Classification at the Border

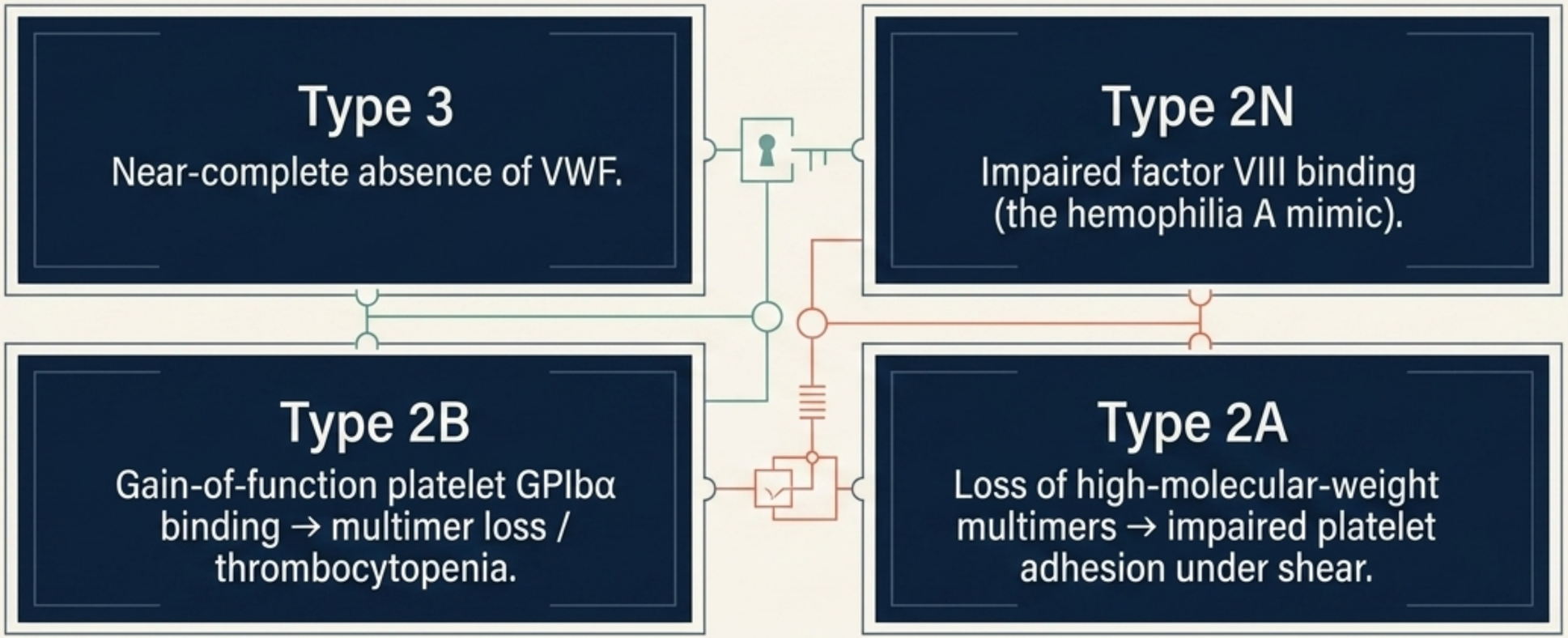
Why classification names mechanism at the center and organizes probability at the border

At the center, classification names mechanism.

At the border, classification organizes probability.

