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

European
von Willebrand Disease
Community

NMOs HANDBOOK

A Comprehensive Guide to **von Willebrand Disease (VWD)**

European
von Willebrand Disease
Community

Introduction
Who We Are

About the EHC

The European Haemophilia Consortium (EHC) is an international non-profit organisation representing **49 national patient organisations** for people with rare bleeding disorders located in the **World Health Organisation (WHO) European region**, including 27 Member States of the European Union and most Member States of the Council of Europe.

The EHC represents approximately **120,000 people** diagnosed with rare bleeding conditions such as haemophilia, von Willebrand Disease (VWD), and other extremely rare bleeding disorders across Europe. However, experts estimate that many more live with an undiagnosed rare bleeding disorder.

About the EHC Von Willebrand Disease Committee

The Von Willebrand Disease (VWD) Committee was set up as a working group in 2020 to lead the 'EHC VWD Platform for Europe'. This platform promotes the formation of a European community of people with von Willebrand Disease (PwVWD), enabling them to find support and 'identity' while also promoting, building, and maintaining a network of European VWD advocates. The working group was transformed into a committee in 2023, which reflects its evolution and development over the past years.

By raising awareness, the Committee aims to drive improvements in **diagnosis, treatment options, and access to care**, both nationally and at the European level, empowering VWD advocates to collaborate with European partners to enhance care for all PwVWD.

With this handbook, the VWD Committee wants to give patients, national member organisations (NMOs), and others interested a summarised overview of VWD with the most important facts as well as helpful links to different, more specific resources.

European von Willebrand Disease Community

Introduction
Who We Are

Terms of Use

This handbook is intended for use by EHC National Member Organisations (NMOs), providing them with essential information on the basics of von Willebrand Disease and guidance on how to begin working towards improving care for their patients.

The content provided here is **for informational purposes only** and should not be used as a substitute for professional medical advice, diagnosis, or treatment. Patients should consult their doctor or a specialist haemophilia treatment centre for personalised guidance.

By using this handbook, you agree to the following:

- You will not distribute, reproduce, or use the handbook for commercial purposes without prior written consent from the European Haemophilia Consortium.
- The information herein is current as of the publication date. However, medical practices and knowledge may evolve, and the EHC assumes no responsibility for the accuracy of information after the publication date.
- This handbook does not establish a patient-healthcare provider relationship. Always follow the guidance of your healthcare provider.

The name “European Haemophilia Consortium (EHC)” and the EHC logo are the exclusive property of the European Haemophilia Consortium. Any use of the name or logo must receive prior approval from the EHC Steering Committee. This rule entails all forms of publication, including print and digital formats. Reprinting, redistribution, or translation of any EHC publication is subject to the permission request.

Requests for review and approval should be submitted to the EHC Communications Team at **communications@ehc.eu** in a timely manner.

Please note: Information and materials in this handbook are intended for general information only. The EHC does not endorse or promote any specific pharmaceutical organisation, drug, or other medical intervention; any reference to a product name is not an endorsement by the EHC.

For any inquiries or additional information, please contact the EHC Communications Team at the email address provided above.

European
von Willebrand Disease
Community

Starting Point

2

A **bleeding disorder** is a condition in which coagulation does not occur as it should, typically due to defects or deficiencies in clotting factors. **VWD is one of the coagulation disorders**, and patients generally struggle to get proper diagnosis and treatment not only in different countries, but also within one country, depending on many factors, such as the national health care situation, availability of trustworthy, reliable information and education, and access to various laboratory tests and treatment options. Even though VWD affects men and women equally, we still see differences in attitudes, access to diagnosis, and treatment provision. This book is a comprehensive guide to all existing information to help NMOs and volunteers distribute correct information to other stakeholders.

It is important for patients, their relatives, and volunteers in NMOs to understand how this bleeding disorder works and what the treatment options are. Not everyone has access to scientific literature or competent advice right away. By empowering patients with knowledge, not only do we strive to improve their **self-advocacy skills**, but also to **provide relevant information** for better advocacy at the national and international levels. We encourage NMOs to nurture environments in which people with VWD and their families may come together and build communities. These communities can be further formalised to become dedicated VWD committees with their own action plan for advocacy, just as previously described in the case with the EHC VWD Committee.

The EHC VWD Committee encourages each NMO to **establish a national VWD committee** by appointing a local ambassador, building a patient and stakeholder network, and organising national activities. To support this, the EHC provides **guidance, mentoring, access to educational resources and campaign materials**, and opportunities to participate in Europe-wide initiatives such as **awareness days, events, and advocacy efforts**. The goal is to help NMOs strengthen national representation and ensure VWD voices are included in broader discussions on care and policy.

The following section of the Guide provides foundational information on bleeding disorders, including an overview of the blood clotting process. It explains how blood functions in healthy individuals and how it behaves in those with VWD. Additionally, it outlines the diagnostic tests used to identify the specific type of coagulation disorder and offers a comprehensive description of each disorder.

European von Willebrand Disease Community

3 Information on Bleeding Disorders

What are bleeding disorders?

'Bleeding disorders' is a generic name for a group of disorders that affect **the ability of blood to clot** in an individual. Bleeding disorders include conditions such as haemophilia A and haemophilia B, von Willebrand Disease (VWD), and extremely rare bleeding disorders (RBDs). These conditions present themselves in either severe, moderate, or mild form.

