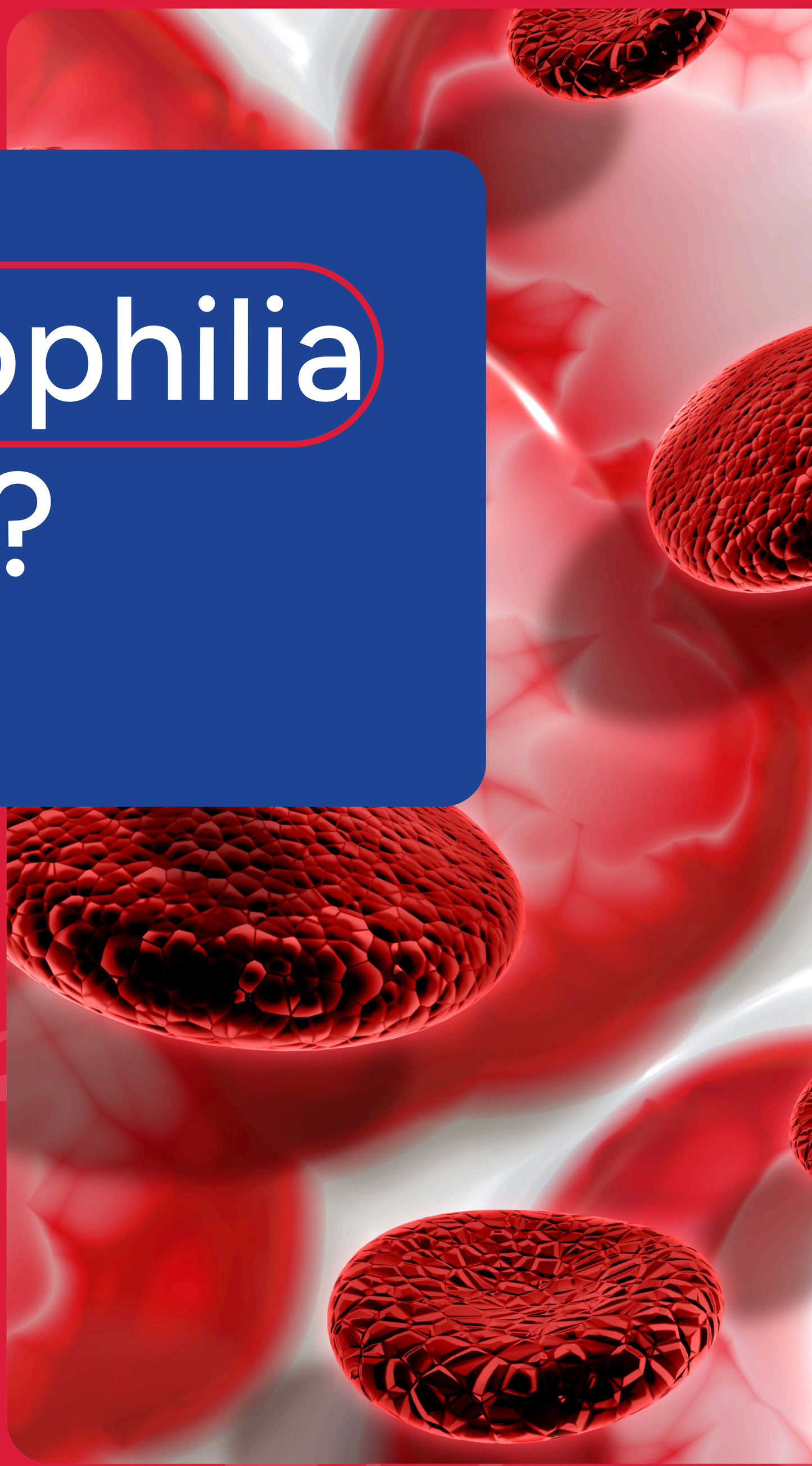
EHC

Empowering the bleeding disorders community

Is haemophilia (fe)male?

a booklet on women and girls with haemophilia and female haemophilia carriers



Foreword

Haemophilia is a rare bleeding disorder characterised by spontaneous or prolonged bleeding due to a lack or reduction in important blood clotting factors, factor VIII or IX. Due to its X-linked inheritance pattern, haemophilia primarily affects males. However, women, particularly carriers of the gene, can also be affected, with reduced factor levels in **up to 30% of haemophilia carriers** and increased bleeding risk in many more.

