HEREDITARY FACTOR X DEFICIENCY (HFXD)

One of the most severe bleeding disorders[1]

Unique severity classification[1]

"Due to the critical role that factor X plays in the coagulation cascade, factor X deficiency is associated with a higher risk of bleeding than deficiencies in other coagulation factors."

- Tarantino MD. *Haemophilia.* 2021;27(4):531-543.

John – Actual patient, diagnosed with severe HFXD at 1 year of age

- Treated on-demand but continued with **pain and frequent muscle/joint bleeds**
- Experienced **cardiac bleed** as adult
- Reported **>150 hospitalizations** for bleeds and/or treatment
- Sustained **severe joint damage,** requiring **total hip replacement** at age 29

Hazel – Actual patient, diagnosed with severe HFXD at age 6 years

- Symptoms prior to diagnosis included **recurrent ankle bruising** with **pain/swelling,** and **abnormal bleeding** after forehead and lip injuries
- Treatments for **misdiagnoses** included multiple **X-rays, splints, and casts. Stroller** was still required at age 5 due to ankle pain

Symptoms of Hereditary Factor X Deficiency (HFXD)

HFXD symptoms can vary and may present across the lifespan[1,2]

Prompt diagnosis and appropriate treatment may help prevent permanent impairment or mortality

In a U.S. survey, 4 years was the mean age at diagnosis of HFXD[3]

Even people with severe HFXD may be undiagnosed as infants, waiting years for proper diagnosis and treatment

John
Actual Patient with Severe HFXD

Diagnosed at 1 year of age

Hazel
Actual Patient with Severe HFXD

HFXD first identified by dentist at age 6 years

Name/photo changed for privacy

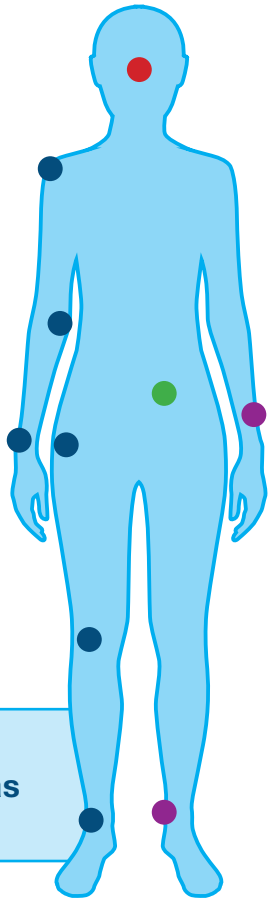
Fernando
Actual patient with Severe HFXD

Endured 25 years of pain, bruising, ad hemarthrosis before diagnosis as adult when an accident caused an ICH and he was hospitalized

Bleed Occurrence In HFXD*[2,4]

Out of 102 people identified with confirmed HFXD, only 42 were symptomatic. Within the symptomatic group:

- The most frequent bleeding symptoms observed were **easy bruising, 23 (55%) and haematoma, 18 (43%)**
- Of those that experienced an **ICH or GI bleed,** these occurred within the **first days after birth** (1–27 days, median 9.7 days)



- Intracranial hemorrhage (ICH) - 21%
- Epistaxis - 36%
- Hemarthrosis - 33%
- Gums - 31%
- Hematomas - 43%
- Gastrointestinal (GI) - 12%
- Easy bruising - 55%

CAN OCCUR ANYWHERE IN BODY

- Excessive bleeding after injury

Symptoms such as joint pain or swelling may be misdiagnosed as arthritis or sprains

*Refers to data collected from one series of patients from three Central European and two Latin American countries in a 2006 study; numbers reflect characterization of the 42 symptomatic patients out of 102 total subjects with confirmed reduced FX activity and identified F10 gene causative mutations (<50% of the sample were symptomatic).

