# Testosterone deficiency or hypogonadism

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UCLA Health

# Hypogonadism or Testosterone deficiency evaluation

## Signs and symptoms along with testosterone < 300 ng/dL (AUA)

Sexual

- **Diminished libido**
- Decreased spontaneous erections
- **Erectile dysfunction (ED)**
- Diminished response to PDE5i (sildenafil/tadalafil)

Non-sexual/ Psychological

- **Diminished energy**/vitality/well being
- Fatigue
- Depressed mood
- Irritability
- Decreased cognition
- Reduced motivation

# Prevalence Hypogonadism

Men 30-79

**5.6%**

Men >70

**18.4%**



UCLA Health

Nguyen, T., Pastuszak, A.T Therapy among prostate cancer survivors. Sex Med Rev 2016

# Prevalence Hypogonadism

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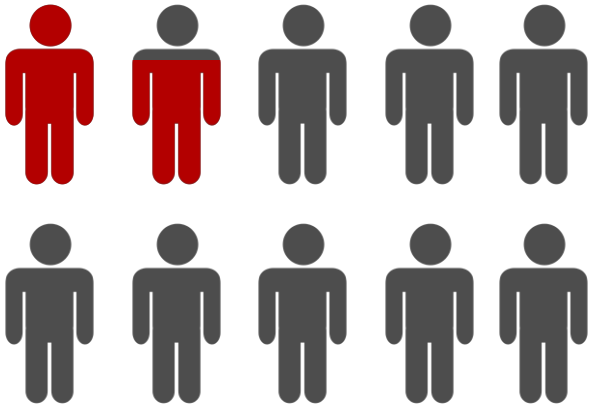
**18.4%**



UCLA Health

Nguyen, T., Pastuszak, A.T Therapy among prostate cancer survivors. Sex Med Rev 2016

# Relevance to primary care

Associated with common conditions: obesity, diabetes, hypertension, COPD, liver failure, OSA, HTN, and HIV infection

- 40-50% of men with DM and metabolic syndrome
- 15% of cancer survivors exposed to radiation or chemotherapy
- 40% for testicular cancer
- Opioid epidemic

# Relevance to primary care

- Patients are going to ask you about this
  - Direct to consumer advertisings on TV and online results in men young/old wondering if they need testosterone therapy
- Or seek out T supplementation outside of traditional channels
  - 2022 JAMA Internal Medicine by Dubin et al: DTC telehealth companies offer T at normal levels, don’t discuss fertility impact, and target supra-therapeutic levels >1000 ng/dL
  - You may get a surprise elevated Hct on routine lab check…

# Hypogonadism or Testosterone deficiency evaluation

## History

- PMhx:
  - radiation/chemo
  - testicular insult
- Shx:
  - Cranial/pituitary
  - Testicular
- Meds/Social hx:
  - Corticosteroids
  - Opioids
  - Anabolic steroids or testosterone

## Exam

- General
  - Beard growth
  - Body hair
- Chest
  - Gynecomastia
- Testicles
  - Size
  - Firmness
  - Mass(es)
- Prostate
  - Size/nodules esp if proceeding with therapy

# Hypogonadism or Testosterone deficiency evaluation

## Medical conditions that should trigger evaluation

Physical/Metabolic

- Decreased bone mineral density
- Anemia
- HIV diagnosis
- Insulin Resistance
- Gynecomastia
- Decreased muscle mass/strength
- Increased body fat

# Hypogonadism or Testosterone deficiency evaluation

## Lab evaluation (guidelines)

- Morning blood testostesterone (before 10am) x 2
  - If common part of practice, you can do both if going to refer then obtain first value and refer simultaneously
- Leutenizing hormone (LH)
- Estradiol – especially if elevated BMI or gynecomastia
- Follicle stimulating hormone (FSH) – if interested in fertility
- Prolactin

# Hypogonadism or Testosterone deficiency evaluation

## Lab evaluation – Guidelines

- Morning blood testostesterone (before 10am) x 2
- Leutenizing hormone (LH) – if T <300
- Estradiol –if elevated BMI, gynecomastia
- Follicle stimulating hormone (FSH) – if interested in fertility
- Prolactin – if T < 300 and LH below normal; or T <150

