

Serious Adverse Events Following Subcutaneous Testosterone Pellet Therapy in Women: A Structured Narrative Review of Published Case Reports

Lucas Caseri Câmara¹, Matheus Hissa Lourenço Ferreira²^a

¹ Department of Clinical Anabolism, College of Governance, Engineering, and Education of São Paulo - FGE-SP, São Paulo, Brazil., ² School of Physical Education, Physical Therapy, and Occupational Therapy, Federal University of Minas Gerais (UFMG)

<https://doi.org/10.64551/001c.163676>



Inquisiva Open

Vol. 2, Issue 1, 2026

Abstract

Objectives

To identify and critically examine published case reports describing serious adverse events potentially associated with subcutaneous testosterone pellet therapy in women, and to assess the strength of the available evidence regarding the safety of this intervention.

Methods

A structured narrative review was conducted following the PRISMA 2020 framework for study identification and selection. PubMed/MEDLINE, Embase, Scopus, and Web of Science were searched from inception to May 12, 2026. Eligible publications were case reports describing women exposed to subcutaneous testosterone pellets who experienced serious adverse events. Methodological quality of included reports was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Case Reports. Findings were synthesized narratively.

Results

The search identified 74 records, of which three case reports met the eligibility criteria. Reported serious adverse events included non-arteritic cilioretinal artery occlusion, severe psychiatric manifestations, and portomesenteric venous thrombosis. The strength of the association varied across reports, and definitive causality could not be established in any case. Methodological reporting quality was generally high, although intervention details were unclear in two reports.

Conclusions

The published case-report evidence identified in this review comprised only three reports. Although theoretical concerns exist regarding dose variability and supraphysiologic exposure with testosterone pellet therapy, published reports of serious adverse events in women remain scarce. These findings highlight the need for improved pharmacovigilance and higher-quality studies.

Keywords: Testosterone, Women, Adverse Drug Reactions, Case Reports, Drug Safety

^a Corresponding Author

Matheus Hissa Lourenço Ferreira

Email: mhlf@ufmg.br

School of Physical Education, Physical Therapy, and Occupational Therapy, Federal University of Minas Gerais (UFMG)

1. INTRODUCTION

Testosterone is a physiologically relevant androgen in women, produced by the ovaries, adrenal glands, and peripheral conversion of steroid precursors.¹ Although historically perceived as predominantly a male hormone, testosterone contributes to female sexual function and several broader physiological processes.^{1,2}

The most established evidence-based indication for testosterone therapy in women is the treatment of hypoactive sexual desire disorder (HSDD) in carefully selected postmenopausal women.²⁻⁴ International consensus statements and clinical practice guidelines acknowledge that appropriately dosed testosterone therapy may improve sexual desire and related aspects of sexual function in this population, while emphasizing the importance of maintaining physiologic dosing and avoiding supraphysiologic exposure.^{2,4}

More recently, alternative administration strategies, including short-term and on-demand testosterone approaches, have also been explored in selected populations, although safety data remain limited and heterogeneous.⁵

Despite these recommendations, important uncertainties remain regarding the long-term safety of testosterone therapy in women, particularly when non-standardized, compounded, or prolonged-delivery formulations are used. Testosterone pellets have gained attention in some clinical settings because of their convenience and sustained hormone delivery. However, concerns persist regarding dose variability, prolonged systemic exposure, limited reversibility once pellets have been implanted, and the potential for supraphysiologic serum testosterone concentrations.²⁻⁴

Serious adverse events attributed to testosterone therapy in women are frequently discussed in clinical and public discourse, yet the extent to which such concerns are supported by peer-reviewed case-based evidence remains unclear. While case reports do not establish incidence or causality, they remain valuable for the early detection of rare or unexpected safety signals and for generating clinically relevant hypotheses regarding potential harm.^{6,7}

Given the ongoing debate regarding the safety of subcutaneous testosterone pellet therapy in women, this review aimed to systematically identify and critically examine published case reports describing serious adverse events potentially associated with this intervention.

2. METHODS

2.1. REVIEW DESIGN

This was a structured narrative review of published case reports describing serious adverse events potentially associated with subcutaneous testosterone pellet therapy in women. The study identification, screening, eligibility assessment, and selection process were conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.⁸ Given the descriptive nature of case-based evidence, clinical heterogeneity of the adverse events, and the

small number of eligible reports, findings were synthesized narratively rather than quantitatively.

2.2. SEARCH STRATEGY

A structured literature search was conducted to identify published case reports describing adverse events potentially associated with subcutaneous testosterone pellet therapy in women. The electronic databases PubMed/MEDLINE, Embase, Scopus, and Web of Science were systematically searched from inception to May 12, 2026.

