Transgender Health for HIV Clinicians

Southeast AETC

Asa Radix, MD, PhD, MPH
Senior Director of Research and Education
Callen-Lorde Community Health Center, NY
2/15/2023

AETC AIDS Education & Training Center Program Southeast

Disclosures

- This program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535 as part of an award totaling $4.2m. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov.

- “Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.”

-

AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinician Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

Faculty Disclosure

- I have not had any relevant financial relationships during the past 24 months

Objectives

Upon completion of this educational activity, you will be able to:

- List key barriers to care among the transgender people seeking health services, including HIV/STI prevention and treatment
- Describe gender-affirming medical and surgical interventions for transgender individuals
- Review HHS Adult ART guidelines for transgender people with HIV
- Describe key components of culturally competent care for transgender patients

How many transgender patients do you currently provide care for (in any capacity)?

A. 0
B. 1-5
C. 6-10
D. >10

How would you rate your competence in dealing with a transgender patient's sexual health concerns?

A. Very comfortable
B. Somewhat comfortable
C. Somewhat uncomfortable
D. Very uncomfortable

Transgender People - Terminology

- Terminology differs across different regional and cultural contexts
- Gender identity different than their assigned sex at birth
  - Transgender woman/ trans woman
  - Transgender man/ trans man
  - Nonbinary/Gender diverse:
  - Cisgender (cis): non-transgender

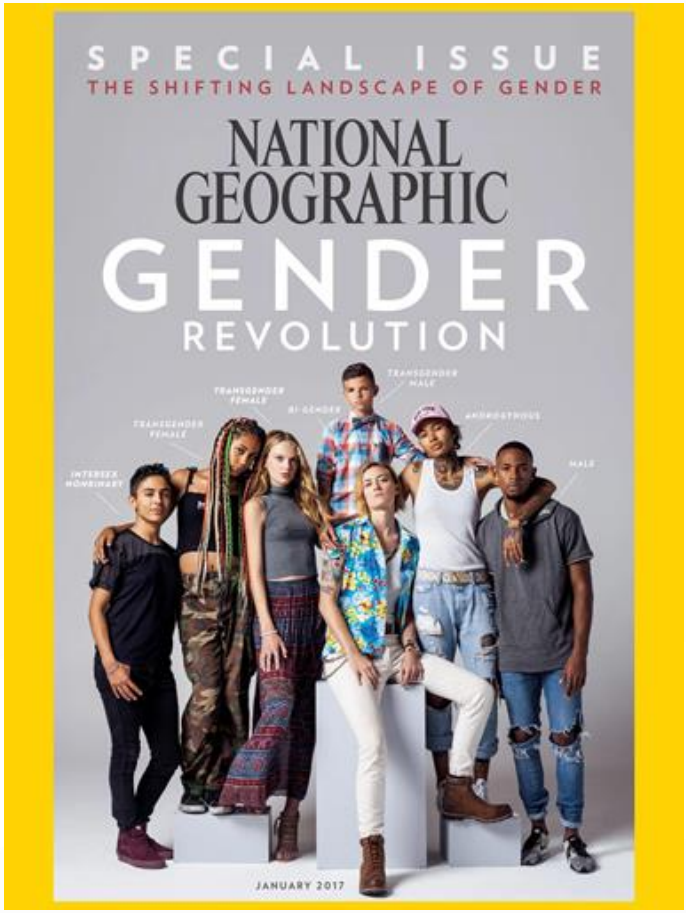


Image source: nationalgeographic.com

How Many People are Trans?

- Approximately 0.5% of adults are transgender
  - Worldwide: 25 million
  - United States: 1.3 million adults
  - Adolescents 13-17: 300,000

>1/3 of trans people identity as non-binary

Winter S, Lancet. 2016; James, S. E., Herman et al, The Williams Institute 2022; The Report of the 2015 U.S. Transgender Survey http://www.ustranssurvey.org/

Transgender Health Disparities

HUMAN RIGHTS VIOLATIONS

Structural & interpersonal Factors

- Social exclusion (housing, employment)
- Legal status
- Mistreated/denied care in healthcare settings
- Poor access to prevention information
- Economic vulnerability
- Violence and victimization

Biologic Factors

- Effects of testosterone
- Effects of estrogen

Individual Factors

- Substance use
- Low self efficacy
- Sex work
- HIV prevention a low priority

Asthma
Anxiety/Depression
Cardiovascular disease
Delays in preventive care
Eating disorders
HIV/STIs
OSA
Overweight/Obesity
Substance use
Tobacco use

Question

What is the proportion of transgender women in the USA who are living with HIV?

A. 7%
B. 14%
C. 42%
D. 77%

Question

What is the proportion of transgender women in the USA who are living with HIV?

