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Testosterone Replacement Therapy Initiation and Follow-Up Evaluation in VA Male Patients

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Abbreviations

CPG	Clinical Practice Guidelines
EHR	electronic health record
FDA	Food and Drug Administration
FSH	follicle-stimulating hormone
FY	fiscal year
LH	luteinizing hormone
TRT	testosterone replacement therapy
VHA	Veterans Health Administration
VA Criteria for Use	VA Pharmacy Benefits Management Services, Medical Advisory Panel, and Veterans Integrated Service Network Pharmacist Executives Testosterone Replacement Therapy (TRT) Criteria for Use

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Executive Summary

Introduction

Hypogonadism (androgen deficiency) is a medical condition of lower levels of male sex hormones, particularly testosterone, than is needed for health. Testosterone hormonal replacement therapy is used in men with hypogonadism diagnosed by clinical signs and symptoms consistent with androgen deficiency and unequivocal low testosterone levels.

Testosterone levels are at their highest during adolescence and early adulthood. As men get older, the testosterone levels decline about 1 percent per year after the age of 30. Thus, low testosterone levels in men are common and increasingly prevalent with aging. However, pharmaceutical companies have aggressively marketed testosterone products directly to men as anti-aging wonder drugs. A U.S. study reported that the predominant users of testosterone products were men between the ages of 40 to 64 who did not have a medical indication for androgen deficiency, suggesting that testosterone was being prescribed to men who were simply reluctant to accept common conditions associated with aging.

Testosterone products are classified by the U.S. Drug Enforcement Agency as Schedule III substances, which have a potential for abuse and may lead to physical or psychological dependence. With the increase in testosterone usage, publications reported adverse events, abuse, and dependence affecting patient safety. In particular, the Journal of the American Medical Association published a study in 2013 that showed VA patients who were on testosterone therapy were associated with increased risk of mortality, heart attack, or ischemic stroke. In 2015, the U.S. Food and Drug Administration (FDA) issued a warning to medical doctors against over-prescribing testosterone-boosting drugs for men because the popular treatments had not been established as safe or effective for common age-related issues like low libido and fatigue. Additionally, in 2009, FDA issued a black box warning (visual alert on the drug's package of serious or life-threatening risks) that required labeling changes in regards to secondary exposures to women and children.

The VA Office of Inspector General (OIG) initiated and conducted a study to assess whether VA providers established androgen deficiency prior to initiating testosterone therapy and the extent VA providers performed follow-up evaluation after initiating the therapy, in accordance with the 2010 Endocrine Society Clinical Practice Guidelines (CPG) that are consistent with current VA guidelines.[1] Specifically, the OIG

[1] VA Pharmacy Benefits Management Services, Medical Advisory Panel, and Veterans Integrated Service Network Pharmacist Executives, *Testosterone Replacement Therapy (TRT) Criteria for Use* (VA Criteria for Use), February 2016. At the time of the OIG study initiation in January 2014, the current VA Criteria for Use were not yet in effect although several Veterans Integrated Service Networks had developed locally written criteria that were consistent with the Endocrine Society 2010 CPG recommendations. The OIG has included discussion of the current VA Criteria for Use as they affect current prescribing practices.

- Described new (incidence) and all (prevalence) VA male patients dispensed with outpatient testosterone in fiscal year (FY) 2014 and their baseline characteristics.
- Evaluated whether VA providers diagnosed men with hypogonadism after establishing clinical signs and symptoms consistent with androgen deficiency followed by biochemical confirmation through unequivocal low testosterone levels as well as follicle-stimulating hormone and luteinizing hormone tests, prior to hormone replacement therapy initiation.
- Determined whether VA providers documented discussion of the risks and benefits of testosterone therapy, prior to therapy initiation.
- Assessed the extent to which VA providers conducted follow-up evaluations within 3–6 months after testosterone replacement therapy initiation, with the recommended laboratory testing, documentation of improvement of symptoms, assessment of adverse effects, and adherence to therapy, prior to therapy continuation.

The OIG integrated and analyzed VA's administrative files, as well as the data file from electronic health records review of a statistical sample of patients (in order to obtain information that was not readily available in the VA administrative data), for the population of nearly 112,000 VA male patients who filled at least 1 outpatient testosterone prescription from VA in FY 2014. The OIG followed retrospectively approximately 23,000 male patients through September 30, 2015, who were initiated on testosterone replacement therapy in FY 2014, to gain insight on VA's initiation of testosterone replacement therapy and follow-up evaluations.[2]

Results and Recommendations

New (Incidence) and All (Prevalence) VA Male Patients Dispensed with Outpatient Testosterone in FY 2014 and Baseline Characteristics. The OIG determined that 111,455 male patients were prescribed testosterone, which accounted for 2.2 percent (prevalence) of all 5,181,607 VA male patients who had at least 1 outpatient clinical encounter at VA in FY 2014. This VA prevalence is similar to a non-VA study on the 2011 prevalence of testosterone replacement therapy estimated at 2.91 percent.[3] Among the 111,455 VA male patients on testosterone, 1 out of 5 (22,936/111,455) was initiated on testosterone therapy in FY 2014. The incidence of initiating testosterone therapy in male patients in FY 2014 was 1 out of 250 (22,936/5,181,607) VA male patients who had at least 1 outpatient encounter at VA in FY 2014. The average patient age (at the first outpatient testosterone prescription in FY 2014) was 58.3 and the median age was 61.

Hypogonadism Diagnosis and Etiology Prior to Testosterone Replacement Therapy Initiation. The Endocrine Society CPG (pages 2537, 2538, and 2540) and current VA Criteria for Use recommend establishing the presence of clinically significant

[2] The OIG used the most current data that were available at the time this evaluation was initiated.
[3] Baillargeon, J et al. Trends in Androgen Prescribing in the United States, 2001 to 2011, *Journal of American Medical Association* 2013; 173(15):1465-1466.

signs and symptoms of androgen deficiency prior to confirming the diagnosis of hypogonadism by measuring at least two testosterone levels, as well as follicle-stimulating hormone and luteinizing hormone levels to distinguish between primary and secondary hypogonadism prior to therapy initiation. The OIG found that VA providers did not generally establish the presence of clinical signs and symptoms consistent with androgen deficiency for any of the patients prior to performing biochemical confirmatory testosterone level tests and did not complete follicle-stimulating hormone and luteinizing hormone tests to distinguish between primary and secondary hypogonadism, prior to their testosterone replacement therapy initiation.

The Endocrine Society CPG specifically recommends against screening for androgen deficiency using testosterone tests. The OIG's assessment indicated that VA providers might have used testosterone tests to screen for, rather than to confirm, hypogonadism.

VA providers generally did not establish clinical signs and symptoms consistent with androgen deficiency prior to biochemical confirmatory testosterone level tests, and might have used testosterone tests to screen for hypogonadism. The OIG estimated that 3 out of 4 patients presented with clinical signs and symptoms of androgen deficiency and 1 out of 11 patients had two low testosterone tests in the morning to confirm low testosterone level within 1 year prior to VA providers initiating testosterone replacement therapy. However, fewer than 1 out of 50 patients had their clinical signs and symptoms of androgen deficiency established prior to their biochemical confirmatory testosterone level tests, suggesting that VA providers might have used testosterone tests to screen for, rather than to confirm, hypogonadism.

In addition, the OIG estimated that within 1 year prior to VA providers initiating testosterone replacement therapy, 61.2 percent had at least 1 testosterone test. This data further indicated that VA providers might have used testosterone tests to screen for, rather than to confirm, hypogonadism.

VA providers did not consistently perform both follicle-stimulating hormone and luteinizing hormone tests in order to distinguish between primary and secondary hypogonadism, prior to initiating testosterone replacement therapy. The OIG determined that 7 out of 50 patients had both follicle-stimulating hormone and luteinizing hormone tests in order to distinguish between primary and secondary hypogonadism, prior to VA providers initiating testosterone replacement therapy. However, VA providers had not established clinical signs and symptoms consistent with androgen deficiency for any of the patients before performing biochemical confirmatory testosterone level tests, as well as completing both follicle-stimulating hormone and luteinizing hormone tests, prior to initiating testosterone replacement therapy.

The OIG also noted that although 7 out of the 50 patients had both follicle-stimulating hormone and luteinizing hormone tests within 1 year prior to VA providers initiating testosterone replacement therapy, 9 out of 50 patients had luteinizing hormone test alone.

Discussion of Risks and Benefits of Testosterone Replacement Therapy Prior to Initiation. The Endocrine Society CPG (pages 2539 and 2551) and current VA Criteria for Use recommend discussing the risks and benefits of testosterone replacement therapy prior to initiation. The OIG determined that VA providers documented a discussion of the risks and benefits of testosterone replacement therapy with approximately 1 out of 3 patients before therapy initiation.

Follow-Up Evaluation Within 3–6 Months After Testosterone Replacement Therapy Initiation. The Endocrine Society CPG (pages 2538 and 2550) and current VA Criteria for Use recommend that providers follow up and evaluate patients within 3–6 months after starting the therapy. Recommendations include (a) evaluating improvement of androgen deficiency symptoms, (b) assessing adverse effects of therapy, and (c) monitoring hematocrit levels. Among the estimated 9,485 patients whose therapy was initiated by VA providers and who were alive at 6 months after therapy initiation and continued on the therapy, the OIG estimated that:

- Approximately 1 out of 4 patients was evaluated for symptoms improvement.
- One out of 3 patients was evaluated for adverse effects.
- Nearly 1 out of 3 patients' hematocrit levels was monitored.