For general guidance only; symptoms in individuals may vary and can occur at any age

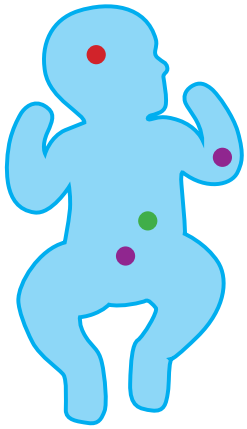
HFXD in Special Populations

Bleeding may start at any age and HFXD may create unique problems for special populations[2]

Neonates[1,4]

Neonates with HFXD can be at high risk for severe, life-threatening bleeds, including intracranial hemorrhages (ICH)

- ICH due to HFXD:
  - Occurs most commonly in the neonatal age group
  - Is likely to recur and be spontaneous



Unique signs in neonates

- Abnormal bleeding from the umbilical stump or circumcision site
- Abnormal bruising or bleeding
- Intracranial hemorrhage (ICH)
- Gastrointestinal (GI) bleeding

Carly
Mother of Actual Patient with Severe HFXD

Carly's child was diagnosed following ICH at birth and had recurrent ICH at 5 weeks, resulting in developmental challenges

Women and Girls[5,6]

An estimated 1 in 5 women and girls experience heavy menstrual bleeding, and among those, **about 1 in 4 have a bleeding disorder.** Females face additional bleeding risks as they enter reproductive age:

- Menorrhagia
- Pregnancy and childbirth complications, including:
  - Miscarriage
  - Uterine bleeding
  - Postpartum hemorrhage
  - Preterm labor

Name changed for privacy

Olivia
Actual Patient with Severe HFXD

Diagnosed as neonate and did well on prophylaxis until menarche, when menorrhagia "spiraled everything out of control"

HFXD, hereditary factor X deficiency

For general guidance only; symptoms in individuals may vary and can occur at any age

HFXD Baseline Severity Classification

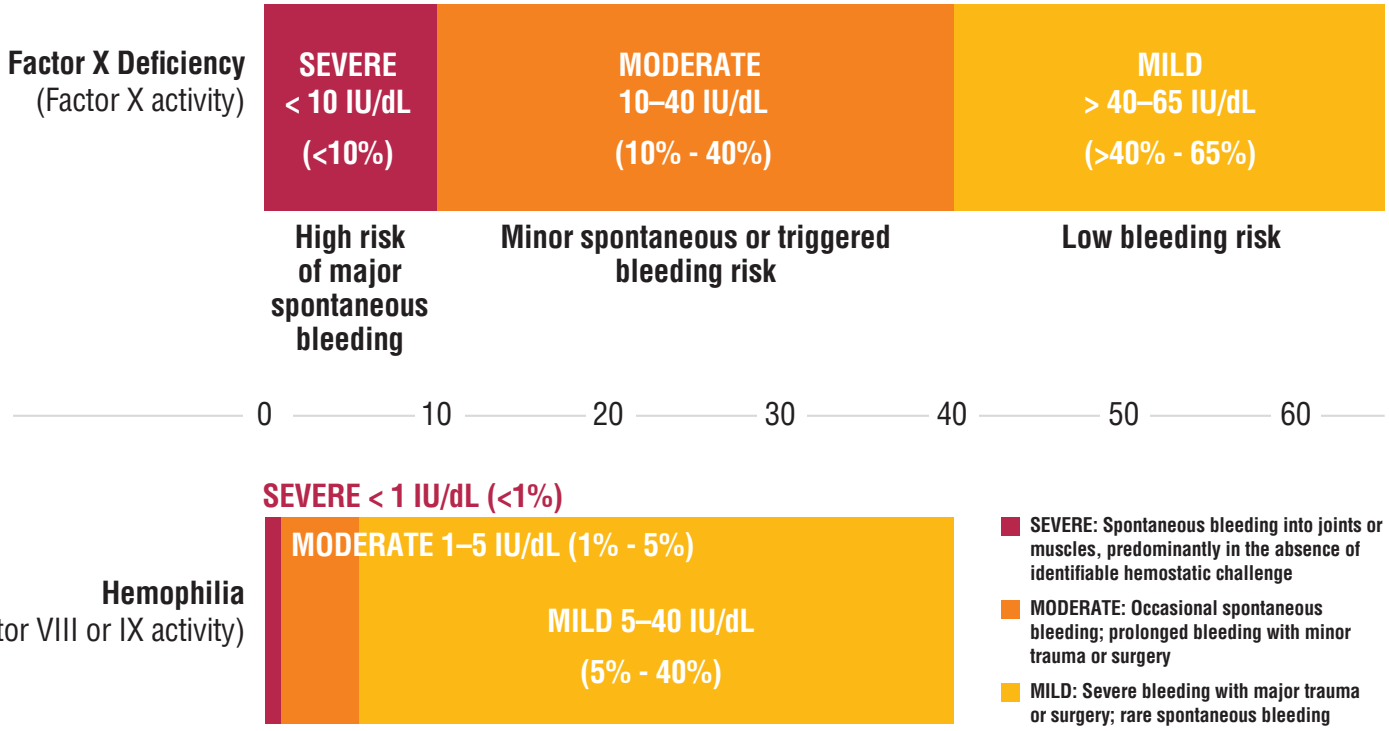
Understanding HFXD baseline severity classification and how it differs from hemophilia[7-10]

