Providing Gender-Affirming Care to Transgender and Gender-Diverse Individuals Living with and At Risk for HIV

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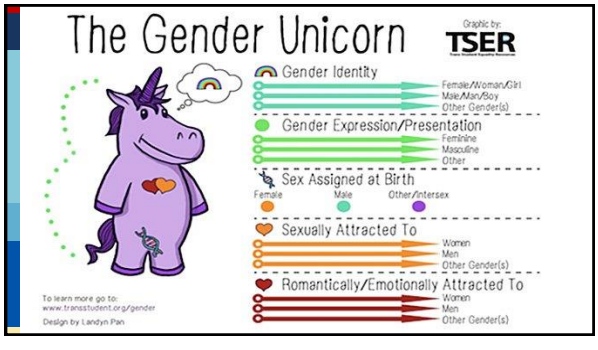
Learning Objectives

After attending this presentation, learners will be able to:

- List key terminology for gender identity and gender affirmation
- Describe best practices for gender-affirming hormone therapy management
- Discuss the epidemiology of HIV in transgender populations
- Identify strategies to improve HIV care and prevention in transgender communities

Slide 3



Key Identity Terms

Female (cisgender)	A person assigned female sex at birth whose gender identity is woman/female
Male (cisgender)	A person assigned male sex at birth whose gender identity is man/male
Transgender	Person whose gender identity and assigned sex at birth do not correspond • Trans woman or transgender female or male-to-female (MTF)* • Trans man or transgender male or female-to-male (FTM)*
Genderqueer	Person who does not follow gender identity and/or expression for assigned sex. May identify as neither, both, or a combo of genders
Nonbinary	Person who does not identify with binary expectations of being strictly a man or woman

*medical model terms (not recommended unless patient uses)

https://www.lgbthealtheducation.org/wp-content/uploads/2020/02/Glossary-2020update-final.pdf

Gender Affirmation

- The process of recognizing, accepting and expressing one's gender identity
  - Medical – hormones, surgery
  - Social/Emotional – Name, pronoun, dress, coming out to others
  - Psychological - Gender validation, internalized stigma/transphobia
  - Legal – Identity documents (name/gender marker)
- Medicalized with the diagnosis of "gender dysphoria," (ICD-10 F64.0) distress related to incongruence between gender identity and sex assigned at birth

APA 2013; Keatley et al 2014; Sevelius 2013; Lawrence 2003; www.lgbthealtheducation.org;

Slide 6

Treatment Guidance

- Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline, 2017. Wylie C. Hembree, et al.
- WPATH Standards of Care for the Health of Transgender and Gender Diverse People, Version 8, 2022. Coleman, E., et al.
- Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People, 2nd edition 2016. Deutsch, M. et al.

J Clin Endocrinol Metab 102: 3869–3903, 2017; Int J Transgender 23:sup1, 2022; Center of Excellence for Transgender Health, Department of Family and Community Medicine, UCSF 2016

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Gender-Affirming Hormone Therapy

Regimen	Typical Dose
Testosterone treatment	
Injectable (short-acting: cypionate, enanthate[2]; long-acting: undecanoate)[1]	20 – 100 mg weekly or 100 – 200 mg every 2 weeks or 750 mg every 4 weeks (initial) then every 10 weeks
Patches, gel 1%[2]	1 – 8 mg/daily (patches); 12.5 – 100 mg daily (gel)
Estrogen treatment	
Oral tablets: micronized estradiol, estradiol valerate[1,2]	1 – 8 mg daily, total (divided)
Estradiol transdermal[2]	50 mcg – 400 mcg/day
Injectable: estradiol valerate or cypionate[1,2]	2 – 10 mg weekly (or < 2 – 40 mg every 2 weeks)
Adjunctive agents	
Spironolactone tablets[2]	25 – 400 mg daily, total (divided)
GNRH agonists[1]	3.75 mg monthly or 11.25 mg every 3 mo (leuprolide acetate); 3.6 mg monthly (goserelin acetate)
Finasteride[2]	1 – 5 mg/day

