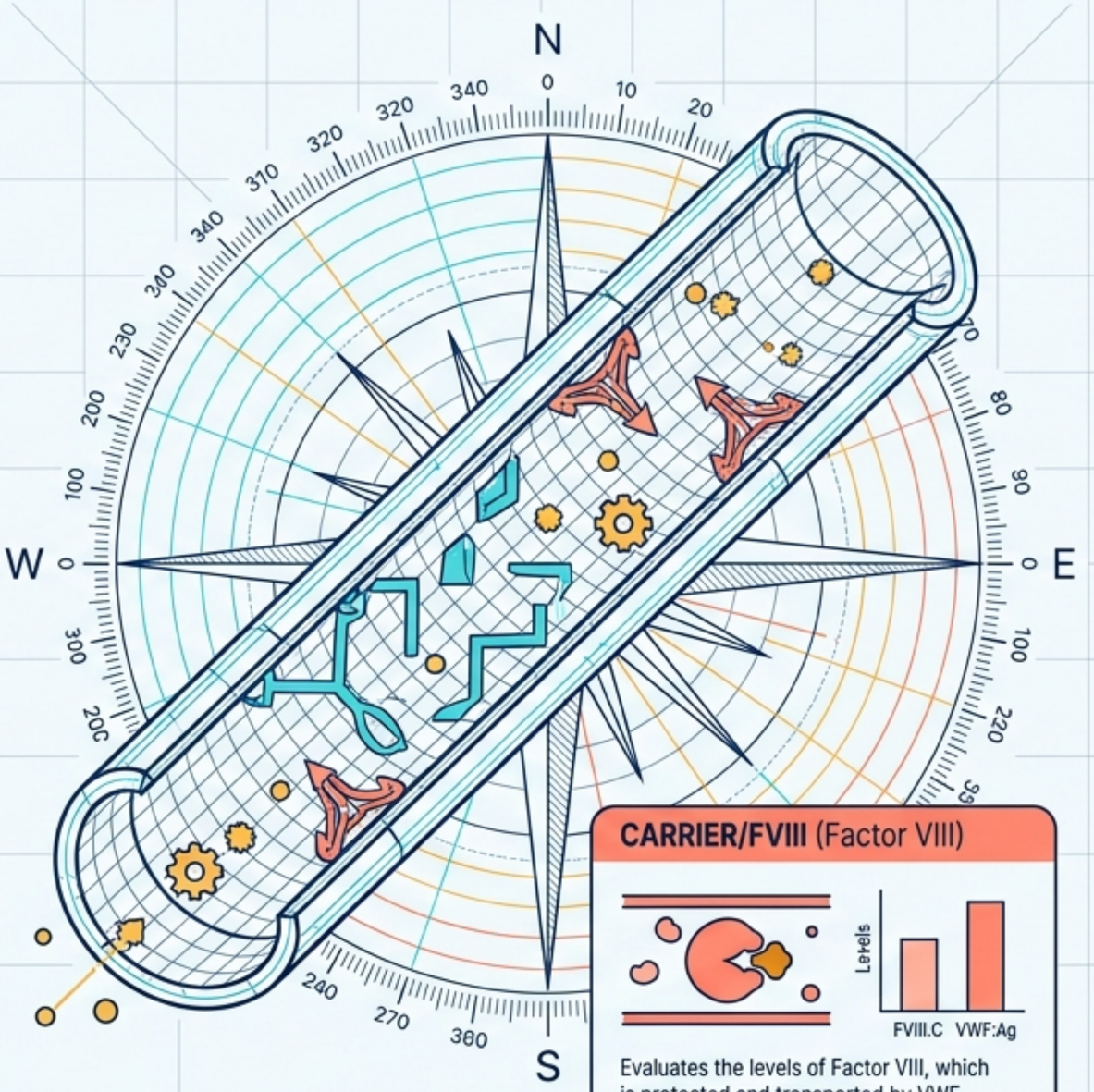
Reading the Map: Principles of First-Line Von Willebrand Factor Testing

Moving from isolated laboratory values to diagnostic pattern recognition.

