PrEP and Transgender Communities: Evidence Informed Practices

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Pronouns: She/Her/Hers
Disclosures

- Research Grants
  - Viiv Healthcare
  - Gilead Sciences
Objectives

- Describe current guidelines for PrEP use
- Review data on PrEP among transgender people
- Identify gender-affirming practices for PrEP implementation
What is PrEP?

- Pre-Exposure Prophylaxis
- Medication used to prevent HIV acquisition
  - Two approved agents: F/TDF and F/TAF
  - Both are also used in combination with other agents for the treatment of HIV
  - Long-acting injectable agent in Phase III trials
    - Cabotegravir LA
- Part of a combination preventive strategy
FDA Approvals

- **July 2012**: FDA approved F/TDF for HIV PrEP in adults who are **at substantial risk** for becoming HIV-infected.

- **May 2018**: FDA expanded indication of F/TDF to include adolescents weighing **at least 35 kg**.

- **October 2019**: F/TAF approved for at-risk adults and adolescents weighing at least 35kg, **excluding receptive vaginal sex**. [No cis women in trial, few trans women]


ADVANCING EXCELLENCE IN TRANSGENDER HEALTH
F/TDF v. F/TAF - What's a Trans Healthcare Clinician to do?

- Overall Facts (DISCOVER trial)
  - F/TAF is “non-inferior” to F/TDF for PrEP
  - Better renal and bone safety measures for TAF v. TDF
    - **eGFR** increased 1.8ml/min with TDF & decreased 2.3ml/min with TAF
      - 1 case Fanconi syndrome with TDF, none with TAF
    - **BMD** increased 0.2-0.5% with TAF & decreased 1-1.1% with TAF
      - BMD tested in subset of 383 participants

- Trans-specific Facts
  - 1% of the 5387 participants were trans women
    - No separate analysis of data from trans women has been presented
    - Approval excludes receptive vaginal sex (no specificity re: neovagina)

http://www.croiwebcasts.org/p/2019croi/104
What is “substantial risk”?  

If you can answer yes to any of the questions below, then PrEP may be one HIV prevention strategy to consider.  

- Do you use condoms sometimes or not at all?  
- Do you get often get STIs in your butt?  
- Do you often get STIs in your vagina?  
- Have you taken post-exposure prophylaxis (PEP) more than once in the past year?  
- Are you in a serodiscordant relationship, where your sexual partner is HIV positive and you are HIV negative?  
- Are you in an open relationship or having anal and/or vaginal sex with multiple partners?  
- Are you having sex with someone whose HIV status you don’t know?  
- Are you having sex with someone in a city or region where the HIV prevalence is high—that is, where there are large numbers of people living with HIV?  

https://prepfacts.org/prep/the-questions/
Box B1: Recommended Indications for PrEP Use by MSM

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- Not in a monogamous partnership with a recently tested, HIV-negative man

Box B2: Recommended Indications for PrEP Use by Heterosexually Active Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

Box B3: Recommended Indications for PrEP Use by Persons Who Inject Drugs

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)
WHO CLINICAL PREP BASICS

Indications for PrEP (by history over the past 6 months):

HIV-negative AND

Sexual partner with HIV who is not virally suppressed, OR

Sexually active in a high HIV incidence/prevalence population AND any of the following:

- Vaginal or anal sexual intercourse without condoms with more than one partner, OR
- A sexual partner with one or more HIV risk factors, OR
- A history of a sexually transmitted infection (STI) by lab testing or self-report or syndromic STI treatment, OR
- Use of post-exposure prophylaxis (PEP), OR
- Requesting PrEP.

Contraindications:

- HIV-positive
- Estimated creatinine clearance <60 ml/min
- Signs/symptoms of acute HIV infection, probable recent exposure to HIV
- Allergy or contraindication to any medicine in the PrEP regimen.

Rx (example): TDF 300 mg + FTC 200 mg PO daily #90 tablets.

Counselling: Link tablet use with a daily routine.

Develop a plan for contraception or safer conception and for STI prevention.
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Does biological vulnerability to HIV differ for trans people?

