

Guneet K. Jasuja, PhD 12th September 2017



Center for Healthcare Organization and Implementation Research

Appointments

- Research Health Scientist at Bedford VAMC
- Research Assistant Professor at BU School of Public Health
- Second Year of HSR&D CDA

Poll Question

- What is your primary role in VA?
 - student, trainee, or fellow
 - clinician
 - researcher
 - Administrator, manager or policy-maker
 Other

Poll Questions

- Are you involved with any aspect of testosterone therapy?
 - Yes
 - No
- If you are involved with testosterone therapy, how are you involved?
 - I am involved in research on testosterone therapy
 - I am involved in prescribing of testosterone therapy
 - I am involved in formulating policy on testosterone therapy.

Broader HSR&D Themes

- Guideline-Concordant Prescribing
- Variation in Prescribing at Different Levels
- Mixed-methods Approach in Understanding Prescribing
- Best Practices and De-implementation of Practices

Aims of CDA

- Aim 1: To identify quantitative patient-, provider-, and site-level predictors of testosterone prescribing in the VA.
- Aim 2: To understand patient, provider, and siteleader perceptions towards testosterone prescribing in the VA.
- Aim 3: To develop and pilot test a multifaceted intervention to optimize testosterone use in the VA.

CDA-Mentoring Team

- Dan Berlowitz (Primary Mentor): Quality of Care
- Allen Gifford: Implementation Science
- Barbara Bokhour: Qualitative Methods
- Adam Rose: Medication Prescribing
- Shalender Bhasin: Hormone Therapy

Outline of Presentation

Background: Testosterone therapy

Work Completed:

- #1: Assessment of Testosterone Prescribing Practices (Aim 0)
- #2: Patient Predictors of Testosterone Prescribing (Aim 1)
- #3: Provider and Site Predictors of Testosterone Prescribing (Aim 1)

Outline of Presentation

Work in Progress:

- #1: Qualitative: Understanding Patient, Provider, and Site Leader Perceptions towards Testosterone Prescribing (Aim 2)
- #2: QI project: Testosterone order check (Extra work)
- #3: Database: Testosterone Prescribing in Patients with HIV (Extra work)
- #4: Database: Effect of Testosterone Therapy on patients taking opioids (Extra work)

Poll Question

Do you know what low testosterone is?



Testosterone: Male hormone

- Age-related decline: After age 30 ~ 1% per year
- <u>Causes of low testosterone</u>: injury to testicles, genetic abnormalities, medications & illnesses.
- <u>Effects of low testosterone</u>: decreased libido, muscle mass, bone density, hemoglobin, increase in weight, cholesterol.
- <u>Treatment</u>: Testosterone Therapy (Symptoms + Low Testosterone Levels)

Testosterone Therapy

Contraindications:

- Absolute: Prostate and Breast cancer
- Relative: Untreated Obstructive Sleep Apnea
- Relative: PSA > 4 ng/ml ; Elevated hematocrit

<u>Measurement of low T:</u>
Initial diagnostic test (before 10 am)

Confirmation of diagnosis by repeat test

Testosterone Therapy

Benefits:

Proven: Increased muscle mass, bone strength.

Potential: Improved cognition

<u>Risks:</u>

- Proven: Increase in red blood cells, growth in prostate cancer, reduced sperm production
- > Potential: Cardiovascular problems

FDA approval of T: Classical hypogonadism (disorders of testes, pituitary, and hypothalamus)

Testosterone Therapy

- In patients with HIV/AIDS
- In transgender populations
- Primarily for hypogonadism/androgen deficiency (low T levels)

Current VA Guidelines:

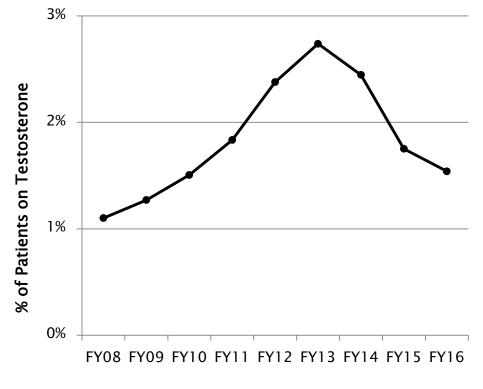
 Pharmacy Benefits Management (PBM) issued criteria for use (CFU) for testosterone therapy in adult men in 2016.