The search strategy was specifically designed to identify case-based reports involving subcutaneous testosterone pellet therapy, combining terms related to testosterone pellets, testosterone implants, and subcutaneous testosterone, along with filters or equivalent search terms for case reports. Complete database-specific search strategies are provided in [Supplementary Table S1](#).

Given the exploratory pharmacovigilance-oriented objective of this review, case reports were intentionally selected as the primary evidence source because they provide individualized clinical descriptions of uncommon or serious adverse events, allowing assessment of temporal association, clinical evolution, alternative explanations, and potential causal plausibility.

2.3. SEARCH SENSITIVITY ANALYSIS

To enhance sensitivity and minimize the risk of missing relevant reports due to indexing limitations of the automatic case report filter, an additional search was performed in PubMed/MEDLINE on June 13, 2026, without using the case reports filter. Free-text terms for study design (“case report”, “case reports”, “case series”) and broader exposure terms (“testosterone therapy”, “androgen therapy”, “testosterone replacement therapy”) were added to the original strategy. This supplementary search did not identify any additional eligible case reports ([Supplementary Table S2](#)).

2.4. ELIGIBILITY CRITERIA

A serious adverse event (SAE) was defined according to the International Council for Harmonisation (ICH) E2A guideline as an event resulting in death, life-threatening illness, hospitalization, persistent disability, or another medically important outcome.⁹ Eligible publications were case reports describing women exposed to subcutaneous testosterone pellet therapy in whom a reported SAE was considered potentially associated with the intervention.

Studies were excluded if they involved male participants; did not include exposure to subcutaneous testosterone pellets; failed to describe an individualized SAE; lacked sufficient clinical detail to establish at least a plausible temporal relationship between testosterone exposure and the reported outcome; or consisted of review articles, editorials, conference abstracts without adequate case-level information, or other non-case-based publications.

2.5. STUDY SELECTION

Study selection was conducted independently by the two authors in a two-stage screening process.

First, titles and abstracts of all retrieved records were screened for potential eligibility. Full texts were subsequently obtained and assessed for studies considered potentially relevant after initial screening. Discrepancies regarding eligibility were resolved through discussion and consensus.

2.6. DATA EXTRACTION

For each included case report, data were extracted using a standardized approach, including author and year of publication, patient age and relevant clinical characteristics, indication for testosterone therapy (when reported), testosterone formulation, dose and duration of exposure, reported serum testosterone concentrations (when available), characteristics of the adverse event, relevant comorbidities or potential confounding risk factors, management of the adverse event, clinical outcome and follow-up, and the authors' interpretation regarding possible causal association. Given the expected clinical heterogeneity and the inherently descriptive nature of case-based evidence, findings were synthesized narratively rather than quantitatively.

2.7. METHODOLOGICAL QUALITY APPRAISAL

Methodological reporting quality of the included case reports was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports,¹⁰ which evaluates completeness and transparency across eight domains, including patient description, clinical history, diagnostic assessment, intervention details, outcomes, adverse event reporting, and clinical lessons. Given the nature of case report evidence, this appraisal was intended to assess reporting quality and methodological completeness rather than formal comparative risk of bias.

2.8. DATA SYNTHESIS AND ANALYTICAL APPROACH

Given the small number of eligible reports, clinical heterogeneity of the adverse events, and the descriptive nature of case-based evidence, quantitative synthesis, incidence estimation, and formal causal inference were not attempted. Instead, this review adopted a case-based translational evidence synthesis approach, integrating individual clinical observations with broader pharmacovigilance and clinical safety considerations. The objective was not to estimate event frequency, but rather to examine the availability, characteristics, and interpretive value of published serious adverse event reports involving testosterone pellet therapy in women.

3. RESULTS

The structured literature search across PubMed, Embase, Scopus, and Web of Science identified a total of 74 records.

After removal of 37 duplicate records, 37 unique records remained for title and abstract screening. Following initial screening, five case reports were considered potentially eligible for full-text assessment. Of these, two were excluded for failing to meet the predefined eligibility criteria, and three case reports were ultimately included in the review for describing adverse events potentially associated with subcutaneous testosterone pellet therapy in women ([Figure 1](#)). A supplementary search in PubMed without the automatic case-report filter and with additional free-text terms for study design and exposure identified no further eligible case reports. The excluded full-text studies and the corresponding reasons for exclusion are detailed in [Supplementary Table S3](#).