- Effect of exogenous hormones on the rectal mucosa
- Effect of exogenous testosterone on internal reproductive tract
- Risk of HIV acquisition in the neovagina
Does biological vulnerability to HIV differ for trans people?

- Effect of exogenous hormones on the rectal mucosa
- Effect of exogenous testosterone on internal reproductive tract
- **Risk of HIV acquisition in the neovagina**
Biologic Risk for HIV Transmission in TW after vaginoplasty (Thailand)

- Estrogen (E) and progesterone (P) are known to impact vulnerability of vaginal epithelium to HIV infection
- No published data on neovaginal HIV vulnerability in TW
- HIV negative participants: 8 TW, 10 CW, 10 MSM
  - Sigmoid & LN biopsies (All) + cervical (CW), neovaginal (TW) swabs

<table>
<thead>
<tr>
<th>Transgender Women</th>
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</thead>
<tbody>
<tr>
<td>Hormone use</td>
<td>8/8</td>
</tr>
<tr>
<td>Median duration of hormone use</td>
<td>7.6 years</td>
</tr>
<tr>
<td>Estrogen + Progesterone</td>
<td>5/8</td>
</tr>
<tr>
<td>Estrogen alone</td>
<td>3/8</td>
</tr>
<tr>
<td>Median time post penile inversion vaginoplasty</td>
<td>1.3 years</td>
</tr>
<tr>
<td>Currently dilating</td>
<td>7/8</td>
</tr>
<tr>
<td>Neovaginal sex</td>
<td>7/8</td>
</tr>
<tr>
<td>Anal sex</td>
<td>8/8</td>
</tr>
</tbody>
</table>
Biologic Risk for HIV Transmission in TW after vaginoplasty (Results)

- CD4/CD8 T cell composition of neovaginal mucosal mononuclear cells (MMC) differs from sigmoid and cervical MMC
- No increase in frequency of neovaginal activated CD4+ or CD4+CCR5+ T cells
- Possible increase in sigmoidal CD4+ CCR5+ target cells for HIV in TW

Differential T cell distribution in Female Genital Tract but not in Sigmoid Colon or Peripheral Blood

Frequency of CD4+ CCR5+ Target Cells in Sigmoid Colon and Peripheral Blood
Biologic Risk for HIV Transmission in TW after vaginoplasty (Results)

- CD4/CD8 T cell composition of neovaginal mucosal mononuclear cells (MMC) differs from sigmoid and cervical MMC.
- No increase in frequency of neovaginal activated CD4+ or CD4+CCR5+ T cells.
- Possible increase in sigmoidal CD4+ CCR5+ target cells for HIV in TW.

**TAKE HOME MESSAGES**

1. The immune system of the neovagina is different from natal vaginas and colons.
2. TW may have anal sex after vaginoplasty.
3. HIV vulnerability in the colon may be greater for TW than other groups.
Does PrEP work as well for trans people?
## PrEP Clinical Trials: Gender Challenges

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Participants</th>
<th>Number</th>
<th>Drug</th>
<th>Modified ITT efficacy of % reduction in acquisition of HIV infection(^a)</th>
<th>Adherence-adjusted efficacy based on drug detection in blood(^b)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>iPrEx</td>
<td>Men who have sex with men and transgender women</td>
<td>2499 FTC-TDF</td>
<td>44 (15-63)</td>
<td>92 (40-99)</td>
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<tr>
<td></td>
<td>Partners</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>HIV discordant couples</td>
<td>4747 TDF, FTC-TDF</td>
<td>67</td>
<td>75 (44-81)</td>
<td>86 (67-94)</td>
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<td></td>
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<tr>
<td></td>
<td>Heterosexually active men and women</td>
<td>1219 FTC-TDF</td>
<td>63 (22-83)</td>
<td>85c NS (55-87)</td>
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<tr>
<td></td>
<td>Injection drug users</td>
<td>2411 TDF</td>
<td>49 (10-72)</td>
<td>74 (17-94)</td>
<td></td>
</tr>
<tr>
<td>Fem-PrEP</td>
<td>Heterosexually active women</td>
<td>2120 FTC-TDF</td>
<td>NR</td>
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</tr>
<tr>
<td>VOICE</td>
<td>Heterosexually active women</td>
<td>5029 TDF, FTC-TDF</td>
<td>NR</td>
<td>-----</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Excluded only those enrolled patients later found to be infected at randomization and those with no follow-up visit or HIV test.