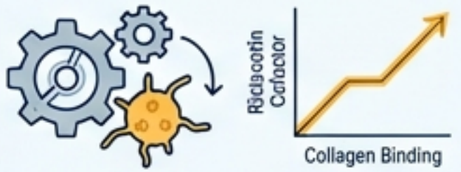


VWF QUANTITY (Antigen)

Measures the total amount of von Willebrand factor protein present in the blood.

The diagnostic quantity baseline.

VWF FUNCTION (Activity)



Assesses the ability of VWF to bind platelets and collagen, crucial for clot formation.

The operational efficacy.

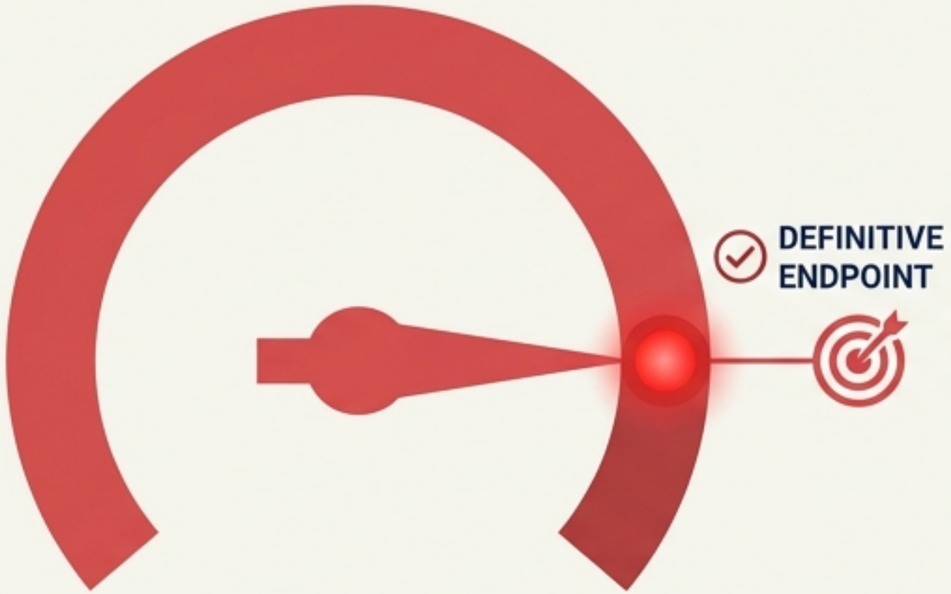
CARRIER/FVIII (Factor VIII)

Evaluates the levels of Factor VIII, which is protected and transported by VWF.

The carrier efficiency check.