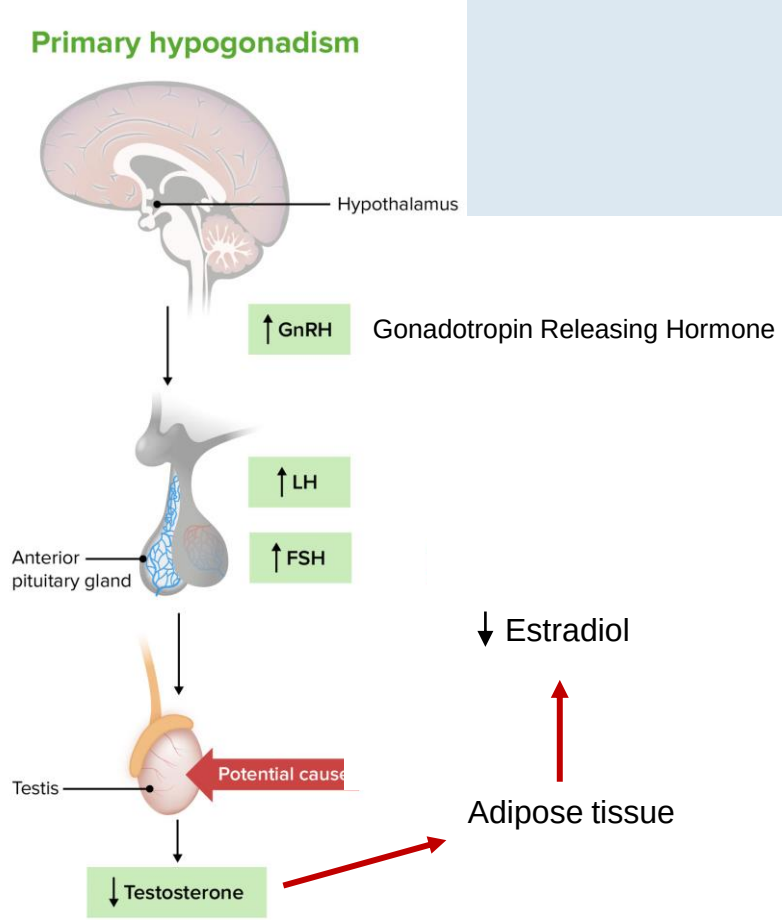
vs

## Real world practice

- **All at once** in am
- Testosterone
- Leutenizing hormone (LH)
- Estradiol
- Follicle stimulating hormone (FSH)
- Prolactin