Cirrincione. Clin Pharmacol Ther. 2021;110:897, transcare.ucsf.edu/guidelines

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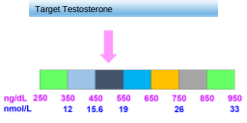
Monitoring Patients on Hormone Therapy



WPATH

Monitoring

	E2 ± antiandrogen	Testosterone
Total testosterone	< 55 ng/dl	Mid normal range
Estradiol*	100-200 pg/mL	<50 pg/mL
Electrolytes	spironolactone	
Lipids	✓	✓
Hematocrit		✓
Liver function		Mild and often transient ↑ ALT/AST
Prolactin	Mild ↑	

*Conjugated or synthetic estrogens can not be monitored by blood tests

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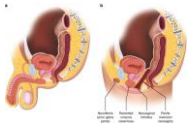
Feminizing Surgery

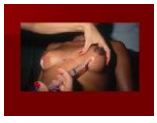
Surgery (2-15%)

- Breast augmentation, orchiectomy, chondrolaryngoplasty, facial feminization, vaginoplasty, labioplasty, vulvopasty
- Increasing numbers of transgender women have genital surgery



Fillers (17-40%)

- Loose fillers (industrial silicone, other substances)
- Injected into breasts, face, hips, buttocks for feminization
- Risk of bloodborne pathogens, migration, inflammation, emboli, disfigurement and death



Poteat, T. CROI Plenary 2016; Drinane, J. Urological Care for the Transgender Patient, 2021

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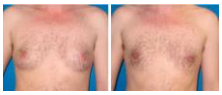
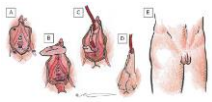
Masculinizing Surgery

- Chest surgery
  - Breast reduction
  - Chest reconstruction
- Facial masculinization
- TAH/BSO
- Penis
  - Metoidioplasty/Metaoidoplasty (meto/meta)
  - Phalloplasty
- Urethroplasty
- Scrotoplasty





Modified ring metoidioplasty (Dr. Ming Chen)

Agarwal JPRAS 2018; Cleveland Clinic 2021

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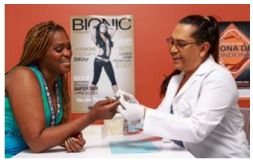
HIV and Transgender People in the US

Prevalence

- USA (18 years and older): 0.39%
- Transgender women 14.1% (8.7%, 22.2%)*
- Transgender men 3.2% (1.4%, 7.1%)*



*Lab confirmed

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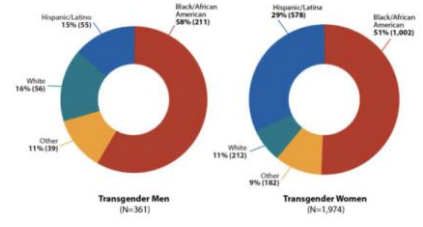
Becasen, J et al. AJPH 2019; Woodring J Natl Health Stat Report. 2015

HIV Diagnoses Among Transgender People in the United States by Race/Ethnicity, 2009-2014



Clark H, AIDS Behav. 2017

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HIV Treatment

Studies show transgender women living with HIV have poorer outcomes across the HIV care cascade, including:

- Lower retention in care
- Lower ART use
- Lower ART adherence
- Lower rates of viral suppression

Baguso et al., 2016; Dowshen et al., 2016; Melendez et al., 2006; Mizuno et al., 2015; Mugavero et al., 2013;Sevelius et al., 2010, 2014; Weiwel et al., 2014; Yehia et al., 2013

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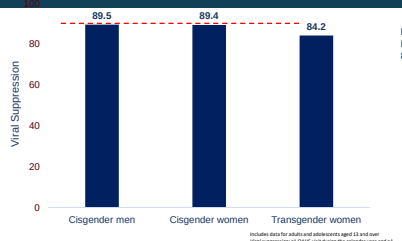
Viral Suppression among Adults and Adolescents Served by the Ryan White HIV/AIDS Program, 2020[a]



Ryan White HIV/AIDS Program, 2020

Includes data for adults and adolescents 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 Guam, Puerto Rico, and the U.S. Virgin Islands.