Factor X Baseline Severity Classification[7]

Determines bleeding risk based on baseline factor X activity (without treatment)

Based on analysis of registry data from the European Network of Rare Bleeding Disorders (EN-RBD) Group; included 45 patients with factor X deficiency out of 592 total patients with a rare bleeding disorder and a mean age of 31 years.[7,8]

Baseline Severity Classification –
Bleeding Risk Ranges for Factor X Deficiency and Hemophilia A[7-10]



Factor X severity classification ranges differ markedly from hemophilia[7-10]

HFXD, hereditary factor X deficiency

HFXD Clinical Bleeding Severity

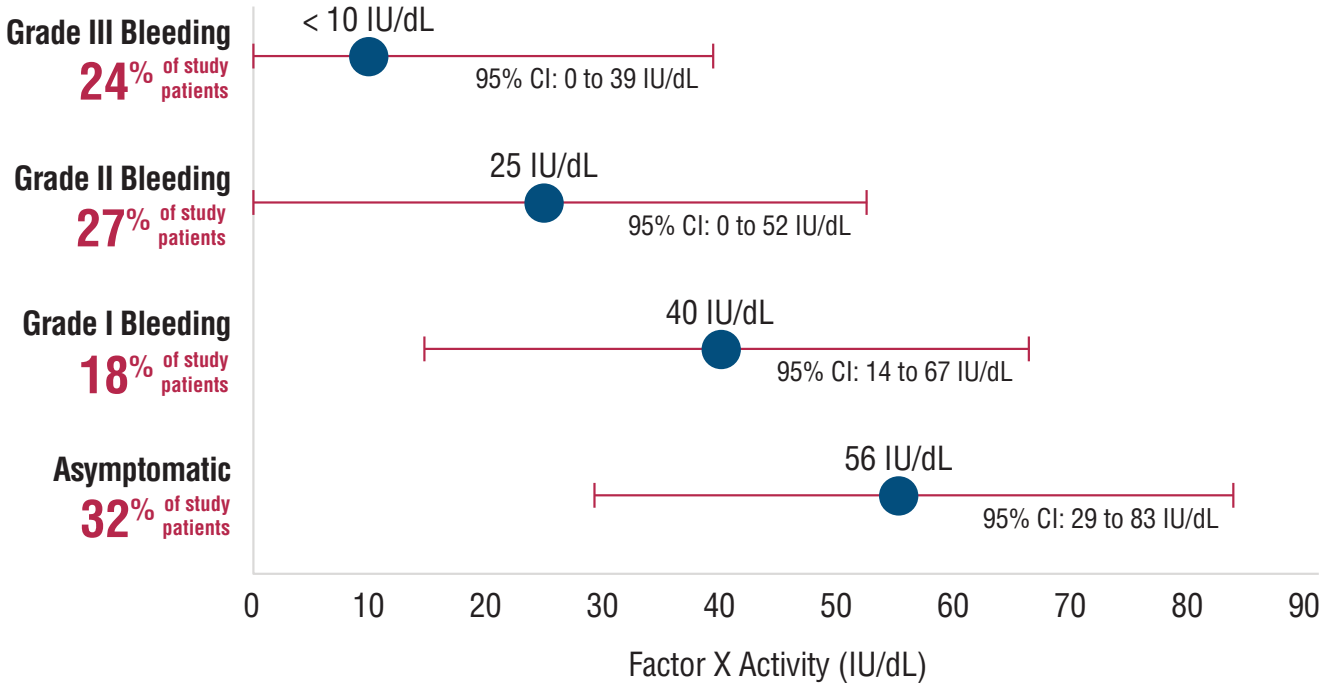
Understanding HFXD clinical bleeding severity grades[8]