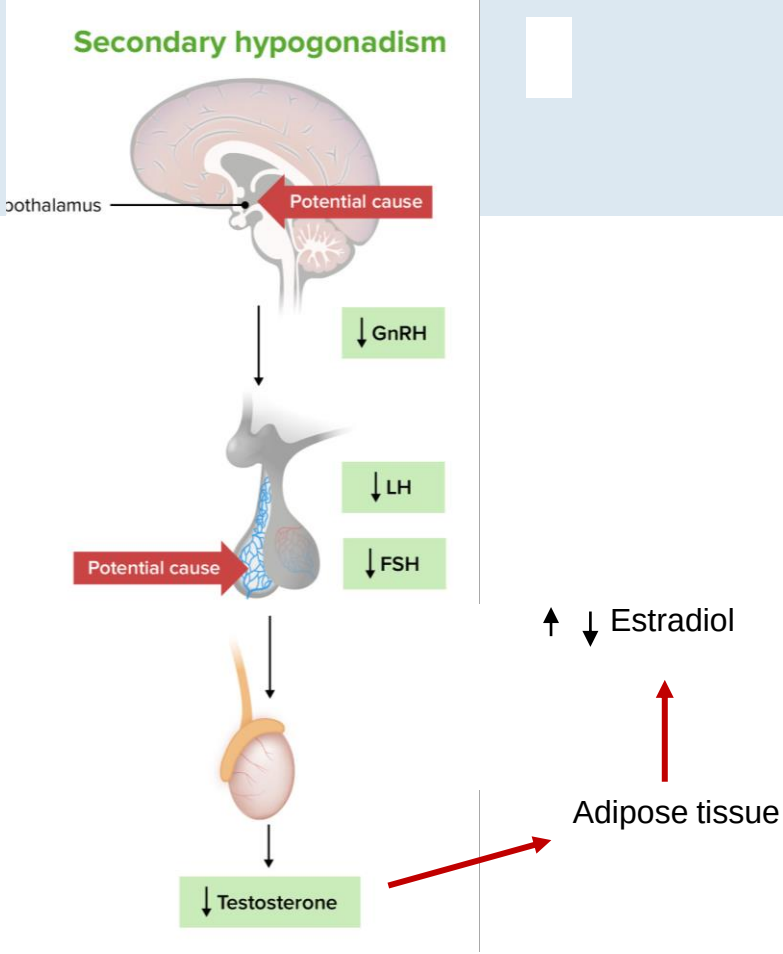
# Hypothalamic-Pituitary-Axis

- Hypergonadotropic hypogonadism (primary)
  - Deficient testosterone production in testicle
  - Pituitary increases LH production
  - Ex – Klinefelter's, treatment testicular ca



# Hypothalamic-Pituitary-Axis

- Hypogonadotropic hypogonadism (secondary)
  - Pituitary issue or suppression - Low LH/FSH
  - Testicle should be able to respond if LH levels can be increased
  - Ex – pituitary adenoma, chronic narcotics, Kallman's syndrome, idiopathic



# Hypogonadism or Testosterone deficiency evaluation

## Lab evaluation - Nuance

- Prolactin
  - Suppresses LH; <80 ng/dL unlikely to be clinically significant unless rising
  - If T < 150 or low T along with low LH/FSH, pituitary MRI prior to/concomitant with referral is helpful
- PSA
  - 40 or older and interested in T therapy; different from PSA screening >55 yo
- Semen analysis
  - interested in fertility, along with FSH

