

# HIV in Sexual and Gender Minority Populations

This is a PDF version of the following document:

Module 6:

[Key Populations](#)

Lesson 7:

[HIV in Sexual and Gender Minority Populations](#)

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<https://www.hiv.uw.edu/go/key-populations/hiv-sexual-gender-minority-populations/core-concept/all>.

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## Background

### Defining Sexual and Gender Minority Populations

Sexual identity and gender identity are highly personal to each individual. It is important to understand that sexual orientation and gender identity are distinct concepts: sexual orientation describes to whom a person feels romantic or sexual attraction toward, whereas gender identity is a person's innermost sense of gender or self, which does not necessarily correspond with a person's assigned sex at birth. The term "sexual minorities" typically refers to individuals who identify as lesbian, gay, bisexual, or any other non-heterosexual identity, whereas the term "gender minorities" refers to individuals who have gender identities that are not associated with their birth sex. Increasingly, there is recognition that self-identification of gender can be nonbinary, with some individuals experiencing a gender identity that is outside the categories of man or woman. Sexual and gender minorities may include lesbian, gay, bisexual, transgender queer, intersex, and asexual (LGBTQIA) individuals, as well as others. Most available epidemiologic and medical literature has focused on lesbian, gay, bisexual, and transgender (LGBT) persons.

### Intersection of LGBT Persons and HIV

Sexual and gender minority populations in the United States experience significant health disparities and poorer health outcomes compared with heterosexual and cisgender peers.[1,2,3] With the exception of lesbian individuals, sexual and gender minority populations have higher rates of HIV and comprise an important group that requires HIV medical care and HIV prevention services.[4,5,6,7]

### LGBT Populations in the United States

In the United States, a 2022 Gallup Poll reported that approximately 7 percent of adults in the United States self-identified as LGBT and this number has increased significantly since 2012 (Figure 1).[8] Of respondents to the Gallup poll who identified as LGBT, 58% responded that they are bisexual, 20% gay, 13% lesbian, 9% transgender, with less than 2% identifying as another sexual orientation. Identifying as LGBT varied markedly by generations: Generation Z (adults born after 1997) were most likely to identify as LGBT, followed next by Millennials (born 1980-1998), then Generation X (born 1965-1985).[8] Notably, approximately 1 in 5 individuals in the age group Generation Z identify as LGBT.[8]

## Terminology

Terms used to describe sexual orientation and gender identity continuously evolve and expand; how these different terms are viewed varies among individuals and cultural communities. Whenever possible, it is best to use the terminology that the person in the clinic or hospital uses to describe themselves, and the best practice is to ask a person what terms they use to describe their sexual orientation and gender. The following glossary is adapted based on terminology used in a number of excellent resources, including The Gay and Lesbian Alliance Against Defamation (GLAAD), the Fenway Institute, and the UC Davis LGBTQIA Resource Center.<sup>[9,10,11]</sup> The following terms are particularly relevant to this review and are listed in alphabetical order:

- **Asexual:** Someone who generally does not feel sexual attraction or a desire for partnered sexuality; some asexual individuals may have sexual activity.
- **Bisexual:** Someone who has sexual and/or emotional attraction to both men and women.
- **Bottom Surgery:** Describes gender-affirming genital surgery. This is distinct from top surgery, which refers to gender-affirming chest surgery.
- **Cisgender:** A person who identifies as the same sex they were assigned at birth.
- **Gay:** Someone who has sexual and/or emotional attraction to people of the same gender. The term “gay” is used more often to describe men than women, while “lesbian” is the more commonly used term to refer to women with same-gender attraction. Some women who have sex with women identify as gay, others as lesbian, and some by other terminology. The term “homosexual” is generally not recommended, unless a person prefers this term to describe themselves, as it is considered offensive and derogatory by many people.
- **Gender:** The identity and/or expression as a man or a woman, or as an individual who falls between or outside the male-female binary categorization.
- **Gender-Affirming Care:** A multidimensional process of aligning one’s social, medical, and legal status with one’s current gender identity.
- **Gender-Affirming Surgeries:** A variety of surgical interventions to align a person’s physical appearance with their gender identity, including but not limited to genital reconstruction.
- **Gender Dysphoria:** Describes discomfort or distress that arises from a discrepancy between a person’s gender identity and sex assigned at birth; this term should not be used interchangeably with gender nonconforming since only some individuals who are gender nonconforming experience gender dysphoria.
- **Gender Expression:** External manifestation of one’s gender, expressed through characteristics, such as name, pronouns, clothing, haircut, and behavior.
- **Gender Fluid:** Describes a person who does not identify as having a fixed gender. Individuals may identify as male, female, or both. They may also identify as a gender outside of the male-female binary construction.
- **Gender Identity:** A person’s gender identity describes a deep, internal sense of their gender.
- **Gender Nonbinary:** A term used to describe individuals whose gender expression is different from conventional expectations of masculinity or femininity. This term should not be used interchangeably with gender dysphoria since only some individuals who are gender nonbinary experience gender dysphoria.
- **Gender Nonconforming:** Another term used to describe individuals whose gender expression is different from conventional expectations of masculinity or femininity.
- **Genderqueer:** A person who experiences their gender identity and/or expression as falling outside the categories of man and woman. This term is not synonymous with transgender but rather is an example of a nonbinary gender identity. Genderqueer individuals may identify as both male and female, neither male nor female, or a combination of male and female.
- **Gender Transition:** Describes the process when a person alters their physical or other aspects of their identity to affirm their desired gender. A transition may include a name change, a different pronoun preference, changes in legal documents, and gender-affirming medical treatments and/or surgeries. The term “gender affirmation” is often used interchangeably with gender transition.

- **GLBT:** Refers to gay, lesbian, bisexual, and transgender persons; often used interchangeably with LGBT (lesbian, gay, bisexual, and transgender).
- **Intersex:** This term is used to describe persons who, without medical intervention, have variations in primary or secondary sex characteristics that do not fit neatly into society's definitions of male or female.
- **Lesbian:** A term used to describe a woman whose sexual and emotional attraction is to other women. Some women may prefer to use the term lesbian, whereas others may identify as gay or otherwise.
- **LGBT:** Refers to lesbian, gay, bisexual, and transgender; often used interchangeably with GLBT—for gay, lesbian, bisexual, and transgender.
- **LGBTQ:** Refers to lesbian, gay, bisexual, transgender, and queer; the Q at the end of LGBTQ may also refer to questioning.
- **LGBTQIA:** Refers to lesbian, gay, bisexual, transgender, queer (or questioning), intersex, and asexual.
- **MSM:** Refers to men who have sex with men. This usually refers to cisgender men and may include men who have sex only with men (gay men), men who have sex with both men and women (bisexual men), and men who have sex with men and individuals of other genders. Not all men who have sex with men identify as gay, so these terms should not be used interchangeably.
- **Nonbinary:** Refers to a person who does not identify as either female or male.
- **Pansexual:** Refers to someone who has physical, romantic, and/or emotional attraction to persons of any sex or gender.
- **Queer:** Describes someone whose sexual identity is not heterosexual, and who may or may not identify as LGBT. The term genderqueer is often used to describe sexual identity.
- **Sexual Orientation:** Describes physical and/or emotional attraction to another person, which is distinct from gender identity. Sexual orientation is often considered to have three distinct dimensions: identity, behavior, and attraction; use of the term sexual preference is not recommended.
- **Same Gender Loving:** A term used primarily in the African American community to describe someone whose sexual and/or emotional attractions are to persons of the same gender.
- **Sex:** The sex (male or female) a person is assigned at birth.
- **They/Them/Their:** These are pronouns that are considered neutral and often used by persons who have a gender identity that is nonconforming or nonbinary.
- **Top Surgery:** Describes gender-affirming chest surgery. This is distinct from bottom surgery, which refers to gender-affirming genital surgery.
- **Transgender:** An umbrella term used to describe someone whose gender identity and/or gender expression differs from what is typically associated with the sex they were assigned at birth. Some now use the term person of trans experience instead of transgender.
- **Transgender Man:** A person who is assigned female at birth but identifies and lives as a man. A transgender man is sometimes referred to as transman, transmasculine, or female-to-male (FTM).
- **Transgender Woman:** A person who is assigned male at birth and identifies and lives as a woman. A transgender woman is sometimes referred to as transwoman, transfeminine, or male-to-female (MTF).
- **Transition:** Usually refers to the process of a transgender person altering physical or other aspects of their identity to affirm their gender identity. A transition may include a name change, a different pronoun, changes in legal documents, and gender-affirming medical treatments and/or surgery.
- **Transsexual:** Describes a person who has a gender identity that is opposite the gender assigned at birth. The use of the term transsexual is controversial and considered outdated by many. It is strongly recommended that clinicians now use the term transgender instead of transsexual.
- **Two-spirit:** This term is used among indigenous people to describe a person who identifies as having both a masculine and a feminine spirit. Some indigenous people use the term two-spirit to describe their sexual, gender, and/or spiritual identity.

## Medical Care for LGBT Persons

### Establishing an Informed and Welcoming Clinic Environment

Beyond insurance obstacles, sexual and gender minorities often struggle with finding medical providers who have training and experience working with LGBT populations and often face discrimination from health care providers.[12,13] In addition, gender identity is increasingly understood to exist along a spectrum, with some individuals not identifying exclusively as male or female, and the lack of data about nonbinary gender minorities presents another obstacle to evidence-based care.[9] Creating an inclusive, culturally responsive, and welcoming clinical environment is an important first step in providing optimal clinical care services for LGBT persons and for reducing HIV acquisition and transmission risk within sexual and gender minority communities. This process can involve training in cultural awareness and diversity, along with educating clinical staff about the unique health needs of sexual and gender minority populations. For LGBT persons living with HIV, the most effective interventions to improve outcomes across the HIV care cascade will differ based on the specific population.

### LGBT Resources for Medical Providers

The lack of medical care data for LGBT and nonbinary gender minorities presents an obstacle to optimal evidence-based care recommendations. Nevertheless, several organizations have generated excellent resources for the medical care of LGBT persons based on the best available evidence and expert opinion. These resources include general LGBT health care and those specific to LGBT persons living with HIV.

- **National LGBT Health Education Center:** The [National LGBT Health Education Center](#)—This program from the Fenway Institute provides educational programs, resources, and consultation to health care organizations with the goal of optimizing quality, cost-effective health care for LGBT people. Many educational resources and webinars, and links to information on technical assistance are available on the website.
- **The Center of Excellence for Transgender Health:** The University of California at San Francisco's [Center of Excellence for Transgender Health](#) website has access to a learning center that includes the extensive [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#).
- **Health Professionals Advancing LGBT Equality:** The organization [Health Professionals Advancing LGBT Equality](#) (formerly known as Gay & Lesbian Medical Association) includes information for patients and medical providers, and a directory of medical providers for LGBT persons.

## Cisgender Men Who Have Sex with Men (MSM)

In the United States, an estimated 1.4% of the adult population self-identifies as gay and 4.2% as bisexual ([Figure 2](#)).<sup>[8]</sup> In this section, the term MSM will be used to describe cisgender men who have sex with men, regardless of whether they identify as gay, bisexual, or another sexual orientation. Medical care for MSM, with or without HIV, should incorporate the same elements of treatment and preventative health interventions as for all patients, while also focusing on health issues that disproportionately impact MSM—in particular, sexually transmitted infections (STIs), mental health conditions, and recreational drug and alcohol use.<sup>[14,15,16]</sup> Medical providers caring for MSM should have awareness that issues may surface due to past experiences of stigma, rejection, and physical and psychological abuse.<sup>[14,15]</sup> Developing a trusting relationship that encourages disclosure of relevant sexual and drug activity and mental health concerns is crucial to providing competent care that can meaningfully improve health outcomes.<sup>[14]</sup> The following discussion will include a discussion of issues related to MSM with HIV (Epidemiology, Knowledge of HIV Status, Mental Health, Substance Use, STI Screening, Anal Cancer Screening, and Immunizations) and MSM who do not have HIV but are at risk of acquiring HIV (Risk for Acquiring HIV, Nonoccupational HIV PEP, and HIV Preexposure Prophylaxis).

### HIV Epidemiology in Cisgender MSM

The Centers for Disease Control and Prevention (CDC) surveillance data uses the term male-to-male sexual contact to include gay, bisexual, and other men who self-report male-to-male sexual contact as their HIV transmission category. Thus, the term male-to-male sexual contact will be used in the following epidemiology summary.

