

Precision Care in Adult Growth Hormone Deficiency

**A Clinical Playbook for Diagnosis,
Titration, and Long-Term Monitoring**

Synthesized from the AACE/ACE Guidelines

The Pathway to Precision Care



Vague Presentation
(Fatigue, Metabolic Syndrome)

Phenotype & Origin Matrix: Understanding the Baseline

Childhood-Onset GHD (CO-GHD)



Etiology

Mostly idiopathic/isolated, congenital defects, or developmental structural issues.

Phenotype

Tends toward lower BMI, lower waist-to-hip ratio, and lower baseline IGF-1

Clinical Risk

High risk of **impaired peak bone mass** and **severe metabolic alterations** if treatment is abandoned at adulthood

Adult-Onset GHD (AO-GHD)



Etiology

Acquired via hypothalamic-pituitary tumors (adenomas, craniopharyngiomas), surgery, or cranial irradiation

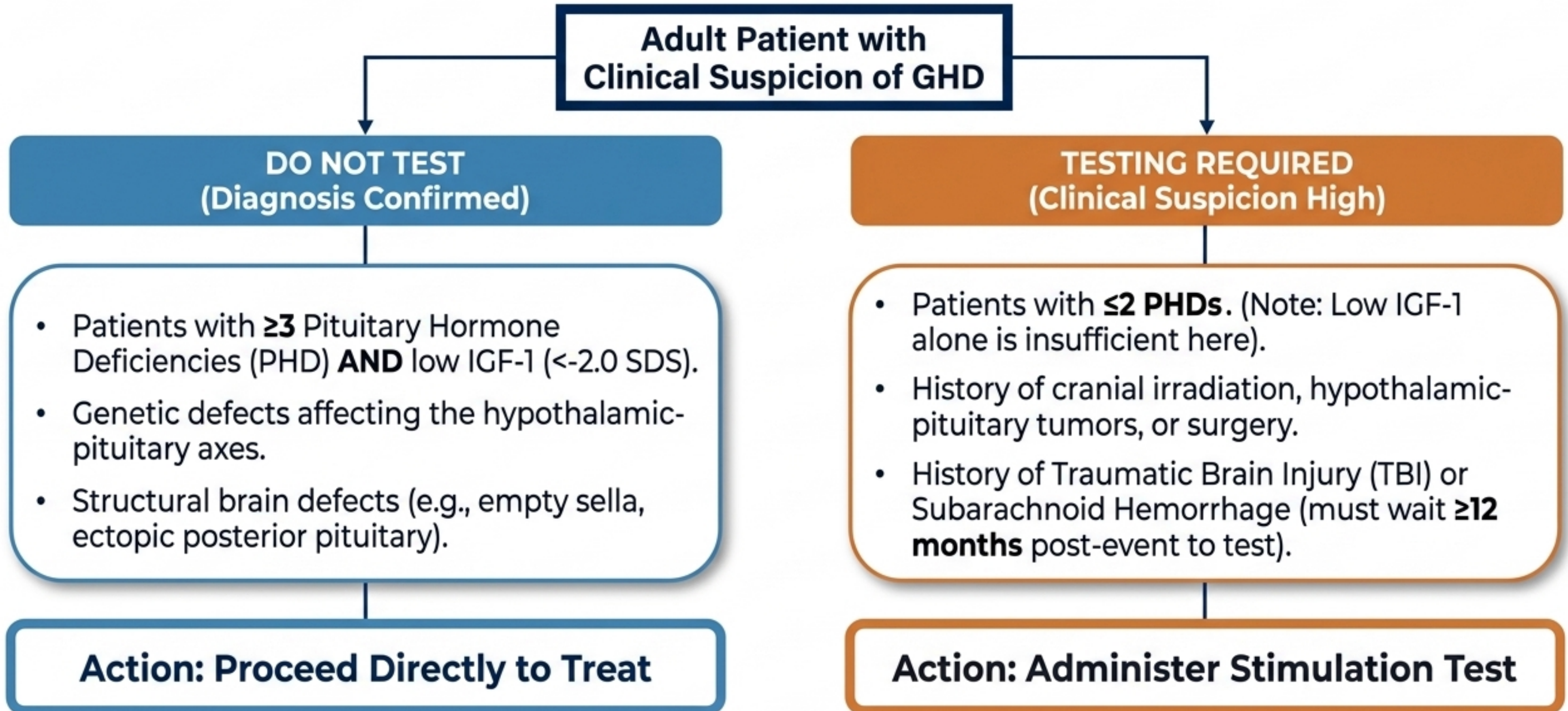
Phenotype

Often presents with features mimicking metabolic syndrome (central adiposity, dyslipidemia)

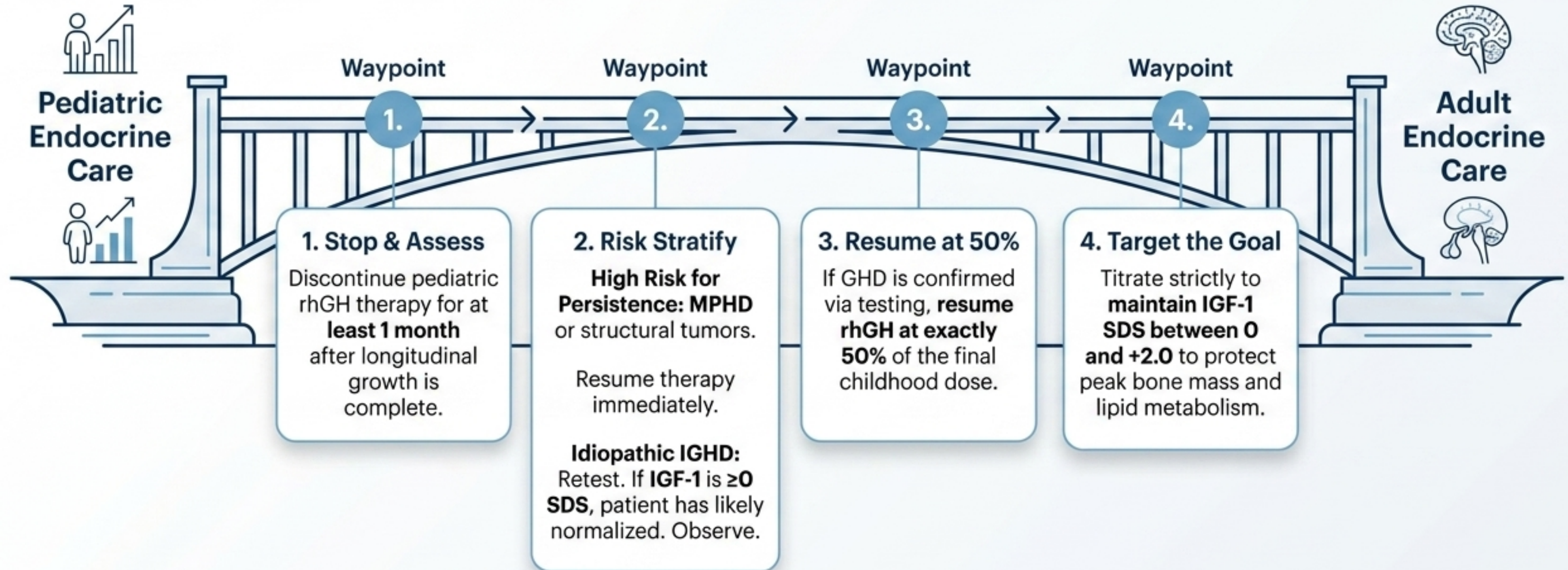
Clinical Risk

Cardiovascular morbidity, increased mortality, frequently co-occurs with Multiple Pituitary Hormone Deficiencies (MPHD)


