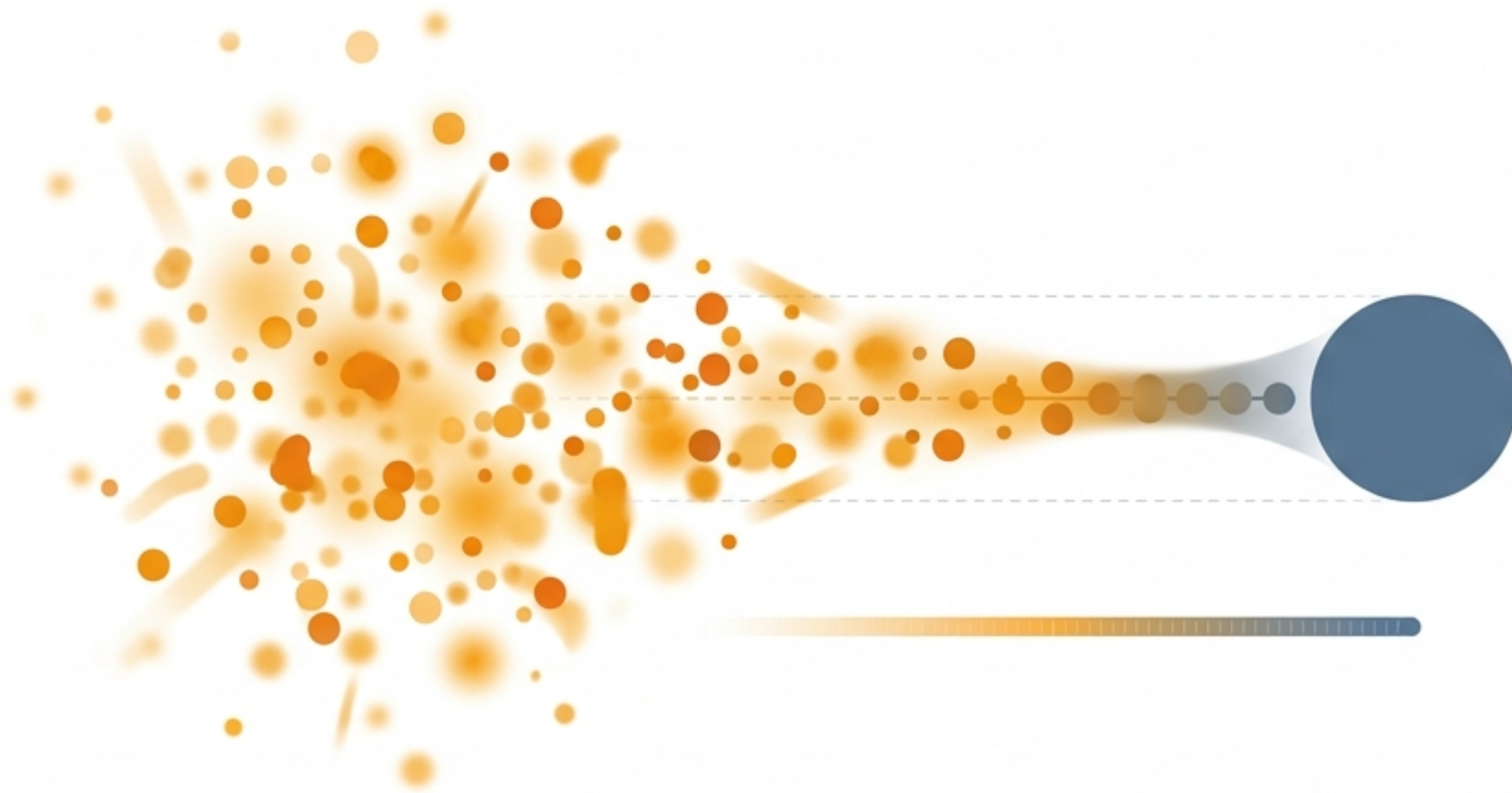
