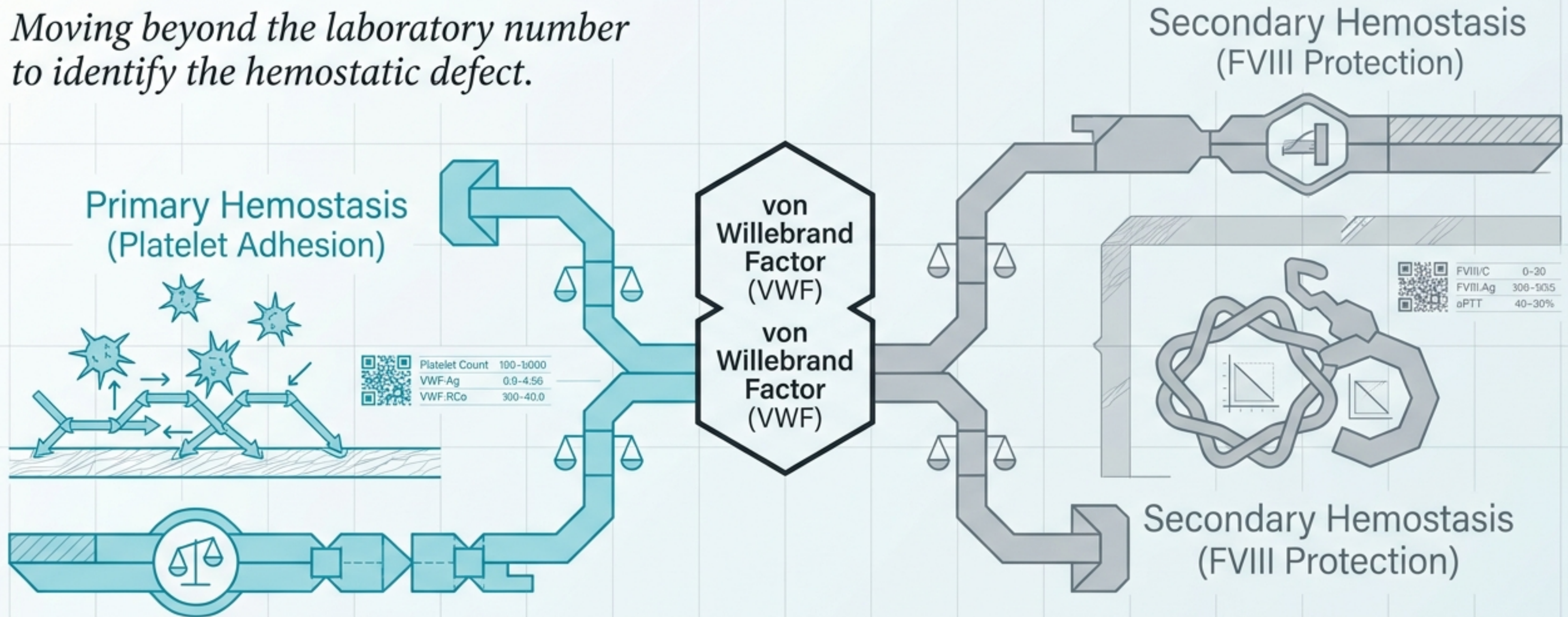


Diagnosing von Willebrand Disease: A Logic of Localization

*Moving beyond the laboratory number
to identify the hemostatic defect.*



“Diagnosis is not the detection of a number. It is the localization of a defect.”

“Diagnosing VWD has historically been framed as ordering the correct laboratory panel and finding a value that crosses a threshold. True expert diagnosis requires identifying which component of hemostasis is failing and which function within that component is impaired.”