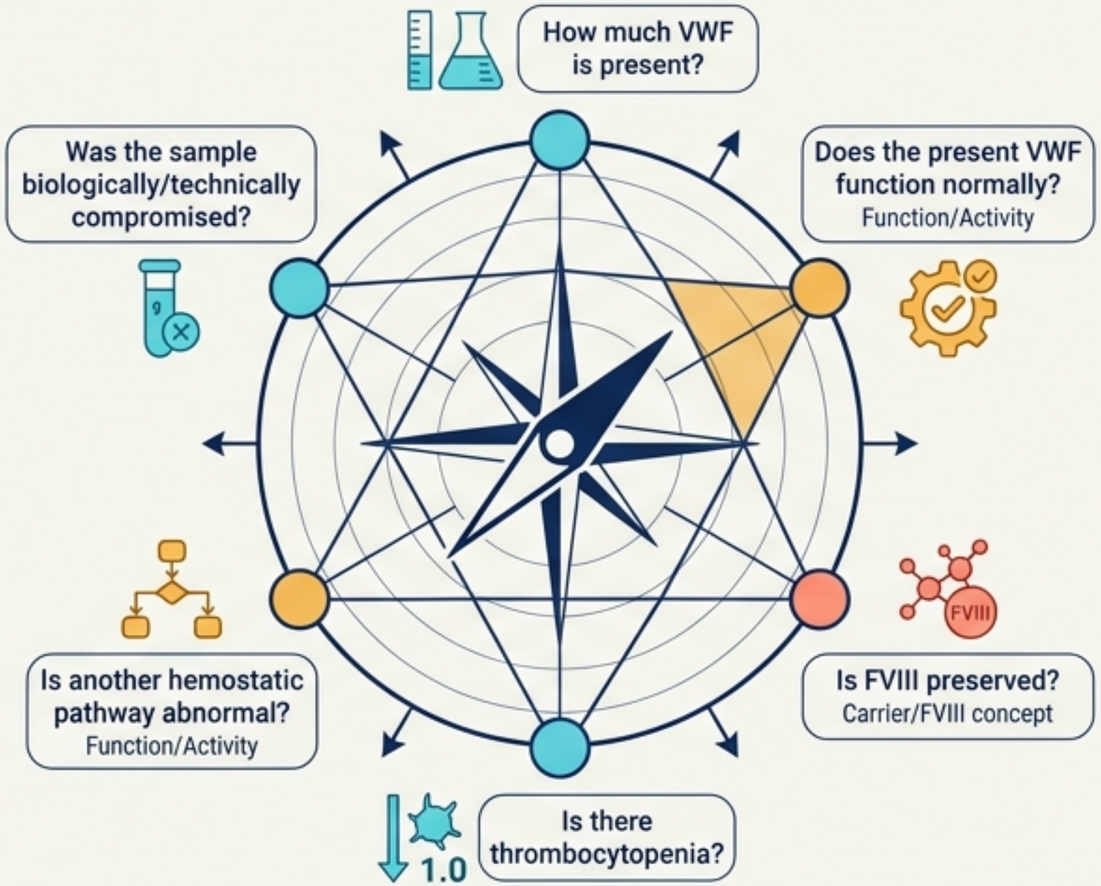
Based on the work of **William Aird**

The Diagnostic Verdict

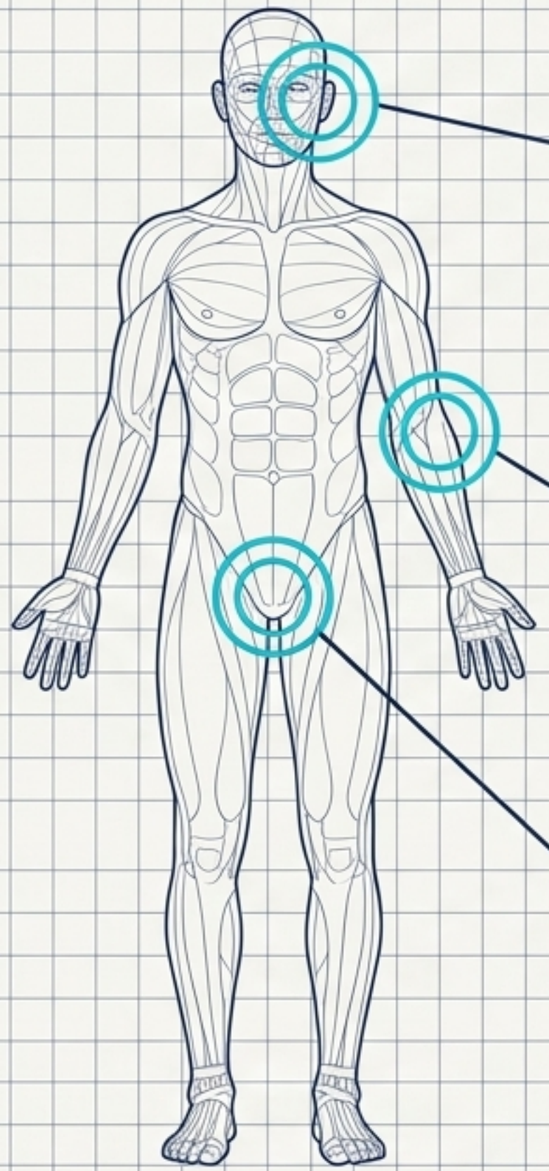


The first VWD panel is often treated as the definitive answer. **It is not.**

The Diagnostic Map



First-line testing creates a map. Clinical reasoning must still read it.