The Endocrine Society CPG (pages 2538 and 2550) suggests, and current VA Criteria for Use recommend, that providers assess patients' adherence to the therapy and measure patients' testosterone level within 3–6 months after starting the therapy. Among the estimated 9,485 patients whose therapy was initiated by VA providers and who were alive at 6 months after therapy initiation and continued on the therapy, the OIG estimated that approximately 1 out of 3 patients received follow-up to evaluate adherence to the therapy. Similarly, for 1 out of 3 patients, the provider ordered testosterone testing.

Among the 12,889 patients in the study population (including therapy initiated by either VA or non-VA providers) who were alive at 6 months after therapy initiation and continued on the therapy, the OIG noted similar estimated follow-up rates, suggesting VA providers followed up with patients even though non-VA providers initiated the therapy in FY 2014.

In summary, VA providers generally did not follow Endocrine Society Clinical Practice Guidelines and current VA Criteria for Use when initiating patients on testosterone replacement therapy or follow-up patients within 3–6 months after the therapy initiation. VA providers largely did not document clinically significant signs and symptoms consistent with androgen deficiency prior to initiating therapy or prior to performing biochemical confirmatory testosterone level tests. This suggests VA providers might have used testosterone tests to screen for, rather than to confirm, hypogonadism. In addition, the OIG found that VA providers generally did not perform both follicle-stimulating hormone and luteinizing hormone tests to distinguish between primary and secondary hypogonadism prior to initiating testosterone replacement therapy. The OIG also found that VA providers did not document a discussion of the risks and benefits of testosterone replacement therapy with approximately 2 out

of 3 patients prior to the therapy initiation. After initiating testosterone replacement therapy, VA providers did not conduct follow-up evaluation within 3–6 months for about 2 out of 3 patients before continuing the therapy.

The OIG recommended that the Under Secretary for Health[4] ensure that when ordering testosterone replacement therapy, providers are in alignment with Veterans Health Administration current guidance related to the initiation and maintenance of testosterone replacement therapy including the following:

- Establish clinical signs and symptoms consistent with androgen deficiency prior to testing patients' testosterone level for confirmation
- Confirm hypogonadism biochemically through repeated testosterone testing prior to initiation of testosterone replacement therapy
- Determine whether the etiology of hypogonadism is primary or secondary prior to testosterone replacement therapy initiation
- Discuss and document risks and benefits of testosterone replacement therapy with patients prior to initiation
- Assess and document patients' symptoms improvement and adverse effects within 3–6 months of initiation before continuing testosterone replacement therapy
- Monitor patients' hematocrit levels within 3–6 months of initiation before continuing testosterone replacement therapy
- Assess patients' adherence to therapy and perform a testosterone level test within 3–6 months of initiation before continuing testosterone replacement therapy

Comments

The Executive in Charge, Office of the Under Secretary for Health, concurred with the recommendations and provided acceptable action plans. (See Appendix E, pages 29–33 for the Executive in Charge comments.) The OIG will follow up on the planned actions for the recommendations until they are completed.

JOHN D. DAIGH, JR., M.D.
Assistant Inspector General for
Healthcare Inspections

[4] Recommendations directed to the Under Secretary for Health (USH) were submitted to the Executive in Charge who has the authority to perform the functions and duties of the USH.

Purpose

The VA Office of Inspector General (OIG) conducted a study to assess the extent VA providers established androgen deficiency prior to initiating testosterone replacement therapy and performed follow-up evaluation of patients within 3–6 months of initiation prior to therapy continuation, in accordance with the Endocrine Society Clinical Practice Guidelines (CPG)[5] and current VA Pharmacy Benefits Management Services Medical Advisory Panel, and Veterans Integrated Service Network (VISN) Pharmacist Executives *Criteria for Use for Testosterone Replacement Therapy (TRT) in Adult Men* (VA Criteria for Use).[6] The objectives were:

- To describe new (incidence) and all (prevalence) VA male patients dispensed with outpatient testosterone in fiscal year (FY) 2014 and their baseline characteristics.
- To evaluate whether VA providers diagnosed men with hypogonadism after establishing clinical signs and symptoms consistent with androgen deficiency followed by biochemical confirmation through unequivocal low testosterone levels as well as follicle-stimulating hormone (FSH), and luteinizing hormone (LH) tests, prior to hormone replacement therapy initiation.
- To determine whether VA providers documented discussion of the risks and benefits of testosterone therapy, prior to therapy initiation.
- To assess the extent to which VA providers conducted follow-up evaluations within 3–6 months after testosterone replacement therapy initiation, with the recommended laboratory testing, documentation of improvement of symptoms, assessment of adverse effects, and adherence to therapy, prior to therapy continuation.

Background

Introduction. Hypogonadism (androgen deficiency) is a medical condition of lower levels of male sex hormones, particularly testosterone, than is needed for health. Testosterone hormone is produced in the testicles of men under the direction of the hypothalamus and pituitary gland located in the brain. The hormone is crucial for male

[5] Bashin, S, Cunningham, GR, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, June 2010, 95 (6): 2536-2559.
[6] VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives, *Testosterone Replacement Therapy (TRT) in Adult Men, Criteria for Use*, February 2016. At the time of OIG study initiation in January 2014, the current VA Criteria for Use for testosterone replacement therapy were not yet in effect although several Veterans Integrated Service Networks had developed locally written criteria that were consistent with the Endocrine Society 2010 CPG recommendations. The OIG included discussion of the current VA Criteria for Use as they are in alignment with the CPG recommendations and affect current prescribing practices.

sexual and reproductive function and responsible for the development of secondary sexual characteristics in men.[7]

Diagnosis of hypogonadism is made only in men with clinical signs and symptoms consistent with androgen deficiency followed by confirmation of the deficiency by low serum testosterone levels.[8] Hypogonadism is classified either as primary or secondary. Primary abnormalities occur at the testicular level while secondary abnormalities occur in the hypothalamus (part of the brain that lies below the thalamus and coordinates hunger, thirst, body temperature, and other various activities in the body) or the pituitary gland (a small oval endocrine gland located on the base of the brain that controls several other hormone-producing glands in the body). Testosterone hormonal replacement therapy is used in men meeting diagnostic and symptomatic criteria for hypogonadism.[9]

Testosterone Use and Adverse Effects. Testosterone products are classified by the U.S. Drug Enforcement Agency as Schedule III substances under the Controlled Substances Act of 1970. Under the Act, drugs are classified into five distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. Schedule III drugs have a potential for abuse, less than substances in Schedules I or II, and abuse may lead to moderate or low physical dependence or high psychological dependence. Testosterone products include injectable, topical (transdermal gel or patch), and oral (buccal) formulations. The most commonly used formulations are testosterone injection and gel.[10]

When medically indicated, testosterone products are beneficial as a hormone replacement therapy in men who are diagnosed with hypogonadism. However, prescribing for unproven indication constitutes a misuse.[11]

Low serum testosterone levels in men are common and increasingly prevalent with aging.[12] Testosterone levels are at their highest during adolescent and early adulthood. As men get older, the testosterone levels decline about 1 percent per year after the age of 30.[13] However, pharmaceutical companies have aggressively marketed testosterone medication directly to men as anti-aging wonder drugs that can treat the so called “low T” conditions, often associated with aging, such as fatigue, loss of libido (sexual desire/drive), depressed moods, decreased muscle strength, and many other

[7] Bashin, S, Cunningham, GR, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. June 2010; 95(6):2536-2559.
[8] Bashin et al, 2010.
[9] Bashin et al, 2010.
[10] VA Pharmacy Benefits Management Services, Testosterone Use FY 2011 through July 2014.
[11] The Journal of American Geriatric Society, 2015, Editorials.
[12] Walsh, T et al. Recent trends in testosterone testing, low testosterone levels, and testosterone treatment among Veterans, *Andrology*, 2015, 3, 287-292.
[13] Harman, SM et al, Longitudinal effects of aging on serum total and free testosterone levels in healthy men. *J Clin Endocrinol Metab*. 2001, 86, 724-731.

symptoms.[14] A U.S. study completed in 2013 reported that the predominant users of testosterone were men between the ages of 40 to 64 who did not have medical indication for androgen deficiency, suggesting that testosterone was being prescribed to men who were reluctant to accept common conditions associated with aging.[15]

With more than a 5-fold increase in prescriptions from 2000 to 2011 reaching a market of $1.6 billion in 2011 in testosterone usage,[16] publications reported adverse events, abuse, and dependence affecting patient safety. In 2010, the New England Journal of Medicine published the results from a clinical trial that evaluated the effect of testosterone administration in men 65 years of age or older who had limitations in mobility and low serum level of total or free testosterone. The trial was stopped before the enrollment had been completed because of significant increase in cardiac, respiratory, and dermatologic self-reported adverse events in the testosterone group than in the placebo group.[17]

In particular, the Journal of the American Medical Association published a study in 2013 that showed an association between VA patients who were on testosterone therapy and an increased risk of mortality, heart attack, or ischemic stroke.[18] In contrast, a study published by the New England Journal of Medicine in 2016 reported that cardiovascular risk of testosterone therapy was inconclusive because of its small (394 patients) sample size.[19] In 2015, the U.S. Food and Drug Administration (FDA) issued a warning to medical doctors against over-prescribing testosterone-boosting drugs for men because the popular treatments have not been established as safe or effective for common age-related issues like low libido and fatigue.[20] Additionally, in 2009, FDA issued a black box warning (visual alert of serious or life-threatening risks associated with the drug) that required labeling changes in regards to secondary exposures to women and children.[21]

[14] Sepkowitz, K. Are you man enough? Beware testosterone treatments, *Newsweek*, June 9, 2013; Perls, T, Handelsman, D. Disease mongering of age-associated declines in testosterone and growth hormone levels, *Editorial JAGS.* 2015.
[15] Gabrielsen, J et al. Trends in Testosterone Prescription and Public Health Concerns, *Urologic Clinics N Am*, 2016, (43): 261-271.
[16] Spitzer, M et al. Risks and Benefits of Testosterone Therapy in Older Men. *Nat Rev Endocrinol*. 2013; 9(7): 414-424.
[17] Basaria, S, et al. Adverse events associated with testosterone administration, *The New England Journal of Medicine*. 2010; 363(2):109-122.
[18] Vigen, R et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels, *Journal of American Medical Association*. 2013, 310 (17):1829-1836.
[19] Snyder, P.J. et al. Effects of Testosterone Treatment in Older Men. *The New England Journal of Medicine*. 2016; 374(7):611-624.
[20] FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use, March 3, 2015.
[21] FDA boxed warning on testosterone gel, September 2009.