3.1. CHARACTERISTICS OF INCLUDED CASE REPORTS

The three included case reports described clinically distinct serious adverse events reported in peri- or postmenopausal women receiving subcutaneous testosterone pellet therapy.¹¹⁻¹³ Reported events included non-arteritic cilioretinal artery occlusion, severe psychiatric manifestations occurring in the context of markedly elevated serum testosterone concentrations after prolonged pellet use, and portomesenteric venous thrombosis in a postmenopausal woman with multiple pre-existing thrombotic risk factors.¹¹⁻¹³ The interval between testosterone exposure and event presentation ranged from 1 month to more than 10 years, and supraphysiologic testosterone concentrations were documented in two reports. Relevant coexisting clinical factors included retinal migraine, obesity, chronic obstructive pulmonary disease, elevated hematocrit, and a personal or family history of psychiatric disorders. Detailed clinical characteristics of the included case reports are summarized in [Table 1](#). Considerations regarding temporal relationships, potential confounding factors, dechallenge/rechallenge findings, and overall interpretation of the reported events are presented in [Supplementary Table S4](#).

3.2. METHODOLOGICAL QUALITY ASSESSMENT

Methodological reporting quality of the included case reports was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports,¹⁰ a standardized tool designed to evaluate the completeness and transparency of case report reporting across eight domains, including patient characteristics, clinical history, diagnostic assessment, intervention, outcomes, adverse events, and key clinical lessons. Most appraisal criteria were fulfilled across the included reports ([Figure 2](#)). Two reports were rated as unclear for the intervention-description domain because details regarding the testosterone pellet formulation and administration were incompletely reported. Item-level JBI judgments and supporting rationale for each assessment are presented in [Supplementary Table S5](#).

Table 1. Clinical Characteristics, Testosterone Exposure, and Adverse Events Reported in Included Case Reports

Author (Year)	Patient characteristics	Indication for therapy	Testosterone exposure	Time to event	Testosterone level (timing)	Relevant risk factors / laboratory findings	Adverse event	Management	Outcome	Causality assessment
Andoh & Light (2026) ¹¹	48-year-old perimenopausal woman	Low testosterone / menopausal symptoms	Subcutaneous testosterone pellets (dose and schedule not reported)	1 month	228 ng/dL (measured after implantation, at time of event)	Retinal migraine; hormonal acne; spironolactone use; negative thrombophilia/stroke work-up; CRP 1.7 mg/dL	Non-arteritic cilioretinal artery occlusion with acute central scotoma	Antiplatelet therapy, aspirin, statin; pellet removal not feasible	Partial visual improvement over 6 weeks; retinal whitening resolved; residual visual field defect persisted	Possible association
Daram et al. (2024) ¹²	58-year-old postmenopausal woman	Libido and energy improvement	Testosterone pellets for >10 years; dose escalation from 200 mg to 250 mg	Long-term exposure; recurrence after re-exposure	Peak 1,171 ng/dL (June 2021); repeat 962 ng/dL; after re-exposure 264 ng/dL; subsequently 144–153 ng/dL	Personal anxiety history; family history of mood and psychotic disorders; concomitant use of GABA, L-theanine, and St. John's wort	Severe psychiatric manifestations (insomnia, agitation, anxiety, paranoid delusions, impulsive thoughts)	Psychiatric hospitalization (2 weeks); psychotropic medications; testosterone discontinuation	Gradual symptom resolution after discontinuation; recurrence after re-exposure; asymptomatic off therapy	Association supported by temporality, dechallenge, and positive rechallenge
Campitruz et al. (2021) ¹³	55-year-old postmenopausal woman	Reduced libido / hypoactive sexual desire	Testosterone pellet therapy (implant; dose and schedule not reported)	2 months	182 ng/dL (measured at time of thrombosis)	Obesity (BMI 30.5 kg/m ²); COPD; hemoglobin 17.5 g/dL; hematocrit 52%; chronic hypoxia	Portomesenteric venous thrombosis with acute abdominal pain	Anticoagulation (LMWH followed by rivaroxaban); testosterone discontinued	Clinical improvement; partial recanalization; no recurrence during follow-up	Possible association

Note: All cases fulfilled the ICH E2A criteria for serious adverse events (persistent disability, hospitalization, or important medical event requiring intervention).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; LMWH, low-molecular-weight heparin. Testosterone concentrations are reported as described in the original case reports. Where information was not available in the source reports, this is indicated as 'not reported'.

