

Clinical Benefits of Testosterone Replacement Therapy in Men: Evidence from A Narrative Review

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ABSTRACT

Testosterone replacement therapy (TRT) has emerged as a cornerstone intervention in men with hypogonadism, with benefits extending beyond sexual health into multiple domains of physical and psychological well-being. This narrative review synthesizes current evidence on the clinical outcomes of TRT, with a particular focus on recreational athletes and men with testosterone deficiency. A comprehensive search of PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar was conducted, covering publications from 1995 to 2025. Eligible studies included randomized controlled trials, observational studies, systematic reviews, and meta-analyses reporting outcomes related to sexual function, musculoskeletal health, bone metabolism, metabolic and cardiovascular parameters, neuropsychological status, and global quality of life. Evidence consistently demonstrates that TRT improves sexual desire, erectile function, and overall satisfaction, while also contributing to fertility potential in carefully selected patients. Musculoskeletal outcomes include increased lean body mass, enhanced muscle strength, and improved recovery from injuries, particularly when combined with structured exercise. In terms of skeletal health, TRT improves bone mineral density and reduces fracture risk in hypogonadal men. Metabolic and cardiovascular benefits include improved insulin sensitivity, reduced fat mass, favorable lipid modulation, and enhanced exercise tolerance. Furthermore, TRT has shown positive effects on mood, vitality, and selected cognitive domains, with additional improvements in global well-being and athletic recovery. Taken together, current evidence highlights TRT as a multidimensional therapy that restores hormonal balance, improves functional outcomes, and enhances overall quality of life in men with testosterone deficiency. While further long-term studies are needed to standardize protocols and confirm benefits in diverse populations, TRT remains an effective therapeutic strategy with broad clinical applications.

KEYWORDS: Testosterone replacement therapy; Hypogonadism; Sexual function; Muscle strength; Bone density; Metabolic syndrome; Cardiovascular outcomes; Cognitive function; Quality of life; Athletic recovery

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1. INTRODUCTION

1.1 Background

Testosterone is a key anabolic hormone responsible for regulating muscle protein synthesis, bone mineral density, erythropoiesis, metabolism, sexual function, and recovery after exercise [1]. In the athletic population, both professional

and recreational, maintaining adequate testosterone levels is essential for preserving lean body mass, muscular strength, and optimal performance [2]. Sports injuries—particularly muscle strains, ligament injuries, and stress fractures—represent a significant burden among athletes, where recovery depends on a complex interplay between

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mechanical rehabilitation, nutrition, and hormonal regulation [3].

Testosterone deficiency, whether absolute or relative, has been associated with impaired muscle healing, reduced exercise tolerance, and delayed rehabilitation outcomes [4]. Furthermore, in recreational athletes, lifestyle factors such as obesity, overtraining, poor sleep, and metabolic disorders can contribute to lower testosterone levels and negatively impact physical performance [5]. Given these challenges, testosterone replacement therapy (TRT) has been explored as a potential strategy to enhance recovery, maintain musculoskeletal health, and improve overall athletic outcomes in men with confirmed deficiency [6].

1.2 Rationale

The clinical importance of testosterone deficiency is underscored by its association with reduced libido, erectile dysfunction, decreased lean body mass, osteoporosis, increased fat mass, fatigue, mood disturbances, and impaired quality of life [1,5]. Testosterone replacement therapy (TRT) aims to restore physiological levels of circulating testosterone, thereby reversing these manifestations and optimizing male health [6]. Over the last two decades, growing evidence has highlighted not only improvements in sexual function but also favorable effects on musculoskeletal strength, bone integrity, metabolic control, and psychological outcomes [2,4,6]. However, while several reviews have addressed TRT in specific populations—such as younger men, older adults, or athletes—there is a need for a comprehensive synthesis that emphasizes its broad clinical benefits across health domains.

1.3 Objective

The objective of this narrative review is to synthesize current evidence on the clinical benefits of testosterone replacement therapy in men, focusing on outcomes related to sexual function, musculoskeletal health, bone metabolism, metabolic and cardiovascular profiles, neuropsychological well-being, and overall quality of life. This review seeks to provide clinicians and researchers with an updated and integrated perspective on the multifaceted role of TRT in male health.

2. METHODS

A comprehensive literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to testosterone and its therapeutic use. The primary keywords included “testosterone replacement therapy,” “TRT,” “hypogonadism,” “androgen deficiency,” “muscle strength,” “athletes,” “metabolic syndrome,” “bone density,” “quality of life,” and “cognitive function.” Boolean operators (AND/OR) were applied to refine the search combinations. The time frame for the literature search was January 1995 to July 2025. Only articles published in English or Spanish and

indexed in peer-reviewed journals were considered. Reference lists of included papers and key reviews were also screened to identify additional eligible studies.