When they have access to adequate diagnosis and treatment, people with bleeding disorders can lead normal and fruitful lives. However, poor access to diagnosis and treatment can have **drastic consequences** on the lives of those affected by these conditions. Bleeds that are not properly managed can be crippling and even life-threatening when they occur, for example, in the brain.

All bleeding disorders fit the description of **rare diseases** as provided by the European Union, which is a condition that affects fewer than 5 people in 10,000. Despite being rare diseases, conditions such as haemophilia and von Willebrand Disease (the most frequent bleeding disorders) are ahead of the curve compared to many other rare diseases, in the sense that both diagnostics and a variety of treatments exist for these conditions.

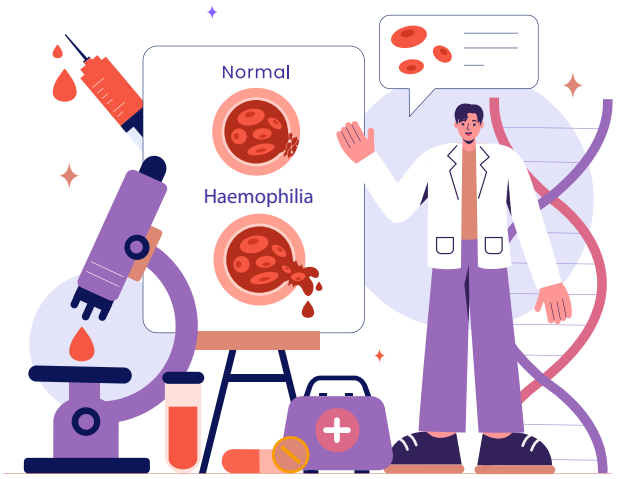
The challenges faced by these patients relate to **underdiagnosis** (when patients with VWD are under the care of ear-nose-throat specialists, rheumatology, gynaecologist, obstetrician, etc. without even knowing they have VWD), as well as to the **lack of access to adequate treatment** (which is often expensive), and **specialised healthcare services**, including specialised coagulation laboratory (which may be located only in one or two cities in a given country).

Furthermore, patients within the European region face great **disparities in access to treatment** and, as a result, **have a different quality of life**. The EHC strives both at the European and national levels to increase the awareness of the daily realities of people with bleeding disorders.

If you are a patient with a bleeding disorder and you are looking for more in-depth medical information, we recommend the following **websites**:

- **The website of your national haemophilia association**
- **The website of the World Federation of Hemophilia**
- **The website of Haemophilia Central**
- **Orpha.net**

European von Willebrand Disease Community



Understanding von Willebrand Disease

What are the key facts about von Willebrand Disease (VWD)?

Von Willebrand Disease (VWD) is the **most common inherited bleeding disorder**, though its impact varies significantly between individuals. The mildest form, **Type 1**, affects up to 1 % of the population, or approximately 10 to 11 per 1,000 people. More severe forms are much rarer: **Type 2 (including subtypes 2A, 2B, 2N and 2M)** is estimated to occur in 0.8 to 2.5 per 1,000, and **Type 3**, the most severe form, affects approximately 1 per 1,000,000.

Although VWD types are categorised by severity, individual experiences often vary. Some people with Type 1 may experience severe bleeding, while others with Type 3 may go long periods without significant symptoms. On average, about 1 in 1,000 people will have bleeding severe enough to require medical attention. The condition affects people of all genders equally, but **women are more likely to be diagnosed** due to symptoms such as heavy menstrual bleeding or complications during childbirth.

European von Willebrand Disease Community

What causes von Willebrand Disease (VWD)?

Individuals with von Willebrand Disease (VWD) have an issue with a clotting protein in their blood called **von Willebrand factor (VWF),** which is essential for controlling bleeding. VWF helps carry Factor VIII (FVIII) to injury sites and assists in binding platelets to the walls of blood vessels, promoting clot formation. When VWF levels are low, FVIII levels also drop, causing clotting to take longer. VWD comes in various types, all stemming from issues with the VWF protein, either due to **insufficient levels or improper function.**

Many people with VWD may not realise they have the condition, as their bleeding may not seem unusually heavy or prolonged. The severity of bleeding varies among individuals, with some experiencing minimal disruption unless injured or undergoing surgery, while others may face significant challenges, even with less severe bleeds like nosebleeds or heavy menstrual flow. Regardless of the type, **bleeding issues are a common aspect of VWD.**

