Perspective
Management and Prevention of HIV Among Transgender Adults

Transgender individuals face discrimination, violence, social exclusion, and other social, political, and economic factors that result in increased vulnerability to HIV. Rates of viral suppression and uptake of preexposure prophylaxis are lower among transgender individuals than the general population. HIV clinics can help improve these rates by promoting inclusivity and tailoring care to the specific needs of transgender patients. This article summarizes an International Antiviral Society–USA (IAS-USA) webinar presented by Asa E. Radix, MD, PhD, MPH, on August 18, 2020. This webinar is available on demand at https://www.iasusa.org/courses/on-demand-webinar-2020-radix/.

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When discussing health-related issues in the transgender population, it is important to be aware of the difference between the terms sex and gender. Sex refers to the biologic and physiologic characteristics that differentiate between males and females and is assigned at birth based on anatomy. Gender refers to an individual’s sense of identity as male, female, or something else on the spectrum (eg, nonbinary, genderqueer, gender diverse, gender nonconforming).

Language around gender identity is evolving, and it is crucial that health care practitioners stay educated about current terminology, which may differ culturally and geographically. Herein, the term trans refers to individuals whose gender identity is different from their sex assigned at birth. Transgender women are those assigned male at birth but have a female or feminine gender identity, and transgender men are those assigned female at birth but have a male or masculine gender identity. The term cisgender is used to describe individuals who are not transgender (ie, whose gender identities are aligned with the sex they were assigned at birth).

An estimated 2.5 million adults worldwide identify as transgender. In the United States, between 1 and 1.4 million adults identify as transgender (35% of those as nonbinary), 4-6 and nearly 2% of high school students identify as transgender or nonbinary. 4, 5

Discrimination and Violence

Many transgender people face discrimination. In a 2015 survey of transgender individuals in the United States, 58% reported experiencing discrimination; 46% reported experiencing sexual or physical assault; 33% reported experiencing discrimination in health care settings; 23% reported that they avoided health care because of discrimination; 15% reported being unemployed; 29% reported living in poverty; 50% reported ever being unhoused; and 50% reported experiencing rejection from their family. 6 In addition, a majority of those surveyed reported being bullied or harassed at school (K–12) because they were transgender: 54% were verbally harassed; 24% were physically attacked; 13% were sexually assaulted; and 17% dropped out of school as a result of severe mistreatment. 6

In 2019, 27 transgender women were reported murdered in the United States. 7 In 2020, as of August, 28 transgender women had been reported murdered in the United States. 8

Vulnerability to HIV

Transgender-specific vulnerabilities to HIV are often rooted in transphobia or in negative attitudes and beliefs about transgender people that lead to discrimination. Some of the structural, interpersonal, biologic, and individual factors that increase vulnerability to HIV for transgender individuals are shown in the Table. These factors include high rates of violence and victimization, as well as high prevalence of depression, suicidality, and substance use. Transgender individuals have high rates of sex work, which is often a result of exclusion from the workforce. Mistreatment and discrimination in health care settings can lead transgender individuals to avoid medical care, resulting in missed opportunities for HIV testing, lack of access to HIV prevention services, reduced diagnosis of and treatment for sexually transmitted infections.

<table>
<thead>
<tr>
<th>Vulnerable Factors</th>
<th>Structural and Interpersonal</th>
<th>Biologic</th>
<th>Individual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inconsistent condom use</td>
<td>- Social exclusion (eg, housing, employment)</td>
<td>- Effects of testosterone (eg, atrophic vaginitis)</td>
<td>- HIV prevention is a low priority</td>
</tr>
<tr>
<td>Substance use</td>
<td>- Legal status</td>
<td>- Effects of estrogen on tissue receptors</td>
<td>- Mood disorders</td>
</tr>
<tr>
<td>Low self-efficacy</td>
<td>- Mistreated or denied care in health care settings</td>
<td>- Sexually transmitted infections</td>
<td>- Suicidality</td>
</tr>
<tr>
<td>Sex work</td>
<td>- Poor access to prevention information</td>
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infections (STIs), lack of engagement in care, and poor medication adherence.