Women are often still predominantly perceived as mere carriers of haemophilia, a misconception that can limit their access to proper healthcare and delay timely diagnoses within medical systems. Furthermore, women and girls are frequently the only group identified as haemophilia carriers, reinforcing another persistent bias that requires attention. It is crucial to recognise that **both males and females can be carriers of haemophilia from a genetic standpoint.** In this booklet, the EHC specifically addresses female carriers and women and girls with haemophilia as part of its advocacy and awareness-raising efforts.

Up to

30%

of haemophilia carriers have reduced factor levels

The EHC advocates for the **EU Strategy for Women's Health**, which aims to achieve health equity, increase awareness, improve diagnostic practices, and standardise care protocols to better manage and support both female haemophilia carriers and women and girls with haemophilia.

Personal Story

My name is Lisa[1], and I am German. I am the mother of a 25-year-old daughter with severe haemophilia A, caused by a de novo mutation. When she was diagnosed, my husband and I had no idea what this would mean for her future. To better understand the condition and be better prepared, I joined the Haemophilia Society in my country. Soon after, I became a volunteer and an advocate, working to give greater visibility to women and girls with bleeding disorders.

Back in

2000

physicians still claimed that haemophilia was a disorder affecting only men, with women merely considered “carriers.”

Step by step, healthcare professionals began to change the way they described the condition. Patient organisations played a crucial role in raising awareness of women and girls with bleeding disorders. Today, the terminology has evolved together with improved access to diagnosis, treatment, and care. However, I believe that we must continue advocating for earlier and more accurate diagnoses for all women with bleeding disorders, regardless of their condition or location. Access to prophylaxis when necessary is essential. Let’s not forget that women experience monthly bleeding, and for many, heavy menstrual bleeding significantly impacts their quality of life.

[1] For privacy reasons, the name, country, and age in this story have been changed.

Transmission of haemophilia in females: most common cases

Parents	Daughter's inheritance	Likelihood of gene transmission
Mother carrier or mother with haemophilia + father without haemophilia (X*X + XY)	Carrier or woman with haemophilia (X*X) or non-carrier (XX)	50% chance carrier and/or less than 30% chance to be affected by haemophilia, 50% chance non-carrier
Mother carrier or mother with haemophilia + father with haemophilia (X*X + X*Y)	Both X are mutated: woman with haemophilia (X*X*) or carrier (X*X*) or One X is non-mutated: woman with haemophilia (X*X) or carrier (X*X)	Can be affected by haemophilia, 100% chance carrier

Transmission of haemophilia in females: rare and extremely rare cases

Parents	Daughter's inheritance	Likelihood of gene transmission
Spontaneous Mutation	Haemophilia (X*X*) or spontaneous mutations only in one X chromosome (X*X)	The condition of (X*X*) is rare - where one mutation is inherited and the second is de novo. If both mutations are de novo - extremely rare.
Carrier (X*X) + skewed X-Inactivation	Inheritance unpredictable. Mild Symptoms (X*X) while in cases of extremely skewed inactivation of non-mutated X, the woman may have severe or moderate haemophilia even in the presence of a single mutated gene	Unpredictable, depends on the X-inactivation balance
One X-chromosome from an affected parent and the other one from a de novo mutation	Inheritance unpredictable. Moderate or severe symptoms	Unpredictable
X-chromosome abnormalities such as monosomy X (Turner syndrome, 45 X)	Inheritance unpredictable. Can be mild, moderate or severe	Unpredictable

Carriers or patients?

Due to X-linked inheritance, the diagnosis of haemophilia is traditionally assigned to males, with the misconception that female carriers are unaffected. However, **up to 30% of carriers** have reduced factor levels and haemophilia. Moreover, there is increasing evidence of an elevated bleeding tendency in haemophilia carriers, even in the presence of normal factor VIII/IX levels. As the term "haemophilia carriers" focuses on risk to their offspring, it can hamper diagnosis, clinical care, and research for the affected women.[2]

In 2021, the International Society on Thrombosis and Hemostasis (ISTH) Scientific and Standardization Committee (SSC) approved a new nomenclature[3] that defines five clinical categories for women who carry haemophilia in their FVIII/FIX genes. This nomenclature accounts for personal bleeding history and baseline plasma FVIII/IX level.

2021

New nomenclature to define five clinical categories of female haemophilia carriers

[2] van Galen KPM, d'Oiron R, James P, et al. . A new hemophilia carrier nomenclature to define hemophilia in women and girls: communication from the SSC of the ISTH. J Thromb Haemost. 2021;19(8):1883-1887. - PMC - PubMed

[3] Ibid.