The Triage Flowchart: Identifying Testing Candidates



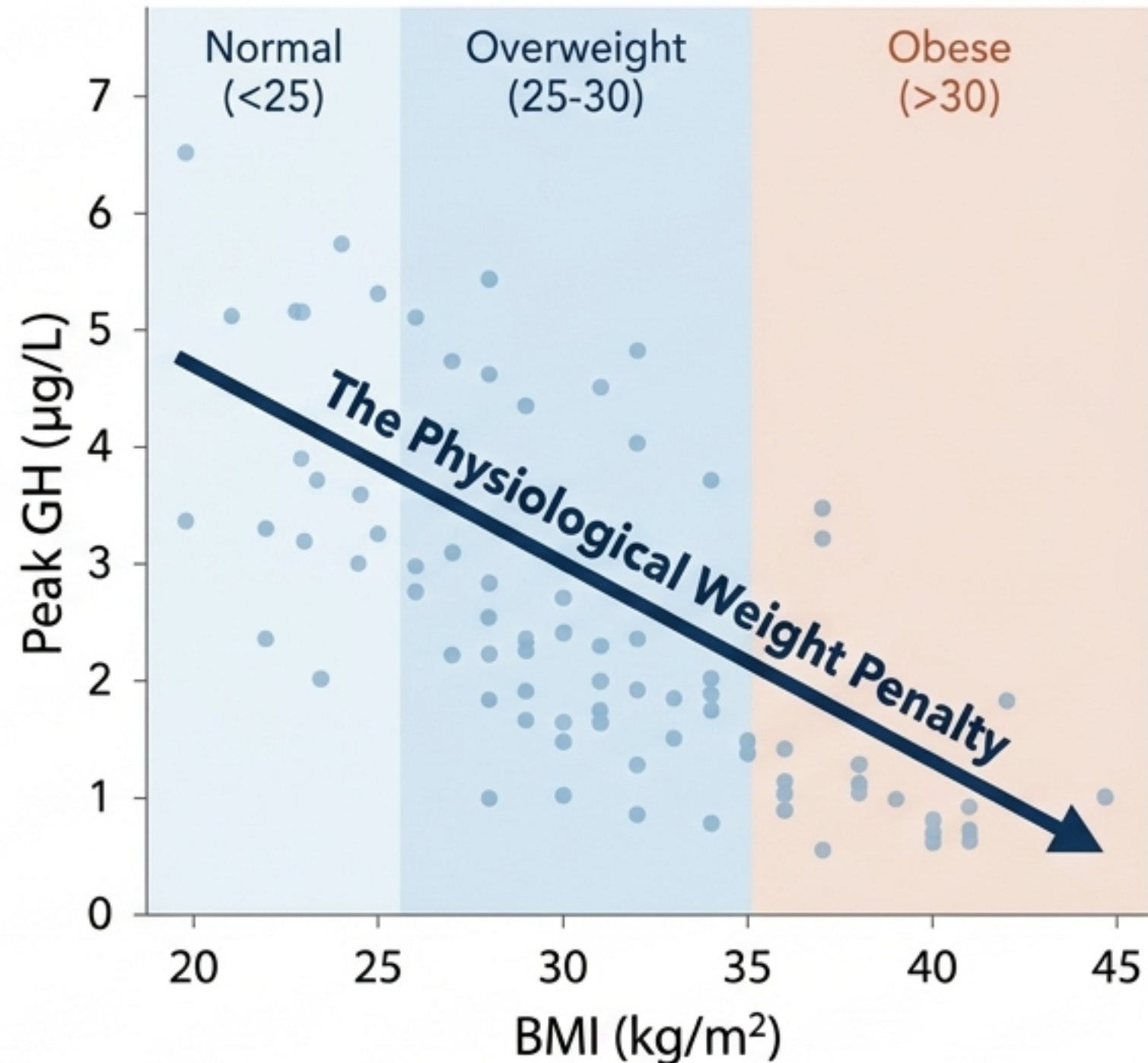
The Transition Bridge: From Pediatric to Adult Care