Data on global HIV prevalence among transgender individuals are limited, largely because transgender women are often placed in the same category as men who have sex with men, especially in low- and middle-income countries. In a 2013 meta-analysis that examined 15 countries, the estimated global prevalence of HIV among transgender women was 19%, and transgender adults were 49 times more likely to have HIV than all adults of reproductive age. In the United States, HIV prevalence is estimated to be 0.39%. HIV prevalence is several times higher among transgender women (14.1%) and transgender men (3.2%).

According to the Centers for Disease Control and Prevention 2018 HIV Surveillance Report, 9,959 transgender women and 403 transgender men are living with HIV in the United States, with more than two-thirds being African American or Latinx (Figures 1 and 2). Overall, new diagnoses of HIV in transgender people increased between 2014 and 2018.

**Antiretroviral Therapy and Viral Suppression**

When people are diagnosed with HIV, it is crucial that they are engaged in care and initiated on antiretroviral therapy (ART) as early as possible. Rates of viral suppression are lower among transgender individuals than the general population for a variety of reasons: prioritization of transition-related medical care over HIV care, fears about drug interactions between hormones and HIV, low adherence to antiretroviral medications, negative experiences with care practitioners and health systems, fear of discrimination, stigma, mental health issues, substance use, and unstable housing. Data from the Ryan White HIV/AIDS Program from 2018 show an overall rate of viral suppression among transgender individuals of 81.8%, approximately 5% lower than all individuals living with HIV. Rates are lower in younger transgender individuals; 67.8% among those aged 20 to 24 years and 72.7% among those aged 25 to 29 years. Rates are also lower among those in temporary or unstable housing (74.1% and 68%, respectively).

Studies from the Program Enhancing Engagement and Retention in Quality HIV Care for Transgender Women of Color, funded by Health Resources and Services Administration (HRSA) between 2012 and 2017, investigated ways to improve the HIV care continuum for transgender women. Interventions found to improve HIV outcomes included integrating HIV care with hormone therapy, peer health navigation, and contingency management (eg, a cash incentive for keeping appointments or achieving viral suppression). Additional studies of such interventions are underway.

**Interactions Between ART and Gender-Affirming Hormone Therapies**

A concern often raised is the possibility of drug-drug interactions between ART and gender-affirming hormone therapy, especially regimens containing estrogen. The first step in the metabolism of estrogen is hydroxylation in the liver by cytochrome P450 enzymes. Some hormone levels may be elevated or lowered, depending on the components of the ART regimen.

Although there are no data that specifically examine interactions between hormones used by transgender people and ART, recommendations regarding
potential interactions have been extrapolated from research on oral contraceptive medications containing ethinylestradiol. The antiretroviral drug classes with the least potential for interactions with gender-affirming hormone therapy are unboosted integrase strand transfer inhibitors and nonnucleoside reverse transcriptase inhibitors. ART regimens containing cobicistat-boosted elvitegravir or cobicistat- or ritonavir-boosted protease inhibitors may increase levels of testosterone and finasteride. ART regimens containing ritonavir-boosted protease inhibitors, efavirenz, etravirine or nevirapine, may decrease levels of estradiol, testosterone, and finasteride.

**PrEP Efficacy in Transgender Individuals**

HIV preexposure prophylaxis (PrEP) was first approved by US Food and Drug Administration for use based on results of the iPrEx (Preexposure Prophylaxis Initiative) study, which reported 29 transgender women in the study population (approximately 1% of participants). A later subanalysis identified additional transgender women in the study population, including people who did not identify as transgender but were taking estrogen, which increased the number of transgender women included to approximately 359 (14% of participants). Among transgender women in the study, PrEP initially appeared to be ineffective as the number of seroconversions was the same among people who were or were not taking PrEP (hazard ratio, 1.1). However, further examination of the data revealed that transgender women had extremely low adherence to PrEP. Among those assigned to PrEP who seroconverted, most had no detectable levels of PrEP drugs in their blood; among those who had levels consistent with taking more than 4 pills per week, no seroconversions were noted. Subsequent analyses have shown baseline characteristics that may explain differences in PrEP efficacy between transgender women and cisgender men who have sex with men.30

The iFACT (Interaction between the use of feminizing hormone therapy and Antiretroviral agents Concomitantly among Transgender Women) Study, conducted in Thailand, examined interactions between PrEP and feminizing hormones among 20 transgender women. The investigators found that estrogen levels were not affected by PrEP but that tenofovir exposure was reduced by approximately 12% in the presence of feminizing hormones. In a small study of PrEP in North Carolina, in 4 transgender women taking feminizing hormones, 4 cisgender men, and 4 cisgender women, concentrations of tenofovir in blood and in rectal tissue were similar, although there were lower ratios of tenofovir diphosphate and deoxyadenosine-triphosphate in rectal tissue of transgender participants. The clinical significance of these data are unclear, considering the small sample sizes; however, they did show that estrogen levels do not change with PrEP use.