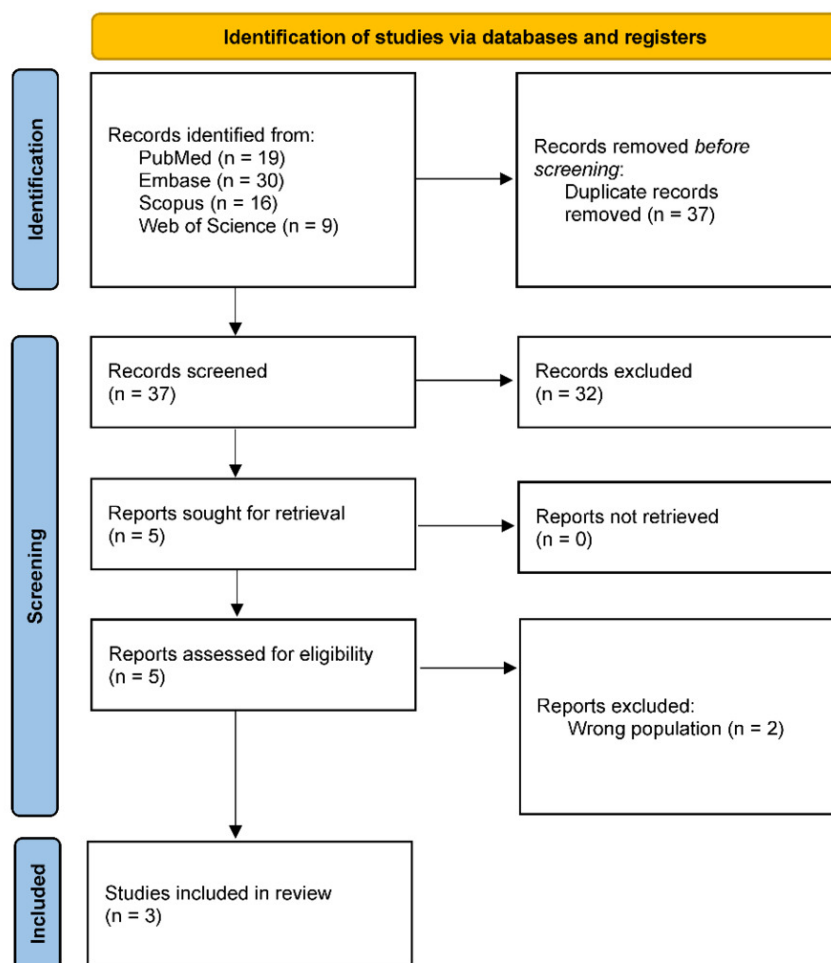


Figure 1. PRISMA 2020 Flow Diagram of Study Identification, Screening, Eligibility Assessment, and Inclusion

4. DISCUSSION

The principal finding of this review was the identification of only three peer-reviewed case reports directly describing adverse events potentially associated with subcutaneous testosterone pellet therapy in women.¹¹⁻¹³ These reports involved clinically significant but heterogeneous events, including non-arteritic cilioretinal artery occlusion, severe psychiatric manifestations, and portomesenteric venous thrombosis. While these events raise legitimate safety concerns, interpretation of causality requires caution.

In the ophthalmologic case, the patient had a prior history of retinal migraine, although extensive systemic evaluation did not identify thrombophilia or another clear alternative etiology.¹¹ In the psychiatric case, the presence of markedly elevated testosterone concentrations, prolonged exposure, dose escalation, and recurrence after re-exposure strengthen the plausibility of a causal relationship, although this scenario may represent supraphysiologic exposure rather than monitored physiologic replacement.¹² In the thrombotic case, the authors acknowledged concomitant prothrombotic risk factors, including obesity, chronic obstructive pulmonary disease, elevated hematocrit, and possible chronic hypoxia.¹³

Taken together, these reports suggest possible safety signals, but they do not establish definitive causality. Their primary value lies in hypothesis generation and clinical vigilance rather than causal inference.¹⁴

4.1. REGULATORY AND CLINICAL CONTEXT

Testosterone therapy in women remains an area of ongoing clinical and regulatory debate. Although testosterone has demonstrated therapeutic benefit in selected clinical contexts, particularly for postmenopausal women with hypoactive sexual desire disorder, concerns remain regarding long-term safety, appropriate dosing, and formulation selection.²⁻⁴

A key distinction must be made between physiologic therapeutic use and supraphysiologic, poorly monitored, compounded, or non-standardized use. This distinction is especially relevant for pellet formulations, which may be associated with prolonged exposure, limited reversibility once implanted, and increased risk of achieving supraphysiologic serum testosterone levels. The psychiatric case identified in this review particularly illustrates this concern, as testosterone concentrations substantially exceeded expected physiologic female ranges.¹²