# Hypogonadism or Testosterone deficiency evaluation

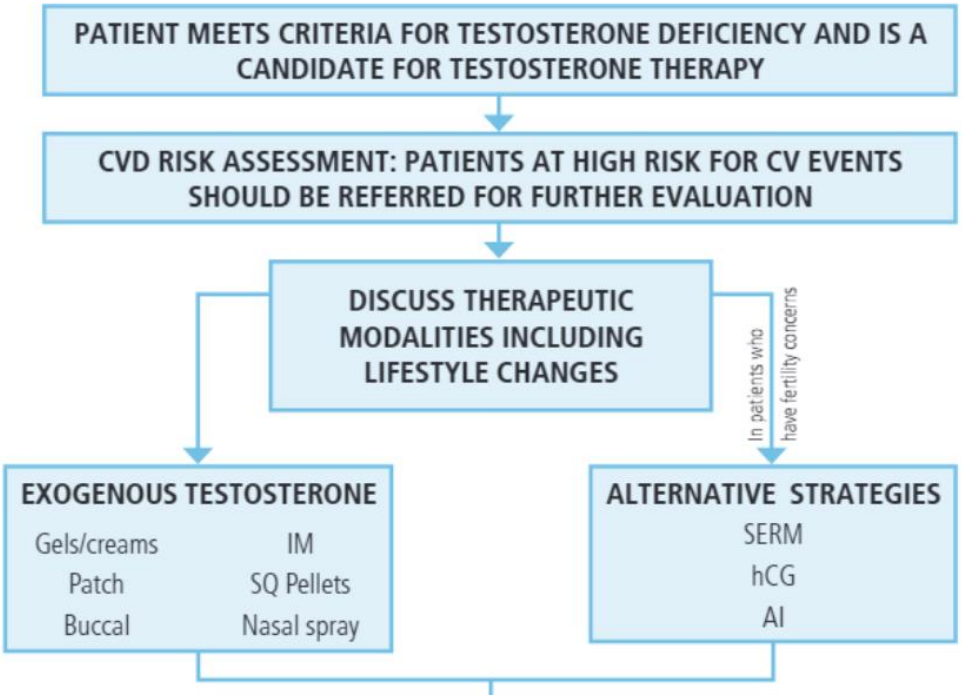
## Lab evaluation - Nuance

- Free testosterone, Sex hormone binding globulin (SHBG)
  - In symptomatic men with low-normal testosterone, can consider treatment if free T (or calculated free T based on SHBG) is < 80 – 100 pg/mL.
  - Not guideline based, done by experts with high comfort in this space
- Karyotype
  - Hypergonadotropic hypogonadism and small testes, rule out Klinefelter's disease

# Testosterone Deficiency: CVD risk

## CVD risk assessment

- Absolute contraindication – Recent cardiovascular event (MI, stroke, TIA) last 6 months
- 3 studies between 2013-2015 raised concerns about CV risk
  - RCT of 209 pts, two retrospective studies
  - Off-label dosing, methodologic flaws like poorly matched comorbidities in groups

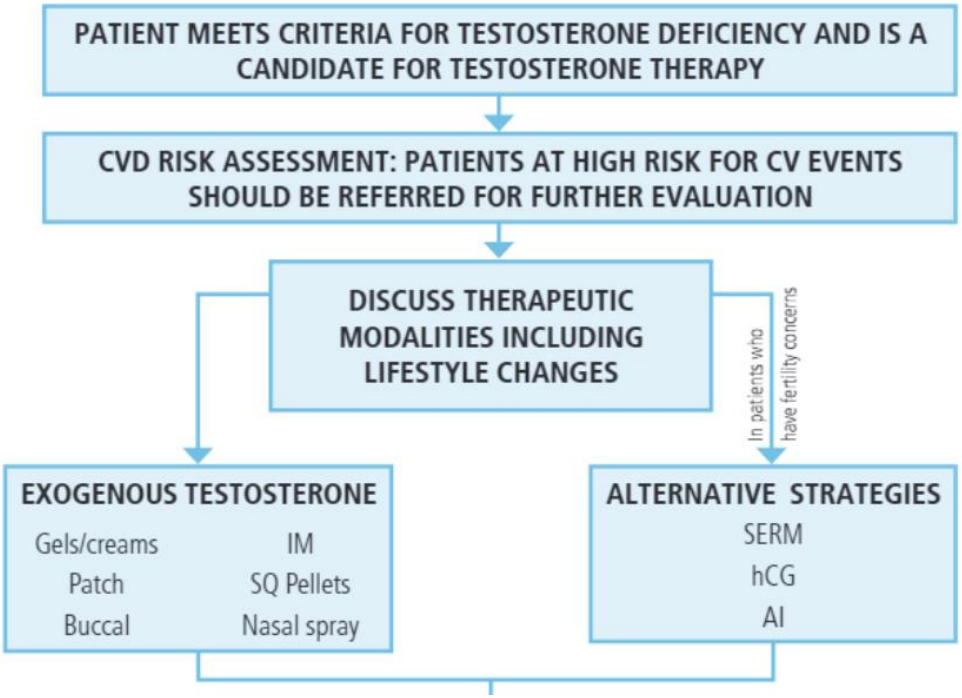


# Testosterone Deficiency: CVD risk

## CVD risk assessment

Since studies resulting in FDA black label warning:

- **3 additional, recent RCTs failed to show elevated risk for CVE with T supplementation**
- Controversy in this space, very recent update
- Get cardiologist buy-in, refer to uro. load the boat



# Testosterone Deficiency: CVD risk - update

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 13, 2023 VOL. 389 NO. 2

Cardiovascular Safety of Testosterone-Replacement Therapy

A.M. Lincoff, S. Bhasin, P. Flevaris, L.M. Mitchell, S. Basaria, W.E. Boden, G.R. Cunningham, C.B. Granger, M. Khera, I.M. Thompson, Jr., Q. Wang, K. Wolski, D. Davey, V. Kalahasti, N. Khan, M.G. Miller, M.C. Snabes, A. Chan, E. Dubcenco, X. Li, T. Yi, B. Huang, K.M. Pencina, T.G. Travison, and S.E. Nissen, for the TRAVERSE Study Investigators*