The Diagnostic Arsenal: Stimulation Tests Compared

	Status & Cut-point	Drawbacks / Benefits	Contraindications	Cost
Insulin Tolerance Test (ITT)	Historical 'Gold Standard' (Cut-point $\leq 5.0 \mu\text{g/L}$)	Requires inducing severe hypoglycemia. Labor-intensive.	 Elderly, seizure disorders, cardio/cerebrovascular disease.	\$
Glucagon Stimulation Test (GST)	Most common alternative.	Takes 3-4 hours, IM injection, frequent GI side effects. Highly dependent on BMI.	None major, but extreme caution in glucose intolerance.	\$
Macimorelin Test	FDA Approved (Dec 2017). Oral administration (Cut-point $\leq 2.8 \mu\text{g/L}$)	Benefits: Simple, fast (90 mins), well-tolerated.	Potential QT prolongation drug interactions.	\$\$\$

The Weight Penalty: Adjusting GST Cut-points for Obesity



The Problem

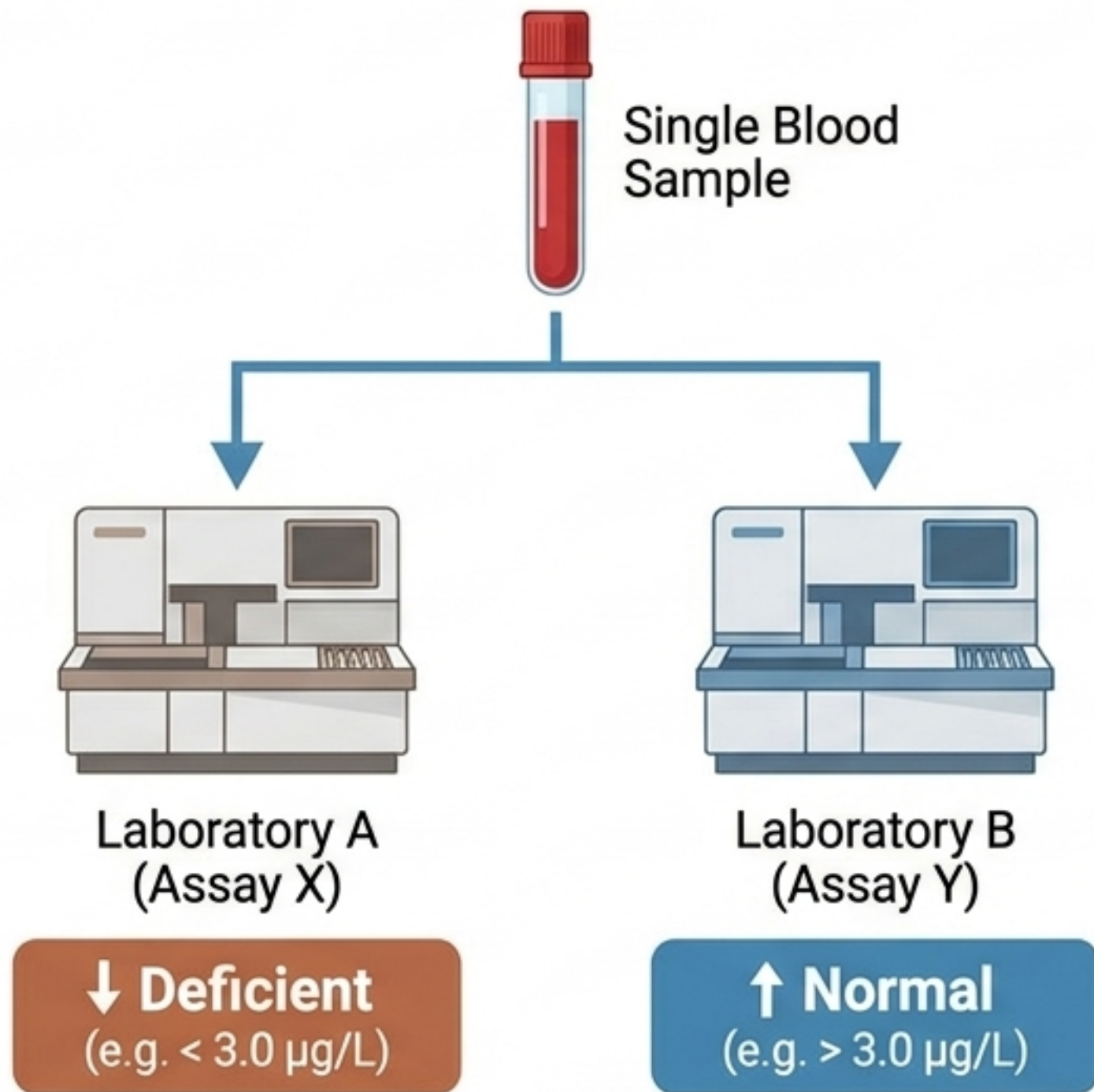
Obesity is a state of functional, relative GHD. Increased BMI decreases glucagon-induced GH stimulatory effects. Using a standard 3.0 µg/L cut-point on an obese patient generates false positives.