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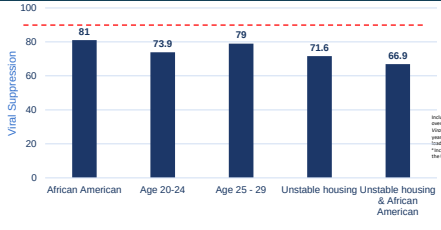
Viral Suppression among Transgender Adults and Adolescents Served by the Ryan White HIV/AIDS Program, 2020[a]

N = 9316 transgender individuals



Ryan White HIV/AIDS Program, 2020

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.

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Factors Associated with Viral Non-suppression

- Prioritization of transition-related medical care over HIV care
- Concerns 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

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Drug-Drug Interactions (GAHT and ART)

- ART with least potential to impact gender affirming hormone therapy (GAHT)
  - **All NRTIs**
  - **Unboosted INSTIs**
  - **NNRTIs: RPV, DOR**
- ART that may increase GAHT
  - EVG/c, PI/r & PI/c increase testosterone, finasteride and dutasteride 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

Monitor dose of GAHT based on desired clinical effects, adverse effects and hormone concentrations.

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Table 17, DHHS ART Guidelines 2022

ARS Question #1 Answer

Providers caring for transgender women living with HIV on antiretroviral therapy (ART) should

A. Discontinue gender affirming 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

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Medical Comorbidities: Weight Gain

- HIV: ART meds (eg, **INSTI, TAF**)
- GAHT
  - Can cause weight redistribution and changes in muscle mass
  - Although muscle mass reduction can occur with feminizing HT, **estrogens known to cause weight gain**
  - Increased body mass typically results from testosterone therapy, but weight gain can vary
- Life stressors

Considerations:

- **ART**: Switching ART is **not recommended** by current guidelines, could consider switch to NNRTI-based regimen
- **GAHT**: Reduce estrogen dose, if patient amenable
- **Lifestyle**: Diet and exercise
- **Other**: If diabetic or prediabetic, consider GLP-1 agonist

Bansi-Matharu. Lancet HIV 2021. 8:e711. transcare.ucsf.edu/guidelines; transcare.ucsf.edu/patients/information-testosterone-hormone-therapy; Block. Am J Epidemiol. 2009;15:181; DHHS Adult and Adolescent ART Guidelines. Sept 2022; Kumar. AIDS 2020. Abstr OAB0605; Monroe. Clin Infect Dis. 2015. 60:453.

Medical Comorbidities: Cardiovascular Risk

- HIV
  - Impact of viremia/inflammation
  - ART meds (protease inhibitors, abacavir)
- GAC
  - Increased venous thromboembolic risk with transgender individuals taking estrogens
  - Possible increased risk for HTN, dyslipidemias, and stroke
- CV risk factors and life stressors

Considerations:

- **ART**: Consider avoiding PIs (except ATV) and ABC; TAF in patients with hyperlipidemia
- **GAC**: Use estrogen injectables or patches instead of pills for patients ≥ 40 years old
- **Lifestyle**: Smoking cessation

Hsue. J Infect Dis. 2012;205:S375. Lundgren. Curr Opin Infect Dis. 2018;31:8; DAD. Lancet. 2008;371:1417; Vehkavaara. Thrombo Haemost. 2001;85:619; Canonico. Circulation. 2007;115:840; cdc.gov/heartdisease/risk_factors.htm; Block. Am J Epidemiol. 2009;15:181; DHHS Adult and Adolescent ART Guidelines. Sept 2022; Patel. IDWeek 2021. Abstr 822.