Factor X Clinical Bleeding Severity[8]

Assigns clinical bleeding grade based on documented bleeds*

From a cross-sectional study using EN-RBD data from 34 patients with hereditary factor X deficiency.[8]

Clinical Bleeding Severity Grades and Factor X Activity[2]
(mean, 95% confidence interval [CI])



Grade III: Spontaneous major bleeding—hemarthrosis, CNS, GI, umbilical cord, intramuscular hematomas requiring hospitalization.
Grade II: Spontaneous minor bleeding—bruising, ecchymosis, minor wounds, oral cavity, epistaxis, menorrhagia.
Grade I: Bleeding after trauma or drug ingestion (antiplatelet or anticoagulant therapy).
Asymptomatic: No documented bleeding episodes.

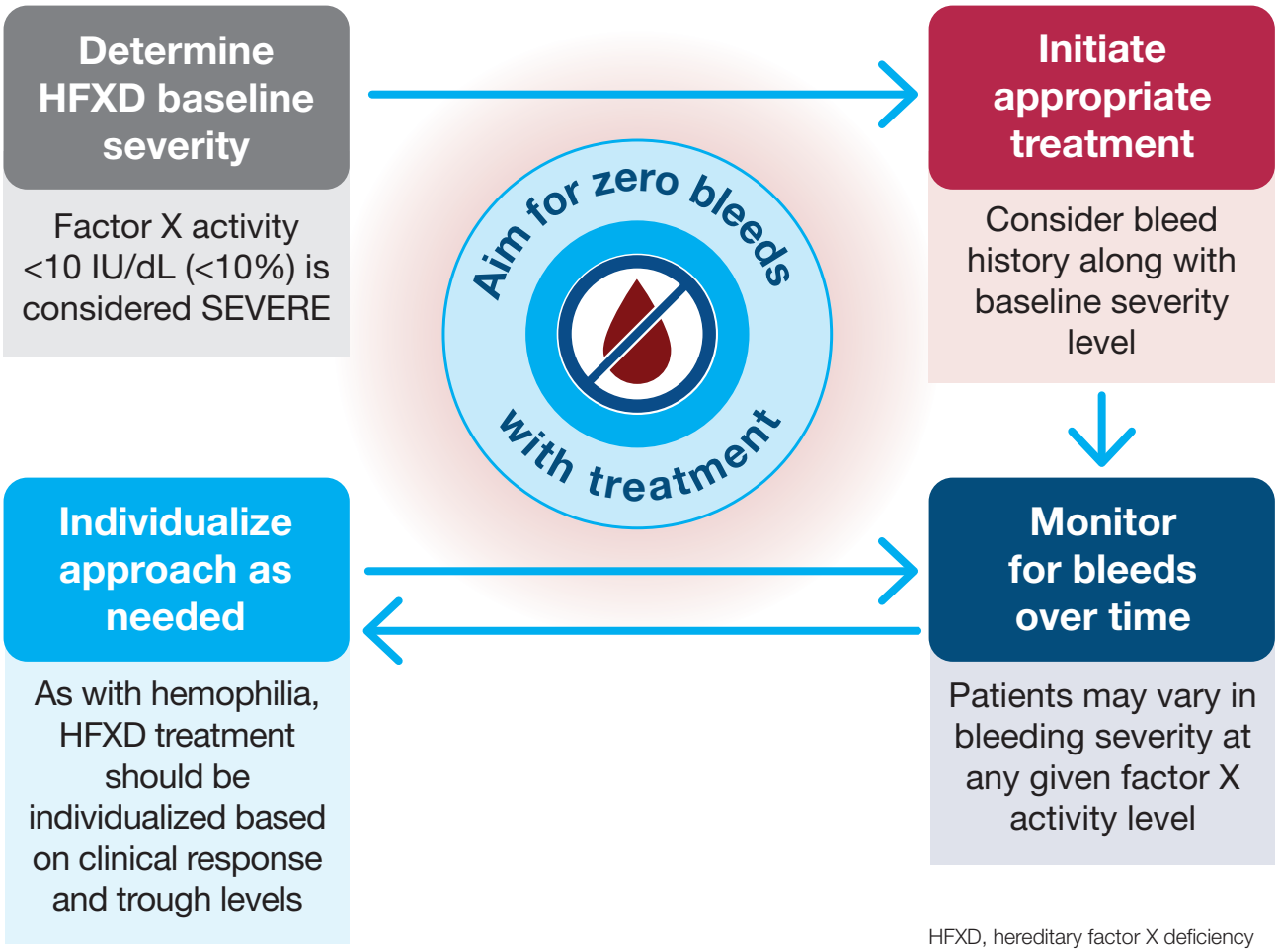
Clinical bleeding severity strongly correlates with factor X activity level[8]

