Efficacy and safety of testosterone treatment in postmenopausal female sexual interest and arousal disorder

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ABSTRACT

Background: Female sexual interest and arousal disorder (FSIAD) is the most prevalent sexual dysfunction in postmenopausal women.

Objective: To systematically review and summarize the existing evidence on the efficacy and safety of testosterone, mainly in transdermal formulations, for the treatment of FSIAD in postmenopausal women.

Method: A systematic review was conducted, including randomized controlled trials, systematic reviews, and meta-analyses. The eligibility of 105 articles was assessed, and 13 were ultimately included in the synthesis following the PRISMA procedure.

Results: Compared with placebo, testosterone was associated with significant improvements in the frequency of satisfactory sexual activity, orgasm, sexual desire, and personal distress related to low desire. Most adverse events were mild and well tolerated. No data indicated severe short-term adverse effects, although long-term safety data remain limited.

Conclusion: The short-term efficacy in improving sexual function and safety of testosterone (especially transdermal) in naturally or surgically menopausal women with FSIAD, either with or without estrogen +/- progestogen hormone therapy, has been demonstrated in this systematic review. Testosterone use was associated with an increase in androgenic adverse effects such as acne or hair growth, but was not associated with any serious adverse effects.

KEYWORDS

Testosterone, menopause, postmenopause, sexual dysfunction, libido, sexual desire, hipoactive sexual desire, sexual arousal disorder.

Introduction

Menopause, whether physiological or iatrogenic, is a life stage characterized by the permanent cessation of ovarian function and is associated with physiological, psychological, and cultural changes that influence sexuality in a biopsychosocial manner.

Female sexual interest and arousal disorder was first described in the diagnostic criteria of the DSM-5, in which, based on the available literature, the assessment of sexual desire and arousal disorders was combined into a single diagnosis [1]. However, many studies on the subject have used the DSM-IV classification, in which hypoactive sexual desire disorder (HSDD) was included within the category of sexual desire disorders and was defined by the absence or significant reduction of sexual thoughts or fantasies and/or desire for and receptivity to sexual activity, causing personal distress [2]. These indicators must persist over time (minimum of 6 months) and cannot be attributed to a mental illness, drug effects, other health problems, or relationship difficulties.

It is estimated that female sexual interest and arousal disorder (FSIAD) affects approximately 1 in 10 women of all ages and is the most prevalent female sexual dysfunction among postmenopausal women. Menopausal status has a significant impact on the prevalence of HSDD, with several studies showing higher rates in women who undergo surgical menopause at younger ages (16%–26%) compared with women in natural premenopause (7%–14%) [3]. In a European sample of women aged 50 to 70 years, the prevalence of HSDD was 9% in women with natural menopause and 12% in women with surgical menopause [2].

The proportion of women with low sexual desire increases with age, whereas the proportion experiencing distress related to low desire decreases over time. These data should be considered when proposing treatment, as a woman who does not report concern or distress about low desire would not meet the diagnostic criteria for

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FSIAD [2]. Low sexual desire is also associated with emotional or psychological distress, low self-esteem, and depression. Therefore, FSIAD leads to a significant deterioration in quality of life [2,3].

When FSIAD is present in postmenopausal women, after excluding other causes such as systemic diseases, mood disorders, and relationship problems, testosterone is an evidence-based therapy and is therefore included in clinical practice guidelines [2]. Despite this biological evidence, barriers to androgen therapy remain among both healthcare professionals and patients. This review analyzes the efficacy, safety, and clinical relevance of testosterone therapy (mainly in transdermal formulations) in postmenopausal women with baseline FSIAD, focusing primarily on randomized placebo-controlled clinical trials.

Methods

Literature search methodology

PubMed and MEDLINE were searched, along with a manual search, for studies published from 2000 to April 2025. To identify all relevant articles, the following search strategy was used: [("testosterone"[MeSH Terms] OR "testosterone"[All Fields]) AND ("menopause"[MeSH Terms] OR "menopause"[All Fields] OR "postmenopause"[MeSH Terms] OR "postmenopause"[All Fields]) AND ("sexual dysfunction, physiological"[MeSH Terms] OR "sexual dysfunction"[All Fields] OR "libido"[MeSH Terms] OR "libido"[All Fields] OR "sexual desire"[All Fields] OR "hypoactive sexual desire"[All Fields] OR "hypoactive sexual desire disorder"[All Fields] OR "sexual arousal disorder"[All Fields])]. This strategy was adapted and applied to different electronic databases.