\(^b\) The percentage of reduction in HIV incidence among those with tenofovir detected in blood, compared with those without detectable tenofovir.

\(^c\) Finding not statistically significant.

F/TDF efficacy demonstrated in studies of cis MSM, heterosexual couples, & injection drug users

Adherence challenges for cis and trans women

F/TAF efficacy demonstrated in studies of cis MSM, no disaggregated data for TW are available, and neither cis women nor trans men were included in efficacy trial


PrEP in Transgender Women: iPrEx

- Trans women on F/TDF: 339/2499 (14%)
- Lack of efficacy: HR 1.1
  - TDF detected in no trans women at seroconversion
  - No seroconversions observed in trans women with TDF levels consistent with > 4 pills/week
  - TDF levels not linked to behavioral risk

### Clinical Trials with women

<table>
<thead>
<tr>
<th>Clinical Trials with women</th>
<th>PrEP Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEx¹ (trans women)</td>
<td>18%</td>
</tr>
<tr>
<td>FEM-PrEP² (cis)</td>
<td>24%</td>
</tr>
<tr>
<td>VOICE³ (cis)</td>
<td>29%</td>
</tr>
</tbody>
</table>

Exogenous hormones alter F/TDF Pharmacology in PLHIV

- **WHY**: Estradiol increases activity of nucleotidase enzymes, which could decrease the active form of tenofovir (TFVdp) while increasing a competing nucleotide dATP

- **WHO**: HIV+ people on F/TDF regimen (4 TW, 4 CW, 2CM)
  - All with HIV RNA < 50; CW all post-menopausal

- **WHAT**: Serum and rectal biopsies at one time point

- **HOW**: measure serum estradiol & rectal NRTI concentrations

- **RESULTS**:
  - Highest estradiol in TW, highest testosterone in CM
  - Reduction in rectal TFV (TFVdp:dATP) among TW
  - TFV lower with higher estradiol or progesterone

Cotrell et al. 2018; TUPDX0106
Drug Interactions between F/TDF and hormones: The iFACT study

- **WHO:** 20 TW who had not received hormones x 6 months
  - None had undergone orchiectomy. All were HIV negative.

- **WHAT:** Estradiol 2 mg and cyproterone 25 mg weeks 1-5, then 8-15 F/TDF started week 3

- **HOW:** Intensive serum PK assessment of estradiol, testosterone, and TFV

- **RESULTS:**
  - Estradiol exposure was not affected by PrEP
  - Lower plasma TFV in the presence of hormone therapy
    - Unclear if this is clinically significant

Hiransuthikul et al. 2018; TUPDX0107LB
Multiple Compartments

- **WHO**: 8 HIV- TW on various hormone regimens, 8 HIV- CM not taking hormones
  - Minimum plasma estradiol concentration for TW: 100pg/ml

- **WHAT**: Directly observed therapy of F/TDF for 7 days
  - Blood drawn at 1,2,4,6,8, and 24 hours + colon biopsy at 24 hours after last dose

- **HOW**: Blood 1,2,4,6,8, and 24 hours + colon biopsy at 24 hours after last dose

- **RESULTS**:
  - Lower TFV, FTC, and active analytes in blood and rectal tissue in TW
  - Reduction consistent with approximately 5 doses/week
  - No impact of F/TDF on estrogen levels

Shieh E et al (presenter Hendrix C). HIVR4P, Madrid, abstract OA23.03, 2018
Summary of Data on F/TDF for PrEP among Trans Women

Implications for trans men using hormonal contraception?
Little data on PrEP pharmacology among transgender men on T