Selected Recommendations from the Endocrine Society CPG and Current VA Criteria for Use for Management of Testosterone Therapy in Men with Androgen Deficiency Syndromes.

In June 2010, the Endocrine Society revised its CPG that replaced the version published in 2006. The CPG recommends that prior to initiating male patients on testosterone replacement therapy, clinicians perform the following:[22]

- Establish the presence of signs and symptoms consistent with hypogonadism (CPG pages 2536, 2537, and 2538)
- Confirm low testosterone level for men presenting with signs and symptoms of hypogonadism through initial measurement and repeating at least once, using a blood sample drawn in the morning (CPG pages 2537, 2538, and 2540)
- Measure levels of FSH and LH prior to the start of testosterone therapy to distinguish between primary and secondary hypogonadism (CPG page 2537)
- Discuss risks and benefits prior to initiating testosterone therapy (CPG pages 2539 and 2551)
- Follow-up and evaluate patients within 3–6 months after initiating therapy and then annually (CPG pages 2538 and 2550) to include provider evaluation of
    - Improvement on symptoms, adverse effects, and adherence
    - Testosterone level
    - Hematocrit (usually expressed as a percentage, it is the proportion, by volume, of red blood cells in the blood) level

At the time of OIG's study concept initiation in January 2014, the current VA Criteria for Use were not in effect. While VA did not have a system-wide guidance for replacement therapy in 2014, several Veterans Integrated Service Networks had developed locally written Criteria for Use adopting the Endocrine Society 2010 CPG recommendations.[23] The current VA Criteria for Use issued in February 2016,[24] endorsed the Endocrine Society CPG discussed in this report.

[22] Bashin, S, Cunningham, GR, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, June 2010, 95 (6): 2536-2559.
[23] Testosterone therapy guidelines comparison chart: Endocrine CPG/OIG/PBM/various Veterans Integrated Service Networks Criteria for Use.
[24]VA Pharmacy Benefits Management Services. *Testosterone Replacement Therapy (TRT) in Adult Men, Criteria for Use,* February 2016. Although not current at the time of the events discussed in this report, the OIG has included discussion of the current VA Criteria for Use as they affect current prescribing practices.

Scope and Methodology

The study population contained all VA male patients who filled at least one outpatient (injectable, buccal, transdermal, or topical) testosterone prescription from VA in FY 2014 and who did not have any prior prescription in FY 2013. The OIG followed the patients through September 30, 2015.

To address the study objectives, the OIG reviewed pertinent policies and guidelines on testosterone replacement therapy. The OIG also conducted a literature review on testosterone use and adverse events. OIG team members met and discussed testosterone prescribing and follow-up requirements with VA subject matter experts. Additionally, the OIG researched VA administrative data tables housed in VA Corporate Data Warehouse (CDW).

The OIG identified the study population using the administrative data centrally housed in VA CDW. The OIG then analyzed VA administrative data on outpatient chemistry laboratory test results for the study population to determine whether patients in the study population completed serum tests for testosterone hormone levels, FSH and LH tests, prior to initiation of testosterone replacement therapy.

The OIG also reviewed the electronic health record (EHR) for a random sample (1,091) of patients from the study population, in order to obtain information that was not readily available in the VA administrative data. This information included whether:

- VA or non-VA clinical providers initiated the hormonal replacement therapy in FY 2014,
- VA clinical providers documented clinical signs and symptoms consistent with androgen deficiency and the discussion of risks and benefits prior to the therapy initiation, for the VA-initiated patients, and
- VA clinical providers conducted a follow-up evaluation between 3–6 months (91–183 days) after initiating the therapy, for patients who continued on the therapy.

Study population. The OIG included all VA male patients in the study population who were initiated on testosterone replacement therapy in FY 2014. The OIG defined testosterone therapy initiation as the filling of the first outpatient testosterone prescription from a VA outpatient pharmacy or consolidated mail outpatient pharmacy in FY 2014, and no prior prescription in FY 2013.

The OIG identified the study population using the administrative data centrally housed in VA CDW. The OIG first identified Internal Entry Numbers in the VA National Drug file for testosterone products (Appendix A). The products included intramuscular testosterone injections, buccal, transdermal testosterone patches, or topical testosterone gel formulations. The OIG then searched the VA outpatient pharmacy data table (CDWWORK.Phm.RxOutpat), which contained all VA filled outpatient prescription records, to get the list of patients who filled at least one outpatient prescription of the

testosterone products in FY 2014 (based on DispensedDate). For the list of patients who filled at least one outpatient prescription of the testosterone products in FY 2014, the OIG checked each of the outpatient prescription records to determine whether the patients received any of the testosterone products in FY 2013. The OIG identified VA male patients for the study population by including all those male patients who filled at least 1 outpatient prescription of the testosterones on our list (Appendix A) in FY 2014, but did not fill any testosterone prescriptions during FY 2013.

Administrative Data and Study Variables. After the OIG identified the study population, the OIG then used the unique VA patient identifier (PatientICN) and linked the population to VA outpatient chemistry laboratory test results data (CDWWORK.CHEM.PatientLabChem) to obtain test result records for serum testosterone, FSH and LH tests, completed in FY 2013 and FY 2014, respectively.

Laboratory evaluation to determine low testosterone level. For each patient in the study population, the OIG identified if and when the patient had low serum testosterone levels repeated in the morning (prior to 12:00 p.m.) within 1 year (366 days) prior to testosterone replacement therapy initiation. The OIG defined the testosterone level as low, if the clinical laboratory reported the test result to be below the laboratory established normal reference range for usual day-to-day clinical decision-making. For example, the clinical laboratory may define the test result as low if the measured testosterone level was below 280 ng/dL (nanograms/deciliter). The OIG considered a testosterone level was low in the morning if the low test result was measured on the blood sample that was drawn prior to 12:00 p.m.

The OIG identified low testosterone test results from the morning blood samples by searching through the VA outpatient chemistry laboratory test results data for each patient in the study population. The OIG first researched Logical Observation Identifiers Names and Codes (LOINC) to identify LOINC (Appendix B) designated for total, free, free/total ratio, and bioavailable testosterone tests. LOINC was developed by the Regenstrief Institute in 1994 to provide a universal standard for identifying laboratory and clinical test results to facilitate exchange of health information across different systems.

In order to capture testosterone tests not assigned a LOINC, the OIG also searched the VA outpatient chemistry laboratory test results data using Topography of '%SERUM%' and LABCHEMTESTNAME of '%TESTO%, excluding LABCHEMTESTNAME (1) starting with %Z%, to exclude made-up test names or inactive tests, or (2) containing the word %DIHYDROTESTOSTERONE%, %FEMALE%, or %WOMEN%.

If multiple tests were completed from a same blood sample on the same day, the OIG considered the test result low if any of the test results were low. Therefore, for the same blood specimen, the OIG verified if any of the test results were low, regardless of the specimen's test time.

After identifying all low testosterone results from the morning blood samples tested in FY 2013 and FY 2014 for the study population, the OIG used the test completion date

for each patient to determine whether the test was performed prior to the therapy initiation in FY 2014.

Laboratory evaluation to determine follow-up testosterone level. Using the similar approach, the OIG determined if providers tested testosterone levels, regardless of low test levels or not, within 3–6 months (90-183 days) after initiation prior to continuing the therapy. The OIG defined a patient in the study population as continuing the therapy if the patient was alive 183 days (6 months) from initiation and had filled at least one outpatient testosterone prescription after 183 days of initiation (the first prescription date).

Laboratory evaluation to determine primary or secondary hypogonadism. For each patient in the study population, the OIG determined if and when they had any serum FSH and LH tests within 1 year prior to their testosterone treatment initiation in order to distinguish between primary (testicular) and secondary (pituitary-hypothalamic) hypogonadism.

The OIG first identified the LOINC for FSH (Appendix C) and LH tests (Appendix D). Using the LOINC, the VA outpatient chemistry laboratory test result data for each patient in the study population was then searched to determine if FSH and LH tests were conducted within 1 year prior to the therapy initiation.

To capture the FSH test results not assigned a LOINC, the OIG also searched the outpatient chemistry lab test data to include test results with Topography of '%SERUM%' and (LABCHEMTESTNAME was %FSH% or %FOLLICLE STIMULATING HORMONE%) and (LABCHEMTESTNAME not starting with %Z% or containing the word %FEMALE% or %WOMEN%). Similarly, to capture the LH test results not assigned a LOINC, the OIG also searched the outpatient chemistry lab test data to include test results with Topography of '%SERUM%' and (LABCHEMTESTNAME was %LH% or % LUTEINIZING HORMONE%) and (LABCHEMTESTNAME not starting with %Z% or containing the word %FEMALE% or %WOMEN%).

After identifying all FSH and LH results completed in FY 2013 and FY 2014 for the study population, the OIG used the test completion date for each patient to determine whether a test was performed within 1 year prior to the therapy initiation in FY 2014.