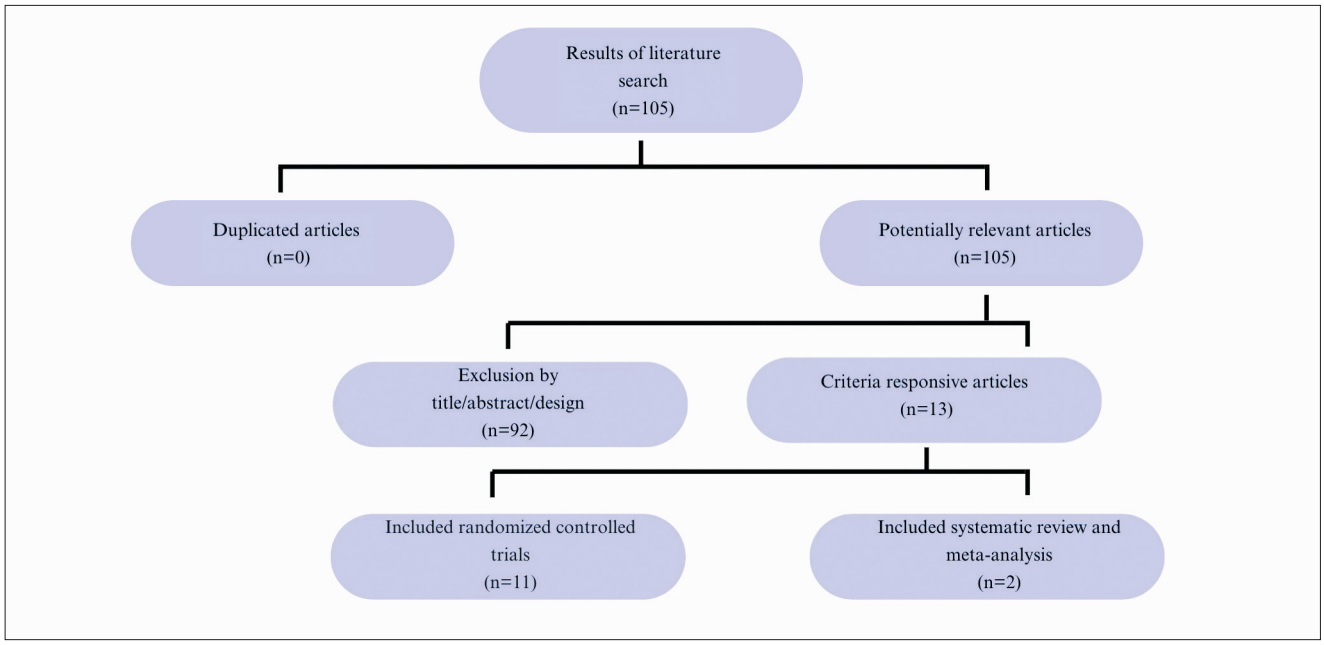
Study selection

The publication time frame was limited including studies from 2000 to 2025. Meta-analyses, randomized controlled trials (RCTs) and systematic reviews were considered in this review. There was no language limitation and publications were included if the full text of the article was available. Articles based on animal models or evaluating other treatments for FSIAD were excluded as were those focusing on male sexuality. Studies were selected if the target population was postmenopausal women (with or without estrogen hormone therapy) and in natural or surgical menopause (with unilateral or bilateral oophorectomy), with FSIAD who were administered testosterone and compared with placebo or no treatment. Studies where the population was premenopausal women with FSIAD were excluded. The testosterone preparation used was in the form of a patch, gel or oral formulation. Studies using dehydroepiandrosterone (DHEA) were excluded, but not those including methyltestosterone. A reviewer (PTC) assessed trial eligibility and selected data from articles that may be most relevant to the treatment of FSIAD with testosterone in postmenopausal women, using a pre-specified protocol (information was collected on trial participant characteristics, type of intervention, how outcomes were measured and quality of studies) and, another reviewer (CCB) checked for any potential errors that may have occurred during data extraction, as outlined in Table 1.

The primary outcome measure was satisfactory sexual activities (SSA). Secondary outcomes were sexual desire (in most studies using the Profile of Female Sexual Function (PFSF)), distress associated with low sexual desire (mostly assessed with the Personal Distress Scale [PDS]), other domains of sexual function (arousal, orgasm, pleasure, sexual self-image), clinical relevance of treatment benefits and adverse effects (AE) in terms of safety and tolerability.