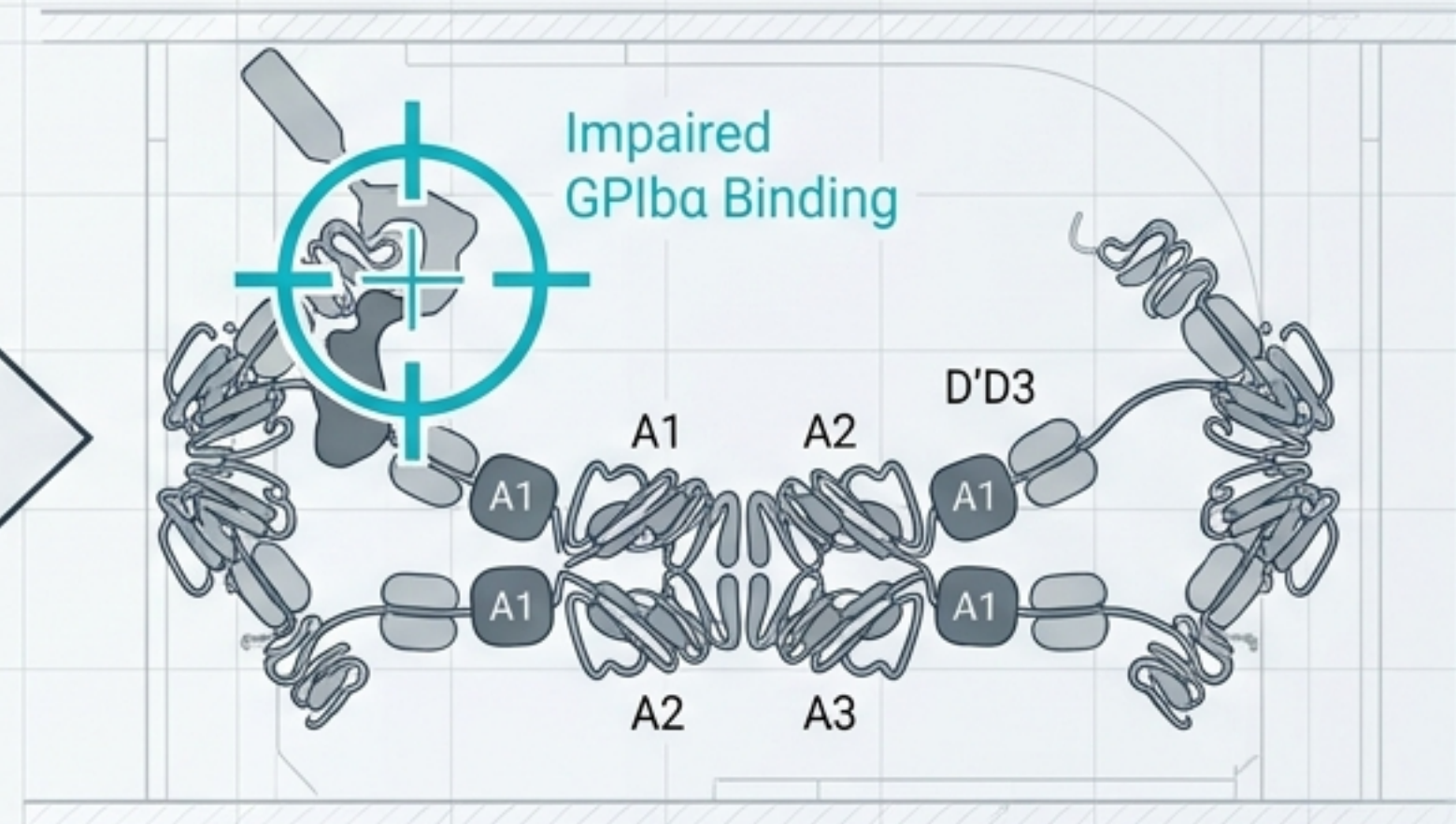
The Old Paradigm

Test A:	45 units	(Ref: 40-60)
Test B:	120 units	(Ref: 100-150)
VWF:Ag:	32 units	(Ref: >50)

Pattern-Matching

From Pattern-Matching
to Localization

The New Paradigm



Localization of Defect

Step 1: Localize the Bleeding System

A bleeding score is not a verdict; it is a structured way of asking whether the phenotype is plausible.