However, patients may vary in their bleed severity relative to factor X activity level, so ongoing monitoring for bleed occurrence is crucial[8]

*Bleeding episodes were classified into four bleeding severity categories relying on bleed location, potential clinical impact, and spontaneity; patients were assigned to a category if they had at least one documented bleeding episode matching the defined bleeding severity and no episode matching the higher severity grade. Linear regression analysis was performed, adjusting for age at data collection, sex, and center where diagnosis was made.

HFXD, hereditary factor X deficiency

The HFXD management approach should be similar to that of hemophilia[7,8,10]



HFXD, hereditary factor X deficiency

Key Insights from Hemophilia Guidelines May Guide the Management of HFXD[10]

Aim for zero bleeds.

- Preventing bleeds in hemophilia can help prevent musculoskeletal damage, pain, and other outcomes including disability or death

Monitor for bleeds over time.

The hemophilia guidelines caution against a "wait and see" approach for bleeds

- Waiting may lead to onset and progression of bleeding symptoms with resulting pain and/or joint damage
- Even a single joint bleed can lead to arthropathy
- Unchecked, hemarthrosis can progress to ultimately manifesting as joint destruction

Management of HFXD should aim for zero bleeds, while incorporating an understanding of baseline severity, individual patient characteristics, and clinical response

References: 1. Tarantino MD. *Haemophilia.* 2021;27(4):531-543. **2.** Peyvandi F, et al. *Blood Reviews.* 2021;50:100833. **3.** Branchford B, et al. *Blood Coagul Fibrinolysis.* 2024;35(3):73-81. **4.** Herrmann FH, et al. *Haemophilia.* 2006;12:479-489. **5.** Byams V, et al. *J Women's Health*. 2022;31(3):301-309. **6.** Shapiro A. *Expert Opin Drug Metab Toxicol.* 2017;13(1):97-104. **7.** Peyvandi F, et al. *J Thromb Haemost.* 2012;10:1938-1943. **8.** Peyvandi F, Palla R, et al. *J Thromb Haemost.* 2012;10:615-621. **9.** Peyvandi F, et al. *Brit J Haematol.* 1998;102:626-628. **10.** Srivastava A, et al. *Haemophilia.* 2020;26(Suppl 6):1-158. doi: 10.1111/hae.14046.

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