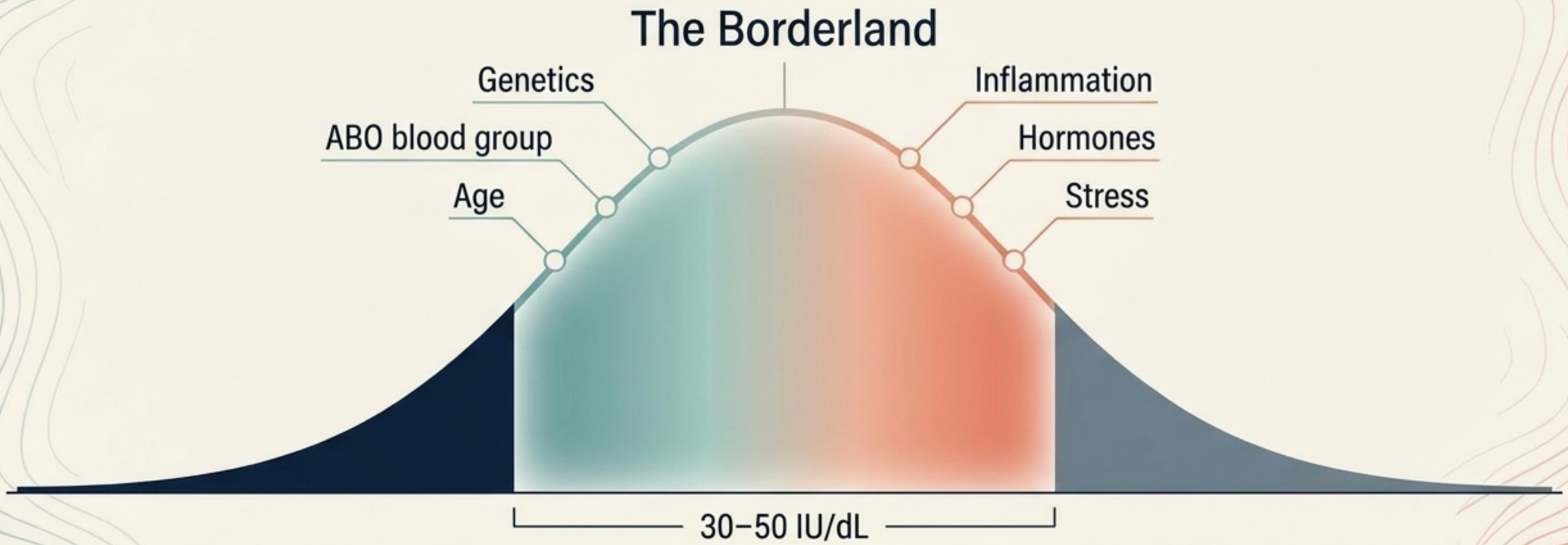
Laboratory thresholds must do work they were never biologically designed to do. The center-to-border distinction is not a cliff. It is a gradient.

Where classification works seamlessly, the label names a distinct biological failure



In these settings, the subtype does not merely describe a laboratory pattern. It explains why the pattern exists.

