# Allyship with Trans and Gender Diverse (TGD) Clients: The Pharmacist's Role

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# Disclosures

- No relevant disclosures
- Received funds for talks from:
  - Rainbow Health Ontario
  - CAMH (Trans and Gender Diverse Healthcare ECHO)
  - Gay Men's Sexual Health Alliance

  - (None of which is felt to meaningfully influence my recommendations today)

- All gender-affirming hormone therapy is off label

This presentation will highlight

**THREE KEY POINTS**

with time for questions & discussion.

**1.** 2SLGBTQIA+ people represent diverse communities

**2.** Trans and gender diverse (TGD) people experience significant health disparities

**3.** Addressing health inequities faced by TGD ppl requires individual actions & inclusive environments

# Key Takeaway #1

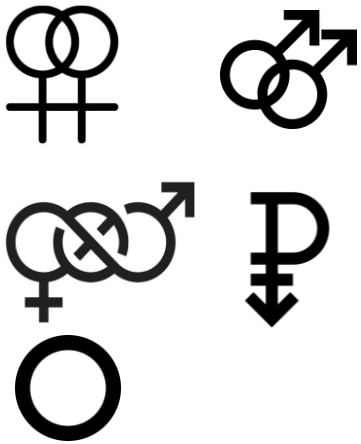
**2SLGBTQIA+** people represent diverse communit**ies** of gender and sexual minorities.

It's important to be familiar with language and terms that may be used.

## Gender Identity

- Transgender
- Transmasculine
- Transfeminine
- Gender non-binary
- Gender fluid
- Gender queer
- Pangender
- Cisgender
- Etc.

## Sexual Orientation



- Lesbian
- Gay
- Bisexual
- Pansexual
- Asexual
- Straight/heterosexual
- Etc.

## Two-spirit

# Terminology

- **Trans(gender)*** – Individuals whose **gender** is different from their **birth sex assignment**. E.g.:
  - **Trans man**: FTM (female to male) –
    Assigned female at birth (**AFAB**) but identifies as a male
  - **Trans woman**: MTF (male to female) –
    Assigned male at birth (**AMAB**) but identifies as a female
  - **Non-binary**: gender identity not exclusive to male/female
  - **Gender non-binary; Gender fluid; Gender queer; Pangender**
  - **etc.**

**Pronouns** are important! (never assume, always ask)

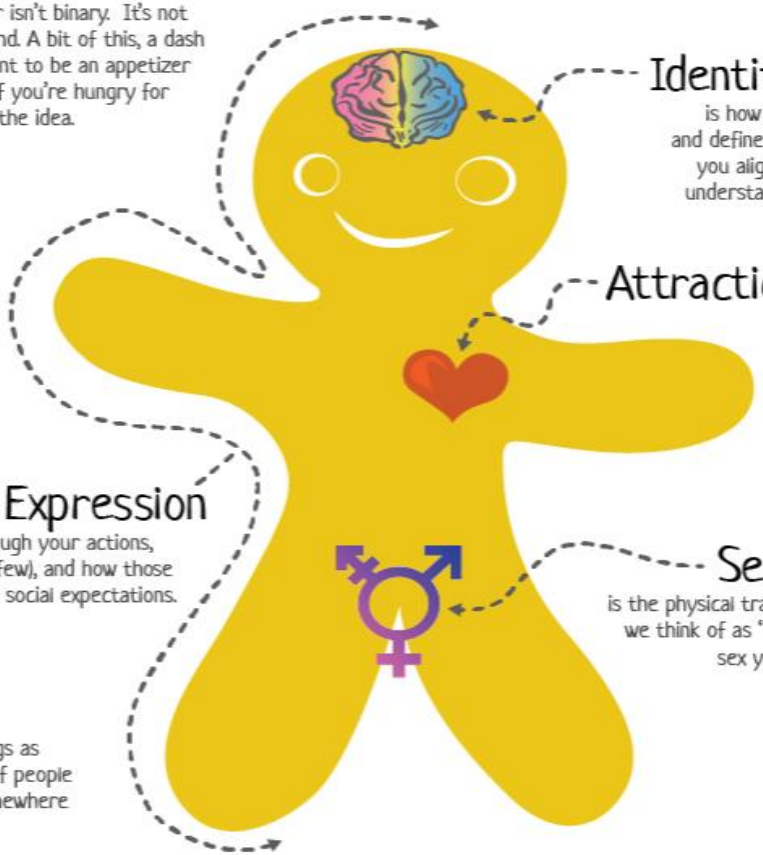
*some trans people identify as ***transsexual***, but this term is older and is not typically used to refer to the community as a whole

(Bass & Nagy, 2021)

# The Genderbread Person

by it's pronounced METROsexual .com

Gender is one of those things everyone thinks they understand, but most people don't. Gender isn't binary. It's not either/or. In many cases it's both/and. A bit of this, a dash of that. This tasty little guide is meant to be an appetizer for gender understanding. It's okay if you're hungry for more after reading it. In fact, that's the idea.



## Identity

is how you, in your head, experience and define your gender, based on how much you align (or don't align) with what you understand the options for gender to be.

## Attraction

is how you find yourself feeling drawn (or not drawn) to some other people, in sexual, romantic, and/or other ways (often categorized within gender).

## Expression

is how you present gender (through your actions, clothing, and demeanor, to name a few), and how those presentations are viewed based on social expectations.

## Sex

is the physical traits you're born with or develop that we think of as "sex characteristics," as well as the sex you are assigned at birth.

We can think about all these things as existing on continuums, where a lot of people might see themselves as existing somewhere between 0 and 100 on each

# Key Takeaway #2

Trans and gender diverse (TGD) people experience **significant health disparities** (aka, **preventable differences in health outcomes**) across a wide variety of domains.

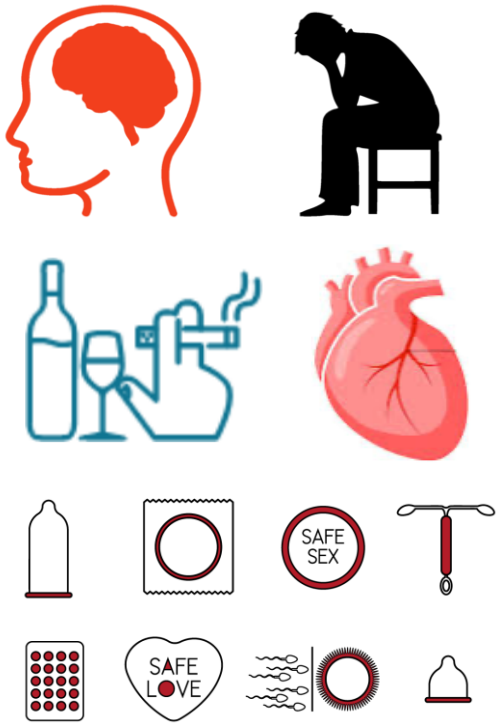
Inequities may be widened for people with other **intersecting** identities (e.g. race, Indigeneity, physical ability, etc).

