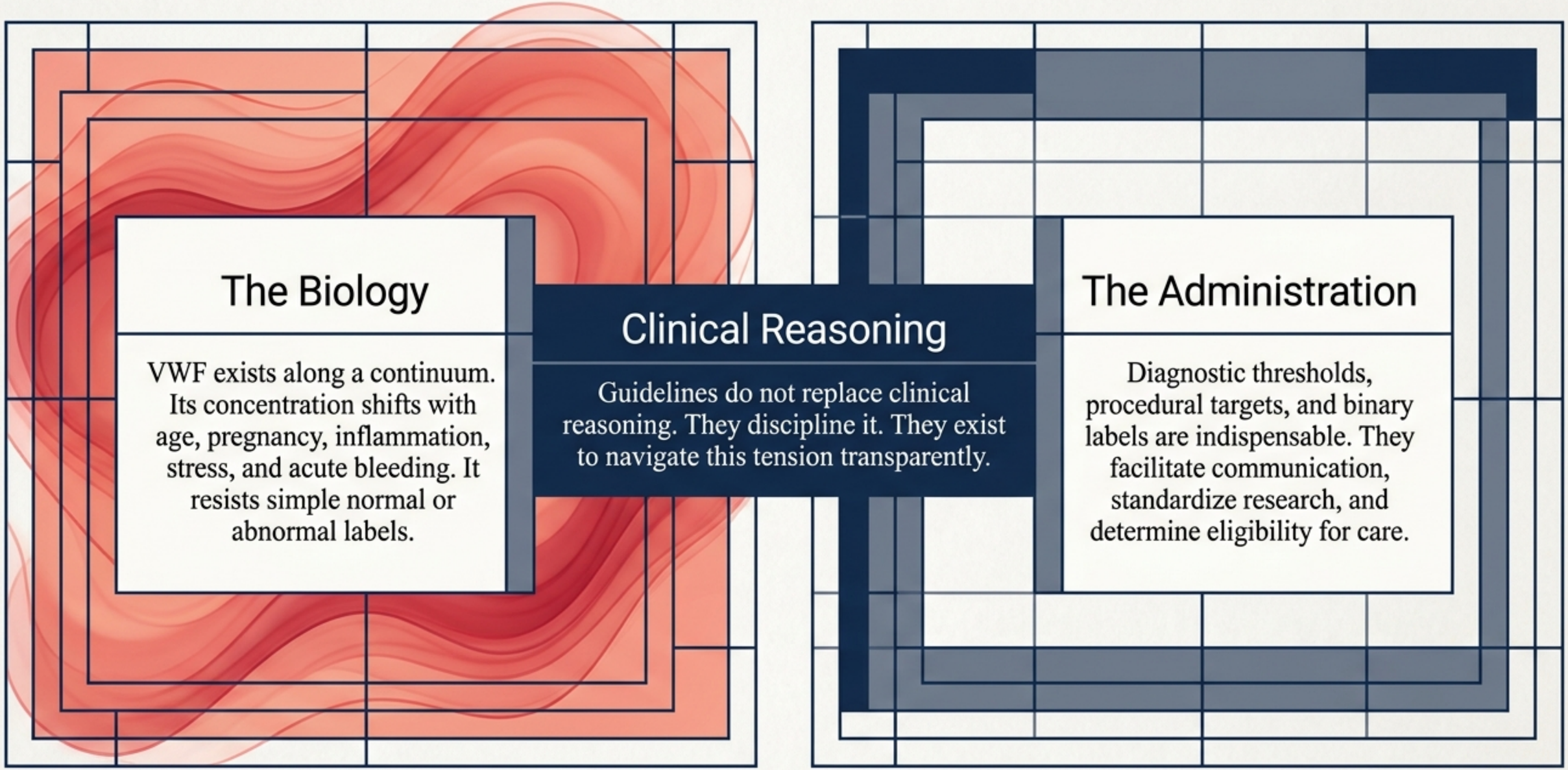
Clinical Practice Guidelines in von Willebrand Disease