The Precision Solution

- BMI <25 (Normal) or BMI 25-30 with high pretest probability: Cut-point $\leq 3.0 \mu\text{g/L}$
- BMI >30 (Obese) or BMI 25-30 with low pretest probability: Cut-point $\leq 1.0 \mu\text{g/L}$

Warning: Exercise extreme caution interpreting GST in patients with glucose intolerance; hyperglycemia inversely correlates with peak GH.

The Assay Heterogeneity Trap

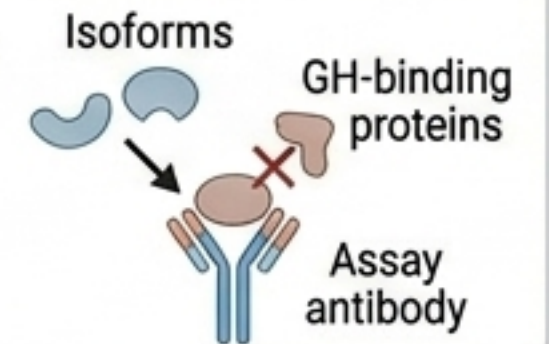


The Trap

Serum GH and IGF-1 levels can demonstrate up to a 2.5-fold difference across laboratories for the exact same sample.

The Culprits

- Measurement of different isoforms (22 kd vs 20 kd).
- GH-binding protein interference.
- Lack of harmonized calibration standards.



The Precision Protocol

- Use the exact same IGF-1 assay from the exact same laboratory for a patient's entire longitudinal follow-up.
- Demand labs report in mass units (using NIBSC standard 98/574) and provide IGF-1 in specific SDS values (Z-scores).

The Titration Dial: Setting the Initial Dose

Rule #1: Never use weight-based dosing in adults. (It induces fluid retention and side effects).

0.1 - 0.2 mg/day (Low Start)



Target Patient: Age >60 years, Obesity, concurrent Diabetes Mellitus, or previous gestational DM.

0.2 - 0.3 mg/day (Standard Start)