# TGD Health Inequities/Disparities

TGD patients experience differences in:

- Health care access and engagement
- Mental health
- Safety, incl intimate partner violence and abuse
- Substance use
- Cardiovascular disease
- Sexual health & STIs
- Preventive care and screening

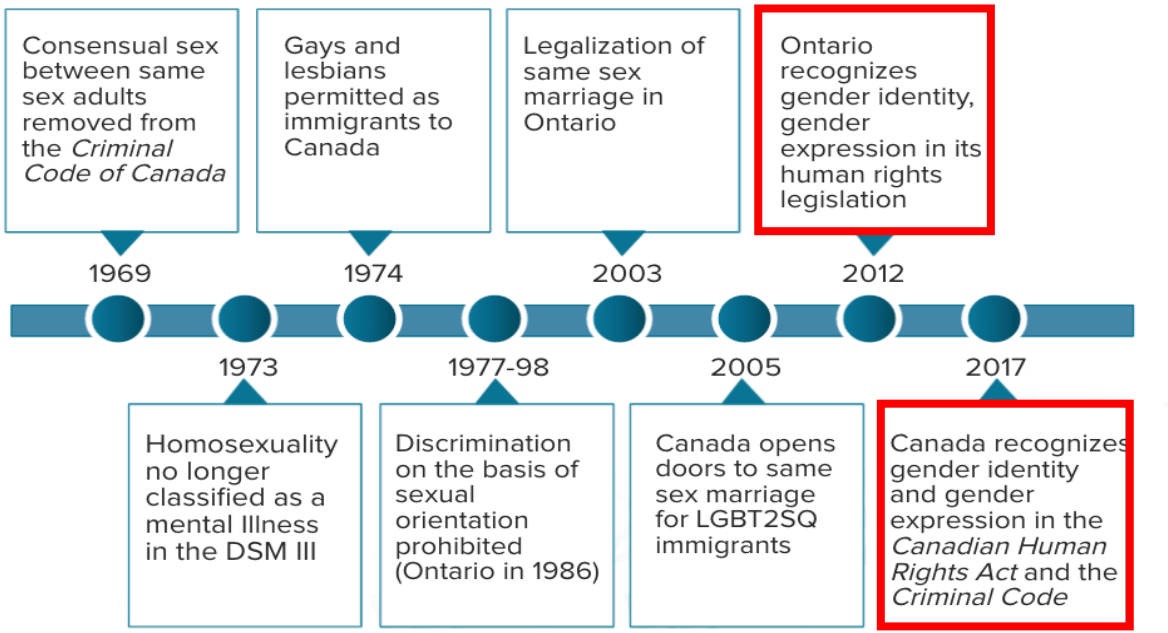
& more



# Why the Health Disparities?

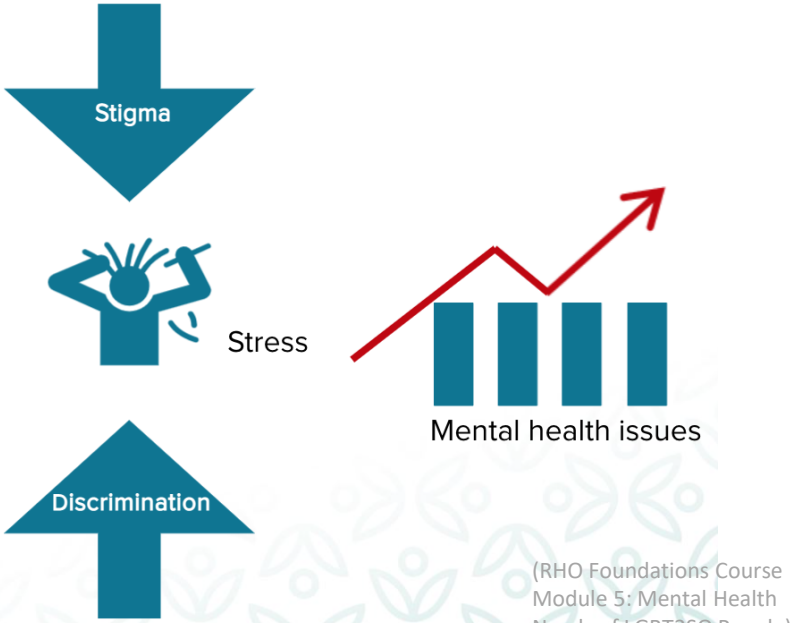
# **Barriers to Care** + the Law

canadian law




Recognize the oppressive systems and institutions that have resulted in these disparities.

# 2SLGBTQ+ populations experience ***minority stress***:




(RHO Foundations Course Module 5: Mental Health Needs of LGBT2SQ People)

**Microaggressions**: brief and commonplace daily verbal, behavioural, or environmental indignities that communicate hostile, derogatory, or negative **slights and insults** toward members of oppressed groups (Nadal, 2008)

# Barriers as experienced by **trans women living with HIV**

- **Interactions with HCPs or staff**
  - Discrimination
  - Denial of services
  - Lack of training (& lack of literature)
  - Agencies not perceived as welcoming
- **Health system navigation issues**
  - Lack of trans specific services
  - Disjointed health care delivery models
  - Siloed care
  - Discrimination in social services
  - Geographic barriers

(Munro 2017)

**1 in 2** trans Ontarians reported discomfort discussing trans health issues with their family physician

**>1/3** of trans Ontarians reported at least one trans-specific negative health care experience with their family physician

Bauer GR, Zong X, Scheim AI, Hammond R, Thind A. Factors impacting transgender patients' discomfort with their family physicians: a respondent driven sampling study. PLoS ONE 2015; 10(12): e0145046.