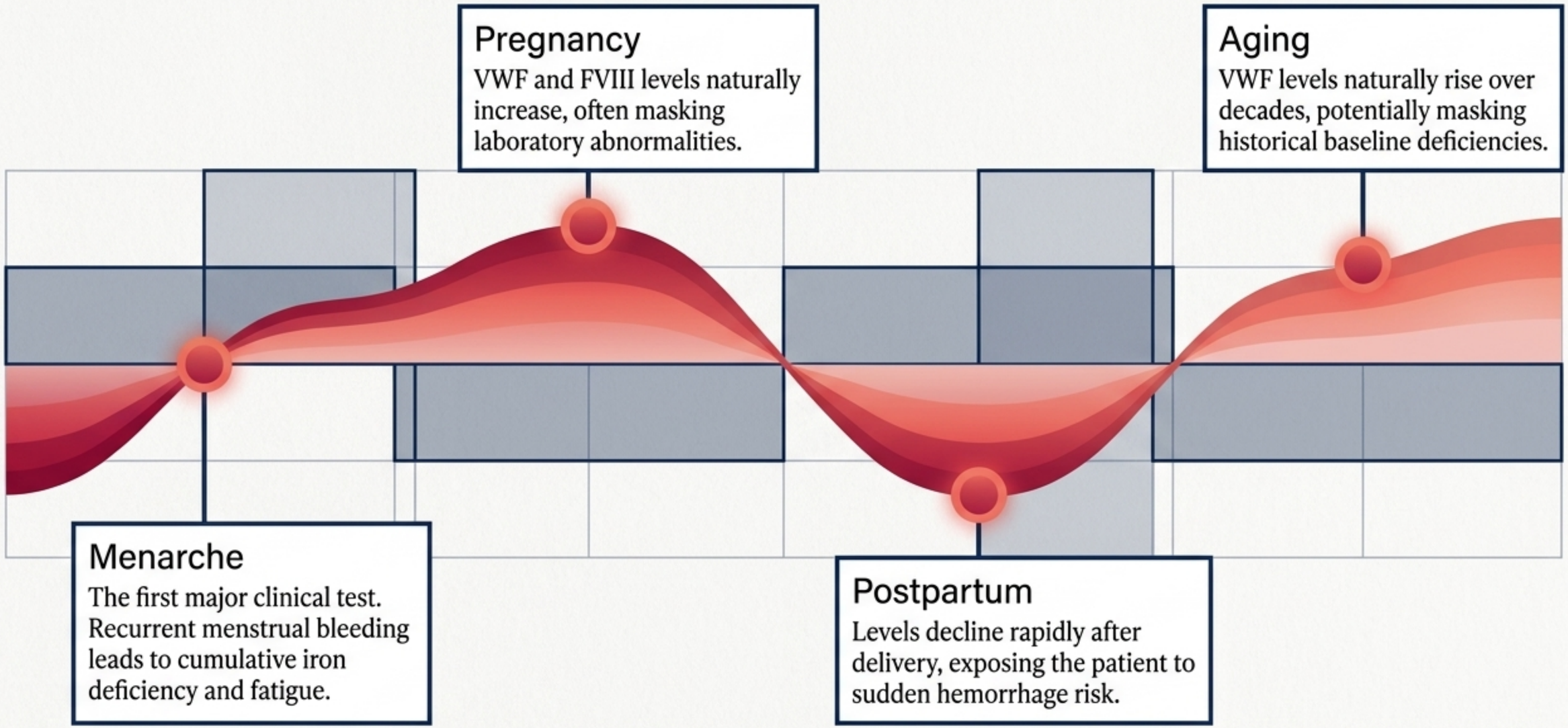
Where Evidence Ends and Judgment Begins

Navigating the tension between continuous biology and categorical medicine.

