THE REUNION PROJECT

LTS TOOLKIT SERIES WEBINAR:

RECLAIMING YOUR VITALITY

UNDERSTANDING HORMONE HEALTH, TESTOSTERONE, AND AGING WITH HIV

MARCH 25, 2026

featuring

Long-Term Survivor Nelson Vergel,
Author of *"Built to Survive"*



Aging with HIV is Complicated





Multimorbidity: 2 in 3 patients report at least two other health conditions alongside HIV.

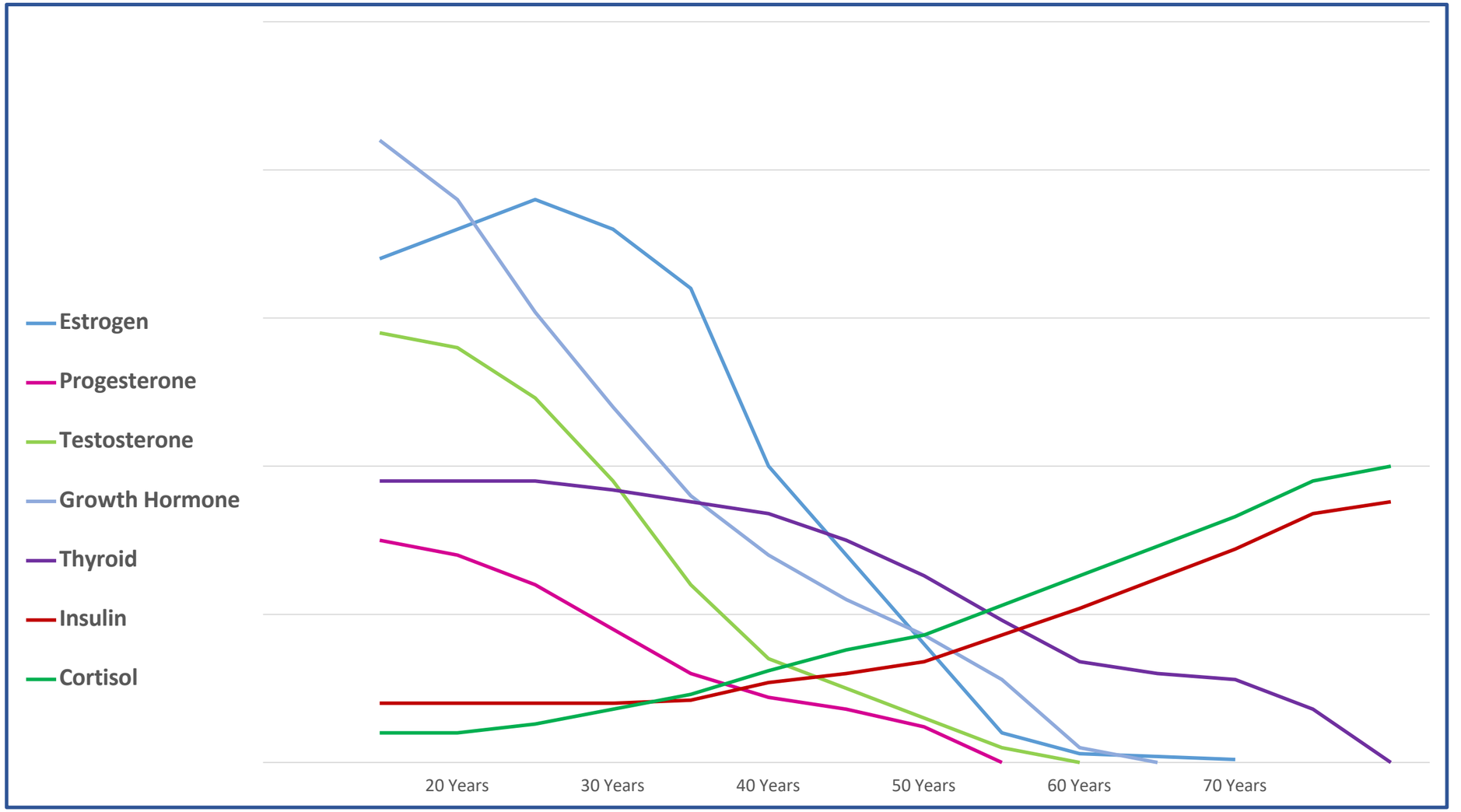


Mental Toll: 64% of respondents report mental health concerns like depression.



The Bottom Line: If you are feeling exhausted, weak, or depressed, you are not alone, and it is not “just in your head.”

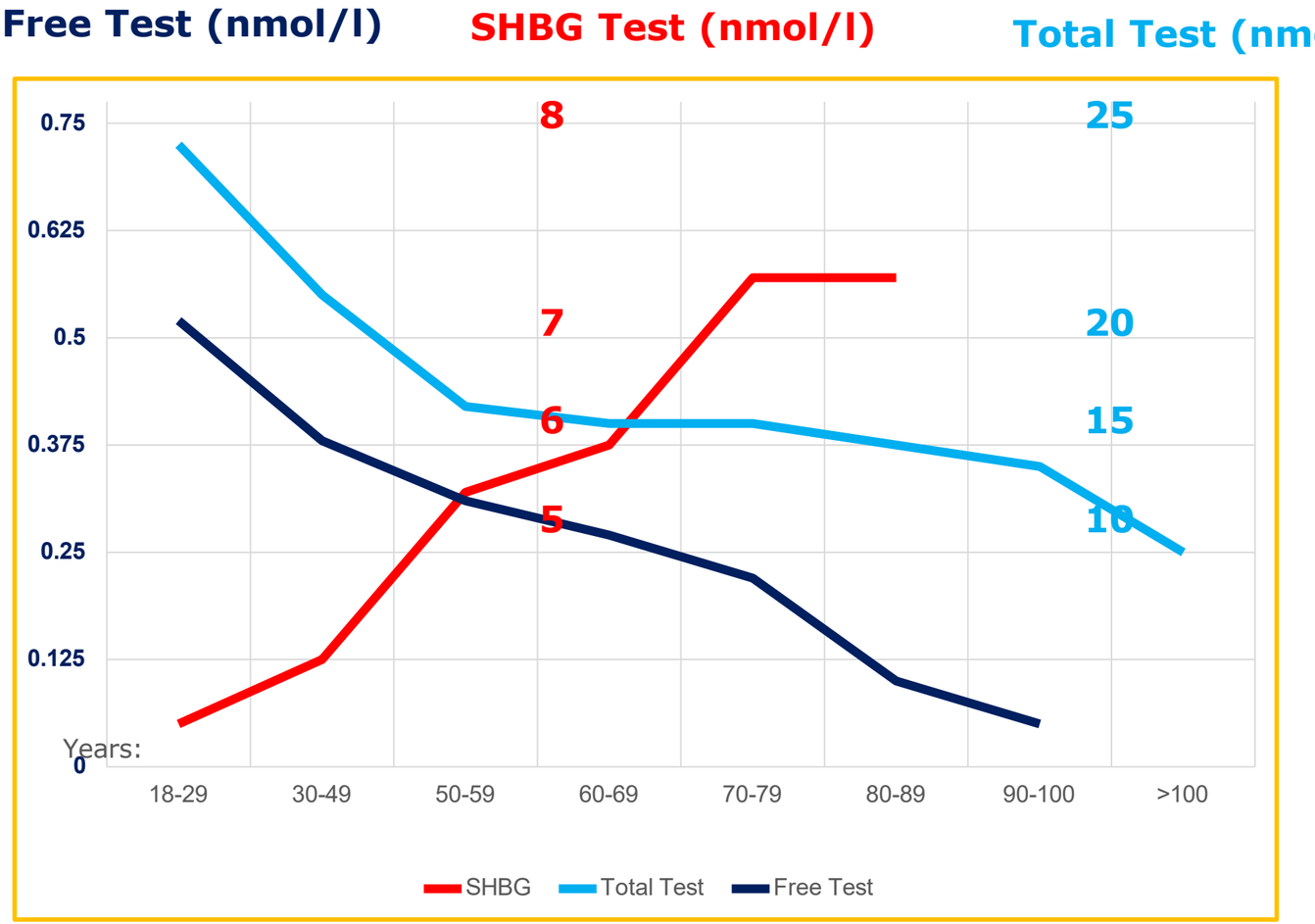
Age-Related Change of Hormones in Women and Men