Studies were included if they evaluated the effects of testosterone replacement therapy in men with clinically confirmed testosterone deficiency, reported outcomes in at least one relevant domain such as sexual function, musculoskeletal health, bone metabolism, metabolic or cardiovascular parameters, neuropsychological status, or quality of life, and were designed as randomized controlled trials, observational studies, systematic reviews, meta-analyses, or narrative reviews. Publications had to be available in recognized peer-reviewed journals. Exclusion criteria comprised animal or in vitro studies, case reports or series with fewer than 10 patients, abstracts, conference proceedings, editorials, non-peer-reviewed sources, and articles focusing exclusively on female populations or on testosterone use for non-medical enhancement such as anabolic steroid abuse. Two reviewers independently screened titles and abstracts for relevance, and potentially eligible full texts were retrieved. Any disagreements were resolved through discussion and consensus to ensure that the selected studies provided a representative overview of the clinical benefits of testosterone replacement therapy.

3. CENTRAL BODY

3.1 Sexual Function and Fertility

Testosterone plays a central role in regulating male sexual health, and its deficiency is strongly associated with decreased libido, erectile dysfunction, and impaired sexual satisfaction. Several clinical trials have demonstrated that testosterone replacement therapy significantly improves sexual desire and erectile function in hypogonadal men, particularly when baseline testosterone levels are markedly reduced [7,8]. Improvements in nocturnal penile tumescence and overall sexual satisfaction have also been consistently reported, underscoring TRT’s impact on both physiological and psychological components of male sexual health [9].

Beyond sexual desire and erectile function, TRT has been shown to influence fertility parameters. While exogenous testosterone is known to suppress spermatogenesis through feedback inhibition of the hypothalamic–pituitary–gonadal axis, clinical evidence indicates that restoring physiological testosterone levels in men with true hypogonadism can improve semen volume, sperm motility, and overall reproductive potential when carefully managed [10]. These effects appear most relevant in men with secondary hypogonadism, where pituitary or hypothalamic dysfunction contributes to reduced endogenous testosterone production. TRT has also been associated with broader psychosocial outcomes, as enhanced sexual function contributes to improved relationship satisfaction, quality of life, and psychological well-being [11,12]. Collectively, the evidence highlights the importance of identifying and treating testosterone deficiency not only to restore sexual health but

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also to support fertility potential and holistic well-being in men.

3.2 Musculoskeletal Health

Testosterone is a key anabolic hormone that regulates skeletal muscle growth and maintenance, exerting its effects primarily through stimulation of protein synthesis and inhibition of muscle catabolism. Clinical and experimental evidence demonstrates that testosterone replacement therapy significantly increases lean body mass, improves muscle strength, and enhances physical performance in hypogonadal men [13,14]. These effects are particularly relevant in the prevention of sarcopenia, a condition strongly associated with aging and physical inactivity.

Beyond muscle mass, TRT contributes to faster recovery after musculoskeletal injuries, including ligament and tendon lesions, by promoting collagen synthesis and tissue remodeling [15]. Such benefits have implications not only for aging men but also for recreational athletes, where delayed recovery often limits performance and participation. Studies have shown that testosterone therapy can enhance rehabilitation outcomes when combined with structured resistance training, amplifying gains in strength and endurance [16].

Importantly, increases in muscle mass achieved with TRT translate into functional improvements such as better mobility, reduced risk of falls, and improved exercise tolerance, thereby contributing to both athletic performance and long-term health [17,18]. Collectively, these findings emphasize the role of testosterone as a cornerstone of musculoskeletal integrity and function, supporting its therapeutic use in men with documented deficiency.

3.3 Bone Metabolism and Density

Testosterone plays a fundamental role in skeletal homeostasis by stimulating osteoblast proliferation, reducing osteoclast activity, and enhancing bone mineralization. Hypogonadism is strongly associated with reduced bone mineral density, increased bone turnover, and a higher risk of osteopenia and osteoporosis in men. Clinical studies have consistently shown that testosterone replacement therapy improves bone mineral density, particularly in the lumbar spine and femoral neck, where age-related bone loss is most pronounced [19,20].

Longitudinal trials demonstrate that sustained TRT not only increases bone mineral content but also improves bone geometry and strength indices, translating into a reduced risk of fractures in hypogonadal men [21]. These skeletal benefits are observed both in older adults with late-onset hypogonadism and in younger men with primary or secondary androgen deficiency. Importantly, the beneficial effects of TRT on bone health are amplified when combined with weight-bearing exercise and adequate nutritional support, underscoring the multidimensional approach required for optimal skeletal outcomes [22].

Beyond density, TRT has been associated with reductions in bone turnover markers, reflecting an improved balance

between resorption and formation. Meta-analyses further support the protective role of testosterone on skeletal health, with evidence pointing to clinically meaningful improvements in bone mass and reduced fracture incidence over time [23,24]. These findings confirm TRT as a cornerstone therapy in men with androgen deficiency and skeletal fragility.

3.4 Metabolic and Cardiovascular Outcomes

Testosterone deficiency is strongly associated with metabolic derangements, including increased visceral adiposity, insulin resistance, dyslipidemia, and the development of metabolic syndrome. Clinical and epidemiological studies have consistently demonstrated that low testosterone levels predict a higher risk of type 2 diabetes and adverse cardiovascular outcomes in men. Testosterone replacement therapy has been shown to reduce fat mass, improve insulin sensitivity, and lower fasting glucose and glycated hemoglobin levels, thereby contributing to improved glycemic control in men with hypogonadism and metabolic syndrome [25,26].