A total of 105 articles were reviewed –104 from the PubMed search and 1 from hand search– and 13 studies (12 from PubMed and 1 from hand search) were ultimately included in the synthesis [2]. The eligibility process is outlined in Figure 1 with a flow chart following the PRISMA statement.

Figure 1. PRISMA Flow-chart showing the article selection process.



Assessment of methodological quality and data extraction

The quality of studies included in the systematic review was assessed using the National Heart, Lung, and Blood Institute (NIH) Study Quality Assessment Tool to evaluate allocation, blinding of participants and investigators, and other sources of bias [4] (Table 2). The final assessment was reached by consensus between the two review authors (PTC and CCB).

Table 2. Quality assessment of the studies included in the systematic review.

Criteria	Buster et al. [4]	Simon et al. [5]	Shifren et al. [6]	Davis et al. [7]	Davis et al. [8]	Braunstein et al. [9]	Nachtigall et al. [10]	Panay et al. [11]	El-Hage et al. [12]	Kingsberg et al. [13]	Lobo et al. [14]
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	YES	NR	YES	YES	NR	NR	NA	YES	YES	YES	NR
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	I	NR	YES	YES	NR	YES	NA	YES	YES	YES	YES
4. Were study participants and providers blinded to treatment group assignment?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
5. Were the people assessing the outcomes blinded to the participants' group assignments?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	NO
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	YES	YES	YES	YES	YES	YES	YES	YES	NR	YES	YES
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	NO	NO	NO	NO	NO	NO	NO	NO	YES	NA	YES
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	NO	YES	YES	YES	YES	YES	NA	YES	YES	NA	YES
9. Was there high adherence to the intervention protocols for each treatment group?	YES	YES	YES	NO	YES	NO	NO	NO	YES	NA	YES
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	YES	NR	NR	YES	NR	NR	NR	NR	NR	NA	NR
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	YES	YES	YES	NR	YES	YES	NO	NR	YES	NR	NR
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
Quality assessment (poor, fair, good)	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	FAIR	GOOD	GOOD	GOOD	FAIR

I: Indeterminate; NA: Not Applicable; NR: Not Reported.

Results

Literature search

The selection process is outlined in Figure 1. Of the 105 publications identified, 13 were selected for evaluation as they met the established inclusion criteria. The remaining 92 articles were excluded, mainly based on the title, but also due to study design and synthesis (Table 3).

Study characteristics

During the study period (2000–April 2025), a large number of studies evaluated the use of testosterone in postmenopausal women, either for the treatment of HSDD or for the assessment of changes in sexual desire in women without a diagnosis of sexual dysfunction. As shown in Table 1, two systematic reviews and 11 RCTs were included, with study populations ranging from 36 to 8,961 participants. Most studies demonstrated improvement in sexual function compared with placebo in postmenopausal women with HSDD; only one study specifically considered the diagnosis of FSIAD. Most studies analyzed transdermal testosterone at 300 μg/day (alone and/or in combination with estrogens +/- progestogens), although other routes of administration and doses were also evaluated.

The most widely used tool to assess sexual outcomes with testosterone treatment was the number of satisfactory sexual activities, although other validated questionnaires were also applied. The trials had a maximum follow-up of 24 weeks for efficacy and up to 4 years for safety.

Table 3. List of articles excluded from the systematic review.