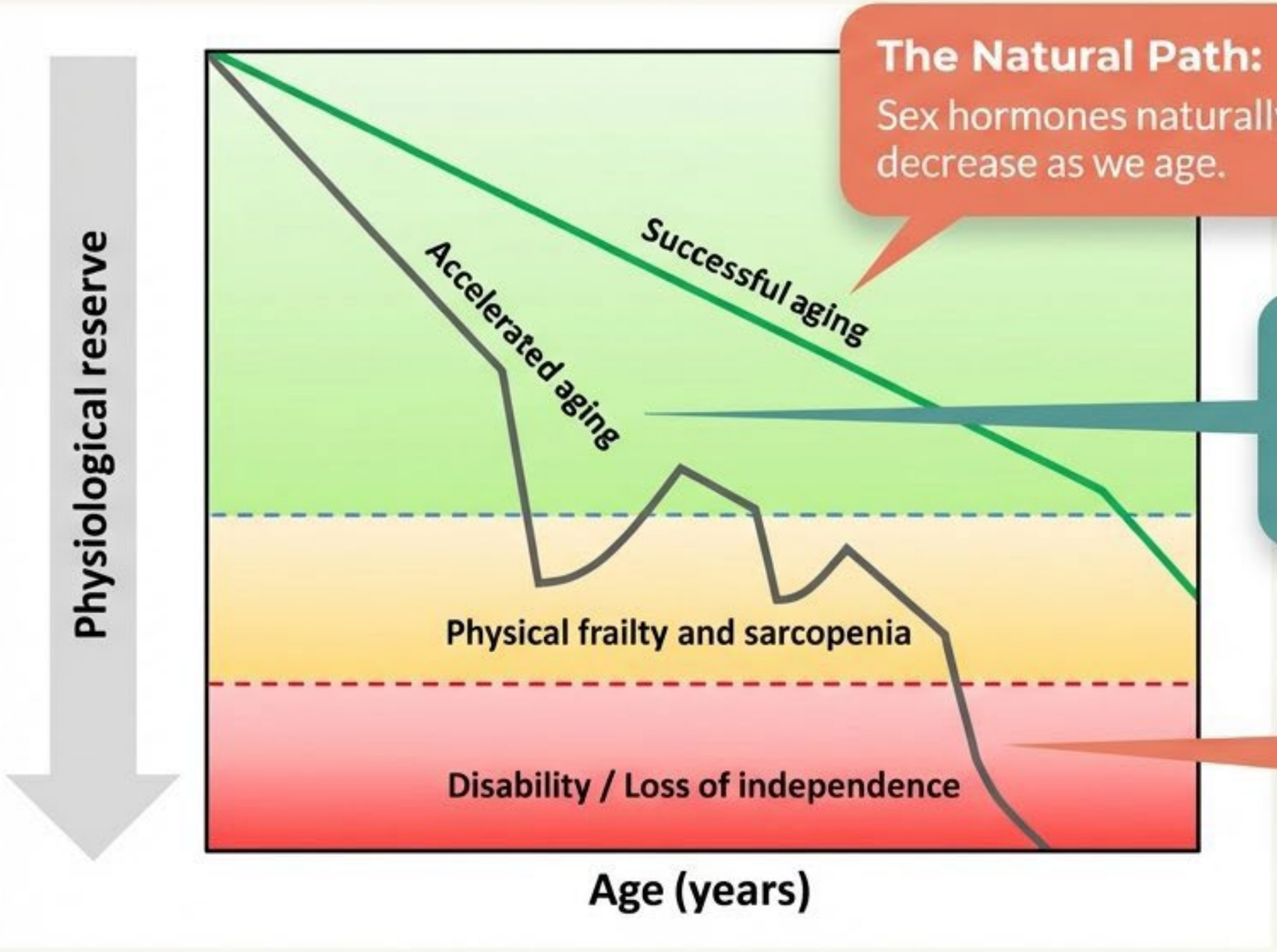
As we age, hormones change. Sex hormones like estrogen, progesterone, and testosterone decrease both in men and women. Growth hormone and thyroid function also decrease in both genders. Unfortunately, insulin from the pancreas and cortisol from the adrenal glands tend to increase as we age due to inflammation and insulin resistance.

Age-related Decline in Free and Total Testosterone Levels

As we age total and free testosterone decrease as sex hormone binding globulin increases. These changes can affect quality of life, decrease muscle mass, and increase fat mass in men and women. Some argue that these changes are natural and are made by evolution to slowly get us ready for death. I disagree with this view and believe that we can extend our disability-free life by normalizing these hormones.



The Hidden Culprit: Accelerated Hormone Decline



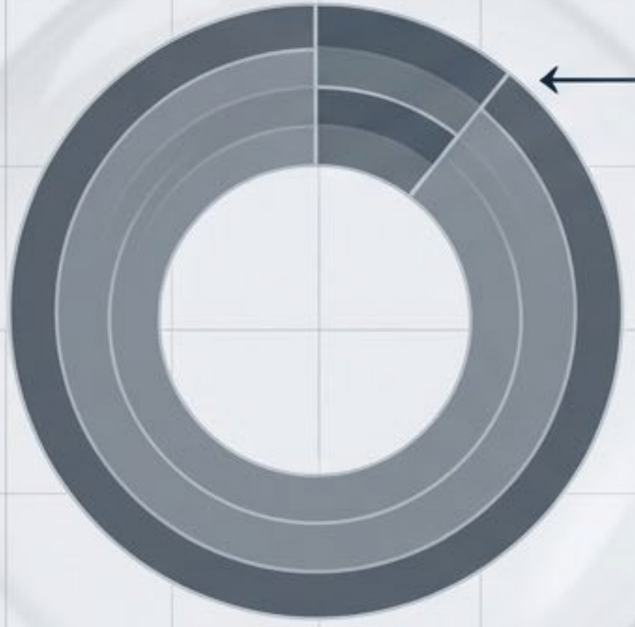
The Natural Path:
Sex hormones naturally decrease as we age.

The HIV Factor:
Chronic inflammation accelerates this decline, draining your physiological reserve much faster.

The Result:
A premature drop into physical frailty, muscle loss, and chronic fatigue.

The Hidden Prevalence: A Disproportionate Burden

General Male Population



6–12%
Prevalence

Massachusetts Male Aging Study. Onset strongly correlates with advanced age.

Men Living with HIV (HAART-Era)



~26%
Baseline Prevalence

Spikes up to 47.9% in ART-naive populations.

Premature Onset: Unlike the general population, hypogonadism frequently presents in MLWH well under the age of 50, independent of typical aging curves

What is Testosterone Deficiency (TD)?





A Note for Women Living with HIV

The Problem

Women with HIV frequently suffer from low adrenal function and extreme loss of lean body mass due to low testosterone.

The Treatment Gap

There are currently zero FDA-approved testosterone formulations specifically for women in the United States.

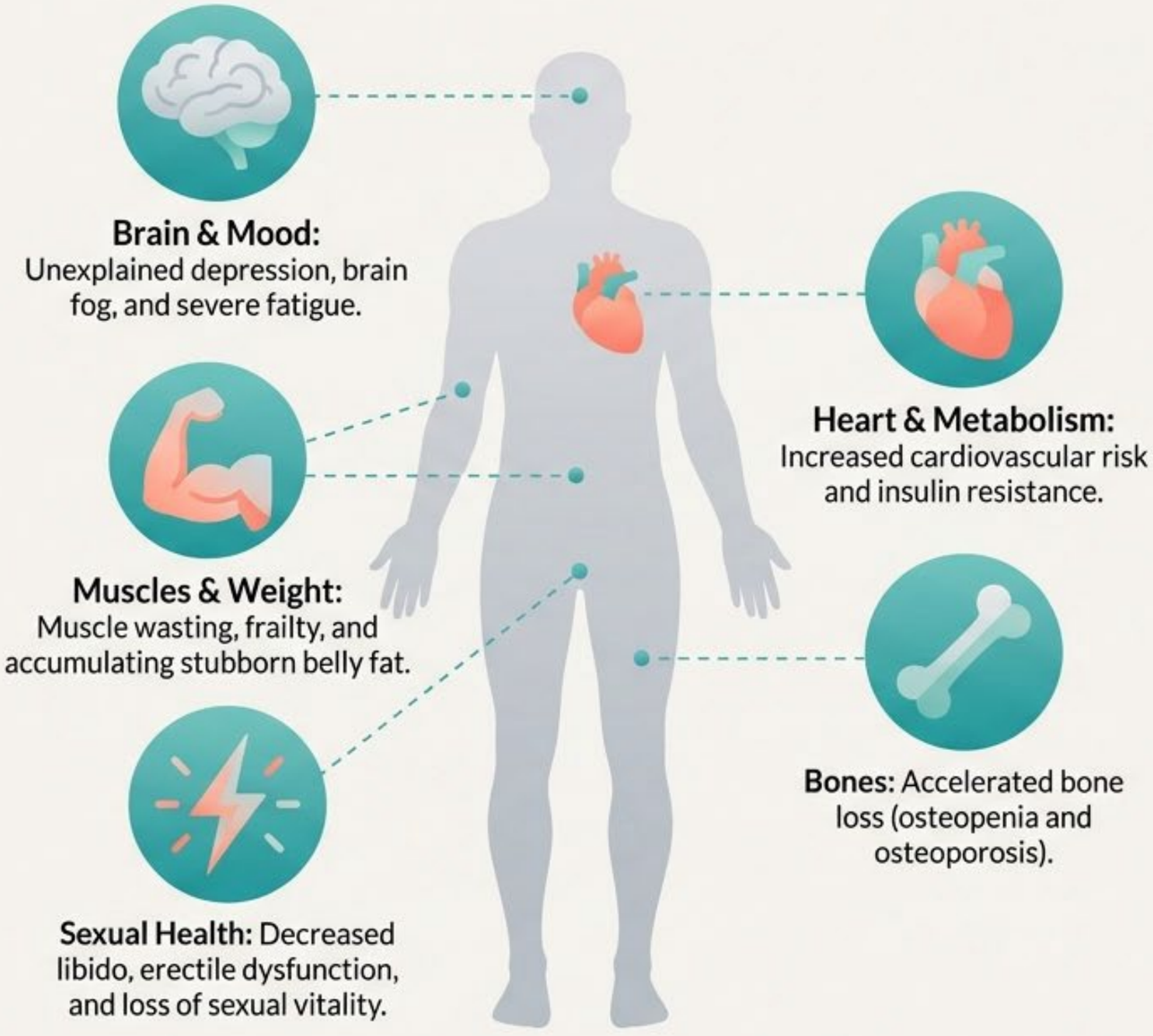
The Solution

Doctors safely prescribe “off-label” compounded transdermal creams or extremely low-dose patches (150–300 micrograms).

Monitoring

Treatment requires close doctor supervision to watch for side effects like acne or voice changes.

Spotting the Signs of Low Testosterone



Brain & Mood:
Unexplained depression, brain fog, and severe fatigue.

Heart & Metabolism:
Increased cardiovascular risk and insulin resistance.

Muscles & Weight:
Muscle wasting, frailty, and accumulating stubborn belly fat.

Bones: Accelerated bone loss (osteopenia and osteoporosis).

Sexual Health: Decreased libido, erectile dysfunction, and loss of sexual vitality.