#### HIV Prevalence

This includes estimates for persons living with diagnosed and undiagnosed HIV. In the CDC 2021 HIV prevalence estimates, male-to-male sexual contact was reported as the transmission category for an estimated 59% (716,900 of 1,212,400) of persons 13 years of age and older living with HIV, plus an additional 5% (62,900) reporting male-to-male sexual contact and injection drug use as the transmission category ([Figure 3](#)).<sup>[17]</sup>

#### HIV Incidence

These numbers represent estimates for new HIV infections that are believed to have occurred during 2021 in the United States. Among the estimated new HIV infections, male-to-male sexual contact was the identified transmission category in 66% (21,100 of 32,100) of the estimated new HIV infections; male-to-male sexual contact and injection drug use comprised an additional 4% (1,300 of 32,100) ([Figure 4](#)).<sup>[17]</sup> Among the estimated new HIV infections in 2021 attributed to male-to-male sexual contact, 13,000 (38%) occurred in Black men, 9,300 (34%) in Hispanic men, and 8,200 (23%) in White men.<sup>[17]</sup>

### Knowledge of HIV Status in Cisgender MSM

Overall, in the United States, based on data from 2021, an estimated 12.8% of persons with HIV are unaware of their HIV status.<sup>[17]</sup> In that same year, an estimated 14.2% of persons in the transmission category of male-to-male sexual contact were living with undiagnosed HIV.<sup>[17]</sup> Knowledge of their HIV status is important so that MSM with HIV have the opportunity to engage in care and attain health benefits from antiretroviral therapy, and MSM without HIV can take measures to prevent infection. In addition, for MSM who are diagnosed with HIV, knowledge of their HIV status and treatment with antiretroviral therapy can dramatically reduce the risk of HIV transmission to sex partners.<sup>[18,19]</sup>

### Mental Health in Cisgender MSM with HIV

Several studies have also shown that MSM with HIV have a greater risk of major depressive disorder than MSM who do not have HIV, with one meta-analysis reporting that 10.4% of MSM living with HIV met criteria for depression compared with 5.7% of MSM without HIV.[20] Significant stigma and discrimination against MSM, particularly MSM with HIV, persists and may accentuate other factors that contribute to depression. Medical providers should be aware of the high rates of mood disorders in MSM with HIV, perform appropriate screening, and be prepared to offer or refer for appropriate behavioral counseling and pharmacologic treatment.

## Substance Use in Cisgender MSM

Substance use is common among MSM with HIV, including a high rate of alcohol and illicit drug use (methamphetamine, cocaine, poppers, and other club drugs) in the context of sex.[14,21,22] In a convenience sample of MSM with HIV living in 6 United States cities, one-third of the respondents reported alcohol use at least once a week, and 30% reported use of cocaine, poppers, or marijuana.[23] One study showed a correlation between heavy alcohol use in MSM with HIV and condomless anal intercourse with HIV-seronegative or HIV-seropositive partners.[21] Another study found that recent use of methamphetamine was associated with increased levels of rectal mucosa inflammatory cytokines, regardless of HIV serostatus, a finding that may at least partially explain the increased risk of HIV acquisition and transmission in MSM who use methamphetamine.[24] Screening for substance use and referral for treatment (if indicated) is important for providers caring for MSM, though most interventions and treatment programs have not yet been tailored to the MSM population.[14]

## Screening for Sexually Transmitted Infections in Cisgender MSM with HIV

Among MSM with HIV infection, rates of STIs are high, but are significantly decreased by risk reduction counseling and at least biannual screening (and quarterly STI screening for MSM at high risk offers even greater benefit).[25] According to the 2021 STI Treatment Guidelines, the following screening schedule is recommended for sexually active MSM living with HIV.[26]

- **Chlamydia:** Testing for chlamydia should be performed at the initial HIV visit and at least annually thereafter; testing is recommended more frequently (e.g., every 3 to 6 months) for MSM who have multiple partners or if their sex partners have multiple partners. The preferred testing method is a *Chlamydia trachomatis* nucleic acid amplification test (NAAT). The testing sites should include all anatomic sites of exposure during sexual activity within the prior year, including urethral and/or rectal tests if the person has had potential exposure at those sites. A urine sample should be obtained to screen for urethral infection, and a swab from the rectum is used as the screening method for rectal infection. Routine testing for oropharyngeal chlamydia infection is not recommended.
- **Gonorrhea:** Testing for gonorrhea should be performed at the initial HIV visit and at least annually thereafter; testing is recommended every 3 to 6 months for MSM who are sexually active and at risk, or have sex partners with multiple partners. The testing for gonorrhea should occur regardless of the history of condom use. The preferred testing method for *Neisseria gonorrhoeae* is a NAAT. The testing sites should include all anatomic sites involved in sexual activity within the prior year, including urethral (urine), rectal (swab), and/or pharynx (swab).
- **Syphilis:** Testing for syphilis should be performed at the initial visit and at least annually thereafter; testing is recommended every 3 to 6 months if sexually active and at risk, or if sex partners have multiple partners. For sexually active MSM, testing for syphilis should occur regardless of the history of condom use. In the United States, rates of primary and secondary syphilis have increased significantly among MSM in recent years. All men newly diagnosed with HIV should be screened for syphilis. The preferred screening method is serologic testing, which requires a blood draw.
- **Hepatitis A Virus (HAV):** The recommended screening test is antibody to HAV (IgG-anti HAV).[27] Individuals who are nonimmune (IgG anti-HAV titer less than 10 mIU/mL) should receive the hepatitis A vaccine series.[27]
- **Hepatitis B Virus (HBV):** Screening should consist of hepatitis B surface antigen (HBsAg), hepatitis



B core antibody (anti-HBc total), and hepatitis B surface antibody (anti-HBs).[28] Men who have sex with men who are nonimmune to hepatitis B should be vaccinated.

- **Hepatitis C Virus (HCV):** Guidelines recommend annual HCV testing for sexually active MSM with HIV.[26,29] Screening for HCV infection is generally done with an antibody-based blood test, with all positive antibody tests followed by an HCV RNA NAT to determine if the individual has resolved or chronic HCV infection.

## Screening for Anal Cancer in Cisgender MSM with HIV

The incidence of anal cancer in the general population is 2 to 3 per 100,000 person-years, but among MSM, the incidence is higher; for HIV-seronegative MSM, the rate is 5 per 100,000 person-years, and for MSM living with HIV, the rate jumps to 77.8 per 100,000 person-years.[30] Anal Papanicolaou (Pap) smear testing is an option to screen for HPV-induced anal dysplasia. This test, using atypical squamous cells of undetermined significance as the cutoff for abnormal, has an estimated sensitivity for dysplasia of 81 to 87% and a specificity of 39 to 41%.[30] A phase 3 study (ANCHOR) conducted at multiple sites in the United States randomized individuals with HIV who were at least 35 years old and who had biopsy-proven high-grade squamous intraepithelial lesion (HSIL) to receive either treatment of the HSIL lesion(s) or have active monitoring.[31] The major finding from this study was that persons in the treatment arm had a significantly reduced risk of incident anal cancer.[31] Nevertheless, at this time, existing national guidelines do not currently recommend routine screening for anal cancer (using anal Pap testing) in MSM, regardless of HIV status.[32,33]

## Enteric Infections in MSM with HIV

Men who have sex with men (MSM) with HIV who engage in rectal sex, especially with oral-anal contact, may contract enteric infections, such as *Shigella* species, *Campylobacter* species, *Giardia* species, and others. In recent years, outbreaks of sexually acquired enteric organisms with specific antibiotic resistance patterns have occurred.[34] Therefore, for MSM with diarrhea, a sexual history is important, as is testing for enteric pathogens, such as with stool culture and/or stool polymerase chain reaction (PCR) testing. Untreated HIV may also raise the risk of transmission of enteric pathogens; a person with HIV and low CD4 or viremia may have higher shedding of organisms when they have an enteric infection, and a person with untreated HIV may also be more susceptible to enteric infections.

## Immunizations in Cisgender MSM with HIV

Men who have sex with men should receive routine, age-appropriate vaccinations according to the Advisory Committee for Immunization Practices (ACIP) immunization schedule.[35] The ACIP schedule also identifies MSM as a special health category for whom hepatitis A and hepatitis B vaccinations are indicated.[27,35] All MSM who are 26 years of age and younger, including those with HIV, should also receive the 9-valent human papillomavirus (9vHPV) vaccine series if they have not already received it.[35] For MSM with HIV who are 27 through 45 years of age and who have not received the HPV vaccine, routine administration of the HPV vaccine is not recommended, but can be considered based on shared clinical decision-making.[32,35] The CDC also recommends mpox vaccination for MSM, with or without HIV, who may be at elevated risk of acquiring monkeypox virus, including those individuals who, within the prior 6 months, have acquired a bacterial STI, had more than one sex partner, engaged in sex at a commercial sex venue (sex club or bathhouse), or who have a sex partner with any of these risk factors.[36]

## Risk Factors for Acquiring HIV in Cisgender MSM

A combination of individual-level and sociostructural factors underlie the elevated risk for HIV transmission and acquisition among MSM.[37] Individual factors associated with HIV acquisition include number of sex partners, use of drugs or alcohol during sex, and condomless anal intercourse.[38,39,40] In recent years, the use of apps and online tools to find anonymous partners has emerged as another individual-level HIV risk

factor, with data showing that MSM who initiate sexual encounters online have higher rates of condomless anal intercourse.[41] Structural risk factors that contribute to HIV risk are layered, with poverty, unemployment, incarceration, and racism converging to increase risk in vulnerable communities, most notably in African American MSM.[42] Ethnographic research has shown that sexual orientation-based discrimination in one's home or social neighborhood also increases HIV acquisition risk behavior.[42]

## **Nonoccupational Postexposure Prophylaxis (nPEP) in Cisgender MSM**

In the United States, most persons receiving nonoccupational postexposure prophylaxis (nPEP) or preexposure prophylaxis (PrEP) are MSM.[43] Accordingly, medical providers who care for MSM should develop competence to provide nPEP in order to help prevent HIV infection. The use of nPEP involves a strategy whereby antiretroviral therapy is administered to an individual within 72 hours after a potential high-risk exposure to HIV has occurred.[44] In 2016, the Centers for Disease Control and Prevention (CDC) issued updated nPEP recommendations.[44] The topic of nPEP is addressed in detail in the lesson on [Nonoccupational Postexposure Prophylaxis](#) in Module 5 (Prevention of HIV).

## **Preexposure Prophylaxis (PrEP) in Cisgender MSM**

Similar to nPEP, most of the persons in the United States who are eligible for, and are receiving HIV preexposure prophylaxis (PrEP), are MSM. There are three medications that are FDA-approved in the United States for HIV PrEP in MSM: oral tenofovir DF-emtricitabine, oral tenofovir alafenamide-emtricitabine, and long-acting injectable cabotegravir. Multiple large clinical trials (iPrEx, IPERGAY, PROUD, DISCOVER, HPTN 083) involving MSM with ongoing exposure to HIV have demonstrated a substantial reduction in the rate of HIV acquisition with the use of HIV PrEP.[45,46,47,48,49] In 2021, the CDC also released their most recent update to the HIV PrEP Guidelines, which includes recommendations for selecting appropriate HIV PrEP candidates, choosing HIV PrEP medication, obtaining a baseline and follow-up laboratory evaluations, and other relevant considerations for clinical care for individuals interested in or receiving HIV PrEP.[50] The topic of HIV PrEP is addressed in detail in the lesson on [HIV Preexposure Prophylaxis](#) in Module 5 (Prevention of HIV).



## Cisgender Women Who Have Sex with Women (WSW)

In the United States, an estimated 1.0% of the adult population self-identifies as lesbian and 4.2 as bisexual ([Figure 5](#)).<sup>[8]</sup> In general, women who have sex with women (WSW) should receive medical and preventative health care services similar to those provided to women who have only male partners.<sup>[15,51]</sup> When compared with heterosexual women, cisgender WSW were 30% less likely than heterosexual women to have an annual routine medical examination, and bisexual women were more than twice as likely to not seek medical care.<sup>[52]</sup> It is important to create a nonjudgmental, welcoming, candid, and inclusive clinical environment. Given the very limited data on HIV in WSW, most of the content in the sections that follow will focus on general issues of health in WSW.

### HIV Epidemiology in WSW

Based on available data, cisgender women who have sex only with other cisgender women appear to have a very low risk of acquiring HIV. <sup>[53,54]</sup> Among WSW, there are several reported cases of HIV transmission.<sup>[55,56,57,58,59]</sup> Data from the National HIV Surveillance System does not include information specific to WSW, primarily due to the rare HIV infections involving WSW. Early in the HIV epidemic, the possibility that HIV could be transmitted woman-to-woman among cisgender women was questioned.