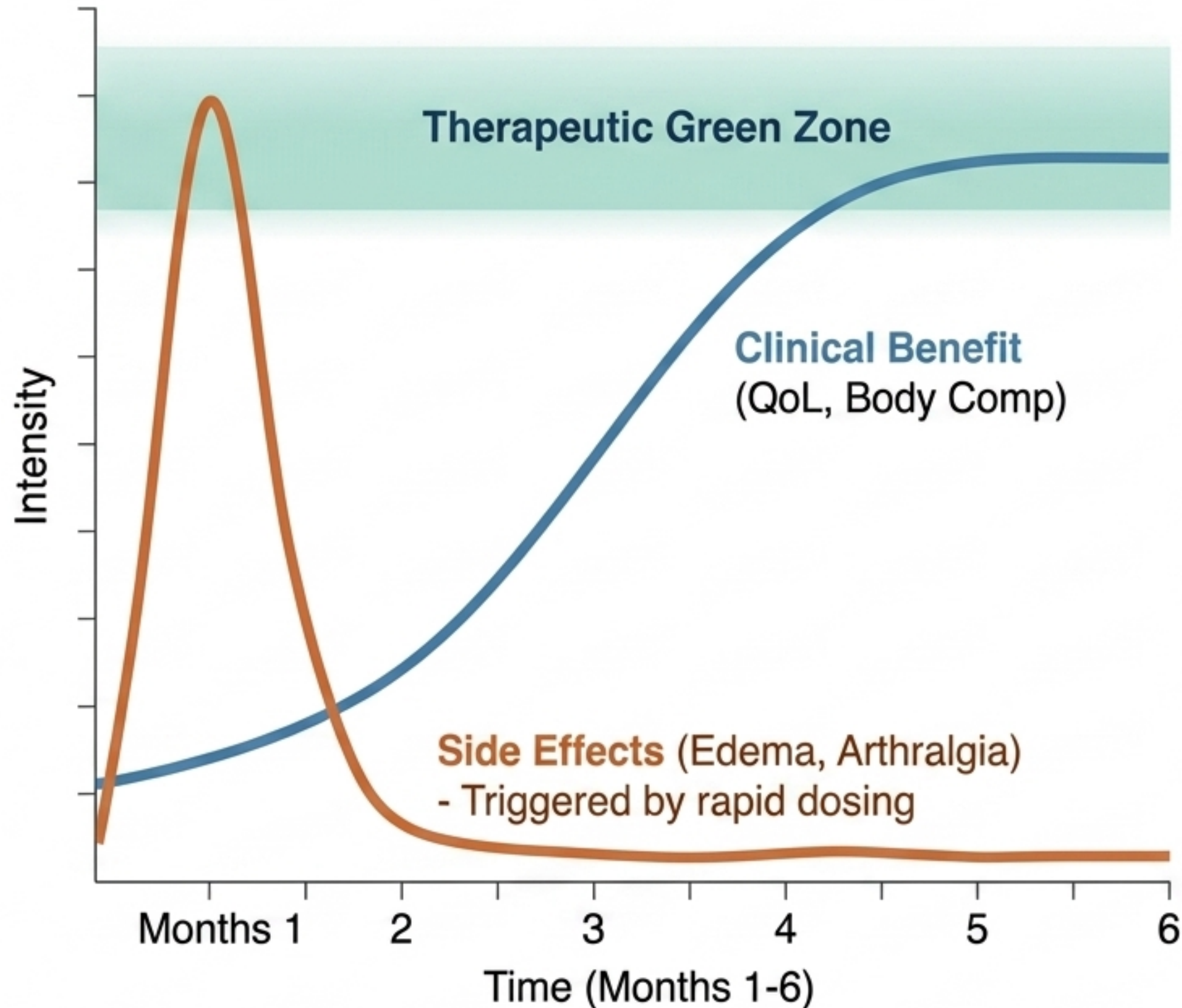
Target Patient: Age 30 - 60 years.

0.4 - 0.5 mg/day (High Start)



Target Patient: Age <30 years, Transition patients, or Women on oral estrogen therapy.

The “Start Low, Go Slow” Activation Curve



The Green Zone Target

Aim for an age-adjusted **IGF-1 SDS** between **-2 and +2**.

The Titration Rhythm

Increase doses by microscopic increments of **0.1 to 0.2 mg/day** every **1 to 2 months** based on laboratory feedback.

The Side Effect Spike

Fluid retention, myalgia, and worsening glucose tolerance are almost entirely correlated with initiating therapy at **too high a dose** or titrating **too rapidly**.