Head / Face

Epistaxis, oral mucosal bleeding, excessive bleeding after dental work.

Skin / Limbs

Easy bruising, procedural bleeding.

Pelvis

Heavy menstrual bleeding, postpartum hemorrhage

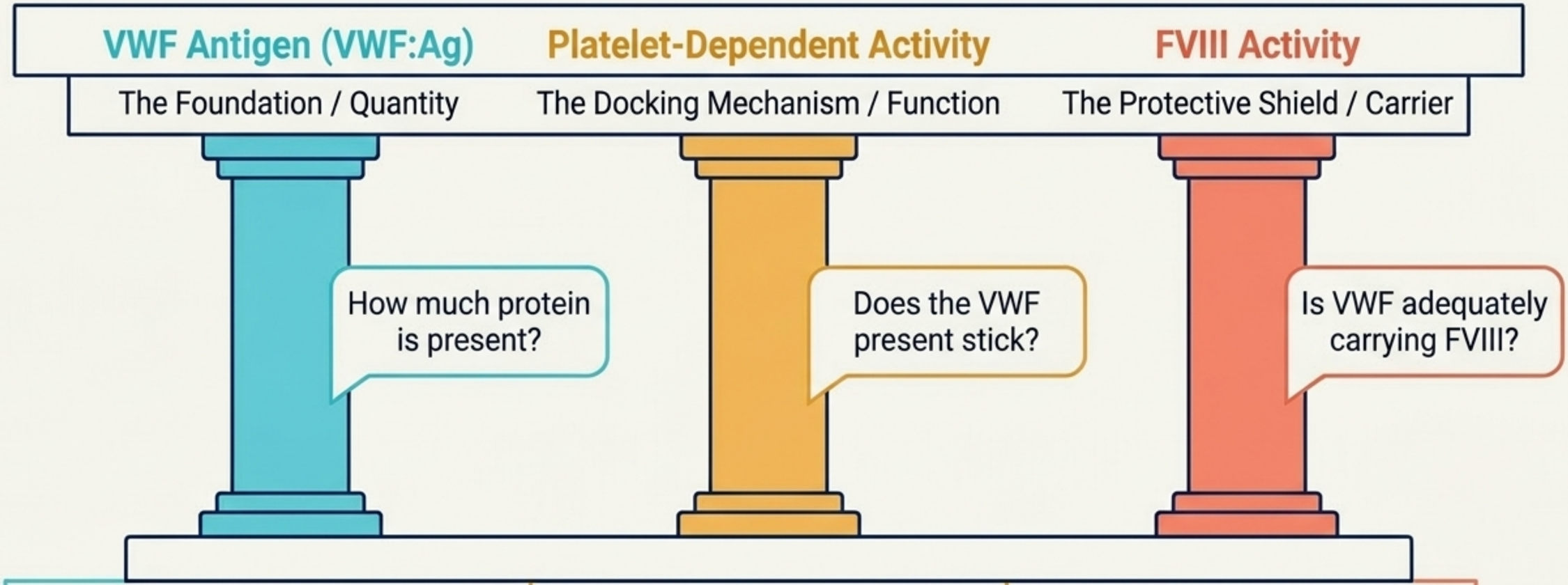
The question is not “Which panel diagnoses VWD?”

The question is “Does this patient’s bleeding pattern justify evaluating the VWF system?”

Modern guidelines emphasize bleeding history and formal assessment tools. History does not replace the lab, and the does not replace history.

VWD sits at their intersection.

The Core Triad of First-Line Testing



Estimates amount of VWF protein. Does not confirm function or explain bleeding. Low values can be physiologic variation, blood group effect, or preanalytic artifact.

Historically VWF:RCo. Modern guidelines prefer newer assays (VWF:GPIbM, VWF:GPIbR) due to improved reproducibility and fewer assay artifacts.

