Testosterone Therapy: Medical Evidence for Both Men and Women

Maple, K. and Monis, A.
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Abstract

Testosterone therapy has become common in the United States and worldwide. While hormone testosterone is primarily associated with male physiology, it plays an important role in the health of both genders.

For men, testosterone therapy is mainly prescribed to manage hypogonadism symptoms such as low libido, muscle loss, and fatigue. Emerging evidence indicates the potential benefits of testosterone therapy for cardiovascular health, cognitive functioning, and other aspects of health.

For women, testosterone therapy is prescribed to tackle sexual dysfunction, mood disorders, and decreased energy, especially in postmenopause. However, the use of testosterone therapy in women is less commonly discussed and researched.

The primary objective of this white paper is to examine clinical research and current evidence on testosterone therapy in men and women alike. The paper outlines the benefits, potential side effects, and various uses of testosterone therapy. An overview of medical evidence on this subject aims to deepen understanding of applications of testosterone therapy in both genders and emphasize the need for further research focusing on long-term effects.

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Introduction

Testosterone therapy, also known as testosterone replacement therapy (TRT), is a hormone treatment designed to address testosterone deficiencies or imbalances by supplementing or replacing the hormone. Modern testosterone therapy began in 1935 when the hormone was chemically synthesized by Adolf Butenandt in Göttingen and Leopold Ruzicka in Basel. In the U.S., testosterone therapy has been approved by the FDA since the 1950s for men with classical hypogonadism, though it is also used off-label for issues such as low energy and sexual dysfunction. While often less discussed, testosterone therapy has been used in women for over 80 years to treat symptoms of perimenopause and menopause.

Testosterone is a hormone produced in both men and women—mainly in the testicles for men and the ovaries for women. As the primary androgen, testosterone drives the development of male characteristics and is naturally found at higher levels in men. It plays a crucial role in various bodily functions, including sperm production, red blood cell formation, bone and muscle strength, fat distribution, and libido. In women, testosterone helps enhance libido, though most of it is converted into estradiol.

As people age, testosterone levels decline, a process that can be accelerated by unhealthy lifestyle factors. Testosterone deficiency or imbalance in both men and women can lead to a wide range of symptoms, such as muscle loss, increased body fat, erectile dysfunction, depression, low libido, insomnia, osteoporosis, hot flashes, and fertility issues.

Problem Statement

The importance of testosterone in maintaining overall health is well established, with research showing that levels of this hormone naturally decrease with age in both men and women. Since hormonal imbalances can have a wide range of effects on both mental and physical health, testosterone therapy has become a key area of study, with a focus on its impact on overall

well-being. While testosterone therapy has been in use for decades, much remains to be explored and understood about its long-term effects and broader therapeutic potential.

Literature Review

This white paper included studies by P.J. Snyder, H.M. Behre, G. Colleluori, Z. Zhang, S. J. Diem, and O.J. Ponce to provide a detailed overview of the effects of testosterone therapy in males and females alike. We also considered findings from K.M. Pencina, A.M. Lincoff, S. Kadamoto, A.S. Mangolim, and T. Goodale, which focused on the impact of testosterone therapy on cardiovascular health, anemia, and metabolic functioning.

Additional studies and pieces of evidence by Y. Barnouin, C.F. Ingram, A. Kimball, and G. El-Hage explored the use of testosterone therapy in specific populations including postmenopausal women, women with sexual dysfunction, and patients with anorexia nervosa. Moreover, research by A.L. Hirschberg, M. Uloko, J.X. Yang, and E.J. Hermans shed more light on the role of testosterone in physical performance, bone health, and psychological effects in women.

The literature included in this paper extends beyond the basic effects of testosterone therapy and provides further insights into efficacy, safety, and long-term outcomes in men and women alike.

Methodology

The primary goal of this white paper is to review and evaluate the evidence regarding the effects of testosterone therapy on various physiological and metabolic functions in both men and women. The studies and research included focus on testosterone therapy's role in enhancing bone health, muscle mass, sexual function, and overall quality of life. Additionally, the white paper examines its impact on cardiovascular health, psychological well-being, and metabolic regulation.

