Controversies in Testosterone Treatment 2020

in Cisgender and Transgender Men

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Controversies in Testosterone Treatment
2020 in Cisgender and Transgender Men

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Poll Question

In your current practice, how many patients do you prescribe testosterone to:

1)  I don’t prescribe testosterone
2)  <10
3)  10-20
4)  >20
Disclosures

- Dr Brown has served as a consultant to ViiV Healthcare, Gilead, Merck, Theratechnologies, and Janssen
Objectives

- To understand the potential risks and benefits of testosterone treatment in the older cisgender male
- To be familiar with the findings of the T Trials and the clinical questions that still remain
- To understand what is known about the risks of testosterone for gender-affirming therapy in transgender men
Male Hormonal Status
Changes with Age as SHBG Increases

Prevalence of Serum T < 300 ng/dl in the NHANES Population

Rohrmann, J Clin Endocrinol Metab. 2007 Jul;92(7):2519-25
Over 10 years, FT declined significantly in both HIV-infected and HIV-uninfected men (p<0.001),
No difference in the rate of decline over time by HIV status (1.1% per year for HIV+ vs -1.0% for HIV-, p= 0.913)
**Signs and Symptoms of Hypogonadism**

<table>
<thead>
<tr>
<th>More Specific</th>
<th>Less Specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ libido</td>
<td>↓ energy, motivation, confidence</td>
</tr>
<tr>
<td>↓ spontaneous erections</td>
<td>depressed mood</td>
</tr>
<tr>
<td>gynecomastia</td>
<td>↓ concentration/memory</td>
</tr>
<tr>
<td>↓ body hair</td>
<td>sleep disturbance</td>
</tr>
<tr>
<td>Small testes</td>
<td>anemia</td>
</tr>
<tr>
<td>infertility</td>
<td>↓ muscle bulk and strength</td>
</tr>
<tr>
<td>↓ bone density, fracture</td>
<td>↑ body fat</td>
</tr>
<tr>
<td>hot flushes</td>
<td>↓ work performance</td>
</tr>
</tbody>
</table>

Bhasin, JCEM, 2010
Relationship of Serum Testosterone to Sexual Symptoms

Wu, NEJM, 2010

(233 ng/dL)
(244 ng/dL)
(317 ng/dL)
Explosion of Testosterone Use the US

Layton, JCEM, 2014
Endocrine Disorders in Men Infected with Human Immunodeficiency Virus

ADRIAN S. DOBS, M.D.
MICHAEL A. DEMPSEY, M.D.
PAUL W. LADENSON, M.D.
B. FRANK POLK, M.D.

Gonadal, adrenal, and thyroid functions were evaluated in 70 men seropositive for human immunodeficiency virus (HIV) infection, clinically categorized as asymptomatic (n = 19), AIDS-related complex (ARC) (n = 9), or acquired immunodeficiency syndrome (AIDS) (n = 42). Twenty of 40 men (50 percent) with AIDS were hypogonadal. Mean serum testosterone concentrations in both ARC (292 ± 70 ng/dl) and AIDS (401 ± 30 ng/dl) men were significantly less than in

Baltimore, Maryland
High Prevalence of Testosterone Use among Older HIV-Infected Men

## TTh Prevalence at Most Recent Visit, by HIV and age 2012-2015

<table>
<thead>
<tr>
<th>Age</th>
<th>HIV+</th>
<th>HIV-</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Prevalence</td>
</tr>
<tr>
<td>&lt;50</td>
<td>463</td>
<td>5.6%</td>
</tr>
<tr>
<td>50-59</td>
<td>482</td>
<td>17.2%</td>
</tr>
<tr>
<td>60+</td>
<td>341</td>
<td>25.5%</td>
</tr>
<tr>
<td>Total*</td>
<td>1286</td>
<td>17.0%</td>
</tr>
</tbody>
</table>

*Total prevalence is direct standardized for age, with 95% CI

- 99% of men on TTh reported having a prescription from a health provider
## Self-reported Reasons for TTh use, by HIV status (can give >1)

