Testosterone: Prescribing Issues

GEORGE T. KOULIANOS, MD, FACOG

Introduction

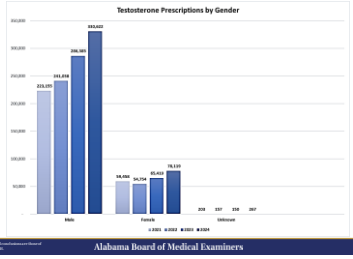
- Nationally, testosterone prescriptions have increased from 7.3 million to more than 11 million between 2019 and 2024. Conservative estimate IQVIA.com
- Increased awareness
- Fueled the rise of questionable clinics selling testosterone and other treatments as a cure all to those who don't need it
- According to the American Urological Association, up to a third of men taking testosterone have never been diagnosed with a deficiency
- 25% of testosterone therapy patients have never had a serum testosterone level checked before starting treatment
- 50% of patients on testosterone therapy have never had a serum testosterone level checked after starting treatment

New York Times, Jan 25, 2025, American Urologic Association 2024

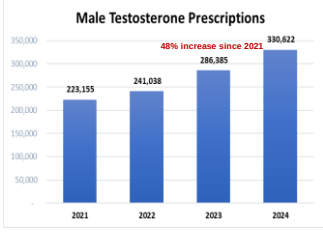
Introduction

- Testosterone is a schedule III-controlled substance with the potential to cause significant adverse effects if prescribed for inappropriate indications and without proper medical supervision

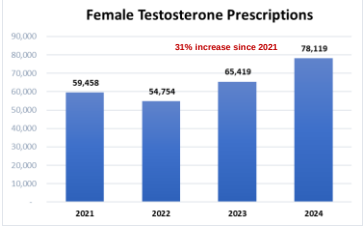
Testosterone Prescriptions by Gender*



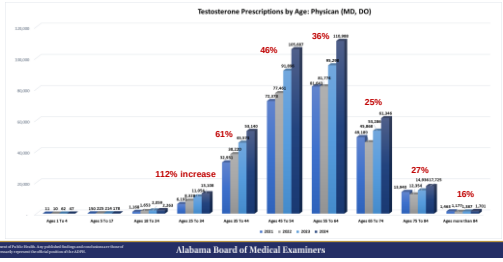
Male Testosterone Prescriptions*



Female Testosterone Prescriptions*

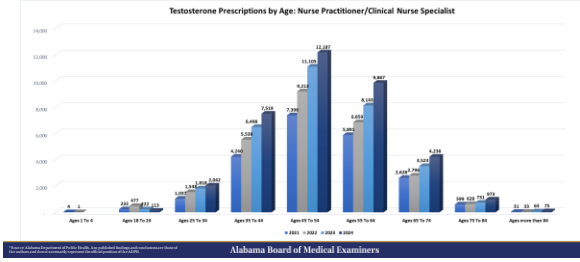


Testosterone Prescriptions by Age: Physician (MD, DO)*



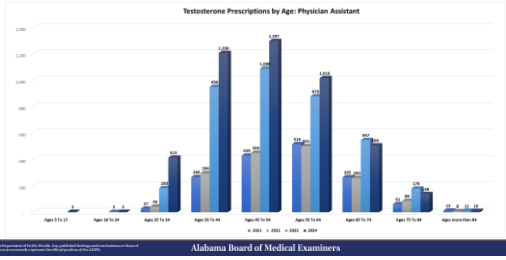
Alabama Board of Medical Examiners

Testosterone Prescriptions by Age: NP/Clinical Nurse Specialist*



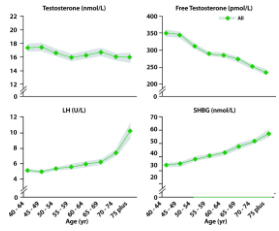
Alabama Board of Medical Examiners

Testosterone Prescriptions by Age: Physician Assistant*



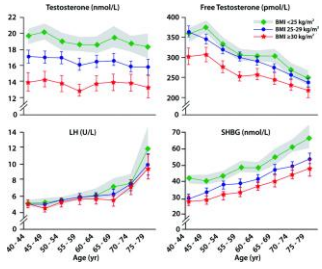
Alabama Board of Medical Examiners

Relationship between age and testosterone



J Clin Endocrinol Metab 2008;93:2737

Relationship between age, BMI and hormones



Clin Endocrinol Metab 2008;93:2737

Who is a candidate for androgen supplementation?