The patient presents a continuum, but the guideline requires categories

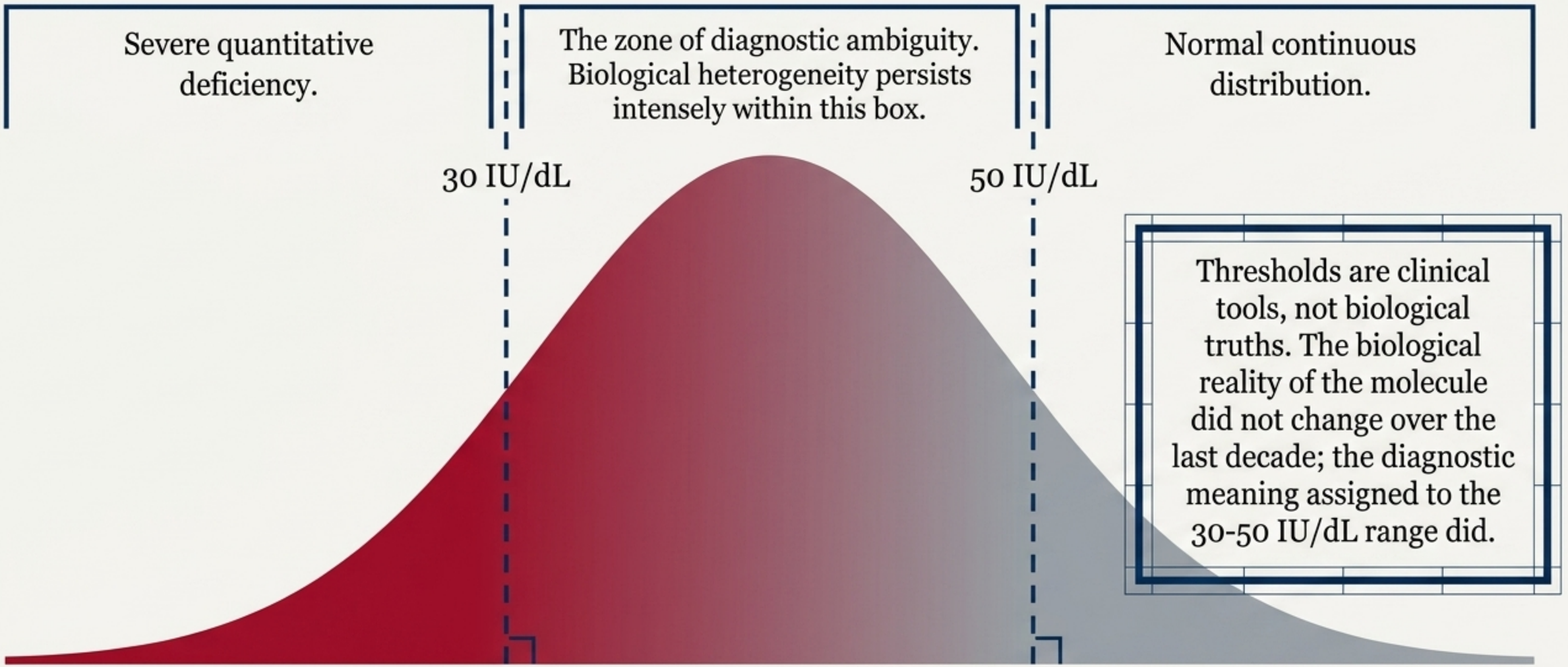


A laboratory result is an observation, not a permanent property



Key Takeaway: The biology creates uncertainty before the evidence ever begins.

There is no natural biological cliff at 30 or 50 IU/dL

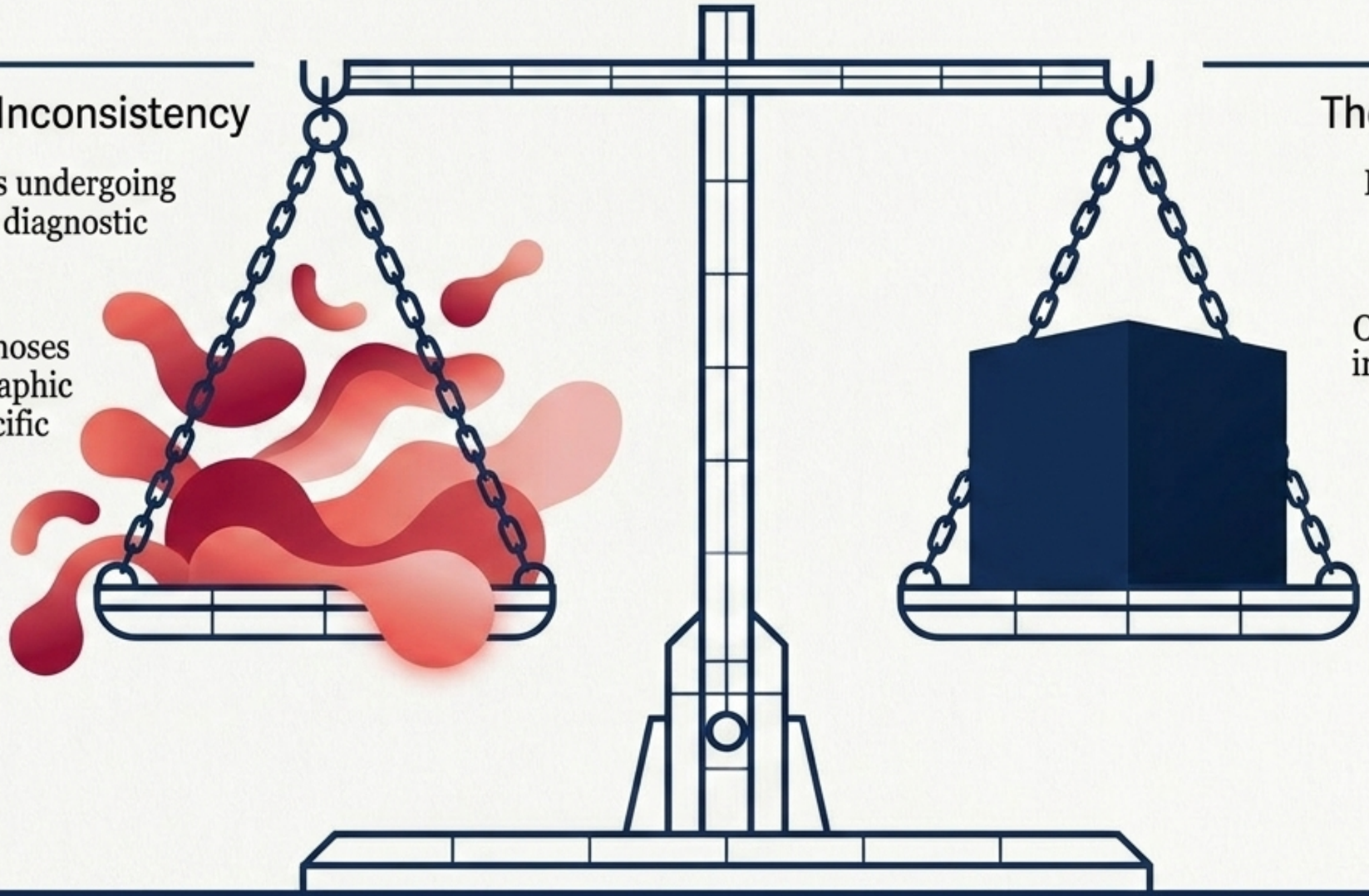


Medicine continually balances inconsistency against rigidity

The Risk of Inconsistency

Similar patients undergoing vastly different diagnostic evaluations.