### Risk Factors for Acquiring HIV in WSW

For many women, sexual identity categories do not necessarily align with sexual behavior.<sup>[60]</sup> For example, the National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 reported that among sexually experienced women 19-59 years of age in the United States, 7.1% reported ever having sex with a woman, and of these women 53% reported their sexual orientation as heterosexual, 28% as bisexual, and 19% as lesbian.<sup>[60]</sup> In one survey of 6,935 women who self-identified as lesbian, 77% reported at least one lifetime male partner.<sup>[61]</sup> In addition, in a separate survey, 96.6% of women who had ever had sex with women reported they had also previously had sex with a male partner.<sup>[60]</sup> Thus, when ascertaining HIV acquisition and transmission risks among WSW, it is important to clarify past and recent sexual history since women may have acquired HIV from a male partner.<sup>[60,62]</sup> In addition, WSW can acquire HIV from injection drug use.

### Sexually Transmitted Infections in WSW

Relatively limited data exist regarding the risk of STIs, including HIV, among cisgender women who have sex with other cisgender women.<sup>[63,64]</sup> The following summarizes the risk of STIs among WSW, based on available data and as outlined in the 2021 STI Treatment Guidelines: (1) transmission of HPV can occur between female sex partners, (2) transmission of HSV is inefficient but can occur, (3) transmission of syphilis can rarely occur, (4) transmission of *Chlamydia trachomatis* occurs more frequently than previously thought, (5) bacterial vaginosis is common.<sup>[65,66,67,68,69,70]</sup> Women who have sex with women often do not use barrier protection, both because of the perceived low risk of sexually transmitted infections and also because there is no risk of pregnancy with cisgender female partners.<sup>[71,72]</sup>

### Mental Health in WSW

Several studies have suggested that WSW have higher rates of depression, anxiety, suicidal ideation, and/or suicide attempt, as compared to other women.<sup>[52,73,74,75]</sup> In the 2013 and 2014 National Health Interview Survey, lesbian women reported a 1.34-fold increased risk of moderate psychological stress and a 1.45-fold increased risk of severe psychological stress when compared with heterosexual women.<sup>[76]</sup> As with other sexual minority groups, stress from discrimination and rejection has been proposed as one reason for the higher prevalence of mental health disorders.<sup>[6,15,74]</sup> Primary care providers should be aware of the increased prevalence of mood disorders in WSW and be prepared to offer or refer for appropriate behavioral counseling and pharmacologic treatment.

## **Substance Use in WSW**

A large systematic review found that women who identified as lesbian had higher rates of alcohol dependence, drug dependence, and any substance use disorder than women who identified as heterosexual.[74] In addition, in the 2013 and 2014 National Health Interview Survey, women who identified as lesbian reported a 2.6-fold higher rate of heavy current alcohol consumption than women who identified as heterosexual.[76] Screening for substance use disorders should be offered to WSW, with referral to appropriate behavioral and pharmacologic treatment programs if needed.

## **Screening for Breast, Cervical, and Anal Cancer in WSW**

There is theoretical concern that WSW are at increased risk of breast cancer due to higher rates of nulliparity, smoking, obesity, and alcohol use.[77] It is unclear, however, whether these behavioral factors, which are known to increase the risk of breast and gynecologic cancers, actually translate into significantly higher cancer rates in WSW; this uncertainty stems from the lack of data on sexual orientation in national databases and registries that collect information on cancer incidence and mortality.[78] Since there are no unique guidelines for breast cancer screening in WSW, screening should follow general breast cancer screening guidelines for all women.[79,80] Because HPV infection is common in WSW, the 2021 STI Treatment Guidelines recommend offering cervical cancer screening to all women, regardless of sexual orientation or sexual practices.[65] There are no recommendations to routinely perform screening for anal cancer in WSW (or in cisgender women who have sex with men).

## Transgender Women

In the United States, approximately 0.6% of the adult population, or about 1.1 million persons, self-identify as transgender.[8,81] The following information is intended to provide a brief overview of HIV epidemiology in transgender women, followed by an introduction to medical care for transgender women and for nonbinary individuals who desire feminization. Excellent comprehensive documents that provide guidance for gender-affirming care are available through Fenway Health, the Center of Excellence for Transgender Health, the Endocrine Society, and the World Professional Association for Transgender Health (WPATH).[9,82,83,84] We recommend reviewing and using the following resources when providing gender-affirming clinical care for transgender people.[9,83,85]

- Fenway Institute (Boston, MA): [Medical Care of Trans and Gender Diverse Adults](#)
- Center of Excellence for Transgender Health (San Francisco, CA): [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#)
- The World Professional Association for Transgender Health (WPATH): [Standards of Care for the Health of Transgender and Gender Diverse People, Version 8](#)

## HIV Epidemiology in Transgender Women

Transgender women in the United States have an HIV prevalence estimated at 14.1%.[81,86] The following summarizes data on transgender women living with diagnosed HIV in the United States (Figure 6).[87]

- **Number of Transgender Women Living with Diagnosed HIV:** The 2021 CDC surveillance data reported 13,111 transgender women living with diagnosed HIV in the United States and the number of reported transgender women living with diagnosed HIV in the United States has increased steadily from 2017 through 2021.[87,88]
- **Transgender Women Living with HIV by Age Group:** Among the transgender women living with diagnosed HIV in the United States in 2018, approximately 50% were 25 to 39 years of age.[88]
- **Transgender Women Living with Diagnosed HIV by Racial/Ethnic Group:** There were marked racial disparities among transgender women living with diagnosed HIV in the United States in 2021, with Black transgender women accounting for more than 45% (6,106 of 13,110) of transgender women living with HIV.[88]
- **Transgender Women Living with Diagnosed HIV by Region:** In the United States, based on residence, the highest number of transgender persons living with diagnosed HIV in 2021 resided in the South.[89]
- **Transgender Women and Knowledge of HIV Status:** In the United States, transgender women living with HIV have a relatively higher percentage of persons who have undiagnosed HIV than the estimated overall 14% of persons living with HIV in the United States who have undiagnosed HIV.[90,91,92]

## Risk Factors for Acquiring HIV

Multiple intersecting structural, interpersonal, and individual vulnerabilities place transgender women at disproportionate risk for acquiring HIV.[93,94] An early study conducted in San Francisco identified four risk factors independently associated with a higher HIV seroprevalence in transgender women: African American race, a history of injection drug use, low education level, multiple sex partners, and self-identified African American race (due to racism and other sociostructural factors).[95] Other studies have revealed that sexual activities that increase the risk of HIV acquisition, including condomless anal intercourse, drug use during sex, and exchange of sex for money, are more common among transgender women than among other groups.[96,97,98] Several studies have shown that transgender women engaging in sex work are much more likely to acquire HIV than cisgender female sex workers.[94,99,100] Compounding these risks, transgender women can be harder to reach for prevention efforts, especially since transgender persons are often impacted by multiple layers of stigma, discrimination, and trauma.[101]

## Approach to Gender-Affirming Care for Transgender Women

The approach to gender-affirming therapy for transgender women and gender nonbinary persons desiring feminization is generally the same regardless of HIV status, except that drug interactions between hormonal therapies and antiretroviral agents need to be considered in persons with HIV.[102] For individuals desiring feminization, options include medical interventions (hormonal therapy), surgery (e.g., bilateral orchiectomy, vaginoplasty, breast augmentation, facial feminization procedures, tracheal cartilage shave, and voice surgery), and cosmetic procedures (e.g., electrolysis).[9,82,103] The decision to take gender-affirming hormones or to have gender-affirming surgery is a significant one, and a medical provider-client discussion regarding the risks and benefits of gender-affirming treatment is essential.[104,105] Psychotherapy is generally recommended but not required, for the receipt of gender-affirming treatment.[82]

### Principles of Feminizing Hormone Therapy

The most common approach to feminizing hormone therapy is to use estrogen to promote female secondary sexual characteristics in conjunction with an antiandrogen to suppress male secondary sexual characteristics.[105] To date, no randomized controlled trials comparing various hormonal-affirming protocols have been conducted, and management remains largely based on expert opinion.[9,82,84,105] Prior to initiating hormonal therapy, WPATH recommends all the following criteria should be met: (1) persistent, well-documented gender dysphoria, (2) capacity to make a fully informed decision about treatment, (3) adult (or legally able to give informed consent), and (4) reasonably controlled medical or mental health conditions, if present.[82] Note that additional criteria are required for the use of feminizing hormone therapy in children and adolescents. Since gender-affirming hormonal therapy is off-label and may be associated with serious complications, many experts recommend having the client sign an informed consent document prior to starting hormonal treatments; other experts recommend simply documenting the informed consent process in the medical chart.[9,82,105] A sample consent form is available in the Fenway Health document—The Medical Care of Transgender Persons.[9]

### Goals of Feminizing Hormone Therapy

Specific feminizing goals may include breast development, redistribution of body subcutaneous fat, reduction in body hair, softening of the skin, diminution in muscle mass, atrophy of the testicles, and slowing of scalp hair loss.[105] Transition is a gradual process, with the onset of most feminizing effects occurring within several months (Figure 7); maximal feminizing effects usually require at least 2 to 3 years (Figure 8).[106] Transgender women naturally have varying levels of and tissue responses to estrogen and testosterone.[105] Most experts recommend monitoring serum estradiol and serum testosterone levels approximately every 3 months during the first year of feminizing hormone therapy (or until a stable level is reached) and then at least twice yearly thereafter, with a goal of obtaining levels equivalent to normal levels for premenopausal females—100-200 pg/mL for estradiol and less than 50 ng/dL for testosterone.[84] Doses of estrogen and antiandrogen should be adjusted to maintain these levels. Some gender nonbinary and other individuals may desire feminization, but not full gender transition, and therefore, estradiol goals may be lower.

### Estrogen Feminizing Hormone Therapy

The mainstay of all feminization protocols is estrogen therapy with 17-beta estradiol (commonly referred to as estradiol), since this compound is considered bioidentical to the estrogen produced by an ovary.[105] Many types of estradiol products are available, including various oral, transdermal, and injectable formulations; these different estrogen medications will generate similar effects if used at equipotent doses.[107] The estradiol dose required for adequate feminization is highly individualized based on a person's goals. All transgender women and gender nonbinary individuals initiating estrogen feminization therapy should start on a low dose and titrate upward as needed, depending on the clinical response. The doses required to achieve the desired effects are generally at least two to three times higher than doses typically used for hormone replacement therapy in postmenopausal cisgender women.[9,105,108,109] Taking doses far in excess of the recommended doses in an effort to achieve more rapid and greater responses is not recommended due to

potential adverse effects. The following summarizes the major estrogen preparations used for feminizing hormone therapy.[\[9,82,84,105\]](#)

- **Oral Estrogen:** Use of oral or sublingual estradiol is relatively inexpensive and is easily titrated. Multiple brands of oral estradiol (17 beta-estradiol) are available. The starting dose for estradiol is usually 2 mg once daily orally and increased to 4 mg once daily after 4 to 12 weeks. The dose should be titrated and adjusted based on clinical response and serum estradiol levels; the maximum recommended dose of estradiol is 6 mg/day. Oral or sublingual estrogen use may cause a higher risk of venous thromboembolism than injectable or transdermal forms of estrogen. Ethinyl estradiol, which is a synthetic estrogen used in oral contraceptive preparations, or conjugated equine estrogen tablets are not recommended for feminizing hormonal therapy because of an increased risk of venous thromboembolism and/or cardiovascular disease.
- **Transdermal Estrogen:** The use of transdermal estradiol is preferred by many experts for feminizing hormone therapy because the transdermal preparation provides a steady level of estrogen and overall lower estrogen exposure. The lower exposure to estrogen is particularly important for individuals who have a higher baseline risk of thromboembolism (e.g., smokers, those 40 years of age and older, or those with a history of venous thromboembolism). In addition, transdermal estrogen avoids first-pass liver metabolism and thus may have an advantage over oral agents in the setting of liver disease. There are many brands of estradiol transdermal; the usual starting dose is 0.025-0.05 mg/24 hours, applied once or twice weekly, with the patch strength increased over 4 to 12 weeks to a dose of 0.1-0.2 mg/24 hours. Estrogen patches are more expensive than most oral estrogens and may not be covered by insurance.
- **Parenteral Estrogen:** Parenteral estradiol formulations (estradiol valerate or estradiol cypionate) may be a good option for some individuals, especially if the oral or transdermal preparations fail to achieve target estradiol levels. The recommended starting dose for estradiol valerate is 5 to 10 mg intramuscular (IM) every 2 weeks, increasing to a usual maintenance dose of 10 to 20 mg IM every 2 weeks. The estradiol cypionate recommended dose is 2 to 10 mg IM every week.

