Clinical Insights | WOMEN'S HEALTH

Gender-Affirming Feminizing Hormone Therapy

Zil Goldstein, FNP; Matthew D. Krasowski, MD, PhD; Dina N. Greene, PhD

Gender-affirming care is associated with improved mental health and quality of life for transgender people.[1,2] Health disparities are well documented in the gender-diverse population, many of which are associated with societal discrimination and health care access. In this article, we provide basic tools and knowledge to facilitate the medical care of transgender women or nonbinary people who are receiving feminizing gender-affirming hormone therapy (fGAHT) (**Figure**).

CME at jamacmelookup.com

Diagnosis of Gender Incongruence

Gender develops with the sense of self and is deeply rooted in identity and belonging. Gender incongruence is a persistent desire to change gender for more than 6 months.[1] Gender dysphoria is the extreme distress experienced by some transgender people due to their gender incongruence and from interacting with a world that identifies them as their sex assigned at birth. Affirming gender socially and/or use of fGAHT can facilitate relief of gender incongruence and dysphoria.

Pretreatment assessment for people requesting fGAHT should occur in an environment that is safe to share experiences of gender. Creating a respectful health care environment with the use of correct names and pronouns is critical.[3] Institutional use of sexual orientation and gender identity fields in electronic health records can improve general health care interactions for gender-diverse patients and alleviate ambiguity with sex-specific procedures for clinicians.[4]

During the initial visits, areas of feminization that are most important to the individual should be emphasized; these baseline goals are critical for monitoring therapy and include breast growth, skin softening, erectile function, and subcutaneous fat redistribution.[1] Institutions can develop templates to facilitate the collection of this information or it can be included in clinical documentation. Universal tools to select or monitor fGAHT treatment goals are not currently available.

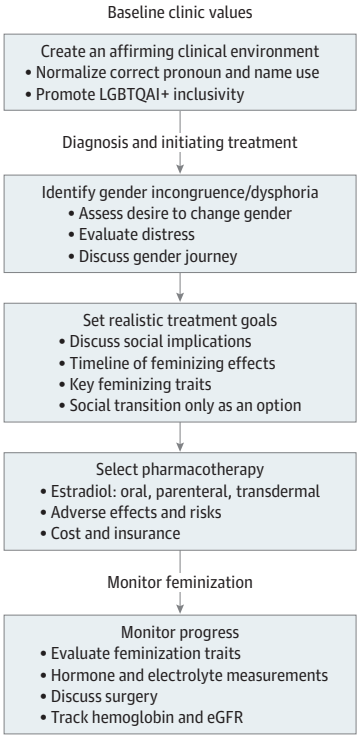
Treatment Selection

Standard of care for fGAHT includes estradiol, which can be administered orally, parenterally (intramuscular or subcutaneous), or transdermally.[1] Formulation is selected based on patient preference, health insurance coverage or out-of-pocket costs, goals of feminization, comfort with the administration route, and risk of adverse effects. The estrogen used for fGAHT (17β-estradiol) is different from that used in most combined hormonal contraception (ethinyl estradiol); however, the risks of combined hormonal contraception use broadly apply to fGAHT, including a low absolute risk of thromboembolism and mood changes attributable to hormone use. Choosing an appropriate estradiol formulation can mitigate some of these risks. For example, the risk of thromboembolism is lowest with transdermal hormone regimens; therefore, such formulations are preferred for individuals who smoke tobacco, are older than 45 years, and/or are at elevated risk for thromboembolism.[5] Data on parenteral estrogen are limited, but the risks are likely similar to oral estrogen. Combined informed consent should guide treatment selection.

Guidelines provide standard dosing for each preparation.[1] Oral estradiol is prescribed at 2 mg per day for the first 2 weeks before increasing to 4 mg per day. Parenteral estradiol valerate is prescribed at 10 mg per week. Transdermal estradiol is prescribed at 0.1 to 0.2 mg every 24 hours.

In addition to estrogen, adjunct antiandrogens are often coprescribed to enhance gonadal suppression and improve feminization.[1] In the US, the primary antiandrogen is spironolactone (50-100 mg, twice daily), but finasteride (1-5 mg/day) and leuprolide (most commonly 11.25-22.5 mg/3 months) may also be used. Antiandrogens typically decrease erectile function, which may or may not be desirable. Spironolactone may also affect mineralocorticoid pathways and electrolyte concentrations (most notably potassium), but this is rarely a concern in healthy adults. Common surgical procedures that reduce dysphoria for transgender women and nonbi-

Figure. Recommended Continuum of Care for Gender-Affirming Feminizing Hormone Therapy



eGFR indicates estimated glomerular filtration rate; LGBTQAI+, lesbian, gay, bisexual, transgender, queer/questioning, intersex, asexual, and more.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by thuy hoang on 07/01/2025

nary people include facial feminization, orchiectomy, vaginoplasty, and breast augmentation.[1]

Monitoring Feminization

Follow-up care for fGAHT should address the physiological changes that accompany estrogen therapy.[1] Monitoring and confirming the feminization goals established at the baseline visit are integral because there are no metrics, scores, or standardized checklists to assign as consistent with feminizing, and there will be variable goals for and effects on feminization across individuals. Questions like, "What have you noticed so far?", "How do you feel about the changes you are noticing?"or "What else would you like to see?" can guide treatment and should be revisited on follow-up. Phenotypic changes are visible within weeks of initiating therapy and plateau after approximately 2 years of hormone use. Fertility may diminish with use of fGAHT, but likely returns with cessation.