# Social determinants of health: Overeducated and underemployed

- Trans PULSE survey (n=433 trans people in Ontario)
  - 71% of respondents had some post-secondary education
  - 50% made less than $15,000 per year


(Bauer 2010)

Slide credit: Dr. Ian Armstrong

# Key Takeaway #3

Addressing **health inequities** faced by for trans and gender diverse ppl requires **individual actions** and inclusive (health care and other) **environments.**

# Addressing Health Inequities: Overcoming Barriers to Care

- Create safe, inclusive, non-judgmental spaces
- Trust
- Respect for privacy & confidentiality
- Culturally competent and culturally safe care
- Anti-discrimination policies & staff training

http://www.ohtn.on.ca/Pages/Knowledge-Exchange/Rapid-Responses/Documents/RR79.pdf


# Basic Concepts we teach Health Care Providers

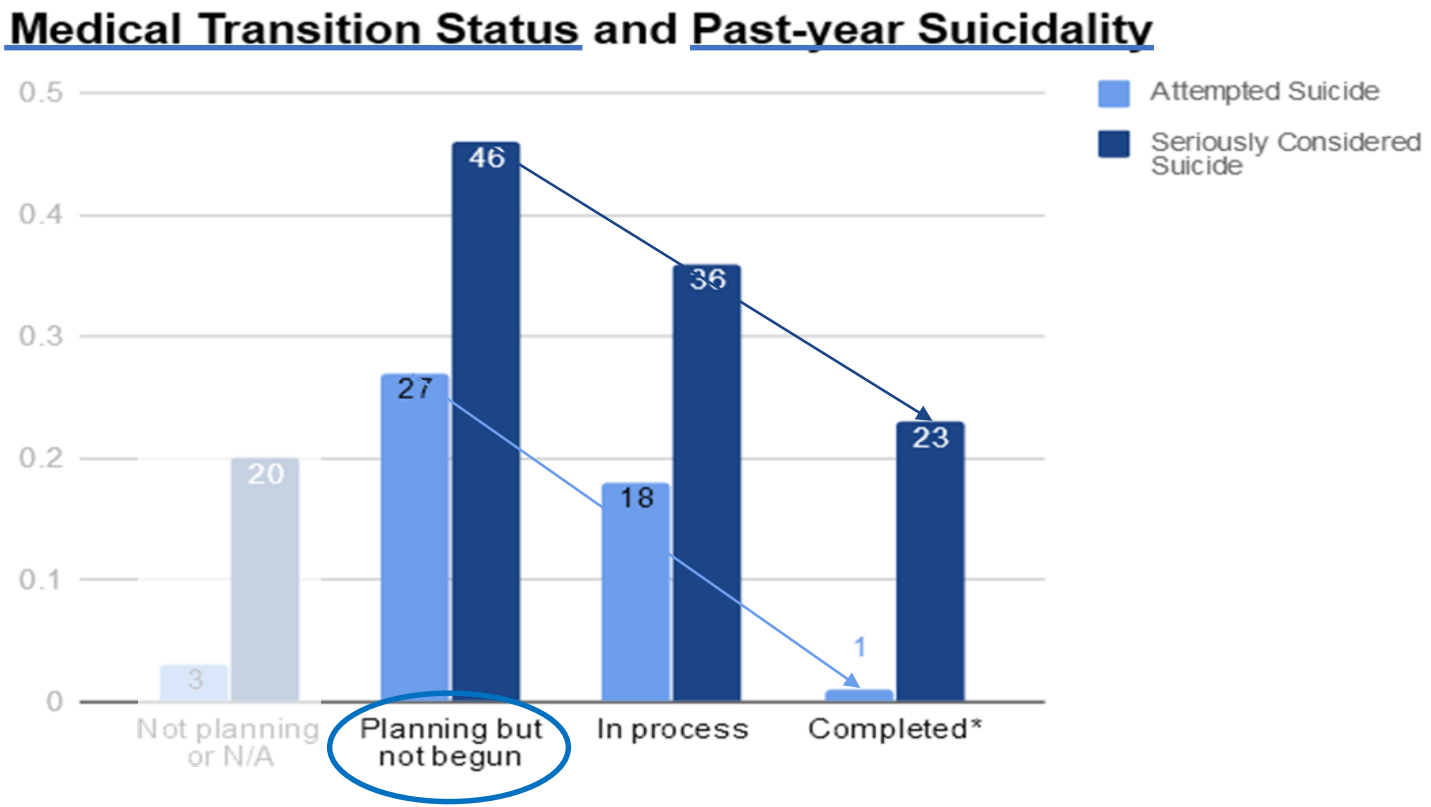
- Have positive space/non-discrimination policy? Is there a positive space sticker or sign?
- Identity: correct name? Gender identity? What pronouns do you use? (gender-affirming language)
- Avoid assumptions
- Ask open-ended questions when possible
  - For example, “Do you have a partner?” rather than, “~~Do you have a boyfriend or girlfriend?~~”
- Don’t ask sensitive questions that are unnecessary
- *Apologize if you make a mistake!*

# Hormone Therapy for TGD Patients

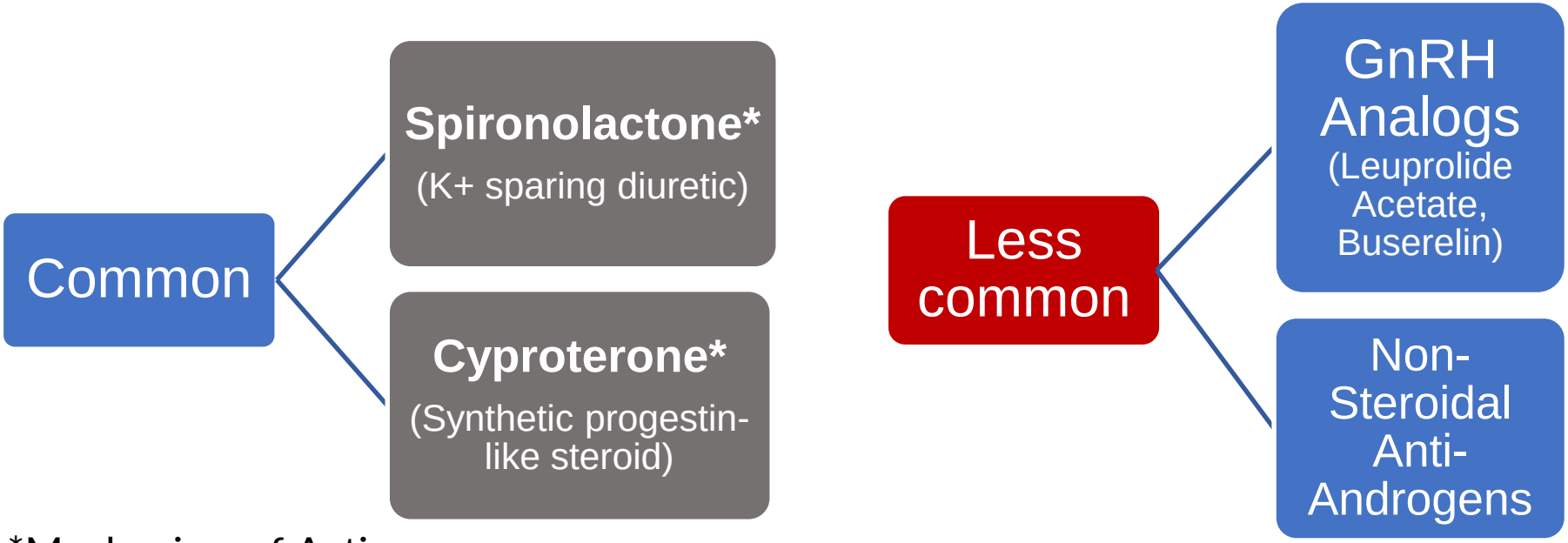
- A significant aspect of TGD healthcare for ***some*** clients
- May involve:
  - Testosterone therapy (‘masculinizing therapy’)
  - Estrogen therapy (‘feminizing therapy’)
  - Hormone blockers—e.g.:
    - Cyproterone
    - Spironolactone
    - Leuprolide
- Pharmacist's Role: Ensuring proper dosing, monitoring side effects, and adherence counseling.