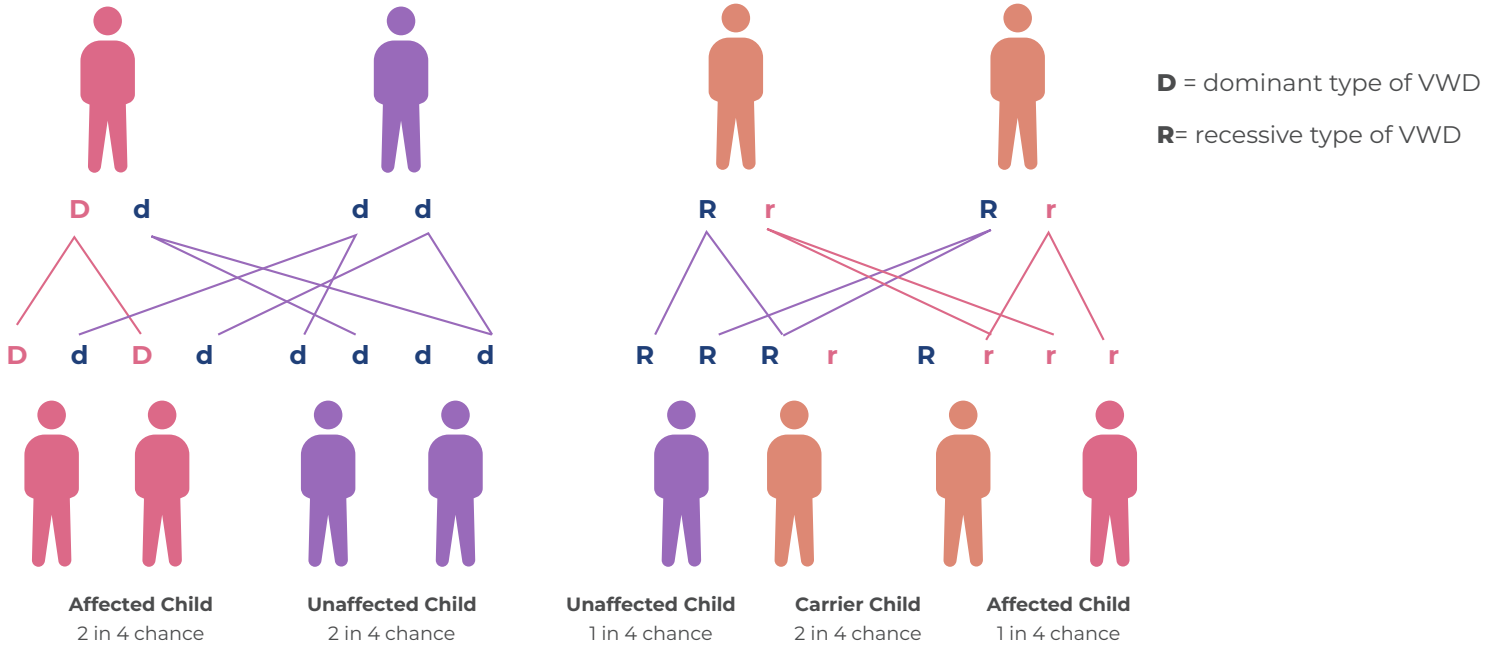


***Figure 1.** Inheritance of VWD Source: [World Federation of Hemophilia (WFH), 2023, **www.wfh.org**].

A parent who has a dominant type of VWD has a 1 in 2 (50%) chance of having a child who has VWD with each pregnancy.

If both parents carry a recessive gene for VWD, with each pregnancy there is a 1 in 4 (25%) chance of having a child who has VWD.

Note: It's important to note that the inheritance of "low VWF" or type 1 VWD, where plasma VWF levels range from 30-50 IU/dL, is more intricate and may not adhere to typical genetic patterns.

European von Willebrand Disease Community

What types of von Willebrand Disease (VWD) exist?

Von Willebrand Disease (VWD) is divided into three primary types, each requiring tailored treatment strategies. The **severity** of the condition within each type **can range from mild to severe**, though there is no universally accepted system to categorise severity. Medical professionals evaluate the severity using **bleeding assessment tools (BAT)** along with lab tests, and the severity may change over time. The presentation of bleeding symptoms can vary significantly between individuals, even within the same type, influenced by the activity of von Willebrand factor (VWF). While the bleeding phenotype tends to be more important than the VWD type, knowing the specific type can still provide valuable insight for treatment and genetic inheritance, as both can differ between types. For individuals whose VWD type is unclear, it is essential to seek medical attention for any bleeding episodes.

Type 1 VWD

Type 1 VWD is the most prevalent form of the condition. Individuals with type 1 VWD have VWF levels that are lower than usual, which can range from mildly reduced to significantly low. There is also a variation known as **type 1C**, in which the VWF has a shorter lifespan in the body, meaning, it breaks down more quickly than normal.

Type 2 VWD

Type 2 VWD is characterised by an abnormality in the structure of VWF, even though its levels may appear normal. This structural defect impairs the function of VWF, resulting in reduced VWF activity. Type 2 VWD is further divided into subtypes:

- **In type 2A,** the VWF protein is defective, making it difficult for VWF to properly bind to platelets.
- **In type 2B,** there is excessive binding of VWF to platelets in the blood, reducing the amount of free VWF available to help stop bleeding at injury sites.
- **Type 2M** involves issues with VWF's ability to bind to platelets, despite the protein's structure being normal.
- **Type 2N** is marked by problems with VWF binding to FVIII, leading to significantly low levels of FVIII.

Type 3 VWD

Type 3 VWD is typically the most severe form of the disorder, characterised by extremely low or absent levels of VWF.

European
von Willebrand Disease
Community

The signs and symptoms of von Willebrand Disease

5

The primary **symptoms** of VWD often include but are not limited to:

- Heavy or extended menstrual bleeding, lasting longer than a week,
- Frequent or long-lasting nosebleeds,
- Unexplained bleeding in the mouth,
- Easy bruising or bruises that persist,
- Bleeding in muscles,
- Prolonged bleeding from minor cuts or in the mouth,
- Gastrointestinal bleeding, affecting both the upper and lower tracts,
- Extended bleeding after injury, surgery, dental procedures, or childbirth,
- Joint bleeding, which occurs in more severe cases but can also be seen in mild and moderate VWD forms.

Individuals with VWD may experience few or no symptoms, while those with more severe forms may face significant bleeding issues.

