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INVITED REVIEW

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The efficacy, safety, and outcomes of testosterone use among transgender men patients: A review of the literature

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Abstract

Introduction: Gender dysphoria is the discrepancy between biological sex and gender identity. This can be debilitating for transgender populations, including transgender men (TM), individuals who were assigned female at birth but who identify as men, that can benefit from hormonal therapy with testosterone products to address gender dysphoria.

Methods: We aim to summarize the efficacy, safety profile, and outcomes of the different testosterone replacement treatment (TRT) in the TM population. A search of the published literature regarding the various FDA-approved TRT was performed in PubMed, Web of Science and Cochrane Library from 2007 to date.

Results: We complied two groups of TRT based on route of administration including the conventional testosterone therapies (intramuscular and subcutaneous injectables, and transdermal gels) and newer testosterone therapies (oral, buccal, and nasal gels). For the conventional testosterone therapies, we identified nine studies discussed conventional TRT in TM population including one randomized trial, four prospective studies, one retrospective study and three reviews. For newer testosterone therapies, we identified three studies discussed newer TRT in TM population including one prospective study and two reviews. Articles were then compiled and analyzed. Albeit majority of TRT data stemming from conventional TRT, there appear to be an overwhelmingly safety and efficacy profile in TM population translated with increased free testosterone levels comparable to male range, menses cessation, anxiety/depression decline and improved quality of life.

Conclusion: Testosterone therapy can be impactful for TM population with improved safety, efficiency, quality of life and function. With the rise of the newer FDA-approved TRT, randomized studies are warranted to determine its safety and efficacity in this TM population.

KEYWORDS
buccal testosterone, injectable testosterone, nasal testosterone, oral testosterone, testosterone gels, transgender men

1 | INTRODUCTION

Approximately 0.5% of the world population experiences gender dysphoria, a discrepancy between one's biological sex and gender identity.[1] For this group, gender dysphoria can be debilitating, leading to increased risks of affective, adjustment, and anxiety disorders.[2,3] Traditionally, transgender patients utilize cross-sex hormone therapy to address the impact of gender dysphoria.[4] These therapies have led to improved anxiety and depression among transgender populations after hormonal treatments.[2,5,6] Among transgender men (TM), individuals who were assigned female at birth but who identify as men, testosterone is conventionally used before definite gender-affirming surgeries. Testosterone suppresses female secondary sex characteristics and induces masculinization.[7] Features of the therapy include deepening of the voice, increased body hair, and the cessation of menses.[2,8]

The standard administration of testosterone for TM is an intramuscular or subcutaneous testosterone, short-term release injection, commonly with testosterone cypionate or testosterone enanthate.[9,10] These injectable esters are administered 7–21 days in doses of 100–250 mg and have shown great result in the process of masculinization.[11] Following these injectable esters is testosterone undecanoate, a long-lasting injectable therapy, which has also shown promise in maintaining stable levels of testosterone, estradiol, and dihydrotestosterone.[12,13] Transdermal testosterone gels, the second most conventional form of therapy, have also been more widely used among the transgender population.[10] Although injectables and gels currently dominate the testosterone market, newer formulations and methods of administration have emerged in recent years. Oral, buccal, and nasal delivery systems have begun to be used for testosterone therapies among TM, but there is paucity of data on safety and efficacy of these innovative delivery mechanisms. Figure 1 summarizes up-to-date FDA-approved testosterone therapies for adult-onset hypogonadism.