## Antiandrogen Feminizing Treatments

Antiandrogens are used to lower testosterone levels (or block tissue effects of testosterone) and thereby enhance the impact of estrogen formulations.[\[105,106,108,110\]](#) The most common antiandrogen strategies used for this purpose consist of a combination of one or more of the following: agents that block androgen production (spironolactone), 5-alpha reductase inhibitors that block the conversion of testosterone to the more potent form dihydrotestosterone (finasteride and dutasteride), and bilateral orchiectomy surgery.[\[9,84,105\]](#)

- **Spironolactone:** Most experts in the United States recommend spironolactone as the antiandrogen agent of choice for transgender women or gender nonbinary individuals who desire feminization. This medication works by directly inhibiting testosterone secretion and by inhibiting androgen binding to androgen receptors. The dose of spironolactone ranges from 25 to 300 mg per day. The usual starting dose is 25 to 50 mg once daily, increasing every 2 to 4 weeks to a typical dose of 200 mg once daily (or 100 mg twice daily). The maximum dose is 300 mg daily, usually given in divided doses.
- **5-Alpha Reductase Inhibitors:** The 5-alpha reductase inhibitors work as antiandrogens by partially blocking the conversion of testosterone to the more potent androgen dihydrotestosterone. These agents have relatively weak activity in persons with low testosterone levels (low substrate). Two 5-alpha reductase inhibitors uptake inhibitors—finasteride and dutasteride—have been used as a component of feminizing therapy. Finasteride is usually started at a dose of 1 mg once per day and titrated to the desired effect, up to a usual dose of 2.5-5 mg once daily. Dutasteride is given at a dose of 0.5 mg once daily. The 5-alpha reductase inhibitors are often used in transgender women or gender nonbinary persons who have male-pattern baldness.
- **Progestins:** The use of progestins, such as medroxyprogesterone acetate or micronized progesterone, can suppress testosterone secretion, but the use of progestins for trans feminine individuals is controversial. Many experts do not advise the routine use of progestins as part of

feminization therapy because of an increased risk of cardiovascular disease and breast cancer, particularly in older persons who are also taking conjugated estrogen.

- **Gonadotropin Releasing Hormone (GnRH) Agonists:** The GnRH agonists are synthetic analogs of natural GnRH. Chronic use of GnRH agonists causes down-regulation of GnRH receptors, which results in decreased secretion of sex hormones (androgen and estradiol). These agents are also referred to as luteinizing hormone-releasing hormone (LHRH) agonists. Specific agents occasionally used as part of feminization therapy include leuprolide, goserelin, and nafarelin. These GnRH agonists are very expensive and typically reserved for delaying puberty in transgender youth. The use of GnRH agonists is not part of routine feminization therapy for transgender adult women. When these agents are used, the typical doses are leuprolide 3.75 mg to 7.5 mg IM once monthly and goserelin 3.6 mg subcutaneous implant monthly.
- **Orchiectomy:** Bilateral orchiectomy may be considered for select transgender women who are intolerant of antiandrogen therapy; if the scrotum is removed with the orchiectomy, it will reduce the amount of skin available for labiaplasty, should labiaplasty be desired in the future. If a person has a bilateral orchiectomy, they will no longer require antiandrogen therapy.

## Potential Adverse Effects of Feminizing Hormonal Therapy

Estrogen therapy may potentially cause a wide range of adverse effects, including venous thromboembolism, cardiovascular events, depression, hypertension, hyperthyroidism, glucose abnormalities, sexual dysfunction, and prolactinoma.[109,111,112,113] The use of estrogens is contraindicated in anyone with known estrogen-responsive cancer and should be used cautiously in patients with a history of thromboembolism, severe thrombophlebitis, diabetes, liver disease, renal disease, cardiac disease, hyperlipidemia, preexisting biliary disease, or a strong family history of estrogen-responsive malignancy. Because smoking further increases the risk of thromboembolism among persons taking estrogen therapy, smokers should be counseled to quit smoking prior to starting gender-affirming estrogen therapy.[46,114] The risks and benefits must be reviewed with patients prior to starting estrogen therapy. Side effects associated with spironolactone therapy include hypotension and hyperkalemia, and the drug is contraindicated in those with renal insufficiency or baseline serum potassium of greater than 5.5 mEq/L.

## Monitoring on Feminizing Hormone Therapy

Regardless of the regimen chosen, all persons receiving gender-affirming hormonal treatment require close follow-up to evaluate the effectiveness of the therapy and to monitor for adverse effects. The following summarizes recommendations for routine baseline laboratory studies and laboratory monitoring.[9,84,105]

- **Baseline Laboratory Studies:** The recommended routine baseline studies for individuals initiating hormonal feminizing therapy should include a basic metabolic panel (including blood urea nitrogen, creatinine, and potassium), aminotransferase levels, lipid profile, and a fasting glucose or hemoglobin A1c level. A baseline prolactin level is indicated only if the patient has a history of hyperprolactinemia or pituitary adenoma, or is also taking medications that increase prolactin levels, such as antipsychotics.
- **Monitoring Serum Estradiol and Testosterone Levels:** Most experts recommend monitoring serum estradiol and serum testosterone approximately every 3 months during the first year of transition (or until a stable level is reached) and then at least twice yearly thereafter, with a goal for levels equivalent to normal levels for premenopausal females—100 to 200 pg/mL for estradiol and less than 50 ng/dL for testosterone. The doses of estrogens and antiandrogens should be adjusted to maintain these levels.
- **Monitoring for Toxicity:** For persons receiving spironolactone, serum potassium, blood urea nitrogen, and creatinine should be checked 2 to 4 weeks after starting or changing the dose of spironolactone. Subsequently, routine twice-yearly monitoring should include a basic metabolic panel (e.g., blood glucose, potassium, blood urea nitrogen, and creatinine) and a lipid panel. A serum prolactin level should be performed yearly as a screen for prolactinoma, which can develop in transgender women or gender nonbinary individuals taking estrogen therapy; some experts only



recommend obtaining prolactin levels for 2 to 3 years, assuming the levels remain normal and the person has no symptoms that would suggest a prolactinoma.

## Key Drug Interactions between Hormonal and Antiretroviral Treatments

Hormonal therapies, like other medications, can interact with other pharmacologic treatments. Although drug interactions can occur between certain antiretroviral medications and hormonal therapies, taking antiretroviral medications is not a contraindication to starting or receiving hormonal treatment.[\[115,116\]](#) There are no known significant drug interactions between the most commonly used anti-androgen, spironolactone, and antiretroviral medications. The major concern for drug interactions, as outlined below, is the concomitant use of estrogens and antiretroviral medications.

- **Nucleoside Reverse Transcriptase Inhibitors (NRTIs):** Although NRTIs are generally considered not to cause major changes in estrogen levels, several small studies have reported that estrogen feminizing hormone therapy may lead to lower plasma tenofovir levels in transgender women taking oral tenofovir-based HIV PrEP.[\[117,118\]](#) Another relatively small study found that levels of active tenofovir metabolites were similar for transgender women taking tenofovir DF with estradiol (with or without spironolactone) as compared to cisgender men (based on historical control data) and remained within the range thought to be effective.[\[119\]](#) Furthermore, for transgender women, tenofovir DF-emtricitabine or tenofovir alafenamide-emtricitabine as daily dosing has proven effective as part of antiretroviral treatment and as daily HIV PrEP. Based on these pharmacologic data showing possible lower levels due to estradiol, non-daily tenofovir DF-emtricitabine dosing (such as on-demand or 2-1-1 dosing) is not recommended as HIV PrEP for transgender women who take estrogen feminizing hormone therapy.
- **Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs):** Some NNRTIs interact with estrogens, due to similar metabolism through the cytochrome P450 system. Available pharmacokinetic data suggest that efavirenz, etravirine, and nevirapine may significantly lower estradiol levels.[\[116,120\]](#) If one of these NNRTIs needs to be given concomitantly with estradiol, the dose of estradiol should be adjusted as needed based on clinical effects and measured serum hormone levels or, if possible, the antiretroviral NNRTI could be switched to another medication that does not have this interaction.
- **Integrase Strand Transfer Inhibitors (INSTIs):** There are no known significant drug interactions between estradiol and INSTIs.[\[121\]](#) Thus, non-boosted INSTI-based antiretroviral therapy is preferred in persons receiving estradiol.
- **Protease Inhibitors (PIs) and Boosting Agents:** Boosting agents (ritonavir and cobicistat) and some PIs interact with estrogens via cytochrome P450 system metabolism. Ritonavir-boosted PIs potentially decrease blood levels of estrogens, whereas cobicistat can potentially increase or decrease estrogen levels.[\[116\]](#) If a boosting agent or PI needs to be concomitantly given with estradiol, the dose of estradiol should be adjusted as needed based on clinical effects and measured serum hormone levels.

## Gender-Affirming Surgery

Many surgical treatments are available for transgender women and gender nonbinary individuals, depending on their needs and goals. Options include breast and/or chest surgery (“top surgery”), genital surgery (“bottom surgery”), and other interventions, such as facial feminization surgery, vocal cord surgery, and thyroid cartilage reduction.[\[84,122,123,124\]](#) A full discussion of surgical options and outcomes is beyond the scope of this Topic Review, but it is important to note that many studies show that surgical intervention can improve well-being and sexual function.[\[82,122,124\]](#)

## Health Care Maintenance

### Cardiovascular Disease

Data on the effects of estrogen on cardiovascular disease risk in transgender women are mixed.[\[109,111,113,126\]](#) Some older studies suggested transgender women have an increased risk of developing cardiovascular disease, but these studies were confounded by the use of ethinyl estradiol, a formulation of estrogen that is not recommended for transgender women. There are no cardiovascular disease screening guidelines that are specific to transgender women or gender nonbinary individuals taking estrogen. Because many experts now consider HIV as an independent cardiovascular risk factor, clinicians caring for transgender women with HIV should screen for and consider aggressive management of cardiovascular risk factors.

## **Bone Health**

It remains unclear whether assessment of bone mineral density in transgender women should be based on sex assigned at birth or assigned gender.[\[106\]](#) In addition, there is no consensus for obtaining bone mineral density testing in transgender women. The Center of Excellence for Transgender Health recommends (1) obtaining bone density evaluation in all transgender persons beginning at age 65 and (2) considering bone density evaluation in transgender women aged 50 to 64 years who have osteoporosis risk factors or who, at any age, had orchiectomy surgery and have not taken estrogen therapy for at least 5 years.[\[127\]](#) Because HIV infection and some antiretroviral medications can increase the risk of osteoporosis, transgender women with HIV may have an even higher risk of developing osteoporosis. The HIV Primary Care Guidelines recommend bone density screening for all men living with HIV older than age 50, postmenopausal women living with HIV, and those individuals with other osteoporosis risk factors; no specific recommendations exist for transgender women with HIV.[\[128\]](#)

## **Cancer Screening**

No standardized cancer screening recommendations exist for the transgender or gender nonbinary populations. In general, the recommendation for cancer screening should be based on whether the body part meets the criteria for screening.[\[129\]](#) For example, transgender women on estrogen therapy without known elevated breast cancer risk should follow standard breast screening guidelines.[\[79,80\]](#) For transgender women, most experts recommend prostate cancer screening in accordance with guidelines for the general population.[\[130\]](#) Note that for transgender women on estrogen therapy, the prostate volume is reduced, and prostate-specific antigen (PSA) will be lowered; some experts have recommended adjusting the upper limit of normal to 1.0 ng/mL in transgender women receiving hormonal therapy.