Author. Journal. Year	Author. Journal. Year	Author. Journal. Year
Parish et al. Menopause. 2023	Terrier et Terrier. Prog Urol. 2016	Stevens et al. J Clin Pharm Ther. 2017
Mayer et al. Ann Pharmacother. 2020	Koochaki et al. J Womens Health (Larchmt). 2021	Segraves et al. J Clin Psychopharmacol. 2004
Cacioppo. Sex Med Rev. 2017	Tajik et al. J Obstet Gynaecol. 2022	Basson et al. J Womens Health Gend Based Med. 2002
Gao et al. J Sex Med. 2015	Katz et al. J Sex Med. 2013	Caruso et al. Urology. 2004
Saadat et al. Curr Drug Metab. 2017	Halvaiepour et al. J Sex Marital Ther. 2021	Fabre et al. J Sex Med. 2011
Kingsberg et al. Curr Med Res Opin. 2020	Clayton et al. J Sex Med. 2018	Meston et Worcel. Arch Sex Behav. 2002
Kamrul-Hasan et al. Medicine (Baltimore). 2024	Althof et al. J Sex Med. 2019	Heiman et al. J Psychosom Obstet Gynaecol. 2006
Yazdani et al. BMC Womens Health. 2023	Simon et al. Menopause. 2014	Liao et al. J sex Med. 2008
Razali et al. Curr Neuropharmacol. 2022	Caruso et al. BJOG. 2001	Berman et al. J Urol. 2003
Lim-Watson et al. Sex Med Rev. 2022	Laan et al. J Sex Med. 2008	Kay et al. Hum Psychopharmacol. 2017
Tetik et Ö. J Sex Marital Ther. 2023	Stephenson et Meston. J Sex Med. 2010	De Rogatis et al. J Sex Med. 2009
McCool et al. Sex Med Rev. 2016	Clayton et al. Womens Health (Lond). 2016	Safarinejad et al. BJU Int. 2010
Frühauf et al. Arch Sex Behav. 2013	Leddy et al. J Sex Med. 2012	Basson et Brotto. BJOG. 2003
Gera et al. Anticancer Res. 2018	Bloch et al. Eur Neuropsychopharmacol. 2013	Simon et al. J Sex Med. 2020
Lerner et al. Clinics (Sao Paulo). 2022	van Nes et al. J Sex Med. 2018	Johnson-Agbakwu et al. Clin Ther. 2018
Johnson et al. Obstet Gynecol. 2024	Stanton et al. Behav Res Ther. 2019	Pastor. Ceska Gynekol. 2011
Thurston et al. J Clin Invest. 2022	Meston et al. Arch Sex Behav. 2008	Caruso et al. Fertil Steril. 2006
Jaspers et al. JAMA Intern Med. 2016	Caruso et al. Gynecol Endocrinol. 2018	Diamond et al. J Sex Med. 2006
Thurston et al. JAMA Netw Open. 2022	Tuiten et al. Womens Health (Lond). 2018	Ferguson et al. J Sex Marital Ther. 2003
Ramezani et al. Psychother Res. 2018	de Souza et al. Menopause. 2016	Padma-Nathan et al. J Sex Marital Ther. 2003
Thurman et al. J Sex Med. 2024	Johnson et al. J Sex Med. 2024	Zang et al. Beijing Da Xue Xue Bao Yi Xue Ban. 2010
Kingsberg et al. Obstet Gynecol. 2019	Velten et al. J Consult Clin Psychol. 2024	Claret et al. Pharm Res. 2006
Clayton et al. J Womens Health (Larchmt). 2022	Sadeghi et al. Complement Ther Med. 2020	Bloemers et al. J Sex Med. 2019
Spielmans. J Sex Res. 2021	Vale et al. Gynecol Endocrinol. 2018	Simon et al. J Sex Med. 2019
Alexander et al. Spinal Cord. 2011	Muin et al. Fertil Steril. 2017	Coleman et al. Clin Ther. 2001
Portman et al. J Sex Med. 2017	Akhtari et al. Daru. 2014	Caruso et al. J Sex Med. 2019
Simon et al. J Womens Health (Larchmt). 2022	Goldfischer et al. J Sex Med. 2011	Clayton et al. Clin Ther. 2017
Fabre et al. J Sex Med. 2011	White et al. Am Heart J. 2012	Rubio-Aurioles et al. J Sex Marital Ther. 2002
Thorp et al. J Sex Med. 2012	Chudakov et al. J Sex Med. 2010	Yang et al. Int J Impot Res. 2008
Derogatis et al. J Sex Med. 2012	Poels et al. J Sex Med. 2013	
Farahi et al. J Sex Med. 2024	Van Rooij et al. J Sex Med. 2013	

Table 1. Relevant studies addressing the impact of testosterone as a treatment in postmenopausal women with FSIAD.

