

Editorials: *Controversies in Family Medicine*

Should Family Physicians Screen for Testosterone Deficiency in Men?

No: Screening May Be Harmful, and Benefits Are Unproven

ADRIANE FUGH-BERMAN, MD, *Georgetown University Medical Center, Washington, District of Columbia*

On September 17, 2014, an advisory committee of the U.S. Food and Drug Administration (FDA) recommended changing the labeling of testosterone products to exclude use in men with age-related decreases in testosterone.¹ The FDA usually follows the advice of its advisory committees.

Aging adults have always been a profitable market. In recent years, testosterone patches, gels, and other topical and injected preparations have been marketed as a youth-restoring tonic and disease preventive. Sales for testosterone therapies topped \$2 billion in 2012 and continue to grow in dozens of countries.²

AbbVie, the pharmaceutical arm of Abbott that manufactures Androgel, the leading testosterone therapy, maintains several websites that promote testosterone therapy. Questions at IsItLowT.com include: “Are you sad and/or grumpy?” “Has there been a recent deterioration in your work performance?” “Have you noticed a decrease in your enjoyment of life?” and “Are you falling asleep after dinner?” This widely used questionnaire, originally titled the ADAM (Androgen Deficiency in the Aging Male) test, was created by an endocrinologist for a testosterone manufacturer; the inventor told the *New York Times* that he drafted the questionnaire in 20 minutes in the bathroom, and later admitted “It is not ideal.”² These questions demonstrate how pharmaceutical companies use nonspecific symptoms to foster disease states and then convince physicians that these conditions are real. In this case, the disease state is marketed to consumers as Low T, and to physicians as late-onset hypogonadism.

AbbVie’s Drive for Five website cites low testosterone levels as one of five risks to men’s health, along with high blood pressure and high levels of cholesterol, blood glucose, and prostate-specific antigen. In fact, obesity and many chronic diseases are associated with low testosterone levels, but association does not prove causation, and there is no reliable evidence that testosterone treatment improves any chronic disease.



This is one in a series of pro/con editorials discussing controversial issues in family medicine.

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No consistent relationship has been proven between testosterone levels and symptoms purportedly associated with Low T.³ Decreased energy, increased body fat, reduced muscle mass and strength, and reduced sex drive are nonspecific symptoms associated with aging. Testosterone may increase libido, but testosterone levels do not correlate with sexual function.

In addition to the question of whether low testosterone levels correlate with actual symptoms, there is another worrisome issue: whether the laboratory-determined testosterone level for a specific patient actually means anything. Testosterone levels peak when men are in their 20s; after 40 years of age, they decline by about 1% to 2% per year.⁴ Testosterone levels are usually highest in the morning, are inconsistent, and can vary hourly, daily, weekly, and seasonally. Levels are affected by glucose ingestion, triglyceride levels, exercise, and sexual activity.⁵ Competition also affects testosterone levels.⁶ Sample centrifugation, storage, and transport conditions can also affect levels, and results vary among laboratories.⁵ Although older men as a group have lower levels than younger men, there is a wide range of normal at all ages. Standardized, age- or ethnicity-adjusted normal testosterone concentration ranges are lacking.⁵ Not only do assays vary in sensitivity, accuracy, and precision, but no single assay is markedly superior to another,⁵ and there is no consensus on what constitutes a low level, with ranges varying from 200 to 350 ng per dL (6.9 to 12.2 nmol per L).

The increasing use of testosterone should be expected to have adverse effects on men’s health. In men with intact testicles, the risks outweigh the benefits. Testosterone therapy has been linked to polycythemia, breast cancer, worsening congestive heart failure, worsening symptoms of benign prostatic hyperplasia, gynecomastia, sleep apnea, testicular atrophy, azoospermia, and, possibly, an increased risk of prostate cancer.⁷ Testosterone therapy has also been linked to thromboembolic ►

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events, especially in persons with thrombophilia and hypofibrinolysis.⁸ Testosterone may be inadvertently transferred to partners, children, or pets; the consequences of this are not known.

In addition, there is consistent and growing evidence that testosterone therapy causes heart attacks. A study of 209 men older than 65 years, the only placebo-controlled trial of testosterone therapy that specifically examined cardiovascular disease and mortality end points, was stopped early because of an increased risk of cardiovascular events.⁹ Cardiovascular risks have been noted in other trials as well. A meta-analysis of 2,994 men in 27 trials identified 180 myocardial infarctions and other cardiovascular-related events; testosterone therapy significantly increased risk (odds ratio = 1.54), with a number needed to harm of, at best, 90.¹⁰ Trials funded by the pharmaceutical industry found no increased risk, whereas independently funded studies found that treatment doubled risk (odds ratio = 2.06).¹⁰

A recent retrospective cohort study of 8,709 male veterans with total testosterone levels less than 300 ng per dL (10.4 nmol per L) who underwent coronary angiography between 2005 and 2011 found that testosterone therapy was associated with increased rates of mortality, myocardial infarction, and stroke.¹¹

Testosterone testing leads to testosterone treatment, which is inappropriate for the vast majority of patients. Testosterone treatment should be reserved for patients who are truly hypogonadal (e.g., those with uncorrected cryptorchidism or Klinefelter syndrome). There is no point in screening men for a disease state for which the treatment has unproven benefits and proven risks. Although testosterone labeling is likely to change, the promotion of testosterone testing and treatment in

normal men may continue. Family physicians should just say no.

Address correspondence to Adriane Fugh-Berman, MD, at ajf29@georgetown.edu. Reprints are not available from the author.

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