The iBrEATHe (Interactions Between Truvada and Hormone Therapy) study, a pharmacokinetic substudy of the Triumph Project (a PrEP demonstration project in transgender populations), investigated drug-drug interactions between PrEP and estradiol in transgender women and testosterone in transgender men. The study included 24 transgender men and 24 transgender women who were taking testosterone and estradiol, respectively. Participants received daily PrEP for 4 weeks, directly observed by video or in person. Investigators measured the participants’ serum hormone levels and tenofovir diphosphate levels weekly for 4 weeks and found that serum hormone levels were not affected by oral PrEP.

**The PrEP Care Continuum**

Data on the PrEP care continuum for transgender people are limited. The multisite LITE (Leading Innovation for Transgender Women’s Health and EmPowerment) study, examined PrEP uptake among 1,100 transgender women without HIV across 6 US cities. Participants received baseline HIV and STI tests and then ongoing testing every 3 months. Of participants who were sexually active, 82% had heard of PrEP but only 22% had ever taken it, only 13% had taken PrEP in the last month, and only 9% had been adherent to PrEP in the last week. In a US study that enrolled 1,808 transgender men 24.3% met 1 or more criterion for PrEP eligibility, but only 34% of those had received information on PrEP from their care practitioner and only 11% were taking PrEP.

Many transgender individuals meet criteria for PrEP use, but only approximately 9% to 10% of those individuals take it. Several studies have examined key barriers to PrEP uptake in this population, including lack of knowledge about PrEP, mistrust of medical practitioners and researchers, concerns about interactions between PrEP medications and hormone therapy, low perceived HIV risk, HIV stigma, and lack of transgender-inclusive marketing. Facilitating PrEP uptake among transgender individuals requires implementing transgender-competent services, such as prescribing hormones in the HIV clinic, providing educational and promotional materials about PrEP, and ensuring that clinicians are recommending PrEP whenever appropriate and advising about the lack of interactions between PrEP and gender-affirming hormones. Because many transgender individuals are underinsured or uninsured, linking them to insurance or to medication assistance programs is also important.

**Inclusivity in the HIV Clinic**

To help engage and retain transgender individuals in care, the clinic environment should be made as inclusive as possible. Having a 2-step question on clinic intake forms that asks 1) current gender identity and 2) sex assigned at birth ensures that a patient’s gender identity is known and provides the physician with information to provide appropriate preventive care. Clinic staff should take special care to use an individual’s chosen name and pronouns consistently. Staff should also avoid using gendered titles (eg, Mr, ma’am) until they have verified a pa-
tient’s gender identity and language-preference. A common mistake is misgendering patients based on assumptions (eg, assuming during a phone call that someone with a deeper voice is a cisgender man). Additionally, clinics should ensure that the psychosocial and material needs of their patients can be easily met (eg, gender-neutral restrooms are provided); that educational materials or brochures featuring transgender individuals are available; that nondiscrimination, diversity, and confidentiality policies are clear and known; and that practitioners are able and willing to prescribe hormones when appropriate (see Box).

**Individualized Care**

Gender affirmation refers to the process of being recognized and supported in one’s gender identity and expression, and may include social, legal, and psychological components, as well as medical interventions such as hormones and surgeries. Some individuals may change their name and pronouns and nothing else, or they may take hormones and decide against surgery, or vice versa. Medical care for a transgender individual should be individualized based on their goals, which may or may not include medical intervention.

**Box. Features of Quality Care for Transgender Individuals**

- Gender identity determined by the patient and not via laboratory or psychometric tests
- Primary care practitioners and HIV specialists able to prescribe and monitor hormones
- Care provider and clinic staff knowledgeable about:
  - Diverse gender identities
  - Hormone regimens and guidelines
  - Preventive care after medical or surgical interventions
  - Surgeries and postoperative management

**References**

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