Author	Year	n	Design	Population	Intervention	Follow-up	Efficacy results	Safety results	QA
Ribera et al. [2]	2024	8961	Narrative review including 9 randomized double-blind clinical trial controlled with placebo	Postmenopausal women with HSDD	Testosterone in different formulations and doses compared to placebo	From 16 weeks up to 2 years	Moderate therapeutic benefit in the use of T vs. placebo	There is no evidence of severe long-term AE (2 years)	NR
Achilli et al. [3]	2017	3035	Systematic review and meta-analysis including 7 randomized and controlled clinical trials	Postmenopausal women with HSDD	Patches twice weekly: delivering 300 µg of testosterone/day (associated or not with another HTM) (n=1,350) vs. placebo (n=1,379)	24 weeks	Testosterone group vs. placebo: - Significant increase in SSA frequency with testosterone + HTM vs. placebo (p<0.00001) and testosterone (without HTM) vs. placebo (p<0.0001) - Significant increase in sexual desire (PFSF) (p<0.00001) and decreased anxiety (PDS) (p=0.00001)	- Significant increase in androgenic AE, acne and hair growth vs. placebo - There are no significant differences in both groups regarding total AE and/or severe AE	NR
Buster et al. [5]	2005	533	Randomized double-blind clinical trial controlled with placebo	Surgically menopausal women with HSDD (concomitant therapy with oral or transdermal estrogens)	Patches twice weekly: delivering 300 µg of testosterone/ day (n=267) vs. placebo (n=266)	24 weeks	Testosterone group vs. placebo: - Significant increase in SSA frequency (mean change 1.56 vs. 0.73 episodes/4 weeks, p=0.001) - Significant increase in sexual desire (PFSF) (mean change 10.57 vs. 4.29, p<0.001) and decreased anxiety (PDS) (p=0.009)	AE were similar in both groups (p>0.05), with the exception of androgenic AE which are greater in the testosterone group (mostly mild)	Good
Simon et al. [6]	2005	562	Randomized double-blind clinical trial controlled with placebo	Surgically menopausal women with HSDD (concomitant therapy with oral or transdermal estrogens)	Patches twice weekly: delivering 300 µg of testosterone/ day (n=283) vs. placebo (n=279)	24 weeks	Testosterone group vs. placebo: - Significant increase in SSA frequency (△ 2.10 vs. 0.98 episodes/4 weeks, p=0.0003) - Significant increase in sexual desire (PFSF) (p=0.0006) and decreased anxiety (PDS) (p=000.6)	There are no significant differences in both groups with respect to AE	Good
Shifren et al. [7]	2006	549	Randomized double-blind clinical trial controlled with placebo	Women with natural menopause +/- hysterectomy preserving at least 1 ovary (FSH>30 IU/L) + treatment with oral estrogens + treatment with progestogen (if uterus) and with HSDD	Patches twice weekly: delivering 300 µg of testosterone/ day (n=276) vs. placebo (n=273)	24 weeks	Testosterone group vs. placebo: - Significant increase in SSA frequency (mean change 2.1 +/- 0.28 vs. 0.5 +/- 0.23 episodes/4 weeks, p=0.0001) comparable increase with de population ITT (testosterone vs placebo: 1.92 +/- 0.26 vs. 0.5+/-0.21 episodes/4 weeks, p<0.0001) - Significant increase in sexual desire (PFSF) and decreased anxiety (PDS) both with a p=0.0001	There are no significant differences in both groups with respect to AE	Good
Davis et al. [8]	2008	814	Randomized double-blind clinical trial controlled with placebo	Postmenopausal women with HSDD without estrogen therapy	Patches twice weekly: delivering 150 µg of testosterone/day (n=267) o 300 µg of testosterone/ day (n=267) vs. placebo (n=277)	24 weeks (patients were followed up to 52 weeks to provide further safety data)	Testosterone group vs. placebo: - Significant increase in SSA frequency in the group who received 300µg testosterone/ day in comparison with placebo (2.1 vs. 0.7 episodes/4 weeks, p<0.001) but in the group who received 150µg testosterone/ day (1.2 vs. 0.7 episodes/4 weeks, p=0.11) - Significant increase in sexual desire (PFSF) in both doses vs. placebo (300µg p<0.001 and 150µg p=0.04) and decreased anxiety (PDS) (300µg p<0.001 and 150µg p=0.04)	- Androgenic AE are higher in the 300µg group compared to placebo. - 4 breast cancer diagnoses in the group that received testosterone compared to none with placebo	Good