Symptoms of Testosterone Deficiency (Hypogonadism)

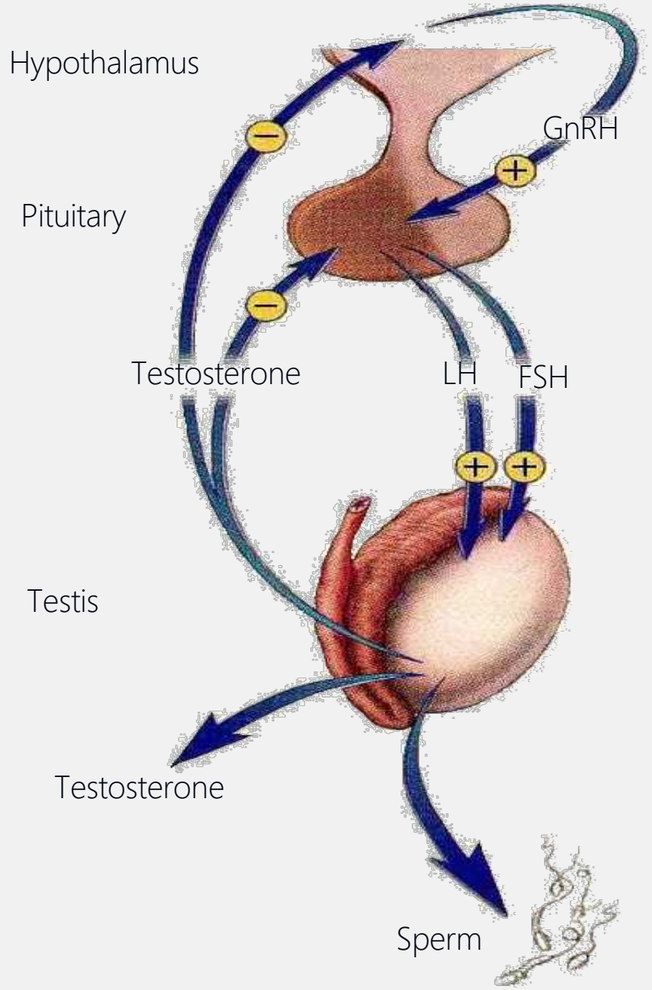
Q What symptoms are characteristic of testosterone deficiency?



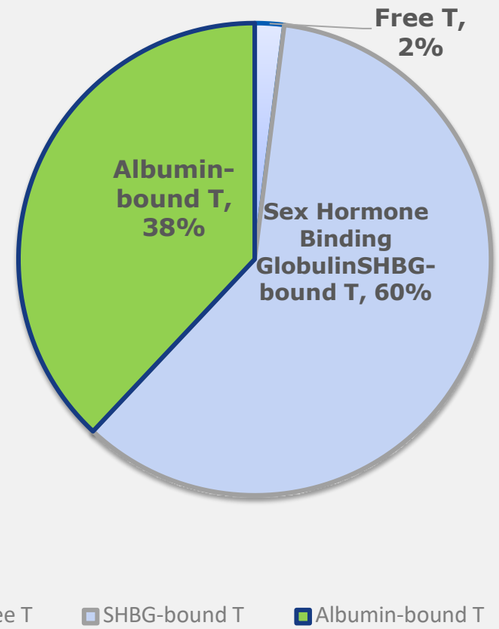
- **Decreased libido**
- Decreased vitality
- **Fatigue**
- **Mood changes**
- Insomnia
- Anemia
- Delayed ejaculation
- Hot flushes
- **Erectile dysfunction**
- Decreased muscle mass
- Increased visceral body fat
- Testicular atrophy
- Weakness
- Osteopenia / Osteoporosis
- Loss of facial, axillary, and pubic hair

Morales et al. CUAJ 2014;4:269-75; Bhasin et al. J Clin Endocrinol Metab 2010;95:2536-59

Production and Regulation of Testosterone



Adapted from Bagatell CJ, Bremner WJ. N Engl J Med. 1996;334:707-715.

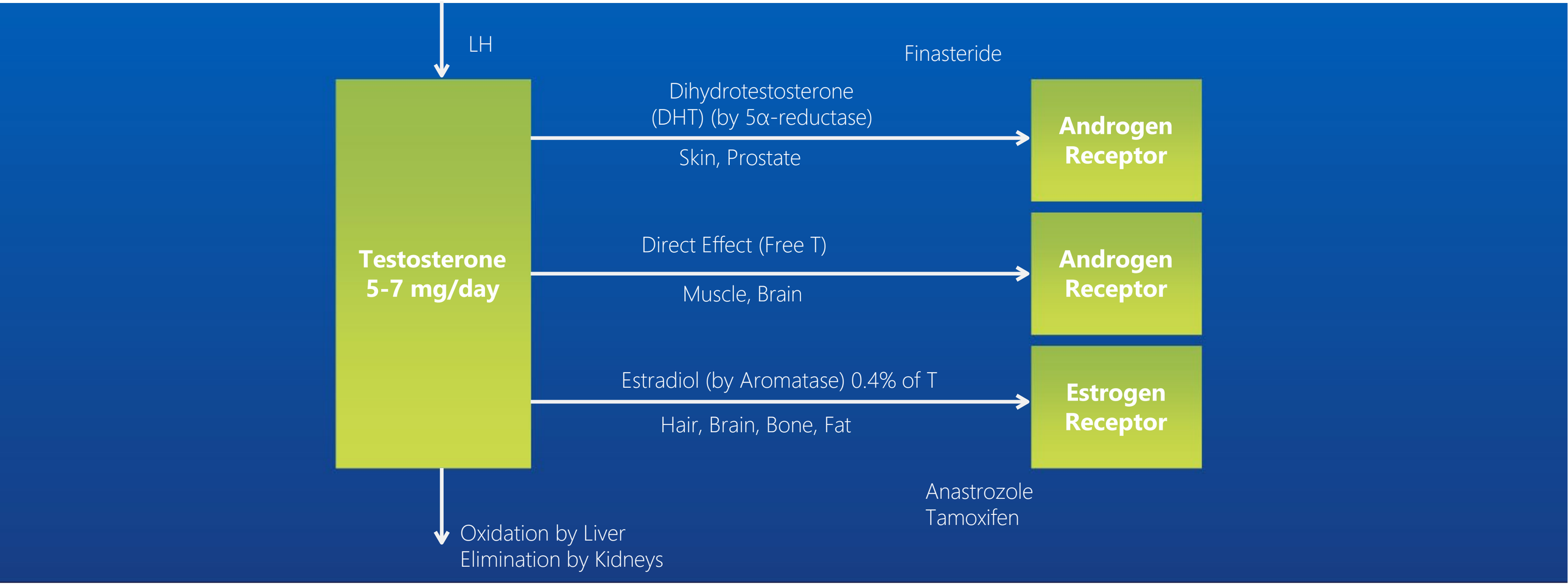


T = testosterone
Only 2% is free testosterone
and 98% is bound to albumin + SHBG
Bioavailable T= Free T + Albumin Bound T

Adapted from Braunstein GD. In: Basic & Clinical Endocrinology. 5th ed. Stamford, Conn: Appleton & Lange; 1997:403-433.

EMPOWER

Testosterone Metabolites and Their Functions



What T Level is Defined as “Low”? Different Guidelines Disagree

Suggested testosterone thresholds for diagnosis of testosterone deficiency

Body	Total Testosterone	Free Testosterone (calculated or EqD)
EAA, ISA, and ISSAM (2009)	<350ng/dl (12.1 nmol/l)	<65pg/ml (<225 pmol/l)
TES (2010)	<300ng/dl (<10.4 nmol/l) or <200ng/dl (<6.9 nmol/l) (panelist disagreement for older men)	<50-90 pg/ml
EAU(2012)	<350ng/dl (12.1 nmol/l)	<84 (<243 pmol/l)
Expert opinion (2014)	<400ng/dl (13.9 nmol/l)	80-100 pg/ml (1.5 ng/dl) (by radioimmunoassay)

Abbreviations: EAA – European Academy of Andrology; EAU – European Association of Urology; EqD – equilibrium dialysis; ISA – International Society of Andrology; ISSAM – International Society for the Study of the Aging Male; TES – The Endocrine Society.

The Danger of Relying Solely on Total Testosterone

The Clinical Trap: Total T levels can be highly misleading in states of obesity, type 2 diabetes, or advanced aging due to fluctuating sex hormone-binding globulin (SHBG). A physician may see a normal Total T level while the biologically active androgen exposure is actually critically deficient.

Total Testosterone Result



Hidden Clinical Reality (Low Free T)

- Fatigue & Lethargy
- Loss of Muscle Mass
- Decreased Libido
- Metabolic Dysfunction

The Paradigm Shift: From Acute Wasting to Chronic Frailty

Pre-HAART Era



Type: Primary Hypogonadism

Driver: Direct testicular damage, opportunistic infections, severe AIDS-related wasting syndrome.

Prevalence: 30-50% presenting with acute cachexia.

Timeline Progression

Current HAART Era

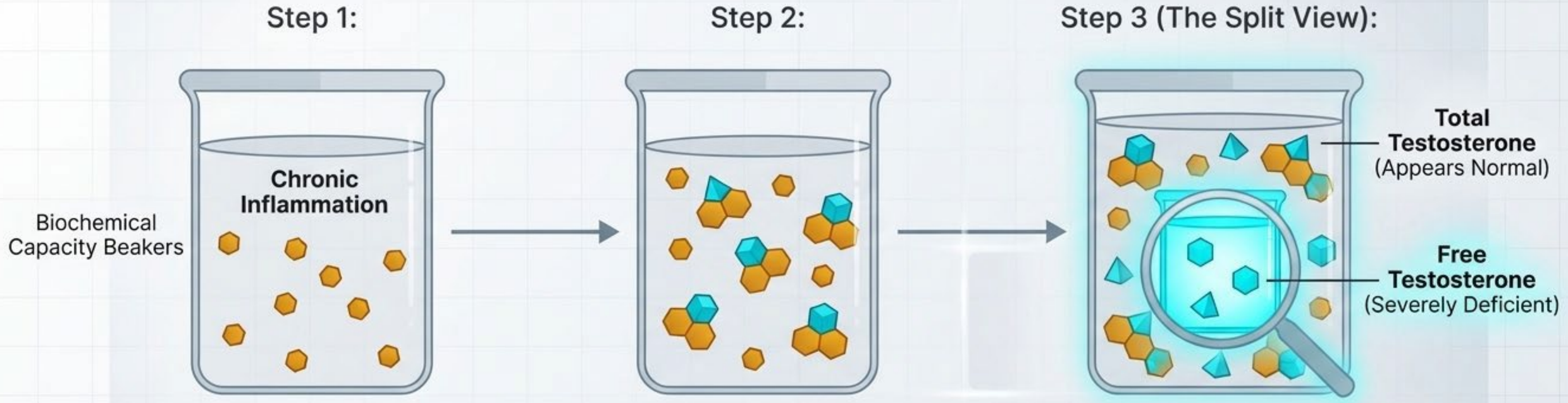


Type: Secondary (Functional) Hypogonadism (>80% of modern cases)

Driver: Hypothalamic-pituitary suppression, chronic systemic inflammation, metabolic shifts

Presentation: Frailty phenotype, altered body fat distribution, normal or inappropriately low Luteinizing Hormone (LH).