Biology is continuous, but clinical care requires decisions

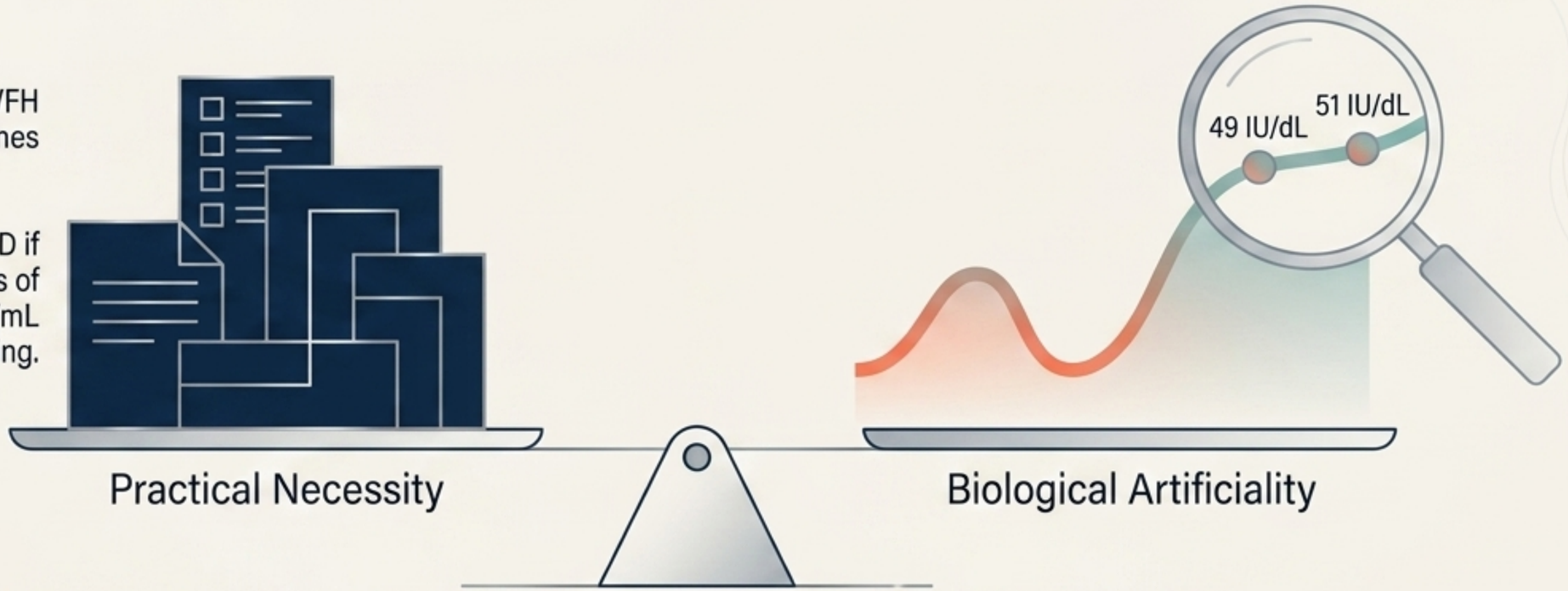


There is no natural cliff between normal VWF, low VWF, and mild type 1 VWD. In this broad middle zone, the number must be interpreted rather than simply obeyed.