Similar to males, with reduced levels (<0.40 IU/ml) women are now characterised as having haemophilia:

1. Women and girls with **mild haemophilia** (FVIII/IX >0.05 and <0.40 IU/ml)
2. Women and girls with **moderate haemophilia** (FVIII/IX between 0.01–0.05 IU/ml)
3. Women and girls with **severe haemophilia** (FVIII/IX <0.01 IU/ml)

Two additional new categories were added to recognise that haemophilia carriers may still be at risk of bleeding:

4. **Symptomatic haemophilia carriers** (FVIII/IX ≥0.40 IU/ml with a bleeding phenotype)
5. **Asymptomatic haemophilia carriers** (FVIII/IX ≥0.40 IU/ml without a bleeding phenotype)

Female patients with FVIII or FIX levels <0.40 IU/mL should be considered and managed as any other persons with haemophilia. Clinicians should be aware that bleeding may also occur in carriers with FVIII/FIX levels of ≥0.40 IU/mL, with an impact on their health-related quality of life.

Global Perspective

While haemophilia is rare in women, with a global population of 4 billion males and 3.95 billion females, **there are over 1 million females predicted to be affected by haemophilia worldwide.**[4]

In the 2023 World Federation of Hemophilia (WFH) Report on the Annual Global Survey[5] on a total number of around 390,630 persons with haemophilia only 2.41% (9,416) worldwide were female.

However, under the new ISTH SSC nomenclature, 28% of females are expected to have levels < 40 IU/dL and a diagnosis of haemophilia, while more than a quarter of females with normal factor levels will have significant bleeding and meet the criteria for the symptomatic carrier.

Global Context

The prevalence of haemophilia among women and girls is significantly lower than in men. The exact numbers are challenging to determine due to underreporting and overlooked or delayed diagnoses. Many women and girls with mild forms of haemophilia or those who are carriers may not be diagnosed, leading to underrepresentation in registries*.

* Important: Registries in different countries may have varying inclusion criteria, impacting the data. Careful consideration is required before analysing and comparing the data.

Approximately 20-30% of girls and women who are carriers have reduced clotting factor levels. Approximately 10–30% of them experience bleeding symptoms ranging from mild to severe.

4 Women and girls with inherited bleeding disorders: focus on haemophilia carriers and heavy menstrual bleeding. Hermans C, Johnsen JM, Curry N. Haemophilia. 2024;30:45–51. - PubMed

5 Annual Global Survey 2023. World Federation of Hemophilia. 2023:14-15 - WFH

Symptoms

Although men/boys and women/girls with haemophilia and symptomatic carriers have similar symptoms, such as bleeding into joints and tissues, and excessive bleeding from invasive procedures or injuries, women can experience additional gender-related complications during menstruation, pregnancy, labour, and delivery. Some clinicians are not familiar with bleeding disorders in women, resulting in many women and girls going undiagnosed or experiencing delays in diagnosis. This may result in undertreatment and poor quality of life.

For women and girls, heavy menstrual bleeding is the most common bleeding symptom.

Bleeding in Symptomatic Carrier Females and Women and Girls with Haemophilia

- Easy bruising
- Spontaneous bleeds
- Heavy or prolonged menstrual bleeding (menorrhagia) - **use the 7-2-1- rule to assess your bleeding.** Available in different languages[6]. Heavy menstrual bleeding often has an underrated impact on the quality of life
- Excessive bleeding after injuries, surgeries, or childbirth
- Frequent nosebleeds (epistaxis)
- Spontaneous joint bleeds (hemarthrosis), similar to those seen in males with haemophilia
- Internal bleeding
- Fatigue
- Iron deficiency/anaemia
- Others

Recording your bleeding symptoms can help you get diagnosed! To assess normal/abnormal bleedings use ISTH-SSC Bleeding Assessment Tool[7]

Female carriers may have no bleeding abnormalities: a majority of women and girls carrying the affected haemophilia gene do not express low levels nor bleeding symptoms. However, it is important to understand that men and women with the same factor level may have **different quality of life** due to menstrual bleeding in females.

Note: Zero annualised bleeding rates (ABRs) are unachievable in most female carriers and women with haemophilia of reproductive age because monthly menstruation is normal and physiological.

6 Women and Bleeding Disorders Focus Area - EHC Community website

7 Rodeghiero F et al. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. J Thromb Haemost 2010; 8: 2063-2065 (plus supplementary material) - ISTH-SSC Bleeding Assessment Tool

Important to know

Diagnosis in girls has to occur during childhood in order to be prepared for menarche and potential abnormal uterine bleeding.