In addition to metabolic benefits, TRT has been associated with favorable changes in cardiovascular physiology. Improvements in endothelial function, reductions in arterial stiffness, and enhanced exercise tolerance have been reported, suggesting a protective vascular effect [27]. Several clinical trials also support beneficial effects on lipid metabolism, including reductions in total cholesterol and triglycerides, as well as modest increases in high-density lipoprotein cholesterol [28].

Importantly, long-term observational data indicate that men treated with testosterone exhibit lower rates of major adverse cardiovascular events compared with untreated hypogonadal men, although results remain heterogeneous depending on study design and population [29]. Meta-analyses further support that when TRT is prescribed in appropriately selected patients with adequate monitoring, it exerts neutral to beneficial effects on cardiovascular outcomes [30]. Collectively, these findings underscore the therapeutic potential of TRT in improving metabolic health and reducing cardiovascular risk in hypogonadal men.

3.5 Neuropsychological and Cognitive Effects

Testosterone deficiency has been consistently associated with fatigue, depressed mood, anhedonia, and reduced quality of life. Several randomized trials and meta-analyses suggest that testosterone replacement therapy (TRT) can alleviate depressive symptoms and improve selected domains of cognition and well-being. In a meta-analysis of 27 randomized controlled trials including 1890 men, TRT significantly reduced depressive symptoms, with stronger effects observed at higher dosages [31,32,33]. In terms of cognition, results remain heterogeneous. In healthy older men, testosterone supplementation improved both spatial and verbal memory after six weeks of treatment [31], while the Cognitive Function Trial of the Testosterone Trials found no improvement in verbal memory or executive function after 12

months of therapy in older men with age-associated memory impairment [32].

In the context of major depressive disorder, results have also been mixed. One randomized trial in hypogonadal men with major depression showed no superiority of TRT over placebo in alleviating depressive symptoms, although improvements in sexual function were observed [34]. Conversely, another trial in men with refractory depression demonstrated significant improvement when testosterone gel was used as adjunctive therapy compared with placebo [35]. In patients with mild Alzheimer's disease, testosterone treatment improved caregiver-reported quality of life, although cognitive benefits were modest, suggesting that the neuropsychological effects of TRT may extend beyond cognition to broader aspects of psychological well-being [36].

Taken together, current evidence indicates that TRT may confer positive effects on mood, vitality, and selected cognitive domains in hypogonadal men, although outcomes vary according to population, dose, formulation, and duration of treatment [31,32,33,34,35,36].

3.6 Global Well-being and Athletic Recovery

Beyond specific domains such as sexual, metabolic, and musculoskeletal health, testosterone replacement therapy (TRT) exerts broad effects on global well-being, vitality, and athletic recovery. Hypogonadal men frequently report reduced energy, impaired motivation, and diminished sense of vitality, all of which negatively impact daily functioning and athletic participation. Randomized trials and longitudinal studies have consistently shown that TRT enhances overall quality of life, improves physical activity tolerance, and restores vitality in men with testosterone deficiency [24,37]. In the athletic context, testosterone contributes to faster recovery following strenuous exercise by modulating protein turnover, glycogen replenishment, and muscle repair. Evidence suggests that TRT, when prescribed for hypogonadal men, improves recovery times and decreases the risk of overtraining syndromes, enabling athletes—both professional and recreational—to maintain consistent performance [38]. Enhanced exercise tolerance and reduced fatigue have also been reported, highlighting the hormone's central role in sustaining endurance and physical resilience [39].

The psychosocial impact of TRT is equally significant. Improvements in self-perception, motivation to engage in physical activity, and overall mood contribute to greater adherence to training regimens and healthier lifestyle choices. Importantly, TRT has been associated with increased participation in structured exercise programs, which synergistically amplifies its benefits on muscle mass, bone health, and cardiovascular function [39]. Collectively, these findings underscore TRT as a multidimensional therapy that not only restores hormonal balance but also enhances recovery, vitality, and global well-being in men with hypogonadism.

4. CONCLUSION

Testosterone replacement therapy (TRT) has demonstrated consistent and clinically meaningful benefits across multiple domains of male health, ranging from sexual function and fertility to musculoskeletal integrity, bone metabolism, metabolic regulation, cardiovascular performance, and neuropsychological well-being. In both clinical populations and recreational athletes with documented hypogonadism, TRT contributes to enhanced vitality, improved recovery, and overall quality of life. The accumulated evidence underscores its role not only in reversing the classical manifestations of testosterone deficiency but also in supporting long-term physical performance and holistic health outcomes. Despite these favorable findings, further large-scale and long-term trials are needed to fully delineate the scope of TRT benefits across diverse populations, especially in younger and recreationally active men. Future research should aim to standardize treatment protocols, optimize dosing strategies, and explore synergistic effects with structured exercise and nutritional interventions. Collectively, the available literature positions TRT as a cornerstone intervention in male health, with the potential to improve not only clinical outcomes but also overall well-being and functional capacity.

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