Divergent diagnoses based on geographic location or specific provider.



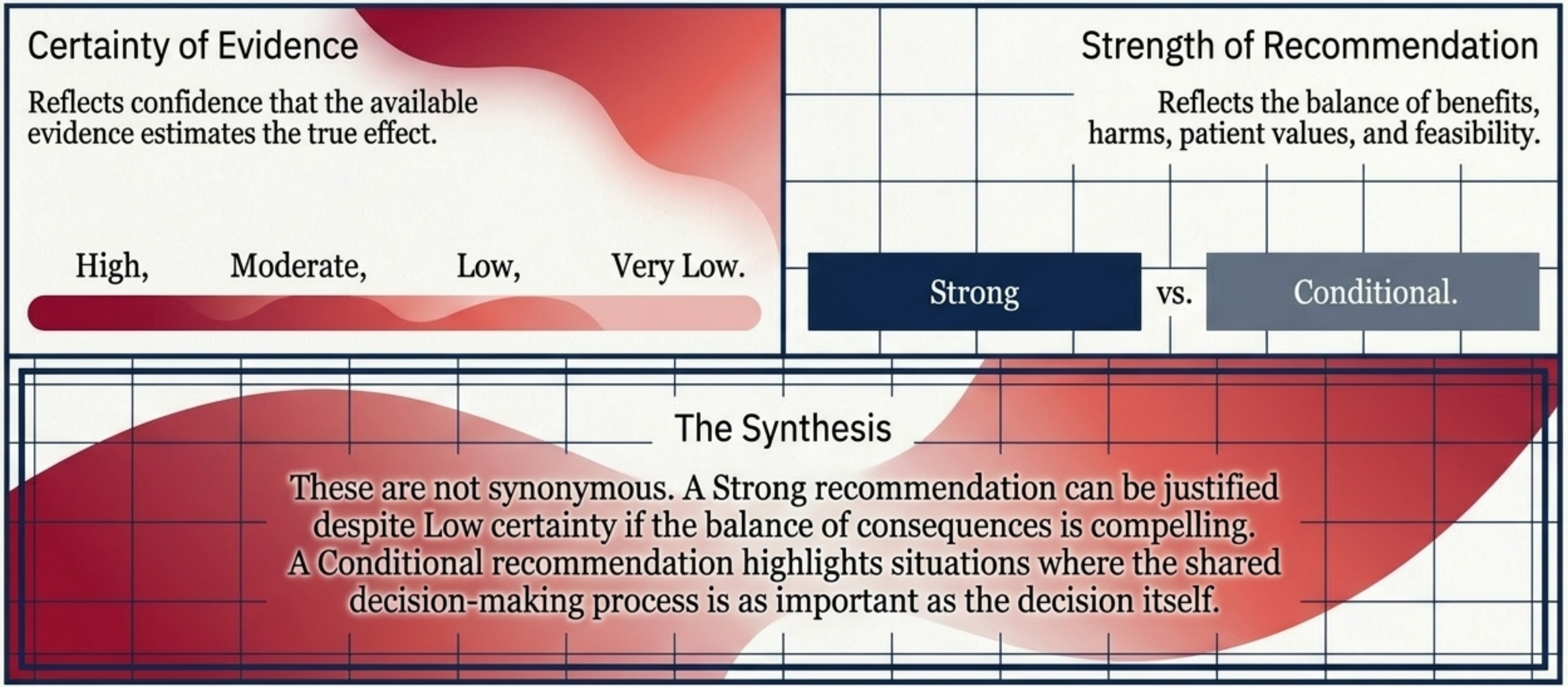
The Risk of Rigidity

Forcing every patient into predefined categories.

Overlooking clinically important differences in unique biology, personal values, and circumstances.

Modern guidelines begin with defined clinical questions and systematic evidence review. They seek to reduce inconsistency without mandating rigidity.