The **severity of symptoms often correlates with the type of VWD**, with people with type 1 typically having mild symptoms, type 2 individuals experiencing moderate symptoms, and type 3 individuals having severe symptoms. However, even those with milder forms of VWD can still encounter serious bleeding episodes that affect their quality of life. In some cases, VWD may not be diagnosed until heavy bleeding occurs after a serious injury, surgery, dental procedures, or childbirth. To assess the severity and create a personalised treatment plan, doctors use validated **bleeding assessment tools (BATs)**. Women are more likely to show symptoms of VWD, often experiencing heavier or prolonged menstrual bleeding and increased bleeding after childbirth compared to men.

European
von Willebrand Disease
Community

Methods for diagnosing VWD 6

There are people who may live with VWD for a long time without realising it, as they may not experience noticeable symptoms or only have mild ones. This is often the case for men, who may only find out when undergoing surgery or if a female relative is diagnosed. Additionally, some people remain **undiagnosed** because their doctors might not recognise VWD, leading to their symptoms being overlooked or misattributed to other conditions.

If your doctor believes you may have a bleeding disorder, they might recommend various tests following an evaluation of your symptoms through BAT. To prevent a prolonged diagnostic journey, which could take over 15 years, it's important to see **a haematologist who specialises in bleeding disorders and has access to advanced laboratories.** These tests are typically performed at a dedicated bleeding disorders treatment centre.

Diagnosing von Willebrand Disease requires evaluating both VWF and FVIII levels and their activity in the blood. However, routine **blood tests alone cannot definitively diagnose VWD**. Since VWF and FVIII levels can vary under different circumstances, such as in the presence of anaemia or during bleeding, such as menstruation, these tests may need to be repeated. If you're taking a contraceptive pill, it's crucial to inform your doctor, as higher doses of the pill can raise VWF levels, potentially making the diagnosis more challenging.

In addition to laboratory tests, your **medical history** plays a key role in the diagnosis. Your doctor will want to know several details, including:

- When you first experienced bleeding symptoms,
- The areas of your body that have been affected by bleeding,
- The onset and duration of the bleeding episodes,
- How frequently the bleeding occurs,
- Whether anyone in your family has a history of bleeding problems.

European
von Willebrand Disease
Community

Testing process

Testing for von Willebrand Disease (VWD), particularly type 1, can be challenging because VWF levels are sensitive to various factors that can cause **fluctuations**. One factor is **pregnancy,** as VWF levels naturally rise during this time. **Oestrogen and some birth control pills** can also increase VWF levels in the bloodstream. Stress, even in mild forms like nervousness or crying during a blood test, can cause a temporary spike in VWF levels, which can make testing especially difficult in children. **Physical activity**, too, can elevate VWF levels, as can **active infections**. Additionally, a person's **blood type** plays a role, with people who have blood type O typically having lower VWF levels compared to those with blood types A, B, or AB. This is why doctors need to know a patient's blood type when interpreting VWF test results. **Thyroid issues** can also affect VWF levels, and your doctor may check thyroid function to rule out other causes for any symptoms. The optimal time for testing is during the periods when VWF is physiologically at the lowest level.

Diagnostic blood tests for VWD

To diagnose VWD, doctors usually order several blood tests to account for the various types of the condition. Due to the many factors that can influence VWF levels, these tests might need to be repeated. Some key tests used to diagnose VWD include the **ristocetin cofactor test**, where normal platelets and the antibiotic ristocetin are introduced into the plasma, and a machine measures how well the platelets stick together. This test is important for diagnosing VWD.

The von Willebrand factor **antigen test** measures the concentration of VWF in the blood, while the **VWF multimers test** examines the different components of the VWF protein to determine the specific type of VWD. The **Factor VIII level test** measures the amount of Factor VIII in the blood, since low levels of VWF can also result in low Factor VIII levels. The **bleeding duration or platelet function analyser (PFA) test** or measuring the aggregation of platelets is sometimes used to evaluate bleeding issues, although it is not always reliable for diagnosing VWD, as many individuals with the condition may show normal results. Therefore, other tests are necessary to make a proper diagnosis of VWD.

Genetic testing offers the most precise results in certain countries, helping your doctor choose the best treatment. To identify the type of VWD, including for inheritance patterns or treatment options, ask your doctor about referring you for genetic testing.

If your country does not offer such testing or proper diagnosis, you can seek help through **ERN-EuroBloodNet,** which may help you access blood testing in another country.

More about **diagnosis:**

ASH ISTH NHF WFH 2021 guidelines on the diagnosis

European von Willebrand Disease Community

Medical treatment for VWD

7

The treatment of VWD focuses on **promoting blood clotting** to prevent excessive bleeding. This can be achieved using medications such as **tranexamic acid or aminocaproic acid**, which help to control bleeding, or **desmopressin and VWF concentrates**, which boost plasma VWF levels. The specific treatment plan depends on factors such as the type of VWD, the patient's VWF levels, and the severity of bleeding or any upcoming surgical procedures. For individuals with mild forms of VWD, treatment may not be necessary unless they are undergoing surgery or dental procedures.

It's important to **contact your treatment centre** in the following situations:

- When planning for surgery, medical procedures, or any invasive dental work (such as tooth extractions);
- If you are pregnant;
- If you experience moderate to severe bleeding;
- If bleeding persists for more than six weeks after childbirth or surgery; or
- If you have particularly difficult or heavy periods.