Dosing Modification Matrix: Manual Overrides



Factors Increasing Dose

- Patient is young (< 30 years).
- Serum IGF-1 remains unacceptably low despite compliance.
- Patient begins Oral Estrogen (Estrogen exerts a first-pass effect on the liver, blunting IGF-1 synthesis).
- Patient transitions from transdermal to oral estrogen.



Factors Decreasing Dose

- Patient is elderly.
- Serum IGF-1 exceeds +2 SDS.
- Patient experiences worsening glucose tolerance or frank diabetes.
- Fluid-retention side effects emerge (edema, arthralgia).
- Patient discontinues oral estrogen (or switches to transdermal).

Precision Monitoring Dashboard: Long-Term Surveillance

Interval: Assess all parameters at 6- to 12-month intervals once maintenance dose is established.



Metabolic & Cardiovascular

- Fasting glucose, Hemoglobin A1c, Lipid profiles.
- Blood pressure and heart rate.



Bone & Body Composition

- BMI, Waist circumference, Waist-to-hip ratio.
- DXA scans (repeat every 2-3 years if initial scan is abnormal).



Hypothalamic-Pituitary Interactions

- Free T4 (GH increases T4-to-T3 conversion, potentially unmasking central hypothyroidism).
- Morning cortisol (GH alters cortisol metabolism, potentially unmasking adrenal insufficiency).



Structural & Quality of Life

- Baseline and periodic MRI for post-surgical tumor remnants.
- Annual QoL-AGHDA specific patient questionnaire.

Safety Guardrails: Navigating High-Risk Comorbidities



Glucose & Diabetes Mellitus

The Risk: GH therapy temporarily induces **insulin resistance** during the initial titration phase.

The Rule: If DM develops or worsens, **hold or reduce the GH dose. Optimize antidiabetic medications FIRST** before attempting to resume GH at lower doses.



Malignancy & Secondary Neoplasms

Absolute Contraindication: Active malignancy or active proliferative diabetic retinopathy.

The "5-Year Wait" Protocol: For adult survivors of cancer, consider low-dose rhGH **ONLY after ≥ 5 years of verified cancer remission**, and **strictly in conjunction with oncology oversight**.

Cautionary Note: Childhood cancer survivors treated with cranial irradiation face modestly increased risk of Secondary Neoplasms (SN).

Illicit Use & WADA Detection Protocols

The Reality of Abuse

Off-label prescription for athletic performance or “anti-aging” is federally illegal.

It produces no documented increase in aerobic capacity or strength, but significantly increases side effects.

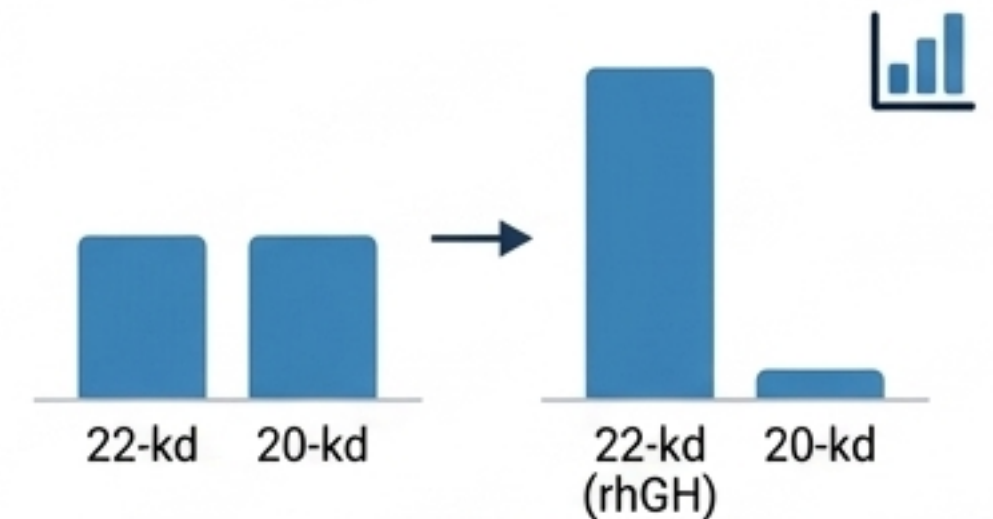
How WADA Detects Abuse

Urine testing fails due to GH’s 22-minute IV half-life. Detection requires sophisticated blood tracking.