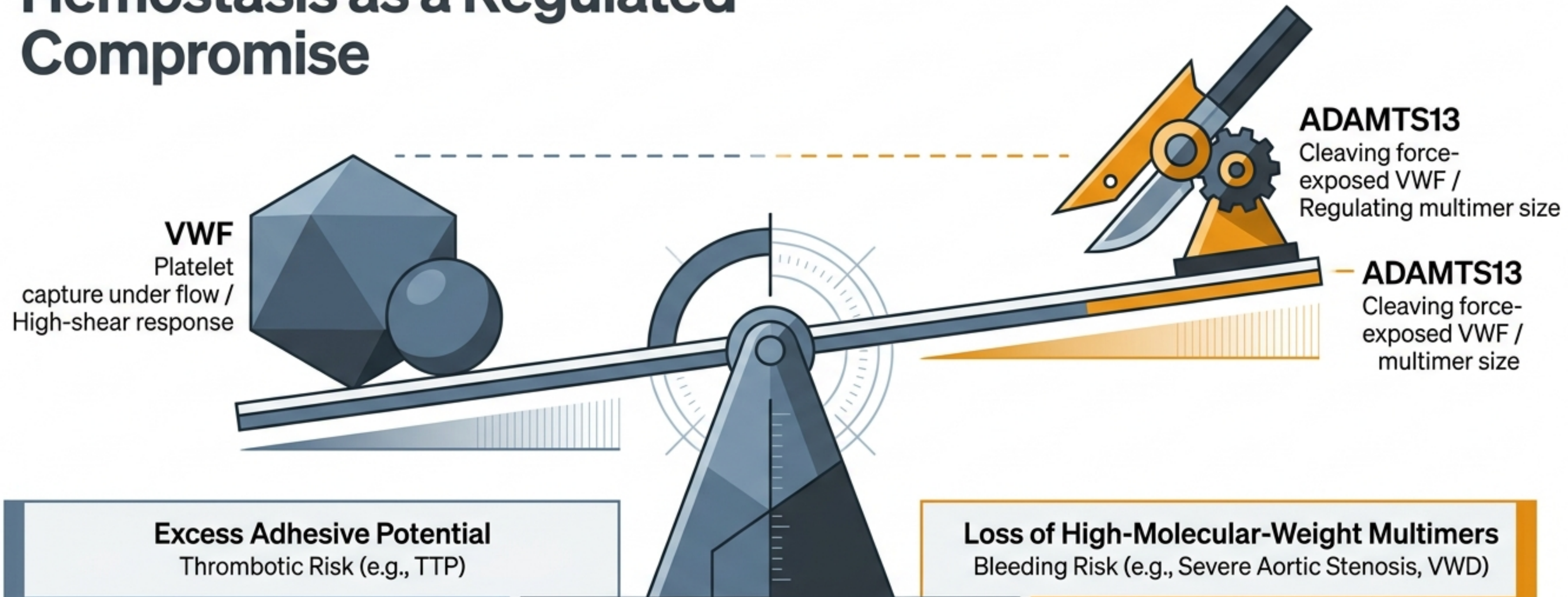