Reduced VWF leaves FVIII unprotected from clearance. Severe type 3 or type 2N VWD can mimic hemophilia A.

Context vs. Exclusion: De-biasing the Routine Labs

CBC & Platelets

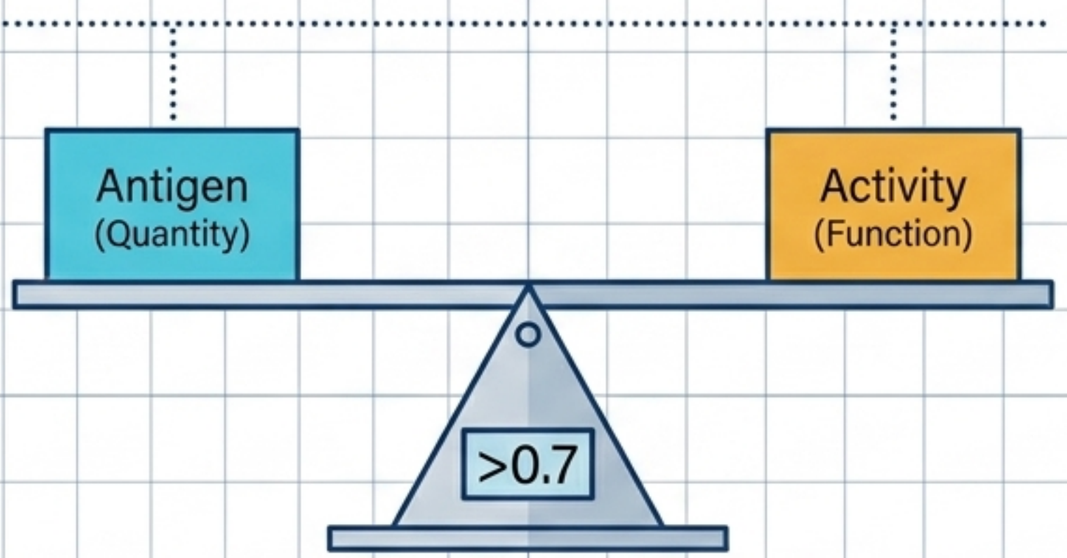
Provide context (e.g., chronic iron deficiency, or thrombocytopenia seen in type 2B VWD), but normal counts do not rule out VWD.

PT & aPTT

Normal values do not exclude VWD. The aPTT is only prolonged if FVIII is sufficiently reduced.

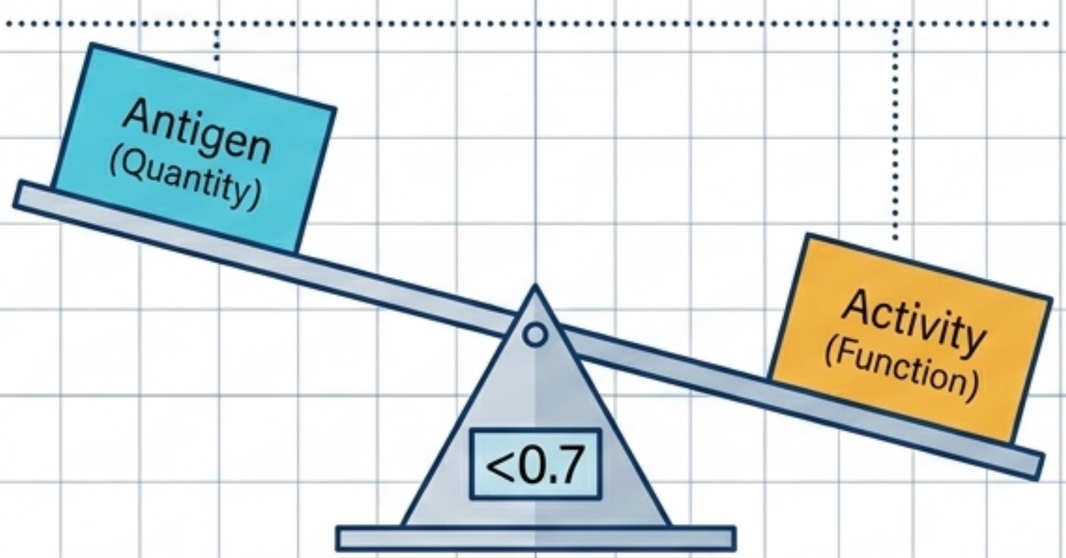
Routine labs provide context. They are not reliable rule-out tests for VWD.