The SHBG Diagnostic Trap



Chronic HIV inflammation drives up Sex Hormone-Binding Globulin (SHBG) production.

Elevated SHBG acts as a biochemical sponge, binding to active testosterone molecules.

While the outer Total Testosterone measurement looks adequate, the active Free ingredient is critically starved.

The Illusion of Normalcy: Relying on Total Testosterone misses the diagnosis. Elevated SHBG masks the deficiency, leaving patients in a state of undetected, compensated, or overt functional hypogonadism.

Clinical Action Pathway



1. Screen (Beyond Sex)

Actively deploy the ADAM questionnaire in MLWH under 50. Look for the frailty phenotype (unexplained fatigue, muscle loss, depression), not just erectile dysfunction.



2. Test (The Free T Imperative)

Never rely solely on Total Testosterone. Always order a morning draw of Total T, SHBG (to calculate Free T via Vermeulen), LH, and FSH to classify primary vs. secondary.



3. Treat (Targeted Restoration)

For confirmed, symptomatic secondary hypogonadism, initiate tailored Testosterone Therapy to break the frailty loop and restore lean metabolic mass.
Monitor hematocrit and cardiovascular risk regularly.

The Diagnostic Matrix: Unmasking the Defect

1. Which Testosterone to Measure?

Total Testosterone (TT)	Calculated Free Testosterone (cFT)
Flawed in MLWH. Highly susceptible to SHBG alterations.	The Gold Standard for MLWH. Calculated via the Vermeulen equation (incorporating TT and SHBG). Liquid chromatography-tandem mass spectrometry (LC-MS/MS) preferred.

2. Locating the Defect (The Gonadotropin Panel)

Primary Hypogonadism	>80% of MLWH Cases Secondary Hypogonadism
Biomarkers: Low cFT + Elevated LH/FSH	Biomarkers: Low cFT + Low/Normal LH/FSH
Pathology: Testicular failure	Pathology: Hypothalamic-pituitary suppression

The Landscape of Testosterone Measurement

Total Testosterone (Total T)	Calculated Free T (cFT)	Directly Measured Free T (mFT)
Standard first-line test. High availability, low cost.	Standard clinical workaround using mathematical formulas.	The True Gold Standard (Equilibrium Dialysis LC-MS/MS).
❌ Highly vulnerable to SHBG alterations. Misleading in metabolic syndrome and aging.	❌ Inherent algorithmic bias (e.g., Vermeulen formula has ~20% positive bias vs. gold standard).	✅ Technically demanding, historically lacked robust reference data. This new dataset solves the reference gap.

How Can One Increase Testosterone Naturally?

Good Sleep Quality and Hygiene

Weight Loss if Overweight

Avoiding Environmental Toxins

Glucose Control

Exercise

Note: There is no effective OTC testosterone booster

Beyond the Prescription: A Holistic Approach



Fixing the Foundation

Addressing sleep, nutrition, and reducing opioid use can naturally boost hormones.

Functional Hypogonadism



Resistance Training

Lifting weights combined with TRT is proven to exponentially increase lean muscle and functional capacity.



Targeting Belly Fat

Reducing visceral fat naturally reduces the “sponge” effect, raising your own testosterone.

Your Next Doctor's Appointment

- ☑ "I have been experiencing fatigue, muscle loss, and mood changes, and I'd like to check my hormones."
- ☑ "Because I have HIV, I know my SHBG might be elevated. Can we specifically order a FREE Testosterone test?"
- ☑ "I'll make sure to schedule the lab visit between 7:00 AM and 10:00 AM for accuracy."
- ☑ "If I am low, can we discuss modern treatment options like oral pills or auto-injectors?"

HYPOGONADISM DIAGNOSIS



- Requires signs/symptoms + low total testosterone level
  - Normal and low testosterone levels should be defined for each assay. There is an ongoing effort by the US Centers for Disease Control and Prevention (CDC) to harmonize testosterone assays to the same standard, which should to harmonize normal ranges. The International Society of Andrology defines low testosterone levels <231 ng/dL and borderline levels 231-346 ng/dL. The Endocrine Society uses <300 ng/dL



- Initial labs: fasting 7-10 AM serum total testosterone; if low total testosterone, repeat and include LH, FSH, PRL



- Measure free and total testosterone level in men with borderline low total testosterone or whom alterations in SHBG are suspected



- Evaluation of androgen deficiency should **not** be done during any acute or subacute illness



- DEXA scan recommended for all men with severe testosterone deficiency or fragility fracture



TRT Contraindications

- 🧬 Breast or untreated prostate cancer
- 🩸 Hematocrit >50%
- 😴 Untreated severe sleep apnea
- ⚠️ Severe LUTS (Lower Urinary Tract Symptoms), IPSS >19
- ❤️‍🩹 Uncontrolled CHF (Congestive Heart Failure), NYHA III–IV
- 👶 Fertility desired (nuanced)

The Newest, Easiest Ways to Treat TD



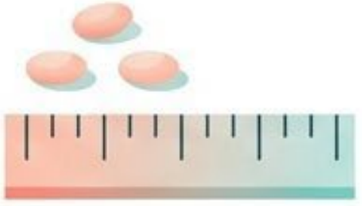
1. Auto-Injectors

Just like an EpiPen. A tiny, virtually painless needle goes just under the skin once a week. No more deep muscle jabs.



2. Modern Oral Pills

The newest breakthrough. Twice-daily pills taken with food. Completely eliminates needles and the risk of transferring gels to loved ones.



3. Long-Acting Implants

Tiny pellets placed under the skin by a doctor that provide steady hormone levels for 3 to 6 months at a time.

The Evolution of Treatment

The Past



Deep-muscle shots.
Highly effective but require needles and cause hormonal "peaks and valleys."

The 2000s



Daily Transdermal Gels.
Steady hormone levels, but carry a risk of accidentally transferring to partners or pets.

The Present



Modern breakthroughs.
Practically painless and highly convenient options.

Evolution of Testosterone Therapy

1935-1937

Testosterone first synthesized

- Oral 17a-methyltestosterone
- Injectable esterified 17β-hydroxy Testosterone
- Subdermal pellets

1979

Depo-Testosterone (testosterone cypionate)

- intramuscular injection



1995

Androderm (testosterone)

- transdermal patch



2000

Androgel (testosterone)

- transdermal gel



2014

Natesto (testosterone)

- nasal gel



2018

Xyosted (testosterone enanthate)

- subcutaneous injection (autoinjector)



July 2022

KYZATREX™ (testosterone undecanoate)

- capsules



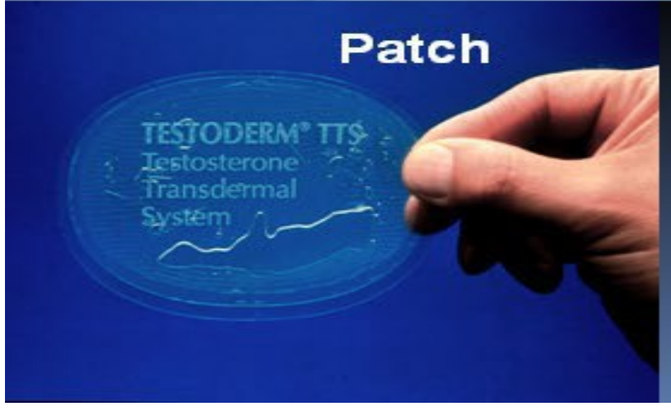
All trademarks are property of respective owners.

Please see Important Safety Information, including Boxed Warning, on slides 3-4 and accompanying Full Prescribing Information.

Testosterone Options









Fortesta (2 % gel)