Data expected from California PrEP demonstration project soon (I-BrEATHe: DOT with 24 TM & 24 TW)
CDC Guidelines on F/TDF for PrEP: Compartments and Steady State

- PrEP effective for *receptive anal sex* after 7 days of use with a minimum adherence of 4 pills per week
- CDC recommends 20 days of daily use for all other acts

**Transgender Specific PK Questions**
- What are PrEP concentrations in the neovagina? When do they reach steady state? Does this vary by surgery type?
- Does exogenous testosterone effect PrEP efficacy and time to achieve steady state in the vaginal and/or rectal mucosa?

http://www.cdc.gov/hiv/basics/prep.html
PrEP Compartments and Steady State

- PrEP effective for receptive anal sex after 7 days of use with a minimum adherence of 4 pills per week.
- CDC recommends 20 days of daily use for all other acts.
- Transgender Specific PK Questions
  - What are PrEP concentrations in the neovagina? When do they reach steady state? Does this vary by surgery type?
  - Does exogenous testosterone affect PrEP efficacy and time to achieve steady state in the vaginal and/or rectal mucosa?

http://www.cdc.gov/hiv/basics/prep.html
Although the effectiveness of PrEP for transgender women has not yet been definitively proven in trials, and trials have not been conducted among transgender men, PrEP has been shown to reduce the risk for HIV acquisition during anal sex and penile-vaginal sex. Therefore, its use may be considered in all persons at risk of acquiring HIV sexually.
Comprehensive HIV Prevention

Figure 1. Comprehensive HIV prevention processes. Conceptual framework illustrating the interplay between processes to halt both the acquisition and transmission of HIV. The primary HIV prevention cycle, left, begins with HIV testing. Risk and needs assessments, linkage to services, engagement in risk-reduction prevention interventions and HIV testing are repeated for as long as an individual remains at risk for HIV acquisition.

Horn et al. JIAS 19, no. 1 (2016).
PrEP Continuum

Engagement in the PrEP Continuum: Trans Women
PrEP Indication: LITE Baseline Data

- 1,125 trans women
- Enrollment online (30%) and in person (70%)
- 30% living with HIV at baseline

PrEP Indication among HIV-negative LITE Participants at Baseline

- Indicated for PrEP based on above
- Condomless receptive anal sex
- Current engagement in sex work
- Laboratory confirmed STI
- Self-reported STI in last 3 mo
- Sexual partner living with HIV
PrEP Continuum: LITE Baseline Data

HIV-Negative & Sexually Active Participants

- 100% Sexually active in last 12 mo
- 82% Ever heard about PrEP
- 27% Lifetime PrEP use
- 16% Recent PrEP use (30 days)
- 11% PrEP adherent (7 pills/week)

Among current PrEP users:
- 97% reported exogenous hormone use
- 65% reported 0 missed doses in prior 7 days
Among the 18% of ALL who reported lifetime PrEP use
Engagement in the PrEP Continuum: Trans Men
Testosterone associated with changes in sexual behavior

- N=122 TM in San Francisco
- Cross-sectional survey & 2 FGDs (n=14)
- Attributed testosterone to:
  - New sexual behaviors (69%)
  - Changes in attraction (49%)
  - Increased sex frequency (72%)

Figure 2. Proportion of participants reporting cisgender men who have sex with men and transwomen sexual partners before and after testosterone use, San Francisco, 2014–2015.

Sexual behavior in prior 6 months

- 45 had sex with cis men
  - 97 partners
  - 856 sex acts (oral, anal, vaginal)
  - 13.8% condomless receptive vaginal
  - 0.8% condomless receptive anal

- 27 had sex with trans women
  - 39 partners
  - 1062 sex acts (oral, anal, vaginal)
  - 9.5% condomless receptive vaginal
  - 2.4% condomless receptive anal

Figure 3.

