Gender-Affirming Care for People with HIV: Estrogen and Androgen Blocker Use in Transgender and Gender Diverse (TGD) Individuals

Marvin Alviso, MD AAHIVS
Educational Faculty Full Circle Health Boise Program, Boise Idaho

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No conflicts of interest or relationship to disclose

There are no FDA-approved medications for gender-affirming care

Disclaimer

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Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities

Feminizing hormones

- Estrogen - 17 B Estradiol, conjugated equine estrogen, synthetic estrogen ethinyl estradiol
- Androgen Blocker
- Progesterone

Feminizing hormones

HORMONE	Dosage		
	Initial Low	Initial Typical	Maximum Typical
ESTROGEN			
Estradiol oral/sublingual	1 mg QD	2 mg BID	3 MG BID
Estradiol transdermal	50 mcg	100 mcg	100-400 mcg
Estradiol valerate IM	< 20 mg q2 wk	20 mg q2 wk	40 mg q2 wk
Estradiol cypionate IM	< 2 mg q2 wk	2 mg q2 wk	5 mg q2 wk
ANDROGEN BLOCKER			
Spironolactone	25 mg QD	50 mg BID	200 mg BID
Bicalutamide	25 mg QD/ two times a week		50 mg QD/two times a week
Finasteride	1 mg QD		5 mg QD
Dutasteride			0.5 mg QD

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Feminizing hormones

HORMONE	Dosage		
	Initial Low	Initial Typical	Maximum Typical
PROGESTAGEN			
Medroxyprogesterone acetate	2.5 mg HS		5-10 mg HS
Micronized progesterone			100-200 mg HS

Effects of estrogen and antiandrogen treatment in transgender women

Psychological and CNS
↓Gender dysphoria
↓Anxiety
↓Depression
↓Perceived Stress
↑Quality of life

Sexual Health
↓Sexual desire

Blood
↓Hemoglobin and hematocrit

Blood Pressure
↓Systolic blood pressure

Voice
No Change

Hormone concentrations
↓Testosterone
↓Lutenizing hormone
↓Follicle-stimulating hormone
↑Prolactin

Lipid and metabolism
↑LDL, cholesterol
↑Triglycerides
↑Sex hormone binding globulin

T'Sjoen, G., Arcelus, J., Gooren, L., Klink, D. T., & Tangpricha, V. (2019). Endocrinology of Transgender Medicine. Endocrine reviews, 40(1), 97–117. https://doi-org.offcampus.lib.washington.edu/10.1210/er.2018-00011

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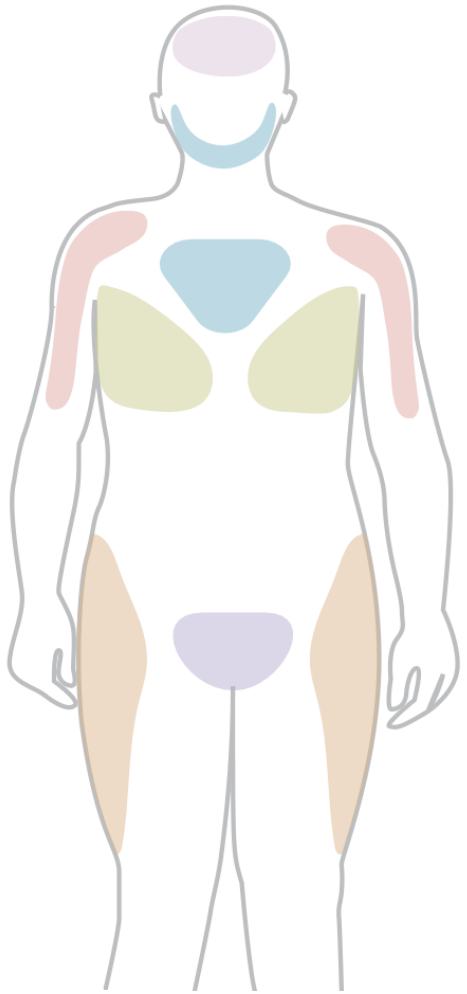
Effects of estrogen and antiandrogen treatment in transgender women