A. 7%

B. 14%

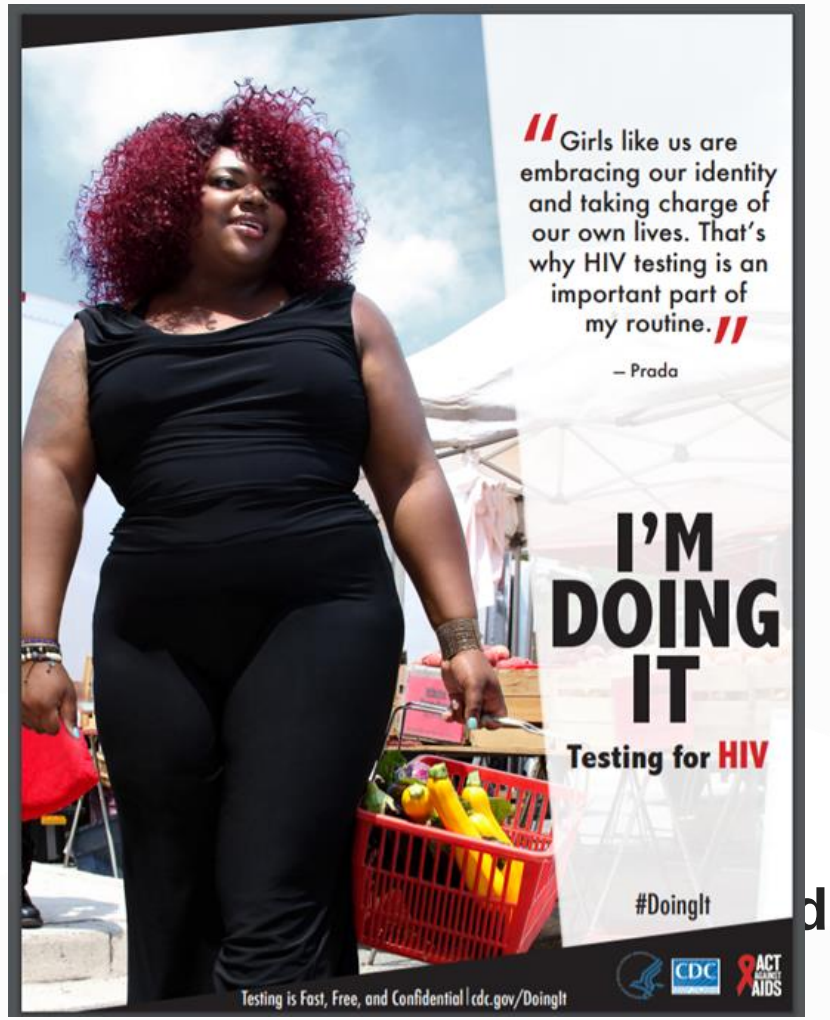
C. 42%

D. 77%

HIV and Transgender People in the US

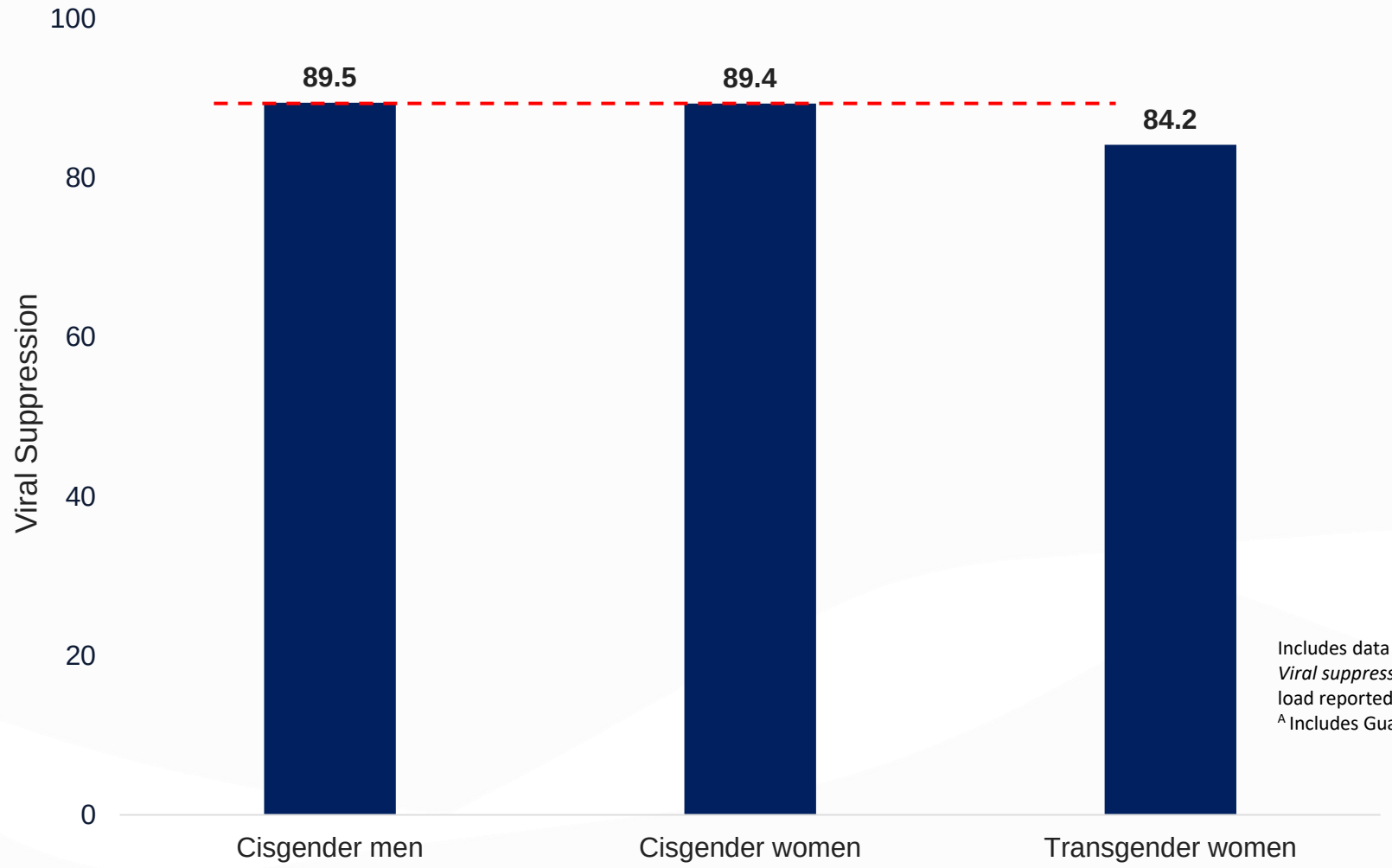
Prevalence

- USA (all adults): 0.39%
- Transgender women 14.1% (8.7%, 22.2%)*
  - Black 44.2%
  - Hispanic 25.8%
  - White 6.7%
- Transgender men 3.2% (1.4%, 7.1%)*
  - Sexual partners cisgender men only 11%



Becasen, J et al. AJPH 2019; Woodring J Natl Health Stat Report. 2015; Radix et al, JIAS 2022

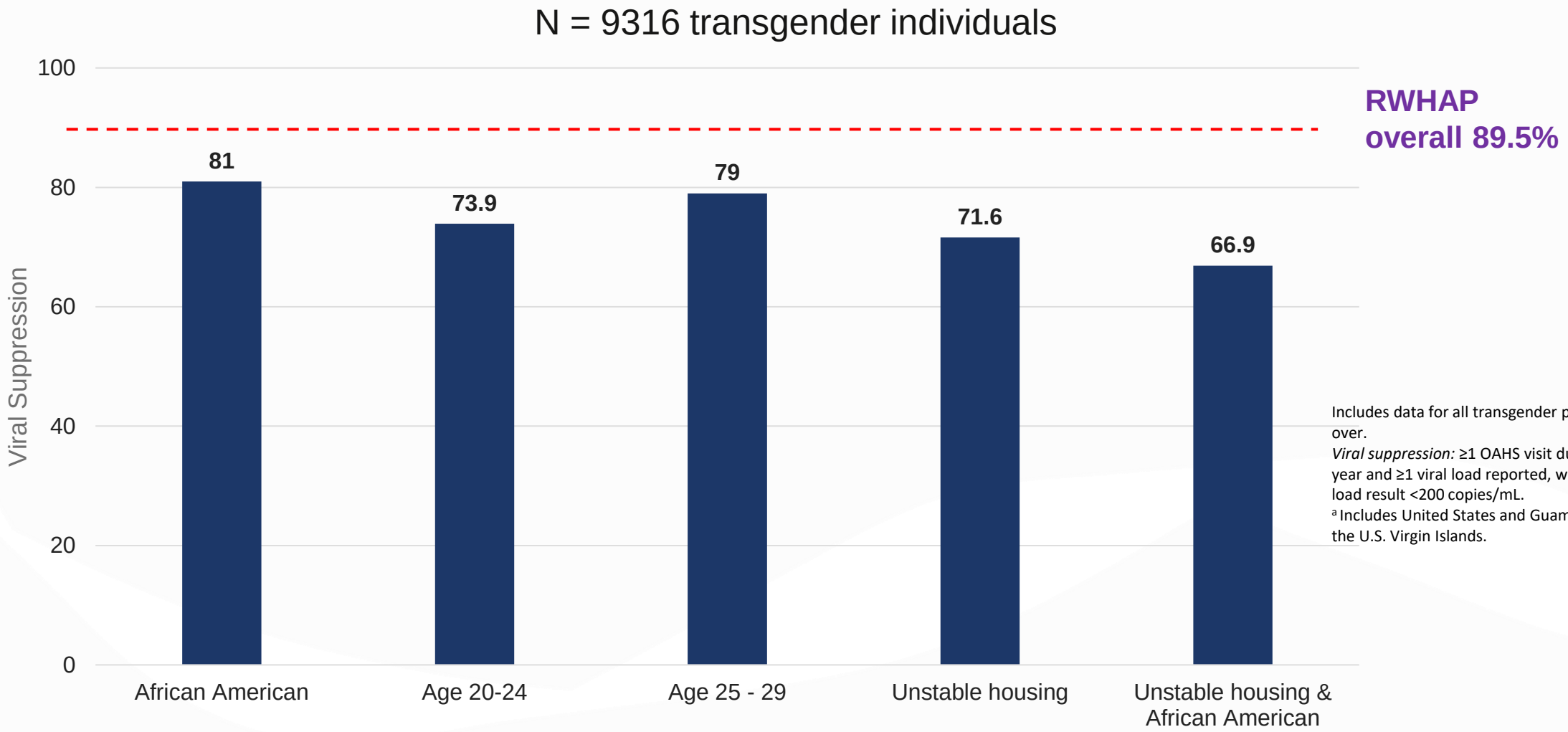
Viral Suppression among Adults and Adolescents Served by the Ryan White HIV/AIDS Program, 2020[a]



RWHAP
N= 561,416
89.5%

Includes data for adults and adolescents aged 13 and over
Viral suppression: ≥1 OAHS visit during the calendar year and ≥1 vi
load reported, with the last viral load result <200 copies/mL.
[A] Includes Guam, Puerto Rico, and the U.S. Virgin Islands.

Viral Suppression among Transgender Adults and Adolescents Served by the Ryan White HIV/AIDS Program, 2020[a]



Includes data for all transgender people aged 13 and over.

Viral suppression: ≥1 OAHS visit during the calendar year and ≥1 viral load reported, with the last viral load result <200 copies/mL.

[a] Includes United States and Guam, Puerto Rico, and the U.S. Virgin Islands.