Medical Comorbidities: Bone Health and Renal Impairment

- Bone health
  - TGW at increased risk for osteoporosis
    - Risk factors: underutilization of hormones after gonadectomy or use of androgen blockers with insufficient estrogen
- Renal impairment
  - Changes of body composition and lean body mass may impact creatinine levels

Considerations:
For bone health

- **ART**: Switch TDF to TAF
- **Lifestyle**: light weights and exercise

For renal impairment

- **ART**: Switch TDF to TAF
- **Dosing Considerations:** CrCl and IBW calculations should be based on gender identity after patient has been on hormone therapy for >6 months

transcare.ucsf.edu/guidelines/bone-health-and-osteoporosis; Collister. Can J Kidney Health Dis. 2021;8; Tao. Int J Infect Dis. 2020;93:108; Stevenson. Endocrinol Metab Clin North Am. 2019;48:421; Webb. Am J Health Syst Pharm. 2020;77:427.

Facilitating HIV Care Engagement

Gender Affirmation

- Having HIV care providers that affirm their gender (e.g., use chosen name and pronouns) were **more likely** to be virally suppressed.
  - Making access to GAHT contingent upon ART adherence associated with **lower likelihood** of viral suppression.

Integration of HIV Care with Gender Care

- Associated with higher rates of viral suppression
- Decreases the number of provider visits
- Makes it easier to discuss important concerns about HIV and gender health care

Peer Navigation

- Having visible transgender staff in the clinic facilitates engagement in care.

Trauma-Informed

- Recognizing and interacting with TPLW as women
- Accounting for various forms of violence, stigma and discrimination affecting TPLW

Chung C, Transgender Law Center, 2016; Dowshen N, Trans Health, 2017; Lacombe-Duncan, Health and Social Care, 2020.

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HIV Prevention

- PrEP uptake suboptimal for transgender populations
  - Low PrEP adherence and persistent
- Cabotegravir LA – cannot use with silicone/fillers buttocks
- Discuss options
  - Transgender women – daily FTC/TDF, daily FTC/TAF*, CAB LA
    Transgender men – daily FTC/TDF, CAB LA

*daily FTC/TAF has not been studied in individuals engaging in vaginal sex acts

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

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CDC 2021 PrEP Update: Identifying Persons at Substantial Risk of Acquiring HIV Infection

2017 Guidance on Substantial Risk of Acquiring HIV Infection

- MSM
  - Sexual partner with HIV
  - Recent bacterial STI
  - High number of sexual partners
  - History of inconsistent or no condom use
  - Commercial sex work
- Heterosexual women and men
  - Same as MSM plus in a high HIV prevalence area/network
- PWID
  - Injecting partner with HIV
  - Sharing injection equipment

- Sexually active adults and adolescents who had anal or vaginal sex in the past 6 months **AND** any of the following
  - Sexually active partner with HIV (especially if partner has an unknown or detectable viral load)
  - Bacterial STI in past 6 months
  - History of inconsistent or no condom use with sexual partner(s)
- PWID
  - Partner with HIV **OR** sharing injection equipment

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PrEP Uptake

Black Transgender women, *USA* (Eaton LA, 2017), n=54	• **47% (n=23)** knew about PrEP • **5% (n=3)** were currently taking PrEP
Transgender Women, *SF, USA* (Wilson, 2015), n=233	• **14% (n=32)** had heard of PrEP • **1% (n=2)** were willing to take PrEP
Transgender Women, *SF, USA* (Wilson, 2022), n=201	• **94%** had heard of PrEP • **45% had taken PrEP in the last 12 months**

Eaton, L. AIDS Behav 2017, Wilson, EC. PLOSOne 2015, Wilson, EC. AIDS Behav 2022

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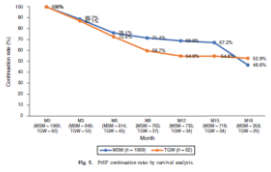
PrEP Persistence



PrEP Discontinuation in San Francisco Department of Public Health Clinics

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 – --)