Precision & Reliability in VWD Testing

Moving from isolated numbers to integrated biological patterns.

Hemostasis as a Regulated Compromise



The goal of hemostatic treatment is proportionate hemostasis—enough support to reduce bleeding risk without creating avoidable thrombotic risk.



The Illusion

VWF levels are reported as exact numbers.
They look definitive.

They are not.

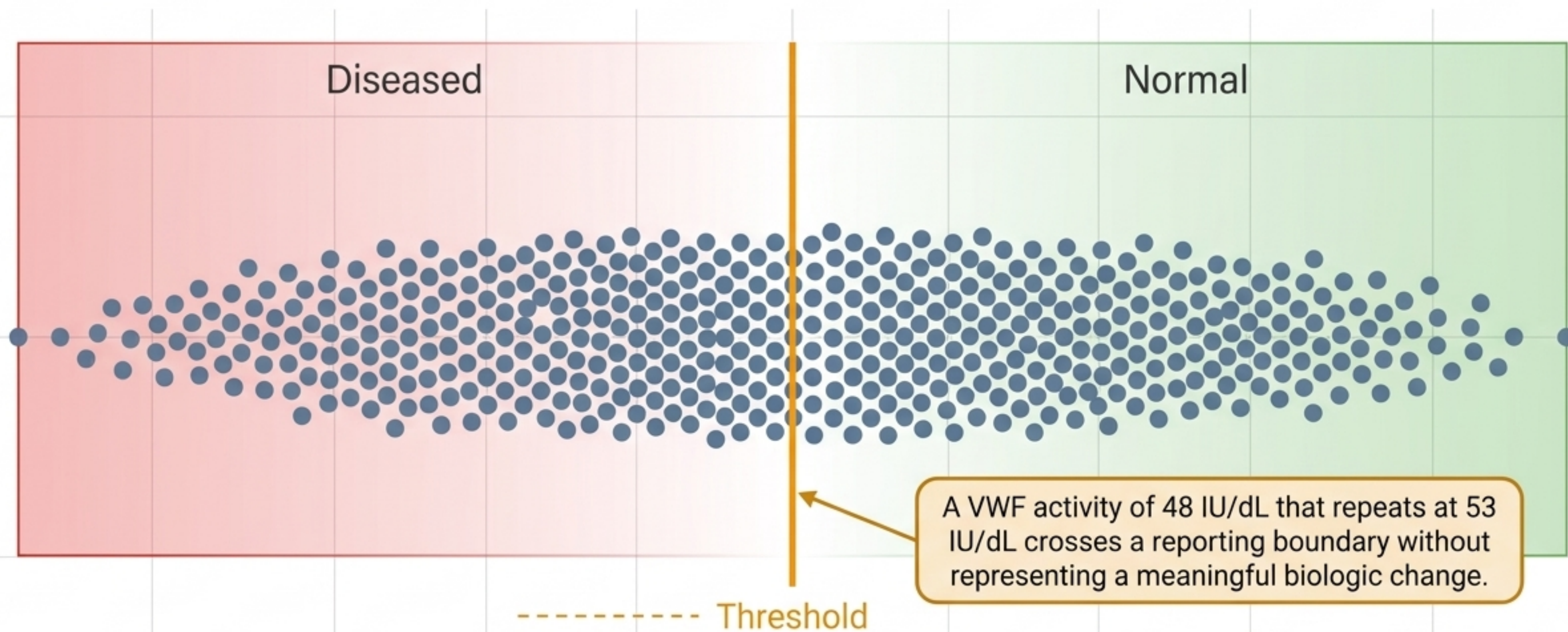
The Reality

A single draw captures a moment, not necessarily
baseline biology.

Plasma VWF spans a wide physiologic range and
is actively influenced by stress, exercise,
pregnancy, surgery, aging, and comorbid disease.

A profoundly abnormal value (e.g., 8 IU/dL) is a clear signal.
But near thresholds, small movements create outsized clinical ripples.

Categorical Boxes vs. Continuous Biology



The diagnostic label can move more than the underlying biology. This is not diagnostic failure; it is the friction of forcing a continuous protein into rigid categorical boxes.

<30 IU/dL

Strong Signal

30–50 IU/dL

The Gray Zone / Integration Required

>50 IU/dL

Provisional Normal



Certainty Dissolves

Some bleed, some do not.
Some normalize with age,
some remain low.

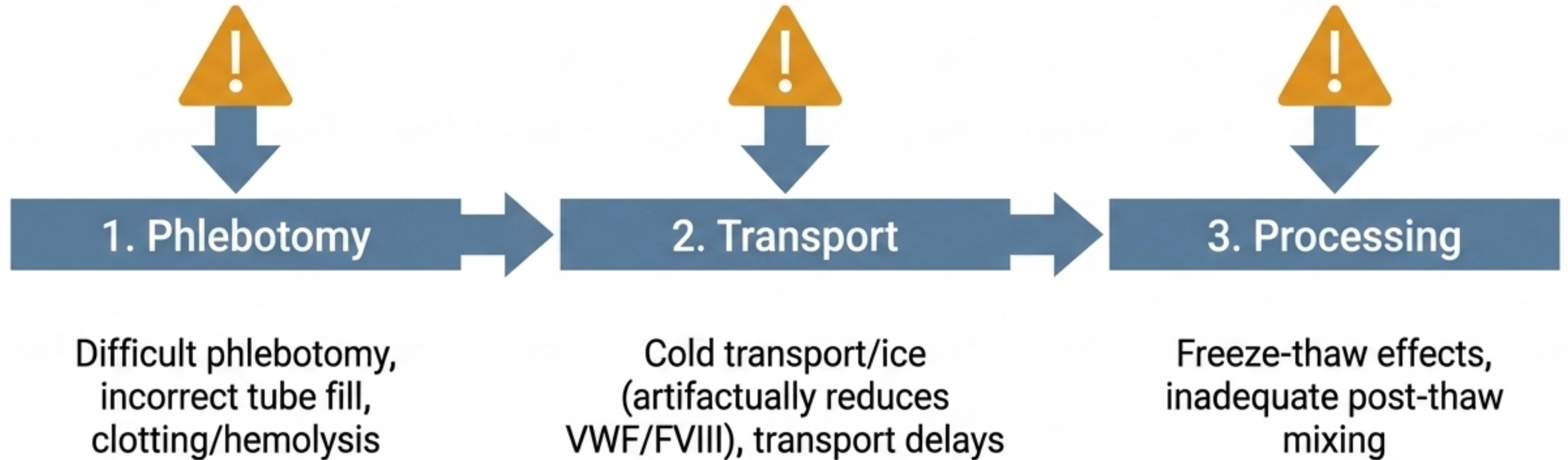
Vulnerability

Highly sensitive to small
changes in sample handling,
assay method, and timing.