Buccal





Androgel packets



Testim tubes

Gels



Androgel pump for higher doses

Not to scale

Underarm lotion



Axiron

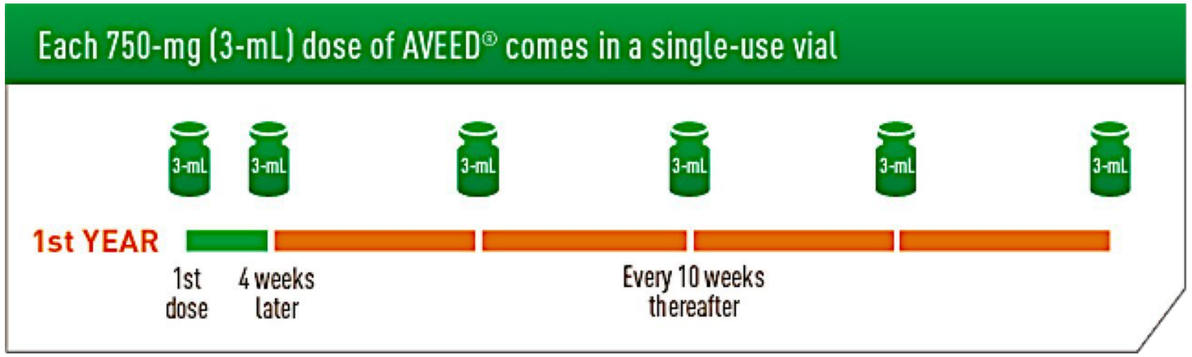


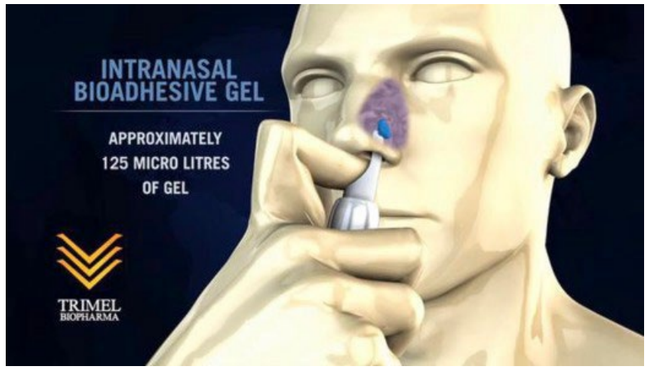
EXCELMALE
Your Men's Health Community

Newer Testosterone Products









Oral Testosterone Undecanoate Twice Per Day







Testosterone enanthate injected subcutaneously once per week



Latest FDA Approved TRT Options

EMPOWER

TRT-RELATED COMPOUNDED PRODUCTS

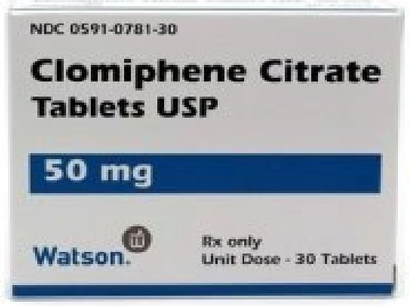
















Pellets

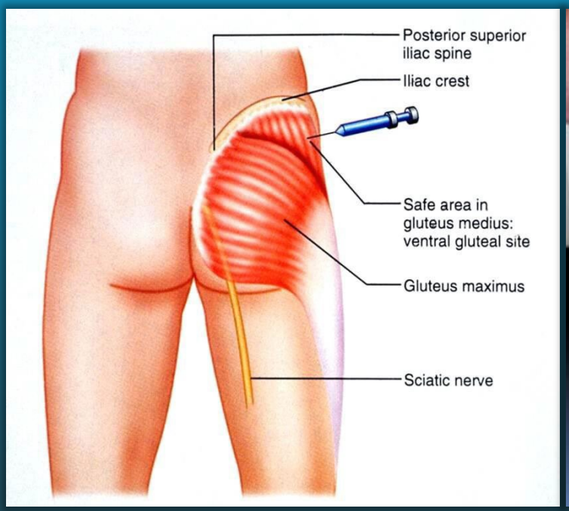
TRT Options And Dosing

Route	Formulation	Dose regimen	Pharmacokinetics	Advantages	Disadvantages
Transdermal gels	AndroGel 1% AndroGel 1.62% Fortesta, 2% Axiron, 2% Testim, 1% Compounded creams: 200mg/cc	• Gel (Androgel 1% or 1.6%, Testim 1%) • Start 5-10 g of 1% gel/day (provides 50-100 mg T daily) • Lotion (Axiron): 60 mg once daily applied to axilla (30-120 mg/d) • Fortesta 2% gel 60 mg/d • Compounded cream: 1 cc daily. New method: scrotal application	Steady state in 48-72 h	Quick onset. Physiologic pattern Stable serum levels. Easy self-administration. Compounded cream can be applied to scrotum for increasing DHT.	Cost or insurance issues. Possible site irritation with alcohol based gels. Transference risk. Variable response. Unreliable absorption.
Oral buccal	Striant 30 mg tablet	30 mg BID	Peak serum levels within 30 min	Quick onset. Physiologic pattern .Easy to use	Gum/mouth irritation/altered taste. Twice per day. Kissing transference.
Injection (shorter acting)	Enanthate 200 mg/ml injection-Cypionate 100 or 200 mg/ml injection	200 mg q 2 weeks or 100-150 mg IM q week	Half-life 5-7 days, rapid onset and offset	Inexpensive.	Supraphysiologic levels. Pain. May cause higher hematocrit. Peaks and nadirs.
Injection (longer acting)	Aveed (undecanoate) 750 mg/ml	750 mg IM q week x2, then q 10 weeks thereafter	Normal serum levels maintained for up to 10-12 weeks	Long duration Stable serum levels. Less frequent injections. Better compliance.	Large IM injection Office injection. Rare post-injection cough.
Subcutaneous pellets	Testopel 75 mg pellet Compounded pellets (100-200 mg)	Testopel 16 pellets q 3-4 months. Compounded 6 pellets q 3-4 months	Serum level peaks at 1-month, normal levels maintained 3-4 months	Long duration. Stable serum levels. Better compliance.	Procedural insertion. Pellet extrusion. Potential bruising or infection
Topical patches	Androderm 2 and 4 mg patches	2-6 mg (1-3 patches) q day	Maintain physiologic levels for 24 h	Mimics circadian patterns Ease of use	Skin irritation at application site. Disclosure
Nasal	Natesto 5.5 mg	11mg (2 pump actuations) TID	Peak serum levels within 40 min, short half-life	Quick onset. Easy to use. Minimal contact transference	Intranasal irritation. High peaks. Twice per day

IM: intramuscular; TID: three times daily; BID: twice daily

Modified and Adapted from McBride JA, Carson CC, Coward RM. Diagnosis and management of testosterone deficiency. Asian J Androl 2015;17:177-86

Testosterone Injection Sites for Deep and Shallow IM & Subcutaneous Methods







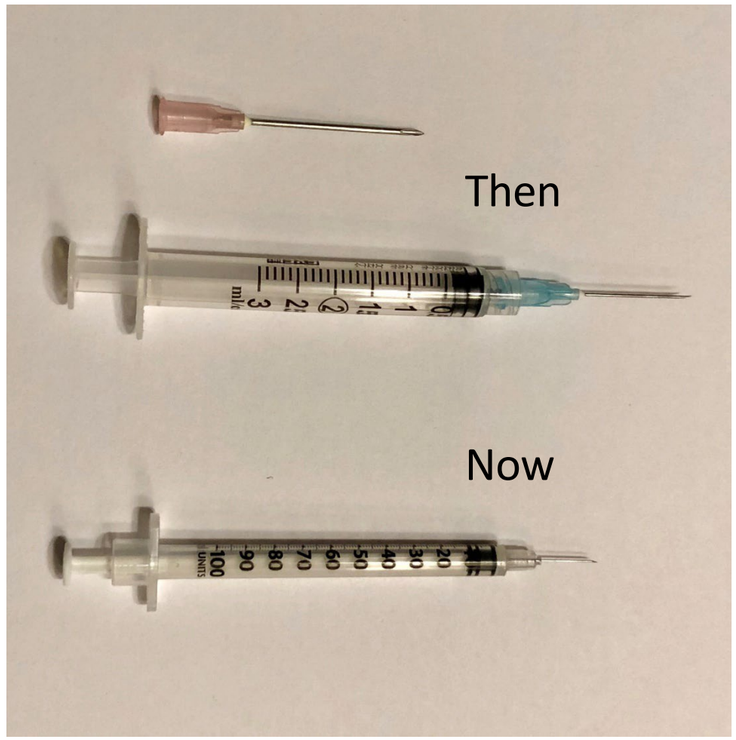


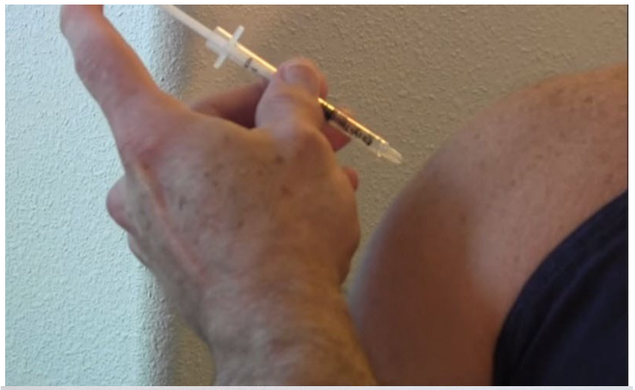
Testosterone Injections: Then and Now

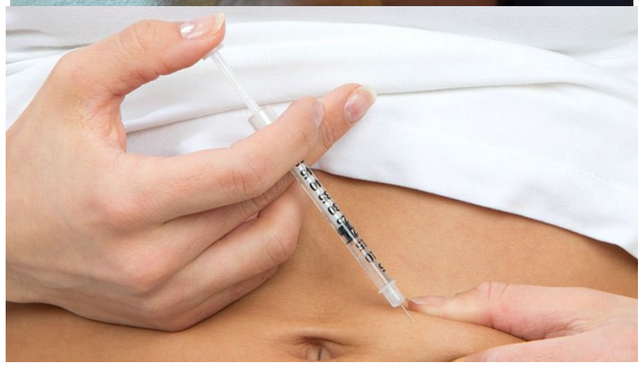
Then: 18 gauge loading syringe, 23 gauge 1 inch injection syringe

Now: 27 gauge ½ inch syringe used for loading AND injecting:

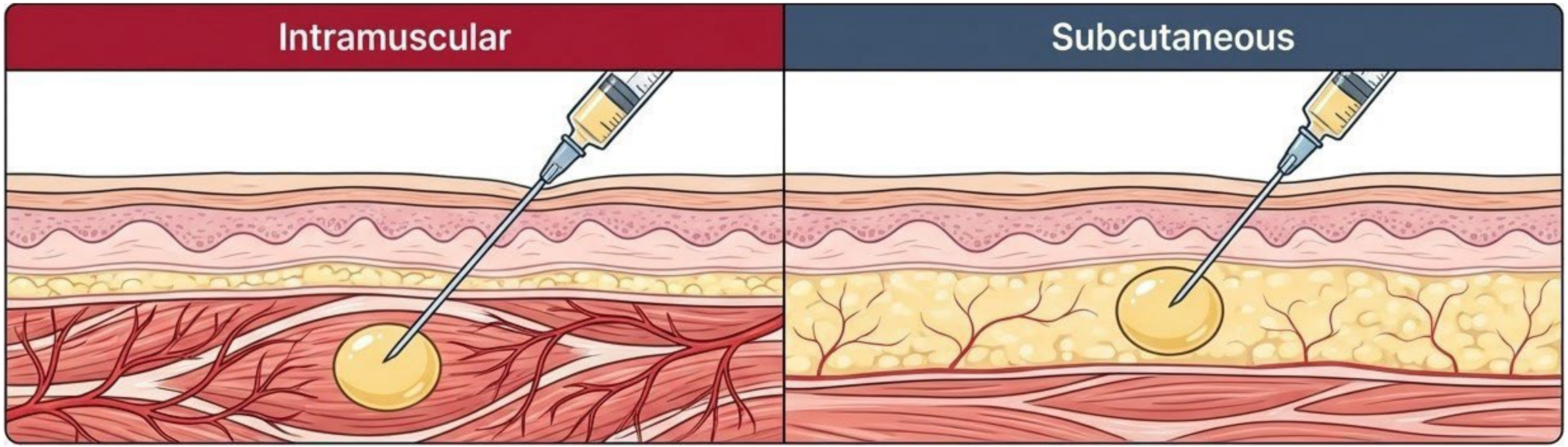
- Less pain
- Less testosterone and supply waste
- Good penetration
- Only one hand needed
- No aspiration needed
- Not advised for testosterone injection volume over .5 cc
- Sites:
  - Shallow IM: Deltoids, Quads, Glutes
  - Subcutaneous: Abdominal area







The Science of Stability: Why Injection Site Matters



Intramuscular (IM) Tissue

Highly vascularized. Blood and lymphatic flow are significantly influenced by physical activity and muscle contractions.