PHYSICAL EFFECTS	REVERSIBILITY	TIME COURSE (YEARS)
Softening of skin/decreased oiliness	Reversible	
Body fat redistribution	Reversible/Variable	
Decreased muscle mass/strength	Reversible	
Thinned/slowed growth of body/facial hair	Reversible	
Male Pattern Baldness	Reversible	
Breast growth	Irreversible	
Decreased testicular volume	Variable	
Decreased libido	Variable	
Decreased spontaneous arousals	Variable	
Decreased sperm production	Variable	
Erectile dysfunction	Variable	

Bourns, Amy. “Guidelines and Protocols for Comprehensive Primary Care with trans and non-binary patients ” Rainbowhealthontario.ca, Province of Ontario, CA, https://www.rainbowhealthontario.ca/TransHealthGuide/

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Laboratory monitoring for transgender patient on estradiol and antiandrogen

	BASELINE	3 MONTHS	6 MONTHS	12 MONTHS	YEARLY	AS NEEDED
CMP	☑	☑		☑	☑	
Lipids	☑ ☑		☑ ☑	☑ ☑		☑ ☑
Fasting glucose of Hgba1c	☑ ☑		☑ ☑	☑ ☑	☑ ☑	
Estradiol		☑	☑	☑		☑
Free and Total Testosterone		☑	☑	☑		☑
Prolactin	☑ ☑ ☑					☑ ☑ ☑

☑☑ if clinically indicated
☑☑☑ only if symptomatic

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Drug-drug interaction with HIV medications

- Medications that ↑ ethinyl estradiol
  - ATV, RPV, ETR, FPV
- Medications that ↓ ethinyl estradiol
  - ATV/r, DRV/r, EVG/c
- No effect
  - DTG, MVC, TDF, RAL
- No studies
  - DRV/c. ATV/c

Radix A, Sevelius J, Deutsch MB. Transgender women, hormonal therapy and HIV treatment: a comprehensive review of the literature and recommendations for best practices. J Int AIDS Soc. 2016 Jul 17;19(3 Suppl 2):20810. doi: 10.7448/IAS.19.3.20810. PMID: 27431475; PMCID: PMC4949308.

Drug-drug interaction with HIV medications

- Antiandrogen spironolactone although metabolized by cytochrome P450, no relevant DDI with ART though this mechanism
- Finasteride when combined with ETR, EFV and NVP may decrease level of finasteride, the clinical significance is unknown

Radix A, Sevelius J, Deutsch MB. Transgender women, hormonal therapy and HIV treatment: a comprehensive review of the literature and recommendations for best practices. J Int AIDS Soc. 2016 Jul 17;19(3 Suppl 2):20810. doi: 10.7448/IAS.19.3.20810. PMID: 27431475; PMCID: PMC4949308.

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Goals of therapy

- The goal of feminizing hormone therapy is the development of female secondary sex characteristics and suppression/minimalization of male secondary sex characteristics
- The general approach to therapy is to obtain physiological female range of estradiol and testosterone using estradiol and androgen blocker
- Serum estradiol goal : 100-200 pg/mL
- Serum testosterone goal: < 55 ng/dL
- Normal K+ and creatinine for patients on spironolactone, AST/ALT if on bicalutamide

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Safety data specific to transgender women using cross sex hormones

Cardiovascular disease

- Data suggest that gender-affirming hormonal therapy (GAHT) may worsen the risks of MI, stroke, or any CVD compared to cisgender women or men
  - Transgender women were more than two times more likely to have MI's compared to cisgender women, but not compared to cisgender men
  - Transgender women were more likely to have had a stroke, MI, or any CVD compared to cisgender women
- ↑ Serum TG (> 24 months) with no changes in LDL and HDL and total cholesterol
- Cardiovascular risk calculators are sex-specific
- CV morbidity/mortality is attributed to the use of ethinyl estradiol but not 17B Estradiol