The Directive

Values here cannot stand
alone. They require integration
of bleeding history, family
history, and clinical setting.

The Preanalytic Funnel



Preanalytic problems can push the diagnosis in either direction—making a normal person look like type 1 VWD, or making type 1 look like type 2. A repeat draw is not redundancy; it is quality control.

The Acute-Phase Mask: The Problem of False Reassurance



The interpretive trap is simple: "The number is normal, so the disease is absent."
The better question is: "Was the patient's biology normal when the sample was drawn?"

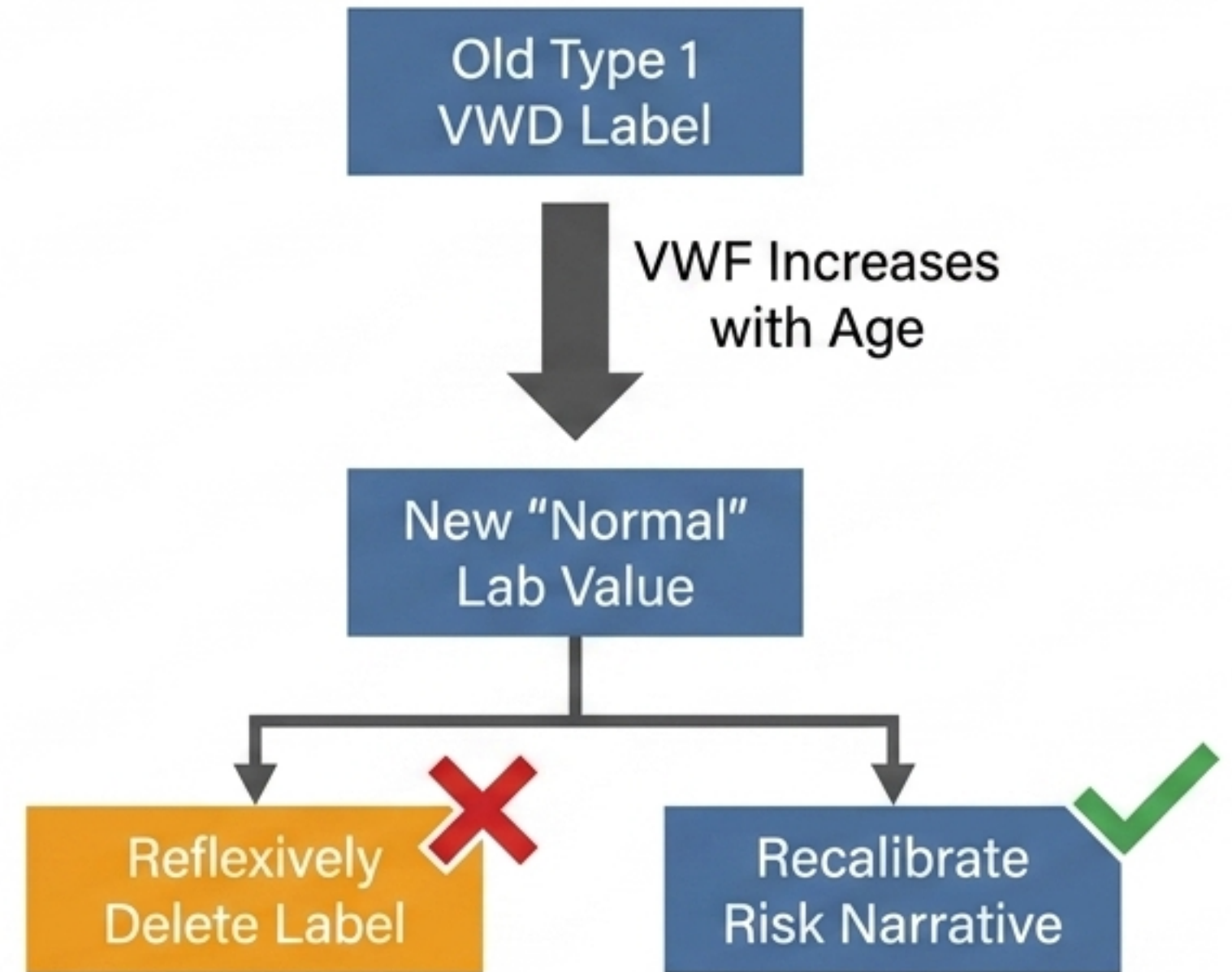
For VWD, "normal" is not only
a reference range.
It is a biological context.