Approaches to Effective Care

Desmopressin (DDAVP): Benefits, Limitations, and Considerations

Desmopressin (DDAVP) helps the body **release stored VWF,** increasing plasma levels of both VWF and FVIII, which in turn **promotes blood clotting**. It is an affordable and easy-to-administer treatment, available as an injection or a nasal spray. However, **it doesn't work for everyone**. Doctors have to do a mandatory test and monitor the patient's response to DDAVP before treatment is needed. Moreover, this test can also help identify the type of VWD. DDAVP is often effective for treating type 1 VWD and can help manage bleeding in certain forms of type 2 VWD. However, it is not suitable for type 1C VWD, as its effects are short-lived, nor for type 3 VWD, as there is no response to the drug.

In emergencies or during surgery, DDAVP can be used to **control bleeding**. Some individuals may experience side effects such as dizziness, flushing, or palpitations, which may improve if the drug is administered more slowly. When DDAVP isn't effective, or if there's a high risk of significant bleeding, **factor concentrates may be used instead**. DDAVP is **not** recommended for people with active cardiovascular disease, seizure disorders, children under 2 years old, or those with type 1C and 3 VWD undergoing surgery. It should **not** be used for more than three consecutive days.

European von Willebrand Disease Community

VWF Concentrates, Prophylactic, and Hormonal Options:

There are two main types of VWF concentrates available for treatment. The first is **plasma-derived**, which is purified from blood and contains VWF along with varying amounts of FVIII. The second type is **recombinant**, which is produced in a laboratory without the need for blood donations. These concentrates are the preferred choice for treating **type 3 VWD, most forms of type 2 VWD**, and for **managing serious bleeding or major surgeries** across all types of VWD.

For **bleeding in mucous membranes**, such as those in the nose, mouth, intestines, or uterus, medications like **tranexamic acid, aminocaproic acid, or fibrin glue** can be used. These treatments help maintain existing clots but do not directly assist in forming new ones.

Hormonal treatments, such as oral contraceptives, can be helpful for some women and girls with VWD. These medications not only help regulate heavy menstrual bleeding but also serve as a method of contraception. For those who do not wish to become pregnant, an **intrauterine device (IUD)** may be an effective alternative for managing heavy periods, as it can provide up to five years of relief. However, the contraceptive pill should not be considered the default treatment option simply because it is widely available and easy to use. **Exogenous hormones** can significantly affect a young woman's life, and these effects are not always positive. For women experiencing heavy periods while trying to conceive, hormone treatments are not an option. Instead, alternative treatments such as **antifibrinolytic agents, DDAVP, or VWF concentrates** may help manage heavy menstruation.

For individuals with VWD who have a history of severe and frequent bleeding episodes, **long-term prophylaxis** with a VWF concentrate is typically recommended. Prophylactic treatment involves the regular administration of a haemostatic agent, either intravenously, subcutaneously, or through other methods, to prevent bleeding, particularly life-threatening episodes or recurring joint bleeds.

Like all medications, these treatments come with the potential for side effects. It's important for those with VWD to **consult with their healthcare provider** to discuss the possible risks associated with treatment.

European
von Willebrand Disease
Community

8

Available Treatments for Individuals with Congenital Bleeding Disorders in Europe

In this section, we list the main types of **treatments** currently available for congenital bleeding disorders:

- Factor concentrates
- Non-replacement therapies
- Prothrombin complex concentrate (PCC)
- Desmopressin
- Antifibrinolytic drugs
- Fibrin glue
- Platelet transfusions
- Hormonal contraceptives
- Intrauterine devices (IUDs)

For more detailed information about each treatment listed above, we encourage you to consult the **EHC Academy**, where additional guidance and educational materials are available. You can also find product authorisation details on the **European Medicines Agency (EMA)** website and your national regulatory authority. For information on reimbursement, please contact your national health insurance provider.

Additional treatment resources:

- **Haemophilia Central website** – guidelines, treatment centres, product info
- **European Haemophilia Safety Surveillance website** – data on treatment products available in Europe

European von Willebrand Disease Community

9 Managing Menstrual Health and Iron Deficiency in Women and Girls with VWD

Women and girls with VWD often experience more pronounced symptoms than men due to **menstruation** and **childbirth**. Girls, in particular, may face heavier bleeding when they first start their periods. As they get older, women with VWD commonly deal with **longer and heavier menstrual cycles**. This excessive blood loss can lead to **iron deficiency**, which, if left untreated, can develop into **anaemia**.

Iron levels are crucial for maintaining health because low iron can cause symptoms such as **fatigue** and **weakness.** This is a common concern for women with VWD. Regular **testing** for low iron levels, through ferritin tests, and checking haemoglobin levels to detect anaemia, is important. If iron levels are low, taking **iron supplements** can help restore them and prevent anaemia. However, if supplements are ineffective, **iron transfusions** may be necessary to significantly boost iron levels. It's also important to address the **underlying cause** of heavy bleeding, such as prolonged periods, as untreated bleeding will cause iron levels to drop again.

What qualifies as "excessive" bleeding can vary between individuals. On average, blood loss during a normal period is around 30–40 ml. Losses of 80 ml or more are considered heavy. Although it's difficult to measure blood loss directly, some **signs of excessive bleeding include:**

- Periods lasting longer than 7 days.
- Changing pads or tampons more often than every 2 hours, or 10+ during the day
- Passing clots about the size of a one-euro coin,
- Experiencing low iron levels repeatedly.