Factors Related to Viral Suppression

- Prioritization of transition-related medical care over HIV care
- Fears about drug interactions between hormones and HIV
- Lower adherence self-efficacy
- Negative experiences with providers/health systems
- Fear of discrimination
- HIV stigma
- Mental health issues
- Substance use
- Unstable housing

Sevelius J, et al. J Assoc Nurses AIDS Care. 2010 ; 21(3): 256–264; Sevelius J, et al. AIDS Care. 2014 August ; 26(8): 976–982; Chung, et al. 2016. Transgender Law Center; Reback CJ 2019; Reback CJ 2018;

Question

Transgender women at risk for HIV are less likely to receive PrEP than cisgender men. What are some of the reasons for this disparity?

A. Worried about interactions with hormone therapy
B. Mistrust of providers and researchers
C. Low HIV-risk perception
D. Lack of trans-inclusive marketing
E. All of the above

Question

Transgender women at risk for HIV are less likely to receive PrEP than cisgender men. What are some of the reasons for this disparity?

A. Worried about interactions with hormone therapy
B. Mistrust of providers and researchers
C. Low HIV-risk perception
D. Lack of trans-inclusive marketing
E. All of the above

HIV Prevention

- PrEP uptake suboptimal for transgender populations (<15%)
- Low PrEP adherence and persistence
- Discuss options
  - Transgender men – FTC/TDF, CAB LA
  - Transgender women – FTC/TDF, FTC/TAF, CAB LA
- No clinically significant drug-drug interactions
- Cabotegravir LA – be aware of silicone/fillers buttocks

Reisner et al, LGBT Health 2021; Cooney et al, Ann. Epid 2022; Grant et al, CID 2021

PrEP Persistence

- Few data on PrEP persistence for trans people

Median days of PrEP use prior to discontinuation	
Men who have sex with men	292 (222 – 347)
Sero-different couple	331 (183 – 391)
Transgender women who have sex with men	120 (69 – 178)
Injection Drug Use	30 (30 – --)
High-risk heterosexual	350 (85 – --)

PrEP Discontinuation San Francisco Dept of Public Health Primary Care Clinics

Facilitators to PrEP in Trans People

- Trans-competent services
- Empowerment approach
- Hormones prescribed at clinic
- Materials/health promotion
- Recommended by medical provider

Reisner et al., *AIDS Behav*. 2017; Restar et al., *AIDS Behav*. 2018; Wood et al., *J Adolesc Health*. 2017; Wilson et al., *Global Public Health* 2019; Klein & Golub. AIDS Patient Care and STDs 2019

How would you rate your competence with initiating and managing gender-affirming hormone therapy?

A. Very comfortable
B. Somewhat comfortable
C. Somewhat uncomfortable
D. Very uncomfortable

Case

45-year-old transgender woman requests estrogen therapy. Past medical history includes HIV, hypertension and hyperlipidemia. Her medications include atorvastatin 20 mg daily, lisinopril 20 mg daily, dolutegravir, emtricitabine & tenofovir alafenamide

- How will you assess this individual for hormone therapy?
- What dosing would you consider?
- What changes do you expect to see on estrogen?
- What additional aspects of care would you address?

General Approach to Hormone Management

- Recreate the hormonal milieu aligned with gender identity and patient goals
- Initiate low doses of hormones
  - Estrogen + androgen blocker
  - Testosterone
- Titrate as tolerated, not to exceed maximum doses
- Monitor hormone levels and response to treatment

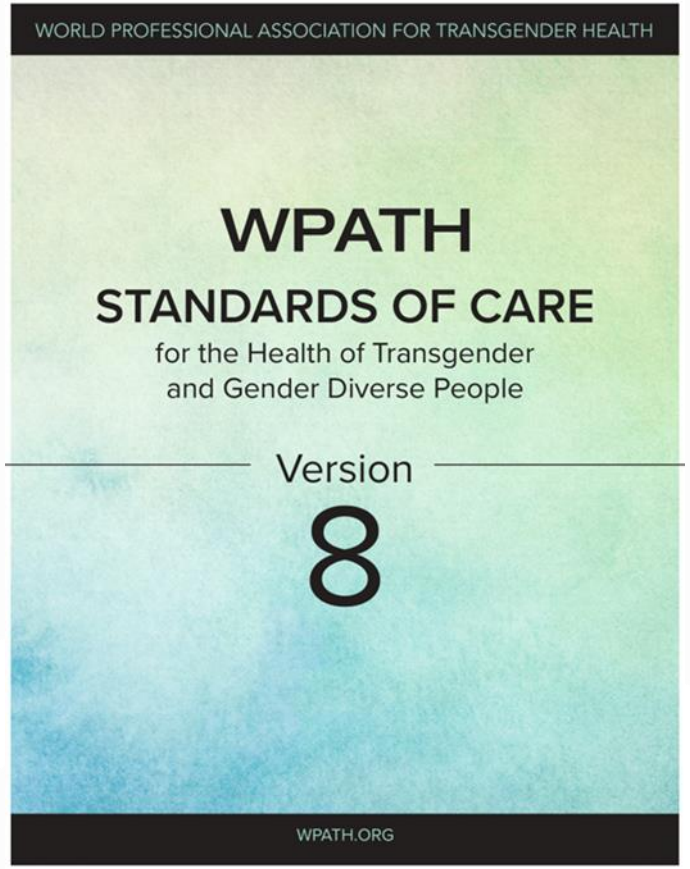


Image source: WPATH.org

Gender-affirming Hormone Therapy

Feminizing	
Estrogens	Estradiol oral (2 mg QD - 6 mg PO QD) Estradiol valerate IM (20 mg IM every 2 weeks) Transdermal estradiol* (25-300 mcg daily)
Androgen blockers	Spironolactone (100 mg – 300 mg QD) GnRH agonists Finasteride for androgenetic hair loss

*Transdermal estradiol recommended age>45, CVD risk factors/VTE
Not recommended: bicalutamide (insufficient data), conjugated estrogens, ethinyl estradiol

Coleman E et al, IJTH 2022

Response to Estrogen Therapy

Effect	Expected Onset	Max Effect	Reversible or Permanent
Breast growth	3-6 months	2-3 years	**Permanent**
Thinning of body hair	6-12 months	>3 years	Reversible
Softening of skin	3-6 months	unknown	Reversible
Body fat redistribution (more feminine)	3-6 months	2-5 years	Reversible?
Decreased muscle mass/strength	3-6 months	1-2 years	Reversible
Decreased sperm, reduced fertility	variable	variable	Reversible?
Decreased testicular volume	3–6 mo	2–3 y	Reversible?

Hembree et al JCEM 2017, Coleman et al IJT 2012

Gender-affirming Hormone Therapy

Masculinizing Hormones	
Testosterone	Testosterone cypionate or enanthate, 50 - 100mg SC weekly or 100 – 200 mg every 2 weeks IM Testosterone gel 50-100 mg/day Testosterone transdermal patch 2.5–7.5 mg/day Testosterone Undecanoate 750 mg every 10 weeks

Coleman E et al, IJTH 2022

Response to Testosterone Therapy

Effect	Expected Onset	Expected Max Effect	Reversible or Permanent Effect
Facial/body hair growth	1-6 months	1-2 years	**Permanent**
Skin oiliness/acne	1-6 months	1-2 years	Reversible
Body fat redistribution	3-6 months	2-5 years	Reversible
Deepened voice	3-12 months	1-2 years	**Permanent**
Increased muscle mass/strength	6-12 months	2-5 years	Reversible
Male pattern baldness	>12 months	variable	**Permanent**
Cessation of menses	2 months	6 months	Reversible
Clitoral enlargement	3-6 months	1-2 years	**Permanent**

Hembree et al 2009, Dahl et al 2006, Coleman et al 2012

How often should hormones be monitored?

Testosterone Therapy
• Testosterone and Hgb/HCT every 3 months in the first year then 1-2 times/year • Target level is 400-700 ng/dL
Estrogen/androgen blockers
• Evaluate every 3 months (with dose changes) in the first year then 1-2 times/yr • Serum testosterone levels <50 ng/dL. • Serum estradiol 100-200 pg/mL. • On spironolactone - monitor serum electrolytes (K^+) and kidney function • Primary care screening

Coleman E et al, IJTH 2022; Hembree WC et al, J Clin Endocrinol Metab 2017

Case

A 44-year-old trans woman presents with a one-day history of a painful, swollen left leg. Ultrasound - thrombus in the left posterior tibial vein

PMH: HIV, stable on ART, VL UD, Smoker 2PPD

Meds: Congugated estrogens (CEE) 10mg daily, spironolactone, DTG, TDF/FTC

She is started on rivaroxaban. What is your advice to reduce her risk of a similar event?