Davis et al. [9]	2006	77	Randomized double-blind clinical trial controlled with placebo	Surgically menopausal women with transdermal estrogen therapy and with HSDD	Patches twice weekly: delivering 300 µg of testosterone/day (n=37) vs. placebo (n=39)	24 weeks	Testosterone group vs. placebo: - Not significant increase in SSA frequency (p=0.06) - Significant increase in sexual desire (PFSF) (p=0.02) and decreased anxiety (PDS)	There are no significant differences in both groups with respect to AE	Good
Braunstein et al. [10]	2005	447	Randomized double-blind clinical trial controlled with placebo	Surgically menopausal women with estrogen therapy and with HSDD	Patches twice weekly: delivering testosterone in dose 150 µg/d (n=107), 300 µg/d (n=110) or 450µg/d (n=111) vs. placebo (n=119)	24 weeks	Testosterone group vs. placebo: - The group who received 300µg testosterone/day in comparison with placebo: significant increase in SSA frequency (p=0.049) and in the sexual desire (p=0.05) - The group who received 150µg testosterone/day showed no significant evidence and the group of 450 µg testosterone/ day similar evidences like 300 µg testosterone/day. Marginally significant linear dose-response trends were observed for SSA and sexual desire at 24 weeks (p=0.06 in both)	There are no significant differences in both groups with respect to AE	Good
Nachtigall et al. [11]	2011	837	Open-label extension of a randomized double-blind placebo-controlled clinical trial	Surgically menopausal women with HSDD and with concomitant therapy with oral or transdermal estrogens	Patches twice weekly: delivering 300 µg of testosterone/day (n=837)	4 years	NR	There is no significant increase over time in new AE, severe AE or withdrawal from the study due to them.	Fair
Panay et al. [12]	2010	272	Randomized double-blind clinical trial controlled with placebo	Natural menopausal women with HSDD	Patches twice weekly: delivering 300 µg of testosterone/day (associated or not with another HTM) (n=130) vs. placebo (n=142)	24 weeks	Testosterone group vs. placebo: - Significant increase in SSA frequency (mean change 1.69 vs. 0.53 episodes/4 weeks, p=0.0089) - Significant increase in sexual desire (PFSF) (p=0.0007) and decreased anxiety (PDS) (p=0.0024)	AE with higher percentage in the placebo group compared to testosterone	Good
El-Hage et al. [13]	2007	36	Crossover study randomized double-blind controlled with placebo	Surgically menopausal women (hysterectomy with uni- or bilateral ovarian excision) + estrogen therapy and with HSDD	Administration of 1% testosterone cream (10 mg of testosterone/day) during 12 weeks	6 months (12 weeks with testosterone/ placebo + 4 weeks of wash-out period + 12 weeks of cross group	Testosterone group vs. placebo: - Significant increase in sexual function (BISF-W) 8.76 vs. 0.54 (p=0.0001) - No significant changes in mood, depression and stress (DASS, p=0.52); POMS, p= 0.76)	There are no significant differences in both groups with respect to AE	Good
Lobo et al. [14]	2003	218	Randomized double-blind clinical trial controlled with placebo	Postmenopausal women with estrogen therapy and with HSDD	Methyltestosterone (1.25 mg) + estrogens (0.625 mg) (n=107) compared with only estrogens (0.625 mg) (n=111)	16 weeks	The combination methyltestosterone + estrogen increases SIQ score significantly more than estrogen alone (2.8 ± 1.6 vs. 2.4 ± 1.4, p 0.047), sexuality being a secondary result	- Common AE with higher incidence in the methyltestosterone + estrogen group vs the estrogen group - Severe AE: one case of endometrial hyperplasia in each group	Fair
Kingsberg et al. [15]	2007	132	Post hoc study of 2 randomized double-blind clinical trial controlled with placebo (N=1094)	Surgically menopausal women and estrogen therapy with HSDD	Patches twice weekly: delivering 300 µg of testosterone/day (n=64) vs. placebo (n=68)	24 weeks	- 52% of women with T in front of 32% of women with placebo (p= 0.025) reported significant improvements regarding their clinic ≥ 90% of women who reported improvement with T would continue with treatment if it were available	NR	Good

QA: Quality Assessment; NR: Not Rated; HTM: Hormonal Treatment of Menopause; BISF-W: The Brief Index of Sexual Function for Women, ITT: Intention-To-Treat; SAL: Sexual Activity Log; DASS: Depression, Anxiety and Stress Scale; POMS: Profile of Mood States; SIQ: Sexual Interest Questionnaire; PDS: Personal Distress Scale; PFSF: Profile of Female Sexual Function.

Primary outcome measure: satisfactory sexual activity

Several studies have shown that transdermal testosterone at 300 μg/day improves satisfactory sexual activity (SSA) compared with placebo [2,3,5–12] (Table 1). In women with surgical menopause (WSM), the 300 μg/day testosterone patch significantly increased SSA, with a mean change of 1.56 activities per 4 weeks (corresponding to a 51% increase from baseline) compared with 0.73 activities per 4 weeks in the placebo group (p<0.001) [5] (Table 1). In this same study, significant differences were observed as early as week 5. Braunstein et al. [10] (Table 1), using a similar design in women with WSM, also reported a significant improvement from baseline of 0.58 SSA per week, representing a 79% increase, compared with a 43% increase in the placebo group (p=0.049).

