

Testosterone therapy to be put to the test

Concerned that American men may be embracing the same kind of misguided sex-hormone use that brought calamity to women, the government is funding a national study to see whether older men with low testosterone benefit from boosting it.

By [Marie McCullough](#)

The Philadelphia Inquirer

 enlarge

BONNIE WELLER / MCCLATCHY NEWSPAPERS

University of Pennsylvania endocrinologist Peter Snyder is leading a \$45 million clinical trial to see whether older men with low testosterone benefit from boosting it.

Information online

The T Trial: www.ttrial.org

ADVERTISING

PHILADELPHIA — Concerned that American men may be embracing the same kind of misguided sex-hormone use that brought calamity to women, the government is funding a national study to see whether older men with low testosterone benefit from boosting it.

Led by University of Pennsylvania endocrinologist Peter Snyder, the \$45 million clinical trial, which last month began recruiting 800 men older than 64, is by far the largest ever to compare the effects of the quintessential male hormone with a placebo. It will investigate whether in some men, symptoms of aging such as ebbing energy, lower libido and muddy memory are partly due to testosterone deficiency.

It is, Snyder said, an "unprecedented opportunity" to shed light on the question: Is unusually low testosterone pathological or just a natural part of aging?

Still, sponsors say, the "T Trial" (the logo is a T inside a male symbol) will not follow enough men for enough years to settle larger questions such as: What are the risks? And could younger, healthier men benefit from heightened testosterone?

Millions of them are not waiting for answers. Sales of male hormone products, worth \$809 million last year, keep rising, a trend that worried experts say justifies public investment in careful studies.

"Viewed by some as an anti-aging tonic, the growth in testosterone's reputation and increased use by men of all ages in the United States has outpaced the scientific evidence," concluded an Institute of Medicine expert panel that recommended the new research.

In 2002, when a 15-year-long, \$725 million government trial called the Women's Health Initiative (WHI) showed that menopausal hormone therapy was risky for women's hearts, blood vessels, brains and breasts, women and their doctors were stunned. After all, a vast body of research showed that estrogen's cardiovascular and bone benefits outweighed the slightly increased chance of breast cancer. Population studies, risk-factor studies, even many small, placebo-controlled trials showed this.

The lesson of the WHI was that a mammoth, long, costly, rigorous trial — the kind drug companies have no incentive to do — was the only way to tease out rare but real risks.

Questions remain

In 2002, when the National Institute on Aging announced plans for a 6,000-man, \$100 million trial — not a Men's Health Initiative, but close — there was an uproar. Unlike estrogen's research record, testosterone's was scant and inconsistent. No one had proved that it prevented or relieved anything in aging men, so trying to tease out the dangers was premature.

Institute of Aging officials "ran into some internal political problems," Snyder recalled. "They were accused of risking men's health."

So they asked the Institute of Medicine — an independent, authoritative, scientific advisory group — to weigh in.

Its panel reviewed all available research, then recommended midsize trials. If these show no benefits, the panel said, then larger versions "are not indicated."

Six years later, the T Trial is finally up and running at 12 medical centers across the country.

The design addresses a number of sticking points, including the fact that experts can't even agree on what "low" testosterone is.

Testosterone levels in the blood fluctuate widely depending on the time of day, and measurement methods vary in accuracy. Men who are obese or have diabetes tend to have depressed levels. And a study of middle-class Californians found almost half who were older than 50 fell below the generally accepted "low" threshold of 300 ng/dl (nanograms of testosterone per deciliter of blood), suggesting it's fairly normal.

Also, testosterone declines gradually but not dramatically with age — unlike estrogen, which plummets around age 50.

That's why the whole notion of "andropause" — male menopause — remains controversial.

'Andropause' doubted

Richard Casey, a Canadian endocrinologist and men's health researcher who has advised testosterone product manufacturers, is among experts who dismiss andropause as a marketing tool. His prescription? Get off the sofa.

"If there is a symptom complex that will respond better to exercise than andropause, I don't know of it," he said. "Here's an idea for patients: Tell them to take the \$1,200 they'll spend on testosterone gel per year and join a health club. ... They'll have money left over for their new clothes!"

To focus on men most likely to be suffering from genuine deficiency, the T Trial is enrolling men who have testosterone below 250 ng/dl and at least one complaint that may be related — trouble with walking, thinking, energy or libido. Remarkably, few of the 31 small testosterone trials done to date enrolled men with such health profiles.

Another challenge for T Trial designers was safety. Some studies suggest testosterone increases PSA, the blood marker for prostate cancer; aggravates sleep apnea; and raises stroke risk by overproducing blood-thickening red cells. Theoretically, testosterone could even increase the risk of male breast cancer, since some of it is converted to estrogen.

To err on the side of safety, the T Trial is excluding men with a long list of conditions that might be worsened by boosting testosterone. The trial will be stopped if dangers become apparent during the year of treatment.

Testosterone is already approved to treat "hypogonadism" — the production of little or no hormones by the sex glands — due to birth defects, radiation, infection or other causes. But hypogonadism is not what most men are using testosterone products for.

Prescriptions soared from 648,000 in 1999 to 3.3 million last year, fueled by the 2000 approval of Solvay Pharmaceuticals' AndroGel, the first rub-on testosterone product, according to the market research firm IMS Health. (Testosterone also comes in injections, patches, implantable pellets and absorb-through-the-gums forms; it isn't readily absorbed from pills.)

Patrick Walsh, the renowned prostate-cancer surgeon at Johns Hopkins University, said he hoped results of the T Trial would lead to more sensible use.

"Right now, hormones are being tinkered with recklessly," Walsh said. "Men come in to see me who went to another doctor for vague symptoms. Without measuring testosterone or anything else, that doctor put them on 'androgen replacement therapy.' They show up on my door two years later with high-grade prostate cancer. Did the testosterone cause it? I don't know."



http://seattletimes.nwsourc.com/html/nationworld/2010494158_malehormones13.html