Thresholds are necessary for standardization, but they are not nature

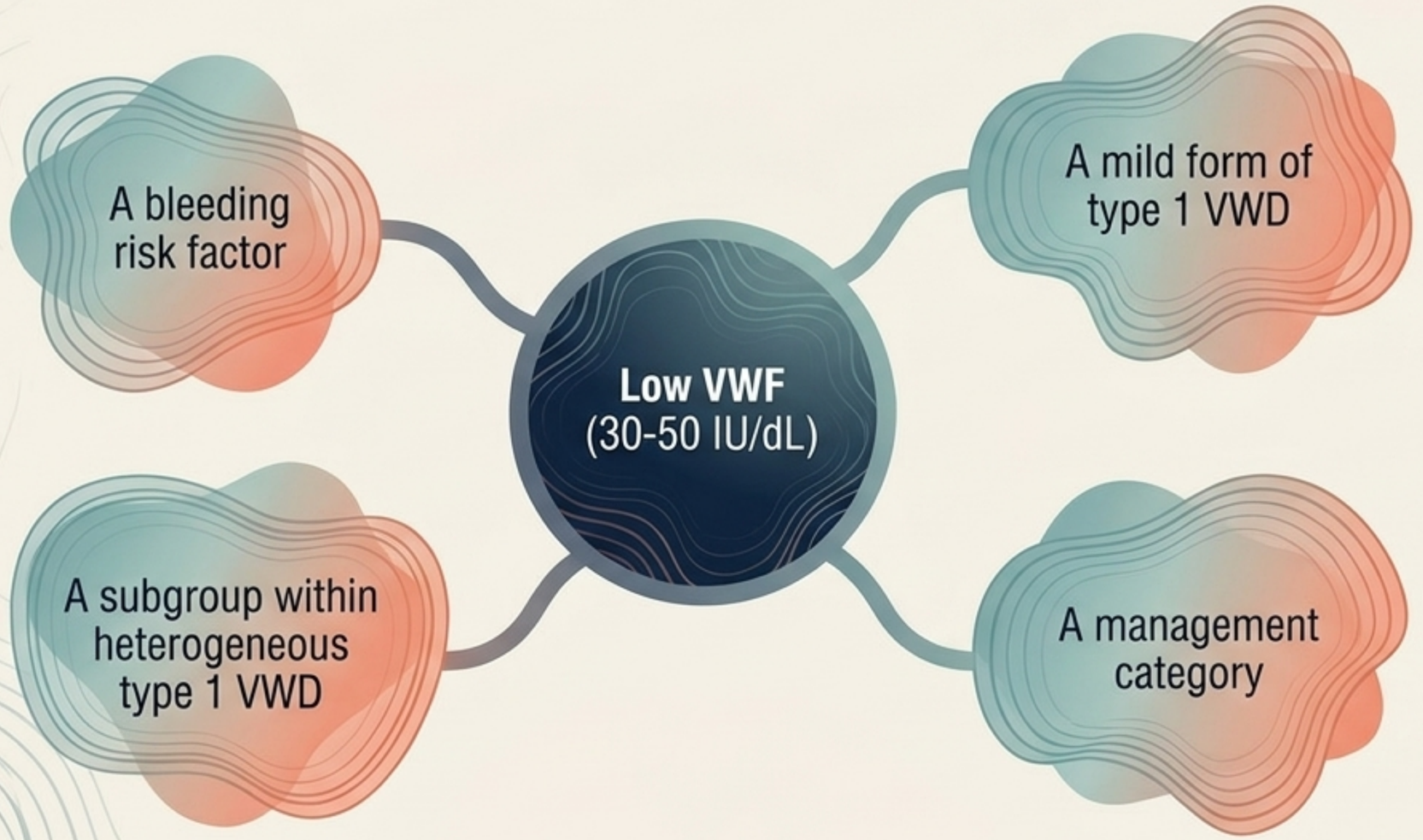
2021 ASH/ISTH/NHF/WFH Guidelines

Diagnose Type 1 VWD if <0.30 IU/mL regardless of bleeding, or <0.50 IU/mL with abnormal bleeding.



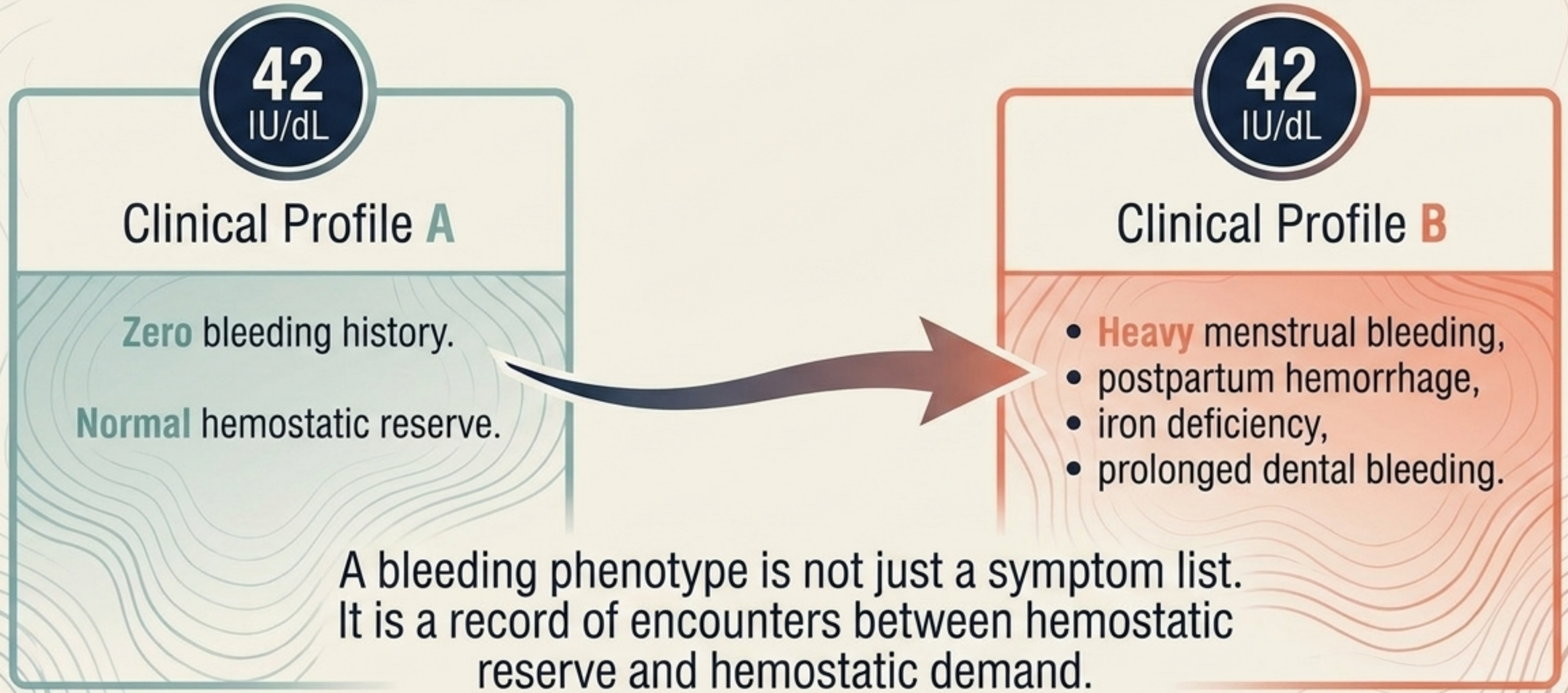
A VWF level of 49 IU/dL is not biologically transformed by becoming 51 IU/dL. The number matters, but it does not carry the whole diagnosis.