A. Discontinue her estradiol treatment only
B. Discontinue both estradiol and spironolactone
C. Discuss tobacco cessation
D. Switch to transdermal estradiol (patch)
E. C and D

Case

A 44-year-old trans woman presents with a one-day history of a painful, swollen left leg. Ultrasound - thrombus in the left posterior tibial vein

PMH: HIV, stable on ART, VL UD, Smoker 2PPD

Meds: Congugated estrogens (CEE) 10mg daily, spironolactone, DTG, TDF/FTC

She is started on rivaroxaban. What is your advice to reduce her risk of a similar event?

A. Discontinue her estradiol treatment only
B. Discontinue both estradiol and spironolactone
C. Discuss tobacco cessation
D. Switch to transdermal estradiol (patch)
E. C and D

Medical Risks

Testosterone Therapy	Estrogen Therapy
Erythrocytosis (hematocrit >50%) Severe liver dysfunction transaminases 3 x ULN	Thromboembolic disease
Uncertain	
Coronary artery disease? Cerebovascular disease? Breast or uterine cancer? Hypertension?	Breast cancer Macroprolactinoma Coronary artery disease Cerebrovascular disease Cholelithiasis Hypertriglyceridemia

Hembree et al J Clin Endocrinol Metab, 2017

Key Points

- ✓ Venous thromboembolism (VTE) is increased with gender affirming hormones (highest with ethinyl estradiol & conjugated estrogens)
- ✓ Transdermal estradiol is recommended age>45, CVD risk factors/VTE

Question

Transgender women living with HIV who initiate antiretroviral therapy (ART) should

A. Discontinue their hormonal treatment
B. Reduce the doses of their estrogen therapy by 50%
C. Stop ART if they want to continue hormones
D. Monitor hormone levels if an interaction with ART is likely

Question

Transgender women living with HIV who initiate antiretroviral therapy (ART) should

A. Discontinue their hormonal treatment
B. Reduce the doses of their estrogen therapy by 50%
C. Stop ART if they want to continue hormones
D. **Monitor hormone levels if an interaction with ART is likely**

Drug-Drug Interactions (GAHT and ART)

- ART with least potential to impact gender affirming hormone therapy (GAHT)
  - Unboosted INSTIs
  - NNRTIs: RPV, DOR
- ART that may increase GAHT
  - EVG/c, PI/r & PI/c increase testosterone and finasteride levels
- ART that may decrease GAHT
  - PI/r decreases estradiol
  - EFV, ETR, NVP decrease estradiol, testosterone, finasteride
- ART with unclear effect on GAHT
  - EVG/c and PI/c on estradiol

Key Points

- ✓ Hormone therapy is not a contraindication to ART
- ✓ Titrate GAHT based on desired clinical effects, adverse effects and hormone concentrations

Case

57-year-old African American transgender woman has been on estrogen therapy for 5 years. She underwent penile-inversion vaginoplasty 5 years ago. Past medical history includes HIV and hyperlipidemia. Her medications include dolutegravir, emtricitabine & tenofovir alafenamide

Does she need a cervical cancer screen?

A. Yes
B. No
C. I'm not sure

Case

57-year-old African American transgender woman has been on estrogen therapy for 5 years. She underwent penile-inversion vaginoplasty 5 years ago. Past medical history includes HIV and hyperlipidemia. Her medications include dolutegravir, emtricitabine & tenofovir alafenamide

Does she need a cervical cancer screen?

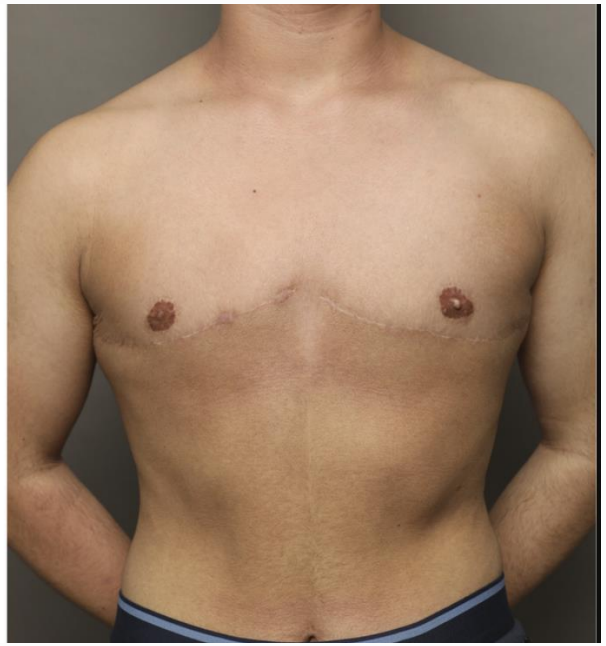
A. Yes
B. No
C. I'm not sure

Gender Affirming Surgeries

Gender Affirming Surgery	Estimated Prevalence Among Trans People in the US (%)
Trans men	
Top surgery	36
Hysterectomy	14
Phalloplasty	3
Metoidioplasty	2
Hysterectomy	14
Phalloplasty	2
Metoidioplasty	2
Trans women	
Vaginoplasty	5-13
Breast surgery	11

Nolan, Urol Clin N Am, 2019; USTS NCTE 2017)

Chest Masculinization



Procedures

- Double incision
- Keyhole
- Purse-String
- Nipple grafts

Image: Sood et al., 2021. Annals of Plastic Surgery, 86 (2), 142-145

Metoidioplasty

- Simple metoidioplasty “clitoral release”
- Can be combined with hysterectomy, oophorectomy, vaginectomy, scrotoplasty
- Urethroplasty (urethral lengthening)