Evidence certainty is not the same as recommendation strength



Guidelines overlap, but they are not interchangeable

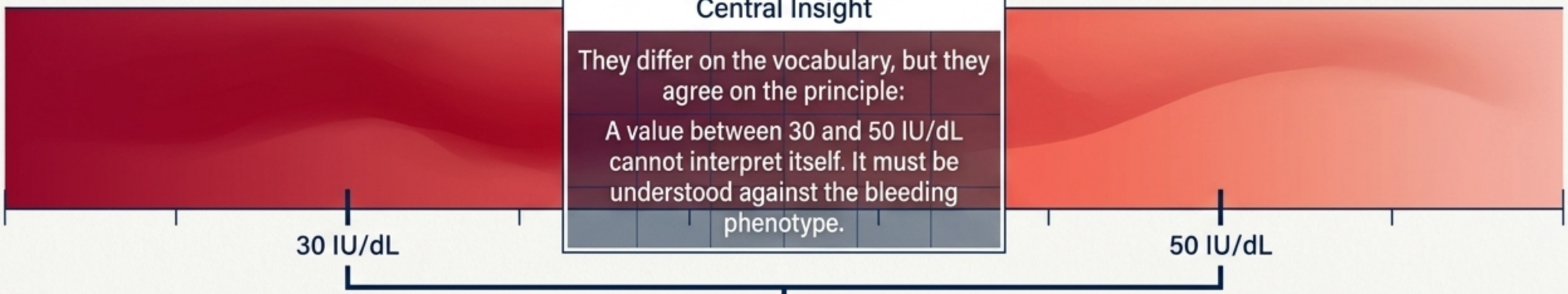
Guideline	Scope & Strength	Main Limitation
2008 NHLBI	Broad US framework. Established baseline for subtype evaluation and VWF replacement.	Predates current GRADE framework and newer assays.
2011 Nordic	Regional specialist centers. Operationalizing repeat testing and centralized expertise.	Procedural targets require adaptation to current standards.
2014 UKHCDO	Practical diagnostic categories. Formalized the Low VWF concept.	Predates the 2021 international framework.
2021 Int'l Diagnosis	11 prioritized questions. Transparent recommendations on thresholds and age normalization.	Leaves longitudinal reassessment to clinical interpretation.
2021 Int'l Management	Specific procedural/prophylaxis questions. Clear evidence-to-decision guidance.	Not a comprehensive treatment manual for complex bleeding.
2024 UKHCDO/BSH	Laboratory diagnosis. Detailed direction on preanalytical conditions and assays.	Broader clinical management is outside its scope.

Different guidelines assign different meaning to the same numerical range

2021 International Diagnosis Guideline

Label: Type 1 VWD (if abnormal bleeding exists).

Philosophy: Prioritizes reducing underdiagnosis and preserving patient access to specialized care and treatment.



Central Insight

They differ on the vocabulary, but they agree on the principle:

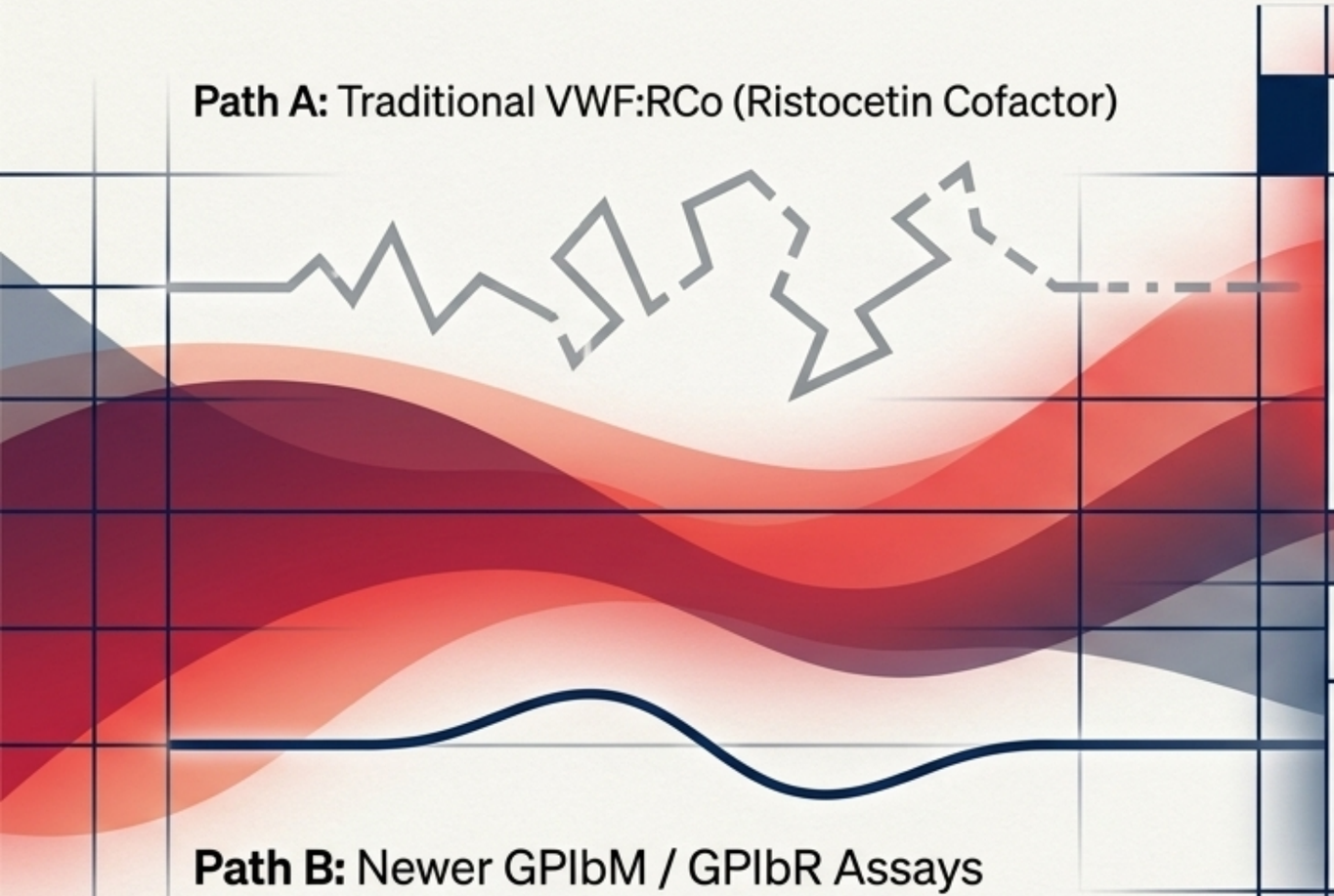
A value between 30 and 50 IU/dL cannot interpret itself. It must be understood against the bleeding phenotype.