Analytic Shifts



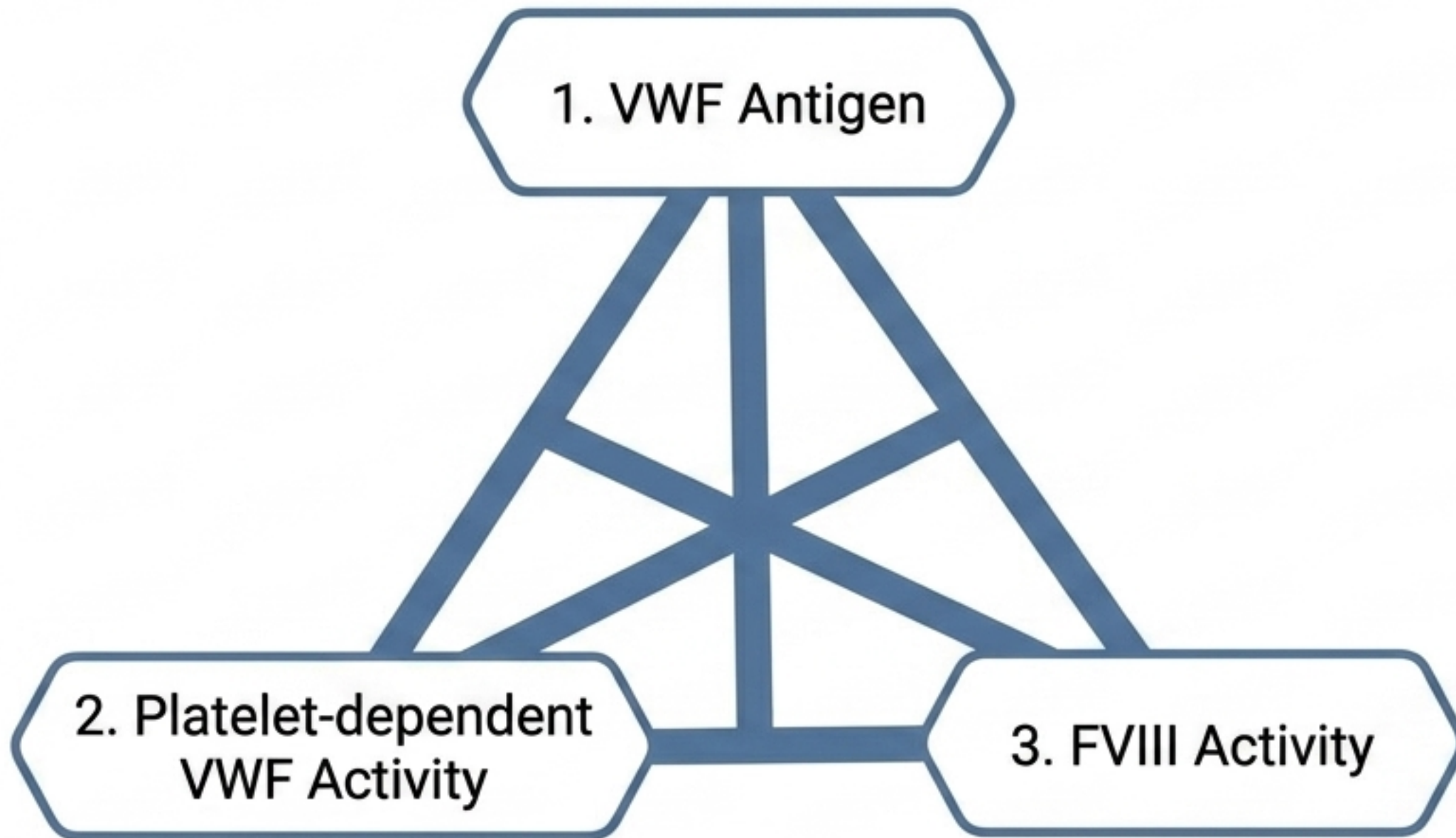
A changed number over a decade may reflect methodology, not biology.