- Men with abnormal testosterone below 300 ng/dl
- Confirmed on subsequent AM lab evaluation
- Exclusion of other related conditions
- Valid symptoms

Valid Symptoms and Low Testosterone < 300 ng/dl

- Persistent fatigue after lifestyle and medical workup
- Decline in muscle mass
- Decline in libido
- Erectile dysfunction
- Depression
- Sleep disturbance
- Idiopathic anemia
- Osteopenia/osteoporosis
- Persistent sleep disturbance with ongoing treatment for sleep apnea

Evaluation

- History and physical exam including genitourinary
  - Penis, scrotum, testes, prostate
  - Breasts
  - General body habitus
- Confirmatory laboratory including fasting early morning serum total testosterone, LLH, Hemoglobin, Hematocrit, Prolactin and PSA

Contraindications to Treatment

- Future fertility
- Active prostate cancer
- Uncertain serum PSA status
- Major cardiac or thromboembolic events in past 6 months
- Cardiac arrhythmia
- Undiagnosed or unmanaged sleep apnea
- Primary or secondary polycythemia
- Active liver and or gallbladder disease

Counseling on Risks of Testosterone Replacement

- Loss of testicular volume and function
- Impaired fertility
- Small increase in risk of thrombotic events (cardiac & cerebral)
- Small increase in risk of cardiac arrhythmia
- Significant risk of secondary polycythemia/erethrocytosis
- Possible risk of major cardiac or thrombotic event if testosterone levels are too high
- Elevated estrogen levels, gynecomastia and mood alteration
- Increase in prostate size and lower urinary tract symptoms

Alabama Board of Medical Examiners

Counseling on Potential Benefits of Testosterone Replacement

Libido	Erectile function	Body composition
Insulin sensitivity	Mood	Bone density

Alabama Board of Medical Examiners

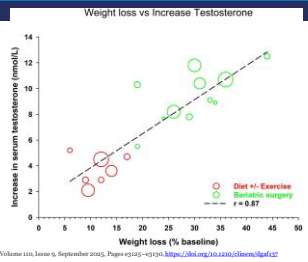
Additional Counseling

All men should be counseled on the importance of a high-quality diet, exercise, sleep quality, stress management, avoidance of marijuana and alcohol, and general medical evaluation

Optimizing these variables will often help patients normalize testosterone levels without needing replacement

Alabama Board of Medical Examiners

Impact of Weight Loss on Serum Testosterone



J Clin Endocrinol Metab, Volume 110, Issue 9, September 2025, Pages e3125–e3130, https://doi.org/10.1210/clinem/dgaf137

Origins of Testosterone Replacement Therapy

- First isolated and synthesized in 1935
- Initial formulations had negligible oral bioavailability and a very short duration of action due to extensive hepatic metabolism
- Testosterone therapy has evolved considerably since the days of the 19th century French physiologist Charles Brown-Sequard, who extolled the virtues of a guinea pig testicular extract in restoring waning potency and virility

Hayes, F.J. JCEM 2000;3020

Treatment Options

Transdermal gel

Intramuscular

Pellets

Oral

3 Month Follow Up Information

- Repeat serum testosterone, hemoglobin, hematocrit and PSA level
- Physical exam by physician
- Evaluate response
- If no benefit is confirmed, testosterone should be discontinued
- Consider referral at any time to urologist or medical endocrinologist
- Adhere to the philosophy of: lowest effective dose
- Consider checking PDMP to identify potential testosterone abuse

Ongoing Treatment Follow Up

- Repeat labs every 6 months
  - Serum testosterone over 800 ng/dl should be considered excessive
- Consider checking PDMP at initiation and annually to identify potential testosterone abuse
- Refer challenging patients to a urologist or medical endocrinologist
- Patients should be seen by their physician at least once per year after steady state has been established
  - Telehealth is not an acceptable visit

Conclusions

- Testosterone replacement therapy is a useful tool in managing the symptomatic testosterone deficient male, but also one that can easily be abused with detrimental health risks to our patients.

Testosterone Therapy for Women

- Current data supports the short-term efficacy and safety of testosterone treatment in post menopausal women with sexual dysfunction due to hypoactive sexual desire disorder (HSDD), after an evaluation has excluded other causes such as relationship, psychological and medication related.
- Limited data supports the use in perimenopausal women.
- Combined hormonal and psychosexual approaches may be beneficial in some cases with mixed etiologies.

NY Times October 22,2025

'I'm on Fire': Testosterone Is Giving Women Back Their Sex Drive — and Then Some

There is no F.D.A.-approved testosterone product for women. Insurance won't cover it. Many doctors won't prescribe it. It's become a cultural phenomenon.