2014 & 2024 UKHCDO Guidelines

Label: Low VWF (cautious categorization).

Philosophy: Prioritizes avoiding premature diagnostic closure. Encourages clinicians to keep looking for other hemostatic defects.

Guideline preferences are rooted in biological failure modes



Traditional VWF:RCo (Ristocetin Cofactor)

Mechanics: Relies on ristocetin binding.

Failure Mode: Vulnerable to VWF sequence variants that alter binding without causing a physiological defect.

Result: False appearance of disease exactly at the boundary where classification is hardest.

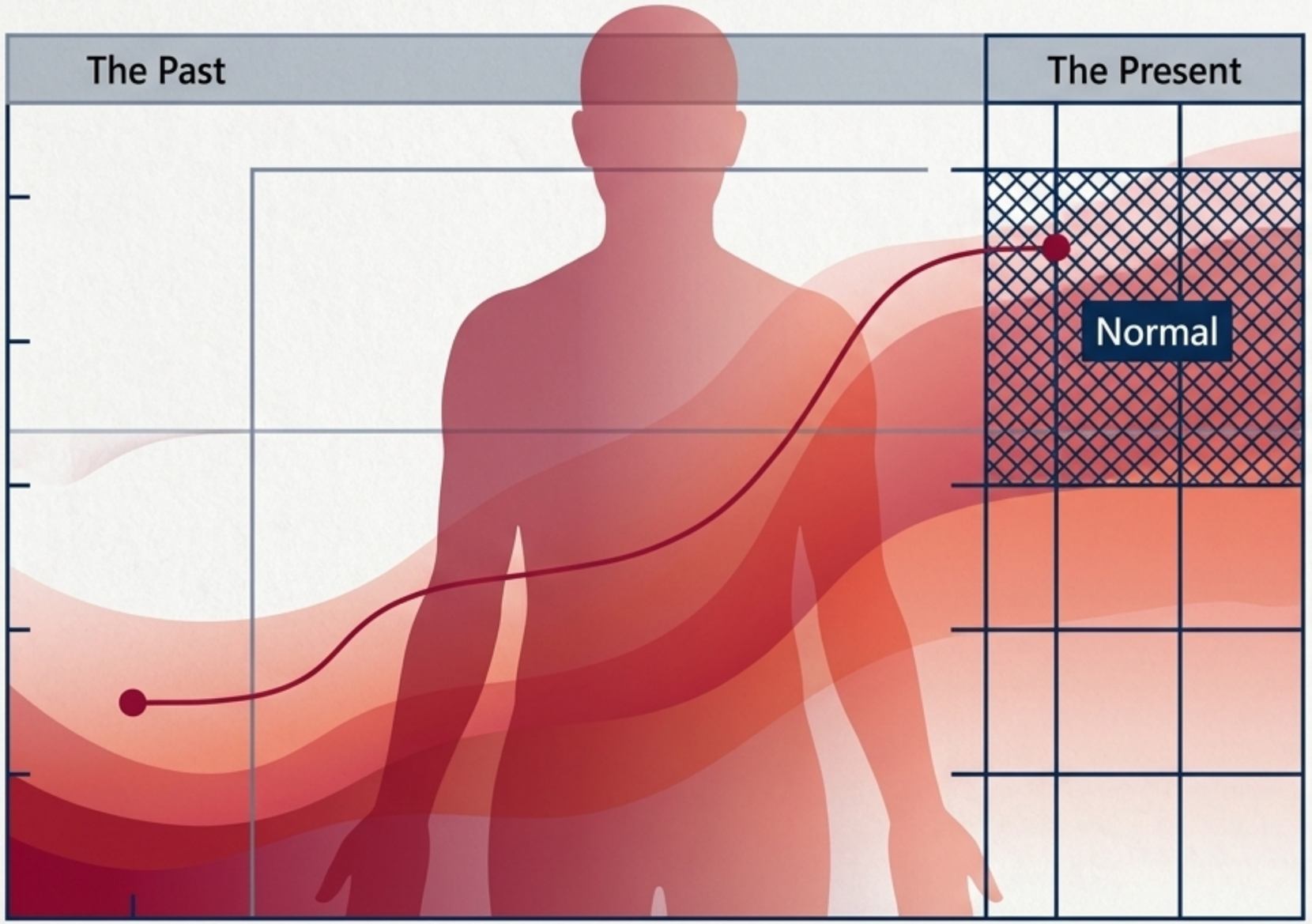
Newer GPIbM / GPIbR Assays

Mechanics: Uses gain-of-function GPIb; independent of ristocetin artifacts.