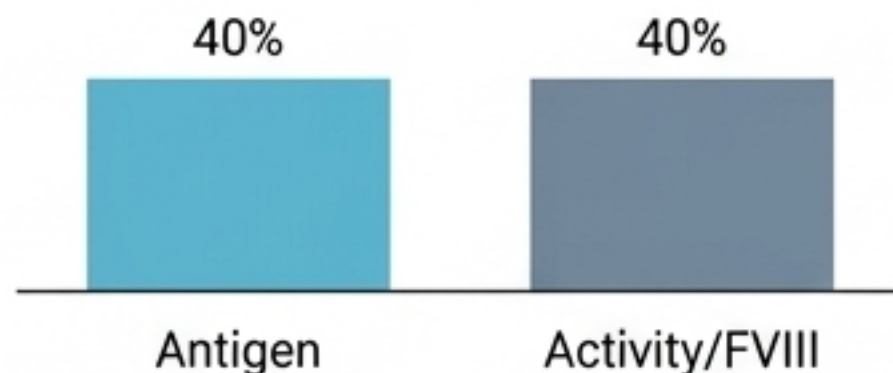
Primary Hemostasis		Secondary Hemostasis	Vascular Integrity
• Mucocutaneous • Epistaxis • Easy bruising • Heavy menstrual bleeding • Immediate procedural bleeding	VWF	• Deep muscle bleeding • Hemarthrosis • Delayed bleeding • Large soft-tissue hematomas	• Hypermobility • Abnormal scarring • Telangiectasias

VWF sits at an interface: Adhering platelets under high shear (Primary) while protecting FVIII from premature clearance (Secondary). This dual-role explains why severe Type 3 or Type 2N VWD can mimic coagulation-factor disorders.

Step 2: Proportionality Encodes Mechanism

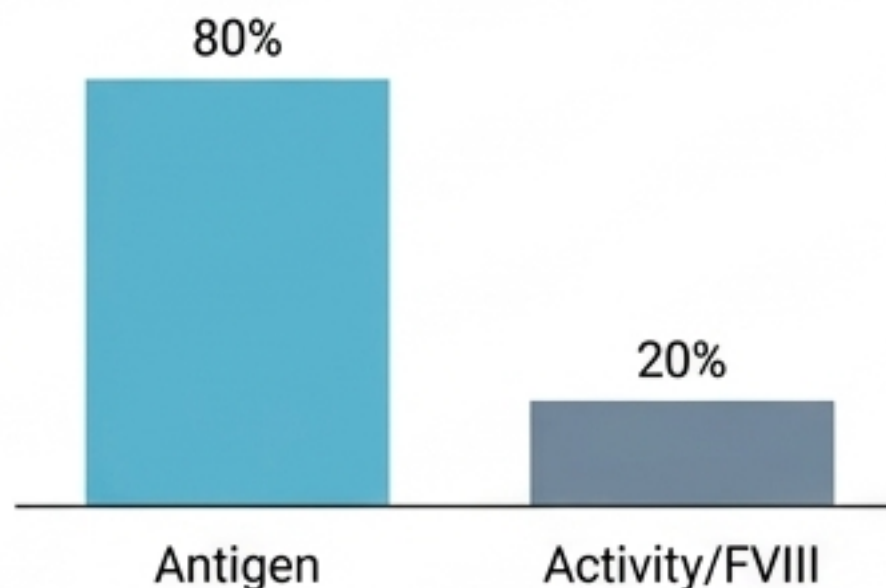
First-line testing (VWF:Ag, Activity, FVIII:C) must be read relationally.

Scenario A: Quantitative Defect



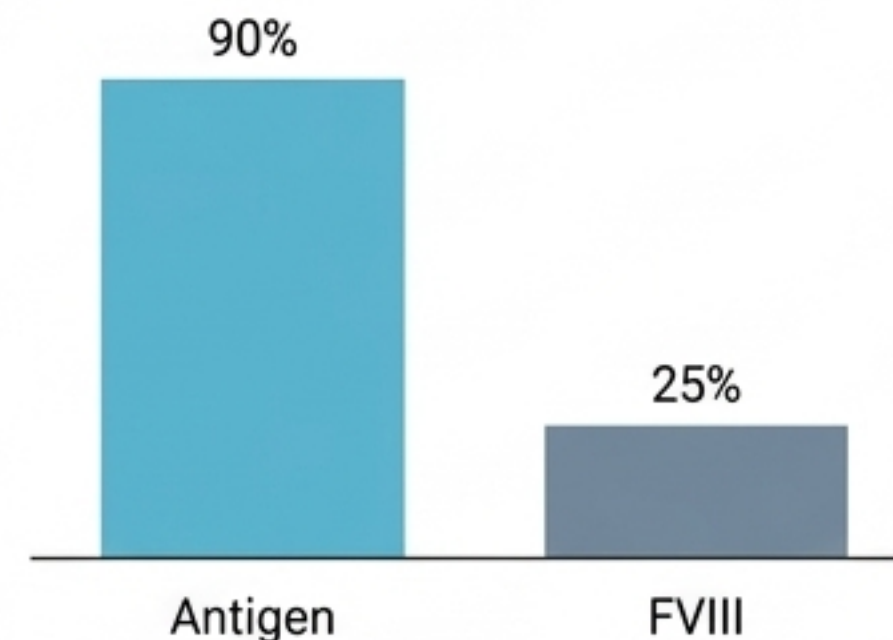
Parallel reduction suggests quantitative deficiency (Type 1 or 3).