If you suspect excessive bleeding, **tracking your menstrual flow** using a bleeding assessment chart can be helpful. This chart can serve as a tool to discuss your symptoms with your doctor and assess your condition more accurately.

Bleeding Assessment Tools (BATs)

- **ISTH/SSC bleeding assessment tool:** a standardised questionnaire and a proposal for a new bleeding score for inherited bleeding disorders:
- **Self-BAT**
- **VWD Test**
- **#TalkingRed Symptom Checker**

European
von Willebrand Disease
Community

Complications

10

This chapter of the guide describes the **physical problems** that can result from bleeding disorders. Problems caused directly or indirectly by a bleeding disorder are called **complications.** You should be aware that not all of these complications will happen to any one person. Such complications can often be prevented or avoided, but, most importantly, they can all be treated. The main purpose of this section is to introduce available options for prevention and treatment. It is meant as a starting point only. For more detailed information or personal guidance, we recommend **contacting your treatment centre.**

- **Inhibitors**

  An inhibitor is a type of alloantibody that targets and blocks clotting factors used in haemophilia treatment, making it harder to manage bleeding episodes. While inhibitors are most common in haemophilia A, they can also occur in haemophilia B or VWD type 3. The severity of inhibitors varies, and treatment depends on their tier. Key therapies include high-dose clotting factors, bypassing agents, and non-factor treatments.

- **Arthropathy**

  Arthropathy in severe VWD occurs in 40% of patients after joint bleeds and is associated with pain, joint damage, functional limitations, and reduced social participation. It is more common in patients with verified joint bleeds compared to those without. Prevention involves managing joint bleeds effectively with clotting factor replacement to minimise joint damage. Treatment may include physical therapy, pain management, and addressing functional limitations. Regular monitoring and early intervention are crucial to reduce the risk of arthropathy and improve patients' quality of life.

- **Thrombotic complications**

  In the treatment of VWD, particularly when using clotting factor concentrates, there is a theoretical risk of thrombotic complications. Excessive increases in factor VIII levels, especially during high-dose or prolonged treatment, or in the presence of other risk factors, can contribute to the development of thrombosis. This risk is especially relevant in certain types of VWD and with certain replacement products that contain both VWF and FVIII. Clinical monitoring is necessary to avoid excessive FVIII accumulation and to manage thrombotic risk appropriately.

- **Synovitis**

  Synovitis is the inflammation of the synovial membrane, often resulting in joint pain, swelling, and reduced mobility. It typically occurs after joint injury when degraded cartilage fragments and extracellular matrix molecules activate synovial cells, leading to the production of inflammatory mediators. This process contributes to cartilage degradation, increased inflammation, and impaired joint

European
von Willebrand Disease
Community

lubrication, perpetuating a cycle of damage. Early intervention is key to preventing and treating synovitis. This includes managing joint injuries, using anti-inflammatory medications and physical therapy. In some cases, intraarticular injections of steroids and/or hyaluronic acid injections may help; this is a general approach if patients experience painful joints. Ongoing monitoring and addressing joint damage are important to prevent long-term issues like osteoarthritis.

Arthropathy

Arthropathy in VWD arises from repeated bleeding into joints, leading to chronic pain, stiffness, reduced range of motion, and structural joint damage. This complication is managed primarily by preventing further bleeds through regular replacement of von Willebrand factor and/or factor VIII. Treatment also includes physical therapy to restore function, pain relief (such as anti-inflammatory medications), and, in some cases, orthopaedic procedures. When bleeding is frequent or severe, long-term prophylaxis is recommended to protect joint health.

Pain management

Pain management involves various approaches to help alleviate, reduce, or control pain, using medications, therapies, exercises, and sometimes procedures. It aims to improve quality of life by helping individuals manage pain from injuries, conditions, or treatments, whether the pain is short-term (acute) or long-lasting (chronic). The goal is not always to eliminate pain entirely, but to enhance daily functioning and well-being through personalised care and adjustments by healthcare providers. Pain can be managed through various methods based on its cause. Pain control medication may be recommended, such as analgetic therapy (which is treatment aimed at reducing pain through medicines that lower pain signals in the body), together with at-home remedies like the RICE method (rest, ice, compression, elevation) and heat therapy help with muscle and soft tissue pain. Lifestyle changes—healthy eating, staying active, hydration, and stress management—can also ease pain. Physical therapy improves movement, while cognitive behavioural therapy (CBT) addresses the emotional side of chronic pain. Complementary therapies such as massage, acupuncture, yoga, may offer additional relief.

Hepatitis

In the past, some blood products used for people with bleeding disorders were contaminated, and this exposed many individuals to hepatitis and HIV infection; this history matters for patients with VWD because these infections can add serious liver or immune related complications to their existing condition. Hepatitis is a medical condition characterised by the inflammation of the liver, often caused by viral infections. The most common causative agents are a group of viruses known as the hepatitis viruses, which include five main types: A (HAV), B (HBV), C (HCV), D (HDV), and E (HEV). In addition to these, other viruses such as herpes simplex virus type 1 (HSV-1), cytomegalovirus (CMV), and Epstein–Barr virus (EBV) can also cause

European von Willebrand Disease Community

hepatitis. Hepatitis can lead to both acute and chronic liver disease, with HBV and HCV being responsible for a significant number of chronic infections worldwide. Treatment and prevention of viral hepatitis vary by virus. Acute cases are managed with supportive care, while antiviral medications like tenofovir for HBV and direct-acting antivirals for HCV treat chronic infections. Vaccines prevent HAV and HBV, and harm reduction practices help prevent HCV. Hepatic encephalopathy is treated with lactulose and rifaximin. Vaccination and infection control are key to preventing the spread.