Similarly, in women with natural menopause (WNM), administration of the 300 μg/day testosterone patch resulted in a mean change of 2.1 ± 0.28 versus 0.5 ± 0.23 SSA per 4 weeks compared with placebo (p<0.0001) [7] (Table 1).

In a study of postmenopausal women not receiving estrogen therapy, a significant increase in SSA frequency was reported in the group receiving 300 μg/day of testosterone compared with placebo (2.1 vs. 0.7 episodes per 4 weeks, p<0.001) [8] (Table 1).

One study [9] (Table 1) reported a non-significant increase in SSA frequency when comparing testosterone with placebo (p=0.06). However, analysis within the testosterone group alone showed a significant increase from baseline (p<0.0001), corresponding to a 148% improvement over baseline values.

In two studies [8,10], the 150 μg/day testosterone patch showed no significant improvement in SSA compared with placebo (1.2 vs. 0.7 episodes per 4 weeks, p=0.11) [8] (Table 1). The 450 μg/day testosterone patch produced results similar to those observed with the 300 μg/day dose, but with a higher incidence of adverse events [10] (Table 1). Treatment with a 1% testosterone cream (10 mg testosterone/day) resulted in a significant improvement in sexual function, as measured by the BISF-W, with a change of 8.76 versus 0.54 with placebo (p=0.0001) [13] (Table 1).

Secondary outcome measures

Sexual desire an associated distress

Most studies reported a significant increase in sexual desire and a significant decrease in distress associated with low desire. These domains were mainly assessed using the PFSF for sexual desire and the PDS for distress [3,5–7,9,12] (Table 1). Similar effects were observed at both testosterone patch dosages (150 μg and 300 μg). Davis et al. [8] (Table 1) showed a significant increase in sexual desire (PFSF) at both doses versus placebo (300 μg p<0.001; 150 μg p=0.04), along with a decrease in distress (PDS) (300 μg p<0.001; 150 μg p=0.04). In the study using 1% testosterone cream [13] (Table 1), no significant changes were observed in mood, depression, or stress, as assessed by the DASS (Depression, Anxiety and Stress Scale; p=0.52) and the POMS (Profile of Mood States; p=0.76).

It should also be noted that the combination of methyltestosterone plus estrogen significantly increased the SIQ (Sexual Interest Questionnaire) score compared with estrogen alone (2.8 ± 1.6 vs. 2.4 ± 1.4, p=0.047), with sexuality as a secondary outcome [14] (Table 1). Improvements were also observed in other domains of sexual function, including arousal, orgasm, pleasure, self-image, and reduced worry [5,9] (Table 1).

Clinical relevance of treatment benefits

Efficacy data are less meaningful without corresponding clinical relevance. In this regard, one study [15] (Table 1) showed that a significantly higher proportion of women in the testosterone group reported a meaningful overall benefit compared with those receiving placebo (33 of 64 women (52%) in the 300 μg/day testosterone patch group vs. 21 of 68 women (31%) in the placebo group; p=0.025). Women receiving testosterone were also significantly more likely to report that the treatment met their expectations than those receiving placebo (30 of 64 women (47%) vs. 18 of 67 women (27%); p=0.03).

Women who reported a benefit were significantly more likely to express willingness to continue testosterone treatment [15] (Table 1). More than 85% of women who experienced a significant benefit reported they were probably or definitely interested in continuing treatment, whereas more than 90% of women who did not experience a significant benefit reported they were probably or definitely not interested in continuing treatment [15] (Table 1).

Adverse effects impacting safety and tolerability

The incidence of androgenic adverse effects (acne and hair growth), mostly mild, was significantly higher in the testosterone group compared with placebo, but there were no significant differences in changes in facial hair [7,9,12,15]. No differences were observed between groups in alopecia or voice deepening [15]. Overall, there was no significant difference in the total number of adverse effects or severe adverse events.

Lipid profile, carbohydrate metabolism, cardiometabolic markers, and renal and hepatic function were not adversely affected. However, recommendations do not extend to women with cardiovascular disease, as they were not included in the clinical trials [2].