The Normalization Conundrum

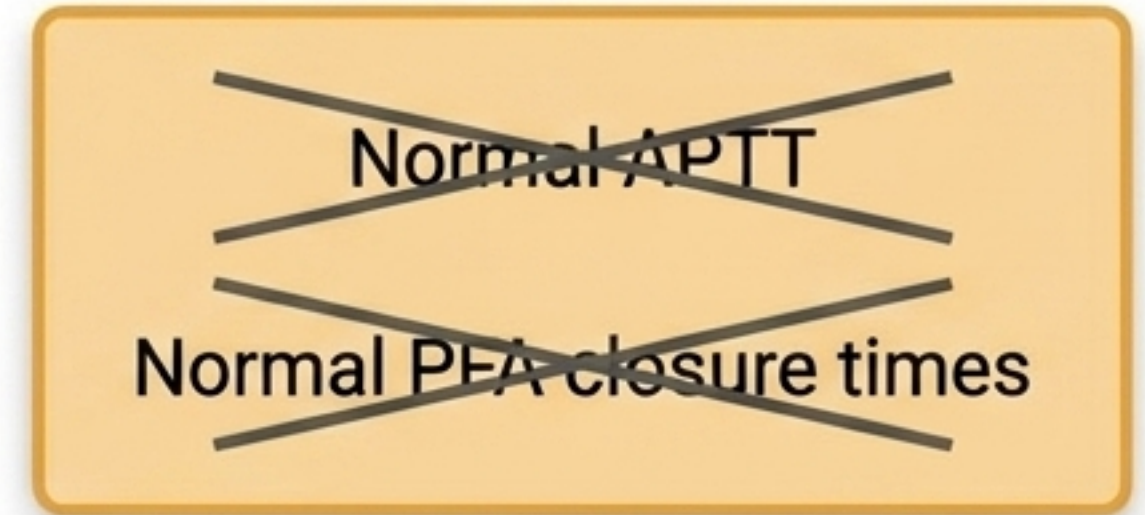


Normalization does not automatically mean the patient is cured or the original diagnosis was wrong. Do not cling to the label, but do not erase it blindly.

The Core Panel Web



The False Escape Hatches



A normal APTT does not exclude VWD. Reagents lack sensitivity, and FVIII may be normal in mild cases. PFA is affected by hematocrit and platelet count.

These broad tests provide context but never replace the core pattern. Additional testing is guided by the core panel, not ordered reflexively.

The Subtyping Prerequisite

Step 2: Assign Subtype

Activity-to-antigen ratios, FVIII-to-VWF relationships, Collagen-binding, Multimers, RIPA

Step 1: Confirm The Foundation

Reproducible baseline, consistent phenotype



Subtyping should be earned. It requires pattern recognition, not just a low value. Assigning a subtype from incomplete, non-baseline, or discordant data invites misclassification.

The 'Why We Repeat' Matrix

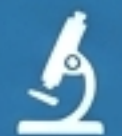
Diagnostic Repeat

**Goal:**

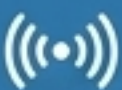
Is the abnormality reproducible at baseline?

**Timing:**

Patient is in baseline health.



Method: Careful sample handling, identical core panel.



Purpose: Seeking the true biologic signal, free from acute-phase noise.

Therapeutic Repeat / Desmopressin Trial

**Goal:**

Can the patient generate a clinically useful rise in VWF/FVIII?

**Timing:**

Administered under controlled challenge.



Method: Timed draws post-administration.



Purpose: Measuring duration and magnitude of therapeutic response.