Success Mode: Better precision and automation.

Conclusion: The recommendation to prefer newer assays is not merely a technical preference; it follows directly from how the older assays biologically fail.

A current value answers one question, but it does not erase history



The Scenario:

VWF levels often normalize as patients age.

The Guideline Directive:

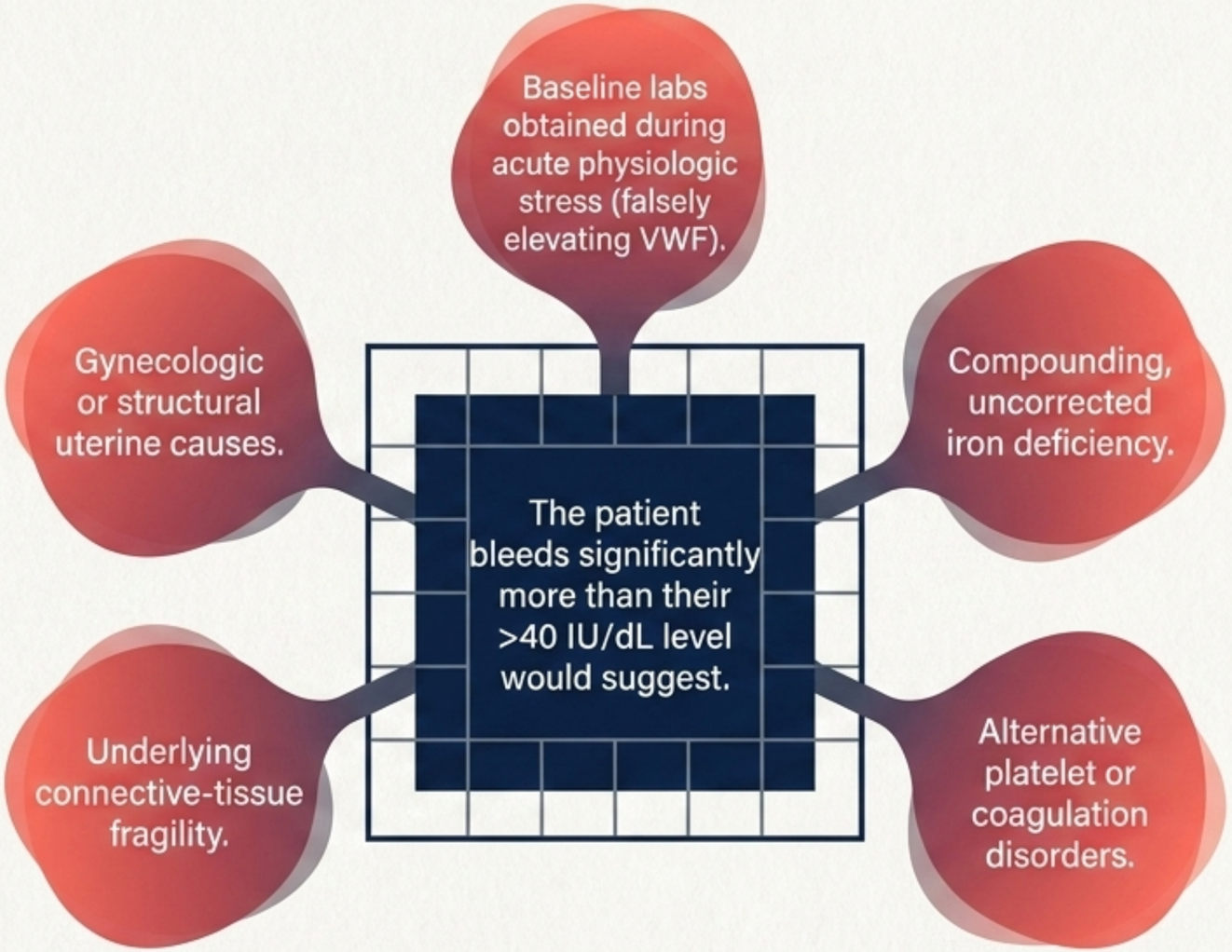
Reconsider, rather than automatically remove, an established Type 1 VWD diagnosis when values normalize.

The Clinical Judgment Required:

Was the original historical diagnosis secure and reproducible? Has the actual bleeding phenotype changed, or just the lab numbers?
What are the surgical consequences of removing the disease label today?