In this review, we aim to provide up-to-date information regarding the efficacy, safety, and outcomes of conventional and newer testosterone treatments for TM population. Although testosterone therapy has been well documented, its use in transgender patients is

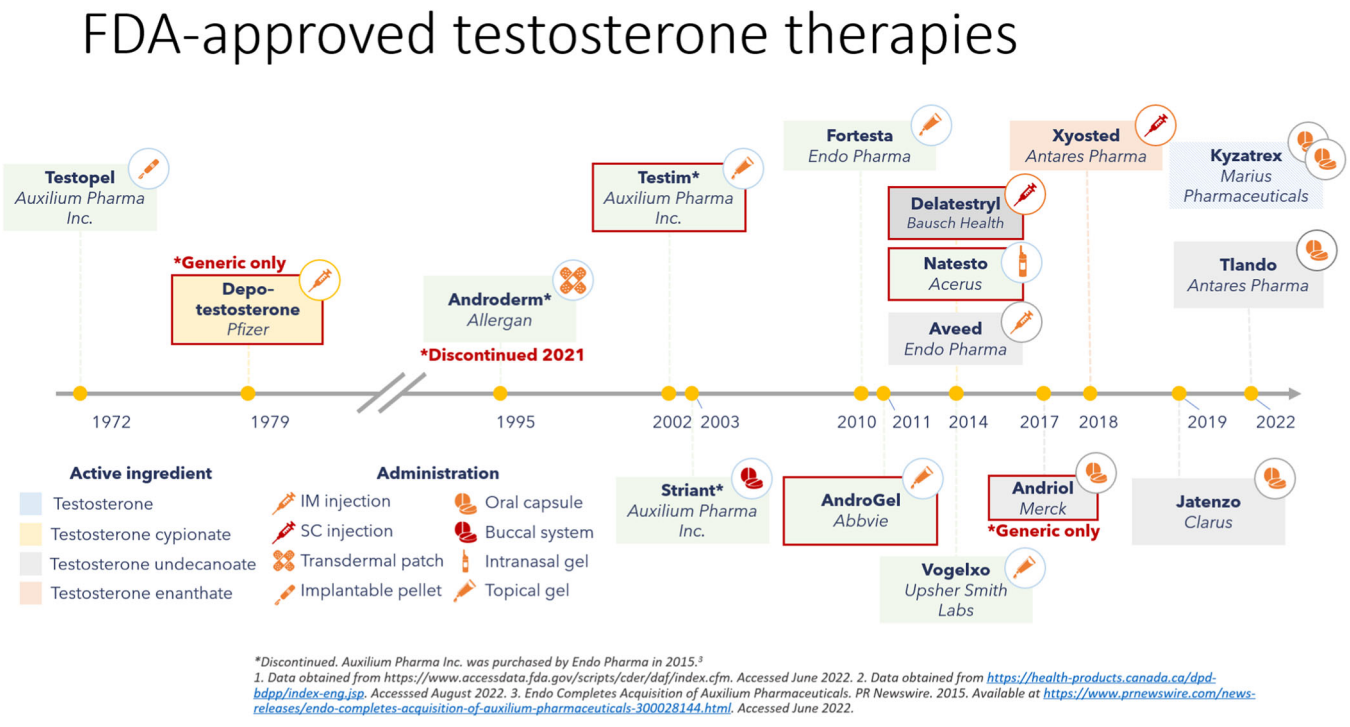

FIGURE 1 List of up-to-date FDA-approved testosterone therapies for adult-onset hypogonadism

limited in the published literature. Furthermore, we hope to provide evidence that can lead to more informed decision-making for health practitioners encountering this at-risk TM population.

2 | METHODS

In this study, we conducted a comprehensive literature review of research articles from 2007 to 2022 via PubMed, Web of Science and Cochrane Database of Systematic Reviews. Search terms with MeSH tool were used for the literature review: TM, injectable testosterone, testosterone gels, oral testosterone, buccal testosterone, nasal testosterone, testosterone outcomes, testosterone efficacy, and testosterone effects. Inclusion criteria for this review were articles that discussed the use, effects, and outcome of testosterone use among TM.

We particularly emphasized articles that reported on the efficacy and outcomes of conventional and newer testosterone therapies among TM in the past decade (Tables 1–4). We complied two groups of TRT based on route of administration including the conventional testosterone therapies (intramuscular and subcutaneous injectables, and transdermal gels) and newer testosterone therapies (oral, buccal, and nasal gels). For the conventional testosterone therapies, we identified nine studies discussed conventional TRT in TM population including one randomized trial, four prospective studies, one retrospective study, and three reviews. For newer testosterone therapies, we identified three studies discussed newer TRT in TM population including one prospective study and two reviews. Articles were then compiled and analyzed.