5246 hypogonadal men, preexisting/high risk of CVD

TRT non-inferior to placebo with respect to major adverse cardiac events

- MI, stroke, death from CVE

7% rate in TRT group vs 7.3% in placebo

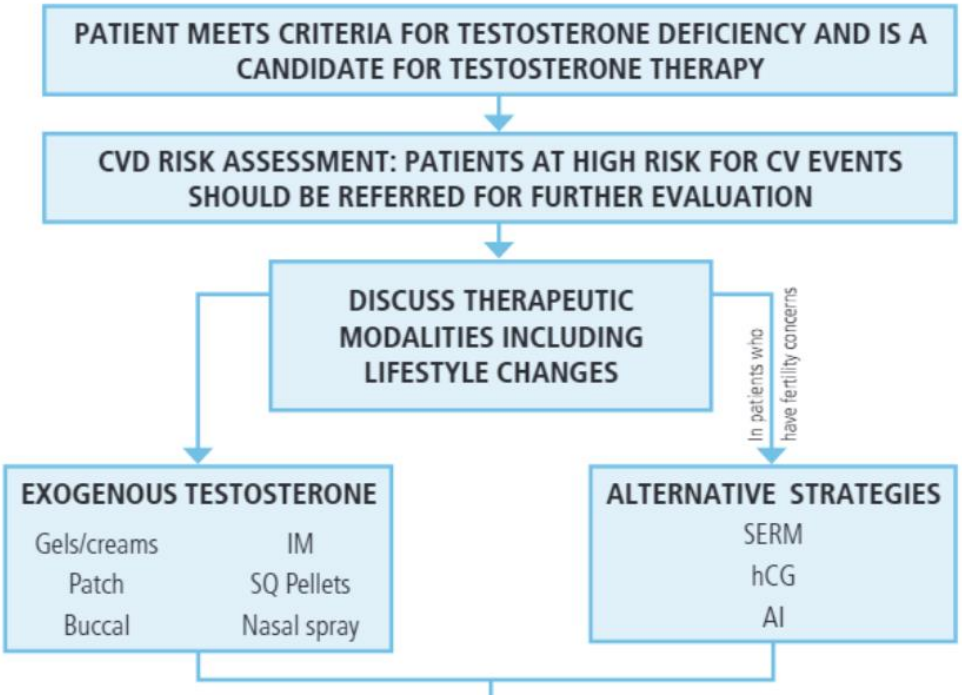
- >1 year of follow-up

Limitation: uses testosterone gel, previous studies with injectable also found no difference

# Testosterone Deficiency treatment

## Lifestyle modification

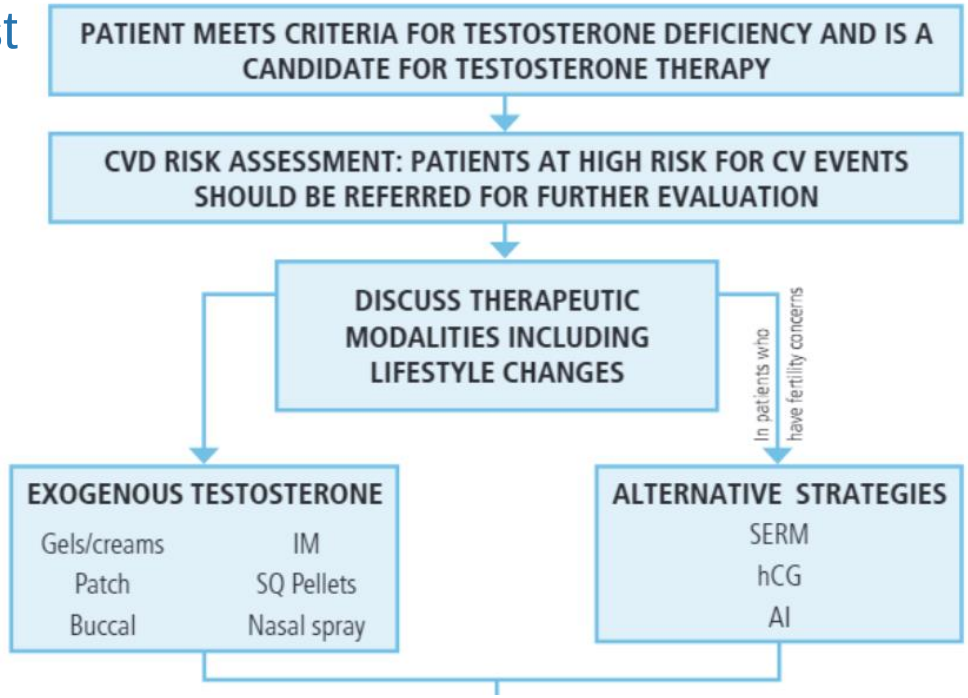
- Weight loss
  - 15% body weight needed to achieve measurable improvements
  - Seen with bariatric surgery; cautious excitement re semaglutide/ozempic
- Moderate-intensity or aerobic exercise
  - 105 minutes weekly for 24 weeks, increase by T by 22 +- 13 ng/dL
  - 236 min weekly, inc T by 59 +- 13 ng/dL