<table>
<thead>
<tr>
<th>Reason</th>
<th>HIV+ (n=196)</th>
<th>HIV- (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Low T level&quot;</td>
<td>90.3</td>
<td>90.3</td>
</tr>
<tr>
<td>&quot;For more strength or energy&quot;</td>
<td>39.8</td>
<td>30.6</td>
</tr>
<tr>
<td>&quot;Fatigue&quot;</td>
<td>38.8</td>
<td>29.0</td>
</tr>
<tr>
<td>&quot;To build muscle&quot;</td>
<td>32.1*</td>
<td>6.5</td>
</tr>
<tr>
<td>&quot;Wasting&quot;</td>
<td>15.3*</td>
<td>1.6</td>
</tr>
<tr>
<td>&quot;Low sexual Desire&quot;</td>
<td>28.1</td>
<td>33.9</td>
</tr>
<tr>
<td>&quot;Erectile Dysfunction&quot;</td>
<td>17.9</td>
<td>11.3</td>
</tr>
<tr>
<td>&quot;To improve athletic performance&quot;</td>
<td>8.2</td>
<td>8.1</td>
</tr>
<tr>
<td>&quot;Anemia&quot;</td>
<td>3.6</td>
<td>0.0</td>
</tr>
</tbody>
</table>
To Treat or Not To Treat? : Weighing Risks and Benefits
Polling Question

60 y/o male with long-standing HIV, well-controlled on TAF/FTC/BIC, complicated by hyperlipidemia, severe lipoatrophy and diabetes mellitus. He reports some fatigue, difficulty maintaining erections, trouble with memory and feelings of depression. DXA shows osteoporosis. Morning free testosterone is low on two occasions.

Would you prescribe testosterone replacement in this patient?

1) Yes
2) No, I don’t prescribe testosterone in older men
3) No, I would prescribe it, but his cardiovascular risk is too high
4) No, I don’t think that he really would benefit from it.
5) Not sure
Potential Benefits of Testosterone Therapy in Older Men

- Fat Mass
- Lean Mass
- Muscle Strength
- Cognition
- Sexual Function
- QOL
- Physical Function
- Bone Health
Adverse Effects of Testosterone Therapy

- Male Pattern Balding
- Acne/Sebum
- ↓ Spermatogenesis
- Sleep Apnea
- Breast
- Prostate
- Cardiovascular
- Erythrocytosis

Bhasin S et al. J Clin Endocrinol Metab. 2010;95:2536
A Cautionary Tale: Women’s Health Initiative

Stopped early in 2002

Main Findings: the Risks

Per 10,000 women after 5 years there was an increased risk of:

• Breast Cancer  (from 30 to 38 cases)
• Coronary Heart Disease  (from 30 to 37 cases)
• Stroke  (from 21 to 29 cases)
A large-scale trial to determine long-term risks and effectiveness should be undertaken only if clinically significant benefits are demonstrated in the initial, shorter studies. The studies should involve only older men who have been diagnosed with low testosterone levels and at least one symptom that might be remedied by the therapy and who are not at high risk for developing prostate cancer.
Testosterone Trials (TTrials): Overview

- Coordinated set of seven placebo-controlled, double-blind trials in 788 men with a mean age of 72 years
  - Sexual Function Trial
  - Physical Function Trial
  - Vitality Trial
  - Cognitive Function Trial
  - Anemia Trial
  - Bone Trial
  - Cardiovascular Trial
Trials: Recruitment

Telephone screens completed  n = 51,085

Ineligible by telephone screen  n = 18,744
Prostate cancer history  n = 3,116
Other cancer history  n = 1,972
Other or no reason  n = 13,856
Declined further screening  n = 6,452

Screening visit 1  n = 23,889

Ineligible by screening visit 1  n = 21,037
Testosterone high  n = 19,189
Prostate cancer risk high  n = 1,616
Other  n = 331
Declined further screening  n = 591

Screening visit 2  n = 2,261

Ineligible by screening visit 2  n = 1,330
No objective impairment  n = 515
Testosterone level high  n = 391
IPSS > 19  n = 147
Other  n = 174
Declined randomization  n = 141