Patient demographics	Yes	Yes	Yes
Patient history / timeline	Yes	Yes	Yes
Clinical condition	Yes	Yes	Yes
Diagnostic methods	Yes	Yes	Yes
Intervention described	Unclear	Yes	Unclear
Post-intervention condition	Yes	Yes	Yes
Adverse events described	Yes	Yes	Yes
Takeaway lessons	Yes	Yes	Yes
	Andoh & Light (2026)	Daram et al. (2024)	Campitruz et al. (2021)

JBİ appraisal

■ Criterion fulfilled

■ Unclear

Figure 2. Methodological quality assessment of included case reports using the Joanna Briggs Institute (JBİ) Critical Appraisal Checklist for Case Reports

Current clinical recommendations for testosterone therapy in women are limited to carefully selected postmenopausal women with hypoactive sexual desire disorder and are intended to achieve physiologic testosterone concentrations. Both the Global Consensus Position Statement² and the ISSWSH Clinical Practice Guideline⁴ caution against testosterone pellet therapy when it produces supraphysiologic exposure or cannot be adequately titrated after implantation. More specifically, the Global Consensus Position Statement excludes pellets and other supraphysiologic formulations from its physiologic-dose recommendations, while the ISSWSH guideline states that pellets are not recommended because implants may produce supraphysiologic concentrations and do not permit dose titration. These concerns apply specifically to pellet formulations and should be distinguished from compounded testosterone preparations in general, which may or may not share the same pharmacokinetic limitations. However, despite these theoretical concerns, published reports of serious adverse events associated with testosterone pellet therapy in women remain scarce. In the present review, only three case reports describing such events were identified. This discrepancy between guideline caution and the limited published evidence of harm underscores the need for improved pharmacovigilance and higher-quality studies before definitive conclusions about safety can be drawn. A recent structured narrative review similarly concluded that, although testosterone pellets provide long-term delivery, most available data derive from observational studies, and both efficacy and safety remain insufficiently characterized.¹⁵

Thus, concerns raised by inappropriate, poorly monitored, or supraphysiologic pellet use should not be generalized to all evidence-based testosterone therapy in women.

4.2. COMPARISON WITH EXISTING LITERATURE

The findings of the included case reports should be interpreted within the context of the broader evidence base on testosterone therapy in women. Randomized controlled trials and meta-analyses evaluating testosterone therapy for hypoactive sexual desire disorder in postmenopausal women have generally demonstrated reassuring short-term safety profiles when physiologic doses are used, with adverse effects primarily limited to acne, hirsutism, and other mild androgenic symptoms, while serious adverse events remain infrequently reported.^{2-4,16} However, these studies have predominantly evaluated transdermal formulations designed to achieve physiologic testosterone concentrations and allow dose titration or treatment discontinuation when necessary. In contrast, testosterone pellet therapy provides prolonged hormone exposure over several months and may result in supraphysiologic testosterone concentrations, with limited ability to modify or reverse exposure once implanted. Consequently, the serious adverse events described in the present review may not be representative of the safety profile observed with physiologically dosed testosterone therapy using titratable formulations. This distinction highlights an important evidence gap, as long-term safety data for pellet therapy remain limited and uncommon serious adverse events may be underrecognized, underreported, or insufficiently characterized in the existing literature.^{4,15}

4.3. CLINICAL IMPLICATIONS

Case reports remain an important component of pharmacovigilance, particularly for rare or unexpected adverse events. However, attribution of harm to hormonal interventions requires careful interpretation. Meaningful assessment of potential causality depends on adequate documentation of clinical indication, dose, formulation, serum hormone concentrations, duration of exposure, coexisting risk factors, concomitant medications, diagnostic exclusion of alternative causes, clinical evolution after discontinuation, and, when applicable, recurrence after re-exposure.^{6, 7,11-13}

Without such detail, isolated anecdotal observations cannot meaningfully inform risk estimation or clinical decision-making. Clinicians considering testosterone pellet therapy should therefore ensure careful patient selection, risk assessment, dose monitoring, and counseling regarding uncertainties in long-term safety.