# Testosterone Deficiency treatment

## Medication options – no fertility interest

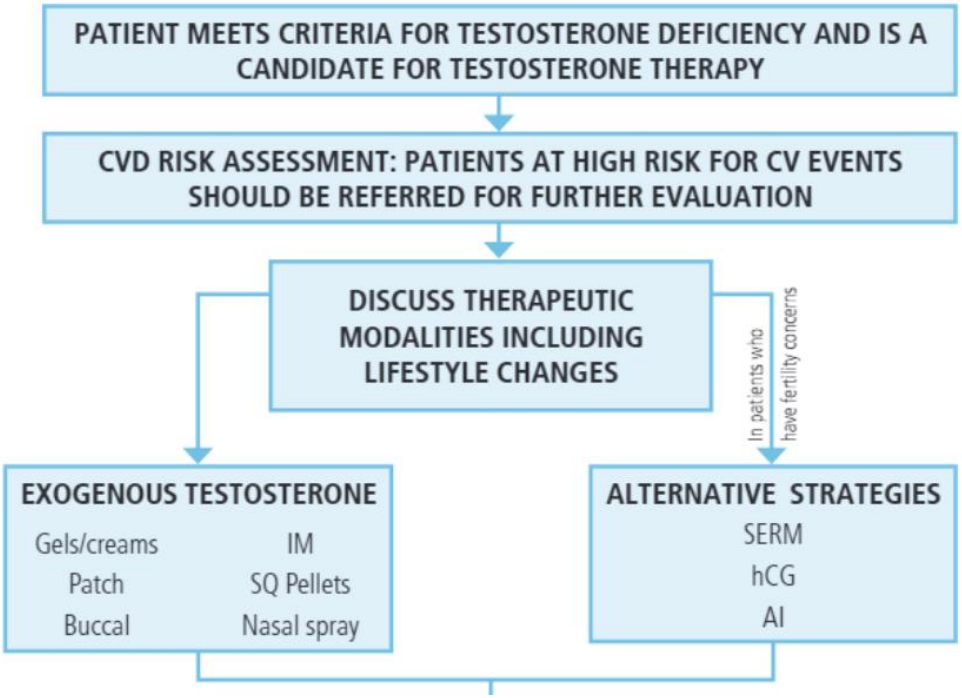
- Testosterone gel
  - 1 or 1.62% formulation, start with two pumps
  - Fewest issues with prior authorization
- Testosterone cypionate
  - Weekly injection, start at 100mg (0.5mL)
  - **Subcutaneous**, lower risk of polycythemia
  - Prescribe needles: 18g + 23g



# Testosterone Deficiency treatment

## Medication options –fertility interest

- Selective Estrogen Receptor Modulator
  - Clomiphene 25mg qod
  - Only effective if LH/FSH levels low-normal
- Aromatase Inhibitor
  - Anastrozole 1mg twice per week
  - Elevated estradiol levels, T <300