Patient demographics. To obtain patient demographics and to determine vital status as of April 8, 2015, the OIG linked the patient information data (CDWWORK.Spatient) to each patient in the study population using the unique VA patient identifier (PatientICN). The OIG excluded a patient from the study population if the patient information data indicated the patient was not a veteran or was a “test” patient. Information about a patient who is not an actual patient (a “test” patient) might be entered into VA administrative data for training/testing purposes.

When the patient information data delivered more than one date of birth for a patient, the OIG first deleted the date of birth that resulted in age under 18 on October 1, 2013. The OIG then took the most recent date of birth to resolve conflicting patient information. For example, if the patient information data showed three dates of birth for

a patient as June 1, 1945, June 1, 1954, and July 15, 2004, the OIG would first delete the birth date of July 15, 2004 (because the age was under 18 as of October 1, 2013) and then selected June 1, 1954 as the patient's date of birth (because June 1, 1954 was more recent than June 1, 1945).

When the patient information data provided a patient more than one date of death, the OIG took the most recent date of death to resolve conflicting patient information. If a patient's date of death was earlier than the first testosterone prescription date (DispensedDate) in FY 2014, the OIG excluded the patient from the study population.

EHR Review of Sampled Patients. In addition to VA clinical providers, non-VA clinical providers might also initiate testosterone replacement therapy. Information on whether VA or non-VA providers initiated the therapy was not readily available in the VA administrative data. The OIG randomly sampled 1,091 patients from the study population for EHR review. The OIG reviewed sampled patients' EHRs to determine whether VA or non-VA clinical providers initiated the testosterone replacement therapy in FY 2014.

For VA-initiated patients, the OIG examined EHRs to determine whether VA clinical providers established clinical signs and symptoms consistent with androgen deficiency and discussed risks and benefits prior to the therapy initiation. The OIG considered that providers established clinical signs and symptoms or discussed risks and benefits if such documentation was found in EHR. Because the signs and symptoms of androgen deficiency are non-specific, it is not uncommon that one or a number of signs or symptoms are mentioned in progress notes unrelated to hypogonadism. Because the OIG did not determine whether documented signs or symptoms were linked to a note that also mentioned testosterone deficiency during the EHR review, the OIG findings of documented signs or symptoms of hypogonadism are over estimated. The OIG's over estimation of documentation does not impact other findings discussed in this report.

For documentation of signs and symptoms of androgen deficiency, the OIG reviewed providers' progress notes back to 18 months from the date of initial prescription in FY 2014. The OIG chose 18 months to allow for providers to establish signs and symptoms prior to testing serum testosterone level (1 year prior to initiation of the therapy) for confirmation of androgen deficiency, because a testosterone test should not be used to screen for hypogonadism (CPG page 2537). For discussion of risks and benefits, the OIG reviewed progress notes within 3 months prior to initiation of therapy.

For patients who continued on the therapy—those alive 183 days (6 months) from initiation and who had filled at least one outpatient testosterone prescription after 183 days of initiation (the first prescription date)—the OIG examined whether providers conducted a follow-up evaluation, either in-person or telephone, between 3–6 months (91–183 days) after initiating the therapy.

The OIG reviewed follow-up evaluations to determine whether providers documented symptoms improvement, adverse effects assessment, medication adherence, and hematocrit levels assessment.

EHR review for obtaining patient information relevant to testosterone replacement therapy initiation. For VA initiated sampled patients, the OIG examined whether providers established clinical signs and symptoms of androgen deficiency (hypogonadism) by documenting in the EHRs at least one of the signs and symptoms listed in Table 1. The OIG reviewed progress notes back to 18 months from the date of initial prescription in FY 2014.

Table 1. Signs and Symptoms To Support Hypogonadism

Incomplete or delayed sexual development
Reduced sexual desire (libido) and activity
Decreased spontaneous erections
Breast discomfort, gynecomastia (enlarged breast in men)
Loss of body hair (axillary and pubic), reduced shaving
Very small (<5ml) or shrinking testes
Increased body fat, body mass index
Height loss, low trauma fracture, low bone mineral density
Hot flushes, sweats
Decreased energy, motivation, initiative, and self-confidence
Feeling sad or blue, depressed mood, dysthymia (persistent depressive disorder)
Diminished physical or work performance
Sleep disturbance, increased sleepiness
Mild anemia (lower than normal red blood cells or hemoglobin)
Reduced muscle bulk and strength
Poor concentration and memory

Source: The Endocrine Society CPG[25]

In addition, the OIG reviewed EHRs to determine whether providers documented discussion of the risks and benefits of the therapy prior to initiation.

EHR review for obtaining patient information relevant to follow-up evaluation. For all sampled patients, whether VA or non-VA initiated, the OIG reviewed providers' documentation of follow-up evaluation for symptoms improvement, adverse effects assessment, medication adherence, and hematocrit levels assessment within 3–6 months (91–183 days) after initiation of the therapy as recommended by the Endocrine Society CPG and current VA Criteria for Use.

[25] Bashin, S, Cunningham, GR, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, June 2010, 95 (6): 2536-2559.

For follow-up evaluation of symptoms improvement, the OIG considered a provider performed the assessment if any provider progress notes were found that indicated symptom improvement, either negative or positive, related to the replacement therapy, within 3–6 months after the therapy initiation.

For adverse effects assessment, the OIG considered a provider conducted the assessment if any progress notes were found that were related to providers' review of body systems within 3–6 months after the therapy initiation. If a provider noted any adverse effect, the OIG examined further whether providers documented any of the adverse effects listed in Table 2.

Table 2. Adverse Effects of Testosterone Replacement Therapy from Review of Body Systems and Testosterone Products

From Review of Body Systems
Cardiovascular: deep vein thrombosis, edema, hypertension, vasodilation
Central Nervous: abnormal dreams, aggressive behavior, anger, anxiety, amnesia, chills
Gastrointestinal: appetite increase, reflux, taste disorder
Skin: acne, alopecia, rash, dry skin, hirsutism
Genitourinary: bladder irritability, increased prostate specific antigen, impaired urination
Endocrine: breast pain/soreness, gynecomastia, hot flashes
Hematologic: anemia, increased hemoglobin/hematocrit, leukopenia, polycythemia
From Testosterone Products
Injection: fluctuation in mood or libido, cough (rare)
Patches: skin irritation
Gel: secondary exposure
Pellets: infection, fibrosis

Source: The Endocrine Society CPG[26]

For medication adherence, the OIG examined whether a provider documented patient compliance such as adherence to dosage regimens and missed dosages. If any progress note was found that indicated patient compliance or non-compliance within 3–6 months after testosterone therapy initiation, the OIG considered that the provider followed up with patients on medication adherence.

[26] Bashin, S, Cunningham, GR, et al. Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, June 2010, 95 (6): 2536-2559.

For monitoring hematocrit levels, the OIG considered that a provider monitored hematocrit levels if a hematocrit level was found in the patient's EHR laboratory section within 3–6 months after the testosterone therapy initiation. However, if the hematocrit value was greater than 54 percent (normal range for men is 38.8 to 50 percent), the OIG checked whether a provider documented relevant actions or interventions; and if the documentation was not found, the OIG considered that hematocrit levels were not monitored.

Statistical Analyses. The OIG performed descriptive data analyses for VA as a whole. Because non-VA clinical providers might also initiate testosterone therapy, and this information was not readily available in the administrative data, the OIG estimated VA-initiated proportion based on our sampled data to derive our study population of male patients who were initiated testosterone therapy by VA providers in FY 2014 and estimated compliance with selected measures in male patients initiated on testosterone replacement therapy by VA providers.

When calculating the proportion (incidence) of VA male patients who were initiated on testosterone replacement therapy in FY 2014, the OIG used the number of men who received at least one episode of outpatient care at a VA health care facility in FY 2014 as the denominator. The OIG used the same denominator for calculating the proportion (prevalence) of VA male patients who were on testosterone replacement therapy in FY 2014.

The OIG performed data analyses using SAS statistical software (SAS Institute, Inc., Cary, NC), version 9.4 (TS1M2).

