Practice Guidelines

Testosterone Therapy for Age-Related Low Testosterone: Guidelines from the ACP

Key Points for Practice

- Testosterone therapy leads to small improvements in erectile and global sexual function in patients with age-related low testosterone levels, but offers no other benefits.
- Consider discontinuing therapy for age-related low testosterone levels unless sexual function improves.
- Consider prescribing intramuscular over transdermal testosterone therapy because of identical benefit and much lower cost.

From the *AFP* Editors

Testosterone levels in men normally diminish with age. For men older than 35 years, testosterone declines by nearly 2% each year. There is no cutoff for low testosterone, although a level of 300 ng per dL (10.41 nmol per L) is used in most trials. One-fifth of patients older than 60 years and one-half of patients older than 80 years have testosterone levels less than 320 ng per dL (11.10 nmol per L), many without symptoms. Treatment of age-related low testosterone is controversial, and no testosterone products are labeled for treatment of age-related effects, including sexual dysfunction. The American College of Physicians (ACP) published guidelines for testosterone therapy in cis gender men with age-related low testosterone based on a systematic review.

Sexual Dysfunction

Testosterone therapy leads to small improvements in global sexual function and erectile function compared with placebo in men with age-related low testosterone levels. The guidelines recommend considering testosterone therapy in cisgender men with age-related low testosterone levels who want to improve sexual function and prescribing replacement therapy only after discussion with the patient. Because of limited evidence, discontinuing testosterone therapy should be considered in patients who do not report improvement in sexual function within 12 months, after an appropriate trial.

Other Age-Related Symptoms

Testosterone therapy does not improve physical or cognitive function compared with placebo. A questionable improvement in objective physical tests is too small to be clinically significant. Testosterone therapy fails to demonstrate clinically significant improvement in fatigue and depressive symptoms. Quality of life is improved with testosterone more than with placebo, although the difference is small. The group suggests not using testosterone therapy to improve energy, vitality, physical function, or cognition.

Harms of Testosterone

Serious adverse events are similar with testosterone therapy and placebo, but studies were not large enough to identify these events. The effect of testosterone therapy on adverse cardiac events is uncertain because few individuals at high risk have been included in trials. Similarly, although testosterone therapy does not appear to increase risk of prostate cancer, trials are underpowered and exclude people at higher risk of dying. Evidence is insufficient to determine if testosterone therapy affects mortality.

Testosterone Formulation

Intramuscular and transdermal testosterone have similar benefits and harms, but intramuscular dosing is less than one-tenth the cost of transdermal formulations. The guideline group suggests that intramuscular administration be used to treat sexual dysfunction.

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This series is coordinated by Michael J. Arnold, MD, contributing editor.

A collection of Practice Guidelines published in *AFP* is available at https://www.aafp.org/afp/practguide.

CME **This clinical content** conforms to AAFP criteria for CME. See CME Quiz on page 13.

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Evidence Limitations

The systematic review included 38 randomized controlled trials and 20 observational studies. Most studies were small, industry-funded, and had moderate to high risk of bias. Most studies followed patients for one year or less, so long-term risks are unknown.

Editor's Note: Testosterone therapy for age-related low testosterone is controversial, and is considered off-label by the U.S. Food and Drug Administration. This systematic review and guideline from the ACP clarifies that benefits of testosterone therapy are limited to small improvements in sexual function. This guideline has been endorsed by the American Academy of Family Physicians. Although similar to the 2017 *AFP* article on testosterone therapy (https://www.aafp.org/afp/2017/1001/p441.html), the current review demonstrates less benefit from treatment than previously reported.—Michael J. Arnold, MD, Contributing Editor

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the U.S. Department of Veterans Affairs or the U.S. government.

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Systematic literature search described? Yes

Guideline developed by participants without relevant financial ties to industry? Yes

Recommendations based on patient-oriented outcomes? Yes

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