# Testosterone Deficiency treatment

## Contraindications to therapy

- Men with locally advanced or metastatic prostate cancer
- Breast cancer
- Hematocrit >54%
- Untreated severe congestive heart failure

## Controversy/SDM – engage urologist

- Prostate cancer or strong family hx
  - Active surveillance
  - Treated w surgery or radiation
- Benign prostatic enlargement with LUTS
- Elevated PSA

December 27, 2023

# Prostate Safety Events During Testosterone Replacement Therapy in Men With Hypogonadism

## A Randomized Clinical Trial

Shalender Bhasin, MB, BS[1]; Thomas G. Travison, PhD[2]; Karol M. Pencina, PhD[1]; et al

» Author Affiliations | Article Information

*JAMA Netw Open.* 2023;6(12):e2348692. doi:10.1001/jamanetworkopen.2023.48692

- 14,304 person-years of follow-up on 5204 men (ages 45-80)
- **Low incidence** of any or high-grade prostate cancer, acute urinary retention, BPH meds or surgical interventions

- **No significant difference** between testosterone treated and placebo treated groups

# Testosterone Deficiency treatment

## Side effects and/or adverse events of exogenous T

- Oligo or azoospermia
  - Usually reversible
- Polycythemia – aim for levels <52-54%
  - Eval and Treat sleep apnea
  - Therapeutic phlebotomy, dose/formulation
- Gynecomastia
  - If E2 levels become elevated
- Dermatologic changes
  - Acne, Androgenic alopecia, allergy rare
- PSA elevation
  - Rise of 0.3 to 0.4 ng/mL, **not associated with Pca risk**
- Mood changes
  - Rare, more associated with supra-therapeutic levels/combination with anabolic steroids

# Testosterone Deficiency treatment

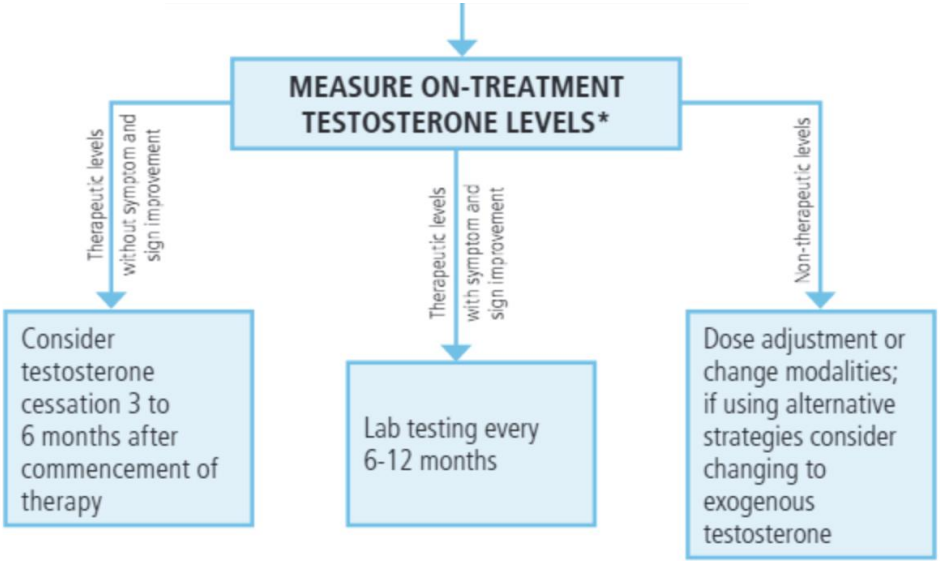
## Side effects and/or adverse events of alternative strategies

- Clomiphene (SERM)
  - Off-label use, not always covered
  - Mood changes in first 2-4 weeks of therapy
  - Vision change, floater – reversible if stop
- Anastrozole (AI)
  - Nausea, anxiety/irritability
  - Limit therapy to 6 month periods - E2 important for bone health
- HCG
  - 3x per week injection
  - Not covered by insurance
  - Pain at injection site, nausea, gynecomastia (if E2 not monitored)