The fragmented taxonomy of the 30–50 IU/dL borderland



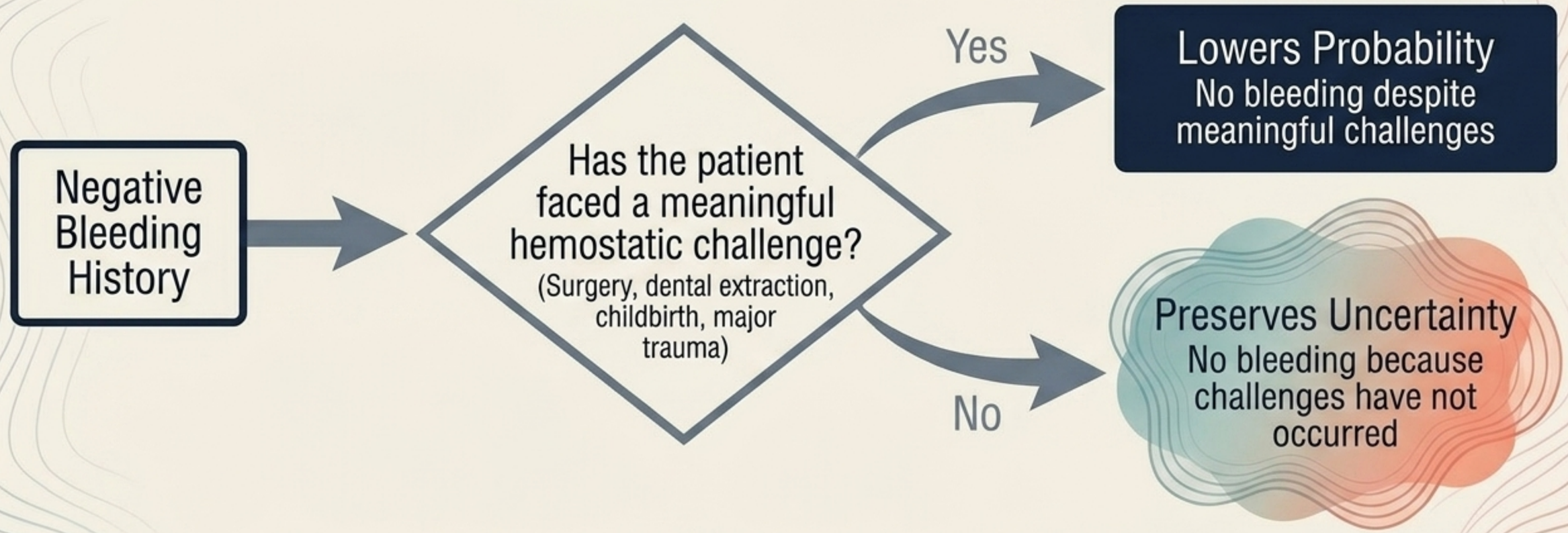
Compared to severe VWD, this range has fewer pathogenic VWF variants, unclear inheritance, and high interference from ABO blood group and hemostatic modifiers.