Scenario B: Qualitative Defect



Disproportionate activity reduction (Ratio < 0.7) suggests qualitative dysfunction (Type 2).

Scenario C: Carrier Defect



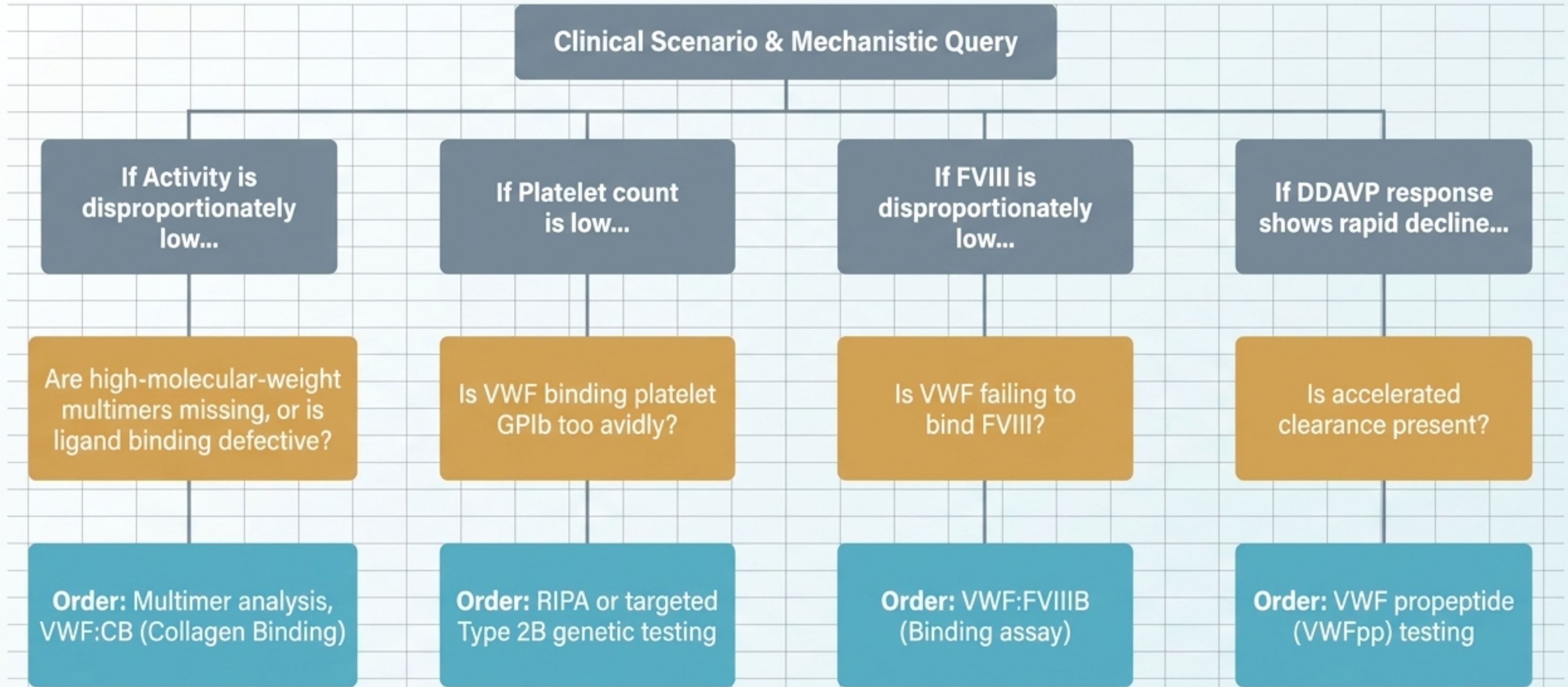
Disproportionate FVIII reduction suggests Type 2N VWD or Hemophilia A.