Subcutaneous (SubQ) Tissue

Less vascularized. Blood and lymphatic flow are more stable and less impacted by physical activity.

> These physiological differences in the injection milieu directly influence the speed, magnitude, and stability of testosterone absorption.

G Nc•tebookLM

The Treatment Balance Scale

Proven Benefits in MLWH

- Significant gains in lean body mass (+1.22 kg to +3.34 kg with T esters).
- Reversal of unintentional weight loss (+1.54 kg overall).
- Improvements in mood, fatigue indices, and bone mineral density preservation.

Clinical Considerations

- Monitor cardiovascular profiles and hematocrit (HGB/erythrocytosis).



Summary Note: TRT should be specifically tailored to symptomatic MLWH exhibiting the chronic frailty phenotype, not prescribed blindly.

But Is It Safe for My Heart?

The TRAVERSE Trial (2023):

A landmark study of 5,246 men proved that testosterone therapy does NOT increase the risk of major cardiovascular events or strokes.

Because of this, the FDA removed the black box heart warning.



HIV-Specific Monitoring:

While it is safe for your heart, HIV+ patients on TRT must regularly monitor their red blood cell count (hematocrit), as testosterone can thicken the blood over time.

System Diagnostics: Clearing the Noise

Liver Toxicity

~~TRT causes severe liver damage.~~

Reality Check: Standard TRT (injections, gels, pellets) bypasses hepatic first-pass toxicity. Liver damage is associated exclusively with oral anabolic steroids, not clinical replacement therapy.

Prostate Cancer

~~TRT creates prostate cancer.~~

Reality Check: TRT does not generate cancer from scratch. It may accelerate existing, undetected prostate cancer, making baseline and annual PSA screening the correct mechanical safeguard.

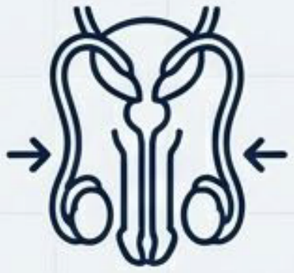
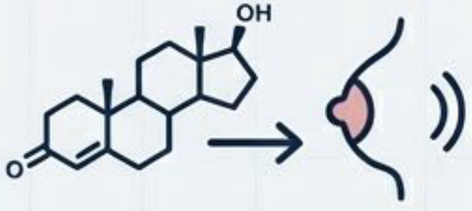
Heart Attacks

~~Testosterone inherently causes heart attacks.~~

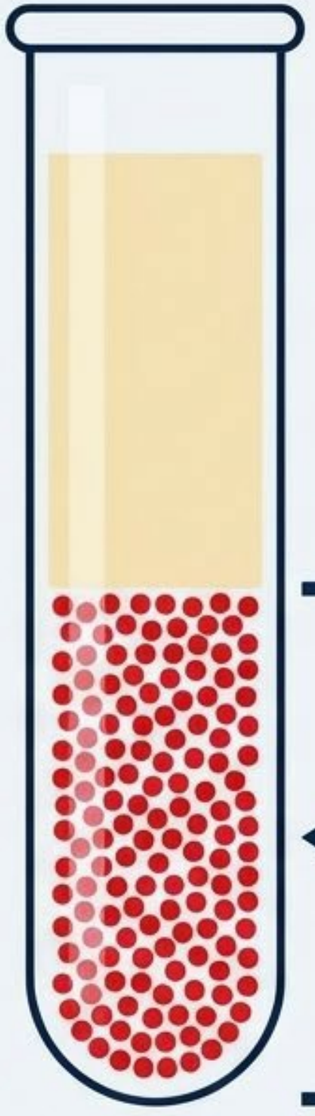
Reality Check: Properly managed TRT improves cardiometabolic function. Cardiovascular risk only spikes when secondary polycythemia (blood thickening) is left unmonitored.

NotebookLM

Secondary System Warnings & Countermeasures

Side Effect (Icon)	Biological Cause & Indicator	Targeted Countermeasure
	Exogenous testosterone shuts down brain signals (LH/FSH), rendering testicles dormant. **Indicator:** Volume reduction, zero sperm count.	Introduce HCG (Human Chorionic Gonadotropin). It mimics LH, maintaining testicular function, size, and preserving fertility.
	Increased sodium retention and mild metabolic shifts, exacerbated by high-sugar diets/alcohol. **Indicator:** Puffy ankles/face, elevated BP.	Restrict alcohol/sugar. Increase cardio. Mild diuretic only if lifestyle interventions fail.
	Excess testosterone converts to estrogen. **Indicator:** Mood swings, nipple sensitivity, excessive water retention.	⚠️ **Caution:** Do not over-suppress. Manage via dose reduction or increased injection frequency before introducing aromatase inhibitors.

The Primary System Limit: Hematocrit



The Hematocrit Variable
Inter Medium

Definition: The exact percentage of your total blood volume occupied by red blood cells.

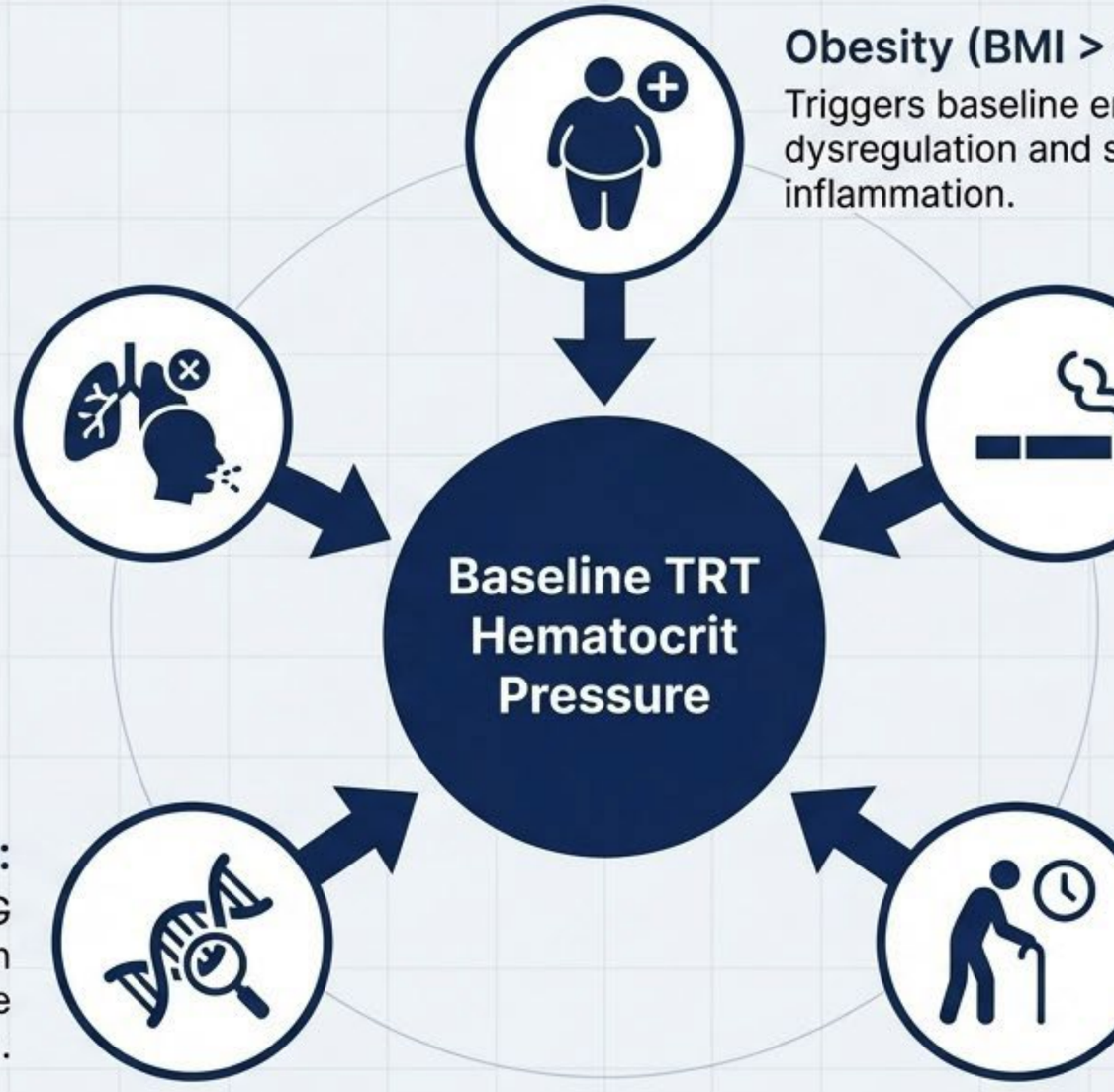
The TRT Effect: Exogenous testosterone stimulates erythropoiesis (blood-building). This is the most common dose-limiting side effect in men.

The Incidence Rate: Up to 66% of men utilizing weekly intramuscular injections will experience hematocrit elevation.

The Mechanical Threat: When hematocrit crosses safe thresholds, blood viscosity increases, forcing the heart to pump sludge instead of liquid, significantly elevating clotting and cardiovascular risk.

NotebookLM

The Risk Multipliers: Compounding Variables



Obesity (BMI > 30):
Triggers baseline erythropoietic dysregulation and systemic inflammation.

Pulmonary Deficits:
COPD, asthma, or chronic bronchitis cause systemic hypoxia, forcing the body to hoard red blood cells.

Smoking:
Introduces independent "smokers" polycythemia" via carbon monoxide hypoxia.

Genetics:
Men with fewer than 20 CAG repeats in the androgen receptor gene are hyper-sensitive to red blood cell production.

Age:
Older men have reduced plasma volume and lower baseline EPO regulation.