Trends in Testosterone Prescribing

- Three fold increase in the US in the last decade
- Peaked in 2013 and has been decreasing since
- Use remains many-fold higher than it was in 2000.
- Reasons for increase in prescribing:
 - Aggressive direct-to-consumer marketing
 - Establishment of low "T" clinics

- Establishment of internet pharmacies in Canada
- Availability of transdermal preparations of testosterone
- Ambiguity of guidelines to distinguish between age-related decline of testosterone and classical hypogonadism
- Declining trend due to heightened FDA activity and media stories.

Proportion of Male Veterans Receiving Testosterone, FY2008-16



Fiscal Year

(Jasuja et al., Patterns of Testosterone Prescription Overuse, Curr Opin Endocrinol Diabetes Obes, 2017).

Work Completed

#1: Assessment of Testosterone Prescribing Practices

 <u>Objective</u>: To examine whether testosterone therapy was preceded by appropriate ascertainment of androgen deficiency and potential contraindications, in accordance with practice guidelines

(Jasuja et al., Ascertainment of Testosterone Prescribing Practices in the VA, Medical Care, 2015).

Methods

- Cross-sectional (FY 2009-12)
- N=111,631 male Veterans
- I year "look back" to check for tests & contraindications
- "Low" testosterone: total testosterone < 300 ng/dL free testosterone < 70 pg/mL
- Exclusions:
 - HIV positive
 - Received testosterone prescription before FY2009
 - No evidence of care in the VA in FY2008

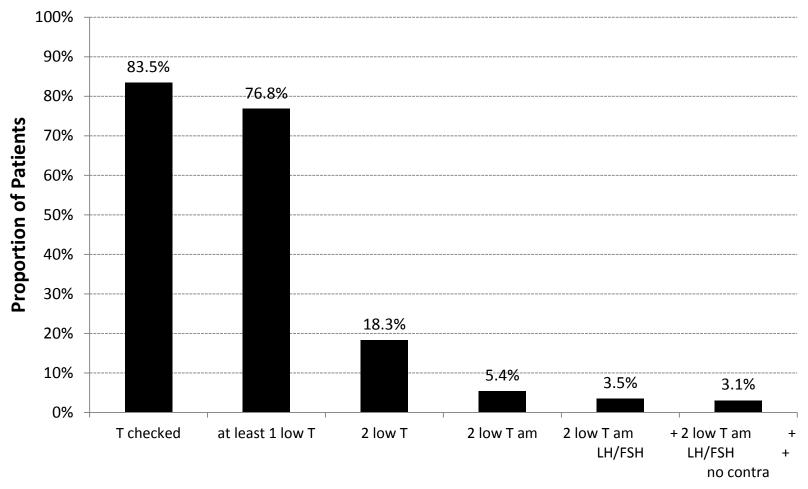
Findings

 New testosterone prescriptions increased from 20,581 in FY09 to 36,544 in FY12 (~78% increase).

Baseline Assessment and Contraindications Before Initiation

Baseline Assessment	
Measurement of baseline PSA level	76%
Measurement of baseline hematocrit level	84%
Measurement of baseline hematocrit and PSA levels	68%
Documentation of Hypogonadism by ICD-9 code	59%
Relative Contraindications	
Obstructive Sleep Apnea	7.5%
Elevated Hematocrit (>50%)	3.5%
PSA level > 4.0	2.3%
Any Relative Contraindication	13%
Absolute Contraindications	
Prostate Cancer	1.4%
Breast Cancer	0.01%
Any Absolute Contraindication	1.4%

Baseline Evaluation



Diagnostic and Baseline Evaluation

Sensitivity Analysis

- We used Medicare data to examine testosterone levels checked outside of the VA.
- Of the patients who had no testosterone levels in the VA at all (n=18,457), 8,237 (about half) were enrolled in fee-for-service Medicare
- Of these, 48% had undergone testosterone testing outside VA.

Conclusions

- Only a small proportion of men receiving testosterone in VA underwent appropriate testing.
- Some received this therapy in spite of important contraindications.
- Promoting a more uniform application of clinical guidelines may facilitate appropriate use of testosterone.

#2: Patient Predictors of Testosterone Prescribing

 <u>Objective</u>: To evaluate patient characteristics associated with receipt of testosterone in the VA.