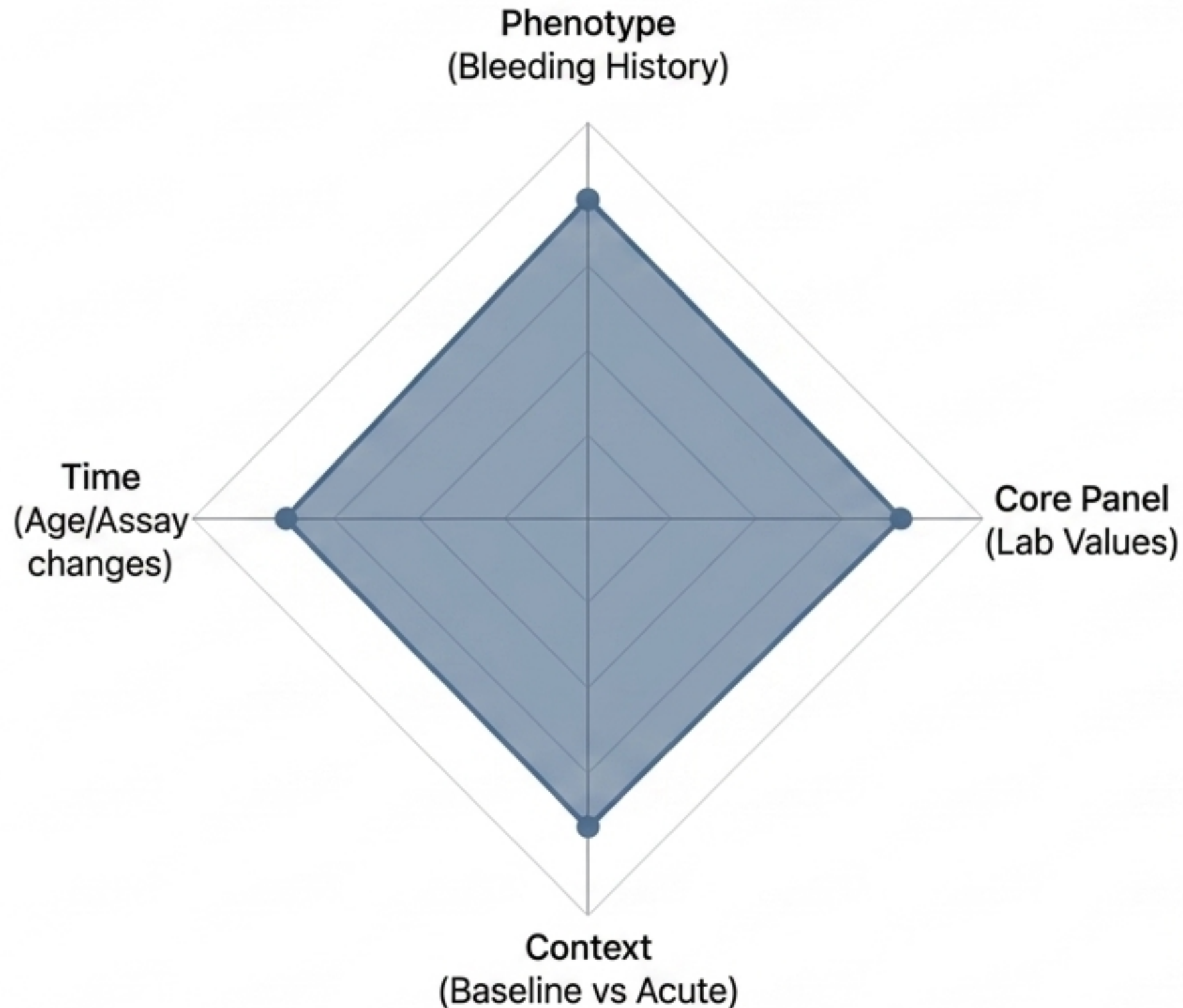
“Repeat labs” is not a vague reflex. It is a targeted biological question.

Guideline Perspectives: The 30–50 IU/dL Range

	Stance	Underlying Priority
2021 ASH/ISTH/NHF/WFH	Diagnoses Type 1 VWD in patients with abnormal bleeding and VWF <50 IU/dL.	Avoiding missed diagnosis and improving access to care.
2024 BSH/UKHCDO	Preserves caution; emphasizes weaker associations between VWF level, bleeding, and variants in this range.	Avoiding overmedicalization; requires confirmation under strict lab conditions.

Thresholds organize decision-making, but they do not replace judgment.
Guidelines provide structure, but cannot eliminate the inherent uncertainty of borderline values.