3 | RESULTS: EVIDENCE SYNTHESIS FOR THIS REVIEW

3.1 | Conventional testosterone therapies: Intramuscular, subcutaneous, and gel testosterone

Short- and long-term intramuscular injections and topical gels are the most common form of testosterone administration for transgender patients. Intramuscular injections have included testosterone cypionate, testosterone enanthate, testosterone propionate, and testosterone ester combination.[14] Advantages of these short-acting injections include general affordability.[14] Disadvantages of these injections include the fact that they require multiple injections and often result in fluctuating serum testosterone levels.[14] For the newer, long-term intramuscular injection, testosterone undecanoate, results show more steady-state serum levels and advantages include less required injections per year.[14] Disadvantages of this injection include its high cost and its invasiveness.[14]

Additionally, 1% testosterone gel is also used for transgender patients. Advantages of the gel is that it achieves serum testosterone concentrations within the male reference range.[15] Disadvantages of gel testosterone include potential transference to another person as well as skin irritation.[16] Despite the advantages and disadvantages of intramuscular injections and topical testosterone gels, they have been widely used in the transgender population. As a result, there has been extensive research conducted on the efficacy, safety, and outcomes of these formulations.

3.2 | Efficacy of conventional testosterone therapies

The most common intended effects of testosterone therapy in transgender patients are to increase free testosterone levels into the normal male range (roughly 450–550 ng/dl),[16] amenorrhea, and deepening of the voice. Other effects include increased facial hair, and for some patients, clitoral enlargement. All of the studies that were included in this review found intramuscular testosterone injections to be effective in producing some or all of these outcomes in the majority of patients. One study of 45 TM patients compared short-acting testosterone enanthate to the longer-acting testosterone undecanoate formulation and a topical gel formulation.[11] All 45 participants achieved amenorrhea and free testosterone levels within a normal male range by 30 weeks.[11] In another study of 85 participants who used intramuscular testosterone enanthate, 87.1% achieved a deepened voice, 52.9% experienced increased facial hair, and 23.5% experienced clitoral enlargement.[17]

Changes in body composition are another common effect of conventional testosterone therapy. Compared to cis-gender women of the same age and race, TM who used testosterone therapy saw an increase in lean muscle mass and a decrease in fat mass at 1-year follow-up.[18] Mueller et al.[19] found that 12 months of testosterone undecanoate therapy produced a significant increase in lean muscle mass without any significant change in BMI, fat mass, or bone mineral density (BMD) in TM.

While intramuscular injection is the most common route of administration for both long- and short-acting testosterone formulations, subcutaneous injections have become increasingly common in recent years. Subcutaneous injection has been found to raise free

TABLE 1 The efficacy of conventional testosterone therapies

Reference	Study type	Testosterone formulation	Efficacy (%)	Efficacy measurement	Pertinent findings
Pelusi et al.[11]	Randomized control	IM testosterone enanthate; IM testosterone undecanoate; topical T-gel	100	TT levels w/in normal male range	Study compared a short-acting IM T formulation, a long-acting IM formulation, and a gel formulation and found no significant difference in efficacy between the three methods of administration.
			100	Amenorrhea	
Kirisawa et al.[17]	Retrospective cohort	IM testosterone enanthate	78.8	Amenorrhea	
			87.1	Deepened voice	
			52.9	Increased facial hair	
			23.5	Clitoral enlargement	
Caenegem, et al.[18]	Prospective case-controlled	IM testosterone undecanoate	[a]	Increased lean muscle mass	
				Decreased fat mass	
Mueller et al.[19]	Prospective cohort	IM testosterone undecanoate	[a]	Increased lean muscle mass	
Olson et al. (2014)	Prospective cohort	Subcutaneous testosterone cypionate	91.4	TT levels w/in normal male range	
			85	Amenorrhea	