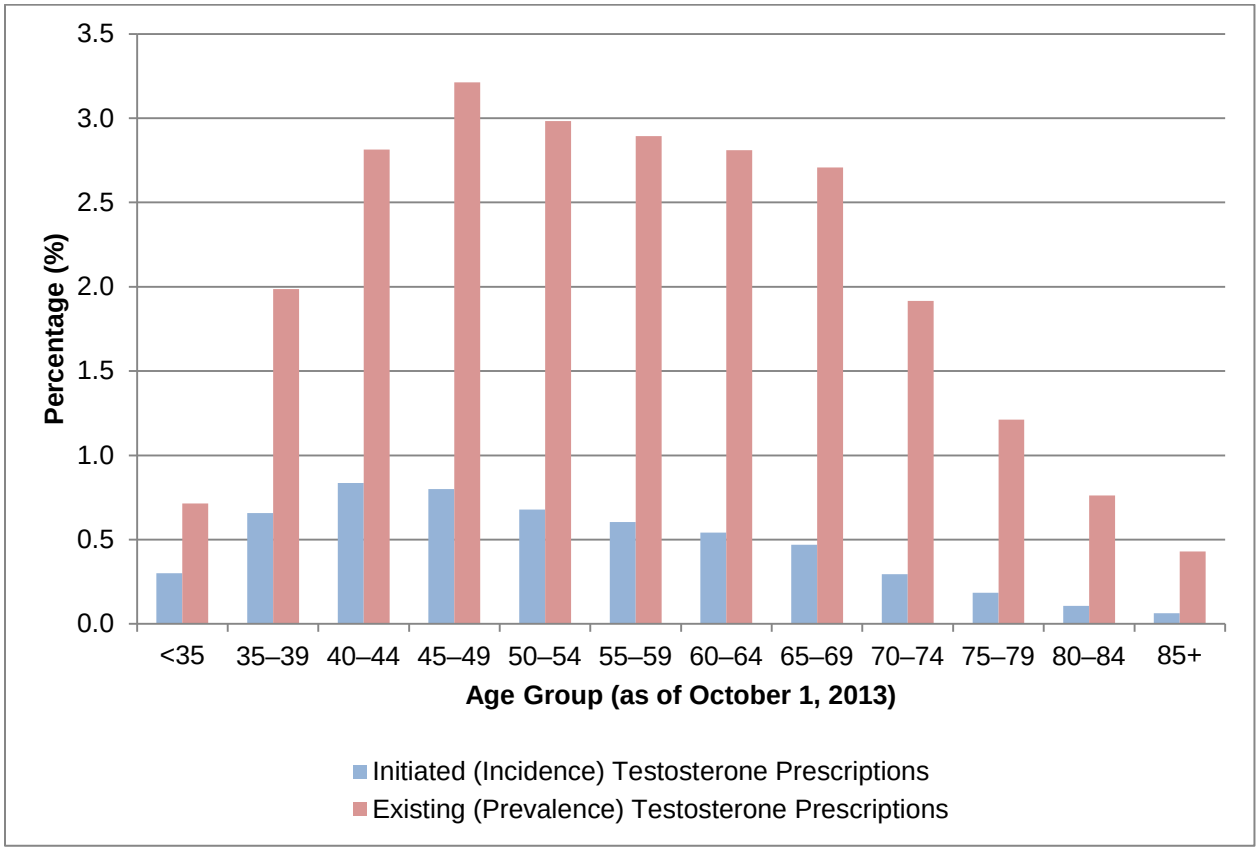
The study was performed in accordance with *Quality Standards for Inspection and Evaluation* published by the Council of the Inspectors General on Integrity and Efficiency.

Results

1. New (Incidence) and Existing (Prevalence) VA Male Patients Prescribed Testosterone

The incidence of initiating testosterone therapy in male patients in FY 2014 was 1 out of 250 (22,936/5,181,607) VA male patients who had at least 1 outpatient encounter at VA in FY 2014. The OIG determined that 111,455 male patients were prescribed testosterone, which accounted for 2.2 percent (prevalence) of all 5,181,607 VA male patients who had at least 1 outpatient clinical encounter at VA in FY 2014. Among the 111,455 male patients on testosterone, 1 out of 5 (22,936/111,455) was initiated on testosterone therapy in FY 2014. The Figure shows the detailed incidence and prevalence of testosterone prescriptions distributions by age in VA male patients in FY 2014.

Figure. New (Incidence) and Existing (Prevalence) VA Male Patients with Testosterone Prescriptions in Fiscal Year 2014 by Age Group



Source: OIG analysis of VA administrative data (FY14AgeDistro)

Because non-VA clinical providers might also initiate testosterone therapy, and this information was not readily available in the administrative data, the OIG reviewed the EHRs of 1,091 patients, randomly sampled from the 22,936 patients who were initiated testosterone therapy in FY 2014, to determine whether a VA or a non-VA provider

initiated the therapy. The OIG estimated (Table 3) that VA providers initiated 3 out of 4 (827/1091) or 75.8 percent of the sampled patient's therapy, non-VA providers initiated 23.6 percent (257/1091). Additionally, 0.6 percent (7/1091) of the sampled patients were started on the therapy prior to FY 2014 (by injection using clinic stock) or initiated while an inpatient in FY 2014.

Table 3. VA and Non-VA Providers Initiation of Testosterone Replacement Therapy in Fiscal Year 2014 in the 1,091 Sampled Patients

	Number of Patients	Percent
VA Initiated	827	75.8
Non-VA Initiated	257	23.6
Other	7	0.6
Inpatient	1	0.1
Injection using Clinic Stock	6	0.5

Source: OIG analysis of sampled patients' EHR review data (FY14TestCompl)

The OIG estimated that VA providers initiated the therapy to 17,386 (75.8 percent) of the 22,936 patients in FY 2014, and was 95 percent confident that the true number of patients initiated by VA providers was somewhere from 16,844 and 17,928. (See also Table 5.)

2. Baseline Characteristics of VA Patients Initiated With Testosterone Replacement Therapy

Table 4 shows the baseline characteristics of the study population, combined and separately by whether sampled for EHR review or not. The average patient age (at the first outpatient testosterone prescription in FY 2014) of the study was 58.3. The median age was 61, meaning half of the patients were under 61 and half were above 61 when dispensed with the first outpatient testosterone prescription in FY 2014. The OIG noted that the age distribution of sampled patients was similar to non-sampled patients.

Table 4. Baseline Characteristics of VA Testosterone Patients in Fiscal Year 2014

	Overall		Sampled for EHR Review		Not Sampled	
	22,936		1,091	4.8%	21,845	95.2%
Age at First Testosterone Prescription in FY 2014						
Mean (standard deviation)	57.8	(12.6)	58.0	(12.7)	57.8	(12.6)
Median	60		61		60	
Distribution	**Number of Patients**	**Percent**	**Number of Patients**	**Percent**	**Number of Patients**	**Percent**
<35	1,254	5.5	61	5.6	1,193	5.5
35–44	2,569	11.2	123	11.3	2,446	11.2
45–54	4,445	19.4	190	17.4	4,255	19.5
55–64	6,618	28.9	320	29.3	6,298	28.8
65–74	6,552	28.6	329	30.2	6,223	28.5
75–84	1,234	5.4	53	4.9	1,181	5.4
85+	264	1.2	15	1.4	249	1.1
Died (death recorded as of April 8, 2015)	223	1.0	7	0.6	216	1.0

Source: OIG analysis of sampled patients' EHR review data (FY14Baseline)

The OIG found that 1 percent of the patients died as of April 8, 2015, the date that every patient in the study population had at least 6 months from therapy initiation (that is, first outpatient testosterone prescription) in FY 2014.

3. Androgen Deficiency Confirmation and Discussion of Risks and Benefits Prior to Testosterone Replacement Therapy Initiation

Prior to initiation of testosterone replacement therapy, the Endocrine Society CPG (pg. 2537, 2538, 2540) and current VA Criteria for Use recommend establishing the presence of clinically significant signs and symptoms of androgen deficiency prior to confirming the diagnosis of hypogonadism through measuring testosterone level repeated at least once, measuring of FSH and LH to distinguish between primary and secondary hypogonadism, and discussing the risks and benefits of testosterone replacement therapy with the patient.

Among the 22,936 patients whose testosterone therapy was initiated in FY 2014, the OIG estimated that VA providers initiated 17,386 (75.8 percent) of the 22,936 patients testosterone therapy, and is 95 percent confident that the true number of patients initiated by VA providers were somewhere from 16,844 to 17,928 (Table 5).

Table 5. Percent (95 percent Confidence Interval) of Male Patients Receiving Confirmatory Androgen Deficiency Diagnosis and Discussion of Risks and Benefits Prior to Testosterone Replacement Therapy Initiation in Fiscal Year 2014

	VA-initiated in the Sampled 827 Patients	Estimated VA-initiated Patients in the Study Population 17,386 with 95 Percent CI (16,844, 17,928) VA Estimates Percent (95 percent CI)
Diagnosed Hypogonadism through A prior to B and C	0	
A. Documented clinical signs and symptoms consistent with androgen deficiency within 18 months prior to testosterone replacement therapy initiation	631	76.3 (73.35, 79.02) [27]
B. Repeated testosterone test in the morning, after the initial low level test result, to confirm low testosterone level within one year prior to testosterone replacement therapy initiation	75	9.1 (7.33, 11.17)
Performed A prior to B	12	1.5 (0.84, 2.51)
C. Conducted FSH and LH tests to determine whether the etiology of hypogonadism is primary or secondary, prior to testosterone replacement therapy initiation	120	14.5 (12.32, 17.02)
Documented Discussion of the Risks and Benefits	269	32.5 (29.49, 35.72)

Source: OIG analysis of sampled patients' EHR review data (FY14TestCompl, FY14TTBefSS)

Based on the EHR review of the sampled patients (Table 5), the OIG estimated that 3 out of 4 patients (76.3 percent; the OIG is 95 percent confident that the true rate is somewhere between 73.35 to 79.02 percent) had documentation of clinical signs and symptoms of androgen deficiency and 1 out of 11 patients (9.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 7.33 to 11.17 percent) had two testosterone tests to confirm low testosterone level in the morning within 1 year prior to their testosterone replacement therapy initiation by VA providers. However, fewer than 1 out of 50 patients (1.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 0.84 to 2.51 percent) had their clinical signs and symptoms of androgen deficiency established prior to their biochemical confirmatory testosterone level tests, suggesting that VA providers may have used testosterone tests to screen for androgen deficiency.

[27] Because the OIG did not determine whether documented signs or symptoms were linked to a note that also mentioned testosterone deficiency during the EHR review, the OIG findings of documented signs or symptoms of hypogonadism are over estimated. The OIG's over estimation of documentation does not impact other findings discussed in this report.

The OIG determined that VA providers documented a discussion of the risks and benefits of testosterone replacement therapy with approximately 1 out of 3 patients (32.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 29.49 to 35.72 percent) prior to initiating therapy.