The Golden Metric: The Activity-to-Antigen Ratio



Type 1 VWD

Antigen and activity decrease proportionately. Ratio is preserved.



Type 2 VWD

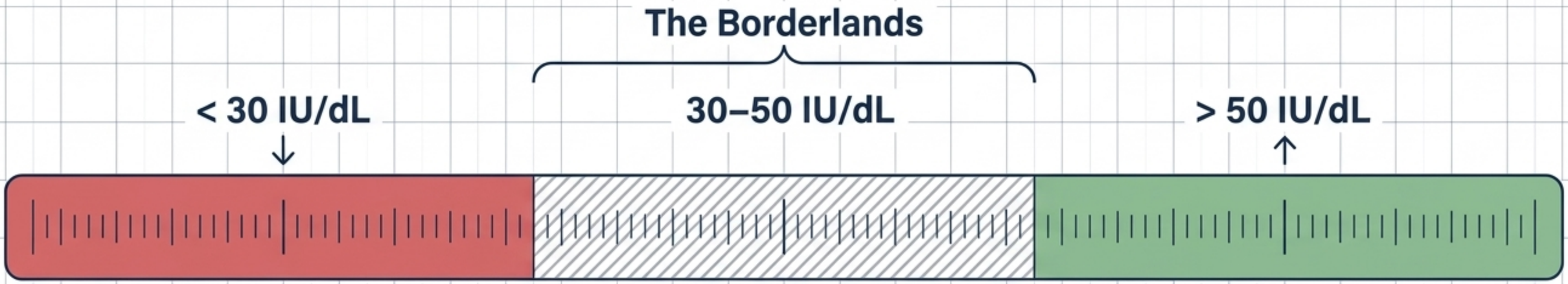
Activity falls disproportionately compared to antigen. Ratio decreases.

The ratio shifts the diagnostic question from “Is the value low?” to “Is the VWF that is present working as expected?” A low ratio signals the **need for second-line testing**.

The Diagnostic Matrix: Three Core Patterns

Pattern 1: Proportional Reduction		Pattern 2: Discordant Reduction		Pattern 3: Normal Panel Despite Bleeding
Antigen	Reduced ↓	**Antigen**	Variable / Reduced	Normal
Activity	Reduced ↓	**Activity**	Disproportionately Reduced ↓	Normal
Ratio	Relatively Preserved	**Ratio**	Reduced (<0.7)	Normal
Consideration	Quantitative deficiency. Type 1 VWD or Low VWF.	Qualitative dysfunction. Type 2 VWD. Second-line testing required.		Physiologic modifiers, platelet/connective tissue disorders. Repeat testing indicated.