Randomized  n = 790

Allocated to testosterone  n = 395

Analyzed  n = 376
No follow-up data  n = 18
Randomized incorrectly  n = 1

Allocated to placebo  n = 395

Analyzed  n = 374
No follow-up data  n = 20
Randomized incorrectly  n = 1
## TTrials: Participant Characteristics

### Table 1. Characteristics of Men Enrolled in Testosterone Trials at Baseline

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Treatment Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>Participants, n</td>
<td>395</td>
</tr>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>72.3 ± 5.8</td>
</tr>
<tr>
<td>Race, n</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>351 (88.9)</td>
</tr>
<tr>
<td>Black</td>
<td>20 (5.1)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>24 (6.1)</td>
</tr>
<tr>
<td><strong>Concomitant conditions</strong></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.0 ± 3.6</td>
</tr>
<tr>
<td>BMI &gt;30, n (%)</td>
<td>246 (62.3)</td>
</tr>
<tr>
<td>Alcohol use, drinks/wk</td>
<td>3.4 ± 5.0</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Current smoker, n</td>
<td>34 (8.6)</td>
</tr>
<tr>
<td>Ever smoker, n</td>
<td>268 (67.9)</td>
</tr>
<tr>
<td>Diabetes, n</td>
<td>144 (36.5)</td>
</tr>
<tr>
<td>Hypertension, n</td>
<td>280 (70.9)</td>
</tr>
<tr>
<td>History of myocardial infarction, n</td>
<td>63 (16.0)</td>
</tr>
<tr>
<td>History of stroke, n</td>
<td>17 (43)</td>
</tr>
<tr>
<td>Sleep apnea, n</td>
<td>76 (19.2)</td>
</tr>
</tbody>
</table>
Trials: Hormone Levels
Ttrials: Sexual Function

Sexual activity—men enrolled in the sexual function trial

Change from baseline in response to question 4 of the psychosocial daily questionnaire

Month

Testosterone (n) 230
- 206
- 208
- 205
- 193

Placebo (n) 229
- 201
- 191
- 191
- 194
Trials: Physical Function

Walking distance—men enrolled in the physical function trial

Walking distance—all men

% of men who walked ≥50 m further than at baseline

Month

Testosterone (n) 191 179 174 172 172
Placebo (n) 196 179 171 159 165

p = 0.20

Testosterone (n) 392 368 358 348 346
Placebo (n) 389 356 339 320 326

p = .003
TTrials: Vitality

Vitality-fatigue—men enrolled in the vitality trial

% of men who scored ≥4 higher than at baseline on the FACT-fatigue scale

Month 0 3 6 9 12
Testosterone (n) 236 219 217 206 203
Placebo (n) 238 207 196 188 191

p = 0.30

Vitality-fatigue—all men

% of men who scored ≥4 higher than at baseline on the FACT-fatigue scale

Month 0 3 6 9 12
Testosterone (n) 394 351 350 337 333
Placebo (n) 394 337 329 317 316

p = 0.22
**TTrials: Cognitive Function**

<table>
<thead>
<tr>
<th>Function Trial</th>
<th>Group</th>
<th>Mean Effect Size</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory, delayed graph recall</td>
<td>Men with age-associated memory impairment (493)</td>
<td>-0.07 (-0.92 to 0.79)</td>
<td>-0.01 (-0.14 to 0.12)</td>
<td>0.88</td>
</tr>
<tr>
<td>Memory, delayed graph recall</td>
<td>All TTrials men (785)</td>
<td>0.09 (-0.57 to 0.75)</td>
<td>0.01 (-0.09 to 0.11)</td>
<td>0.80</td>
</tr>
<tr>
<td>Memory, Benton visual retention test</td>
<td>Men with age-associated memory impairment (492)</td>
<td>-0.28 (-0.76 to 0.19)</td>
<td>-0.09 (-0.24 to 0.06)</td>
<td>0.24</td>
</tr>
<tr>
<td>Hand dexterity, card rotation</td>
<td>Men with age-associated memory impairment (488)</td>
<td>-0.12 (-1.89 to 1.65)</td>
<td>-0.01 (-0.13 to 0.11)</td>
<td>0.89</td>
</tr>
<tr>
<td>Spatial function; trail making test B-A, s&lt;br&gt;</td>
<td>Men with age-associated memory impairment (490)</td>
<td>-5.51 (-12.91 to 1.88)</td>
<td>-0.09 (-0.22 to 0.03)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Testosterone treatment did not improve several aspects of cognitive function in men who had age-associated memory impairment.
Trials: Anemia