The Endocrine Society CPG (page 2537) recommends against screening for androgen deficiency;[28] the current VA Criteria for Use did not address this issue. Although fewer than 2 out of 100 patients (1.5 percent) had their clinical signs and symptoms of androgen deficiency established prior to their biochemical confirmatory testosterone level tests (Table 5), the OIG estimated that within 1 year prior to their testosterone replacement therapy initiation by VA providers (Table 6):

- 9.1 (the OIG is 95 percent confident that the true rate is somewhere between 7.33 to 11.17) percent had two testosterone tests to confirm low testosterone level in the morning,
- 12.8 (the OIG is 95 percent confident that the true rate is somewhere between 10.75 to 15.21) percent had at least two testosterone tests,
- 46.9 (the OIG is 95 percent confident that the true rate is somewhere between 43.61 to 50.25) percent had at least one testosterone test in the morning, and
- 61.2 (the OIG is 95 percent confident that the true rate is somewhere between 57.89 to 64.37) percent had at least one testosterone test.

The above data further suggested that VA providers might have used testosterone tests to screen, rather than to confirm, for androgen deficiency.

[28] A screening test is done to detect potential health disorders or diseases in people who do not have any symptoms of disease. *Johns Hopkins Medicine Health Library*. Accessed March 26, 2018. The Endocrine Society CPG recommends against screening for androgen deficiency in the general population. The CPG recommends making a diagnosis of androgen deficiency only in men with consistent symptoms and signs and unequivocally low serum testosterone levels.

Table 6. Percent (95 percent Confidence Interval) of Male Patients Receiving Testosterone Level and Follicle-Stimulating Hormone and Luteinizing Hormone Tests Prior to Testosterone Replacement Therapy Initiation in Fiscal Year 2014

	Study Population 22,936		Estimated VA-initiated Patients in the Study Population 17,386 (16,844, 17,928)
	Number	Percent	Estimate (95 Percent CI)
B. Performed at least two testosterone tests in the morning to confirm low testosterone level within one year prior to testosterone therapy initiation	2,010	8.8	9.1 (7.33, 11.17)
Performed at least two testosterone tests within one year prior to testosterone therapy initiation	2,984	13.0	12.8 (10.75, 15.21)
Performed at least one testosterone test in the morning within one year prior to testosterone therapy initiation	9,348	40.8	46.9 (43.61, 50.25)
Performed at least one testosterone test within one year prior to testosterone therapy initiation	12,248	53.4	61.2 (57.89, 64.37)
C. Conducted both FSH and LH tests to evaluate whether the etiology of hypogonadism is primary or secondary within one year prior to testosterone therapy initiation	2,763	12.0	14.5 (12.32, 17.02)
Conducted FSH test to evaluate whether the etiology of hypogonadism is primary or secondary, within one year prior to testosterone therapy initiation	4,935	21.5	25.0 (22.26, 28.03)
Conducted LH tests to evaluate whether the etiology of hypogonadism is primary or secondary within one year prior to testosterone therapy initiation	3,340	14.6	18.0 (15.60, 20.72)
Completed both B and C	693	3.0	1.9 (1.20, 3.10)

Source: OIG analysis of VA administrative data (FY14TestCompl)

The OIG determined (Table 6) that 7 out of 50 patients (14.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 12.32 to 17.02 percent) had both FSH and LH tests in order to distinguish between primary and secondary hypogonadism prior to their testosterone replacement therapy initiation by VA providers. The OIG found that VA providers generally did not establish clinical signs and symptoms consistent with androgen deficiency prior to biochemical confirmatory testosterone level tests, and might have used testosterone tests to screen for hypogonadism.

The OIG also noted (Table 6) that although 7 out of the 50 (14.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 12.32 to 17.02 percent) patients had both FSH and LH tests within 1 year prior to initiation of testosterone replacement therapy by VA providers, the OIG estimated that 1 out of 4 (25.0 percent;

the OIG is 95 percent confident that the true rate is somewhere between 22.26 to 28.03 percent) had a FSH test alone. The OIG also estimated that 9 out of 50 (18.0 percent; the OIG is 95 percent confident that the true rate is somewhere between 15.60 to 20.72 percent) of patients had an LH test alone.

Among the study population (including both patients initiated by VA and non-VA providers), the OIG noted lower test rates than the corresponding rates of those patients whose testosterone replacement therapy was initiated solely by VA providers in FY 2014, except for the similar rates in performing:

- At least two morning testosterone tests to confirm low testosterone level,
- At least two testosterone tests, regardless of timing, and
- Two morning testosterone tests to confirm low testosterone, as well as both FSH and LH tests.

4. Follow-Up Evaluation of Patients After Testosterone Replacement Therapy Initiation

The OIG estimated (Table 7) that 9,485 patients in the study population whose therapy was initiated by VA providers were alive at 6 months after therapy initiation and continued on the therapy, and is 95 percent confident the true number was somewhere between 9,077 and 9,894.

The Endocrine Society CPG (pages 2538 and 2550) and current VA Criteria for Use recommend that providers follow up and evaluate patients within 3–6 months after starting therapy. Recommendations include: (a) evaluating improvement of androgen deficiency symptoms, (b) assessing adverse effects of therapy, and (c) monitoring hematocrit levels. The OIG estimated (Table 7) that within 3–6 months after therapy initiation, VA providers evaluated approximately:

- 1 out of 4 patients (24.0 percent; the OIG is 95 percent confident that the true rate is somewhere between 20.43 to 27.96 percent) for symptoms improvement,
- 1 out of 3 (33.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 29.11 to 37.40 percent) for adverse effects,
- 1 out of 3 (30.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 26.26 to 34.35 percent) for hematocrit levels,
- 1 out 3 patients (29.3 percent; the OIG is 95 percent confident that the true adherence rate is somewhere between 25.44 to 33.47 percent) for adherence to the therapy, and
- 1 out of 3 patients (35.7 percent; the OIG is 95 percent confident that the true test rate is somewhere between 31.56 to 40.00 percent) for testosterone testing.

Table 7. Percent (95 percent confidence interval) of Male Patients Receiving Follow-Up Evaluation Within 3–6 Months (91-183 days) After Testosterone Replacement Therapy Initiation, Among Those Who Were Alive at 6 Months After Therapy Initiation and Continued on the Therapy

	Study Population (VA or non-VA providers initiated the therapy) 12,889	Study Population (VA or non-VA providers initiated the therapy) 12,889		Estimated VA-initiated Patients in the Study Population 9,485 with 95 percent CI (9,077, 9,894)	
		Sampled Patient Number 640	VA Estimates Percent (95 percent CI)	Sampled Patient Number 471	VA Estimates Percent (95 percent CI)
Documented clinical symptoms improvement		132	20.6 (17.73, 23.86)	113	24.0 (20.43, 27.96)
Assessed adverse effects		199	31.1 (27.70, 34.70)	156	33.1 (29.11, 37.40)
Monitored hematocrit level		177	27.6 (24.40, 31.12)	142	30.1 (26.26, 34.35)
Evaluated adherence to therapy		168	26.3 (23.06, 29.72)	138	29.3 (25.44, 33.47)
Performed testosterone test	4,299 (33.4%)	206	32.2 (28.76, 35.82)	168	35.7 (31.56, 40.00)

Source: OIG analysis of sampled patients' EHR review data and VA administrative data (FY14TestCompl)

Among the 12,889 patients in the study population (including therapy initiated by either VA or non-VA providers) who were alive at 6 months after therapy initiation and continued on the therapy, the OIG noted (Table 7) similar estimated follow-up rates, suggesting VA providers followed up with patients even though non-VA providers initiated the therapy in FY 2014.

Conclusions

The OIG integrated and analyzed VA's administrative files, as well as the data file from reviewing EHRs of a statistical sample of patients (in order to obtain information that was not readily available in the VA administrative data), for the population of nearly 112,000 VA male patients who filled at least 1 outpatient testosterone prescription from VA in FY 2014. The OIG followed retrospectively approximately 23,000 male patients through September 30, 2015, who were initiated testosterone replacement therapy in FY 2014, to gain insight on the provision of VA testosterone therapy initiation and follow-up.

In this population-based study, the OIG determined that 111,455 male patients were on outpatient testosterone prescription, which accounted for 2.2 percent (prevalence) of all 5,181,607 VA male patients who had at least 1 outpatient clinical encounter at VA in FY 2014. Among the 111,455 male patients on testosterone, 1 out of 5 (22,936/111,455) was initiated on testosterone therapy in FY 2014. The incidence of initiating testosterone therapy in male patients in FY 2014 was 1 out of 250 (22,936/5,181,607) VA male patients who had at least 1 outpatient encounter at VA in FY 2014. The average patient age (at the first outpatient testosterone prescription in FY 2014) was 58.3 and the median age was 61.

Prior to initiation of testosterone replacement therapy, the Endocrine Society CPG (pages 2537, 2538, and 2540) and current VA Criteria for Use recommend establishing clinical signs and symptoms consistent with androgen deficiency prior to biochemical tests through confirmatory testosterone level tests, and measuring both FSH and LH levels to distinguish between primary and secondary hypogonadism. The OIG found that VA providers generally did not document clinical signs and symptoms consistent with androgen deficiency prior to biochemical confirmatory testosterone level tests, and might have used testosterone tests to screen for hypogonadism. The OIG also found that VA providers did not consistently perform both FSH and LH tests to determine whether the etiology of hypogonadism is primary or secondary, prior to testosterone replacement therapy initiation.

OIG's assessment suggests that VA providers might have used testosterone tests to screen for, rather than to confirm, hypogonadism, even though the CPG specifically recommends against using testosterone tests to screen for hypogonadism. Current VA Criteria for Use does not address this issue. The OIG estimated that 3 out of 4 patients (76.3 percent; the OIG is 95 percent confident that the true rate is somewhere between 73.35 to 79.02 percent) whose EHRs included documentation of clinical signs and symptoms of androgen deficiency and 1 out of 11 patients (9.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 7.33 to 11.17 percent) had two testosterone tests to confirm low testosterone level in the morning within 1 year prior to their testosterone replacement therapy initiation by VA providers. However, fewer than 1 out of 50 patients (1.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 0.84 to 2.51 percent) had their clinical signs and symptoms of androgen deficiency established prior to their biochemical confirmatory testosterone level tests, suggesting that VA providers might have used testosterone tests to screen for hypogonadism.