This white paper also highlights the outcomes of testosterone therapy in specific populations, such as hypogonadal men, postmenopausal women, and patients with preexisting conditions, while addressing the potential benefits and risks associated with this treatment approach.

Results/Findings

P.J. Snyder et al. found that testosterone replacement in hypogonadal men improves bone mineral density in the hip and spine, increases fat-free mass, energy, and sexual function, and restores prostate volume from subnormal to normal levels. Interestingly, while testosterone therapy's impact on bone mineral density lasted up to 24 months, its effects on other tissues, such as muscle, lasted only three to six months.

H.M. Behre et al. studied the effects of raising serum testosterone on body composition and quality of life. Results showed that 1% testosterone gel improved lean body mass, fat mass, and overall quality of life in men with low to low-normal testosterone levels, with further improvements over 12 months.

P.J. Snyder also conducted a randomized controlled trial to assess testosterone's effect on fracture incidence, with 2,601 men in the testosterone group and 2,603 in the placebo group. After a median follow-up of 3.19 years, clinical fractures were more common in the testosterone group (3.5%) than in the placebo group (2.46%). Additionally, another study by Snyder et al. revealed that testosterone treatment significantly increased volumetric bone mineral density, especially in the spine, and showed greater impact on trabecular rather than peripheral bone.

G. Colleluori et al. found that testosterone therapy significantly improved skeletal health in hypogonadal men with type 2 diabetes, more so than in those without diabetes. However, a systematic review and meta-analysis by Z. Zhang et al. indicated that the effect of testosterone on bone mineral density and fracture risk remains inconclusive. Despite this, the analysis confirmed improvements in sexual function and quality of life without increasing the risk of all-cause mortality or cardiovascular events.

S.J. Diem et al. reported that testosterone therapy might offer modest improvements in sexual function and quality of life in older men with low testosterone, although it had no significant effect on common signs of aging. They emphasized that the long-term safety and efficacy of testosterone therapy are still unclear. Additionally, O.J. Ponce et al. noted that testosterone therapy improved sexual desire and erectile function but increased the risk of erythrocytosis.

A pivotal study by K.M. Pencina et al. demonstrated that testosterone therapy was more effective than placebo in correcting anemia and preventing its onset in middle-aged and older men with hypogonadism. Conversely, a randomized controlled trial by A.M. Lincoff et al. showed that testosterone therapy was non-inferior to placebo in men with hypogonadism and high cardiovascular risk, though it increased the incidence of atrial fibrillation, acute kidney injury, and pulmonary embolism.

S. Kadamoto et al. confirmed the safety and effectiveness of testosterone therapy for high-risk prostate cancer patients receiving high-dose-rate brachytherapy. Similarly, A.S. Mangolim et al. found that testosterone therapy slightly improved lean body mass and LDL cholesterol in obese men with low testosterone but did not affect blood pressure.

T. Goodale et al. reviewed testosterone therapy’s impact on cardiovascular health, suggesting it may improve myocardial ischemia, exercise capacity, and metabolic markers in men with prediabetes or diabetes. They found no credible evidence that testosterone increases cardiovascular risk and noted its potential cardiovascular benefits.

Y. Barnouin et al. conducted a randomized controlled trial that revealed testosterone supplementation over six months did not improve overall physical function in older, obese, hypogonadal men, though it did reduce the muscle mass and bone density loss often associated with weight loss.

C.F. Ingram et al. reviewed testosterone therapy for female sexual dysfunction, concluding that it is effective in treating postmenopausal women. However, they called for more long-term safety data regarding its effects on cardiovascular health, cognitive function, breast health, and the musculoskeletal system.

A. Kimball et al. studied the use of low-dose testosterone in 90 women with anorexia nervosa, finding that testosterone therapy did not yield sustained improvements in mood or eating disorder symptoms, nor was it superior to placebo.