[a]These studies did not define efficacy measures in percentages.

testosterone levels to a normal range and induce amenorrhea as effectively as intramuscular injection and has the added advantages of reduced pain and irritation at the injection site and lower risk of infection.[20]

One percent topical testosterone gel was also found to be as effective as both long- and short-acting, intramuscular testosterone injections in raising free testosterone levels and inducing amenorrhea.[11] Pelusi et al. found that participants who used a topical gel testosterone formulation gained similarly significant amounts of lean muscle mass compared to intramuscular formulations.[11] Gel testosterone formulations may also require a lower starting dose for transgender patients than those typically administered to hypogonadal cis-gender men to produce the same effects.[15] Table 1 summarizes the efficacy of conventional testosterone therapies in TM population.

3.3 | Safety of conventional testosterone therapies

While conventional testosterone formulations have been extensively studied and found to be safe for long term use in TM, they are not without their various side effects. A common side effect of intramuscular formulations is pain and swelling at the injection site, hence the shift towards subcutaneous injection which uses a shorter needle.[16] Similarly, troublesome acne and weight gain are common adverse, but nonlife threatening, effects of conventional testosterone treatment.[16,17] Unlike injectable testosterone therapies, topical gel testosterone may cause skin irritation, and increase risk of transference of testosterone to partners or children via skin-to-skin contact.[21]

Hypertension is a frequently reported side-effect of conventional testosterone therapy. In one study of 35 transgender patients, two of them dropped out of the study due to hypertension which was not present at baseline.[22] The hypertension resolved after discontinuation of testosterone treatment.[22] Increased hematocrit, hemoglobin, and LDL and decreased HDL have also been observed. In one study of 53 TM, two developed erythrocytosis, LDL increased by an average of 17.7 mg/dl ($p = 0.006$), and HDL decreased by an average of 8.5 mg/dl ($p < 0.001$).[23] There is also evidence to suggest that intramuscular testosterone formulations may increase hemoglobin levels more than gel formulations.[11] Studies about increased risk of cardiovascular disease, stroke, or venous embolism due to testosterone therapy have been inconclusive.[16,21,24]

Psychological side effects are an additional concern of conventional testosterone therapies. The shorter acting IM testosterone formulations have been found to cause

TABLE 2 The safety profile of conventional testosterone therapies

Study	Study type	Testosterone formulation	Complications	Safety profile	Pertinent findings
Mueller et al.[22]	Observational	IM testosterone undecanoate	Hypertension Troublesome acne	Safe	Two patients dropped out of the study due to clinically significant hypertension which resolved after discontinuation of treatment. Five patients reported troublesome acne (14.3%).
Kirisawa et al.[17]	Retrospective cohort	IM testosterone enanthate	Emotional instability Weight gain Acne	Safe	9.4% of patients in this study reported emotional instability but no life-threatening adverse effects were reported in any patients.
Irwig et al.[20]	Review	Varied	Injection site reactions Troublesome acne	Safe	
Madsen et al.[21]	Review	IM testosterone; testosterone gel	Mood, libido, and energy fluctuations (IM) Transference to close contacts (gel)	Safe	
Wierckx et al.[23]	Retrospective cohort	IM testosterone undecanoate	Erythrocytosis Hypercholesterolemia	Safe	