Unexplained anemia

% of men whose hemoglobin increased ≥1 from baseline

Change in hemoglobin from baseline

![Graphs showing the percentage of men whose hemoglobin increased ≥1 from baseline over months, and the change in hemoglobin from baseline. The graphs compare testosterone (n=27) and placebo (n=35) groups, with p-values of 0.004 and 0.016 for the respective comparisons.](image)
Endocrine Society Guidelines
Erythrocytosis

Against T Therapy

Baseline Hct >50%
(these men should undergo further evaluation)

Monitoring
• Hematocrit at 3 & 6 months---then annually
• Older age and T injections at higher risk

Cessation and Referral

Hct >54%
• Evaluate for hypoxia
• Re-initiate T at lower dose once Hct at safe level

Bhasin S et al. J Clin Endocrinol Metab. 2010;95:2536
TTrials: Bone

Effect of testosterone on volumetric bone mineral density

Percent change from baseline

- Trabecular Spine
- Peripheral Spine
- Whole Spine
- Trabecular Hip
- Peripheral Hip
- Whole Hip

p < 0.001
Figure 8. Change from baseline to 12 months in noncalcified coronary artery plaque volume, as determined by CTA, in 138 men treated with testosterone or placebo. Data presented as least square mean ± 95% confidence intervals.
Myriad Effects of Testosterone on CV Function

Testosterone

- Vasorelaxation
  - Relaxation of vascular smooth muscles through voltage and Ca++ dependent potassium channels, activating endothelial nNOS, blocking of L and T type Ca++ channels

- ECG-changes
  - Elongation of T-wave, shortening of QT interval

- Anti-Atherosclerosis

- Anti-Inflammatory Effect
  - Inhibits TNF-α, IL-6, YGAM-1
  - Induces IL-10 (anti-inflammatory cytokine)

- Anti-Thrombotic effect on Platelets

- Peripherial Resistance

- Prothrombic effect on Platelets

- Thrombosis

- Lipid Metabolism
  - Increased expression of SCARB1
  - Increased hepatic cholesterol deposition, expression of LDL, inhibition of leptin

- Vascular and Forming of Blood

- Blood vessel

- Increased endothelial permeability

- Erythrocytosis

- Increased hematocrit

- Clotting enzymes
  - Adhesive molecules (e.g., YGAM-1, YGAM-2)
  - Blood Plasma

- Tissue cells

- Increased fluid retention due to higher expression of Nat/H+
  - exchanger, aquaporin 1

Kharaba, Biomedicine & Pharmacotherapy
Adverse Events in the TOM Trial

On December 31st, 2009, the Trial’s DSMB recommended cessation of enrollment and treatment discontinuation due to increased frequency of CV adverse events.

<table>
<thead>
<tr>
<th></th>
<th>T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV-Related</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Atherosclerotic</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Serious Events</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Total Events</td>
<td>85</td>
<td>65</td>
</tr>
</tbody>
</table>

Testosterone Therapy and Mortality in Older Males with High CVD Risk

Figure 2. Kaplan-Meier Survival Curves With Testosterone Therapy Evaluated as a Time-Varying Covariate

HR, 1.29 (95% CI, 1.04-1.58)
Log-rank P = .02

No. at risk
Testosterone therapy
No 8709
Yes 0
5337
2897
918
206

Vigen, JAMA, 2013
Risk of Non-Fatal MI: Pre vs Post Testosterone Prescription

<table>
<thead>
<tr>
<th></th>
<th>All Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>55,593</td>
</tr>
<tr>
<td>Pre-prescription</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>193</td>
</tr>
<tr>
<td>Rate per 1,000 PY (95%CI)</td>
<td>3.48 (3.02, 4.01)</td>
</tr>
<tr>
<td>Post-prescription</td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>65</td>
</tr>
<tr>
<td>Rate per 1,000 PY (95%CI)</td>
<td>4.75 (3.72, 6.05)</td>
</tr>
<tr>
<td>Rate Ratio (post/pre) (95%CI)</td>
<td>1.36 (1.03, 1.81)</td>
</tr>
</tbody>
</table>