1. The Isoform Test

Pituitary GH secretes multiple isoforms (22-kd, 20-kd). **Synthetic rhGH is strictly 22-kd.**

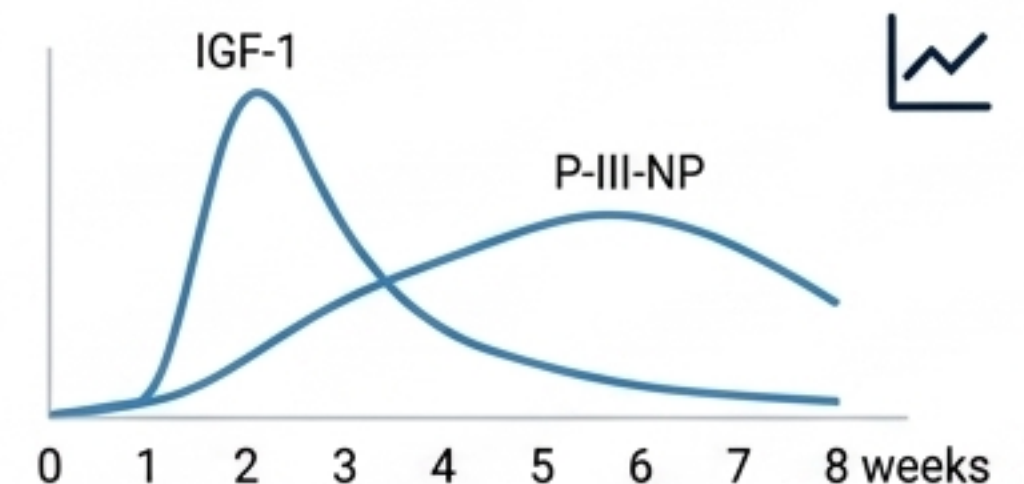
Injection **severely skews** the naturally occurring 22-kd to 20-kd ratio, forensically proving synthetic origin.



2. The Biomarker Array

Measures trailing biological indicators of GH abuse that last for weeks after injection.

IGF-1 spikes within 2 weeks; P-III-NP (collagen turnover marker) peaks at 4-6 weeks.



Precision Care Framework Summary

From Ambiguity to Exactitude

1. Targeted Testing	2. Standardized Assays	3. Individual Titration	4. Vigilant Monitoring
<ul style="list-style-type: none">• DO NOT TEST ≥ 3 PHD with low IGF-1.• Use BMI-adjusted GST cutoffs (3.0 $\mu\text{g/L}$ for normal, 1.0 $\mu\text{g/L}$ for obese).• Or utilize Macimorelin oral test ($\leq 2.8 \mu\text{g/L}$).	<ul style="list-style-type: none">• Stick to one single laboratory.• Demand NIBSC 98/574 mass unit standards.• Target the exact IGF-1 SDS window of -2 to +2.	<ul style="list-style-type: none">• NO weight-based dosing.• Start low: 0.1-0.2 mg/day for elderly/DM.• Start high: 0.4-0.5 mg/day for young/oral estrogen.• Titrate by 0.1-0.2 mg/day every 1-2 months.	<ul style="list-style-type: none">• Test Free T4 and cortisol early (GH unmasks deficiencies).• Track A1c, Lipids, DXA, and QoL longitudinally.• Maintain strict 5-year clearance for cancer remission.