TABLE 3 The outcomes of conventional testosterone therapies

Study	Study type	Testosterone formulation	Success (%)	Outcomes measurement	Pertinent findings
Pelusi et al.[11]	Randomized control	IM testosterone enanthate; IM testosterone undecanoate; topical T-gel	100	Increased satisfaction with T treatment	
Irwig et al.[16]	Review	Varied	[a]	Reduced fertility Endometrial atrophy Thinning of the vaginal wall Altered breast composition	
Kirisawa et al.[17]	Retrospective cohort	IM testosterone enanthate	7.1	Increased sexual desire	
			2.4	Increased aggression	
			48.2	Mastectomy	
			44.7	Gender-affirming surgery	
Caenegem et al.[18]	Prospective case-controlled	IM testosterone undecanoate	[a]	Increased VBD Increased BMD	Increased VBD was found in the distal radius, and increased BMD was found at the total hip.
Mueller et al.[19]	Prospective cohort	IM testosterone undecanoate	[a]	Decreased circulating estrogen, LH, FSH, and prolactin	
Madsen et al.[21]	Review	IM testosterone; testosterone gel	[a]	Aggression fluctuations	
Moravek[24]	Review	Varied	[a]	Reduced fertility	
Colizzi et al.[26]	Longitudinal	IM testosterone ester	[a]	Decreased anxiety and depression	
Motta et al.[27]	Prospective cohort	Varied	[a]	Increased anger expression	Increased aggression was not accompanied by an increase in aggressive behavior or selfharm.

Abbreviations: BMD, bone mineral density; FSH, follicule-stimulating hormone; LH, leutinizing hormone; VBD volumetric bone density.

[a]These studies did not define outcomes measures in success percentages.

TABLE 4 Newer testosterone therapies, applications, advantages, and disadvantages

Application Site	Formulation	Advantages	Disadvantages
Oral	Testosterone undecanoate	▪ Self-administered ▪ Convenient ▪ Modifiable dosage ▪ Quick reversal	▪ Multiple administrations ▪ Short half-life ▪ Unpredictable absorption ▪ Fluctuating T serum levels ▪ Fatty foods
Buccal	Testosterone	▪ Increased bioavailability ▪ Self-administered ▪ Quick reversal	▪ Skin irritation ▪ Multiple administrations ▪ Altered taste ▪ Poor adhesion
Intranasal	Testosterone	▪ Self-administered ▪ Quick reversal	▪ Multiple administrations ▪ Nostril irritation ▪ Contraindications

hormonal fluctuations immediately after an injection and before the next which can lead to mood swings and drastic changes in sexual desire.[21] Emotional instability was also seen in 9.4% of patients in one study of 85 TM.[17] While symptoms of depression and anxiety typically improve after, transgender patients begin hormone therapy, high doses of testosterone could exacerbate severe mental health issues that are not attributed to gender dysphoria.[24]

Despite these potential adverse effects, testosterone therapy has not been found to increase the risk of cancer for TM. The rates of breast cancer are lower in TM than in cis-gender women, likely because so many trans men opt for mastectomy as part of their transition.[16,25] Cervical and vaginal cancers are also relatively rare in TM and many choose to undergo hysterectomies, oophorectomy, and/or sexual reassignment surgery as part of their transition.[16,25] Table 2 summarizes the safety of conventional testosterone therapies in TM population.

3.4 | Outcomes of conventional testosterone therapies

Testosterone therapy has been shown to reduce depression and anxiety associated with gender dysphoria, and improve quality of life for TM.[11,16] In one longitudinal study of 118 transgender patients, the percentage of patients with anxiety dropped from 50% to 17% after 1 year of testosterone treatment.[26] For depression, the percentage dropped from 42% to 23%. In a study comparing short-acting IM testosterone, long-acting IM testosterone, and testosterone gel, all participants across all three groups reported increased satisfaction with life scores after 54 weeks of treatment.[11] Testosterone therapy may also lead to increased sexual desire and sexual activity.[16,17] The psychological outcomes of conventional testosterone therapy are not all positive, however. Increased anger and aggression are notable side effects for some patients.[17,21,27] One study of 52 TM found a significant increase in anger expression and control scores after 7 months of treatment.[27] Increased anger did not appear to be linked to any increase in risk for self-harm, or psychiatric hospitalization. Short-acting IM testosterone formulations may be more likely to cause increased aggression due to the fluctuations in hormone levels between injections.[21]