Navigating the Borderlands

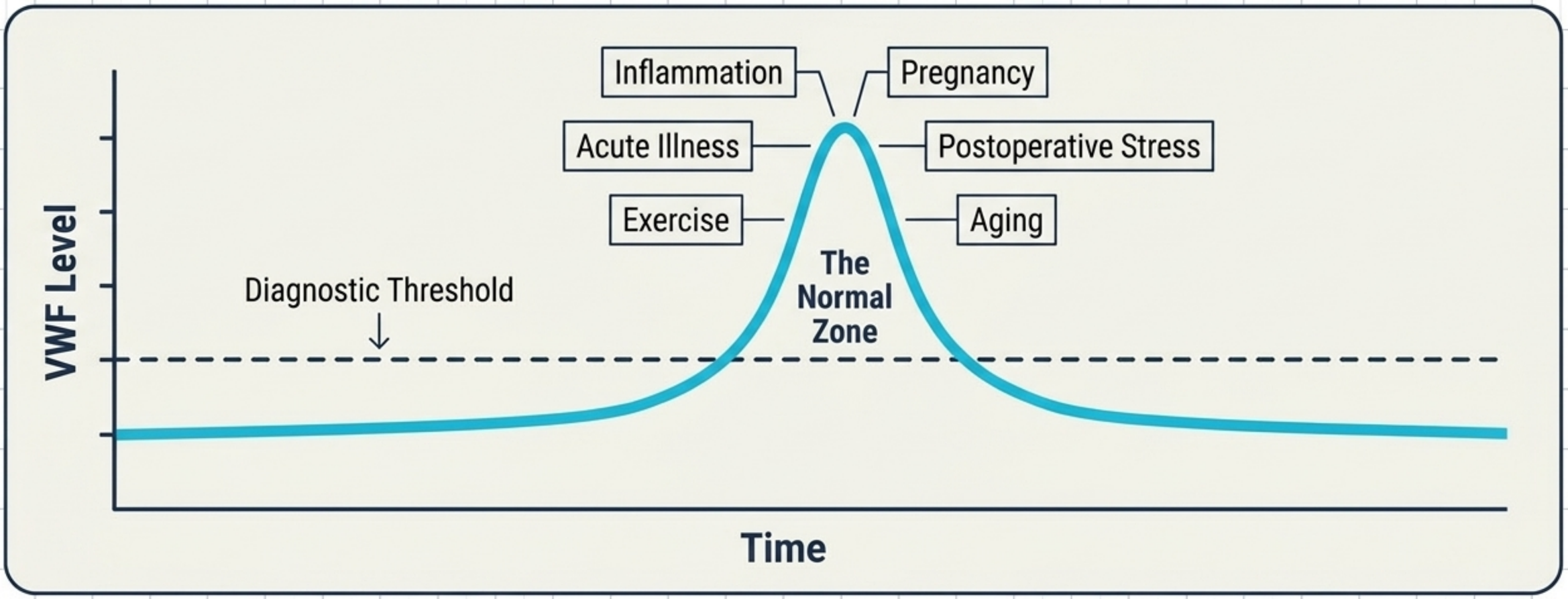


Definitive Deficiency
Supports Type 1 VWD regardless of bleeding history.

Context-Dependent
Supports Type 1 VWD only in patients with abnormal bleeding history.

In the borderlands, the key question is not “Is the value low?” The key question is “Does this value explain the patient’s bleeding phenotype and future risk?”

The Illusion of Normal: Physiologic Modifiers



VWF is highly dynamic. A normal result obtained during a VWF-elevating state may mask underlying disease. Repeat testing at baseline health is biology-aware diagnosis, not indecision.

Preanalytic Pitfalls: The Hazard Zone

Deep Dive

The Cold Exposure Trap

Transporting whole blood on ice can alter VWF and FVIII measurements, leading to misclassification.

Patient Arm → **Processing** → **Transport** → **Laboratory Interface**

- Improper tube filling (disrupts anticoagulant ratio)
- Delayed processing (degradation of factors)
- Inappropriate transport conditions

Clinical Maxim: When the laboratory pattern does not fit the phenotype, sample quality belongs in the differential diagnosis.