## **Mental Health in Transgender Women**

Transgender and gender nonbinary individuals are at risk for mental health disorders and psychological distress due to multiple overlapping risk factors, including gender dysphoria, high rates of psychological and physical abuse, social exclusion, stigma, and victimization.[\[104,131,132\]](#) Available data suggest prevalence rates of depression, anxiety, post-traumatic stress disorder, and substance use disorders are higher among transgender individuals compared to cisgender women or men.[\[132,133\]](#) For transgender women living with HIV, the burden of mental health disorders is likely even higher than for transgender women who do not have HIV, due to added stigma secondary to HIV status.[\[134,135\]](#) Unfortunately, transgender individuals with mental health disorders often face health care discrimination and have difficulty finding appropriate medical and psychiatric providers, as well as difficulty accessing emergency care.[\[136,137\]](#)

## **Substance Use in Transgender Women**

Transgender women have a higher prevalence of substance use disorders compared with cisgender populations.[\[138,139\]](#) Transgender women are at particularly high risk of discrimination and victimization, and research has shown that as many as 35% of transgender people who experience discrimination use drugs and alcohol as a coping mechanism.[\[138\]](#) Another study demonstrated that transgender women who experience physical or psychological abuse due to gender expression or identity have 3- to 4-fold higher odds

of alcohol, marijuana, or cocaine use, as well as 8-fold higher odds of any drug use.[\[132\]](#) Multiple factors may enhance the risk for substance use disorders among transgender individuals, including intimate partner violence, depression, post-traumatic stress disorder, unstable housing, housing discrimination, and engagement in sex work.[\[138\]](#) There is limited research on substance use in transgender women, particularly among transgender women living with HIV.[\[140,141\]](#)

## Transgender Men

This discussion is intended to provide a brief overview of the epidemiology of transgender men and HIV, followed by an introduction to medical care for transgender men and gender nonbinary persons desiring masculinizing therapy. Excellent documents that provide guidance for gender-affirming care are available through Fenway Health, the Center of Excellence for Transgender Health, the Endocrine Society, and the World Professional Association for Transgender Health (WPATH).<sup>[9,82,83,84]</sup> We recommend reviewing and using the following resources when providing gender-affirming clinical care for transgender people.<sup>[9,83,85]</sup>

- Fenway Institute (Boston, MA): [Medical Care of Trans and Gender Diverse Adults](#)
- Center of Excellence for Transgender Health (San Francisco, CA): [Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People](#)
- The World Professional Association for Transgender Health (WPATH): [Standards of Care for the Health of Transgender and Gender Diverse People, Version 8](#)

## Epidemiology

In the United States, there are an estimated 1.0 to 1.4 million adults who self-identify as transgender.<sup>[142,143,144]</sup> Among transgender men living in the United States, an estimated 3.2% are living with HIV.<sup>[86,92]</sup> The following summarizes data on transgender men living with diagnosed HIV in the United States ([Figure 9](#)).<sup>[87]</sup>

- **Number of Transgender Men Living with Diagnosed HIV:** The CDC HIV Surveillance System identified 403 transgender men living with diagnosed HIV in the United States in 2018, but this likely represents a significant underestimate of the true prevalence; the number of reported transgender men living with diagnosed HIV in the United States has increased steadily from 2014-2018.<sup>[87]</sup>
- **Transgender Men Living with Diagnosed HIV by Age Group:** In 2018, most of the transgender men living with diagnosed HIV in the United States were between 25 and 55 years of age.<sup>[87]</sup>
- **Transgender Men Living with Diagnosed HIV by Racial/Ethnic Group:** There were marked racial disparities among transgender men living with diagnosed HIV in the United States, with transgender men who identify as Black accounting for 47% of diagnoses.<sup>[87]</sup>
- **Transgender Men Living with Diagnosed HIV by Region:** Based on residence, transgender men living with diagnosed HIV in the United States were most likely to live in the South or Midwest.<sup>[87,89]</sup>
- **Transgender Men and Knowledge of HIV Status:** Little is known about awareness of HIV status among transgender men. Additional research and reporting are needed to better estimate the undiagnosed HIV fraction among transgender men in the United States.

## Risk Factors for Acquiring HIV

Transgender men appear to face similar discrimination, stigma, victimization, and rates of depression and suicide as transgender women, yet the risk of acquiring HIV is generally lower than in transgender women.<sup>[92]</sup> Some experts, however, have argued that the risk of acquiring HIV in transgender men has been underestimated.<sup>[133,145]</sup> A study of transgender men in San Francisco identified several HIV risk factors, including housing insecurity, injection drug use, and a high number of sex partners. Transgender men who have sex with cisgender men or transgender women represent a subpopulation of transgender men who may be at elevated HIV risk.<sup>[146,147,148]</sup> More research is needed to better estimate HIV risk, describe the complex structural barriers and discrimination that contribute to the elevated risk, and guide HIV prevention efforts among transgender men. It is important to note that the racial disparities in HIV prevalence for transgender men, like for transgender women, stem from long-standing and ongoing institutionalized racism and other sociostructural barriers, not biological differences.

## Approach to Gender-Affirming Care for Transgender Men

The approach to gender-affirming therapy for transgender men and for gender nonbinary persons is usually the same regardless of HIV infection status.[\[102\]](#) For individuals desiring female-to-male transition or masculinizing therapy, options include medical interventions (hormonal therapy) and surgery (e.g., breast reduction, metoidioplasty, phalloplasty, scrotoplasty, and hysterectomy).[\[9,82,103\]](#) The decision to take gender-affirming hormones or to have gender-affirming surgery is a significant one, and a medical provider-client discussion regarding the risks and benefits of gender-affirming treatment is essential.[\[104,105\]](#)

## Principles of Masculinizing Hormone Therapy

The same general principles of hormone therapy apply to transgender men (and nonbinary persons desiring masculinizing therapy) as to transgender women, including the requirement for a thorough baseline evaluation to ensure that patients have well-documented, persistent gender dysphoria, capacity, and age of majority to make fully-informed decisions, and reasonably controlled physical and mental health conditions.[\[82\]](#)

## Goals of Masculinizing Hormone Therapy

Testosterone therapy is the mainstay of masculinizing therapy for transgender men, and it can be delivered through the intramuscular, subcutaneous, or topical route. Specific masculinizing goals often include an increase in facial and body hair, increase in muscle mass, decrease in breast mass, deepening of the voice, and reduction or cessation of menses. Some of these effects, such as changes in voice pitch, muscle mass, and hair growth, usually start to occur within months ([Figure 10](#)), but masculinization is a gradual process, and it generally takes years to experience maximal masculinization effects ([Figure 11](#)).[\[82,84,149\]](#) For transgender men on long-term testosterone therapy, most experts recommend maintaining serum total testosterone levels in the male physiologic range of 400 to 700 ng/dL; ideal levels may be different for gender nonbinary persons and depend on an individual person's goals.[\[84\]](#)

## Testosterone Masculinizing Hormone Therapy

In general, daily administration of transdermal testosterone (gel or patches) approximates physiologic testosterone levels better than parenteral testosterone (intramuscular [IM] or subcutaneous [SQ]), which is typically given every 1 to 2 weeks or even less frequently with some longer-acting injectable preparations. The doses listed below for testosterone masculinizing therapy are suggested initial and maintenance doses.[\[9,84,149\]](#) Implantable testosterone pellets offer another long-acting option, though they require an office visit for placement every 3 to 4 months.[\[9\]](#) With all testosterone preparations, the maintenance doses may need to be adjusted based on testosterone levels, desired masculinizing effects, and adverse effects. Some individuals who desire a more androgynous appearance may prefer lower-dose testosterone therapy. Common physiologic effects in transgender men and gender nonbinary persons receiving testosterone include increased muscle mass and strength, decreased fat mass, acne, increased facial and body hair, scalp hair loss, deepening of the voice, vaginal atrophy, clitoromegaly, cessation of menses, and increased libido.[\[84\]](#)

- **Testosterone Transdermal Patch:** The initial dose for the testosterone transdermal patch is a 2.0 to 2.5 mg patch applied daily and replaced every 24 hours; after 2 to 4 weeks, the dose can be increased to 4.0 to 5.0 mg per day. For the testosterone transdermal patch, the usual maintenance dose is 6.0 to 7.5 mg per day.
- **Testosterone Gel:** There are several testosterone gel preparations used in this setting. The most common is testosterone gel 1.62%, available as a metered-dose pump or packet. The usual starting dose for testosterone gel (1.62%) is 20.25 mg daily, titrating the dose upward over 2 to 4 weeks until a maintenance dose of 40.5 to 81 mg per day is reached.
- **Injectable Testosterone:** The usual starting dose of injectable testosterone (cypionate, enanthate, undecanoate) is 40 to 80 mg injected IM weekly and increased by 20 to 40 mg every 2 to 4 weeks to reach a maintenance dose of 50 to 100 mg IM every week, 100 to 200 mg every 2 weeks, or (with some preparations) 200 to 400 mg every 4 weeks. The injections can be given IM or SQ.

- **Long-Acting Testosterone Undecanoate Injection:** The usual starting dose for the long-acting testosterone undecanoate injection is a 750 mg IM initial dose, 750 mg IM repeated 4 weeks later, with a maintenance dose of 750 mg IM every 10 weeks.
- **Testosterone Pellets:** Each of the testosterone pellets contains 75 mg of crystalline testosterone, and one pellet is implanted subcutaneously in the subdermal space at the upper outer area of the buttock in an office procedure. Following implantation, the pellet slowly releases testosterone. The pellet typically is replaced every 3 to 4 months.
- **Oral Testosterone Undecanoate:** An oral softgel capsule that contains testosterone undecanoate is available with a recommended starting dose is 237 mg twice daily with food. There is little experience with this medication in transgender care and it is generally not recommended as a first-line option.

## Medications for Cessation of Menses

For transgender men and gender nonbinary persons who retain their uterus, testosterone therapy alone may cause cessation of menses within 1 to 6 months.[\[84\]](#) For individuals who continue to have uterine bleeding after several months of testosterone, options include the use of a progestational agent, such as medroxyprogesterone acetate at a dose of 5 to 10 mg daily, depot medroxyprogesterone acetate (DMPA), or endometrial ablation. Transgender men of child-bearing age who are taking testosterone should be counseled that they can become pregnant while taking testosterone and that testosterone use is contraindicated during pregnancy. Thus, appropriate measures should be taken to prevent pregnancy if taking testosterone. Further, since receiving testosterone while pregnant could cause serious toxicity to the fetus, any person receiving testosterone who becomes pregnant should stop the testosterone immediately.

## Potential Adverse Effects of Testosterone Therapy

Common adverse effects of testosterone therapy include erythrocytosis (hematocrit greater than 50%), hepatotoxicity, decreased HDL cholesterol, increased triglycerides, hypertension, weight gain, vaginal atrophy, acne, male pattern baldness, and a possible increase in coronary artery disease.[\[9,84,149\]](#) In addition, masculinizing hormone therapy may cause emotional effects, such as irritability and anger.

## Monitoring of Persons on Masculinizing Hormone Therapy

All patients receiving gender-affirming hormonal treatment require close follow-up to evaluate the effectiveness of the therapy and to monitor for adverse effects. The following summarizes recommendations for routine baseline laboratory studies and laboratory monitoring.[\[9,84,149\]](#)

- **Baseline Laboratory Studies:** The recommended baseline studies for individuals initiating hormonal masculinizing therapy with testosterone include a complete blood count, lipid panel, basic metabolic panel (including blood urea nitrogen, creatinine, and potassium), hepatic aminotransferase levels, and fasting glucose or hemoglobin A1c level.
- **Monitoring Testosterone Levels:** Most experts recommend monitoring serum testosterone levels approximately every 3 months during the first year of transition. Subsequently, it is reasonable to follow testosterone levels every 6 to 12 months, assuming they remain in the goal range.
- **Recommended Testosterone Level:** The Endocrine Society recommends a serum total testosterone level should fall into the physiologic male range of 350 to 1,000 ng/dL for persons receiving testosterone for gender-affirming masculinizing treatment, regardless of the testosterone preparation.[\[84\]](#) The timing of when to check a testosterone level varies based on the testosterone preparation. For testosterone enanthate or testosterone cypionate, it is recommended to check midway between injections; for transdermal testosterone, it is optimal to check at least 2 hours after application (and persons must have been using the topical testosterone for at least 1 week). Maintaining levels higher than 1,000 ng/dL ("supraphysiologic" levels) significantly increases the risk of testosterone-related adverse effects and is not recommended.[\[84\]](#) There may be some instances in which calculation of bioavailable free testosterone may help in clinical decision-making, and there may be instances in which checking an estradiol is indicated, though it is not done routinely; more



detail on this is available in guidelines from the Center of Excellence for Transgender Health.[149]

- **Monitoring for Toxicity:** For persons receiving testosterone, the hemoglobin (or hematocrit) should be followed every 3 months for the first year, then every 6 to 12 months thereafter, assuming it remains in the normal male range (the normal male range should be used, although labs may report normal ranges for women for a patient with female sex assigned at birth). Lipid panel and aminotransferase levels should be followed every 6 to 12 months.