- **Hepatitis A**

Hepatitis A is an inflammation of the liver caused by the hepatitis A virus (HAV). The virus is primarily spread when an uninfected (and unvaccinated) person ingests food or water that is contaminated with the faeces of an infected person. The disease is closely associated with unsafe water or food, inadequate sanitation, poor personal hygiene and oral-anal sex. Hepatitis A is treated with supportive care, focusing on hydration, nutrition, and symptom relief. Avoiding medications like acetaminophen that can harm the liver is important. Prevention includes improved sanitation, safe drinking water, proper sewage disposal, personal hygiene practices like handwashing, and safer sex practices. Hepatitis A vaccines, available as inactivated or live attenuated options, provide effective protection. The vaccine is recommended for those at risk, but it's not licensed for children under 1 year.

- **Hepatitis B**

Hepatitis B is an infection of the liver caused by the hepatitis B virus. The infection can be acute (short and severe) or chronic (long-term). Hepatitis B can cause a chronic infection and puts people at high risk of death from cirrhosis and liver cancer. It can spread through contact with infected body fluids like blood, saliva, vaginal fluids and semen. It can also be passed from a mother to her baby. Hepatitis B can be prevented with a safe and effective vaccine. The vaccine is usually given soon after birth, with boosters a few weeks later. It offers nearly 100% protection against the virus. Acute hepatitis B is treated with supportive care, while chronic cases are managed with antiviral medications like tenofovir or entecavir. Prevention includes the hepatitis B vaccine, given to infants within 24 hours of birth and in two or three doses. To reduce transmission, practice safe sex, avoid needle sharing, and maintain good hygiene. Pregnant women with hepatitis B should take antiviral medications to prevent transmission to their baby.

- **Hepatitis C**

Hepatitis C is a viral infection that affects the liver. It can cause both acute (short-term) and chronic (long-term) illness. It can be life-threatening. Hepatitis C is spread through contact with infected blood. This can happen through sharing needles or syringes, or from unsafe medical procedures such as blood transfusions with unscreened blood products. Symptoms can include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain,

European von Willebrand Disease Community

dark urine and yellowing of the skin or eyes (jaundice). There is no vaccine for hepatitis C, but it can be treated with antiviral medications. Early detection and treatment can prevent serious liver damage and improve long-term health. Hepatitis C is treated with antiviral medications like sofosbuvir and daclatasvir, which can cure most cases in 12-24 weeks. Lifestyle changes, like avoiding alcohol, also help. Prevention includes safe healthcare practices, needle disposal, harm-reduction for drug users, and safe sex with condoms. People at higher risk, like those with HIV or who inject drugs, should take extra precautions.

- **Preventing the spread of hepatitis**

  To prevent hepatitis spread, key measures include vaccination (especially for HBV, HAV, and HEV), ensuring injection and surgical safety, and preventing mother-to-child transmission of HBV. Harm reduction services for people who inject drugs, treatment of chronic HBV and HCV, and improving sanitation, clean water, and food safety are also essential. For hepatitis B and C, targeted interventions to reduce sexual transmission are important. The focus of these efforts will depend on the country's specific context and hepatitis prevalence.

- **How to take care of yourself if you have hepatitis**

  If you have hepatitis A, B, or C, taking care of your liver is essential. For hepatitis A, rest, a balanced diet, and plenty of fluids are typically enough, as it doesn't become chronic. Vaccination is key for prevention, and if exposed, immune globulin or the hepatitis A vaccine should be administered promptly. For hepatitis B and C, follow your doctor's guidance on antiviral medications and avoid alcohol to prevent further liver damage. Eat a healthy diet with fruits and vegetables, avoid raw oysters and harmful chemicals, and engage in regular exercise. Regular check-ups with a hepatologist, vaccinations for flu and pneumococcal disease, and stress management techniques also support overall health. By taking these steps and staying in close communication with your healthcare team, you can effectively manage hepatitis and protect your liver.

- **AIDS and HIV infection**

  HIV (Human Immunodeficiency Virus) attacks the body's immune system, making it harder to fight infections. If left untreated, HIV can progress to AIDS (Acquired Immunodeficiency Syndrome), the most severe stage of the disease. HIV is transmitted through bodily fluids like blood, semen, vaginal fluids, and breast milk, but not through casual contact like kissing or sharing food. The virus can be prevented with antiretroviral therapy (ART), which helps manage the virus and prevent its transmission. HIV is preventable through measures like using condoms, getting tested for HIV and other sexually transmitted infections (STIs), opting for male circumcision, and using harm reduction services for people who inject drugs. While there's no cure, antiretroviral drugs (ART) help prevent the virus from replicating and strengthen the immune system. ART must be taken daily for life to remain effective.

European von Willebrand Disease Community

Financial Planning for VWD: Navigating Costs and Access to Care

The **financial burden** of treating von Willebrand Disease (VWD) can be significant, and varies greatly depending on the country and healthcare system. **In European Union (EU) countries**, healthcare systems generally offer **comprehensive coverage** for rare diseases, including VWD. However, **the level of reimbursement, patient co-payments, and access to specialised centres can differ widely** across member states. For instance, countries like Germany and France have well-established treatment frameworks for bleeding disorders, but even there, the cost of advanced treatments such as clotting factor concentrates can be high for patients without full insurance coverage. In contrast, smaller or less-resourced EU countries may face longer wait times or limited access to specialised care, increasing both direct and indirect costs of treatment.