As one of the main effects of testosterone therapy is amenorrhea, fertility is significantly reduced, although not eliminated, in TM.[16,24] TM who have sex with cis-gender men are still able to get pregnant and should use some form of progestin or nonhormonal contraception if they are not trying to become pregnant.[24] Testosterone therapy significantly decreases circulating estrogen, leutinizing hormone, follicule-stimulating hormone, and prolactin levels.[19] Long term treatment can also lead to endometrial atrophy and thinning of the vaginal epithelium.[16] For these reasons, trans men who do wish to become pregnant and have not undergone a hysterectomy or sexual reassignment surgery can increase their fertility by discontinuing testosterone therapy to restore their circulating hormones to a normal female range.[16]

Hormone therapy is often only one step on the pathway to full medical transition for TM. Long term testosterone therapy does alter breast tissue composition by decreasing adipose and glandular tissue, but this typically does not lead to a reduction in size, so many trans men opt for mastectomy.[16] Some patients may undergo a hysterectomy if testosterone therapy is not sufficient to reach amenorrhea, and vocal therapy may also be desirable for patients who do not achieve satisfactory pitch lowering through testosterone therapy.[16] One study of 85 trans men found that 48.2% underwent mastectomy sometime after receiving IM

testosterone therapy.[17] 44.7% of participants in that study underwent gender-affirming surgery, on average, 39.4 months after beginning testosterone therapy. Last, conventional testosterone therapy has been associated with a small increase in BMD.[18,21] One study of 23 TM found a slight but significant increase in volumetric BMD at the distal radius and in BMD at the total hip when compared to age matched, cis-gender women.[18] Table 3 summarizes the outcomes of conventional testosterone therapies in TM population.

3.5 | Newer testosterone therapies: Oral, buccal, and intranasal testosterone

In recent years, innovations have been made in testosterone administration for transgender patients. These masculinizing treatments have included buccal, intranasal, and oral routes of administration (Figure 1). Buccal administration of testosterone was first introduced in 2003 and requires application of the tablets to the gums of the mouth.[14] Through buccal administration, there is increased bioavailability due to the bypassing of the liver.[14] Advantages of buccal administration include the facts that it is self-administered, and it has a quick reversal. Disadvantages of these tablets include possible skin irritation and the need for multiple administrations daily.[14] Buccal testosterone has also been noted for altered taste and poor adhesion to buccal mucosa, making it a less recommended form of administration.[21]

Nasal testosterone was first approved by the FDA in 2014. This is a noninvasive method of administration that has lower dose levels because of efficient absorption.[14,28] Advantages of nasal testosterone also include the fact that it is self-administered and has quick reversal.[14] Disadvantages of this method include multiple administrations, nostril irritation and contraindications for patients with nasal diseases.[14]

Oral testosterone, the most innovative testosterone administration to date, was approved by the FDA in 2020. Advantages of oral testosterone include convenience, modifiable dosage, and quick reversal.[14] Disadvantages include multiple administrations, short half-life, unpredictable absorption, fluctuating T serum levels, and the fact that is taken with fatty food.[14,21,29] Owing to recent FDA-approval for the use of these newer TRT products, there has been little contemporary data detailing their efficacy, safety, or outcomes in TM population and underpinning the unmet need for research studies on their use.[16] Table 4 summarizes newer testosterone therapies, applications, advantages, and disadvantages.

4 | DISCUSSION

Across all studies, conventional testosterone treatment has been found to be safe for long term use with minimal risk for life-threatening side effects.[30,31] Comorbidities can be monitored and managed through regular blood pressure screenings, metabolic panels, and complete blood count tests.[9] The Endocrine Society Clinical Practice Guideline for transgender patients recommends that clinicians measure patient hormone levels at regular intervals to ensure that their free testosterone levels remain within a normal male physiological range and that estradiol levels are being sufficiently suppressed.[32] Moreover, those at-risk TM patients that could be worsened by the depletion of endogenous hormones or influx of androgens should be addressed and managed with the patient's general physician before beginning testosterone treatment.[32] Hematocrit and hemoglobin levels should be measured every three months for the first year, and then twice a year to monitor the risk of polycythemia.[33]