(Jasuja et al. Who gets Testosterone? Patient Characteristics Associated with Testosterone Prescribing in the Veteran Affairs System: A Cross-Sectional Study. JGIM, 2017)

Methods

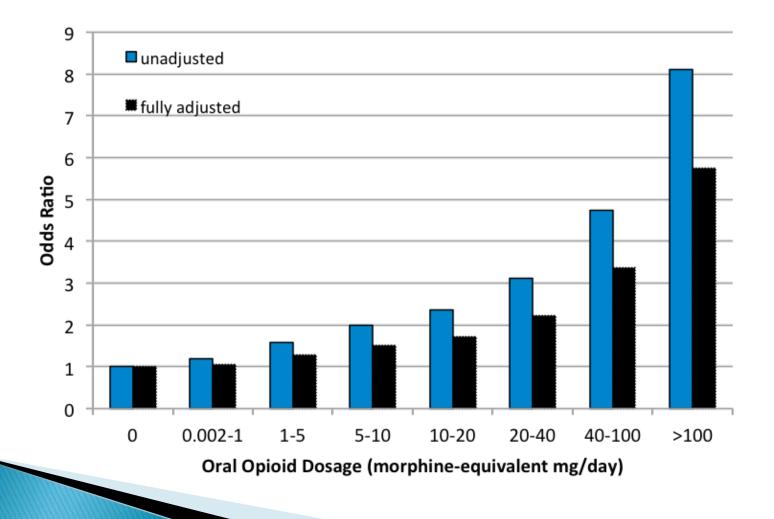
- Cross-sectional (FY 2008-12)
- N=682,915 male Veterans ("On Testosterone"=132,764; "Not on Testosterone"=550,151)
- I year "look back" to check for diagnoses and medications
- Exclusions:
 - HIV positive
 - Received fills only in FY 08
 - No evidence of fills in the VA in FY 08
 - Patients with diagnosed conditions of testes, pituitary and hypothalamus (Classical hypogonadism)
 - Patients with identified gender disorder

Findings

- Only 6.3% of men on testosterone had classical hypogonadism.
- Demographics (age 40-55, White race), conditions (sleep apnea, depression, diabetes) and medications (antidepressants, corticosteroids) associated with higher testosterone receipt (AOR less than 2; p<0.001).</p>
- Use of opioids (>100 mg/equiv. of oral morphine daily) and obesity (>40 kg/m²) were strongest predictors of testosterone.

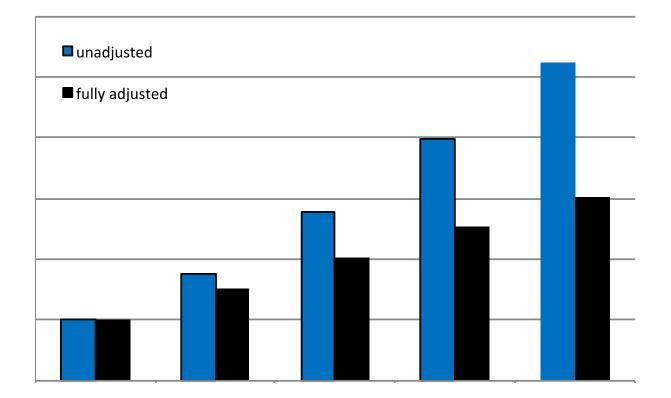


Opioid Dosage as a Determinant of Testosterone Receipt



Findings

ceipt



Conclusions

- Though obesity and opioid use is associated with unapproved, off-label use however, they may be valid reasons for receiving this therapy.
- Need for greater understanding of the context within which testosterone is prescribed.

#3: Provider- and Site-Level Predictors of Testosterone Use

 <u>Objective</u>: To evaluate provider-and site-level determinants of testosterone in the VA.

(Jasuja et al., Provider and Site-Level Determinants of Testosterone Prescribing in the Veterans Healthcare System. JCEM, 2017)

Methods

- Cross-sectional (FY 2008-12)
- N=683,135 patients; N=38,659 VA providers; N=130 stations
- Associated provider who wrote index prescription
- Associated site where the patient had most encounters

Findings: Provider Predictors (Adjusted Model)

Variable	OR (95% CI)
Age (31-40) vs. 61+	1.14 (1.11-1.16)
Age (41-50) vs. 61+	1.15 (1.13-1.17)
Age (51-60) vs. 61+	1.13 (1.11-1.16)
Years in VA (<=1 year)	1.19 (1.17-1.22)
Male gender	1.04 (1.03-1.06)
MD, Endocrinology vs. MD, PCP	2.14 (2.00-2.29)
MD, Urology vs. MD, PCP	1.42 (1.23-1.63)

Findings: Site Predictors (Adjusted Model)