Modern VWF:GPIbM and VWF:GPIbR assays are preferred over classic VWF:RCO (Ristocetin cofactor) due to better precision at low levels and avoidance of false-abnormals from benign polymorphisms.

Step 3: Escalate Only to Answer a Mechanistic Question

Second-line testing should never be reflexive. Every test must be driven by a specific structural query.



Diagnostic Table: VWD Subtypes by Mechanism

Subtype classification is a summary of mechanism, not a memorized label attached to a number.

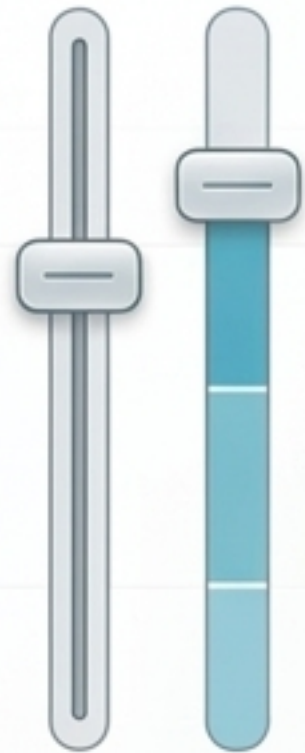
Subtype	Mechanism	Core Diagnostic Question	Clinical Consequence
Type 1	Partial quantitative deficiency	Is the proportional reduction clinically significant?	Often DDAVP responsive
Type 2A	Multimer loss / absent high-molecular-weight forms	Is it defective assembly or increased cleavage?	Reduced platelet adhesion
Type 2B	Hyper-avid platelet GPIb binding	Is there clearance of large multimers and platelets?	CAUTION - DDAVP may worsen thrombocytopenia
Type 2N	Defective FVIII binding	Is this VWD or Hemophilia A?	FVIII drops because VWF fails to protect it
Type 3	Virtually absent VWF	Is this relevant for family counseling?	Usually requires VWF replacement, resembles severe coagulation disorder

Step 4: Separate the Intrinsic Signal from Contextual Noise

VWF is highly dynamic. Failure to account for context is a major source of interpretive error.

System Control Panel

Physiologic Elevation



Stress, inflammation, exercise, acute bleeding.
(Pushes VWF artificially HIGH).

Hormonal Modulation



Pregnancy, estrogen exposure, aging.
(Pushes VWF artificially HIGH).

Preanalytical Errors



Poor sample handling, refrigeration/freezing issues, delayed processing.
(Can create false-abnormals).

Clinical Imperative: Sometimes the most important next test is not an expanded panel. It is repeating the first-line tests correctly under baseline conditions.