Clinicians should recommend quarterly visits for the first year and annually thereafter. For these visits, monitoring estradiol, total testosterone, luteinizing hormone, complete blood cell counts, and basic metabolic parameters is appropriate. Clinicians should also use these visits to ensure that other preventive care services, such as family planning, routine health maintenance, and sexually transmitted infection screening, are performed. Laboratory tests associated with sex hormones have shown substantial shifts toward affirmed gender after 3 months of treatment with fGAHT.[6] For patients receiving existing therapy who are transferring care, these same laboratory tests can be used to establish care and should be followed up annually.

Expert guidelines currently propose 100 to 200 pg/mL (to convert to pmol/L, multiply by 3.671) as an estradiol target range.[1] However, there is limited published evidence supporting a range that narrow, with many publications showing a much wider range of estradiol concentrations for those receiving fGAHT.[7] Testosterone concentrations are recommended to be less than 50 ng/dL (to convert to nmol/L, multiply by 0.0347), which is similar to cisgender women. Higher testosterone concentrations for people using fGAHT may be appropriate depending on the goals of therapy. Many factors are associated with serum estradiol and testosterone concentrations, including fGAHT doses and formulation (including antiandrogen), the timing of serum collection compared with the last dose, and pharmacokinetics.

Most common laboratory tests are minimally or not affected by fGAHT. Hemoglobin and hematocrit levels and red blood cell counts typically decrease with estradiol therapy, an effect largely associated with a decreasing testosterone concentration.[8] Cisgender female reference intervals for these complete blood cell count parameters can be used for those who receive stable fGAHT.

Calculating the estimated glomerular filtration rate (eGFR) for the transgender population is complicated, given that the equations include sex as a variable.[9] For the same creatinine concentration, use of the female variable is associated with an approximately 30% lower eGFR. Consider alternative laboratory parameters, such as cystatin C, when the eGFR at the creatinine concentration is at a clinical threshold.

Even following gender-affirming surgeries, transgender women will retain their prostate, and general prostate cancer screening recommendations should be followed, although a lower prostate-specific antigen cutoff has been proposed.[10] Breast development following estrogen therapy warrants following breast cancer screening recommendations for cisgender women after 5 years of treatment with fGAHT.

Summary

The evidence for providing fGAHT is robust and suggests that the quality of life, including mental health, substantially improves.[2] Instilling comfort and confidence in medical clinicians across the country is critical for maintaining the health of transgender and nonbinary people.

ARTICLE INFORMATION

Author Affiliations: Callen Lorde Community Health Center, Brooklyn, New York (Goldstein); Department of Public Health and Health Policy, City University New York, New York (Goldstein); Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City (Krasowski); Department of Laboratory Medicine and Pathology, University of Washington, Seattle (Greene).

Corresponding Author: Dina N Greene, PhD, DABCC, Department of Laboratory Medicine and Pathology, University of Washington, 1959 NE Pacific St, Seattle, WA 98195 (dngreene@uw.edu).

Published Online: June 30, 2025. doi:10.1001/jamainternmed.2025.1161

Conflict of Interest Disclosures: Dr Krasowski reported scientific advisory board service for Truvian, Inc outside the submitted work. No other disclosures were reported.

REFERENCES

1. Coleman E, Radix AE, Bouman WP, et al. Standards of care for the health of transgender and gender diverse people, version 8. *Int J Transgend Health*. 2022;23(suppl 1):S1-S259. doi:10.1080/26895269.2022.2100644

2. Baker KE, Wilson LM, Sharma R, Dukhanin V, McArthur K, Robinson KA. Hormone therapy, mental health, and quality of life among transgender people: a systematic review. *J Endocr Soc*. 2021;5(4):bvab011. doi:10.1210/jendso/bvab011

3. Nisly NL, Imborek KL, Miller ML, et al. Developing an inclusive and welcoming LGBTQ clinic. *Clin Obstet Gynecol*. 2018;61(4):646-662. doi:10.1097/GRF.0000000000000405

4. Moreira JD, Haack K, White V, Bates ML, Gopal DM, Roepke TA. Importance of survey demographic questions to foster inclusion in medicine and research and reduce health inequities for LGBTQIA2S+ individuals. *Am J Physiol Heart Circ Physiol*. 2023;324(6):H856-H862. doi:10.1152/ajpheart.00152.2023

5. Arrington-Sanders R, Connell NT, Coon D, et al. Assessing and addressing the risk of venous thromboembolism across the spectrum of gender affirming care: a review. *Endocr Pract*. 2023;29(4):272-278. doi:10.1016/j.eprac.2022.12.008

6. Nolan BJ, Cheung AS. Laboratory monitoring in transgender and gender-diverse individuals. *Clin Chem*. Published online February 10, 2025. doi:10.1093/clinchem/hvaf001

7. Winston-McPherson G, Thomas T, Krasowski MD, et al. Estradiol concentrations for adequate gender affirming feminizing therapy: a systematic review. *LGBT Health*. doi:10.1089/lgbt.2024.0407

8. Greene DN, McPherson GW, Rongitsch J, et al. Hematology reference intervals for transgender adults on stable hormone therapy. *Clin Chim Acta*. 2019;492:84-90. doi:10.1016/j.cca.2019.02.011

9. Turino Miranda K, Greene DN, Collister D, et al. A holistic framework for the evaluation of kidney function in a gender-diverse landscape. *Am J Kidney Dis*. 2024;84(2):232-240. doi:10.1053/j.ajkd.2024.01.522

10. Iwamoto SJ, Grimstad F, Irwig MS, Rothman MS. Routine screening for transgender and gender diverse adults taking gender-affirming hormone therapy: a narrative review. *J Gen Intern Med*. 2021;36(5):1380-1389. doi:10.1007/s11606-021-06634-7

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by thuy hoang on 07/01/2025