Standard of care recommendations also include mental health screenings as part of the routine follow-up for all transgender patients.[9] Patients who do not elect for mastectomy, hysterectomy/oophorectomy or sexual reassignment surgery should continue with regular mammograms, breast exams, and cervical cancer screenings as recommended and work with their health care provider to determine if and when the time is right for surgical transition.[16,32]

This comprehensive review highlights that majority of TRT data in TM population were stemming from conventional TRT use and there appear to be an overwhelmingly safety and efficacy profile in TM population clinically proven and translated with increased free testosterone levels comparable to male range, menses cessation, anxiety/depression decline and improved quality of life. Notwithstanding, testosterone therapy can be impactful for TM population with improved safety, efficiency, quality of life and function. With the rise of the newer FDA-approved TRT, randomized studies are warranted to determine its safety and efficacy in this TM population.

5 | CONCLUSION

The use of testosterone to induce masculinization among TM has shown great promise in recent years. More conventional therapies, including intramuscular injections, subcutaneous injections, and transdermal gels, have been extensively studied and show promising efficacy and outcomes with limited safety concerns.

The newer therapies, including oral, buccal, and nasal testosterone formulations, have not yet been extensively studied. As newcomers to the market, increased research is needed to determine the efficacy, safety profile, and outcomes of these formulations among the TM population.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. de Ziegler D, de Sutter P. Transgender men: clinical care and implications in reproductive medicine: introduction. *Fertil Steril*. 2021;116:919-921.
2. T'Sjoen G, Arcelus J, Gooren L, Klink DT, Tangpricha V. Endocrinology of transgender medicine. *Endocr Rev*. 2019;40:97-117.
3. Grannis C, Leibowitz SF, Gahn S, et al. Testosterone treatment, internalizing symptoms, and body image dissatisfaction in transgender boys. *Psychoneuroendocrinology*. 2021;132:105358.
4. Unger CA. Hormone therapy for transgender patients. *Transl Androl Urol*. 2016;5:877-884.
5. Davis SA, St. Amand C. Effects of testosterone treatment and chest reconstruction surgery on mental health and sexuality in female-to-male transgender people. *Int J Sex Health*. 2014;26:113-128.
6. Costantino A, Cerpolini S, Alvisi S, Morselli PG, Venturoli S, Meriggiola MC. A prospective study on sexual function and mood in female-to-male transsexuals during testosterone administration and after sex reassignment surgery. *J Sex Marital Ther*. 2013;39:321-335.
7. Irwig MS. Testosterone therapy for transgender men. *Lancet Diab Endocrinol*. 2017;5:301-311.
8. Hodges-Simeon CR, Grail GPO, Albert G, et al. Testosterone therapy masculinizes speech and gender presentation in transgender men. *Sci Rep*. 2021;11:3494.
9. Costa LB, Rosa-e-Silva A, Medeiros S, et al. Recommendations for the use of testosterone in male transgender. *Revista Brasileira de Ginecologia e Obstetrícia RBGO Gynecology and Obstetrics*. 2018;40:275-280.
10. Overview of Masculinizing Hormone Therapy | Gender Affirming Health Program. https://transcare.ucsf.edu/guidelines/masculinizing-therapy.
11. Pelusi C, Costantino A, Martelli V, et al. Effects of three different testosterone formulations in female-to-male transsexual persons. *J Sex Med*. 2014;11:3002-3011.
12. Jacobeit JW, Gooren LJ, Schulte HM. Safety aspects of 36 months of administration of long-acting intramuscular testosterone undecanoate for treatment of female-to-male transgender individuals. *Eur J Endocrinol*. 2009;161:795-798.