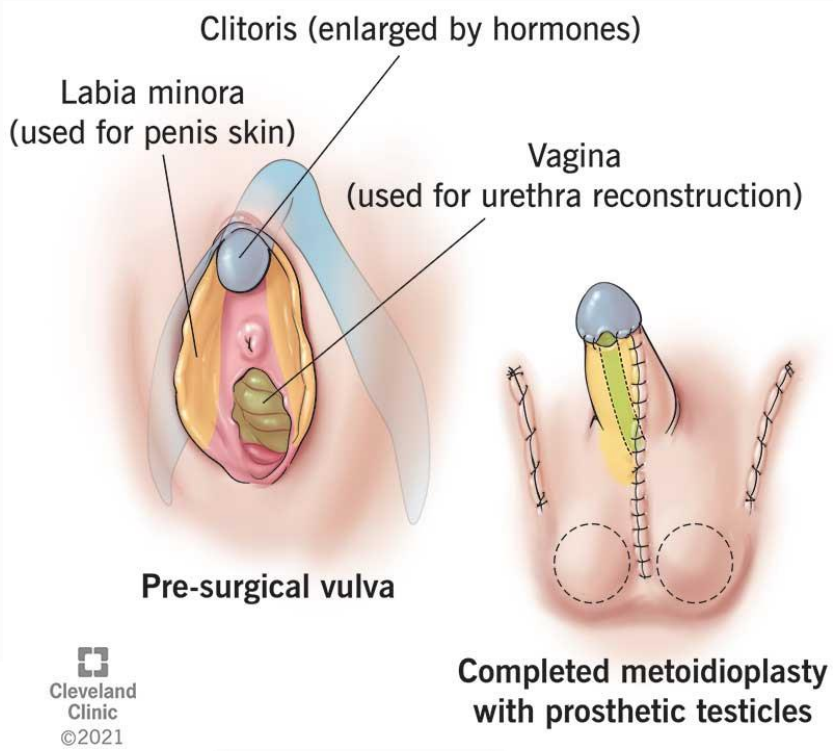
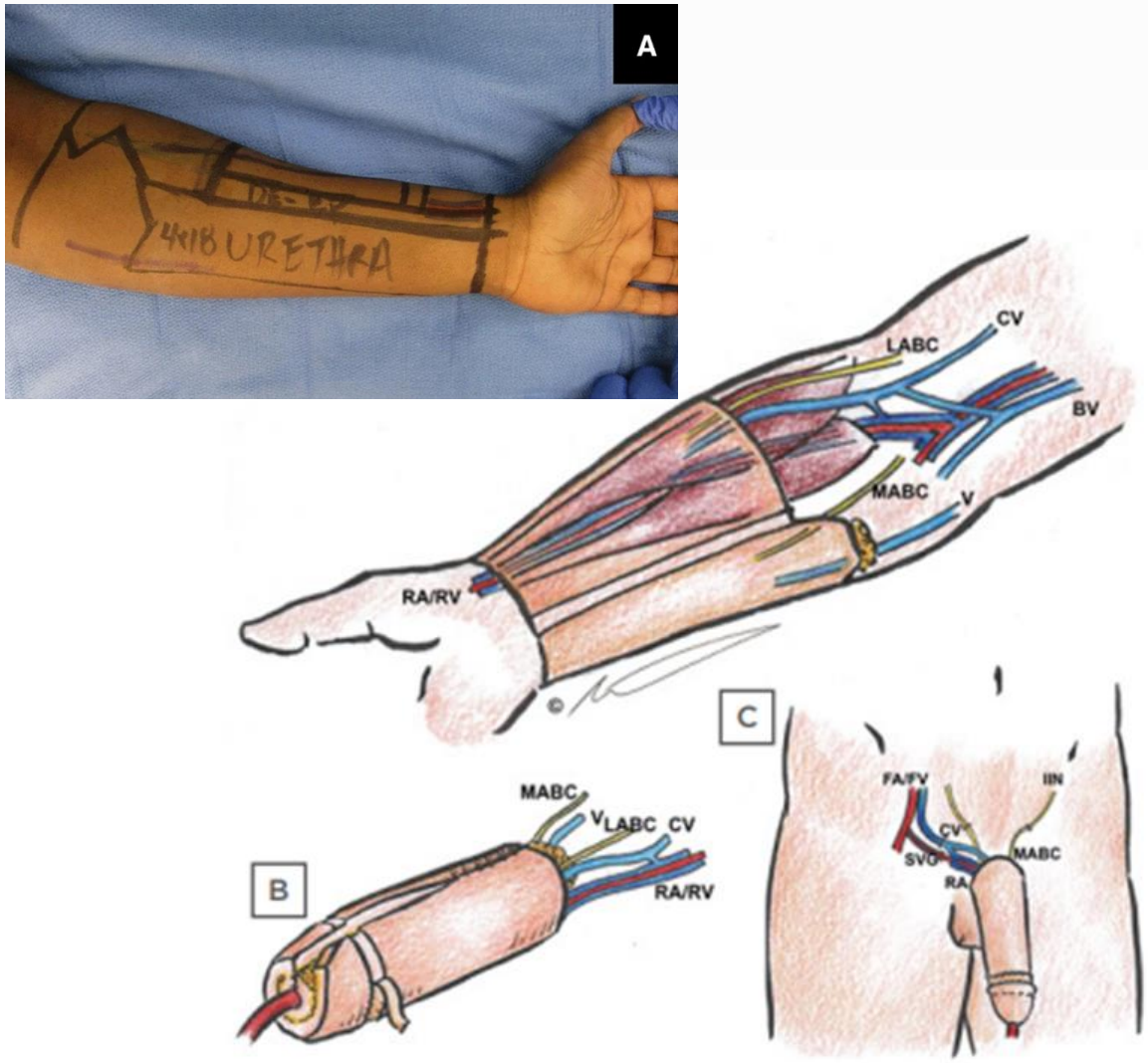


Image: https://my.clevelandclinic.org/health/treatments/21668-metoidioplasty

Phalloplasty

- Radial forearm
- Musculocutaneous latissimus dorsi flap
- ALT (anterior lateral thigh flap)
- Abdominal flap

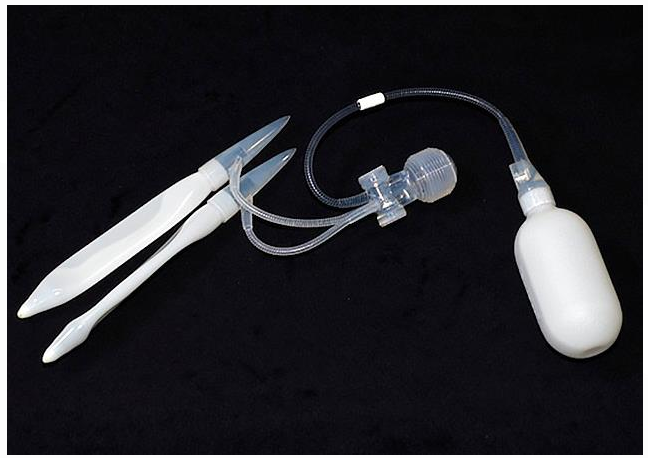


Images: Jahromi, et al. World J Surg 2021; Brazio, et al. EMJ Urol. 2020

Image: https://www.hopkinsmedicine.org/news/articles/gender-affirming-treatment

Other procedures

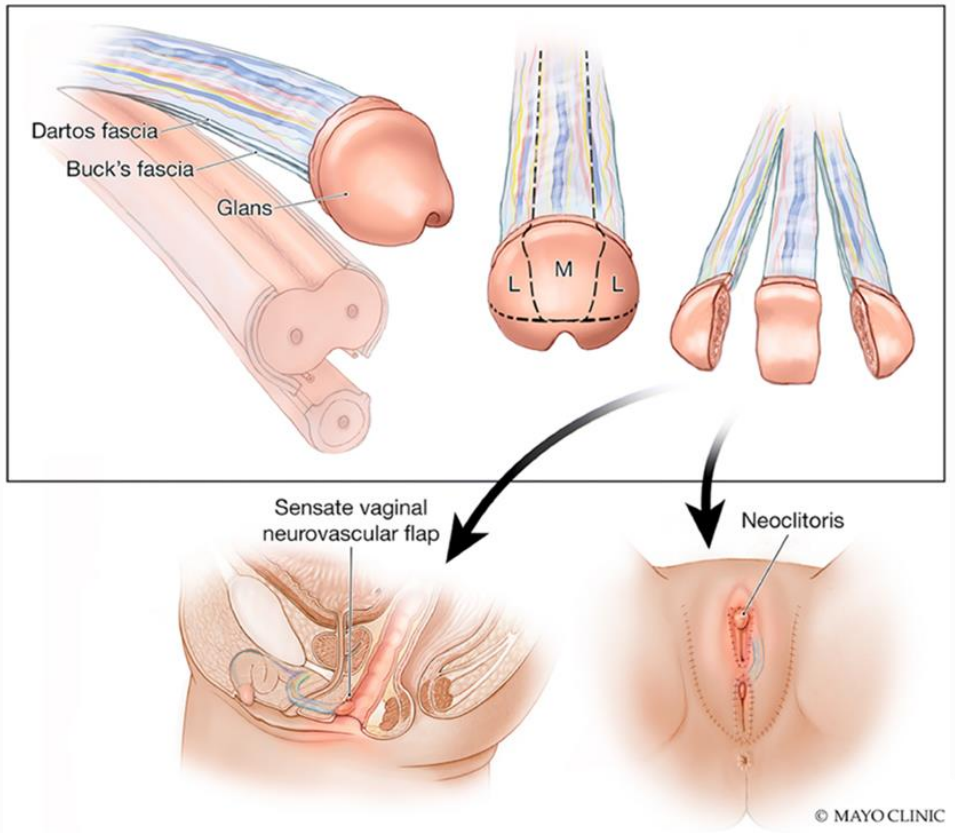
- Vaginectomy / colpoclesis
- Scrotoplasty with testicle implants
  - labia majora used to create a scrotum
- Penile implants (semi-rigid, inflatable)



Images: http://www.drtimnathan-urology.com.au/insertion-of-testicular-prosthesis
https://www.centerforreconstructiveurology.org/erectile-dysfunction/penile-implants-types/#.V6zoOk0rLIU
http://www.phallo.net/penile-implants/coloplast-genesis.htm