RR (95% CI): < 65 yrs 1.2 (0.8, 1.6)
≥ 65 yrs 2.2 (1.3, 3.7)

Finkle, PlosOne, 2014
Meta-Analysis of Benefits/Harms with Testosterone Treatment: CVD Events

**Figure 3.** Primary harm outcomes from RCTs for testosterone treatment vs. placebo.

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Route</th>
<th>Mean Baseline $T$, ng/dL</th>
<th>Follow-up, mo</th>
<th>Industry-Funded</th>
<th>Events/Participants, $n/N$</th>
<th>Peto OR</th>
<th>Peto OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amory et al, 2004 (25)</td>
<td>IM</td>
<td>294</td>
<td>36</td>
<td>No</td>
<td>1/24</td>
<td>7.39</td>
<td>(0.15 to 372.38)</td>
</tr>
<tr>
<td>Basaria et al, 2015 (27)</td>
<td>TD</td>
<td>307</td>
<td>36</td>
<td>Yes</td>
<td>12/155</td>
<td>2.79</td>
<td>(1.02 to 7.61)</td>
</tr>
<tr>
<td>Gianatti et al, 2014 (38)</td>
<td>IM</td>
<td>246</td>
<td>9</td>
<td>Yes</td>
<td>3/45</td>
<td>2.69</td>
<td>(0.37 to 19.77)</td>
</tr>
<tr>
<td>Giltay et al, 2010 (41)</td>
<td>IM</td>
<td>230</td>
<td>7</td>
<td>Yes</td>
<td>0/113</td>
<td>0.07</td>
<td>(0.00 to 1.28)</td>
</tr>
<tr>
<td>Hildreth et al, 2013 (47)</td>
<td>TD</td>
<td>297</td>
<td>12</td>
<td>No</td>
<td>1/96</td>
<td>0.14</td>
<td>(0.02 to 1.17)</td>
</tr>
<tr>
<td>Kenny et al, 2010 (53)</td>
<td>TD</td>
<td>398</td>
<td>12</td>
<td>No</td>
<td>1/69</td>
<td>0.45</td>
<td>(0.05 to 4.46)</td>
</tr>
<tr>
<td>Merza et al, 2006 (60)</td>
<td>TD</td>
<td>230</td>
<td>6</td>
<td>Yes</td>
<td>0/20</td>
<td>0.13</td>
<td>(0.00 to 6.48)</td>
</tr>
<tr>
<td>Nair et al, 2006 (61)</td>
<td>TD</td>
<td>&gt;350</td>
<td>24</td>
<td>No</td>
<td>2/30</td>
<td>1.99</td>
<td>(0.20 to 19.94)</td>
</tr>
<tr>
<td>Ng Tang Fui et al, 2016 (64)</td>
<td>IM</td>
<td>196</td>
<td>13</td>
<td>Yes</td>
<td>1/49</td>
<td>7.70</td>
<td>(0.15 to 388.20)</td>
</tr>
<tr>
<td>Snyder et al (T Trials), 2016 (71)</td>
<td>TD</td>
<td>234</td>
<td>12</td>
<td>Yes</td>
<td>7/394</td>
<td>1.00</td>
<td>(0.35 to 2.88)</td>
</tr>
<tr>
<td>Snyder et al, 1999 (72)</td>
<td>TD</td>
<td>368</td>
<td>36</td>
<td>Yes</td>
<td>4/54</td>
<td>1.35</td>
<td>(0.29 to 6.22)</td>
</tr>
<tr>
<td>Srinivas-Shankar et al, 2010 (75)</td>
<td>TD</td>
<td>316</td>
<td>6</td>
<td>Yes</td>
<td>1/130</td>
<td>1.02</td>
<td>(0.06 to 16.32)</td>
</tr>
<tr>
<td>Svartberg et al, 2008 (77)</td>
<td>IM</td>
<td>239</td>
<td>12</td>
<td>Yes</td>
<td>1/19</td>
<td>7.39</td>
<td>(0.15 to 372.38)</td>
</tr>
<tr>
<td>Tan et al, 2013 (79)</td>
<td>IM</td>
<td>260</td>
<td>11</td>
<td>Yes</td>
<td>2/60</td>
<td>1.97</td>
<td>(0.20 to 19.31)</td>
</tr>
</tbody>
</table>

