

Despite some of the controversies surrounding testosterone gels, a new study of older men found that this treatment had positive effects, from increased sexual activity and more vitality to just feeling better.



# Feeling GOOD:

## TESTOSTERONE GEL AND OLDER MEN

BY GLENDA FAUNTLEROY

*Staving off what happens to our bodies as we age is an enormous industry in the U.S. Both women and men depend on products sold over-the-counter and by prescription to relieve problems that arise as levels of women's estrogen and men's testosterone decrease — and bring a whole host of body changes and symptoms.*

**F**or millions of men in the U.S., boosting decreasing testosterone with gel supplements is a daily regimen — turning it into a reported \$2 billion industry. But do all men experience the benefits they hope for?

In its February 16 issue, the *New England Journal of Medicine* published results from the Testosterone Trials in which a team of investigators aimed to determine whether there were benefits of boosting testosterone levels in men older than age 65.

The 12-month Testosterone Trials were funded in part by the National Institutes of Health as well as AbbVie, the maker of the popular testosterone product AndroGel®. AbbVie donated the testosterone and placebo gel.

Researchers screened 51,085 men but were able to enroll only 790 who met all the criteria. The authors noted that, “relatively few men had a sufficiently low testosterone level to qualify.” Participants were 65 years or older and had serum testosterone levels that averaged less than 275 ng per deciliter. Three separate trials were conducted: the Sexual Function Trial, the Physical Function Trial, and the Vitality Trial. Each man participated in one or more of the three trials. One group received placebo only.



## TESTOSTERONE

# AT A GLANCE

- ▶ **Boosting decreasing testosterone with gel supplements is a current daily regimen of millions of men in the U.S. — turning it into a reported \$2 billion industry.**
- ▶ **Men in the Testosterone Trials who received testosterone reported better sexual function than those in the placebo group. This included more sexual activity, improved sexual desire, and increased erectile function.**
- ▶ **In a 2015 Safety Announcement, the FDA said the popular treatments have not been established as safe or effective for men with common age-related issues like low libido and fatigue.**

Men in the Testosterone Trials were given an initial dose of 5 g daily of AndroGel 1% in a pump bottle. Their testosterone serum levels were tested regularly, and gel doses were adjusted as necessary to keep testosterone levels within the normal range for men 19 to 40 years of age.

“When men get older, their testosterone levels decline and they experience a number of symptoms,” says study co-author Shalender Bhasin, MD, from Brigham and Women’s Hospital, Harvard Medical School. “Some of these symptoms are similar to those experienced by men who have testosterone deficiency. The most common complaints are sexual symptoms, but they often complain of lack of energy or lack of vitality. Older men may also experience decrease in their physical function, their mobility.”

Testosterone gel is often prescribed to offer aging men a boost from these symptoms. AndroGel shares the gel market with brands such as Axiron®, Testim®, and Aveed®. Net sales of AndroGel in 2015 equaled \$692 million, according to Libby Holman, AbbVie’s senior manager of public affairs.

“Testosterone gel is the most commonly prescribed method in the U.S.,” says Bradley Anawalt, MD, chief of medicine at the University of Washington Medical Center, who specializes in male reproductive endocrinology. “In the rest of the world, a long-acting testosterone injection that is administered every ten to 12 weeks is the most common testosterone prescription. This injectable testosterone (testosterone undecanoate) has recently been approved for use in the U.S., but it is very expensive, nearly \$4,000 per year.”

### **Testosterone Therapy “Often Makes Them Feel Better”**

There appears to be little argument to the fact that men with below normal testosterone levels experience a benefit from testosterone gel — and at times multiple benefits.

“The biggest benefit is usually in how men feel,” Anawalt says. “For hypogonadal men, testosterone therapy often makes them feel better. Many men will report improved sexual function and pleasure and some will report improved energy and vitality.”

The Testosterone Trials proved these outcomes. “The most striking and consistent improvements were in sexual function,” Bhasin says. Men who received testosterone reported better sexual function than those in the placebo group. This included more sexual activity, improved sexual desire, and increased erectile function.