Vaginoplasty Procedures

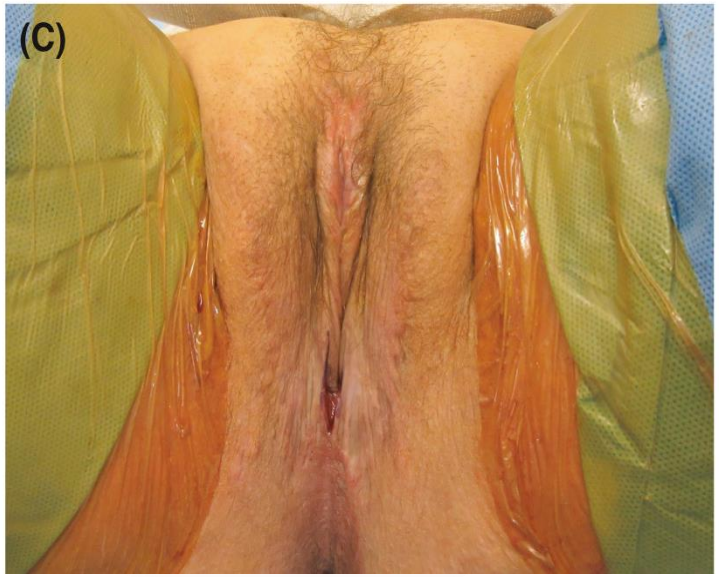
- 1938 - Non-genital skin grafts
- 1956 - Penile skin graft (penile-inversion)
- 1974 - Intestinal graft (colo-vaginoplasty)
- 2018 - Peritoneal graft (Davydov)



R. Abbe, Medical Record, 1898; Banister and McIndoe, Proceedings of the Royal Society of Medicine,1938; Markland and Hastings, Journal of Urology, 1974; Bizic et al, Scientific World Journal, 2014; Jalalizadeh M, Shobeiri SA. Female Pelvic Med Reconstr Surg. 2018; Stowell JT, Abdom Radiol (NY). 2020

Penile inversion vaginoplasty

- Routine exam - inspection (small speculum, anoscope)
- STI screen
- No cervix (pap unnecessary)



Hontscharuk et al, Andrology, 2021

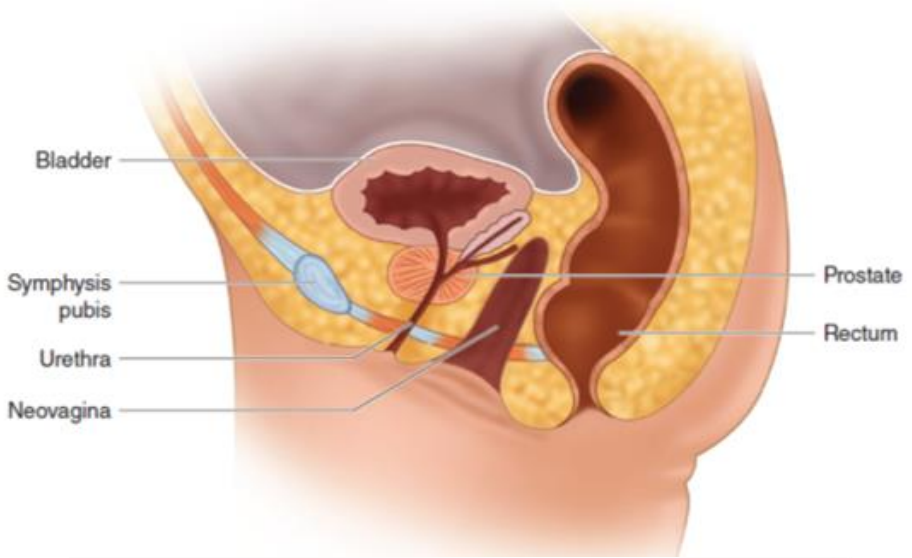


Illustration: Poteat & Radix, 2017 Springer

Facial Surgeries

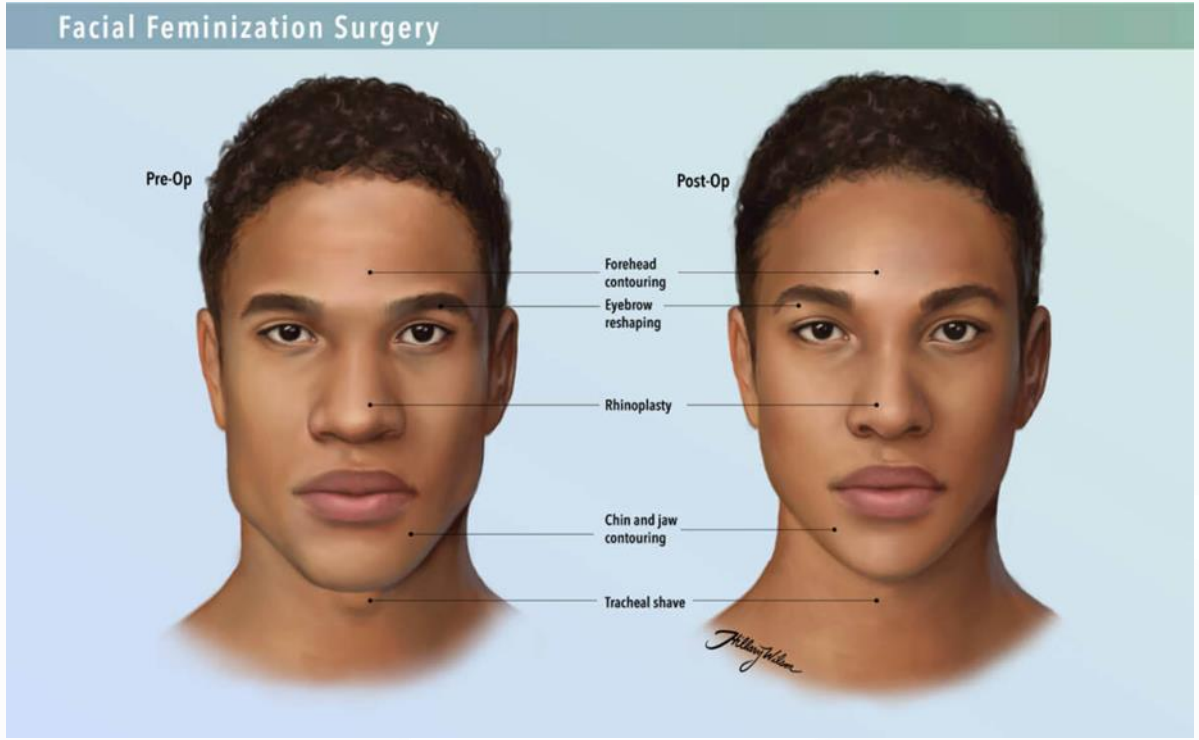
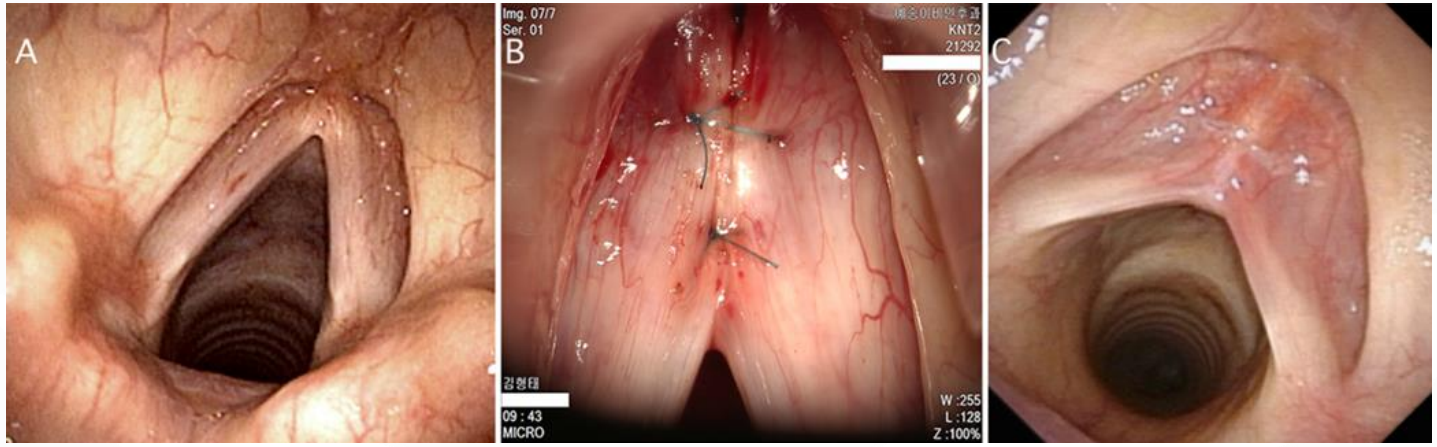