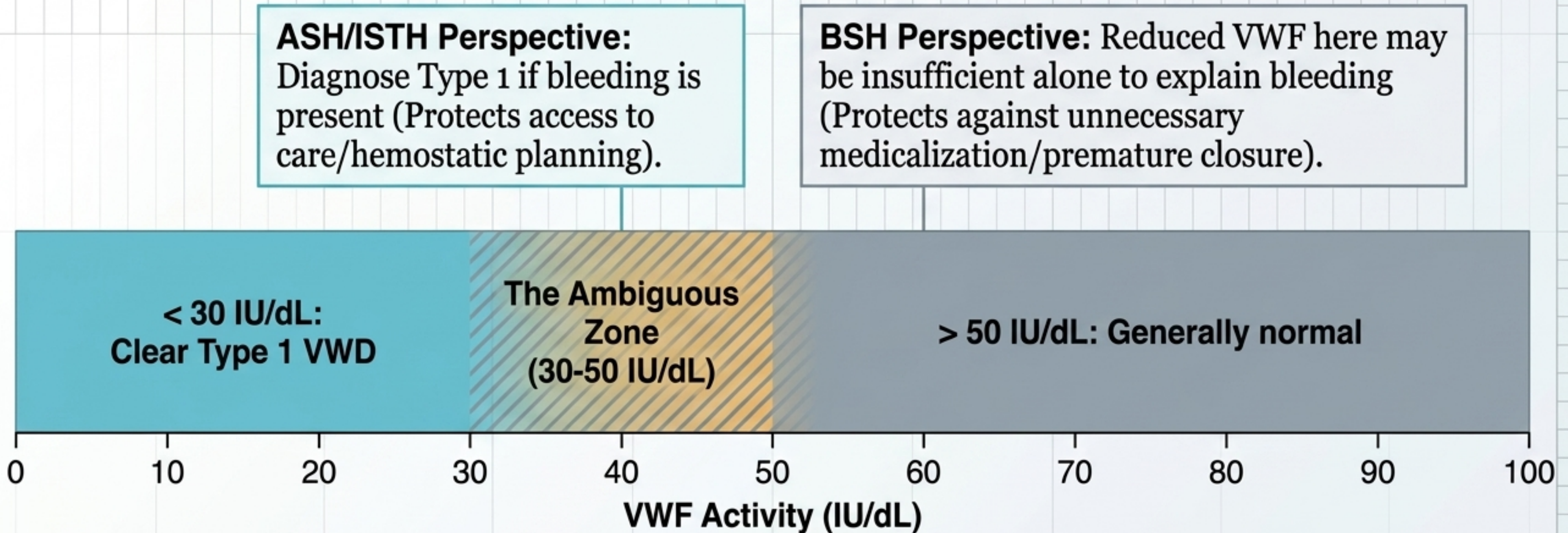
Step 5: Integrate Genetics Without Erasing Phenotype

Genotype can support localization, but it should not override clinical presentation.



Step 6: When Localization Becomes Probability Estimation

The 30–50 IU/dL range does not define a sharp biologic boundary; it requires probability estimation.



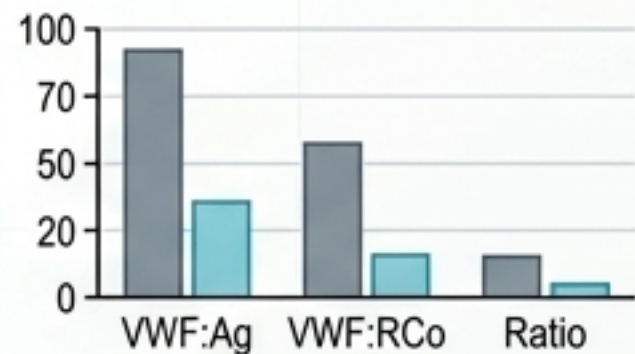
The practical question is not “Does this patient cross a cutoff?”
It is “Does the total evidence justify a disease label and its consequences?”

Diagnostic Pitfalls: The Acquired Mimic & Cognitive Anchoring

The core conceptual error is mistaking a measurement for the mechanism that produced it.

The Acquired Mimic

Chart 1



Patient A: Child with lifelong bleeding + family history.

Diagnosis: Congenital Type 2A VWD.

Chart 2



Patient B: Older adult with new bleeding + high-shear cardiac lesion.

Diagnosis: Acquired von Willebrand Syndrome (aVWS).

**Same pattern. Different diagnosis.
Different treatment.**

The Three Errors



Testing Errors: Sampling during stress, pregnancy, or inflammation.