## Gender-Affirming Surgery

Masculinizing surgical options include chest reconstruction (“top surgery”) and genital surgery (“bottom surgery”).[82,123,124] Genital gender-affirming surgeries include hysterectomy, oophorectomy, vaginectomy, scrotoplasty, phalloplasty, and/or metoidioplasty. Of these surgeries, phalloplasty carries the highest complication rate, but case series have demonstrated high levels of patient satisfaction following the procedure.[150,151] A full discussion of surgical options and outcomes is beyond the scope of this Lesson Review, but is addressed in other more comprehensive resources.[82,123,124]

## Health Care Maintenance

Compared with the available literature on transgender women, less research and guidance exist on the health needs of transgender men.[148,152,153]

- **Cardiovascular Disease:** There are no cardiovascular screening guidelines that are specific to transgender men with or without HIV. Available data suggest that transgender men have cardiovascular risk comparable to non-transgender men. Transgender men have a relatively high rate of smoking (approximately 25%), and all smokers should be encouraged to stop smoking.
- **Bone Health:** Both testosterone and estrogen are protective against osteoporosis. The Center of Excellence for Transgender Health recommends the same osteoporosis screening for transgender men as for transgender women; bone density evaluation should be performed in all transgender men beginning at age 65, in transgender men aged 50 to 64 years with osteoporosis risk factors, and in transgender men of any age who have had oophorectomy and who do not use hormone replacement for at least 5 years.[149]
- **Cancer Screening:** Transgender men and gender nonbinary persons who retain a cervix and uterus should undergo the same screening for cervical cancer as for cisgender women; they should also receive education about signs and symptoms of endometrial cancer.[84,129] There are currently no guidelines for breast cancer screening for transgender men. Mammography is not routinely performed following gender-affirming bilateral mastectomy, but note that cases of breast cancer have occurred in some transgender men following bilateral mastectomy.[154] The risk of breast cancer is higher if breast tissue is left following the surgical procedure for contouring. Transgender men who have undergone mastectomy surgery should have an annual breast examination, with a follow-up mammogram if abnormalities are found in clinical practice.[84] Transgender men who do not have mastectomy surgery should have routine mammogram screening performed based on recommendations for cisgender women. Transgender men receiving testosterone do not develop a prostate, and therefore, there is no risk of developing prostate cancer.

## Mental Health

Transgender persons, including trans men, experience depression and suicidality at a disproportionately high rate, which reflects the elevated burden of mental health issues. One early study found that more than half of transgender men had depression, and almost one-third had attempted suicide.[95] Unfortunately, many studies related to mental health in transgender persons either do not differentiate between transgender men and women, or have very low numbers of transgender men. Thus, the burden of mental health disorders and suicide among transgender men is not well characterized. Recent evidence suggests that access to gender-affirming testosterone therapy improves mental health for many transgender men.[155]

## **Drug Interactions Between Hormonal and Antiretroviral Treatments**

There are limited data on drug interactions between testosterone and antiretroviral therapy. Based on available data, testosterone levels may be increased when given with boosted protease inhibitors and with elvitegravir boosted with cobicistat. The NNRTIs efavirenz, etravirine, and nevirapine may decrease testosterone levels, and the levels of testosterone should be monitored and adjusted as needed. [[116](#), [120](#)]

## Summary Points

- In the United States, for the year 2021, an estimated 7% of adults self-identified as lesbian, gay, bisexual, or transgender (LGBT) persons.
- High rates of stigma and trauma contribute to the numerous barriers for sexual and gender minority populations to obtain optimal health care.
- Terminology to describe sexual and gender minority populations is dynamic and ever-changing. Whenever possible, it is best to ask and use the terminology the individual uses.
- In 2021, cisgender men who have sex with men accounted for 59% of all persons living with HIV in the United States and 66% of the estimated number of new HIV infections.
- Cisgender women who have sex with women have an extremely low HIV incidence and prevalence, but they may be at risk for other STIs.
- For the year 2021 in the United States, persons who identified as transgender women accounted for 1.1% of all persons living with diagnosed HIV and 2.3% of the new HIV infections that year.
- The number of transgender men living with HIV in the United States is very low, accounting for less than 0.1% of all people living with HIV.
- Primary care for sexual and gender minority people should incorporate routine preventative care and focus on issues that disproportionately affect these populations, particularly mental health conditions, substance use disorders, and sexually transmitted infections.
- Gender affirmation is a multidimensional process of aligning one's social, medical, and legal status with one's current gender identity. Gender-affirming care may include both surgical and hormonal options.
- Medical providers should be aware of the potential benefits and risks of gender-affirming hormone therapies and follow available evidence-informed recommendations and protocols. The goals of this therapy depend on an individual's desired effects.

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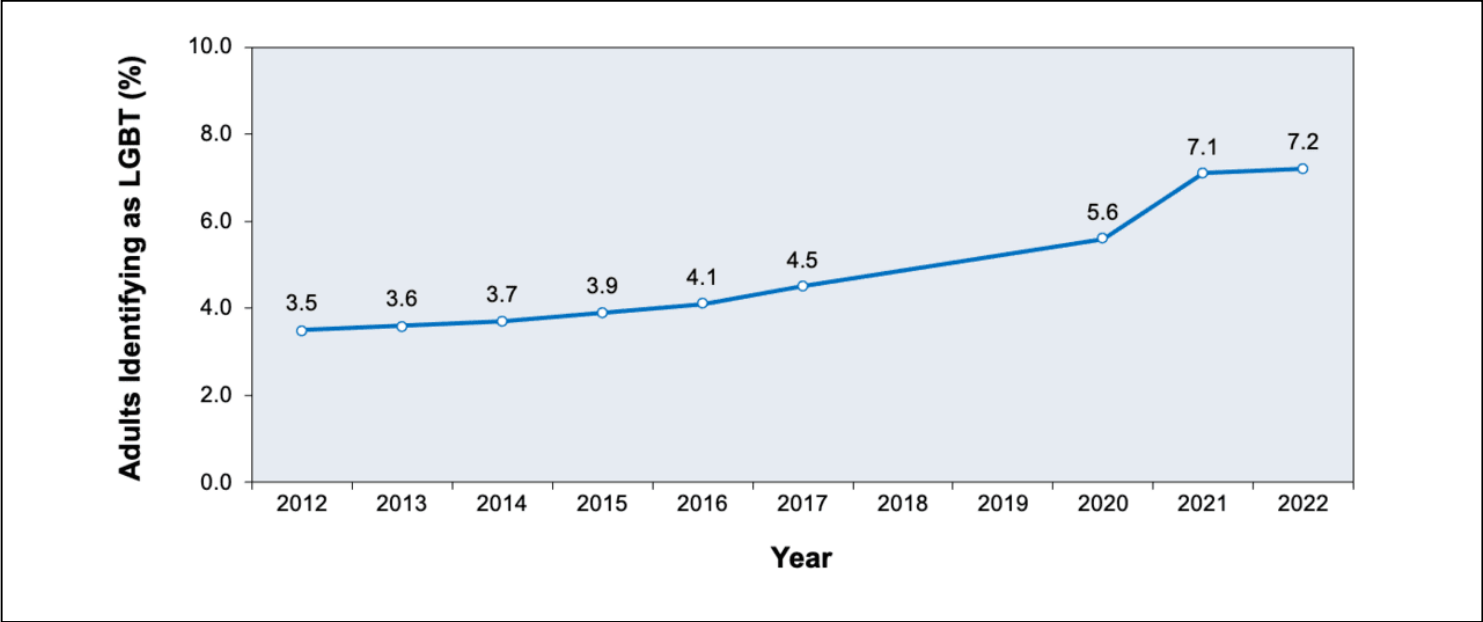
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# Figures

**Figure 1 Percentage of Adults Identifying as LGBT, United States, 2012-2022**

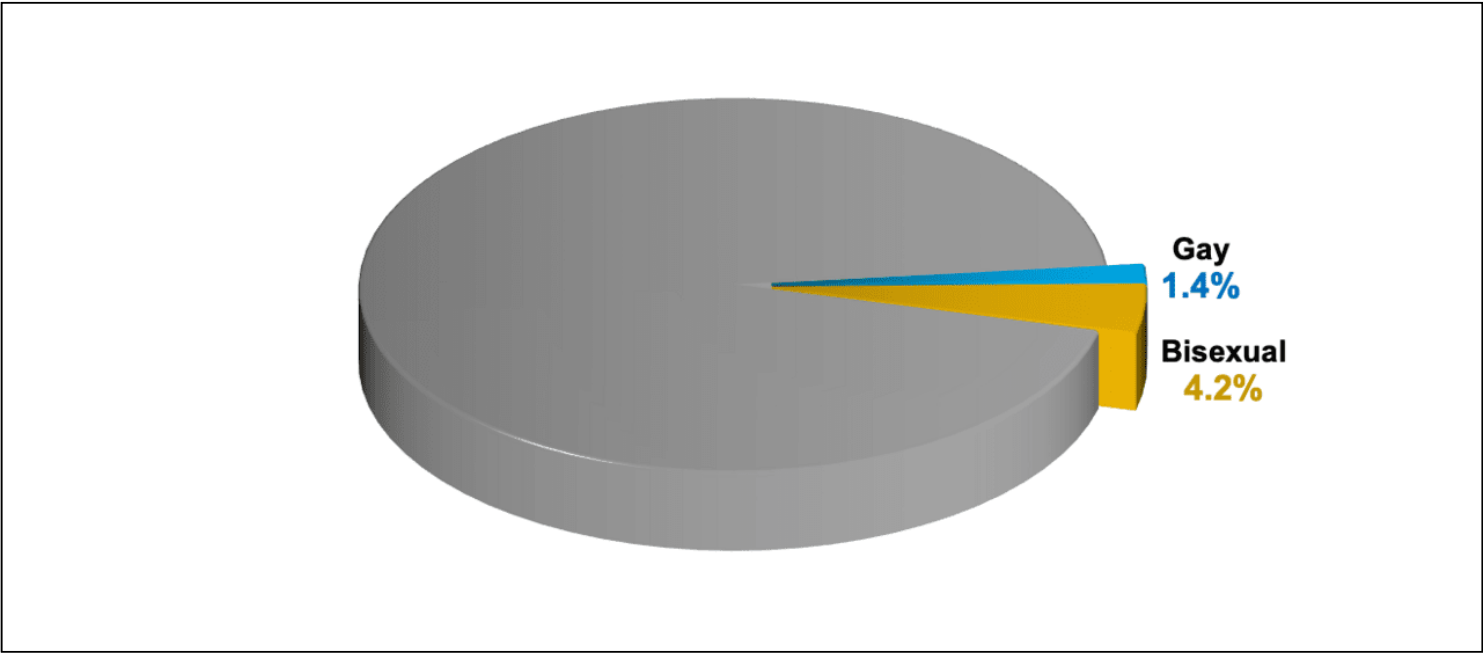
Source: Jones J. U.S. LGBT Identification Steady at 7.2%. Gallup News. February 2023.





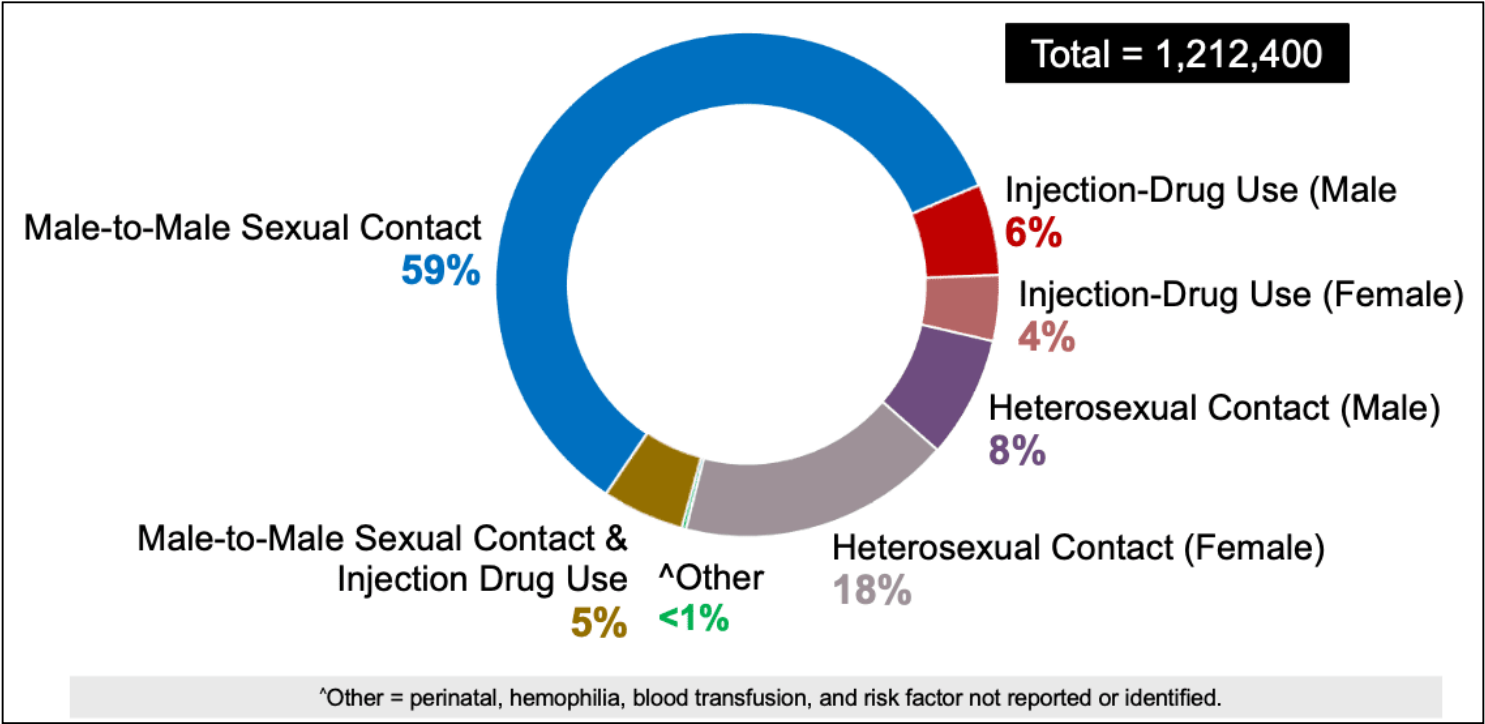
**Figure 2 Percentage of Adults Identifying as Gay or Bisexual, United States, 2022**

Source: Jones J. U.S. LGBT Identification Steady at 7.2%. Gallup News. February 2023.