Although genetic testing is not always performed at a young age, it is important to conduct an assessment of factor levels and evaluation of bleeding symptoms at a young age so as not to miss the follow-up of menarche (the first menstrual period).

Some carriers may not be aware of their condition until they experience excessive bleeding during medical procedures, childbirth, or injuries.

Screening of clotting factor levels can help identify carriers at risk of symptoms and allow for preventive measures.

Factor levels in blood tests may be different depending on the day of the cycle when testing. Always talk to your clinician for interpretation of the blood test results.

For FVIII level interpretation, it is important to know your blood type, group, and history of any recent inflammations. Always talk to your clinician for interpretation of the blood test results.

Emergency Preparedness

Women with haemophilia in the emergency room (ER) should be prepared to advocate for themselves, as their condition is often underrecognised. Advocate for yourself confidently but respectfully to ensure your needs are met in the ER.

1. **Clearly Explain Your Condition** – Inform the ER team that you have haemophilia and describe past bleeding episodes or treatments received. In the case of non-diagnosed women, report to the ER team your family bleeding disorders history - it is not rare to have women with haemophilia in families with haemophilia.

2. **Carry Medical Documentation** - Have a medical alert card, emergency letter from your haematologist, or digital records detailing your diagnosis and treatment plan.

3. **Request a Haematology Consult** – If the ER team is unfamiliar with haemophilia in women, ask for a haematologist to be consulted. Give the contact details of your haemotologist to the ER team.

   Note that factor levels in the ER are always higher due to acute stress response (FVIII), inflammation, infection, or overall dehydration and hemoconcentration!

4. **Advocate for Proper Testing & Treatment** – Ensure that appropriate treatment is administered promptly.

5. **Know Your Medications** – Be aware of your prescribed treatment plan. Tell the ER team about any medication you are taking.

6. **Avoid Certain Medications** – Medications like aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) - e.g., ibuprofen and naproxen- can worsen bleeding and should be avoided unless approved by your doctor.

7. **Follow Up After Discharge** – Arrange a follow-up with your haematologist after any ER visit to ensure proper ongoing care.

Emergency Room Checklist for Women with Haemophilia

Before an Emergency Happens

- Carry a **medical alert card or bracelet** indicating haemophilia (in case they are available in your country).
- Keep an **emergency letter** from your haematologist detailing your diagnosis and treatment plan.
- Know your **clotting factor levels** and treatment options.
- Have a list of **safe and unsafe medications.**
- Store **emergency medication** (if prescribed) at home and know how to use it.