Outside Europe, the costs can be even more variable. In countries with private healthcare systems, such as the **United States**, patients may face substantial out-of-pocket expenses unless they have comprehensive insurance coverage. Even with insurance, the costs of frequent treatments, hospitalisations, and specialised care can lead to high financial strain. In countries with public healthcare systems—for example, in parts of **Latin America or Asia**—treatment may be more affordable, but patients often encounter waiting lists and may lack access to the latest therapies, which can increase long-term costs or complications. As the **CVESS study** on the socio-economic burden of VWD across Europe highlights, treatment costs vary considerably between countries, with some nations facing higher direct medical and indirect costs due to differences in healthcare infrastructure, guidelines, and treatment practices.

European
von Willebrand Disease
Community

For patients and families, **financial planning** for VWD treatment requires a clear understanding of local healthcare systems, insurance options, and potential out-of-pocket costs. It's also crucial to explore **financial assistance programs** from pharmaceutical companies or government-funded initiatives, especially in countries where costs can be high. **Emergency funds or dedicated savings** for long-term care can help manage unpredictable medical expenses. Given the variability in costs and access to care, individuals with VWD should work closely with healthcare providers to navigate treatment options and ensure they are accessing **the most cost-effective and appropriate care available.**

It is important to note that not all healthcare systems have access to the same treatment options. Therefore, it is necessary for **patients to educate themselves when travelling** to other countries to ensure they have planned in case of injury or sickness. Patients should keep in mind that healthcare access rules, medicine documentation needs, and travel insurance **requirements differ between EU or Schengen countries and European states** outside those groups, and they can confirm these details through their national foreign affairs website and the official sites of their destinations.

To get a better understanding of how people with VWD live in your country, we encourage NMOs to **advocate for the use of dedicated scientific registries**, such as the **World Bleeding Disorders Registry (WBDR)**, developed by the World Federation of Hemophilia (WFH). This registry is a partnership between the scientific team at WFH and local Haemophilia Treatment Centres (HTCs), and patients can use their own app, **myWBDR**, to collect data on their bleeds, use of treatment, and other important information in a GDPR-compliant way. Healthcare specialists add core data from patients' medical reports. NMOs can have access to **accumulated national-level data** to support their advocacy efforts, and HTCs also have access to summarised data from their centres. It is also important to mention that the WBDR is linked to the **PROBE study,** which in the future will also collect health-related quality of life data on patients with VWD. This will provide more data to analyse and eventually improve access to treatment and care in different countries.

European
von Willebrand Disease
Community

Resources

12

- The Hemophilia, Von Willebrand Disease & Platelet Disorders Handbook
- European Haemophilia Consortium (EHC) VWD Platform
- EHC-ERN-EuroBloodNet “Topic on Focus on VWD” webinars
- WFH e-Learning Portal
- WFH What is Von Willebrand Disease Handbook
- National Hemophilia Foundation VWD Brochure
- WHO-FIC Foundation on VWD
- Helloclue Article: Everything you need to know about bleeding disorders
- WFH World Bleeding Disorders Registry
- EHC VWD Children’s book

Guidelines:

Diagnosis

- ASH ISTH NHF WFH 2021 guidelines on the diagnosis

Summary

- NBDF VWD Guidelines Toolkit - Diagnosis
- ASH Letter re WVD ICD-10 Codes

Management

- ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease
- NBDF VWD Guidelines Toolkit - Management

BATs

- letstalkperiod.ca Self-BAT
- #TalkingRed Symptom Checker

Medicines

- Response to desmopressin is influenced by the genotype and phenotype in type 1 von Willebrand disease (VWD): results from the European Study MCMDM-1VWD
- Ongoing trials

Ageing

- Haemophilia Foundation Australia (HFA) report on the needs of older people with bleeding disorders

European
von Willebrand Disease
Community

12

Complications

- Understanding Inhibitors in Bleeding Disorders | NBDF
  Alloantibodies in von Willebrand disease | Blood | American Society of Hematology (ashpublications.org)
- Long-term impact of joint bleeds in von Willebrand disease: a nested case-control study - PMC (nih.gov)
- National Hemophilia Foundation - Living With an Inhibitor
- ScienceDirect | Synovitis
- ScienceDirect | Arthropathy
- Cleveland Clinic | Pain Management
- ScienceDirect| Neurologic complications of hepatic viruses
- WHO | Hepatitis A
- WHO | Hepatitis B
- WHO | Hepatitis C
- WHO | Global Hepatitis Programme | Prevention
- CDC | Clinical Care of Hepatitis A
- Hemophilia of Georgia | Taking Care of Yourself if You Have Hepatitis
- WHO | HIV and AIDS

Financial Planning

- The Cost of Von Willebrand Disease in Europe: The CVESS Study

Expert networks

- ERN-EuroBloodNet
- EAHAD (European Association for Haemophilia and Allied Disorders)

Access to care

- EHC Advocacy Toolkit
- EHC Novel Treatment Reviews

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

European
von Willebrand Disease
Community

Contact details:

About the EHC VWD:
community.ehc.eu/focus-area/von-willebrand-disease-vwd

Email:
vwd@ehc.eu