G. El-Hage et al. reported that testosterone cream significantly improved sexual desire and satisfaction in menopausal women with hypoactive sexual desire disorder (HSDD) without causing adverse reactions.

An interesting study by A.L. Hirschberg et al. found that testosterone therapy increased aerobic running time and lean mass in young, physically active women. M. Uloko et al. similarly reported that testosterone therapy is effective for postmenopausal women with HSDD, though more research is needed on its efficacy for premenopausal women.

J.X. Yang et al. discovered a positive relationship between serum testosterone levels and lumbar bone mineral density in middle-aged postmenopausal women, suggesting that increasing testosterone could benefit bone health.

E.J. Hermans et al. found that a single dose of testosterone reduced fear responses in humans, showing potential anxiolytic effects, while R. Goldstat et al. found that testosterone therapy improved mood, well-being, and sexual function in premenopausal women with low libido.

Finally, R.C. Britton et al. reviewed the cardiovascular effects of testosterone in postmenopausal women, suggesting it may improve body composition and insulin sensitivity, though further research is needed to understand the long-term cardiovascular risks.

Discussion

The clinical trials and evidence reviewed in this white paper provide valuable insights into the effects of testosterone therapy on various physiological functions in both men and women. Studies show that testosterone therapy can improve bone mineral density, muscle mass, and sexual function in men with hypogonadism, while also enhancing overall quality of life. However, the duration of these benefits varies. For instance, improvements in bone density can last up to 24 months, whereas effects on energy and muscle mass may only persist for a few months.

Despite the benefits, testosterone therapy is not without risks. Some studies report an increased incidence of fractures in men undergoing testosterone treatment, and others suggest a higher risk of cardiovascular events in certain populations.

In women, testosterone therapy has shown promise in enhancing sexual function, particularly in postmenopausal women. However, concerns about long-term safety, including impacts on cardiovascular health and cognitive function, still need to be addressed.

Overall, the body of research supports the therapeutic use of testosterone for specific conditions, but more comprehensive studies are needed to fully understand its long-term efficacy and safety.

Conclusion

Testosterone plays a vital role in regulating numerous physiological functions in both men and women. It is essential for maintaining bone density, muscle mass, sexual function, and overall physical and mental well-being. Research has shown that testosterone therapy can lead to significant improvements in these areas, particularly for men with hypogonadism and postmenopausal women experiencing sexual dysfunction.

The benefits of testosterone therapy extend beyond sexual health. Studies suggest that it can improve body composition by increasing lean muscle mass and reducing fat, boost cardiovascular health by enhancing blood flow and cholesterol profiles, and elevate energy levels and physical performance. These improvements can contribute to a better quality of life, helping individuals regain vitality and manage age-related declines in physical and sexual function.

However, the potential risks of testosterone therapy underscore the importance of careful monitoring throughout treatment. Some studies have raised concerns about increased risks of cardiovascular events, such as heart attacks or strokes, and potential effects on prostate health in men. In women, long-term safety concerns include impacts on cardiovascular health, cognitive function, and breast health.

Despite its promise, particularly in addressing conditions like hypogonadism, testosterone therapy is not without its complexities. More comprehensive, long-term research is needed to fully understand the risks and benefits, especially for populations outside of the primary treatment groups. This includes further exploration into optimal dosing, the effects of prolonged use, and the therapy's overall efficacy in different demographics. Careful consideration of these factors is essential to ensure that testosterone therapy remains a safe and effective treatment option for both men and women.

