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

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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years:

Dr. Blumenthal has received research support paid to her institution from Gilead Sciences, Inc. (Updated 11/28/22)

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Learning Objectives

After attending this presentation, learners will be able to:

- Use key terminology for gender identity and gender affirmation
- Describe best practices for gender-affirming hormone therapy management
- Discuss HIV treatment and prevention in transgender populations
- Identify strategies to improve HIV and PrEP care in transgender communities

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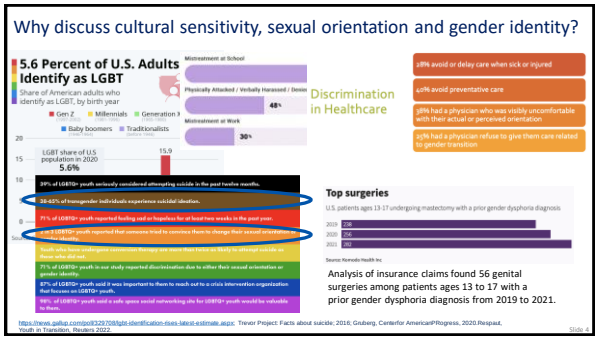

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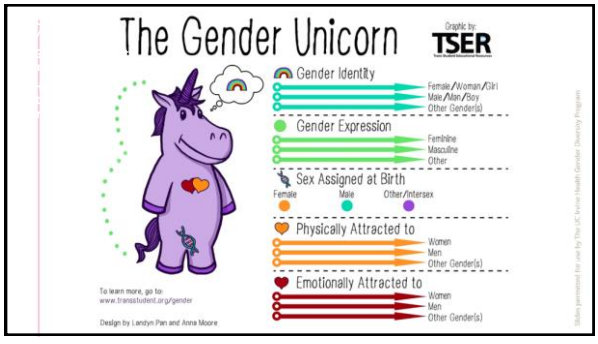

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Key Identity Terms

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

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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;

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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

Target Testosterone

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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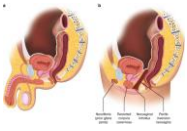
Feminizing Surgery

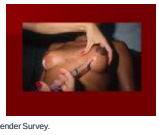
Surgery (4-25%)

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



Fillers (~17%)

- 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; Nolan I, Transl Androl Urol, 2019. James S, Report of the 2015 U.S. Transgender Survey. Drinane J, Urological Care for the Transgender Patient, 2021

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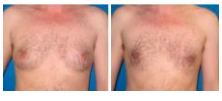
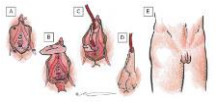
Masculinizing Surgery

- Chest surgery (25-50%)
  - Breast reduction
  - Chest reconstruction
- TAH/BSO (~14%)
- Penis (2-5%)
  - Metoidioplasty/Metaoidoplasty (meto/meta)
  - Phalloplasty
- Urethroplasty
- Scrotoplasty
- Facial masculinization





Modified ring metoidioplasty (Dr. Ming Chen)

Nolan I, Transl Androl Urol, 2019. 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

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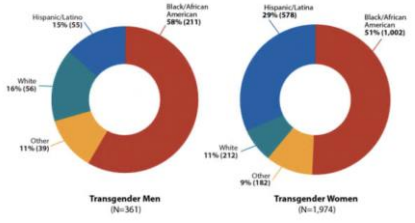
HIV Diagnoses Among Transgender People in the United States by Race/Ethnicity, 2009-2014



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

N = 9316 transgender individuals

Ryan White HIV/AIDS Program, 2020

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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

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Medical Comorbidities: Weight Gain

- HIV: ART meds (e.g., **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.

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Medical Comorbidities: Cardiovascular Risk

- HIV
  - Impact of viremia/inflammation
  - ART meds (protease inhibitors, abacavir)
- GAHT
  - 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
- **GAHT**: 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.

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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.

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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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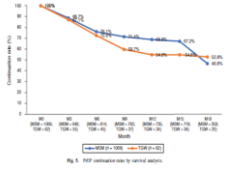
PrEP Persistence

- Prepped for PrEP (P4P): Same day PrEP enrollment program in Ho Chi Minh City[1]
- 1069 MSM and 62 TGW enrolled between Mar 2017 to Jun 2018



- PrEP discontinuation evaluated among those who initiated PrEP in San Francisco Department of Public Health clinics between Jan 2012 and Jul 2017 (N = 348)

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 – --)

- Adjusted analysis of variables associated with PrEP discontinuation: transgender women Hazard Ratio 1.94 (1.36–2.77) (p <0.001) compared to MSM

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Green, Sexual Health 2021; Scott, AIDS 2019

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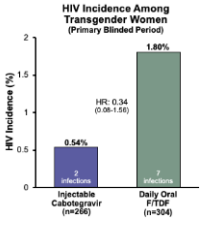
HPTN 083: Gender-Affirming Hormonal Therapy and Long-Acting Injectable Cabotegravir for PrEP

- Subset analysis of transgender women (n=330)
  - Excluded if had silicone implants/ fillers
  - Low HIV risk perception (34%)
  - Self-reported GAHT
    - Cyproterone acetate/ethinyl estradiol (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.

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Drug-Drug Interactions (GAHT and PrEP)

- No interactions observed between LA CAB and GAHT
- No clinically relevant bidirectional effects between FTC/TDF and GAHT found
- TFV-DP concentrations comparable between TGW on GAHT and MSM for those on FTC/TAF

Important to remain vigilant and run DDI check on all medications, not just PrEP medications.

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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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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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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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, low concern for interactions with GAHT
- Clinical competency, GAHT provision, welcoming environment essential to engagement in care

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Acknowledgements

- Jennifer Cocahoba, PharmD
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Question-and-Answer Session

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