

Psychological and Psychiatric Effects of Testosterone Therapy in Men: A Narrative Review

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ABSTRACT

Testosterone is a key androgen with significant influence beyond reproductive physiology, extending to mood regulation, cognition, motivation, and overall psychological well-being. Age-related decline in testosterone and hypogonadism have been associated with depressive symptoms, anxiety, fatigue, and reduced quality of life, underscoring the importance of hormonal balance in mental health. This narrative review aimed to synthesize the current evidence on the psychological and psychiatric effects of testosterone therapy (TRT) in men, with emphasis on its role in depression, anxiety, cognition, aging, and psychiatric disorders. A comprehensive literature search was conducted using PubMed, Embase, PsycINFO, and Cochrane Library, covering studies from 1990 to 2025. Eligible publications included clinical trials, systematic reviews, and meta-analyses evaluating the impact of TRT on psychological or psychiatric outcomes in adult men. Evidence suggests that TRT improves vitality, self-confidence, sexual function, and quality of life in hypogonadal men. Significant reductions in depressive symptoms and enhanced cognitive performance have been reported, particularly in older men and those with clinically low testosterone levels. While TRT appears to reduce fatigue and improve mood, results regarding anxiety remain mixed, and its role in conditions such as schizophrenia and bipolar disorder is still exploratory. Importantly, physiological TRT is generally not associated with increased aggression, distinguishing it from the psychiatric risks of supraphysiological anabolic steroid abuse. Testosterone therapy may confer substantial psychological and psychiatric benefits in men with hypogonadism, particularly in mood and cognitive domains. However, limitations such as heterogeneity in study design, diagnostic criteria, and lack of long-term data warrant caution. Future large-scale, multidisciplinary trials are essential to establish standardized guidelines and clarify the long-term psychiatric safety of TRT.

KEYWORDS: Testosterone replacement therapy; Hypogonadism; Mental health; Depression; Cognition.

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1. INTRODUCTION

1.1 Background

Testosterone is a key androgen that plays a fundamental role not only in sexual and reproductive function but also in

psychological well-being and psychiatric health. Beyond its peripheral effects, testosterone acts on the central nervous system through androgen and estrogen receptors distributed in the limbic system, hypothalamus, and prefrontal cortex,

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influencing mood, cognition, motivation, and emotional regulation [1]. Hypogonadism in men has been consistently associated with fatigue, decreased motivation, low self-esteem, depressive symptoms, and impaired quality of life [2]. Age-related testosterone decline, often termed late-onset hypogonadism, has been linked to increased prevalence of depressive and anxiety disorders, highlighting the importance of hormonal balance in mental health [3].

1.2 Rationale

Recent studies suggest that testosterone replacement therapy (TRT) may exert beneficial effects on mood, depressive symptoms, and cognitive function in men with testosterone deficiency [4]. Moreover, testosterone levels have been inversely correlated with the severity of depressive disorders and may serve as a modifiable risk factor for psychiatric morbidity [5]. At the psychological level, improvements in vitality, confidence, and sexual satisfaction after TRT further support its role in enhancing overall mental health and well-being [6]. However, the literature remains heterogeneous, and concerns about risks such as increased irritability or exacerbation of psychiatric symptoms necessitate a balanced and critical review.

1.3 Objective

The objective of this narrative review is to synthesize the current evidence regarding the psychological and psychiatric effects of testosterone therapy in men. We aim to describe its role in mood regulation, cognition, motivation, and psychiatric disorders, as well as to highlight potential risks and future directions for clinical practice.

2. METHODS

2.1 Literature Search

A comprehensive literature search was conducted using the databases PubMed/MEDLINE, Embase, PsycINFO, and Cochrane Library. The search covered publications from January 1990 to July 2025 to capture both early foundational studies and the most recent evidence on the psychological and psychiatric effects of testosterone therapy in men. Keywords and Medical Subject Headings (MeSH) included combinations of: “testosterone,” “testosterone replacement therapy,” “TRT,” “mental health,” “psychological effects,” “psychiatric disorders,” “depression,” “anxiety,” “cognition,” and “quality of life.” Boolean operators (AND, OR) were used to refine the search strategy. Additionally, reference lists of relevant articles and reviews were manually screened to identify further eligible studies.