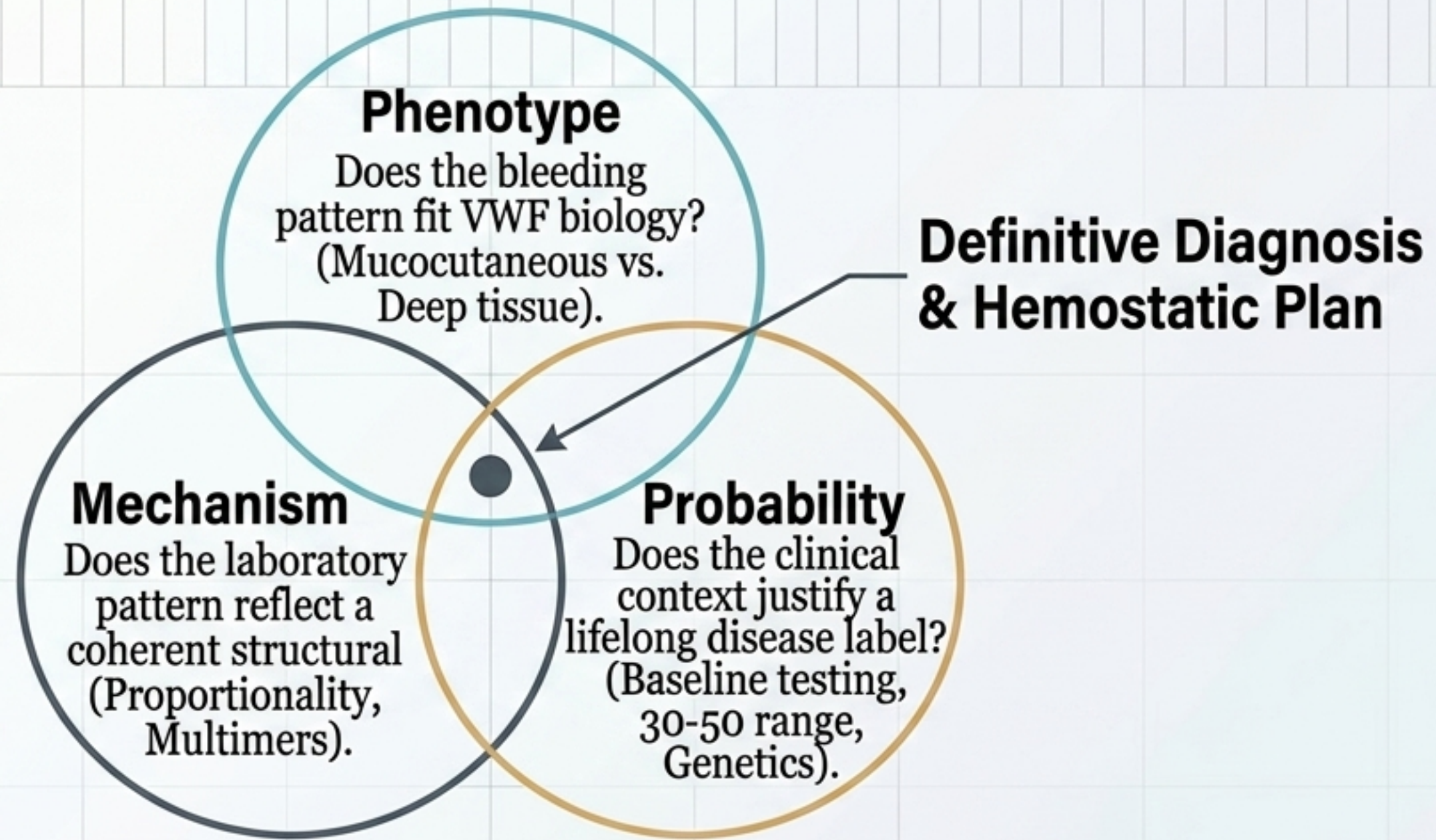
Interpretive Errors: Treating a borderline ratio as definitive without contextualizing the data.



Anchoring Errors: Keeping an old diagnosis without reassessing, or stopping the workup once a mildly low VWF is found.

Synthesis: The 3-Question Bedside Heuristic

True diagnosis only exists at the intersection of phenotype, mechanism, and probability.



Actionable Rule: If the answer to any of the three questions is NO, pause. Repeat testing. Re-localize the bleeding.

Clinical Dashboard: Reflect & Apply

Applying the logic of localization to a real-world presentation.

Lab Panel

VWF:Ag: 43 IU/dL | **VWF Act:** 41 IU/dL | **FVIII:** 96 IU/dL

Platelets/PT/aPTT: Normal | **Blood Group:** O

Phenotype Checklist

Recurrent delayed deep muscle hematomas after minor trauma.

- ✗ Epistaxis
- ✗ Heavy menstrual bleeding
- ✗ Dental bleeding
- ✗ Family history

The Pattern-Matching Trap

VWF is mildly low (30-50 range) with proportional reduction. A reflex label of "Type 1 VWD" might be applied.

The Localization Reality

The phenotype (delayed deep muscle hematomas) points strongly AWAY from primary hemostasis and VWF biology. The VWF value does not explain the physical bleeding.

Verdict: Pattern asks for caution, not a premature label. Re-localize the bleeding mechanism (e.g., coagulation factors, vascular) rather than forcing the VWD label based on a borderline number.