In the Physical Function Trial, the men's six-minute walking distance was measured. There was some improvement in the walking speed in all men who were included in the trial. The percent of men whose six-minute walking distance increased by at least 50 m did not differ significantly between the two groups. However, when men were asked whether their walking ability was better, they perceived that it had improved, according to Bhasin.

Results of the Vitality Trails were mixed. Men who took testosterone showed no benefit over placebo on the fatigue scale. Men on testosterone did, however, report slightly lower depression symptoms. And at the end of the trial, men in the testosterone group were more likely to report that their energy was better compared with those given placebo.

### **Over-Prescribed Despite the Risks?**

The boosts to sexual performance and mood do not come without risks. Several research studies have investigated the possible link between testosterone therapy and an increased risk of prostate cancer and heart problems. There have been mixed results with some studies reporting a benefit to testosterone — with decreased cardiovascular events and decreased mortality — and some showing an increase.

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— BRADLEY ANAWALT, MD, CHIEF OF MEDICINE,  
UNIVERSITY OF WASHINGTON MEDICAL CENTER,  
SEATTLE



**“There’s a lot of hype and misperception about what testosterone does and does not do, but...in men who have low testosterone levels and have low libido there is benefit in terms of improved sexual desire and sexual activity but the magnitude of the benefit is modest.”**

— SHALENDER BHASIN, MD, BRIGHAM AND WOMEN’S HOSPITAL, HARVARD MEDICAL SCHOOL, BOSTON

In a large 2014 UCLA study published in *PLOS One*, researchers analyzed health insurance claims of more than 55,000 men prescribed testosterone and reported that among men 65 and older, there was a two-fold increase in the risk of heart attack in the 90 days after filling an initial testosterone therapy prescription. In men younger than 65 with a history of heart disease, the risk was two- to three-fold in the first 90 days.

While the Testosterone Trials revealed no differences in major cardiovascular events between the testosterone and placebo groups during the 12-month study, Bhasin points out the set of trials were not powered to determine the long-term risks, particularly cardiovascular and prostate risks. “So the risk-to-benefit ratio still remains unclear and much larger and longer randomized trials are needed,” he says.

Taking note of the enormous jump in sales and proven health risks, the Food and Drug Administration (FDA) issued a Safety Announcement in March 2015 against over-prescribing testosterone-boosting drugs. The FDA said the popular treatments have not been established as safe or effective for men with common age-related issues like low libido and fatigue.

The agency required drug makers to add information to the labeling about a possible increased risk of heart attacks and strokes in patients taking testosterone.

The FDA announcement further called for healthcare professionals to prescribe testosterone therapy only for men with low testosterone levels caused by certain medical conditions and confirmed by laboratory tests.

“Many men who are being prescribed T therapy are not being properly evaluated,” Anawalt says. “Some are being started on therapy without having their testosterone blood concentrations measured. Others are being diagnosed with hypogonadism based on a single blood test or tests performed on blood obtained in the afternoon.”

To be diagnosed with hypogonadism, a man must have reproducibly low blood testosterone concentrations on at least two occasions, Anawalt explains. The testosterone measurement should be performed on blood drawn between 7 and 10 a.m. when testosterone concentrations peak. The normal range is based on peak, early morning blood testosterone concentrations, he says.

Bhasin reiterates that while many men may be using the testosterone to enhance sexual performance, the important lesson from the trial is that only men who had consistently low testosterone levels actually improved their sexual desire and function.

“So there’s a lot of hype and misperception about what testosterone does and does not do,” Bhasin says. “But...in men who have low testosterone levels and have low libido there is benefit in terms of improved sexual desire and sexual activity but the magnitude of the benefit is modest.”

FAUNTLEROY IS A FREELANCE WRITER BASED IN CARMEL, IND., AND A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE ABOUT INCREASED RESEARCH OF NATURAL PRODUCTS IN THE MARCH ISSUE.