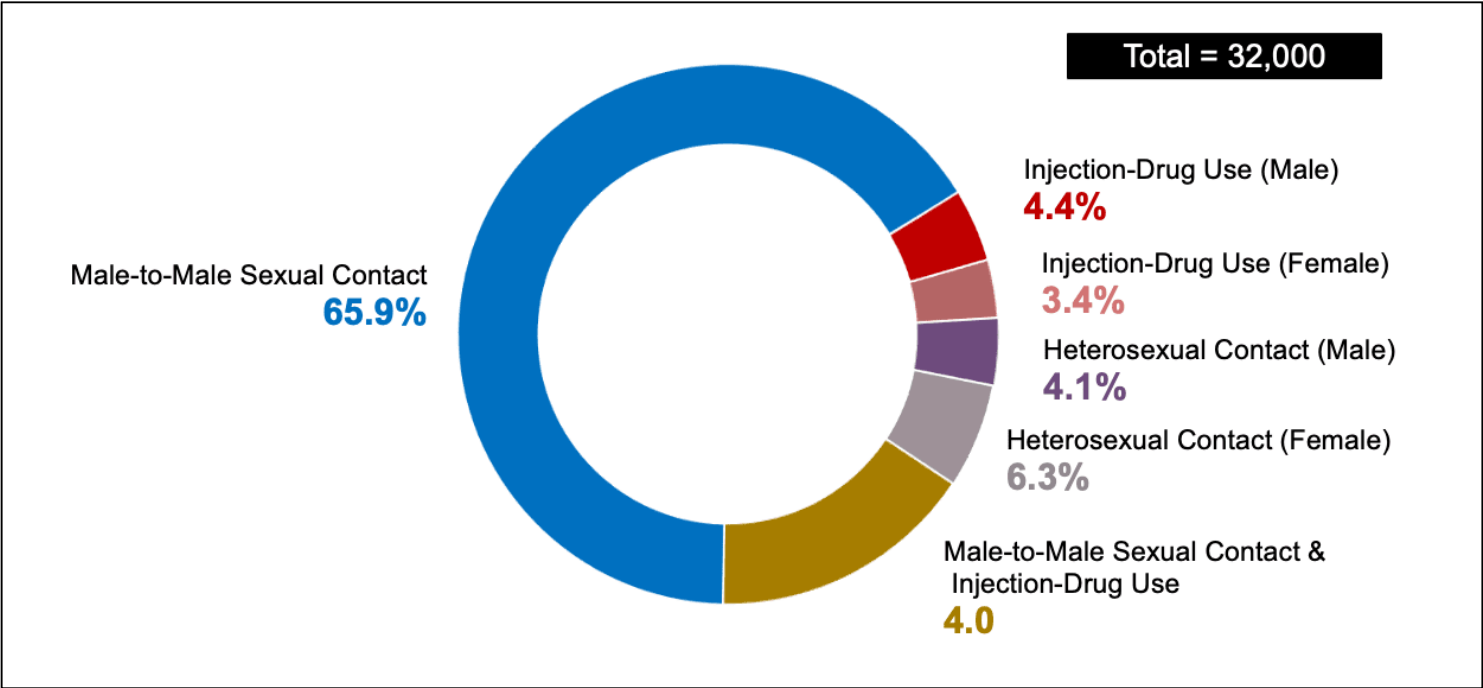
**Figure 3 Estimated Number of Persons Living with HIV, by Transmission Category, United States, 2021**

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.



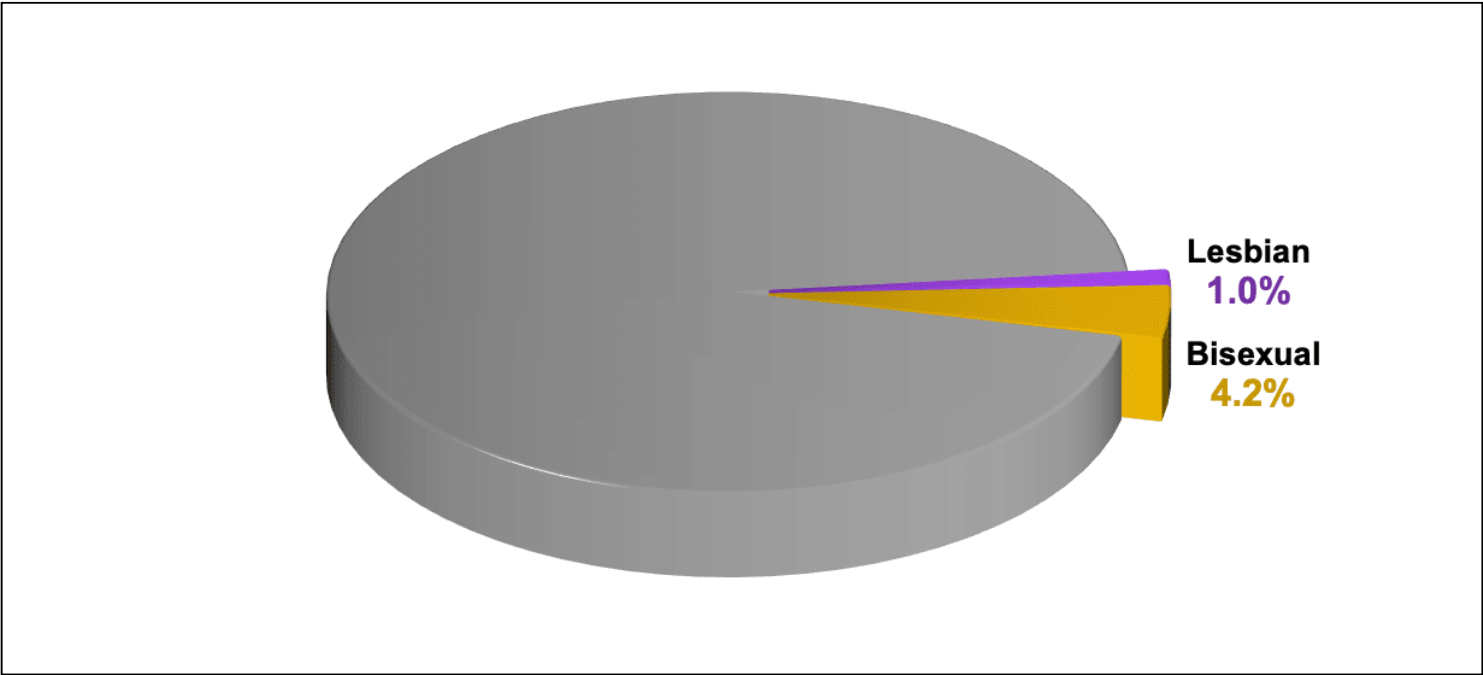
**Figure 4 Estimated Number of New HIV Infections, by Transmission Category, United States, 2021**

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2017–2021. HIV Surveillance Supplemental Report. 2023;28(3). Published May 2023.



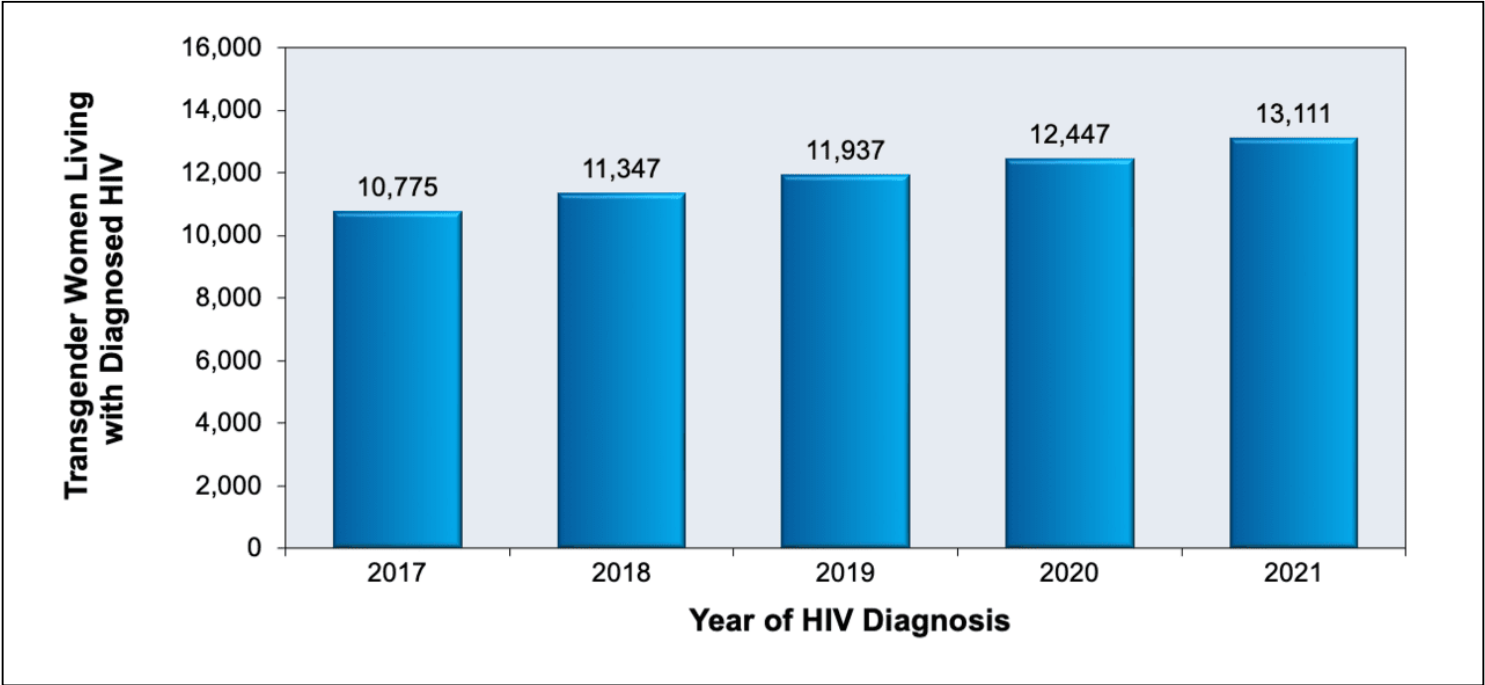
**Figure 5 Percentage of Adults Identifying as Lesbian or Bisexual, United States, 2022**

Source: Jones J. U.S. LGBT Identification Steady at 7.2%. Gallup News. February 2023.