In addition, the OIG estimated that within 1 year prior to their testosterone replacement therapy initiation by VA providers:

- 9.1 (the OIG is 95 percent confident that the true rate is somewhere between 7.33 to 11.17) percent had two morning testosterone tests to confirm low testosterone level,
- 12.8 (the OIG is 95 percent confident that the true rate is somewhere between 10.75 to 15.21) percent had at least two testosterone tests, regardless of timing,

- 46.9 (the OIG is 95 percent confident that the true rate is somewhere between 43.61 to 50.25) percent had at least one morning testosterone test, and
- 61.2 (the OIG is 95 percent confident that the true rate is somewhere between 57.89 to 64.37) percent had at least one testosterone test, regardless of timing.

The above data further indicated that VA providers might have used testosterone tests to screen, rather than to confirm, for hypogonadism.

The OIG also found that VA providers did not consistently perform both FSH and LH tests to determine whether the etiology of hypogonadism is primary and secondary prior to their testosterone replacement therapy initiation. The OIG determined that 7 out of 50 patients (14.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 12.32 to 17.02 percent) had both FSH and LH tests, prior to their testosterone replacement therapy initiation by VA providers. The OIG found that VA providers had not established clinical signs and symptoms consistent with androgen deficiency for any of the patients prior to performing biochemical confirmatory testosterone level tests. The OIG also found that VA providers did not consistently perform both FSH and LH tests to determine whether the etiology of hypogonadism is primary and secondary, prior to testosterone replacement therapy initiation.

Prior to initiation of testosterone replacement therapy, the Endocrine Society CPG (pages 2539 and 2551) and current VA Criteria for Use recommend discussing the risks and benefits of testosterone replacement therapy. The OIG determined that VA providers documented the discussion of the risks and benefits of testosterone replacement therapy with approximately 1 out of 3 patients (32.5 percent; the OIG is 95 percent confident that the true rate is somewhere between 29.49 to 35.72 percent) before therapy initiation.

The Endocrine Society CPG (pages 2538 and 2550) and current VA Criteria for Use recommend that providers follow up and evaluate patients within 3–6 months after starting the therapy. Recommendations include (a) evaluating improvement of androgen deficiency symptoms, (b) assessing adverse effects of therapy, and (c) monitoring hematocrit levels. Among the estimated 9,485 patients whose therapy were initiated by VA providers and who were alive at 6 months after therapy initiation and continued on the therapy, the OIG estimated that approximately 1 out of 4 patients (24.0 percent; the OIG is 95 percent confident that the true rate is somewhere between 20.43 to 27.96 percent), 1 out 3 (33.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 29.11 to 37.40 percent), and nearly 1 out of 3 (30.1 percent; the OIG is 95 percent confident that the true rate is somewhere between 26.26 to 34.35 percent) received recommended follow-up evaluation on symptoms improvement, adverse effects, and hematocrit level, respectively, within 3–6 months after VA providers started the therapy.

The Endocrine Society CPG (pages 2538 and 2550) suggests and current VA Criteria for Use recommends that providers assess patients' adherence to the therapy and measure patients' testosterone level within 3–6 months after starting the therapy. Among the estimated 9,485 patients whose therapy were initiated by VA providers and

who were alive at 6 months after therapy initiation and continued on the therapy, the OIG estimated that approximately 1 out of 3 patients obtained follow-up on adherence to the therapy (29.3 percent; the OIG is 95 percent confident that the true rate is somewhere from 25.44 to 33.47 percent) and testosterone level (35.7 percent; the OIG is 95 percent confident that the true rate is somewhere from 31.56 to 40.00 percent), within 3–6 months after VA providers started the therapy. Among the 12,889 patients in the study population (including therapy initiated by either VA or non-VA providers) who were alive at 6 months after therapy initiation and continued on the therapy, the OIG noted similar estimated follow-up rates, suggesting VA providers followed up with patients even though non-VA providers initiated the therapy in FY 2014.

The OIG concluded that VA providers generally did not follow up with patients 3–6 months after initiating testosterone replacement therapy, in accordance with the Endocrine Society CPG and the current VA Criteria for Use recommendations. VA providers generally did not establish clinical signs and symptoms consistent with androgen deficiency prior to initiating therapy or prior to biochemical confirmatory testosterone level tests, and might have used testosterone tests to screen for hypogonadism. In addition, the OIG found that VA providers did not consistently perform both FSH and LH tests to determine whether the etiology of hypogonadism was primary and secondary hypogonadism, prior to testosterone replacement therapy initiation.

The OIG also found that VA providers did not document the discussion of the risks and benefits of testosterone replacement therapy with approximately 2 out of 3 patients prior to the therapy initiation. After testosterone replacement therapy initiation, VA providers did not conduct follow-up evaluation within 3–6 months for about 2 out of 3 patients before continuing the therapy.

The OIG findings are consistent with those reported in a non-VA study published in 2015 with regard to poor adherence to recommendation of two or more testosterone levels and LH and FSH levels.[29]

The OIG made seven recommendations.

Recommendations

1. The Under Secretary for Health ensures that providers establish clinical signs and symptoms, consistent with androgen deficiency, prior to testing patients' testosterone level for confirmation in alignment with Veterans Health Administration guidance.

2. The Under Secretary for Health ensures that providers biochemically confirm hypogonadism through repeated testosterone testing prior to initiation of testosterone replacement therapy in alignment with Veterans Health Administration guidance.

[29] Muram, D et al. Use of Hormone Testing for the Diagnosis and Evaluation of Male Hypogonadism and Monitoring of Testosterone Therapy: Application of Hormone Testing Guideline Recommendations in Clinical Practice, *J Sex Med*. 2015: 12:1886-1894.

3. The Under Secretary for Health ensures that providers determine whether the etiology of hypogonadism is primary or secondary, prior to testosterone replacement therapy initiation in alignment with Veterans Health Administration guidance.

4. The Under Secretary for Health ensures that providers discuss and document the risks and benefits of testosterone therapy with patients prior to initiation in alignment with Veterans Health Administration guidance.

5. The Under Secretary for Health ensures that providers assess and document patients' symptoms improvement and adverse effects within 3–6 months of initiation before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

6. The Under Secretary for Health ensures that providers monitor patients' hematocrit levels within 3–6 months of initiation, before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

7. The Under Secretary for Health ensures that providers assess and document patients' adherence to therapy and perform testosterone level test within 3–6 months of initiation, before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

Appendix A

National Drug Internal Entry Numbers (IEN) for Testosterone Prescriptions

IEN	DRUG NAME
00513	TESTOSTERONE ENANTHATE 200MG/ML INJ (IN OIL)
00515	TESTOSTERONE CYPIONATE 100MG/ML INJ (IN OIL)
00516	TESTOSTERONE CYPIONATE 200MG/ML INJ (IN OIL)
00524	TESTOSTERONE 75MG PELLET
00530	TESTOSTERONE 4MG/24HRS PATCH
00532	TESTOSTERONE 2.5MG/24HRS PATCH
14775	TESTOSTERONE CYPIONATE 200MG/ML INJ,1ML (IN OIL)
15508	TESTOSTERONE (ANDRODERM) 5MG/24HRS PATCH
16544	TESTOSTERONE 30MG PATCH,SA,BUCCAL
17475	TESTOSTERONE PROPIONATE 2% OINT,TOP
17901	TESTOSTERONE 2% CREAM,TOP
21468	TESTOSTERONE (ANDROGEL) 1% 5GM/PKT GEL,TOP
21470	TESTOSTERONE (TESTIM) 1% 5GM/PKT GEL,TOP
21471	TESTOSTERONE (ANDROGEL) 1% 2.5GM/PKT GEL,TOP
22219	TESTOSTERONE 10MG/PUMP GEL,TOP
22384	TESTOSTERONE 30MG/PUMP SOLN,TOP
22523	TESTOSTERONE 1.62% 20.25MG/PUMP GEL,TOP
22526	TESTOSTERONE 1% 12.5MG/PUMP GEL,TOP
22791	TESTOSTERONE 2MG/24HRS PATCH
24417	TESTOSTERONE (ANDROGEL) 1.62% 1.25GM/PKT GEL,TOP
24551	TESTOSTERONE (ANDROGEL) 1.62% 2.5GM/PKT GEL,TOP
24578	TESTOSTERONE UNDECANOATE 250MG/ML INJ,SOLN,3ML

Source: OIG analysis of VA administrative data

Appendix B

Logical Observation Identifiers Names and Codes (LOINC) Laboratory Codes and LABCHEMTESTNAME for Testosterone Level Tests