4.4. STRENGTHS AND LIMITATIONS

This review has several strengths, including a structured multi-database search, explicit eligibility criteria, a supplementary sensitivity search using broader exposure and case-report terms, and methodological appraisal of included reports using the Joanna Briggs Institute critical appraisal framework.¹⁰ However, important limitations should be acknowledged. First, the analysis was restricted to published case reports, which represent a low level of evidence and are inherently vulnerable to publication bias, incomplete reporting, and uncertain causal attribution. Second, the small number of included reports precludes meaningful generalization regarding incidence, frequency, comparative safety, or the overall risk profile of testosterone pellet therapy in women. Third, spontaneous pharmacovigilance databases, regulatory adverse-event reporting systems, observational studies, and randomized clinical trial safety datasets were not systematically analyzed. Although multiple databases were searched, relevant cases may still have been missed if they were not indexed as case reports or did not use pellet-specific terminology. Therefore, the identification of only three published case reports should not be interpreted as evidence that such events are rare, or as evidence of safety or absence of harm, since underreporting, publication bias, variable clinical recognition, and use of testosterone pellets outside academic settings may all influence the number of cases available in the literature.

4.5. FUTURE RESEARCH DIRECTIONS

The current evidence base underscores the need for more systematic safety evaluation of testosterone pellet therapy in women. Prospective registries, pharmacovigilance analyses, multicenter observational cohorts, and better characterization of dose-response relationships would substantially improve understanding of rare but clinically important adverse events. More transparent reporting of suspected complications would also facilitate more bal-

anced evidence-based regulatory and clinical decision-making.

5. CONCLUSION

The limited number of peer-reviewed case reports identified in this review should not be interpreted as evidence of safety, nor as proof of absence of clinically important risk. Rather, the available literature suggests that serious adverse events may occur under certain circumstances, particularly in the context of supraphysiologic exposure or concomitant risk factors, but remains insufficient to define the true magnitude of risk. Strengthening pharmacovigilance, improving transparency in adverse event reporting, and generating higher-quality safety evidence should be priorities for future research.

CONFLICT OF INTEREST / COMPETING INTERESTS

The authors declare no conflicts of interest relevant to this work.

ETHICS APPROVAL AND CONSENT

This review was based exclusively on previously published literature and did not involve the collection of new data from human participants or animals. Ethical approval and informed consent were therefore not required for this study.

AI TOOL USE DISCLOSURE

Artificial intelligence tools were used for language editing and formatting only. All scientific content, interpretations, references, and conclusions were reviewed and verified by the authors, who accept full responsibility for the final manuscript.

THIRD-PARTY MATERIAL PERMISSIONS

No third-party material requiring permission has been reproduced in this manuscript. The tables and figures were created by the authors based on the data and methods described in the cited sources.

DATA AVAILABILITY

All data analyzed in this review were obtained from previously published sources. The extracted data supporting the findings are presented in the article and its supplementary material.

FUNDING

This research received no external funding.

REPORTING GUIDELINES

The literature search and study-selection process were reported in accordance with the applicable items of the PRISMA 2020 statement.

PREPRINT DISCLOSURE

This manuscript has not been posted as a preprint and has not been previously published.

AUTHOR CONTRIBUTIONS (CREDIT)

Conceptualization: Lucas Caseri Câmara (Lead). Data curation: Lucas Caseri Câmara (Supporting), Matheus Hissa Lourenço Ferreira (Lead). Methodology: Lucas Caseri Câmara (Equal), Matheus Hissa Lourenço Ferreira (Equal). Supervision: Lucas Caseri Câmara (Lead). Writing – original

draft: Lucas Caseri Câmara (Equal), Matheus Hissa Lourenço Ferreira (Equal). Writing – review & editing: Lucas Caseri Câmara (Equal), Matheus Hissa Lourenço Ferreira (Equal). Validation: Matheus Hissa Lourenço Ferreira (Equal). Visualization: Matheus Hissa Lourenço Ferreira (Equal).

ABBREVIATIONS

HSDD, hypoactive sexual desire disorder; ICH, International Council for Harmonisation; JBI, Joanna Briggs Institute; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SAE, serious adverse event.

Submitted: May 12, 2026 EDT. Accepted: June 22, 2026 EDT.

Published: July 02, 2026 EDT.

ISSN: 3068-773X



This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CCBY-4.0). View this license's legal deed at <http://creativecommons.org/licenses/by/4.0> and legal code at <http://creativecommons.org/licenses/by/4.0/legalcode> for more information.