Total: 36/1258 vs. 26/1157

Random-effects model heterogeneity: $I^2 = 18\%$

Diem, Annals Int Med, 2020
Increase in PSA with Testosterone Treatment

Snyder, JCEM, 1999
Of 197 articles relating to testosterone therapy, 44 met inclusion criteria: 11 placebo-controlled, randomized studies; 29 non-placebo-controlled studies of men with no prostate cancer history; and 4 studies of hypogonadal men with history of prostate cancer. Of studies that met inclusion criteria, none demonstrated that testosterone therapy for hypogonadism increased prostate cancer risk or increased Gleason grade of cancer detected in treated vs untreated men.

Shabsigh, IJIR, 2008
Endocrine Society Guidelines
Prostate

**Against T therapy**
- Prostate Cancer
- Nodule
- PSA >4.0 ng/ml
- PSA >3.0 ng/ml (African Americans, Family History)

**Monitoring**
Men ≥40 yrs with PSA >0.6 ng/ml
PSA at 3 & 6 months---then based on AUA guidelines

**Cessation and Referral**
- Nodule
- \(\Delta\) PSA change >1.4 ng/ml
- International Prostate Symptom Score >19

Bhasin S et al. *J Clin Endocrinol Metab.* 2010;95:2536
What's the purpose of the TRAVERSE clinical research study?
This study is testing a testosterone replacement therapy in men with low testosterone (hypogonadism) and a history or risk of heart disease or stroke.

The TRAVERSE study is enrolling now.
Talk to your doctor or contact us today to see if you may qualify.

<< SITE INFO >>
www.studynname.com

Men: It's okay to talk about low testosterone (hypogonadism).
Decreased sexual desire?
Feel fatigued?
Depressed mood?

What you're feeling could be related to low testosterone (hypogonadism).
Gender Affirming Hormonal Therapy for Transgender Men
Effects of Testosterone in Transgender Men

Figure: Effects of testosterone therapy in transgender men

Psychological and CNS
- ↓ Gender dysphoria
- ↓ Anxiety
- ↓ Depression
- ↓ Perceived stress
- ↑ Total grey matter volume
- ↑ Cortical thickness in several areas

Skin
- Acne

Voice
- ↓ Pitch

Muscle
- ↑ Lean mass
- ↑ Cross-sectional area
- Bodyweight
- Grip strength

Blood pressure
- ↑ Systolic blood pressure

Blood
- ↑ Haemoglobin and haematocrit

Lipids and metabolism
- ↑ HDL cholesterol
- ↓ Triglycerides
- ↓ Sex hormone-binding globulin

Hormone concentrations
- ↓ Oestradiol
- ↓ Luteinising hormone
- ↓ Follicle-stimulating hormone
- ↓ Prolactin

Hair
- ↑ Facial and body hair
- ↑ Hair density, diameter, and growth rate
- Alopecia

Breast
- ↓ Breast cancer
- ↓ Glandular tissue
- ↓ Fibrous connective tissue

Reproductive system
- Cessation of menstruation and infertility
- ↑ Clitoral size
- ↓ Vaginal epithelium thickness
- Atrophic endometrium (according to data from some studies)
- Ovarian hyperplasia and polycystic ovaries