The number may be similar.
The probability is not.



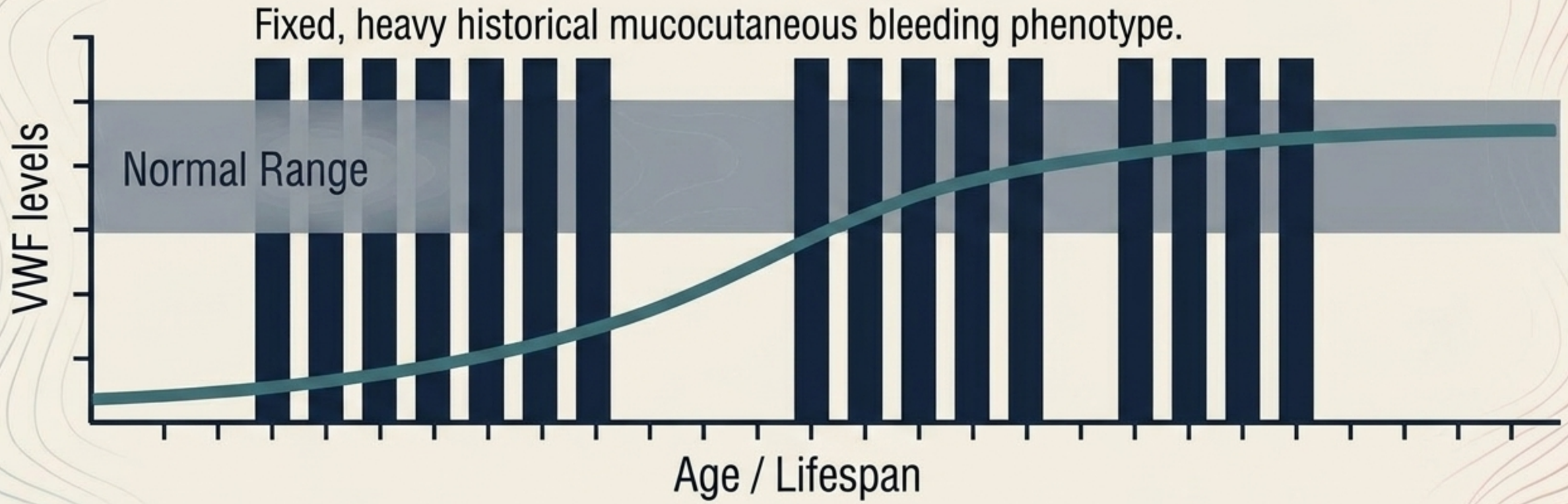
A bleeding phenotype is not just a symptom list.
It is a record of encounters between hemostatic reserve and hemostatic demand.