In one study [8] (Table 1), breast cancer was detected in three women assigned to the testosterone group (one of whom later reported symptoms before randomization, and one of the other two was diagnosed only after four months of therapy). An additional case of breast cancer was reported in one of the testosterone groups at the end of the study extension. The study authors noted that the excess cases of breast cancer in women treated with testosterone could be due to chance; however, they also suggested that a possible causal relationship should be considered. Some epidemiological studies have shown an association between endogenous or exogenous testosterone and breast cancer risk, while others have not. The article [8] also noted that some data suggest that adding testosterone to estrogen plus

progestogen regimens may enhance hormonal stimulation of the breast, and that long-term data from large clinical trials on testosterone use are lacking.

One article [16] reported abnormal uterine bleeding, but no increased risk of endometrial hyperplasia or cancer was detected (biopsy showed atrophy or insufficient tissue). Another article [13] reported the development of virilization after a minimum of six months of treatment with intramuscular testosterone and also described clitoromegaly associated with long-term use of injectable androgen and estrogen therapy.

Discussion

For many years, testosterone has been prescribed to women to relieve a variety of symptoms, although its true risks and benefits remained uncertain [2]. Over the last two decades, however, researchers have devoted significant effort to clarifying its safety and therapeutic value. Transdermal delivery systems—namely patches and gels—offer noninvasive alternatives to injections, avoiding first-pass hepatic metabolism and enabling more physiological delivery through direct skin absorption. However, the two modalities differ in absorption kinetics, variability, ease of use, side-effect profiles, and practical clinical considerations [17]. The patch produces a mean testosterone profile that more closely mimics the circadian rhythm, whereas the gel appears to have greater inter- and intra-subject variability [18]. Both gels and patches effectively raise serum testosterone into the physiological range and improve symptoms of hypogonadism (low libido, mood changes, and loss of muscle mass) [19]. Because patches more closely mimic circadian rhythms while gels produce a flatter profile, some clinicians may prefer the patch when circadian hormonal patterns are a key consideration; conversely, gels may provide more flexibility in dosing and application site [20].

Current evidence suggests that systemic transdermal testosterone, administered at a physiological premenopausal dose (300 µg/day), provides a moderate improvement compared with placebo in postmenopausal women with HSDD unrelated to modifiable causes or comorbidities [21]. Importantly, no severe short-term adverse effects have been documented. Combined approaches that also address psychological and sociocultural factors remain valuable [22]. If testosterone therapy is pursued, counseling should be provided within a biopsychosocial model of sexuality, framing testosterone not as a cure but as a pharmacological aid within a broader, complex process.

Although multiple reviews have addressed testosterone therapy in postmenopausal women, this review emphasizes study populations and measurement tools, underscoring the need for more rigorously designed trials. Only three studies [5,6,12] used psychometric instruments that meaningfully assess female sexual desire and enrolled appropriate participants (postmenopausal women with diagnosed sexual dysfunction). Even with this stricter lens, the findings remain aligned with current scientific society recommendations for systemic transdermal testosterone in postmenopausal women with FSIAD. Still, further well-designed studies are necessary.

There is consensus among multiple international societies recommending testosterone therapy for postmenopausal women with decreased sexual interest (with or without reduced arousal) that causes personal or relational distress and who seek treatment.

Based on the studies evaluated in this review, testosterone therapy—mostly assessed in transdermal formulations at a dose of 300 µg/day—has shown statistically significant and consistent improvements in postmenopausal women with FSIAD across several domains of sexual function. These include the frequency of satisfactory sexual activities, sexual desire, orgasm, pleasure, sexual self-image, and personal distress associated with low sexual desire, in both women with natural and surgical menopause, with or without concomitant estrogen +/- progestogen therapy.

Testosterone therapy is generally well tolerated, with the most frequent adverse effects being mild and androgenic in nature (i.e. acne and hair growth). No significant differences were observed between testosterone-treated groups and placebo in either the total number of adverse effects or the incidence of severe adverse events. Long-term safety data (up to four years) generally show no major adverse events in laboratory parameters.

Patient selection is important. For women with sensitive skin or frequent irritation, gels may be preferable. For those who value a "set-and-forget" device and do not have issues with patch adhesion, a patch may offer more physiological circadian mimicry. Counseling is critical when using gels: patients must understand the risk of transfer to others, the need to apply the product to dry, intact skin, allow it to dry before dressing, and avoid contact with others for a defined period.

Overall, this review consolidates key information on the utility of testosterone in treating female sexual interest and arousal disorder in postmenopausal women, emphasizing its established efficacy and generally favorable safety profile. However, data remain limited regarding well-being, bone health, cognition, menopausal symptoms, mood disorders, breast cancer, cardiovascular disease, and long-term safety.

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Conflict of interest
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