2.2 Selection Criteria

Inclusion criteria were: (1) studies published in peer-reviewed journals, (2) original clinical studies, systematic reviews, or meta-analyses evaluating testosterone therapy in adult men, (3) outcomes related to psychological parameters (e.g., mood, motivation, self-esteem) or psychiatric conditions (e.g., depression, anxiety, cognitive disorders), and (4) articles available in English.

Exclusion criteria were: (1) animal or in vitro studies, (2) case reports or case series with fewer than five patients, (3) studies involving women or transgender populations, (4) articles focusing exclusively on physical or metabolic outcomes without addressing psychological or psychiatric parameters, and (5) non-peer-reviewed publications such as conference abstracts or opinion pieces.

3. CENTRAL BODY

3.1 Physiological Role of Testosterone in the Brain

Testosterone exerts significant effects on the central nervous system through both androgen receptors and aromatization to estradiol, which acts on estrogen receptors widely distributed in the brain [7]. These receptors are particularly abundant in regions critical for emotional and cognitive processing, including the amygdala, hippocampus, hypothalamus, and prefrontal cortex

[8]. Through these pathways, testosterone influences dopaminergic, serotonergic, and GABAergic neurotransmission, thereby modulating mood, motivation, reward, and stress response [9].

Neuroimaging studies have demonstrated correlations between circulating testosterone levels and structural as well as functional changes in brain areas associated with cognitive control and emotion regulation [10]. For instance, higher testosterone levels have been linked with increased activation of the amygdala in response to emotional stimuli, suggesting a role in vigilance and affective reactivity [11]. In addition, testosterone contributes to neuroplasticity and neurogenesis within the hippocampus, mechanisms that may underlie its protective effects against depressive symptoms and cognitive decline in aging men [12].

3.2 Psychological Effects of Testosterone Therapy

Testosterone replacement therapy (TRT) has been shown to improve multiple aspects of psychological well-being in hypogonadal men. One of the most consistently reported benefits is the reduction of fatigue and enhancement of vitality, which directly translates into improved motivation and overall life satisfaction [13]. Patients often report increased self-confidence and assertiveness, which are thought to be mediated by testosterone’s effects on dopaminergic reward pathways [14].

Another critical domain is sexual health and self-perception. Sexual dysfunction, frequently associated with low testosterone, is linked to reduced self-esteem and strained interpersonal relationships. TRT has been shown to enhance libido and sexual performance, indirectly improving self-image and psychological stability [15].

Cognitive effects of TRT have also gained attention. Evidence suggests potential benefits in memory, attention, and executive functioning, particularly in men with low baseline testosterone levels [16]. While findings are not uniform across all studies, meta-analyses indicate that cognitive improvement may be more pronounced in older men or those with clear hypogonadism [17].

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Overall, psychological outcomes of TRT highlight its potential to enhance quality of life beyond physical health. However, these effects may vary depending on baseline hormonal status, treatment duration, and individual psychosocial context, emphasizing the importance of personalized approaches [18].

3.3 Psychiatric Implications of Testosterone

Among psychiatric conditions, depression has been the most extensively studied in relation to testosterone. Low testosterone levels are frequently observed in men with depressive disorders, and TRT has been associated with significant improvements in mood and reduction of depressive symptoms, particularly in men with hypogonadism [19]. Meta-analyses indicate that TRT may serve as an effective adjunctive treatment for mild to moderate depression, though evidence is less conclusive for major depressive disorder without underlying androgen deficiency [20].

The relationship between testosterone and anxiety remains complex. Preclinical studies suggest that testosterone may exert anxiolytic effects via modulation of GABAergic and serotonergic systems [21]. Clinical evidence, however, is mixed: some studies report decreased anxiety levels following TRT, while others show no significant impact, highlighting the need for further investigation [22].