The problem of the untested hemostatic challenge



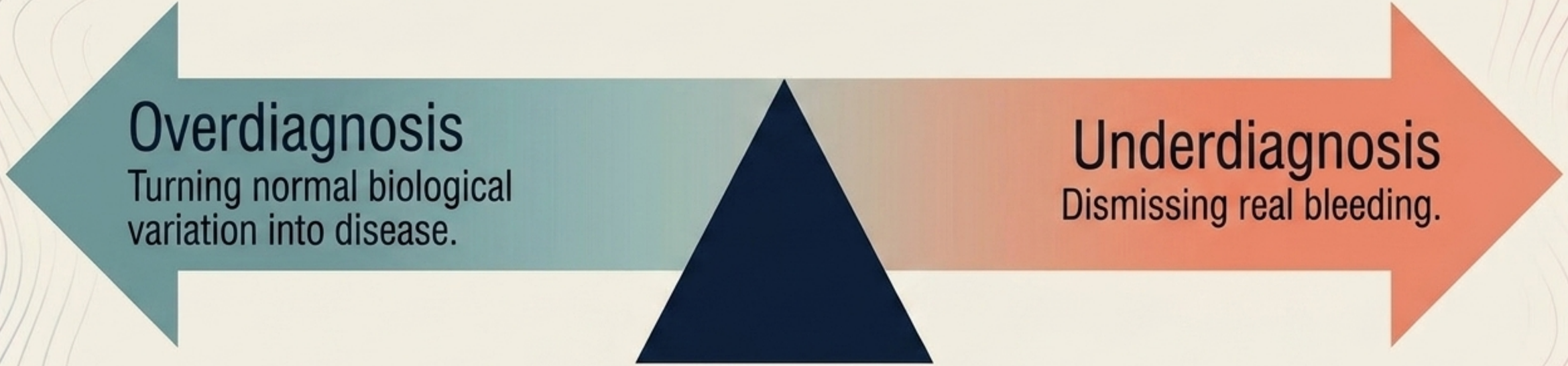
In untested patients (e.g., a child with mild epistaxis, or a young man avoiding major procedures), classification must remain provisional.

Has the diagnosis disappeared, or has the laboratory value changed?



VWF levels often rise with age. The current level matters for current management. The historical phenotype matters for interpretation. Both can be true.

The dual dangers of the borderland



- Unnecessary medicalization
- Patient anxiety
- Distorted family interpretation
- Unneeded treatment

Clinical Judgment: Asking how well the whole pattern fits.