Sexual health
- ↑ Sexual desire
<table>
<thead>
<tr>
<th>Route</th>
<th>Dosing</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enanthate or</td>
<td>Intramuscular</td>
<td>Inexpensive</td>
<td>Peaks and troughs with pharmacokinetics</td>
</tr>
<tr>
<td>cypionate</td>
<td>100–200 mg every 2 weeks (or half dose weekly)</td>
<td>Effective at achieving target testosterone concentrations</td>
<td>Pain with injections</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Increased erythrocytosis compared with other formulations</td>
</tr>
<tr>
<td>Gels (1%)</td>
<td>Topical</td>
<td>Consistent testosterone concentrations</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>25–100 mg per day</td>
<td></td>
<td>Potential transference to women or children on personal contact</td>
</tr>
<tr>
<td>Patch</td>
<td>Topical</td>
<td>Consistent testosterone concentrations</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>2.5–10 mg per day</td>
<td></td>
<td>Skin irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inadequate testosterone concentrations</td>
</tr>
<tr>
<td>Axillary solution</td>
<td>Topical</td>
<td>Consistent testosterone concentrations</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>30–120 mg per day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undecanoate</td>
<td>Intramuscular</td>
<td>Consistent testosterone concentrations</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>750–1000 mg every ten to 14 weeks</td>
<td></td>
<td>Large injection volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Risk of pulmonary oil microembolus (rare)</td>
</tr>
<tr>
<td>Undecanoate</td>
<td>Oral</td>
<td>40–80 mg, 2–3 times per day with meals</td>
<td>Variable testosterone concentrations</td>
</tr>
<tr>
<td>Pellets</td>
<td>Subcutaneous implants</td>
<td>Consistent testosterone concentrations</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>150–450 mg every 3–6 months</td>
<td>Infreqent dosing</td>
<td>Invasive (incision with scalpel)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inflexible dosing</td>
</tr>
<tr>
<td>Buccal</td>
<td>Buccal</td>
<td>--</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td>30 mg twice per day</td>
<td></td>
<td>Gum irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Taste alterations</td>
</tr>
<tr>
<td>Nasal spray</td>
<td>Nasal</td>
<td>11 mg three times per day</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Frequent dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inadequate testosterone concentrations</td>
</tr>
</tbody>
</table>

Availability of certain formulations varies by country.

**Table 2: Testosterone formulations**
**Laboratory Monitoring for Gender Affirming Hormonal Therapy**

**Table 2. Recommended Laboratory Monitoring in Transgender Persons Receiving CSHT***

<table>
<thead>
<tr>
<th>Value</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin A1c or glucose levels</td>
<td>Per USPSTF guidelines Per USPSTF guidelines</td>
</tr>
<tr>
<td>Lipid levels</td>
<td>Per USPSTF guidelines Per USPSTF guidelines</td>
</tr>
<tr>
<td>Estradiol levels</td>
<td>As needed Every 3 mo for the first 6 mo</td>
</tr>
<tr>
<td>Total testosterone levels</td>
<td>Every 3 mo for the first year</td>
</tr>
<tr>
<td>Sex hormone-binding globulin levels</td>
<td>Every 3 mo for the first year</td>
</tr>
<tr>
<td>Albumin levels</td>
<td>Every 3 mo for the first year</td>
</tr>
<tr>
<td>Hemoglobin levels and hematocrit</td>
<td>Every 3 mo for the first year</td>
</tr>
<tr>
<td>Prolactin levels</td>
<td>Only if symptoms of prolactinoma develop</td>
</tr>
<tr>
<td>Blood urea nitrogen, creatinine, and potassium levels</td>
<td>Only if receiving spironolactone</td>
</tr>
</tbody>
</table>

* From reference 67.
CSHT = cross-sex hormone therapy; USPSTF = U.S. Preventive Services Task Force.
Most Common Adverse Effects for GAHT in TGM

- Acne
- Alopecia
- Decreased HDL
- Increased Triglycerides
- Increased Systolic Blood Pressure
Testosterone use among older cisgender men is common, especially among those with HIV. The T Trials showed improvements with sexual function, physical function, mood, hemoglobin, bone density with testosterone in older men over 1 year, and increases in coronary non-calcified plaque. No effect on vitality or cognition.

No RCTs among older cisgender men with HIV.

Long term effects on cardiovascular events and prostate cancer are unclear. TRAVERSE Study will address this.

Gender affirming hormonal therapy in transgender men is generally well tolerated with acne, alopecia, and dyslipidemia as the major adverse effects. Long term risks unclear.
Thank You for Your Attendance!
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