Sudhakar, D, Huang, Z, Zietkowski, M, Powell, N, Fisher, AR. Feminizing gender-affirming hormone therapy for the transgender and gender diverse population: an overview of treatment modality, monitoring, and risks. *Neurourol Urodyn*. 2022; 1- 18. doi:10.1002/nau.25097

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Safety data specific to transgender women using cross sex hormones

- More recently, associations between TAF and dyslipidemia have also been proposed
- With ART, avoiding regimens containing PI, ABC, and TAF may decrease cardiovascular risks

Van Gerwen OT, Blumenthal JS. Providing gender-affirming care to transgender and gender-diverse individuals with and at risk for HIV. Top Antivir Med. 2023 Mar 31;31(1):3-13. PMID: 37018731; PMCID: PMC10089290.

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Safety data specific to transgender women using cross sex hormones

Venous Thromboembolic events

- The risk of thromboembolic events seems to be higher following treatment with estrogen based GAHT
- Type of estrogen therapy and route of administration play a role in thromboembolic events

Relative Thrombotic Risk	Estrogen
	Ethinyl estradiol
High	50 µg
Intermediate	30-35 µg
Low intermediate	20 µg
Moderately Low	Conjugated equine estrogen
Low	Oral estradiol
Low	Injectable estradiol
Very low	Transdermal estradiol

Sudhakar, D, Huang, Z, Zietkowski, M, Powell, N, Fisher, AR. Feminizing gender-affirming hormone therapy for the transgender and gender diverse population: an overview of treatment modality, monitoring, and risks. *Neurourol Urodyn*. 2022; 1- 18. doi:10.1002/nau.25097

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Safety data specific to transgender women using cross sex hormones

Weight gain

- Certain components of ART regimen, particularly INSTI's and TAF, have been associated with weight gain. Estrogen and Progesterone have an added side effect of weight gain.

Bone health

- Fracture rate among users of feminizing hormone is unknown.
- Higher percentage of transgender women have lower BMD and low vitamin D.
- Long term use of TDF have been associated with ↓ in BMD.

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Safety data specific to transgender women using cross sex hormones

Renal impairment

- TDF also affects renal function. TAF is preferred for people with underlying renal disease. Renal parameters, if patient on GAHT > 6 months, calculations should be based on gender identity rather than sex assigned at birth.

Oncological data

- Feminizing hormones could affect the risk of hormone sensitive cancer types including breast and prostate cancer. Prevalence appears to be low among transgender women.
- Combination of age + length of estrogen exposure.
- Lower risk of prostate cancer in transgender female.

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Preventive health screening

- Breast Cancer Screening: Age 50+ > 5 years on hormone estrogen or progesterone
- Cervical Cancer Screening: No
- Osteoporosis: Gonadectomy and 5 years off hormones, do DEXA

Safety data specific to transgender men using cross sex hormones

Cardiovascular

- Testosterone treatment does not result in adverse cardiovascular outcomes
- Many studies report an association between testosterone therapy and increases in Hb (range +4.9-12.5%) and Hematocrit (range +4.4% -17.6%) during first year of treatment

Bone Health

- Limited data on osteoporotic fractures in transgender men on testosterone therapy
- Studies showed that transgender men on testosterone therapy had larger cortical bone size as well as higher BMD

Velho, I., Fighera, T. M., Ziegelmann, P. K., & Spritzer, P. M. (2017). Effects of testosterone therapy on BMI, blood pressure, and laboratory profile of transgender men: a systematic review. *Andrology*, *5*(5), 881–888. https://doi-org.offcampus.lib.washington.edu/10.1111/andr.12382

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Safety data specific to transgender men using cross sex hormones

Oncologic Data

- The role of androgen therapy on cancer risk for transgender males is controversial

Preventive health screening

- Cervical Cancer Screening
- Breast Cancer Screening : No guidelines for patients who had mastectomy
- Osteoporosis: If patient stops using testosterone for 5 years

Sterling J, Garcia MM. Cancer screening in the transgender population: a review of current guidelines, best practices, and a proposed care model. Transl Androl Urol. 2020 Dec;9(6):2771-2785. doi: 10.21037/tau-20-954. PMID: 33457249; PMCID: PMC7807311.

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