13. Meriggiola MC, Armillotta F, Costantino A, et al. Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. *J Sex Med*. 2008;5:2442-2453.
14. Barbonetti A, D'Andrea S, Francavilla S. Testosterone replacement therapy. *Andrology*. 2020;8:1551-1566.
15. Nolan BJ, Zwickl S, Wong AFQ, et al. Testosterone concentrations and prescription patterns of 1% testosterone gel in transgender and gender diverse individuals. *Ther Adv Endocrinol Metab*. 2022;13:204201882210835.
16. Irwig MS. Chapter 10-Testosterone treatment for transgender (trans) men. In: Legato MJ, ed. *The Plasticity of Sex*. Academic Press; 2020:137-157. doi:10.1016/B978-0-12-815968-2.00012-8
17. Kirisawa T, Ichihara K, Sakai Y, Morooka D, Iyoki T, Masumori N. Physical and psychological effects of gender-affirming hormonal treatment using intramuscular testosterone enanthate in Japanese transgender men. *Sex Med*. 2021;9:100306.
18. Van Caenegem E, Wierckx K, Taes Y, et al. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case–controlled study (ENIGI). *Eur J Endocrinol*. 2015;172:163-171.
19. Mueller A, Haeberle L, Zollver H, et al. Effects of intramuscular testosterone undecanoate on body composition and bone mineral density in female-to-male transsexuals. *J Sex Med*. 2010;7:3190-3198.
20. Subcutaneous Testosterone: An Effective Delivery Mechanism for Masculinizing Young Transgender Men | LGBT Health. https://www.liebertpub.com/doi/full/10.1089/lgbt.2014.0018
21. Madsen MC, Heijer den M, Pees C, Biermasz N, Bakker L. Testosterone in men with hypogonadism and transgender males: a systematic review comparing 3 different preparations. *Endocr Connect*. 2022;11(8):e220112.
22. Mueller A, Kiesewetter F, Binder H, Beckmann MW, Dittrich R. Long-Term administration of testosterone undecanoate every 3 months for testosterone supplementation in female-to-male transsexuals. *J Clin Endocrinol Metab*. 2007;92:3470-3475.
23. Wierckx K, Van Caenegem E, Schreiner T, et al. Cross-Sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the european network for the investigation of gender incongruence. *J Sex Med*. 2014;11:1999-2011.
24. Moravek MB. Gender-affirming hormone therapy for transgender men. *Clin Obstet Gynecol*. 2018;61:687-704.
25. Traish AM, Gooren LJ. Safety of physiological testosterone therapy in women: lessons from female-to-male transsexuals (FMT) treated with pharmacological testosterone therapy. *J Sex Med*. 2010;7:3758-3764.
26. Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: results from a longitudinal study. *Psychoneuroendocrinology*. 2014;39:65-73.
27. Motta G, Crespi C, Mineccia V, Brustio PR, Manieri C, Lanfranco F. Does testosterone treatment increase anger expression in a population of transgender men? *J Sex Med*. 2018;15:94-101.

28. Banks WA, Morley JE, Niehoff ML, Mattern C. Delivery of testosterone to the brain by intranasal administration: comparison to intravenous testosterone. *J Drug Target*. 2009;17:91-97.
29. Cocchetti C, Fisher AD. Testosterone in transgender population. In: Mulhall JP, Maggi M, Trost L, eds. *Controversies in Testosterone Deficiency*. Springer International Publishing; 2021:107-121. doi:10.1007/978-3-030-77111-9_9
30. Natale C, Carlos C, Hong J, Khera M, Baum N, Raheem OA. Testosterone therapy after prostate cancer treatment: a review of literature. *Sex Med Rev*. 2021;9(3):393-405.
31. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and management of testosterone deficiency: AUA guideline. *J Urol*. 2018;200(2):423-432.
32. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society* clinical practice guideline. *J Clin Endocrinol Metab*. 2017;102:3869-3903.
33. Nackeeran S, Kohn T, Gonzalez D, White J, Ory J, Ramasamy R. The effect of route of testosterone on changes in hematocrit: a systematic review and Bayesian network meta-analysis of randomized trials. *J Urol*. 2022;207(1):44-51.

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