The Disciplined Stance: Proportional Reasoning



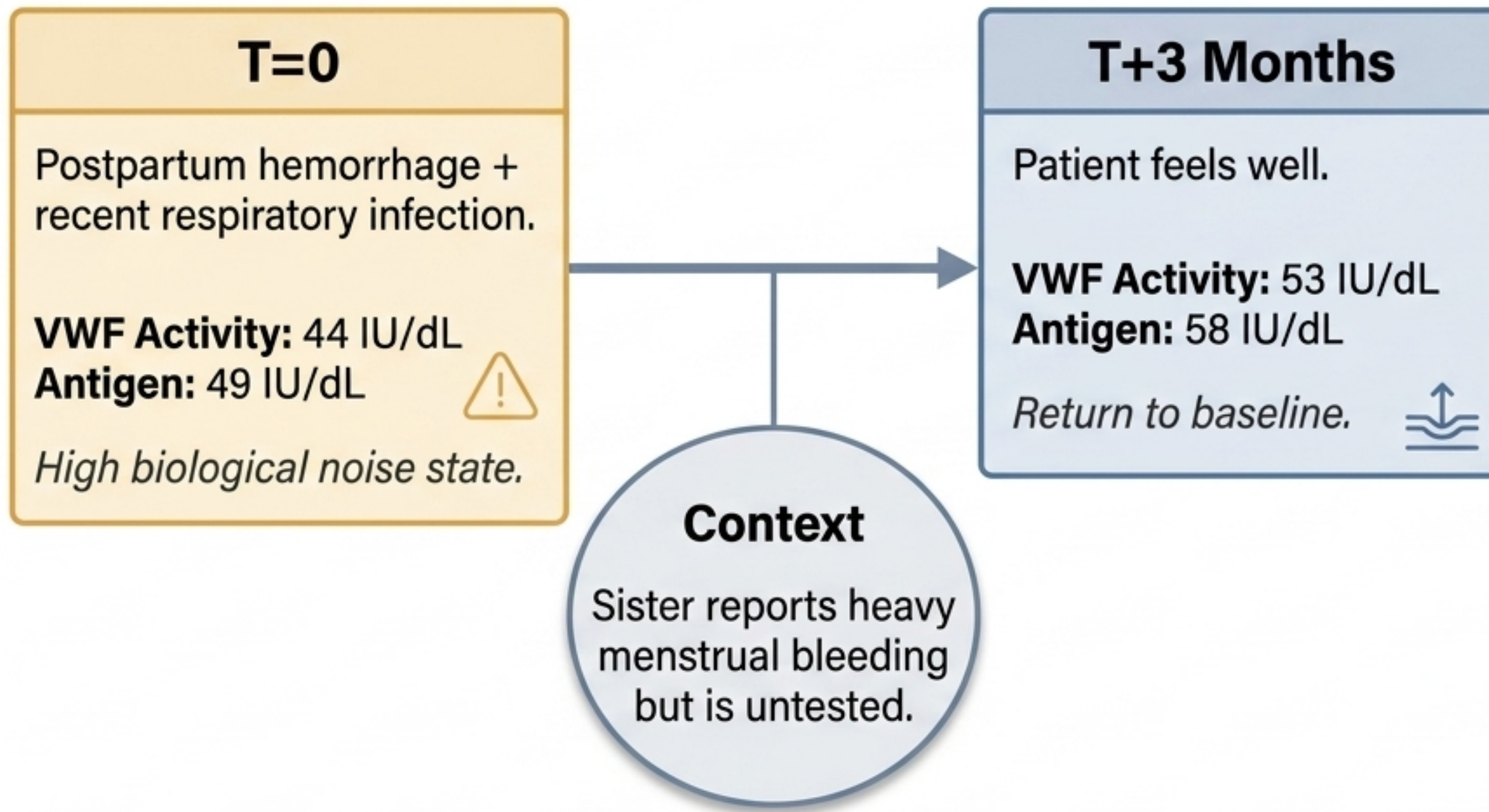
Diagnosis in VWD is an integration problem, not a threshold decision.

How we explain this to patients matters.

- ✗ Poor Framing:** "We repeat because the test is unreliable." (Undermines trust)
- ✓ Disciplined Framing:** "We repeat because VWF naturally fluctuates, and we are trying to understand your true baseline biology." (Protects trust)

**Repetition is not weakness.
It is respect for biology.**

Clinical Application: The 28-Year-Old Patient



Integration Prompts

- What is the diagnostic risk of treating 53 IU/dL as 'normal' and closing the case?
- How does the sister's history change the threshold for future procedural planning?

Takeaway: Do not close the case solely because a repeat value crossed 50 IU/dL if the phenotype and family history remain compelling.

5 Rules for VWD Lab Interpretation

- 1 Treat borderline results (30-50 IU/dL) as provisional until reproduced at baseline.
- 2 Assume physiologic and preanalytic variability is present unless conditions were explicitly stable.
- 3 Revisit historical diagnoses when values normalize with age—recalibrate the risk narrative, do not reflexively delete it.
- 4 Confirm the diagnostic foundation with a complete core panel before attempting to assign a subtype.
- 5 Use structured repeat testing to reduce noise. Repetition is a feature of diagnostic discipline, not a failure of it.