# Why is **gender affirming care** important?

www. transpulsecanada.ca



# Medications: Anti-Androgens

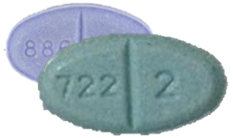



*Mechanism of Action:

- **#1: Blocks peripheral androgen receptors**
- *Secondary* suppression of testosterone synthesis

# Medications: Estrogens

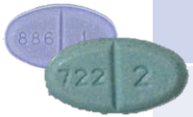
- **Oral (ODB-covered)**
  - 17β-**Estradiol**: lower cost, generally easy adherence
- **Transdermal Estradiol**
  - Avoids 1st pass effect through liver: ↓risk of DVT/PE, ↑ risk of triglycerides
  - Not covered by ODB; very expensive
- **Injectable Estradiol Valerate**—*compounding pharmacy*
  - Avoids 1st pass effect through the liver, but VTE risk suspected to be similar to oral (Connors 2019)
  - Peak and trough effect





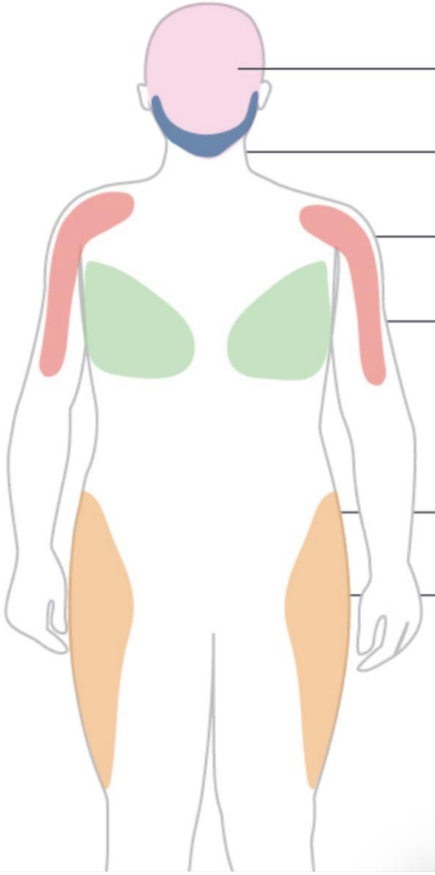

(RHO Webinar: Transition-Related Hormone Therapy in Primary Care, 2020)

# Estrogen + Blocker Dosing


| | Starting dose | Usual dose | Max dose |
|---|---|---|---|
| **Anti-androgens** | | | |
| Spironolactone | 50mg once daily | 100mg BID | 150mg BID (300mg/d) |
| Cyproterone | 10mg q1-2d (usually 12.5mg q1-2d) | 10mg daily | 25-50mg daily |
| **Estrogen** | | | |
| Estradiol PO/SL (Estrace®) | 1-2mg daily | 2mg BID | 3mg BID (6mg/d) |
| Estradiol patch (e.g. Estradot®), apply 2x/week | 50mcg daily | 100-200mcg daily | 400mcg daily |
| Injectable Estradiol Valerate | 3-5mg weekly (IM/SC) or 6-10mg q2wks (IM) | 5-10mg weekly (IM/SC) | 10mg weekly |

# Effects of Estrogen +/- Blocker Therapy



Softening of skin/decreased oiliness

Thinned/slowed growth of body/facial hair[c]

Decreased muscle mass/strength[b]

Breast growth

Body fat redistribution

Decreased testicular volume
Decreased Libido
Decreased spontaneous erections
Decreased Sperm production
Erectile Dysfunction

Variable timeline, variable effectiveness; different levels of reversibility

# Estrogen Risks

*Compared to AMAB not on estrogen

| *Increases* risk | *May* increase risk | Does *not* incr risk |
|---|---|---|
| **VTE** *(route and anti-androgen dependent)* | HTN | Prolactinoma |
| ↑Triglycerides | DM2 | Breast Ca (***inconclusive***) |
| Weight gain | Decr bone density | Prostate Ca |
| | Hyperprolactinemia | |
| ***Likely increases* risk w additional risk factors:** | | |
| Stroke | | |
| Cardiovascular Disease | | |
| Gallstones | | |

(WPATH SoC v8) Coleman et al., 2022

# Estrogen + Blocker Lab Monitoring

In this table, smaller and lighter grey "x"s indicate parameters that are measured under particular circumstances

| Test | Baseline | 4–6 weeks | 3 months | 6 months | 12 months[e] | Yearly | According to guidelines for cis patients, or provider discretion |
|---|---|---|---|---|---|---|---|
| CBC[a] | X | | x | x | X | x | |
| ALT/AST[b] | X | | x | x | X | x | X |
| Creatinine/lytes[c] | X | x | x | x | x | X (spironolactone) | |
| Hba1c or fasting glucose | X | | | | X | | X |
| Lipid profile | X | | | | X | | X |
| Total testosterone | X | | X | X | X | X | |
| Estradiol | X | | X | X | X | X | |
| Prolactin[d] | X | | | | x | x | x (may *consider* q1-2yrs, esp. with cyproterone) |
| Other | Hep B, C | | | | | | |
| | Consider: HIV, syphilis and other STI screening as indicated, frequency depending on risk | | | | | | |

(Sherbourne Health Guidelines, 2019)