Image: https://www.hopkinsmedicine.org/center-transgender-health/services-appointments/faq/facial-gender-surgery

Feminization Laryngoplasty

- During typical male puberty thyroid cartilage enlarges, vocal cords elongate and thicken
- Wendler glottoplasty: - decreases the length of the vocal cords and elevates pitch



Voice clip

Mastronikolis, J Voice 2013; Kim, Laryngology, 2016

Preventive Care - Cancer Screening

Transgender Women & AMAB

- Breast Cancer‡
- Colon Cancer
- (Intestinal vaginoplasty)

- Prostate Cancer - discuss benefits and harms of PSA screening

‡ 5 years of estrogen

Transgender Men & AFAB

- Cervical Cancer*
- Breast/Chest Cancer
- Colon Cancer

* Follow guidelines for cis women

Create a Welcoming Environment

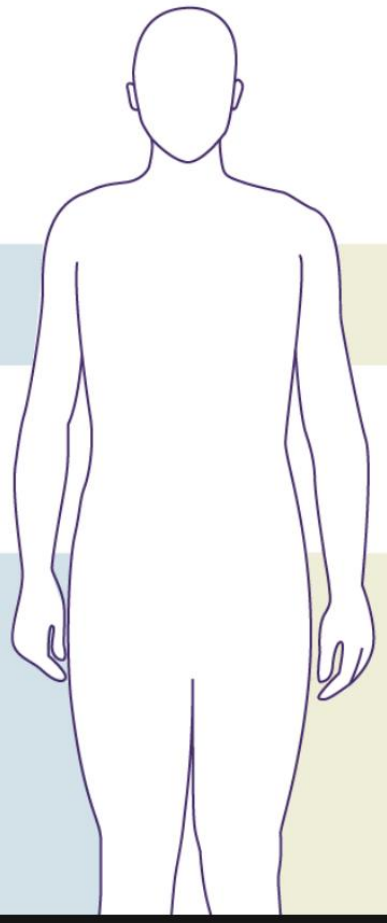
First impressions are important

- **Assess and change current clinical environment**
  - Intake forms inclusive of multiple gender identities and sexualities
  - Affirm gender: Use chosen names and pronouns
  - Knowledgeable providers
  - Assess psychosocial/material needs
  - Use trans images - on education materials, brochures, website
  - Gender neutral/inclusive bathrooms
  - Hire trans-identified staff

Image: Callen-Lorde Community Health Center

Using Less Gendered Language

GENDERED TERMS These terms may be uncomfortable or distressing for trans men to hear.	LESS GENDERED TERMS Try your best to use neutral and inclusive terminology to avoid patient discomfort. If you are unsure, ask what terms your client prefers.
Breasts	Chest
Vulva	External Pelvic Area
Vagina	Genital Opening, Frontal Pelvic Opening, Internal Cana
Uterus, Ovaries	Internal Organs
Pap smear	Cancer screening
Bra, Panties	Underwear
Period, Menstruation	Bleeding



Summary

Transgender individuals

- Experience many health disparities, including HIV
- Clinical competency, hormone provision, welcoming environment essential to engagement in care, use of PrEP and ART

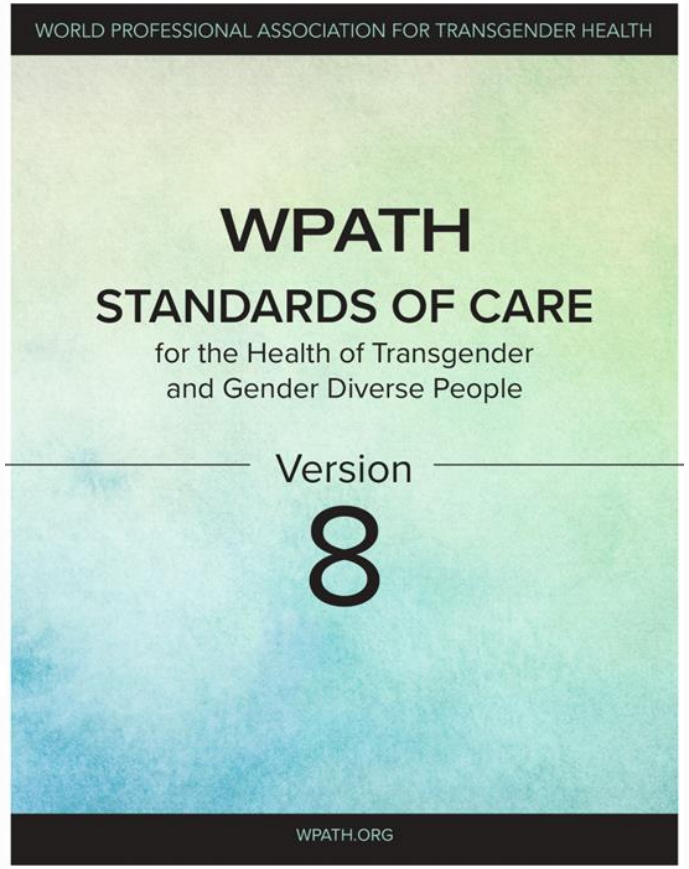
HIV Nexus: A Clinical Resource

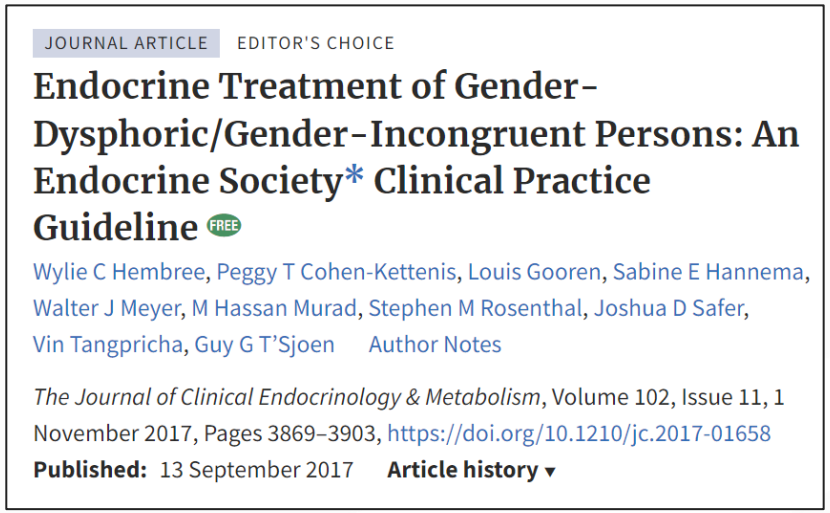
- Serves as a one-stop hub for resources designed to support clinicians
- Contains latest research and information on HIV prevention, screening, and treatment
- Provides access to free continuing medical education programs
- Highlights CDC guidelines and recommendations
- Includes patient education materials