Variable	OR (95% CI)
Region: West vs. Northeast	1.75 (1.45-2.11)
Region: South vs. Northeast	1.63 (1.36-1.95)
Region: Midwest vs. Northeast	1.37 (1.13-1.67)
Care received at CBOC	1.22 (1.20-1.24)

Methods

- Appropriateness prescribing in new T patients FY09-12 (N=99,102 patients; N=12,912 providers; N=129 sites)
- 3 levels of appropriate prescribing
 - Minimal: At least one low testosterone levels
 - At least two low testosterone levels

- Maximal: At least two low AM testosterone levels

Findings: Provider Predictors of Appropriate Prescribing

Variable	2 AM Low T
Provider age (31-40)	1.30 (1.12-1.50)
Provider age (41-50)	1.14 (1.00-1.30)
Provider age (51-60)	1.12 (1.00-1.26)
Provider years in VA (<=1)	0.82 (0.72-0.94)
Male gender	0.88 (0.81-0.96)
MD, Endocrinology	2.14 (1.54-2.97)

Findings: Site Predictors of Appropriate Prescribing

Variable	2 AM Low T
Region: South	0.80 (0.72-0.90)
Care received at CBOC	0.83 (0.77-0.90)
Most complex sites	1.33 (1.18-1.49)

Conclusions

- Findings highlight the opportunity to intervene both at the provider and site-level to improve testosterone prescribing.
- Beyond testosterone, this study provides an example of how to examine contributions to prescribing variation at different levels of the healthcare system.

Work in Progress

#1: Qualitative: Aim 2 of CDA

- Aim 2: To understand patient, provider and site-leader perceptions towards testosterone prescribing in high and low testosterone prescribing sites using qualitative methods
- Completed 22 provider and local leader and 15 interviews with Veterans at 3 high and low sites

Ongoing: Coding and data analyses

#2: Quality Improvement project

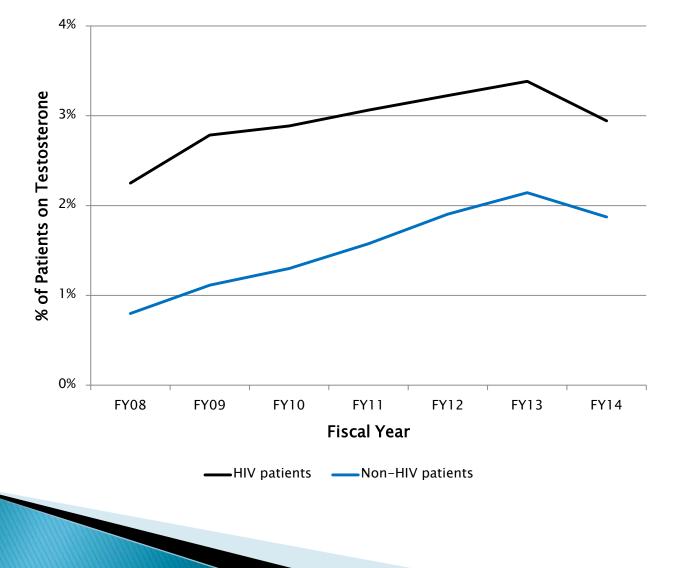
- Development and Implementation of a Testosterone order check: Dr. Eric Shirley, VISN 1 Director of Primary Care
- Alert providers about clinical recommendations in CPRS before prescribing
- Provider given the option of continuing or canceling the new order and provide justification for continuing
- <u>Research Aim</u>: To test the effectiveness of an order check in reducing new testosterone prescriptions in VISN 1.
- Rolled out in 8 VISN 1 sites in Jan. 2016
- <u>Next step:</u> Data analyses: Rate of change in new T prescriptions (Interrupted time series analyses)

#3: Testosterone Prescribing in Patients with HIV

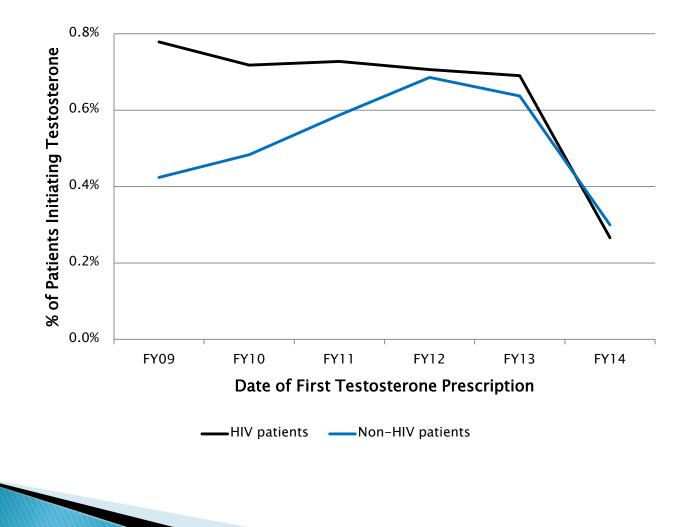
- Use of testosterone in patients with HIV due to hypogonadism and wasting.
- <u>Objective</u>: To compare trends/rates, and guideline concordant appropriate testing in testosterone prescribing in HIV vs. non-HIV population