REFERENCES

1. Burger HG. Androgen production in women. *Fertil Steril*. 2002;77 Suppl 4:S3-S5. doi:[10.1016/S0015-0282\(02\)02985-0](https://doi.org/10.1016/S0015-0282(02)02985-0)
2. Davis SR, Baber R, Panay N, et al. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. *J Clin Endocrinol Metab*. 2019;104(10):4660-4666. doi:[10.1210/je.2019-01603](https://doi.org/10.1210/je.2019-01603)
3. Uloko M, Rahman F, Puri LI, Rubin RS. The clinical management of testosterone replacement therapy in postmenopausal women with hypoactive sexual desire disorder: a review. *Int J Impot Res*. 2022;34(7):635-641. doi:[10.1038/s41443-022-00613-0](https://doi.org/10.1038/s41443-022-00613-0)
4. Parish SJ, Simon JA, Davis SR, et al. International Society for the Study of Women's Sexual Health Clinical Practice Guideline for the Use of Systemic Testosterone for Hypoactive Sexual Desire Disorder in Women. *J Sex Med*. 2021;18(5):849-867. doi:[10.1016/j.jsxm.2020.10.009](https://doi.org/10.1016/j.jsxm.2020.10.009)
5. Yin LB, Bernardino RM, Pace K, et al. On-demand testosterone for the treatment of female sexual dysfunction: a systematic review. *Sex Med Rev*. 2026;14(1):qeag014. doi:[10.1093/sxmrev/qeag014](https://doi.org/10.1093/sxmrev/qeag014)
6. Vandenbroucke JP. In defense of case reports and case series. *Ann Intern Med*. 2001;134(4):330-334. doi:[10.7326/0003-4819-134-4-200102200-00017](https://doi.org/10.7326/0003-4819-134-4-200102200-00017)
7. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *J Clin Epidemiol*. 2014;67(1):46-51. doi:[10.1016/j.jclinepi.2013.08.003](https://doi.org/10.1016/j.jclinepi.2013.08.003)
8. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:[10.1136/bmj.n71](https://doi.org/10.1136/bmj.n71)
9. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). *ICH E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting*. ICH; 1994. https://database.ich.org/sites/default/files/E2A_Guideline.pdf
10. Joanna Briggs Institute. *Checklist for Case Reports*. Joanna Briggs Institute; 2020. https://jbi.global/sites/default/files/2020-08/Checklist_for_Case_Reports.pdf
11. Andoh JE, Light JG. Cilioretinal artery occlusion associated with subcutaneous testosterone replacement therapy. *J Vitreoretin Dis*. Published online April 30, 2026. doi:[10.1177/24741264261442954](https://doi.org/10.1177/24741264261442954)
12. Daram N, Wilhoite M, Hurley E, Kaplan M. Psychiatric manifestations in a postmenopausal woman caused by prolonged testosterone pellet therapy. *O&G Open*. 2024;1(4):053. doi:[10.1097/og9.0000000000000053](https://doi.org/10.1097/og9.0000000000000053)
13. Campitruz MZ, Ortiz-Figueroa LT, Santiago E. Portomesenteric venous thrombosis in a postmenopausal female with testosterone implant: a case report. *J Med Case Rep*. 2021;15(1):280. doi:[10.1186/s13256-021-02805-6](https://doi.org/10.1186/s13256-021-02805-6)
14. Murad MH, Sultan S, Haffar S, Bazerbach F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med*. 2018;23(2):60-63. doi:[10.1136/bmjebm-2017-110853](https://doi.org/10.1136/bmjebm-2017-110853)
15. Pinto da Costa Viana D, Jacobsen L, Gabriel LH, et al. Testosterone pellets in women: revisiting safety and clinical outcomes. *Cureus*. 2025;17(10):e94442. doi:[10.7759/cureus.94442](https://doi.org/10.7759/cureus.94442)
16. Islam RM, Bell RJ, Green S, Page MJ, Davis SR. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data. *Lancet Diabetes Endocrinol*. 2019;7(10):754-766. doi:[10.1016/S2213-8587\(19\)30189-5](https://doi.org/10.1016/S2213-8587(19)30189-5)

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Complete electronic search strategies used in PubMed/MEDLINE, Embase, Scopus, and Web of Science for identification of eligible case reports (conducted on May 12, 2026)

Database	Search strategy
PubMed/ MEDLINE	("testosterone pellets"[All Fields] OR "testosterone pellet"[All Fields] OR "testosterone implants"[All Fields] OR "testosterone implant"[All Fields] OR "subcutaneous testosterone"[All Fields]) AND (casereports[Filter])
Embase (Elsevier)	('testosterone pellet':ti,ab,kw OR 'testosterone pellets':ti,ab,kw OR 'testosterone implant':ti,ab,kw OR 'testosterone implants':ti,ab,kw OR 'subcutaneous testosterone':ti,ab,kw) AND ('case report'/exp OR 'case report':ti,ab,kw)
Scopus	TITLE-ABS-KEY ("testosterone pellet" OR "testosterone pellets" OR "testosterone implant" OR "testosterone implants" OR "subcutaneous testosterone") AND TITLE-ABS-KEY ("case report" OR "case reports")
Web of Science Core Collection	TS=("testosterone pellet" OR "testosterone pellets" OR "testosterone implant" OR "testosterone implants" OR "subcutaneous testosterone") AND TS=("case report" OR "case reports")