In schizophrenia, low testosterone levels have been linked to negative symptoms such as social withdrawal and reduced motivation. Preliminary studies suggest that TRT may alleviate some of these symptoms, though large-scale randomized trials are lacking [23]. In bipolar disorder, testosterone has been implicated in mood regulation, with some evidence suggesting a potential role in stabilizing mood and reducing depressive phases, but concerns remain about its possible contribution to manic or aggressive episodes [24]. The relationship between testosterone and aggression has generated considerable debate. While supraphysiological doses of anabolic steroids have been associated with heightened aggression and impulsive behaviors, physiological TRT in hypogonadal men does not appear to significantly increase aggression [25]. Distinguishing therapeutic use from abuse is therefore critical to understanding the psychiatric implications of testosterone.

3.4 Testosterone in Aging and Andropause

Age-related decline in testosterone, often referred to as late-onset hypogonadism or andropause, has profound implications for men's psychological and psychiatric health. This gradual reduction in circulating testosterone typically begins after the fourth decade of life and is associated with symptoms such as fatigue, irritability, reduced motivation, loss of libido, and cognitive slowing [26]. These manifestations frequently overlap with psychiatric disorders, making diagnosis and management challenging in clinical practice.

TRT in aging men has been shown to improve mood, energy, and overall quality of life, particularly in those with symptomatic hypogonadism [18]. Improvements in psychological domains such as vitality, social functioning, and self-perceived health have been documented in randomized controlled trials. Additionally, studies suggest that testosterone supplementation may reduce depressive symptoms and enhance cognitive performance in older men with low baseline testosterone levels, although findings remain heterogeneous [27].

Importantly, not all elderly men with reduced testosterone benefit equally from therapy. Some evidence indicates that individual variability in receptor sensitivity, comorbidities, and psychosocial context may influence treatment outcomes [28]. Furthermore, clinicians must carefully distinguish between normal aging and clinically significant hypogonadism to avoid overtreatment. A personalized approach considering both biological and psychological aspects is therefore recommended in the management of aging men [29].

3.5 Limitations and Future Directions

The current body of literature evaluating the psychological and psychiatric effects of testosterone therapy in men is limited by significant methodological heterogeneity. Many clinical trials differ in study design, duration of therapy, testosterone formulations, and outcome measures, which complicates direct comparisons across studies [30]. Furthermore, numerous studies are restricted by small sample sizes and short follow-up periods, limiting the generalizability of their findings [4].

Another limitation lies in the variability of diagnostic criteria for hypogonadism. Thresholds for defining low testosterone differ between studies, and symptom-based assessments often overlap with primary psychiatric conditions such as depression or anxiety. This overlap makes it difficult to ascertain whether improvements following TRT are due to correction of hypogonadism, direct psychiatric effects, or placebo responses [31].

Future research should prioritize large-scale, randomized controlled trials with standardized diagnostic and outcome measures to more definitively establish the role of TRT in mental health. Special attention should be given to long-term psychiatric safety, as current evidence predominantly addresses short-term effects [32]. In addition, studies integrating endocrinology and psychiatry are needed to explore patient subgroups most likely to benefit, such as men with treatment-resistant depression or negative symptoms of schizophrenia [1].

4. CONCLUSION

Testosterone plays a fundamental role in men's psychological and psychiatric health, influencing mood, cognition, motivation, and overall well-being. Evidence from clinical and experimental studies suggests that testosterone replacement therapy (TRT) may improve symptoms of

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depression, anxiety, vitality, and cognitive performance, particularly in men with clinically confirmed hypogonadism. These benefits highlight the importance of considering hormonal status when evaluating men presenting with psychiatric or psychological complaints, as testosterone deficiency may represent a modifiable factor contributing to mental health disorders.

Despite these promising findings, significant limitations remain. Current evidence is constrained by methodological heterogeneity, variable diagnostic criteria, and a lack of long-term randomized controlled trials specifically targeting psychiatric outcomes. While physiological TRT appears safe and beneficial, risks of overtreatment and misuse—especially in non-hypogonadal populations—must be carefully weighed. Future research integrating endocrinology and psychiatry is essential to identify patient subgroups most likely to benefit and to establish clear guidelines for safe and effective use of testosterone therapy in mental health practice.

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