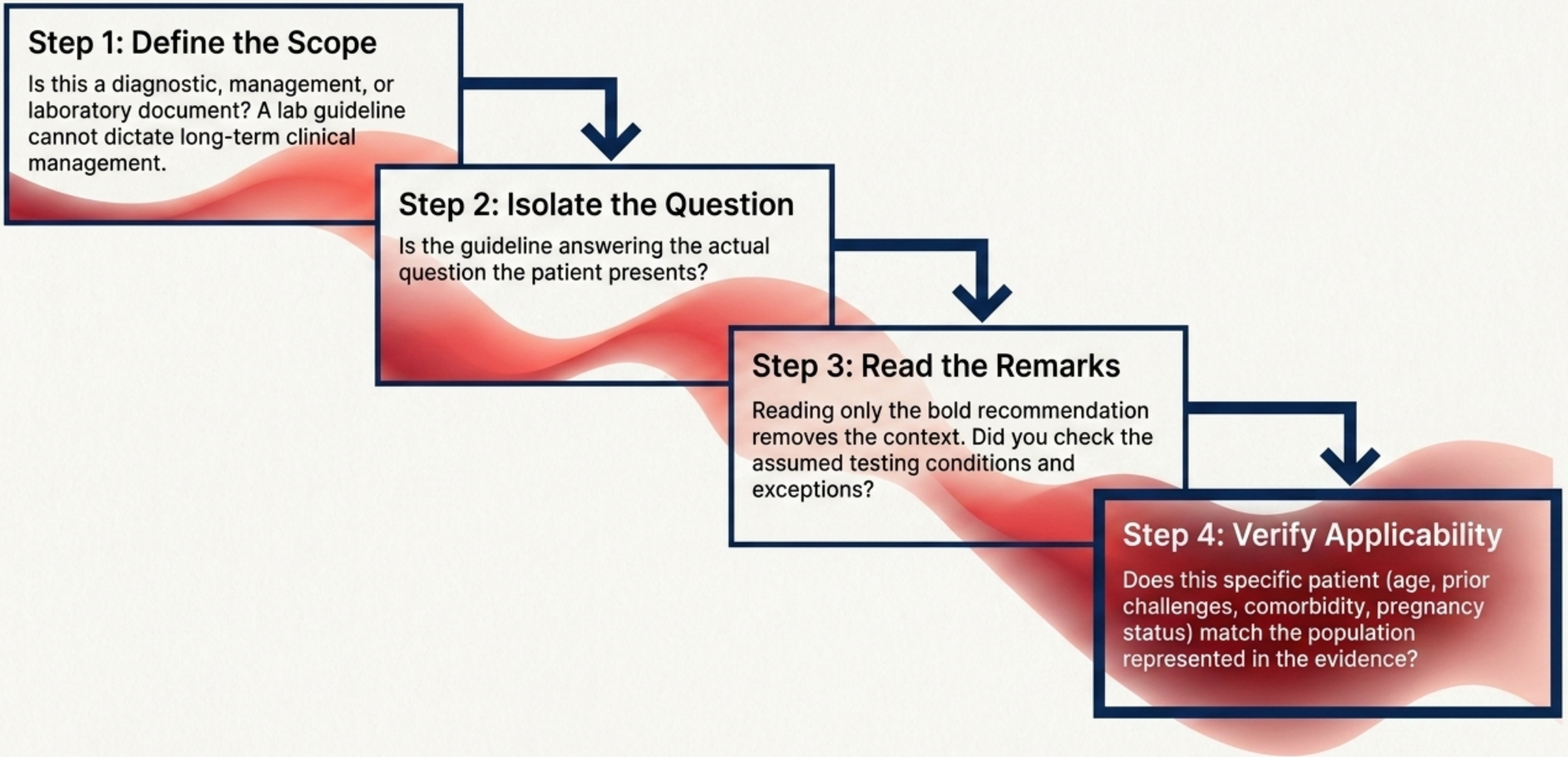
The guideline tells the clinician what not to do automatically. It cannot reconstruct the patient's history.

Identify what the guideline cannot explain



The correct response is not to reject the guideline or dismiss the patient.
It is to identify the biological modifiers the standard test cannot capture.

Applicability should be demonstrated, not assumed



Historical labels do not mandate historical prophylaxis

The Past (Age 24)

Labs: VWF levels 24-29 IU/dL.

Phenotype: Heavy menstrual bleeding, recurrent epistaxis.

Outcome: Secure diagnosis of Type 1 VWD; successful desmopressin response.

The Present (Age 67)

Labs: VWF antigen 78 IU/dL, Activity 74 IU/dL (Normalized).

Scenario: Facing major surgery.

The Clinical Synthesis:

Does she still have VWD? Yes, the historical diagnosis remains secure. However, her current normal values and thrombosis risk dictate the hemostatic support required for this operation. Historical labels do not erase present biology.

Guidelines **make clinical** judgment transparent, not obsolete

What Guidelines Do

- Narrow the field of biological uncertainty.
- Make underlying assumptions visible.
- Improve consistency across healthcare systems.

What Judgment Requires

- Verifying the bleeding phenotype.
- Validating the sample and the assay mechanism.
- Weighing the patient-specific consequences of the decision.

Final Takeaway: The purpose of a guideline is not to eliminate human judgment. It is to make that judgment more disciplined, transparent, and defensible.