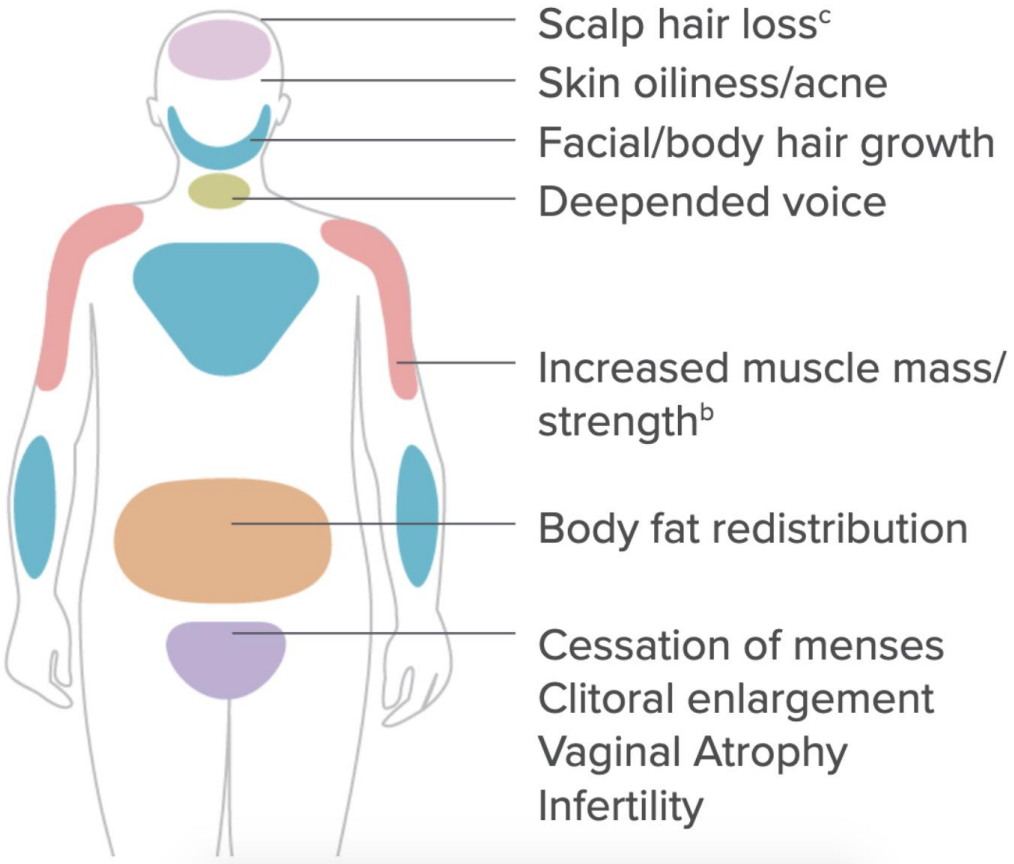
# Medication: Testosterone

- **Injectable** (IM or SubQ injection)
  - Testosterone **enanthate** or **cypionate**
  - Chosen for efficacy, availability, and cost
  - Covered by **ODB** (through EAP – exceptional access program)


- **Transdermal (Gel)**
  - Steadier testosterone level (daily application)
  - Risk of transfer
  - Price is significant barrier


- (Oral testosterone typically avoided d/t hepatotoxicity concerns)

# Effects of Testosterone



# Testosterone Dosing



| | Starting dose | Max dose |
|---|---|---|
| Injectable IM/SC:<br>Testosterone enanthate<br>(Delatestryl®, 200mg/mL)<br>Testosterone cypionate<br>(e.g. Depo-Testosterone®, 100mg/mL) | 20-50mg weekly (**IM/SC**)<br>(or 40-100mg IM q2wks) | 100mg weekly (**IM/SC**)<br>(or 200mg IM q2wks) |
| Testosterone Gel 1%<br>(taro-testosterone gel, Androgel®, Testim®)*<br><br>*only taro-testosterone packets (2.5g, 5g) are covered through ODB EAP | 2 pumps / 2.5g of product (= 25mg test) daily | 4-8 pumps / 5-10g of product (= 50-100mg test) daily |

# Testosterone Risks

*Compared to AFAB not on testosterone

| *Likely Increases* risk | *May* increase risk if additional risk factors | Does *not* increase risk |
|---|---|---|
| **Polycythemia?** (↑ RBCs?) | Cardiovascular disease | Breast cancer |
| Weight gain | ↑Triglycerides | Cervical/uterine/ovarian cancers |
| ↑LDL cholesterol, ↓HDL | DM2 | Osteopenia/osteoporosis |
| Sleep apnea | | |
| HTN | | |

(WPATH SoC v8) Coleman et al., 2022

# Testosterone Lab Monitoring

| Test | Baseline | 3 mos, 6 mos | 12 mos | Annually |
|---|---|---|---|---|
| **Complete Blood Count** ("male range"), **Total testosterone** ("male range," 8.4 - 28.8 nmol/L)<br>• mid-range?<br>• trough? | X | X | X | X |
| **ALT** (liver enzyme) | X | | X | If concerns |
| A1c/fasting glucose, Lipids | X | | X | If other RFs |

- Hep A, B, C, **pregnancy test** (before 1st dose)

# Anatomy and Tips on Terminology Use

- Refrain from referring to body parts as ‘male’ or female’
- Ask pt preferred terms for body parts, or use gender neutral terms

| Consider Avoiding | Consider Using |
|---|---|
| Vagina | Inside the genitals / front hole |
| Vulva | Outside of the genitals |
| Clitoris | Erogenous tissue / erectile tissue |
| Period / Menses | Monthly bleeding |
| Bacterial vaginosis | Bacterial overgrowth in the genitals |
| Atrophic vaginitis | Thinning of the internal genital tissue |
| Breasts | Chest |
| Penis | External genitals / erectile tissue |
| Testes | External genitals / gonads |

# TGD HIV Care

These populations are disproportionately affected by HIV & receiving appropriate gender-affirming care can have positive implications on their HIV care (and vice-versa)

# Epidemiology

- **Transfeminine** individuals have high rates of HIV
  - Estimated prevalence of HIV **~20%** worldwide, or 66 times the odds of general population (Stutterheim 2021)
- **Transmasculine** individuals have a much lower prevalence, although less research
  - Estimated prevalence of HIV **2.56%** worldwide, or 6.8 times the odds of general population
  - **63.3%** of trans men surveyed in Ontario (2009-2010) were gay, bi, or men who have sex with men (Bauer 2013)
    - Of those, 17.5% reported no HIV-related sexual risk in the past year, 73.3% reported low/moderate risk, and 9.2% reported high risk

Slide credit: Dr. Ian Armstrong

Joseph, Where Love is Illegal Photo Project

# Privacy and confidentiality

- Privacy protects vulnerable people from stigma and violence
  - Around HIV status (from family, partners, cultural community, workplace)
  - Around trans status (whether very early or very established in their transition)

Slide credit: Dr. Ian Armstrong

# Attitudes & Adherence

- Many prioritize gender-affirming care & hormone therapy over ART (Transgender Law Centre)
- Concern about drug-drug interactions—led to*:
  - **40%** of trans women **not taking ART or HRT as prescribed**
    - 12% did not take **ART** as directed
    - 12% did not take **hormone therapy** as directed
    - 16% did not take **both** as directed
  - **Only 49% discussed drug-drug-interactions w/ provider**