Green, Sexual Health 2021; Scott, AIDS 2019

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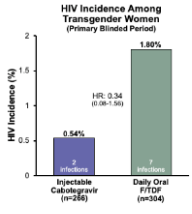
HPTN 083: Gender-Affirming Hormonal Therapy and Long-Acting Injectable Cabotegravir for PrEP

- Subset analysis of transgender women (n=330)
  - Excluded if had silicone implants/ fillers
  - Low HIV risk perception (34%)
  - Self-reported GAHT
    - Cyproterone acetate/ethinylestradiol (27%), estradiol valerate (45%), estradiol (29%), spironolactone (32%)
- HIV incidence (median follow-up: 1.4 years)
  - Lower with long-acting injectable cabotegravir versus daily oral FTC/TDF (0.54 vs 1.80%)
- Initial findings in subset of patients (n=53) suggest that GAHT does not impact cabotegravir concentrations



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Grinsztejn B, et al. *J Int AIDS Soc.* 2022;25(suppl 3):245. Abstract EPLBC04.

Drug-Drug Interactions (GAHT and PrEP)

- No bidirectional effects between TDF/FTC and GAHT found
- No interactions observed between CAB-LA and GAHT

DHHS Adult and Adolescent ART Guidelines. Sept 2022, Grant R et al. Clin Infect Dis 2021, Blumenthal. CROI 2022. Abstr 851, Grinsztejn. AIDS 2022. Abstr EPLBC04.

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ARS Question #2

Which statement is **TRUE** regarding the use of PrEP in transgender people?

A. The CDC recommends "on-demand" PrEP (2-1-1) for use in transgender people

B. Emtricitabine/tenofovir alafenamide is the preferred PrEP option for transgender women due to higher rates of chronic kidney disease

C. Oral PrEP does not affect estradiol or total or free testosterone levels in transgender individuals using hormones

D. Transgender men should avoid oral PrEP due to testosterone use

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Create a Welcoming and Affirming Environment

Assess and change current clinical environment

- Intake forms and EMRs inclusive of multiple gender identities and sexualities
- Use patient chosen names and pronouns
- Knowledgeable providers
- Wrap around services
- Include transgender images on education materials, brochures, website
  - Hire trans-identified staff
  - Gender neutral/inclusive bathrooms

Cahill S, *PLoS ONE*. 2014

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Best Practices in Meeting (ALL) Patients and Collecting Gender Health Data

- Start by introducing yourself, consider using your pronouns, then asking:
  - "What is your name/how would you like to be addressed here?"
  - "What pronouns do you use?"
- Use the two-step method
  - Ask about current gender identity
  - Ask about sex assigned at birth
- Use less gendered language
  - Try to use neutral and inclusive terminology to avoid patient discomfort
- Maintain an up-to-date organ inventory

Deutsch et al, 2013

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Summary

- Transgender individuals experience many health disparities, including HIV and increased risk for HIV
- GAHT and other affirming care important for HIV care engagement
- Medical comorbidities in TLWH may be amplified by GAHT
- Different PrEP administration options available for transgender individuals, no concern for interactions with GAHT
- Clinical competency, GAHT provision, welcoming environment essential to engagement in care

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Acknowledgements

- Jennifer Cocahoba, PharmD
- Asa Radix, MD
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- Jennifer Anger, MD MPH

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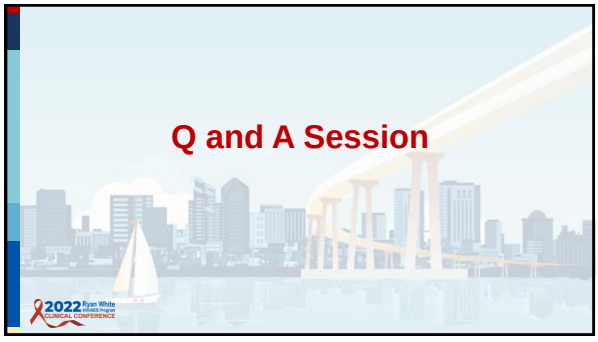
Q and A Session
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