™ aware of HIV risk

Few eligible trans men receive PrEP

- May – July 2017 online recruitment
- N=1808 trans masculine people
- 24.2% eligible by CDC criteria
  - Recent receptive anal or vaginal sex, sex work, sexually transmitted infection (STI)
- PrEP eligibility associated with
  - Low income, gay/bi/queer/pan identity, poly relationship, stimulant/poppers
- Only 48 of PrEP eligible were on PrEP

Few eligible trans MSM receive PrEP

- Nov – Dec 2017 online recruitment
- N=857 trans MSM (843 HIV-negative)
- 54.4% eligible by CDC MSM criteria, 31.2% eligible by heterosexual criteria, 6.6% eligible by IDU criteria
- PrEP indication associated with: meeting partners online, sex not only with cis men, higher perceived risk, greater number partners, partner stigma

- 84.1% heard of PrEP
- 33.3% currently taking PrEP, of lifetime
- 21.8% stopped taking PrEP, of lifetime
- 11.5%
Best Practices

Based on Clinical Experience
Trans - Affirming Advertising
Sex-Positive, Trans-Affirming Info

Sex-Positive Messaging

I LOST MY VIRGINITY
but I still have the box it came in
What is “Sex Positive”?

“An attitude towards human sexuality that regards all consensual sexual activities as fundamentally healthy and pleasurable, and encourages sexual pleasure.”

-- Allena Gabosch
Abstinence only
Abstinence at least preferred

If you don’t use protection, you are stupid and careless

Sex is DANGEROUS!

Your body’s normal functions are gross

Sex is immoral

Monogamy is morally superior and healthier than non-monogamy

Some sex is normal, some deviant

If you don't want sex, something is wrong with you

Your body is flawed and undesirable

Sex is nasty and dirty

SHAME

Sex Negative Prevention Messages

Slide courtesy of Kate Bishop
Sex Positive Prevention Messages

Your body is AMAZING!

Consent is sexy (and required)
All desires are wonderful
You make good decisions about what happens to your body
Explore what you like and learn how to ask for it

Sex work is honorable work

Pleasure is a great reason to have sex
Pleasure is everyone’s birthright
It’s ok to want sex, and
It’s ok not to want sex
Your body belongs only to you

All bodies are desirable are capable are sacred ARE GOOD BODIES
fat scarred gender-variant disabled short swishy butch toothless hairy HIV-positive
Everyone, even the most experienced sexpert, has a list of sexual activities we find icky.

We cannot eliminate our bias by pretending not to have any.

Find your “Yucks” and fix your face.
PrEP for Trans People: Take Home

- **PrEP indicated** for adults and adolescents at risk for sexual transmission of HIV, including transgender people

- **Data are limited** with transgender people
  - New data suggest *potential interactions* between F/TDF for PrEP and estradiol
  - Data also suggest efficacy among trans women who adhere to prescribed dosing

- Best practices include combination HIV prevention strategies and sex-positive, trans-inclusive approaches to PrEP engagement

https://www.sayitwithacondom.com/prep-transgender-condom
Case: Robyn

- 19 y/o transgender woman
- History of rectal STIs and sex work
- Currently in monogamous relationship with a cisgender man
- Prescribed oral estradiol and spironolactone that she takes sporadically
- Had vaginoplasty one year ago and denies anal sex since surgery
- Rapid HIV test negative today
Case Questions

1. Is she a candidate for PrEP? Why or Why not?

2. If she elects to take PrEP, how would you decide whether to prescribe F/TAF or F/TDF?

3. What would you tell her about hormones and PrEP?
Case: Danny

- 30 y/o transgender man
- History of rectal STIs and sex work
- Currently in monogamous relationship with a trans woman
- On injectable testosterone x 6 months
- No menses x 3 months
- Rapid HIV test negative today
Case Questions

1. Is he a candidate for PrEP? Why or Why not?

2. If he elects to take PrEP, how would you decide whether to prescribe F/TAF or F/TDF?

3. What are other key sexual health considerations?
THANK YOU!
Any Questions?
Resources


Citations


Lade JM, To EE, Hendrix CW, Bumpus NN. Discovery of Genetic Variants of the Kinases That Activate Tenofovir in a Compartment-specific Manner. EBioMedicine. 2015;2(9):1145-1152.


Citations


Citations