LOINC	TOPOGRAPHY	LABCHEMTESTNAME
14914-6	SERUM	FREE TESTOSTERONE
15432-8	SERUM	FREE TESTOSTERONE
1639-4	SERUM	TESTOSTERONE (LABCORP)
25986-1	SERUM	TESTOSTERONE, FREE
25987-9	SERUM	ZZFREE TESTOSTERONE
27057-9	SERUM	TESTOSTERONE FREE(PERCENT)
2986-8	Plasma/Serum	TOTAL TESTOSTERONE
2990-0	SERUM	Free Testosterone
2991-8	SERUM	FREE TESTOSTERONE
2993-4	SERUM	TESTOSTERONE -8/7/14
2994-2	SERUM	TESTOSTERONE TOTAL LC/MS/MS(QUEST)
30123-4	Plasma/Serum	TOTAL TESTOSTERONE-IU
35224-5	SERUM	ZZTESTOSTERONE, TOTAL (LC/MS/MS)
35225-2	SERUM	TESTOSTERONE, FREE (QUEST)
6891-6	SERUM	% FREE+WEAKLY BOUND TESTOSTERONE
Missing	SERUM	BIOAVAILABLE TESTOSTERONE
Missing	SERUM	FREE TESTOSTERONE (<11/20/13 SY)
Missing	SERUM	FREE TESTOSTERONE (CALCULATED)
Missing	SERUM	FREE TESTOSTERONE PERCENT
Missing	SERUM	TESTOSTERONE
Missing	SERUM	TESTOSTERONE (% FREE)
Missing	SERUM	TESTOSTERONE FREE
Missing	SERUM	TESTOSTERONE FREE INDEX%
Missing	SERUM	TESTOSTERONE FREE(PERCENT)
Missing	SERUM	TESTOSTERONE TOTAL
Missing	SERUM	TESTOSTERONE, FREE
Missing	SERUM	TESTOSTERONE, FREE AND WEAKLY BOUND
Missing	SERUM	TESTOSTERONE, FREE(CALC)

LOINC	TOPOGRAPHY	LABCHEMTESTNAME
Missing	SERUM	TESTOSTERONE, TOTAL
Missing	SERUM	TESTOSTERONE,% F+WB
Missing	SERUM	TESTOSTERONE,FREE(LC)
Missing	SERUM	TESTOSTERONE-FREE+WEAKLY BOUND
Missing	SERUM	TOTAL TESTOSTERONE
Missing	SERUM	TOTAL TESTOSTERONE (QUEST)
Missing	SERUM	testosterone, free

Source: OIG analysis of VA administrative data

Appendix C

Logical Observation Identifiers Names and Codes (LOINC) Laboratory Codes and VA LABCHEMTESTNAME for Follicle-Stimulating Hormone (FSH) Tests

LOINC	TOPOGRAPHY	LABCHEMTESTNAME
10501-5	SERUM	FSH (11-04)
1477-9	SERUM	FSH
15067-2	PLASMA	FOLLICLE STIMULATING HORMONE(FSH)
15067-2	SERUM	FSH - FOLLICLE STIMULATING HORMONE
2286-3	PLASMA	FOLLICLE STIMULATING HORMONE
2286-3	PLASMA	FSH
2286-3	SERUM	FSH
34434-1	SERUM	LH/FSH RATIO
Missing	SERUM	FOLLICLE STIMULATING HORMONE
Missing	SERUM	FSH
Missing	SERUM	FSH*

Source: OIG analysis of VA administrative data

Appendix D

Logical Observation Identifiers Names and Codes (LOINC) Laboratory Codes and VA LABCHEMTESTNAME for Luteinizing Hormone (LH)

LOINC	TOPOGRAPHY	LABCHEMTESTNAME
10501-5	BLOOD	LH
10501-5	PLASMA	LH (LUTEINIZING HORMONE)
10501-5	SERUM	LUTEINIZING HORMONE (LH)
1599-0	SERUM	LH
2579-1	PLASMA	LUTEINIZING HORMONE
2579-1	SERUM	LUTEINIZING HORMONE
34434-1	SERUM	LH/FSH RATIO
Missing	SERUM	LH
Missing	SERUM	LH*
Missing	SERUM	LUTEINIZING HORMONE
Missing	SERUM	LUTEINIZING HORMONE (LH)

Source: OIG analysis of VA administrative data

Appendix E

Under Secretary for Health Comments

Department of Veterans Affairs

Memorandum

Date: March 8, 2018

From: Executive in Charge, Office of the Under Secretary for Health (10N)[30]

Subj: Draft Report: Testosterone Replacement Therapy Initiation and Follow-Up Evaluation in VA Male Patients

To: Assistant Inspector General for Healthcare Inspections (54)

1. Thank you for the opportunity to review the OIG draft report, Healthcare Inspection: Testosterone Replacement Therapy Initiation and Follow-Up Evaluation in VA Male Patients. I have reviewed the draft report and concur.

2. In certain actions, Veterans Health Administration finds that it would be beneficial if the Office of Inspector General would include a qualifying reference statement such as, "as evidence suggest" or "best available evidence" or the "clinical experts agree" where it applies.

3. Thank you for the opportunity to review the draft report. If you have any questions, please email Karen Rasmussen, M.D., Director, Management Review Service at VHA10E1DMRSAction@va.gov.

Carolyn M. Clancy, M.D.

Attachment

[30] The recommendations for the Under Secretary for Health (USH) were submitted to the Executive in Charge who has the authority to perform the functions and duties of the USH.

VETERANS HEALTH ADMINISTRATION (VHA)

Action Plan

OIG Draft Report – National Review – Testosterone Replacement Therapy Initiation and Follow-up Evaluation in VA Male Patients

Date of Draft Report: February 5, 2018

Recommendations/ Actions	Status	Completion Date

OIG Recommendations

Recommendation 1. The Under Secretary for Health ensures that providers establish clinical signs and symptoms consistent with androgen deficiency, prior to testing patients' testosterone level for confirmation in alignment with Veterans Health Administration guidance.

Executive in Charge Comment: Concur in Principle

Veterans Health Administration (VHA) providers co-manage care with non-VHA providers and lack explicit linkage of symptoms to lab orders in Computerized Patient Record System (CPRS). It is not possible to accurately determine the indication for a first testosterone level although it was noted that the majority of reviewed patients had documented symptoms before prescribing. What is most important is that prior to initial dispensing of testosterone, VHA providers document pertinent clinical signs and symptoms, biochemical confirmation of hypogonadism, an established etiology for the hypogonadism, and symptoms resulting from hypogonadism.

A multidisciplinary workgroup will be formed to evaluate, create and disseminate a plan to include informatics tools or templates to be utilized VHA wide. This plan/template will ensure documentation of the pertinent clinical signs and symptoms warranting evaluation while facilitating patient results reporting for testosterone levels. Furthermore, this template will link to an order set for repeat testosterone testing (repeat morning total and free testosterone) and determination of follicle-stimulating hormone (FSH), and luteinizing hormone (LH) levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 2. The Under Secretary for Health ensures that providers biochemically confirm hypogonadism through repeated testosterone testing prior to initiation of testosterone replacement therapy in alignment with Veterans Health Administration guidance.

Executive in Charge Comments: Concur

This aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and

renewal prescribing of testosterone. Template components will ensure documentation of the results of repeated testosterone testing and determination of etiology, discussion of risks and benefits of therapy, symptomatic and clinical effectiveness of therapy, adverse effects, hematocrit level, patient adherence, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 3. The Under Secretary for Health ensures that providers determine whether the etiology of hypogonadism is primary or secondary, prior to testosterone replacement therapy initiation in alignment with Veterans Health Administration guidance.

Executive in Charge Comment: Concur

The aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and renewal prescribing of testosterone. The template components will ensure documentation of the results of repeated testosterone testing and determination of etiology, discussion of risks and benefits of therapy, symptomatic and clinical effectiveness of therapy, adverse effects, hematocrit level, patient adherence, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 4. The Under Secretary for Health ensures that providers discuss and document the risks and benefits of testosterone therapy with patients prior to initiation in alignment with Veterans Health Administration guidance.

Executive in Charge Comments: Concur

The aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and renewal prescribing of testosterone. The template components will ensure documentation of the results of repeated testosterone testing and determination of etiology, discussion and documentation of risks and benefits of therapy, symptomatic

and clinical effectiveness of therapy, adverse effects, hematocrit level, patient adherence, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 5. The Under Secretary for Health ensures that providers assess and document patients' symptoms improvement and adverse effects within 3–6 months of initiation before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

Executive in Charge Comments: Concur

The aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and renewal prescribing of testosterone. The template components will ensure documentation of the results of repeated testosterone testing and determination of etiology within 3-6 months of initiation before continuing testosterone replacement therapy, discussion of risks and benefits of therapy, symptomatic and clinical effectiveness of therapy, adverse effects, hematocrit level, patient adherence, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 6. The Under Secretary for Health ensures that providers monitor patients' hematocrit levels within 3–6 months of initiation, before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

Executive in Charge Comments: Concur

The aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and renewal prescribing of testosterone. The template components will ensure documentation of the results of repeated testosterone testing and determination of etiology, discussion of risks and benefits of therapy, symptomatic and clinical effectiveness of therapy, adverse effects, monitor the patients hematocrit level, adherence, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Recommendation 7. The Under Secretary for Health ensures that providers assess and document patients' adherence to therapy and perform testosterone level test within 3–6 months of initiation, before continuing testosterone replacement therapy in alignment with Veterans Health Administration guidance.

Executive in Charge Comments: Concur

The aforementioned multidisciplinary workgroup will also evaluate, create and disseminate for use at each facility a restricted medications template for initial and renewal prescribing of testosterone. The template components will ensure documentation of the results of repeated testosterone testing and determination of etiology, discussion of risks and benefits of therapy, symptomatic and clinical effectiveness of therapy, adverse effects, hematocrit level, patient adherence to therapy, and subsequent testosterone levels.

Status:	Target Completion Date:
In progress	February 28, 2019

Appendix F

OIG Contact and Staff Acknowledgments

Contact	For more information about this report, please contact the OIG at (202) 461-4720.
Contributors	Limin X. Clegg, Ph.D. Daisy Arugay-Rittenberg, MT Yoonhee C. Kim, PharmD Kathy Gudgell, RN, JD Nathan McClafferty, MS Ron Penny, MS Jarvis Yu, MS Jackelinne Melendez, MPA, Management and Program Analyst

Appendix G

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