At the Emergency Room

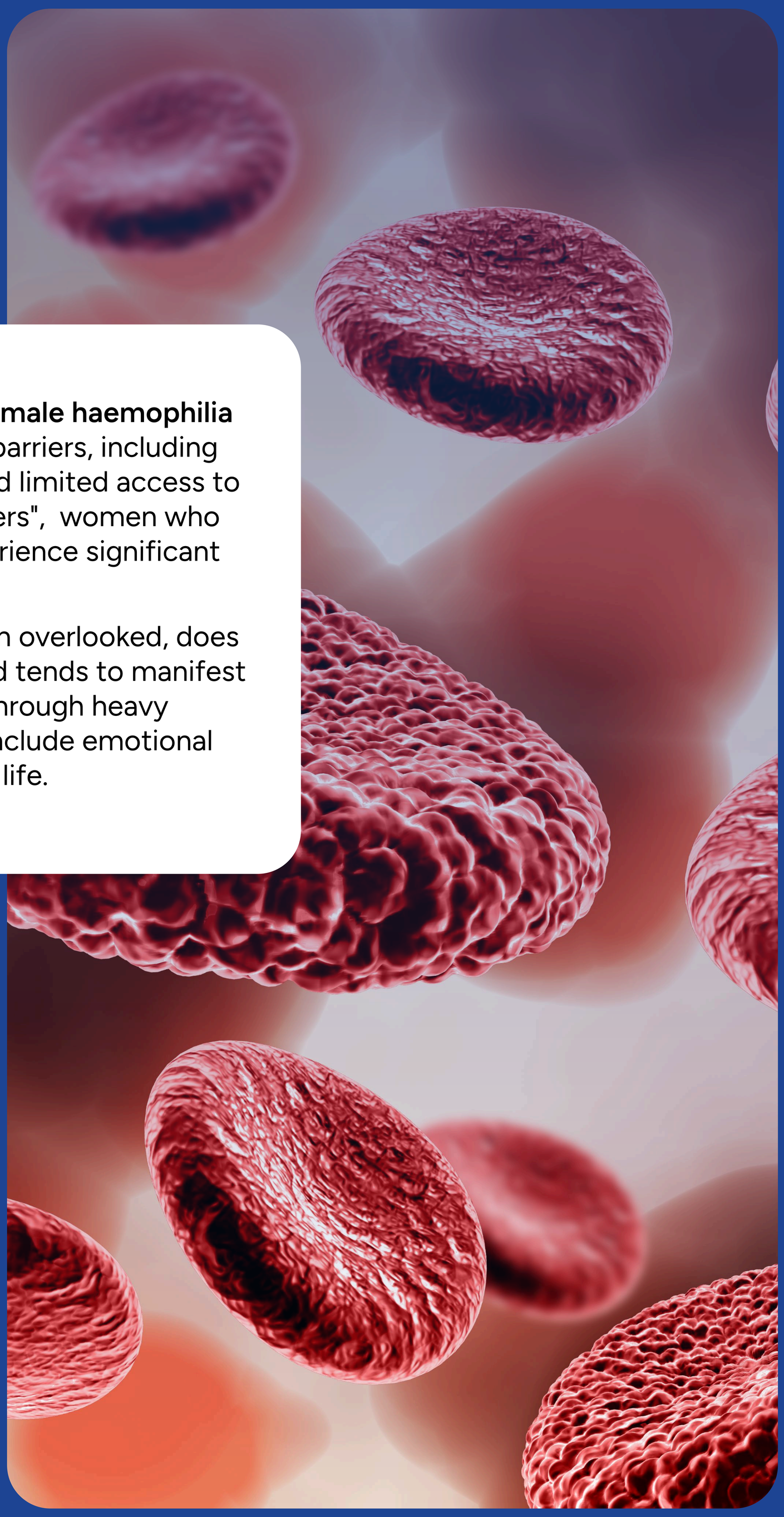
- Inform staff immediately: **"I have haemophilia, and I may need specialised treatment."**
- Show your **medical documentation** to ensure proper care.
- Request a **haematology consult** if the ER staff seem unfamiliar with haemophilia in women. Give the contact details of your haematologist to the ER staff.
- Ensure doctors check for **internal bleeding** (e.g., joints, muscles, gastrointestinal, reproductive).
- Ask for **appropriate blood tests**.
- Confirm **treatment is provided promptly**, especially after injury, surgery, or unexplained bleeding.

After Discharge

- Schedule a follow-up with your **haematologist** to review ER treatment and next steps.
- Monitor for **delayed bleeding symptoms** and return to the ER if needed.
- Rest and recover according to the **doctor's instructions** to prevent re-bleeding.

This checklist can help ensure that women with haemophilia receive the proper care in an emergency.
Keep a copy in your wallet or phone for quick reference.

Taking Action



Women and girls with haemophilia and female haemophilia carriers often face significant healthcare barriers, including lack of recognition, delayed diagnoses, and limited access to care. While traditionally seen as "just carriers", women who inherit haemophilia genes frequently experience significant bleeding and low factor levels.

However, bleeding in such females is often overlooked, does not always correlate with factor levels, and tends to manifest differently than in males—most notably through heavy menstrual bleeding. Symptoms can also include emotional distress, which can impact their quality of life.

Even though recent changes now allow for the diagnosis of haemophilia in females with low factor levels and differentiate between symptomatic and asymptomatic haemophilia gene carriers, raising awareness, improving diagnosis, ensuring accurate classification, and expanding access to emerging treatments remain key.

Policy & Research Needs

The EHC advocates for the EU Strategy for Women's Health aimed at ensuring equal access to healthcare for men and women with haemophilia and dedicated resources to address the unique needs of women and girls dealing with haemophilia, ultimately leading to improved care and quality of life [8]

Furthermore, the EHC calls for a comprehensive EU Plan on Rare Diseases to enhance access to care and treatment for all people living with rare conditions, while also addressing the specific needs of women and girls with bleeding disorders.

To advance the care and management of women and girls with haemophilia and female carriers, it is essential to prioritise their inclusion in clinical research, improve diagnostic accuracy, and establish standardised treatment protocols. Healthcare professionals, researchers, and policymakers must collaborate to ensure equitable access to care, addressing both the physical and psychosocial challenges faced by affected women. Stakeholders should work together to support evidence-based policy changes and enhance education on the unique manifestations of haemophilia in women. A concerted effort is required to close existing gaps and improve health outcomes for this underrepresented population.

8 Van Galen K, Lavin M, Skouw-Rasmussen N, et al. European principles of care for women and girls with inherited bleeding disorders. Haemophilia. 2021;27(5):837-847. - PubMed

EHC

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Contact Information

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