 Methods: Comparison of two cohorts (FY08-14): Patients with HIV on T (N=2, 484) Non-HIV patients on T (N=189,369)

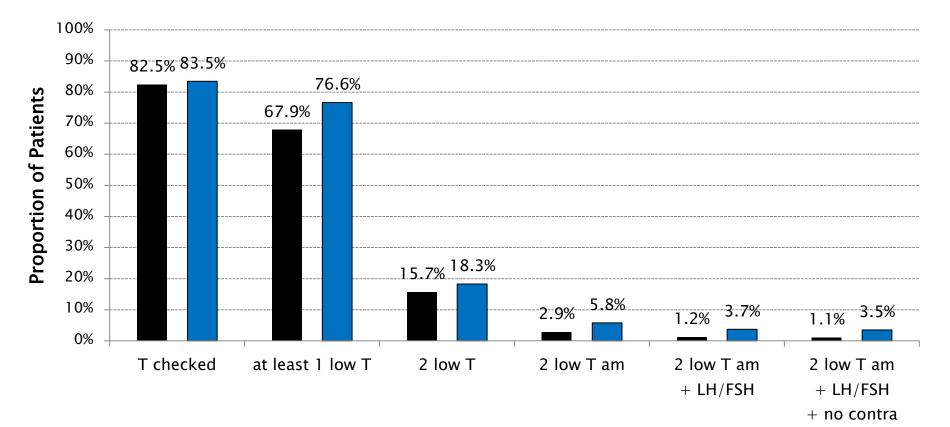
Trends in Testosterone Prescribing in Patients with HIV vs. Non-HIV Patients



Trends in Testosterone Initiation in Patients with HIV vs. Non-HIV Patients



Comparison of HIV and non-HIV Patients on Diagnostic and Baseline Evaluation



Diagnostic and Baseline Evaluation

■ HIV patients ■ Non-HIV Patients

Conclusions

- Trends of prescribing for both groups followed a similar pattern.
- Higher rates of testosterone use in patients with HIV:
 - More androgen deficiency
 - Likelihood of prescribing due to frequent provider visits
 - Greater off-label use in patients with HIV
 - Awareness of testosterone among clinicians who care for patients with HIV
- Findings suggest opportunities for improvement of testosterone treatment practices for HIV-infected men within VHA.

#4: Effect of Testosterone in Patients Taking Opioids

- Suppression of hormonal production with opioid use.
- <u>Objective</u>: To examine effect of testosterone therapy on mortality and cardiovascular outcomes in patients on long-term opioid therapy

- Methods: Comparison of 2 samples on outcomes:
 - Long-term opioids + testosterone
 - Only opioids
- <u>Analyses:</u> Ongoing

Significance of Work

Important beginning to understand the unknown

- Findings will help in advising VA Operations (Pharmacy Benefits Management) in improving testosterone prescribing in the VA
- Application to other medications for optimal prescribing in the VA
- Fits in with the Medication Optimization Program of Boston/Bedford CHOIR.
- Quantitative findings: Need for improvement in provider prescribing practices for testing and documentation.
- <u>Next step:</u> Development and pilot testing of a multi-faceted intervention to optimize testosterone use in the VA

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- <u>Operational Partners</u>
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- <u>Project Team</u>
 Joel Reisman, Omid Ameli, Alex Male, Avy Skolnik, Ryann Engle



 PBM Clinical Guidance-Criteria For Use of Testosterone Therapy in Adult Men

http://www.pbm.va.gov/PBM/clinicalguidance/criteriaforuse/Testoste rone_Replacement_in_Adult_Males_Criteria_for_Use.pdf

 FDA Drug Safety Communication on Testosterone <u>https://www.fda.gov/Drugs/DrugSafety/ucm436259.htm</u>

Questions/Comments

Contact Information

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