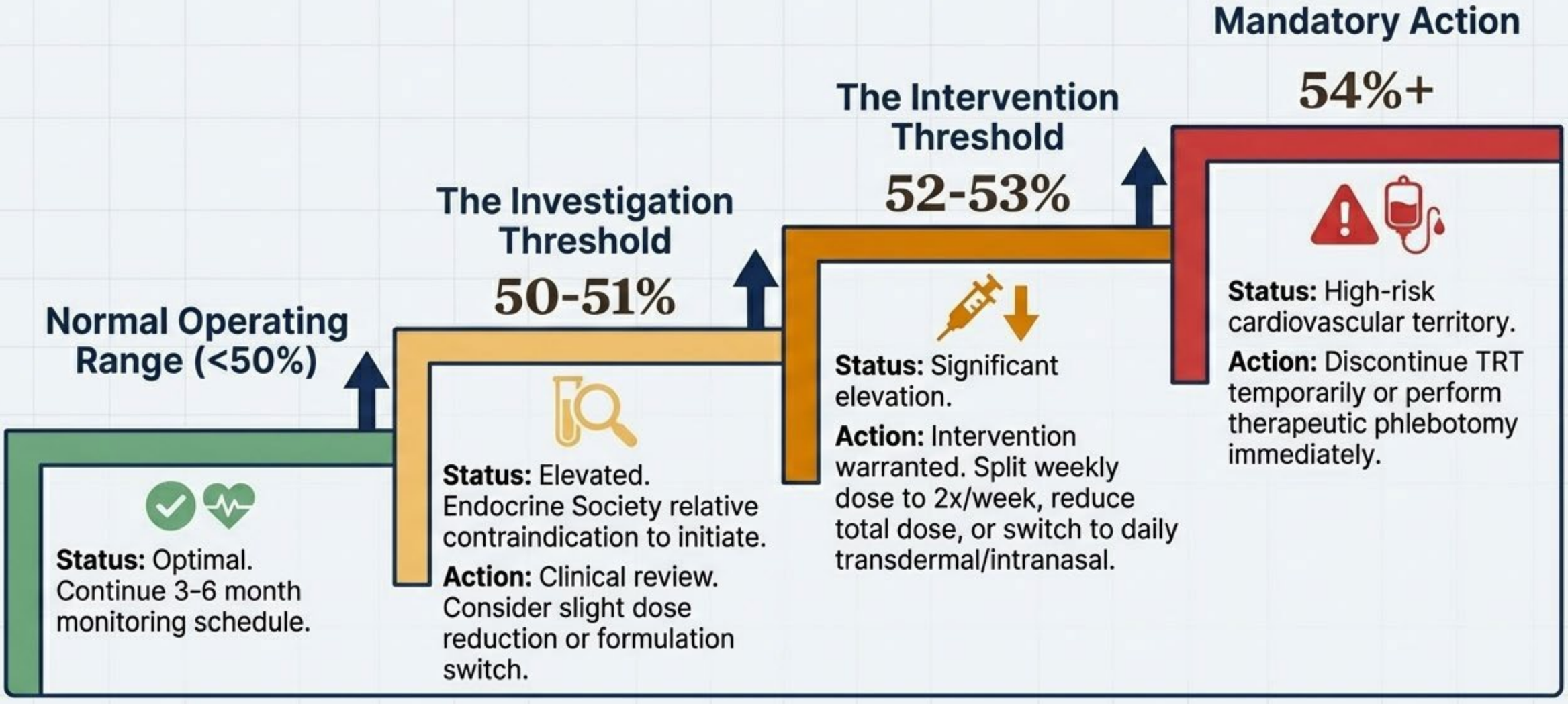
NotebookLM

Delivery Method Risk Matrix

	Testosterone Formulation	Typical Dosing	Erythrocytosis Rate	Hematocrit Change
	**High Risk**			
	Weekly IM Injections	100-200 mg weekly	43% to 67%	+4.4%
	**Moderate Risk**			
	Subcutaneous Pellets	Every 3-6 months	~35%	+1.7%
	Extended-Release IM	1g every 9-12 weeks	~7%	Stable/Mild
	Transdermal Gels	50-100 mg daily	~13%	Minimal
	**Optimal Zone**			
	Oral Undecanoate	Daily with meals	Very low (<1%)	Negligible
	Intranasal Gel	11mg 3x daily	<1.3%	-0.8% (decrease)

NotebookLM

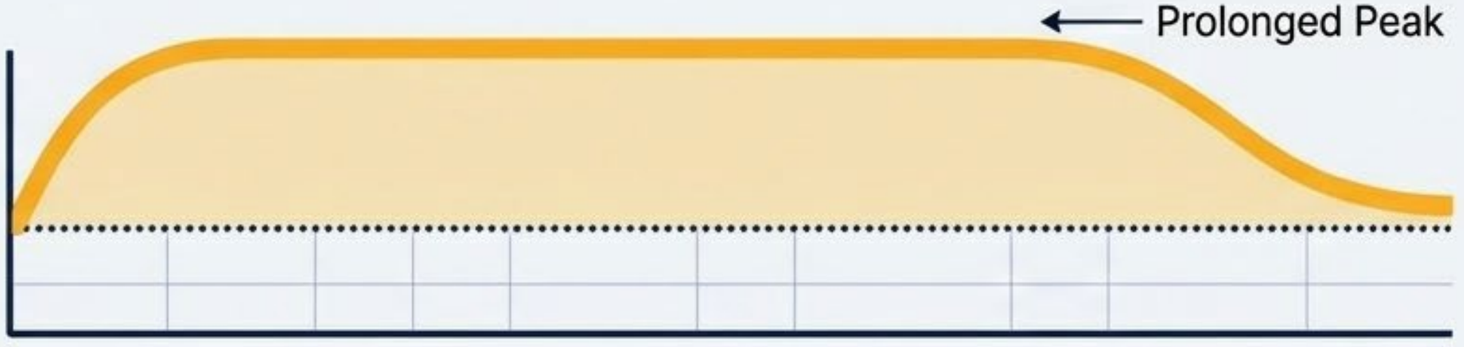
The Clinical Intervention Ladder



NotebookLM

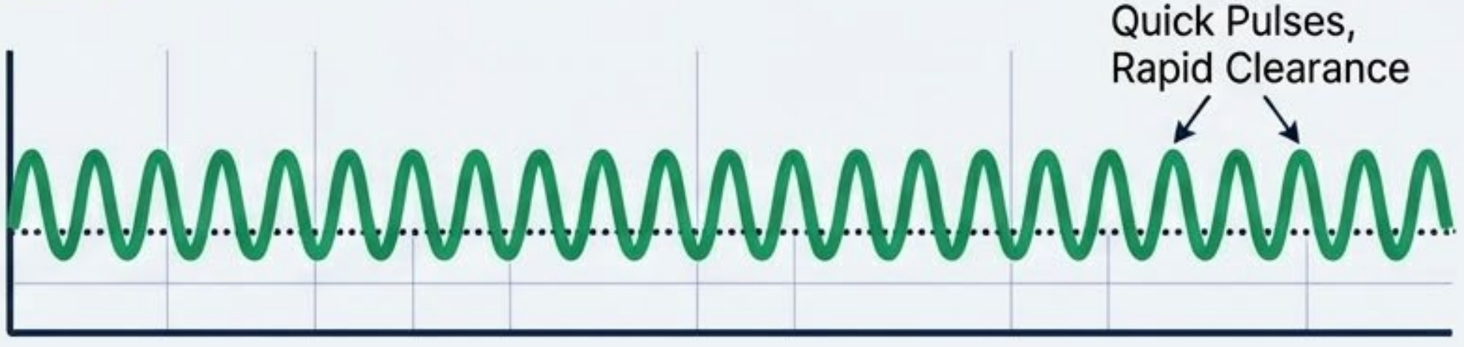
Pharmacokinetics: Why Delivery Drives Risk

Sustained Exposure (Weekly IM Injections)



Weekly injections create sustained, supraphysiologic peaks. The bone marrow interprets this prolonged exposure as a constant command to overproduce red blood cells.

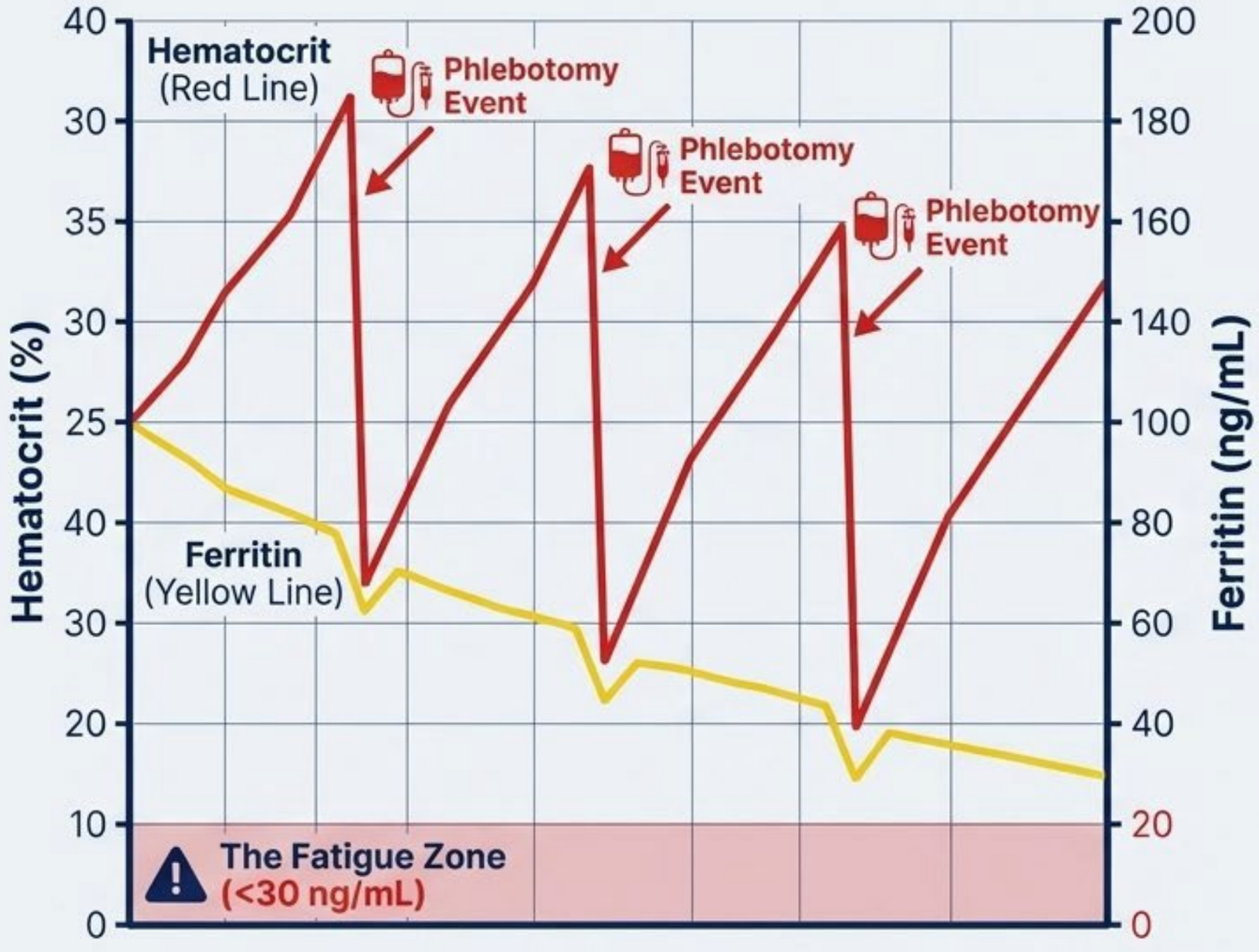
Pulsatile Exposure (Intranasal / Gels)



Daily or multi-daily applications mimic natural physiological pulses. Because testosterone clears quickly from the vascular space, the bone marrow largely ignores the signal, halting excess blood production.