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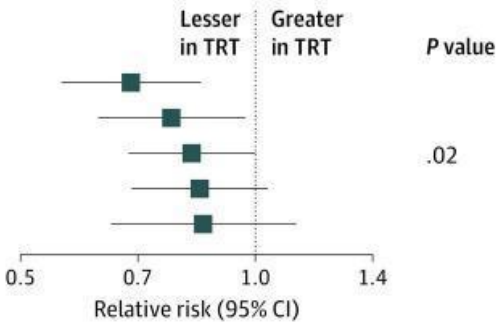
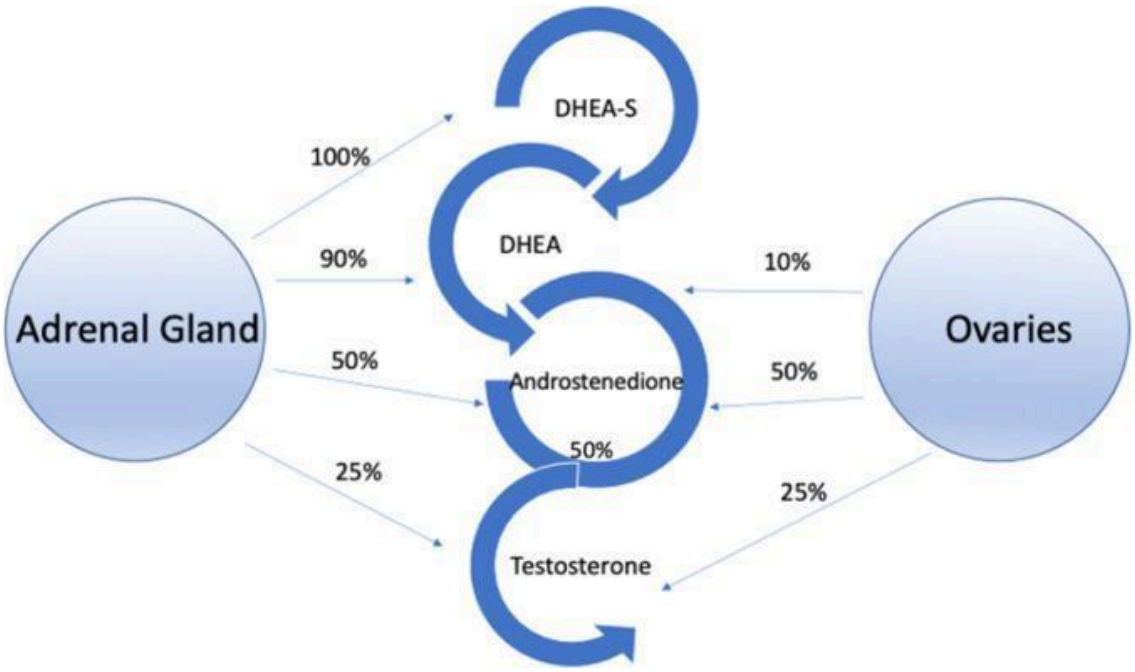
Appendices

Time, mo	Participants experiencing events/total patients, No. (%)		Relative risk (95% CI)
	TRT	Placebo	
6	143/1997 (7)	203/1958 (10)	0.69 (0.57-0.85)
12	137/1934 (7)	171/1894 (9)	0.78 (0.63-0.97)
24	174/1746 (10)	207/1677 (12)	0.83 (0.69-0.99)
36	135/1347 (10)	167/1300 (13)	0.85 (0.70-1.04)
48	51/570 (9)	51/499 (10)	0.86 (0.65-1.13)



Incidence of anemia in participants who didn't have anemia at baseline.

Pencina KM, Travison TG, Artz AS, et al. Efficacy of Testosterone Replacement Therapy in Correcting Anemia in Men With Hypogonadism: A Randomized Clinical Trial [published correction appears in JAMA Netw Open. 2024 Jan 2;7(1):e2355610. doi: 10.1001/jamanetworkopen.2023.55610]. *JAMA Netw Open*. 2023;6(10):e2340030. Published 2023 Oct 2. doi:10.1001/jamanetworkopen.2023.40030



Overview of androgen synthesis in the premenopausal ovary and adrenal gland.

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Conflicts of Interest

At the time of preparing this whitepaper, the authors declared no conflicts of interest.

Contact Information

For any inquiries regarding this whitepaper, please reach out directly to the authors.