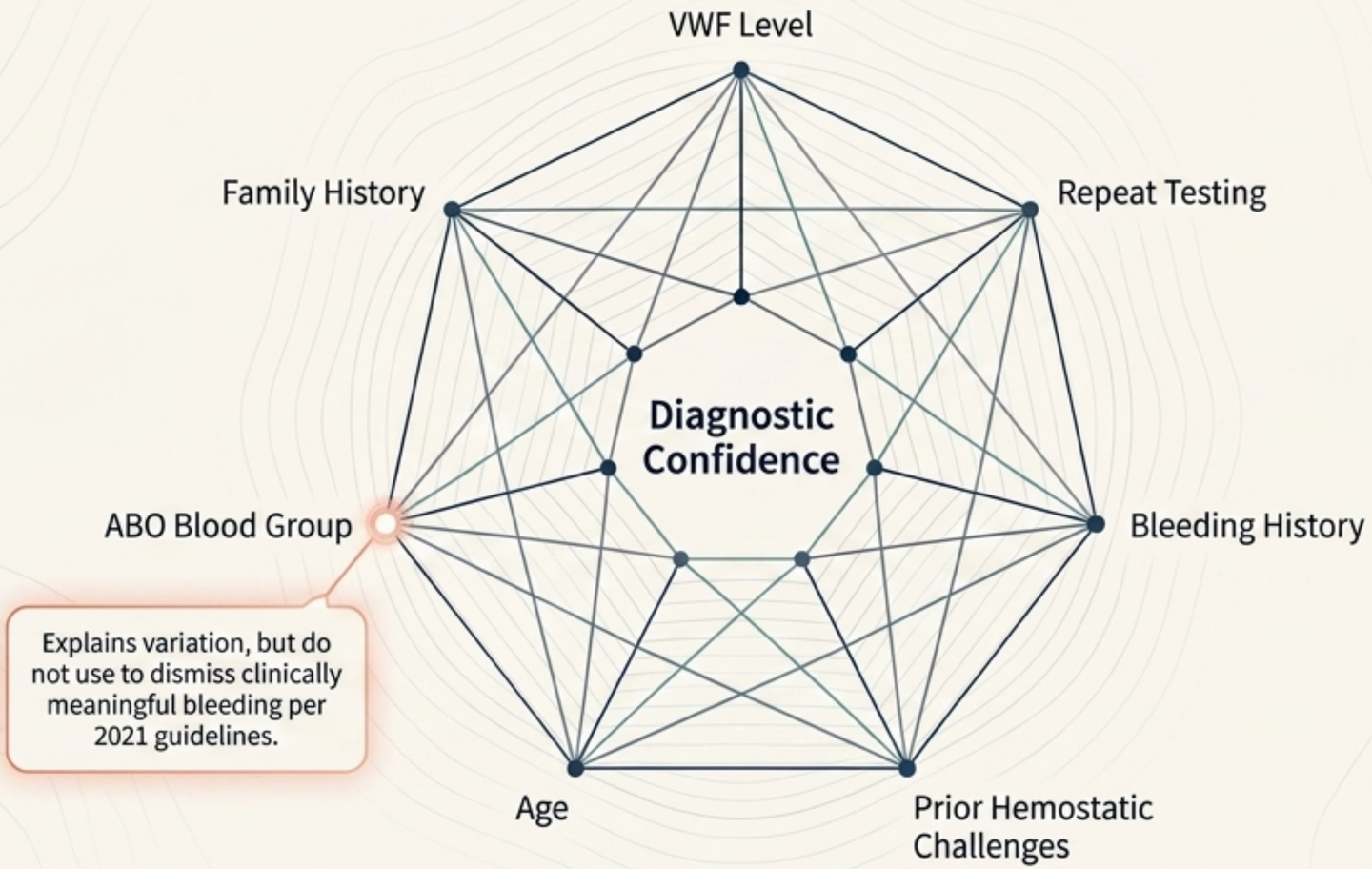
- Untreated heavy menstrual bleeding
- Missed iron deficiency
- Failure to plan for surgery/childbirth

The evidence anchor: Why the border is difficult

Evidence Stream	What it shows	Why it matters
Population	Levels vary continuously	No natural biologic cliff exists.
Genetic	Pathogenic variants rare in 30-50 range	Deficiency is genetically heterogeneous.
Bleeding Cohorts	Referred patients still bleed	Mild lab abnormalities still matter clinically.
Correlation	Severity correlates poorly with absolute VWF	Phenotype cannot be read from the number alone.

The question is not just whether the VWF level is low, but whether the overall pattern supports clinically meaningful VWF-mediated bleeding.

Navigating probability requires weighing a constellation of variables



The diagnosis is strongest when elements align. It is weakest when it rests on a single borderline value without bleeding, without repeat testing, and without a challenge history.

Clinical Application: The Patient Profile

Patient ID: 42-year-old woman.

Phenotype

- Heavy menstrual bleeding since menarche
- Postpartum hemorrhage (first delivery)
- Prolonged bleeding after wisdom tooth extraction
- Easy bruising
- No major surgery other than childbirth
- Iron deficiency

Laboratory Pattern

- VWF antigen: 42 & 46 IU/dL
- Platelet-dependent VWF activity: 39 & 44 IU/dL
- FVIII: mildly reduced
- Ratio: preserved
- Multimers & platelets: normal
- No pathogenic variant identified

The 2021 Guideline View

VWF < 0.50 IU/mL + abnormal bleeding =

Diagnosis: Type 1 VWD

The Biological Reality View

Preserved ratio/multimers = partial quantitative pattern.

Older frameworks call this Low VWF.

Absence of identified variant does not exclude meaningful bleeding in the 30-50 range.

The point is not that one label solves the case. The point is that the label organizes the probability of future bleeding and the need for procedural planning.

At the border, classification is not a verdict. It is a structured way to think.