NotebookLM

The Phlebotomy-Iron Paradox



The Mechanical Reality

Removing one **unit of blood (500mL)** instantly drops **hematocrit by ~3%.** However, it also rips **200-250mg of iron** from the body.

Because TRT forces the body to consume massive amounts of iron, repeated phlebotomies rapidly deplete ferritin stores.

Result: 'Safe' hematocrit, but crushing, iron-deficient fatigue.

The HIF Rebound Effect

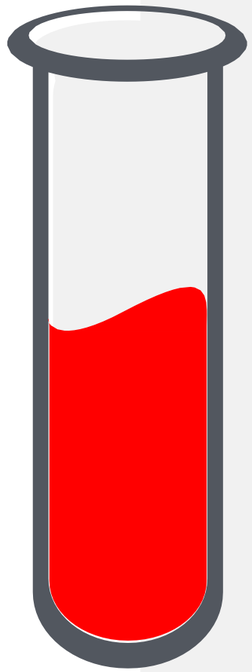
Phlebotomy lowers tissue oxygen. This activates Hypoxia-Inducible Factor (HIF) pathways, which paradoxically signal the kidneys to produce MORE EPO, putting you on an endless treadmill of blood removal.

System Rule: Never prescribe serial phlebotomy without monitoring Ferritin.

NotebookLM

BLOOD TEST MONITORING SCHEDULE: Baseline

- The following are the required blood tests and how to use them for clinical decision making. Patients can get affordable blood tests in most U.S. cities at DiscountedLabs.com



Initial Blood Test – New Patient Starting TRT

- **Testosterone, Free & Total**
- **PSA**
- **LH & FSH**
- **Lipids**
- **CBC**
- **CMP**
- **TSH, Free T3 & Free T4**
- **Sensitive Estradiol**
- **Post baseline:**
  - **If T <200 ng/dL and no current/past use of anabolic steroids or opiates, test for prolactin.**
  - **If free T3 is low and/or TSH is high (> 2.5), perform a complete thyroid panel including antibodies and reverse T3.**

BLOOD TEST MONITORING SCHEDULE (Follow Up)

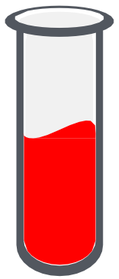


01

6wk Follow up – 6wks after initial Rx

Fasted, morning and well-hydrated conditions:

- CBC
- CMP
- Testosterone, Free & Total
- Estradiol Sensitive
- TSH, Free T3

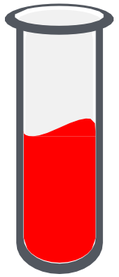


02

6 Month Follow up – 6 months after initial RX

- Testosterone, Free & Total
- PSA (optionally based on week 6 results)
- Lipids
- CBC
- CMP
- Estradiol, sensitive
- Free T3 (if abnormal FT3 was found at baseline and thyroid treatment was provided)

03



Annual Blood Test – Same as 6 months (plus PSA)

Resources

- PoWeRUSA.org
- Subscribe to pozhealth group by sending an email to pozhealth+subscribe@groups.io
- Facebook Group: Pozhealth
- ExcelMale.com
- DefyMedical.com
- EmpowerPharmacy.com
- DiscountedLabs.com

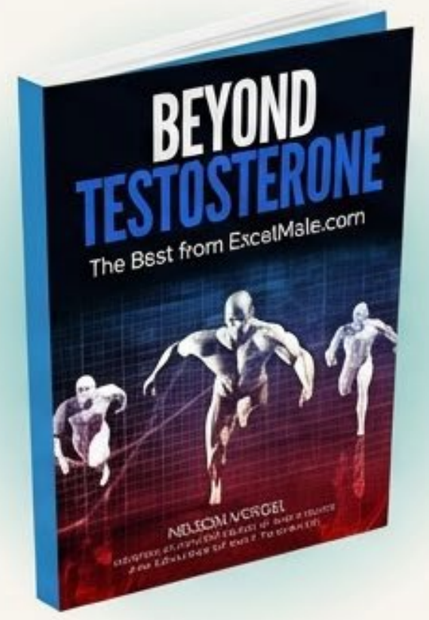
Join the Women's Health and HRT Group on Facebook



Keep Empowering Yourself

EXCELMALE
YOUR MEN'S HEALTH COMMUNITY

PoWeR
PROGRAM FOR WELLNESS RERATION



Community

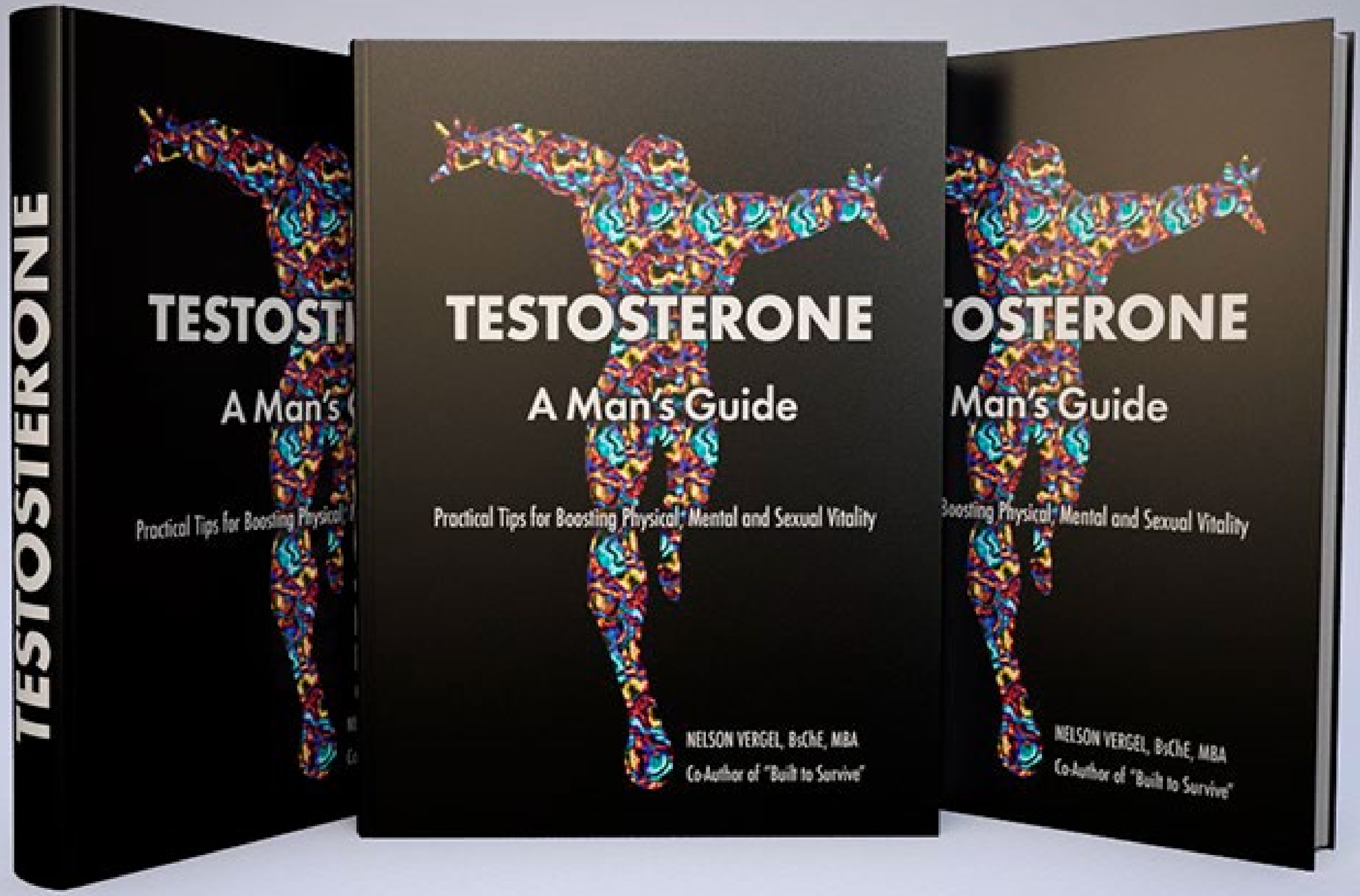
Join the conversation with thousands of others at ExcelMale.com and the Women's Health and HRT Group on Facebook.

Advocacy

Explore the Program for Wellness Restoration at PoWeRUSA.org.

Free Reading

Download the comprehensive 480-page guide 'Beyond Testosterone' at BeyondTestosterone.com.


TESTOSTERONE
TESTOSTERONE
A Man's Guide
Practical Tips for Boosting Physical, Mental and Sexual Vitality
NELSON VERGEL, BsChE, MBA
Co-Author of "Built to Survive"
TESTOSTERONE
A Man's Guide
Practical Tips for Boosting Physical, Mental and Sexual Vitality
NELSON VERGEL, BsChE, MBA
Co-Author of "Built to Survive"

Subscribe to Nelson and Jeff Taylor's Online Information Group:

Send an email to

Pozhealth+subscribe@groups.io

THANK YOU

Questions?