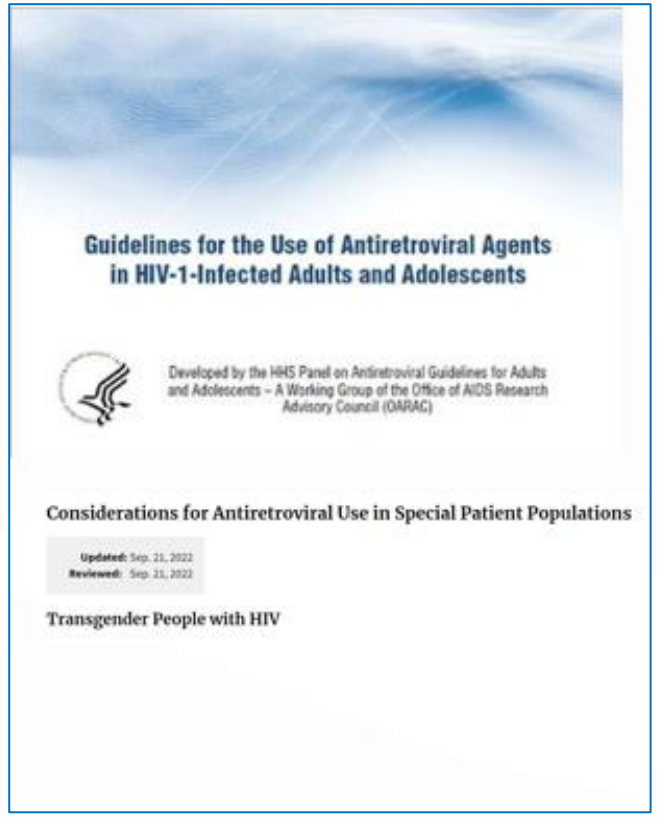
Let's Stop HIV Together for Clinicians

- Clinicians are the front line for preventing new HIV infections and inspiring healthier outcomes for all patients.
- The Centers for Disease Control and Prevention's (CDC's) campaign, Let's Stop HIV Together, offers free resources and tools for health care providers and their patients on HIV screening, prevention, and treatment.

Clinical Practice Guidelines







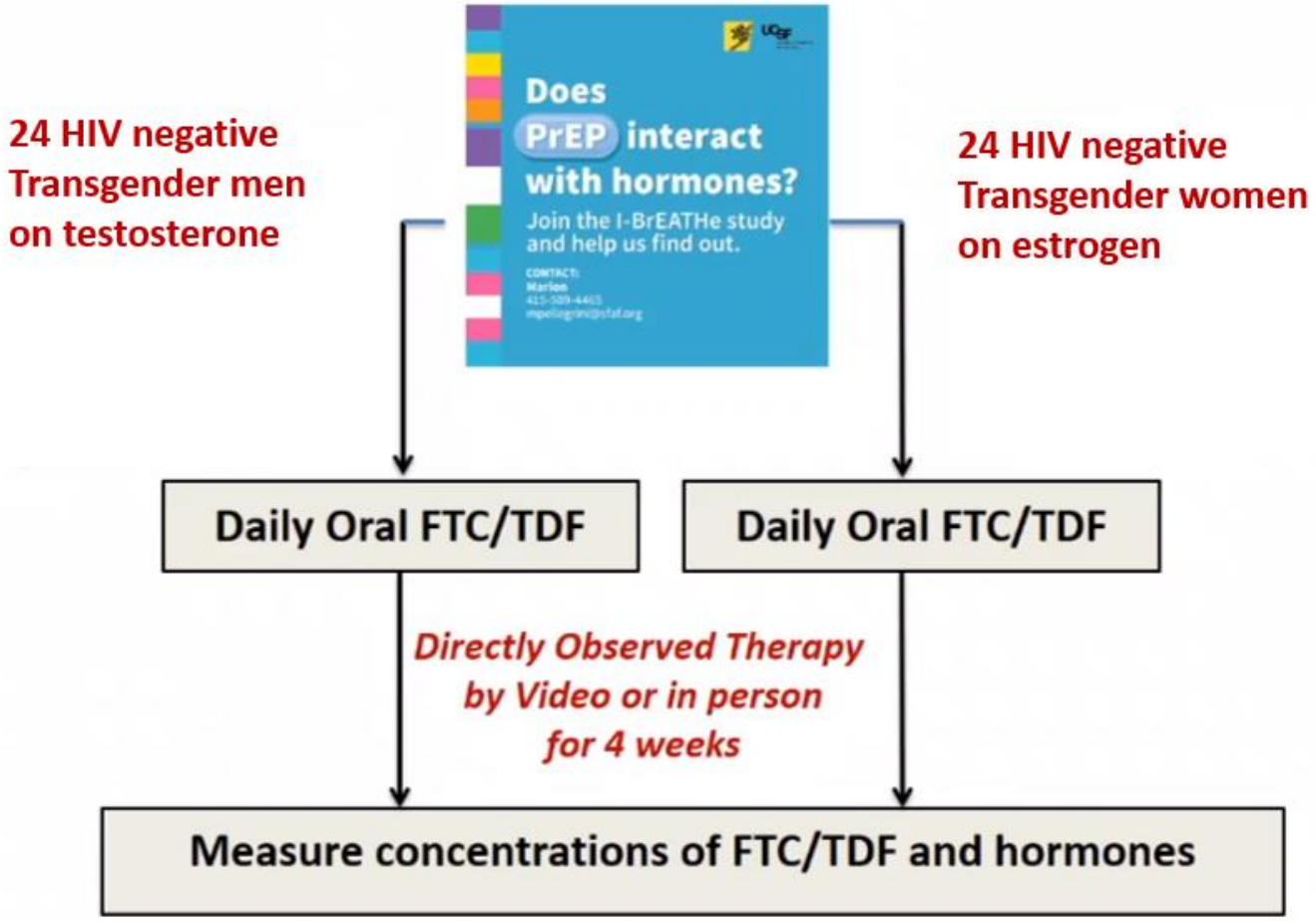
Coleman E et al, IJTH 2022; Hembree WC et al, J Clin Endo Metab 2017; U.S. Department of Health and Human Services, Panel on Antiretroviral Guidelines for Adults and Adolescents. (2021)

Acknowledgements

Richard E. Greene, MD, MHPE, FACP

Thank you

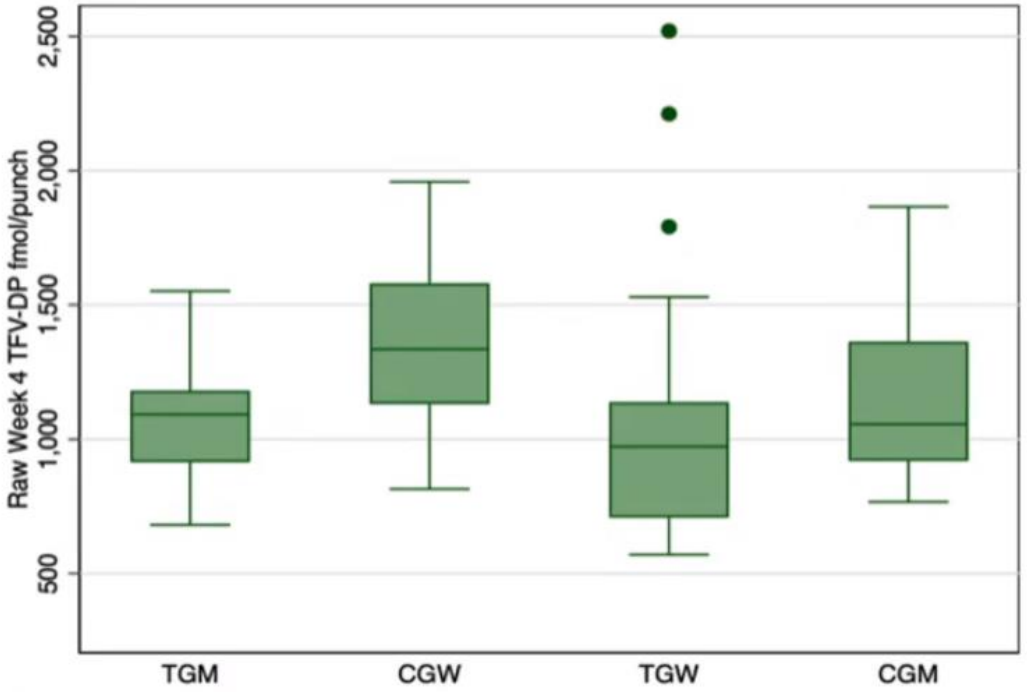
iBrEATHe Study (PrEP)



Grant et al, CID 2021

iBrEATHe Study

TFV-DP concentrations in DBS after 4 weeks of directly observed daily dosing



There were no significant differences between TGM and TGW and CGM;

All participants were projected to achieve highly protective concentrations (>800 fmol/punch).

ant et al, AIDS 2020

Grant et al, CID 2021