

## SUMMARY

PracticeUpdate Editorial Team

**Background:** Testosterone therapy is increasingly promoted. No randomized placebo-controlled trial has been implemented to assess the effect of testosterone therapy on cardiovascular events, although very high levels of androgens are thought to promote cardiovascular disease.

**Methods:** A systematic review and meta-analysis was conducted of placebo-controlled randomized trials of testosterone therapy among men lasting 12+ weeks reporting cardiovascular-related events. We searched PubMed through the end of 2012 using ("testosterone" or "androgen") and trial and ("random\*") with the selection limited to studies of men in English, supplemented by a bibliographic search of the World Health Organization trial registry. Two reviewers independently searched, selected and assessed study quality with differences resolved by consensus. Two statisticians independently abstracted and analyzed data, using random or fixed effects models, as appropriate, with inverse variance weighting.

**Results:** Of 1,882 studies identified 27 trials were eligible including 2,994, mainly older, men who experienced 180 cardiovascular-related events. Testosterone therapy increased the risk of a cardiovascular-related event (odds ratio (OR) 1.54, 95% confidence interval (CI) 1.09 to 2.18). The effect of testosterone therapy varied with source of funding (P-value for interaction 0.03), but not with baseline testosterone level (P-value for interaction 0.70). In trials not funded by the pharmaceutical industry the risk of a cardiovascular-related event on testosterone therapy was greater (OR 2.06, 95% CI 1.34 to 3.17) than in pharmaceutical industry funded trials (OR 0.89, 95% CI 0.50 to 1.60).

**Conclusions:** The effects of testosterone on cardiovascular-related events varied with source of funding. Nevertheless, overall and particularly in trials not funded by the pharmaceutical industry, exogenous testosterone increased the risk of cardiovascular-related events, with corresponding implications for the use of testosterone therapy.

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BMC Medicine

Testosterone Therapy and Cardiovascular Events Among Men: A Systematic Review and Meta-Analysis of Placebo-Controlled Randomized Trials

*BMC Med* 2013 Apr 18;[Epub Ahead of Print], L Xu, G Freeman, BJ Cowling, et al

## Maintaining Testosterone Levels Naturally

Testosterone is a male hormone made primarily in the testicles. Hormones change as we go through the life cycle. What is normal for a 16-year-old is not the same for a 60-year-old.

Although medication for low testosterone ("low T") is being promoted by drug companies, treatment is not as simple as just replacing this hormone. A low level is often due to many other factors. It is not a good idea to start testosterone medication too quickly without exploring other ways to raise testosterone first. Taking medication can stop your own body from making the hormone. Testosterone medication is also not without risks, many of which are unknown with long-term use.

### ***What can I do to maintain or increase my testosterone level naturally?***

1. **Maintain healthy body weight.** This is probably the most important thing a man can do. As belly fat increases, there is an increase in activity of the enzyme "aromatase," which converts testosterone in the fat cells to estrogen. Having less testosterone and more estrogen can deposit fat in areas of the body similar to women (breasts, hips, thighs). It also increases your risk of enlargement of the prostate and even prostate cancer. With every one point drop in your body mass index (BMI), your testosterone level will increase by a point (roughly).
2. **Exercise.** A combination of aerobic (increase in heart rate) and resistance (weightlifting) has been found to increase the production of testosterone. This also helps prevent the most common diseases from which we will die (heart disease and cancer).
3. **Get a good night's sleep.** Most testosterone is made during deep REM (Rapid Eye Movement) sleep. A poor sleep cycle with less time spent in REM has been associated with low testosterone levels. See our handout [\*Improving and Maintaining a Healthy Sleep/Wake Cycle\*](#).
4. **Avoid tobacco products.** Tobacco reduces testosterone.
5. **Limit alcohol.** Alcohol (more than two drinks a day) causes more testosterone to be converted into estrogen.
6. **Wear loose fitting underwear.** Testicles hang away from the body to be cooler. Heat can reduce sperm count and testosterone production. Wear boxers, not briefs.
7. **Avoid xenobiotics.** Xenobiotics are chemicals found in the environment that do not occur naturally in the body. Xenobiotics can act like hormones. Research has shown that the average testosterone level in men has gradually dropped over the years. This may be due in part to all the potential toxins that have accumulated in our environment. The main ones include:



NIH, National Institute on Aging



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- **Bisphenol A (BPA) found in plastics.** Don't microwave food in plastic containers. Avoid plastic containers with the numbers 3, 6, or 7 engraved in the triangle on the product. Some, but not all, #7 containers contain BPA. Those labeled PLA are OK to use as they are made from corn husks. Buy BPA-free water containers. Drinking water out of containers with the numbers 2, 4, 5 or 7-PLA is OK. Don't drink out of Styrofoam containers.
  - **Phthalates.** These chemicals are used in plastics, coatings, lubricants and binders. Many are found in hygiene products such as shampoos and colognes. A useful web site on phthalate free products is <http://lesstoxicguide.ca/>.
  - **Organophosphates.** These are mainly found in pesticides and herbicides. Eat organic products when able.
8. **Manage your stress.** When researchers study long term stress, they measure cortisol in the blood. This is a steroid hormone. When cortisol levels are high, they can increase fat deposits. This in turn results in more testosterone being converted into estrogen.
9. **Eat well.** Poor nutrition is at the root of many diseases. It can also create an imbalance of male hormones.

**Foods to avoid:** Avoid red meat and animal fat, food dyes, and processed foods. Limit caffeine, dairy products, and sugar (by itself or in products).

**Foods to include:** green tea, multi-colored fruits and vegetables, nuts (particularly Brazil nuts, which are rich in selenium. Just two a day are plenty.), fiber (covered by eating fruits and vegetables), ground flax seed (1 tablespoon a day), soy products (e.g., drink soy milk instead of cow's milk).



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10. **Consider over-the-counter supplements.**

**If you want to maintain healthy testosterone levels, the changes discussed above will trump any supplement. The nutrients below inhibit aromatase. Taking them may add to the benefits you will get from lifestyle changes.**

To reduce the aromatase enzyme in your body (which means that you will reduce the amount of testosterone converted to estrogen), try some or all of the following:

- Zinc 20-30 mg if levels are low. (Have this checked by your health practitioner.)
- Quercetin 400 mg daily.
- Grape seed extract 100 mg daily.

You can also get these nutrients by eating nuts, fruits (grapes and citrus) and vegetables.

- Dehydroepiandrosterone (DHEA) 25-50 mg.  
DHEA is a steroid hormone made by the adrenal glands, which are located above each kidney. The body converts DHEA into hormones, such as estrogen and



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testosterone. DHEA levels go down when stress goes up. This can be determined by measuring cortisol levels in the blood. The best way to raise DHEA is to learn to see life in a less stressful way.

### **If your prostate is enlarged (a condition called benign prostatic hypertrophy or BPH), or if you have had prostate cancer...**

Reduce 5-alpha reductase enzyme in your body. This reduces the amount of testosterone that is converted to Dihydrotestosterone (DHT). DHT is more likely to increase the size of the prostate. Consider the following:

- Zinc 20-30 mg if levels are low. (Have this checked by your health practitioner.)
- Saw palmetto 160 mg twice daily,
- Epigallocatechin (ECGC, found in green tea) 200 mg three times a day in the form of mixed catechins (acids found in plants).

***The information in this handout is for general education. It is not meant to be used by a patient alone. Please work with your health care practitioner to use this information in the best way possible to promote your health.***

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### **NOTES:**