* (Braun 2017 – study excluded HIV+ trans women with detectable VL)

# Drug-Drug Interactions

# Drug-drug interactions

## ART + Anti-androgen

- **Spironolactone**
  - No expected interaction with PIs, NNRTIs, INSTIs, NRTIs, CCR5i (but no studies on this)

- **Cyproterone**
  - *May* be ↑ by cobi, ritonavir (**CYP3A4** inhibition)
  - *May* be ↓ by EFV, NVP, ETR (**CYP3A4** induction)
  - No expected effect from NRTIs, INSTIs, CCR5i

(Badowski 2021, Liverpool Interaction Checker, Radix 2016)

# Drug-drug interactions

Potential for bi-directional DDIs btwn hormones and ART/PrEP

- **HIV PrEP w TDF/emtricitabine**: 
  - Slight ↓tenofovir in serum (↓AUC 12%) & rectal tissue with feminizing hormones; clinical significance unknown (Hiransuthikul et al 2019, Cottrell 2019)
  - No significant effect on estradiol levels
- **ART:**
  - Slight ↓efavirenz (↓$C_{24}$ 9%) and ↓tenofovir (↓AUC 14%, ↓$C_{24}$ 17%) with ART, **but 90% virally suppressed at 12 wks** (Hiransuthikul 2021)
  - ↓estradiol (↓AUC 28%, ↓$C_{max}$ 19%, ↓$C_{24}$ 36%) when co-administered w **EFV**-based ART (Hiransuthikul 2021), **but *not* w INSTI-based ART** (Loutfy 2023)

(Leinung 2019)

# Summary

- **Trans women:**
  - Are disproportionately affected by HIV
  - Access HIV care & achieve virologic suppression at lower rates than other populations
- Minimal data on **trans men** and HIV
- Currently **some research** on drug-drug interactions between feminizing hormone therapy and ARVs, **none** on testosterone and ARVs
- **HIV PrEP** does not impact hormone therapy, but unclear if hormone therapy has a clinically significant impact on PrEP

# Questions?

Thank you! jordan.Goodridge@utoronto.ca

# References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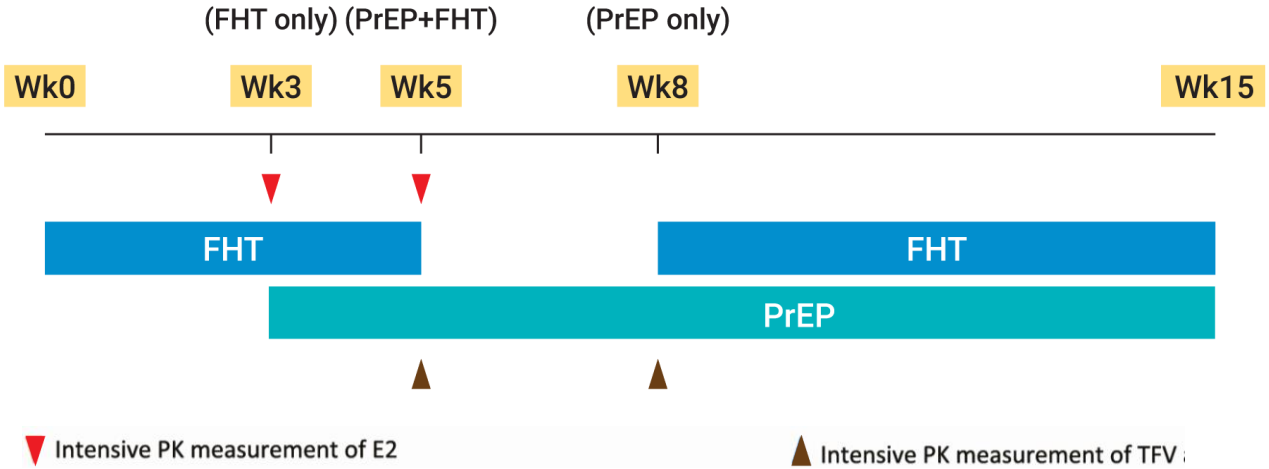
# Appendix

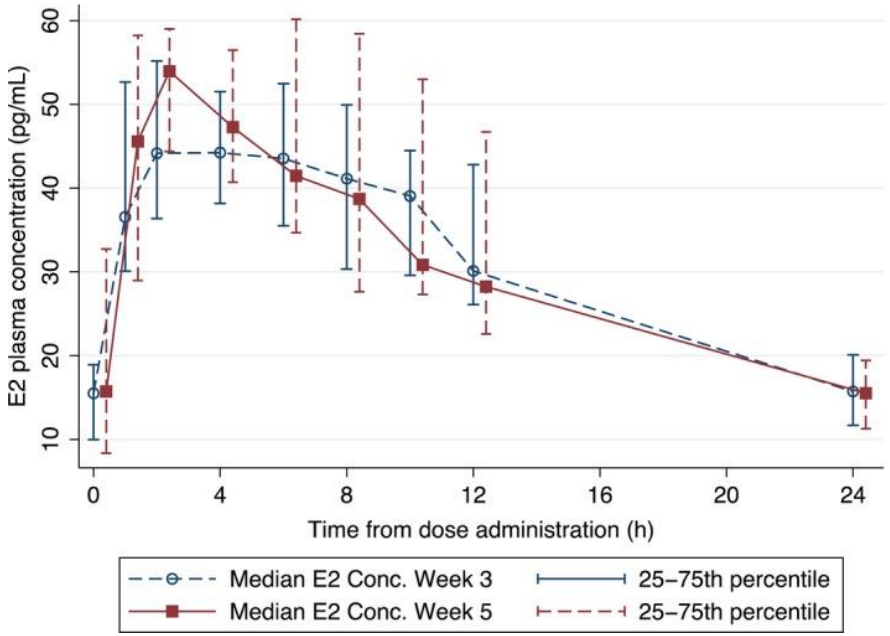
# Drug-drug interactions (PrEP + FHT)

