hypertension, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, KS

Background: von Willebrand disease (VWD) is the most common inherited bleeding disorder known in humans. Accurate and timely diagnosis presents numerous challenges.

Objective: These evidence-based guidelines of the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) are intended to support patients, clinicians, and other health care professionals in their decisions about VWD diagnosis.

www.bloodadvances.com



CLINICAL GUIDELINES

blood advances

ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease

Nathan T. Connell,[1,*] Veronica H. Flood,[2,*] Romina Brignardello-Petersen,[3] Rezan Abdul-Kadir,[4] Alice Arapshian,[5] Susie Couper,[6] Jean M. Grow,[7] Peter Kouides,[8] Michael Laffan,[9] Michelle Lavin,[10] Frank W. G. Leebeek,[11] Sarah H. O'Brien,[12] Margareth C. Ozelo,[13] Alberto Tosetto,[14] Angela C. Weyand,[15] Paula D. James,[16] Mohamad A. Kalot,[17] Nedaa Husainat,[17] and Reem A. Mustafa[17]

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Background: von Willebrand disease (VWD) is a common inherited bleeding disorder. Significant variability exists in management options offered to patients.

Objective: These evidence-based guidelines from the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) are intended to support patients, clinicians, and health care professionals in their decisions about management of VWD.

AMERICAN SOCIETY OF HEMATOLOGY

ISTH International Society on Thrombosis and Haemostasis

NATIONAL HEMOPHILIA FOUNDATION *for all bleeding disorders*

WFH WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA

ASH ISTH NHF WFH 2021 Guidelines on the Diagnosis and Management of VWD

QUESTIONS?

- www.hematology.org/VWDguidelines
- www.isth.org/page/VWDGuidelines
- www.hemophilia.org/bleeding-disorders-a-z/types/von-willebrand-disease
- www.wfh.org/VWDGuidelines

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Become a member and support our global community today.

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COMPASSION to ACTION
Together we can

THANK YOU!

¡GRACIAS!

MERCI!

شكرا

СПАСИБО

STAY SAFE!

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