What First-Line Testing Can (and Cannot) Do

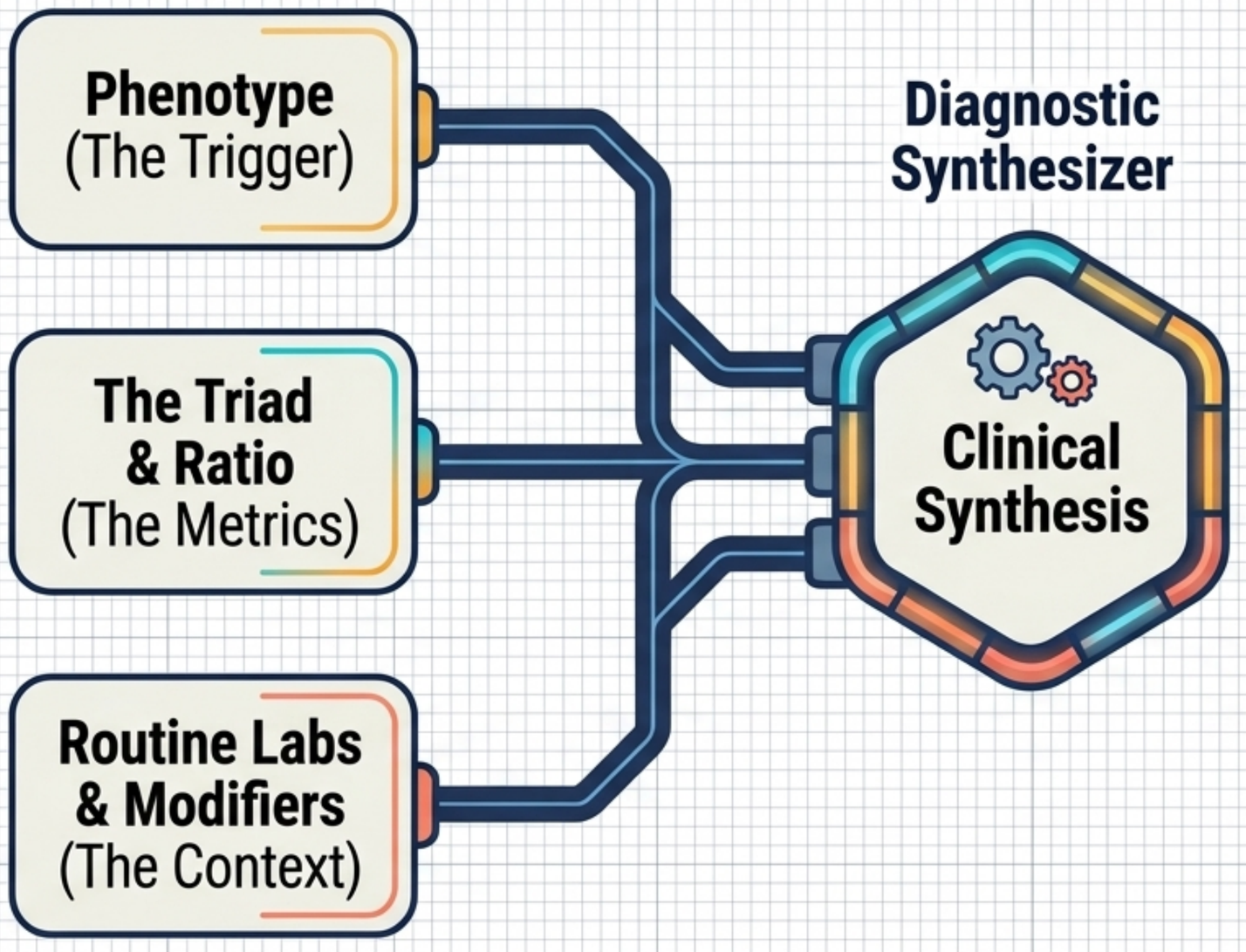
What the Panel CAN Do

- ✓ Support quantitative VWF deficiency.
- ✓ Suggest qualitative VWF dysfunction (via ratio).
- ✓ Identify low FVIII related to impaired carrier function.
- ✓ Guide the selection of second-line testing.
- ✓ Inform peri-procedural planning.

What the Panel CANNOT Do

- ✗ Diagnose VWD without clinical context (phenotype).
- ✗ Exclude all bleeding disorders.
- ✗ Reliably subtype all Type 2 variants.
- ✗ Predict future bleeding risk in isolation.

Clinical Synthesis: The Full Picture



First-line VWF testing is not a verdict. It is a structured conversation with VWF biology.

Antigen asks how much.
Activity asks if it works.
FVIII asks if it carries.

The most useful question is not: What is the number?

It is: What pattern do these numbers create?

Diagnosis begins with a pattern that makes biological and clinical sense, not with a single isolated value.