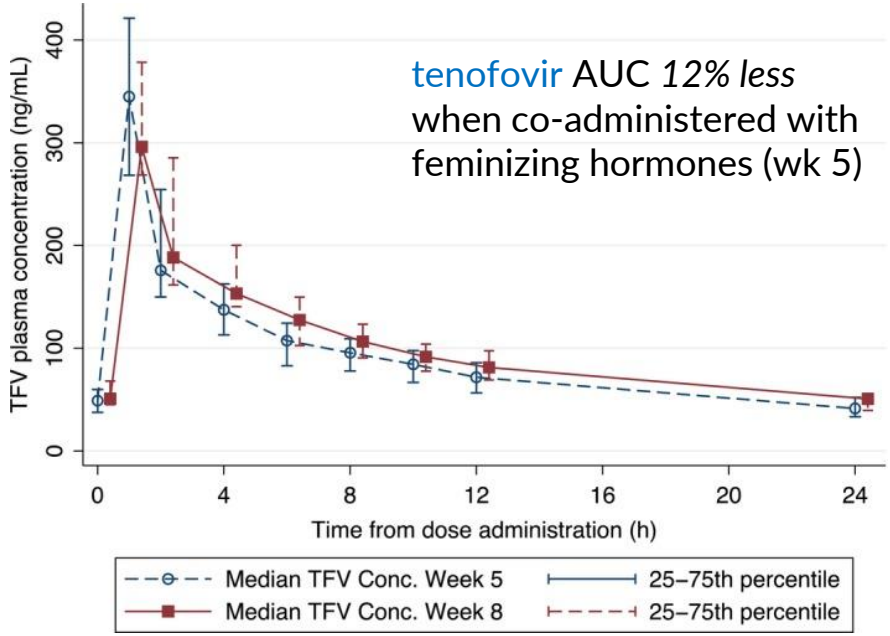



(Hiransuthikul 2019)

- (n = 20 trans women)
- FHT regimen: estradiol 2mg/d + cyproterone 25mg/d

# Drug-drug interactions (PrEP + FHT)



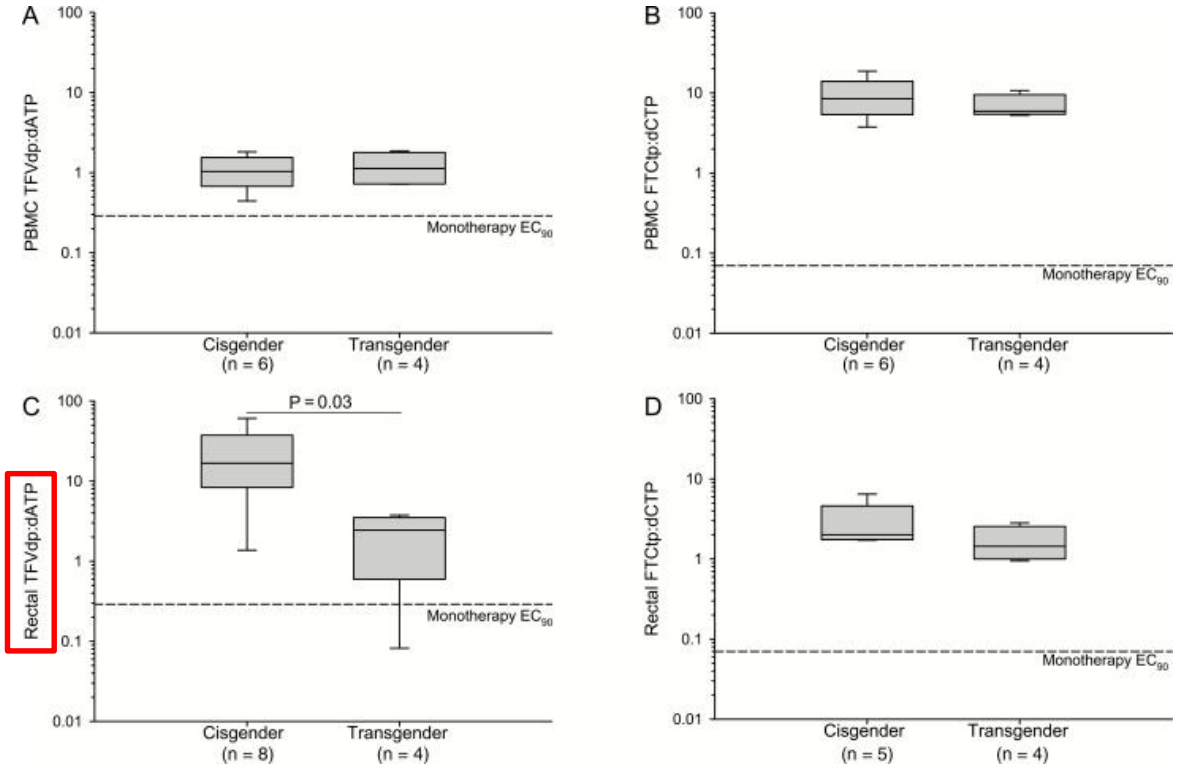




tenofovir AUC *12% less* when co-administered with feminizing hormones (wk 5)

(Hiransuthikul 2019) n=20

- FHT regimen: estradiol 2mg/d + cyproterone 25mg/d

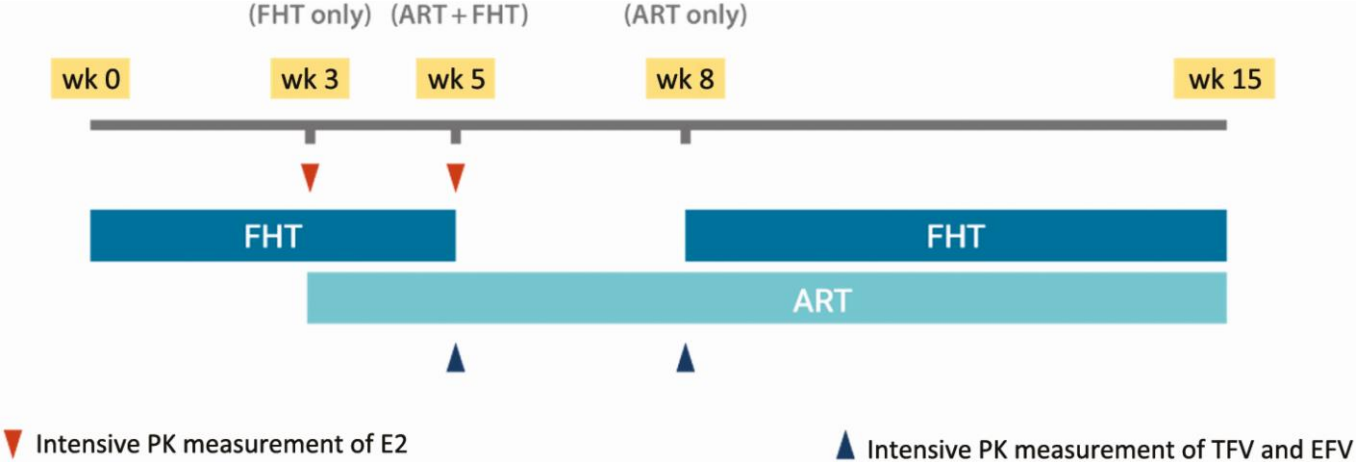
# Drug-drug interactions (**PrEP** + **FHT**)