# Testosterone Deficiency treatment

## Measure on-treatment T levels

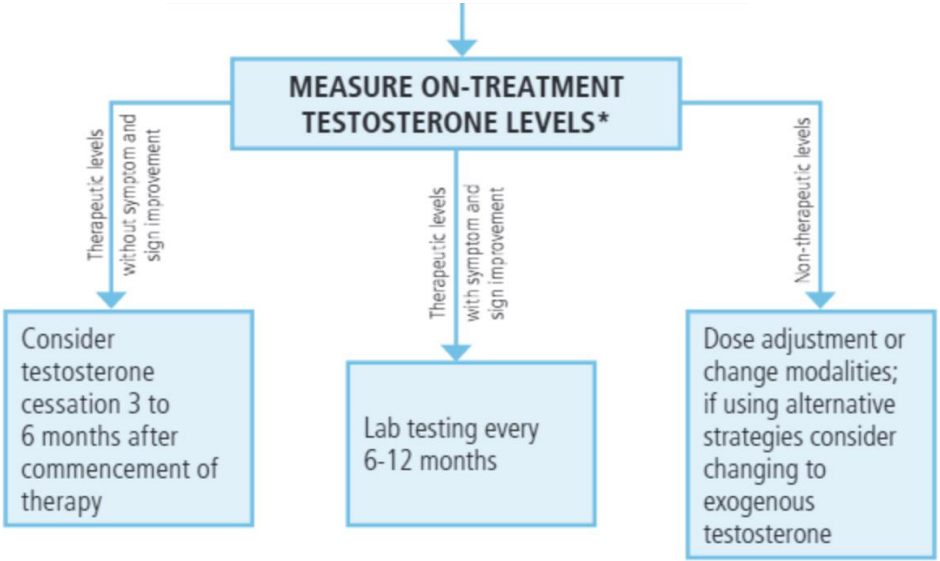
- Target 450-600 ng/dL
- 3-4 weeks after initiation of exogenous
  - Day 6 or 7 before injection (trough)
- 4-6 weeks for alternate strategies
- In addition monitor:
  - Hct/Hgb
  - Estradiol
  - PSA if ≥ 40 – once per year



# Testosterone Deficiency treatment

## Surveillance

- Therapeutic levels but no improvement
  - Switch pharmacotherapy
  - if no improvement in 3 to 6 months stop or refer
- Therapeutic levels + improvement
  - Start surveillance 3 months then extend
- Nontherapeutic levels
  - Change dose or agent



# Testosterone Deficiency – When to refer?

## Depends on patient complexity and your practice

Need help evaluating/managing

- Obtain initial lab evaluation, ask about fertility and refer to urology
  - Consider OSA screen at time of referral
- If fertility concerns, need for semen analysis – MLK Wilmington now offering male fertility eval/management
- Office/staff capacity issues

Plan to manage

- If concern or experiencing side effects/adverse events
- Controversial cases, despite new data:
  - CVD risk
  - Elevated PSA
  - Prostate Cancer
  - Erythrocytosis

Anytime you feel you need help

# ED, Varicoceles, Peyronie's, Male infertility, Vasectomy

## MLK Wilmington clinic

- Mondays
- 3:1 ratio of clinic to OR for now, language-concordant care in Spanish

## UCLA (SM and WW)

- Tues - Friday
- Including video visit new patient consultations

- Even if patient is DHS/county patient, able to schedule surgical consults at MLK as sexual dysfunction/fertility care limited in county system
- Place referral, include my name, and give patient the direct number to our scheduling team: 424-529-6755

# Testosterone Deficiency – Who to refer to?

## Beyond your time in LA

- Urologists who list andrology, hypogonadism in conditions treated
- Urologists who have completed sexual medicine or andrology fellowships
- SMSNA (Sexual Medicine Society of North America) find a provider page:
  - smsna.org/patients then click “Find a provider” on the upper right hand of screen

**Take photo or screen shot**

SMSNA (Sexual Medicine Society of North America) find a provider page