Supplementary Table S2. PubMed supplementary search strategy for sensitivity analysis (conducted on June 13, 2026)

Database	Search strategy
PubMed/ MEDLINE	("testosterone pellet"[tiab] OR "testosterone pellets"[tiab] OR "testosterone implant"[tiab] OR "testosterone implants"[tiab] OR "subcutaneous testosterone"[tiab] OR "testosterone therapy"[tiab] OR "androgen therapy"[tiab] OR "testosterone replacement therapy"[tiab]) AND ("case report"[tiab] OR "case reports"[tiab] OR "case series"[tiab])

Note: This supplementary search was performed without the automatic case reports publication type filter. No additional eligible case reports were identified.

Supplementary Table S3. Full-text articles excluded after eligibility assessment and reasons for exclusion

Study	Citation	DOI / PMID	Reason for exclusion
Patel MH, Brumfiel CM, Breen I, Glembocki D, Luber A	<i>Granulomatous Panniculitis as a Complication of Subcutaneous Testosterone Pellet Therapy.</i> Skinmed. 2023;21(3):203–204.	PMID: 37634108	Wrong population (male participant)
Chiles K, Provet J, Honig S	<i>Injection site abscess with unpredictable testosterone response is an uncommon complication of testosterone pellet implantation.</i> J Sex Med. 2012;9(Suppl):20–21.	DOI: 10.1111/j.1743-6109.2012.02633.x	Wrong population (male participant)

Supplementary Table S4. Causality Considerations and Potential Confounding Factors in Included Case Reports

Author (Year)	Temporal relationship	Serum testosterone level	Alternative risk factors	Response after discontinuation (dechallenge)	Recurrence after re-exposure (rechallenge)	Overall interpretation
Andoh & Light (2026)	Retinal artery occlusion occurred approximately 1 month after pellet implantation	228 ng/dL at time of event	Retinal migraine; hormonal acne; spironolactone use	Not assessable (pellet removal not feasible)	Not applicable	Possible association
Daram et al. (2024)	Psychiatric symptoms developed during long-term exposure and recurred after therapy re-initiation	Peak 1,171 ng/dL; repeat 962 ng/dL; later 264 ng/dL	Personal anxiety history; family psychiatric history; concomitant supplement use	Symptoms improved after testosterone discontinuation	Symptoms recurred after testosterone re-initiation	Association supported by temporality, dechallenge, and positive rechallenge
Campitruz et al. (2021)	Portomesenteric thrombosis occurred approximately 2 months after implantation	182 ng/dL at time of thrombosis	Obesity; COPD; secondary polycythemia; chronic hypoxia	Clinical improvement after discontinuation and anticoagulation	Not performed	Possible association

Supplementary Table S5. Item-Level Assessment of Included Case Reports Using the JBI Critical Appraisal Checklist for Case Reports

Item	JBI Question	Andoh & Light (2026)	Daram et al. (2024)	Campitruz et al. (2021)	Justification / Notes
1	Were patient's demographic characteristics clearly described?	Yes	Yes	Yes	All reports provided age, sex, and relevant demographic information.
2	Was the patient's history clearly described and presented as a timeline?	Yes	Yes	Yes	Clinical history and temporal sequence of exposure and outcome were reported.
3	Was the current clinical condition of the patient on presentation clearly described?	Yes	Yes	Yes	Presenting symptoms, examination findings, and clinical context were adequately described.
4	Were diagnostic tests or assessment methods and the results clearly described?	Yes	Yes	Yes	Diagnostic investigations and relevant results were reported in all cases.
5	Was the intervention(s) or treatment procedure(s) clearly described?	Unclear	Yes	Unclear	Andoh & Light: testosterone pellet therapy was reported, but pellet dose, number of pellets, and procedural details were not provided. Campitruz et al.: only a testosterone implant was reported, without information regarding dose, formulation, implantation protocol, or procedural details.
6	Was the post-intervention clinical condition clearly described?	Yes	Yes	Yes	Follow-up outcomes and clinical evolution were described in all reports.
7	Were adverse events (harms) or unanticipated events identified and described?	Yes	Yes	Yes	The adverse event was clearly documented and discussed in each case report.
8	Does the case report provide takeaway lessons?	Yes	Yes	Yes	All reports included clinical implications or recommendations for practice.

Note: "Unclear" was used when the source case report did not provide sufficient information to allow judgment of the criterion. All other items were clearly reported in the original publications.