(Cottrell 2019)

- Cohort study
- Regimens not listed

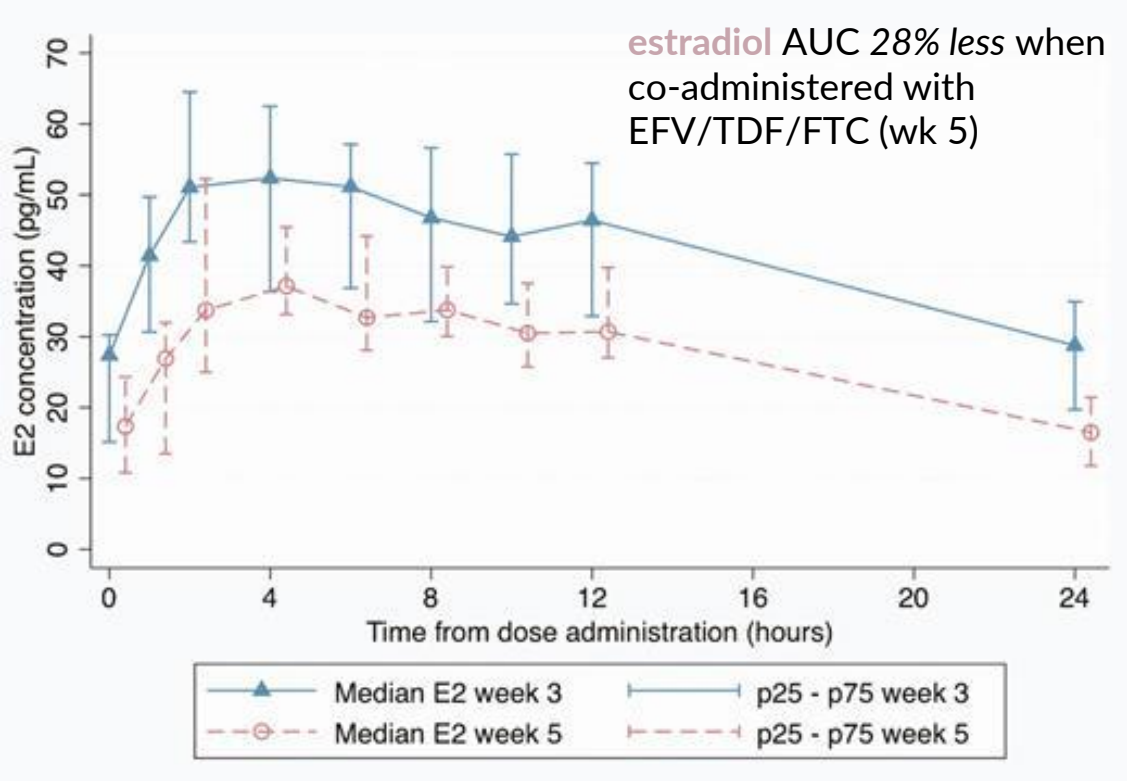
# Drug-drug interactions (ART + FHT)




(Hiransuthikul 2021)

- (n = 20 trans women w HIV)
- **FHT** regimen: estradiol 2mg/d + cyproterone 25mg/d
- **ART**: TFV disoproxil fumarate/emtricitabine/ EFV at 300/200/600 mg

# Drug-drug interactions (ART + FHT)

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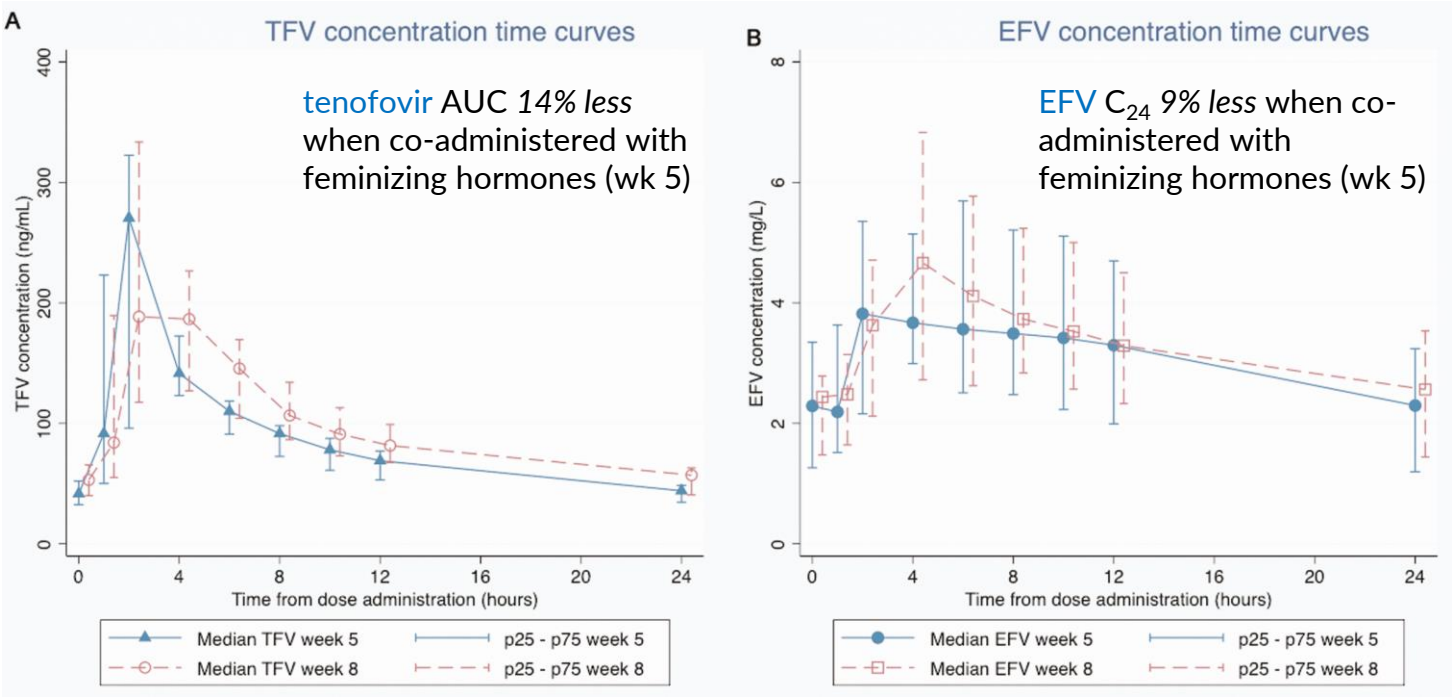


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- ART: TFV disoproxil fumarate/emtricitabine/ EFV at 300/200/600 mg