Changes in Circulating Hormone Levels at Menopause

	Premenopause	Postmenopause
Estradiol	40 – 400 pg/ml	10 – 20 pg/ml
Estrone	30 – 200 pg/ml	30 – 70 pg/ml
Testosterone	20 – 80 pg/ml	15 – 70 pg/ml
Androstenedione	60 – 300 ng/dl	30 – 150 ng/dl

Speroff: *Clinical Endocrinology and Infertility* 9th Ed

Hypoactive Sexual Desire Disorder

- Defined as the absence of sexual fantasies and thoughts and/or desire for or receptivity to, sexual activity that causes the personal distress or difficulties in the relationship lasting for at least 6 months.
- Causes can be multifactorial and can include central processes (i.e. neuroendocrine imbalance, medication, hypogonadism, psychological distress) and cultural factors (religious or cultural emphasis on sexual purity).
- Can be associated with profound negative effects on mood, self esteem, and partner relationships and can cause significant decrease in quality of life.

Utoko et al. 2022 J Sexual Med

HSDD Diagnosis and Evaluation

- Use of a validated self report screening and diagnostic instrument
  - Decreased Sexual Desire Screener (Panay N: Sept 2022 Post Reprod Health;28(3):158)
  - Lab evaluation
    - Total serum testosterone
      - Mid to high range level may not need additional supplementation
    - Sex Hormone Binding Globulin
      - Women with levels above normal range are less likely to benefit from testosterone therapy

HSDD Evaluation and Monitoring

- Checking a free testosterone may provide an insight into the lack of response in women not experiencing an improvement of symptoms with testosterone treatment.

When Testosterone Therapy is Not Recommended

- Infertility
- Sexual dysfunction other than HSDD
- Improvement of cardiovascular, metabolic or bone health
- Depression
- General wellbeing
- Enhance cognitive performance
- Delay cognitive decline
- Treatment of low androgen levels due to hypopituitarism, adrenal insufficiency, surgical menopause, pharmacologic glucocorticoid administration

Testosterone Therapy Contraindications

Hepatic disease

Hyperlipidemia

Treatment Methods

Aim for testosterone concentrations in the physiologic postmenopausal range

Consider a trial of conventional hormone replacement therapy first

No FDA approved products for women

When using male approved products use 1/10th the recommended starting dose for men

Options: Gel, cream, patch (transference risk)

Not recommended: Testosterone implants, IM injections, oral preparations (includes buccal lozenges and troches)

General Concerns: Safety & Efficacy of Custom Compounded Hormone Therapy

- There is a lack of high quality data on the safety and efficacy of custom compounded bioidentical hormone therapy for the management of menopausal symptoms
- Compounded bioidentical menopausal therapy should not be prescribed routinely when FDA approved formulations exist
- Due to lack of regulation, the amount of active medication can be highly variable within a specific dose
- There are no requirements for adverse event reporting, which hinders a definitive evaluation of safety
- Patients requesting the use of compounded bioidentical menopausal hormone therapy should be counseled on the lack of FDA approval of these preparations and their potential risks and benefits

Committee on Clinical Consensus-Gynecology. Compounded Bioidentical Menopausal Hormone Therapy. Obstetrics and Gynecology;142:1266-1273

Testosterone Pellets: Safety Concerns

- The FDA released a letter referencing the lack of reporting of more than 4,200 adverse events, including endometrial cancers, by the BioTE Medical company based in Irving, TX that provides bioidentical hormone pellet therapy
- The global consensus on the use of testosterone in women (which is endorsed by multiple international societies) is clear that the use of these pellets does not represent appropriate care
- We have to tell women that their new mustache, deepened voice, or clitoromegaly is permanent

Dunsmoor-Su R. Testosterone Therapy in Women. Obstetrics and Gynecology 2021;138:809-812

Duration and Monitoring of Treatment

- Serum testosterone, liver function and fasting lipids should be measured at baseline
- Serum testosterone should be measured 3-6 weeks after treatment has started (levels do not always predict response to therapy)
- Evaluate response at 3 to 6 months after treatment start and then every 6 months thereafter
- Discontinue treatment if no response at 6 months

Safety Information

- No safety and efficacy data for testosterone therapy available after 24 months
- Long term effects on cardiovascular risk and breast cancer incidence are not known
- Women on testosterone therapy should be monitored for signs and symptoms of androgen excess every 6 months

Conclusions

- There has been a marked increase in testosterone utilization in both men and women over the past several years.
- Risks have been underappreciated and can be significant
- Patients require careful monitoring
- Long term impacts of therapy in women are not fully appreciated