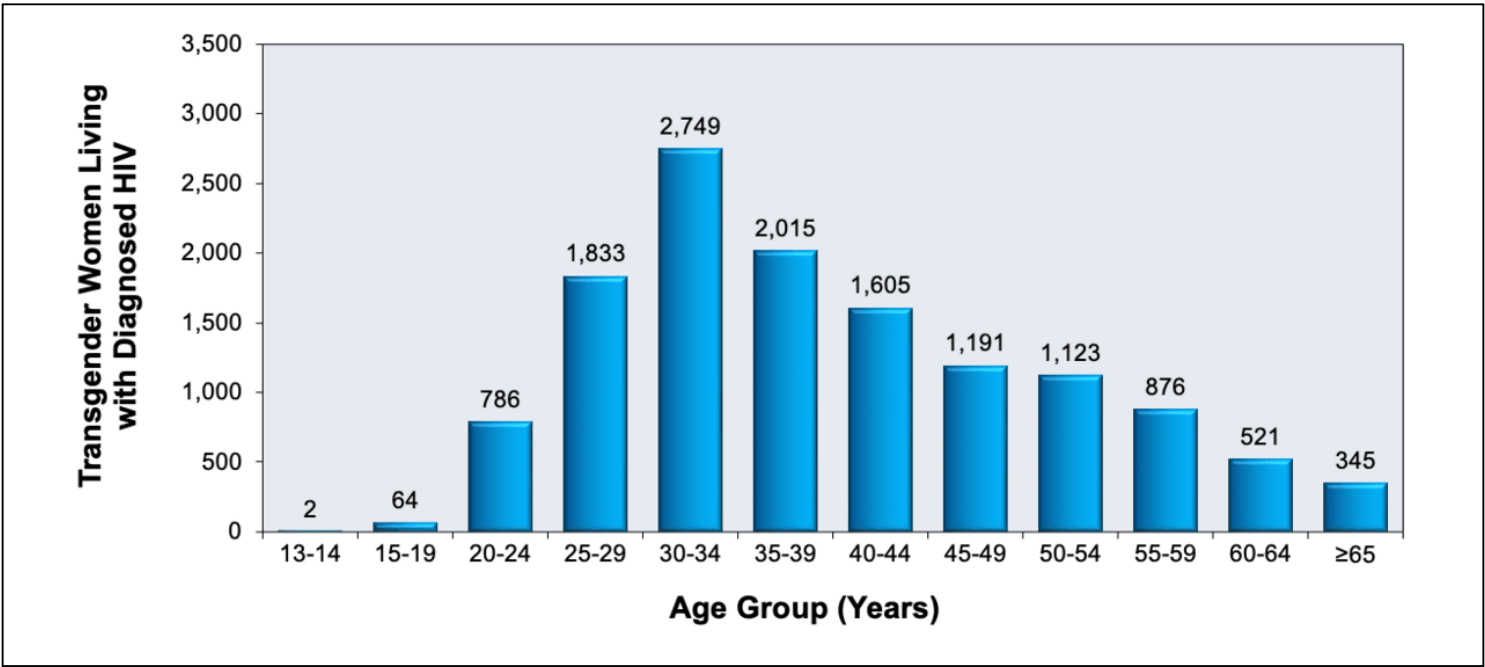
**Figure 6 (Image Series) - Transgender Women and HIV Epidemiology, United States (Image Series) - Figure 6 (Image Series) - Transgender Women and HIV Epidemiology, United States**  
**Image 6A: Transgender Women Living with Diagnosed HIV, 2017-2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



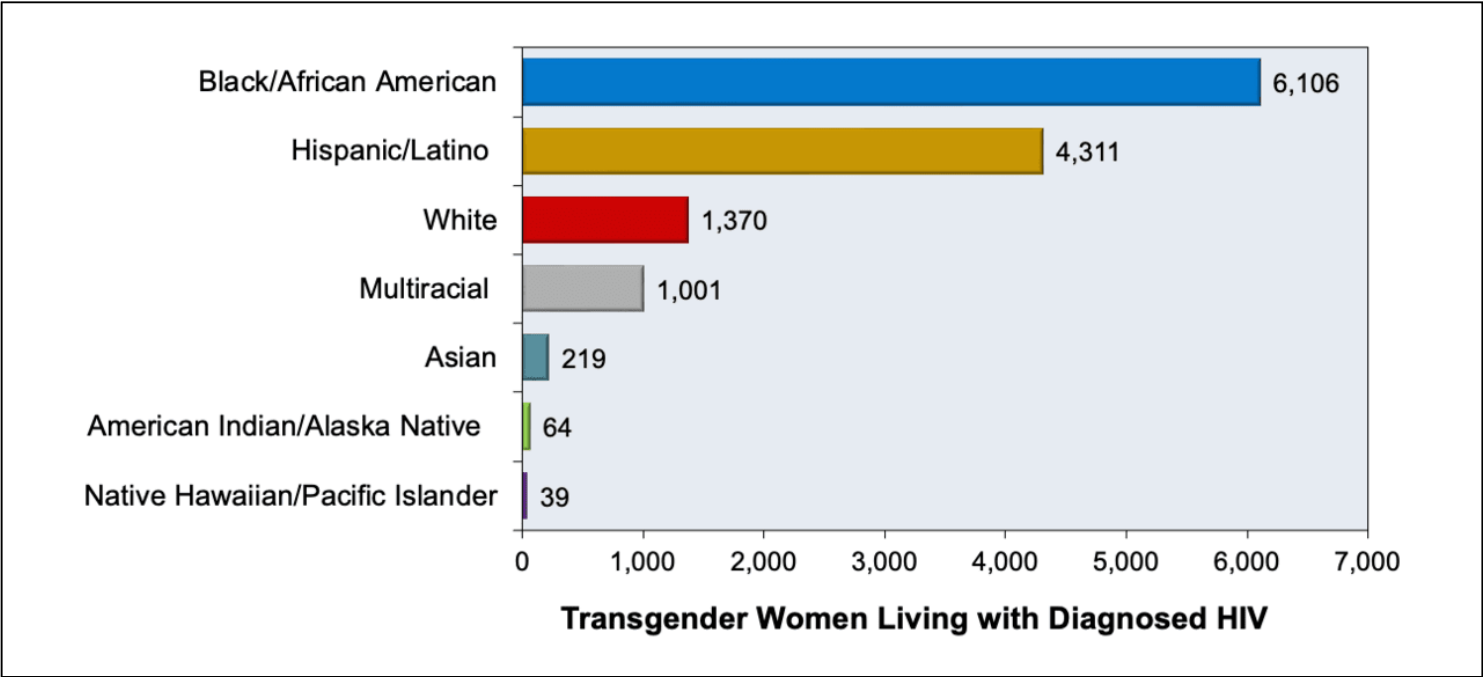
**Figure 6 (Image Series) - Transgender Women and HIV Epidemiology, United States**  
**Image 6B: Transgender Women Living with Diagnosed HIV, by Age Group, 2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



**Figure 6 (Image Series) - Transgender Women and HIV Epidemiology, United States**  
**Image 6C: Transgender Women Living with Diagnosed HIV, by Race/Ethnicity, 2021**

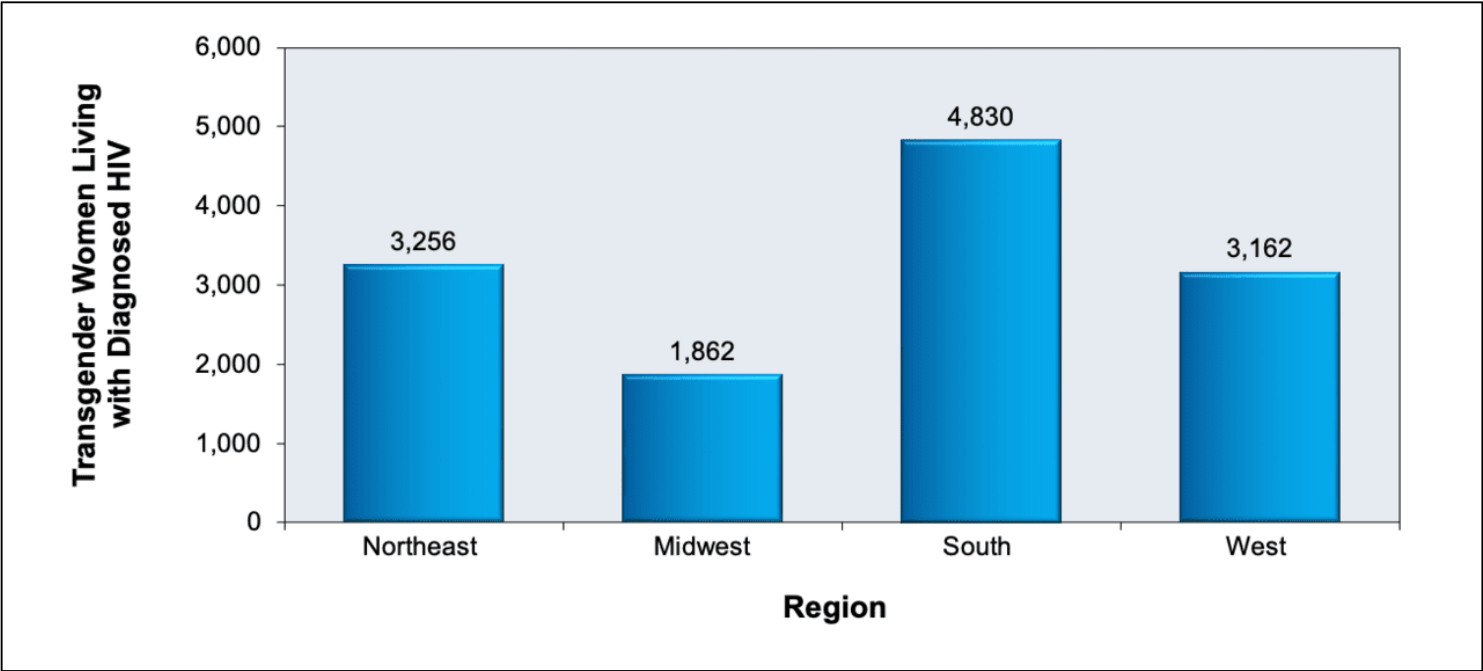
Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.





**Figure 6 (Image Series) - Transgender Women and HIV Epidemiology, United States**  
**Image 6D: Transgender Women Living with Diagnosed HIV, by Region, 2021**

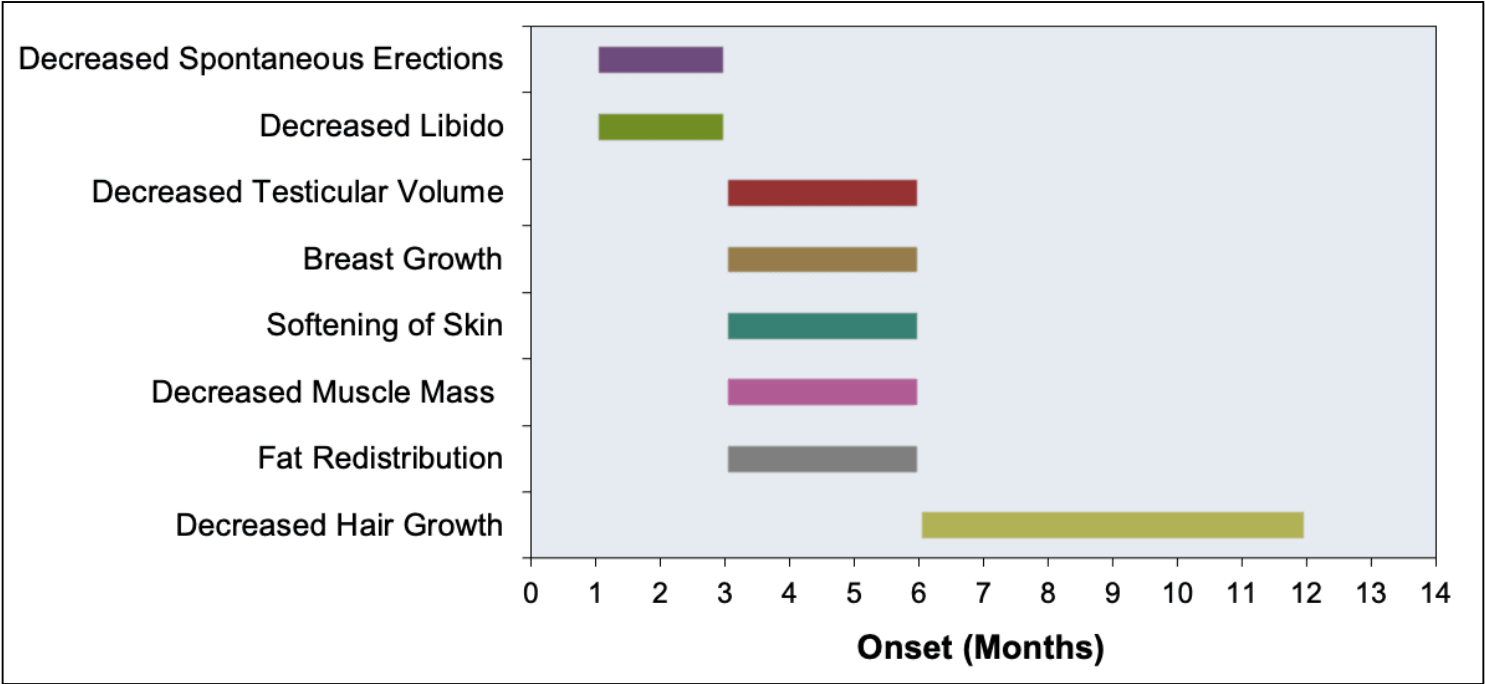
Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



**Figure 7 Onset of Feminizing Effects with Gender-Affirming Hormone Therapy in Transgender Women**

This figure shows the approximate time for onset of effects of gender-affirming hormone therapy in transgender women. Note that gender-affirming hormone therapy in transgender women has little impact on voice changes.

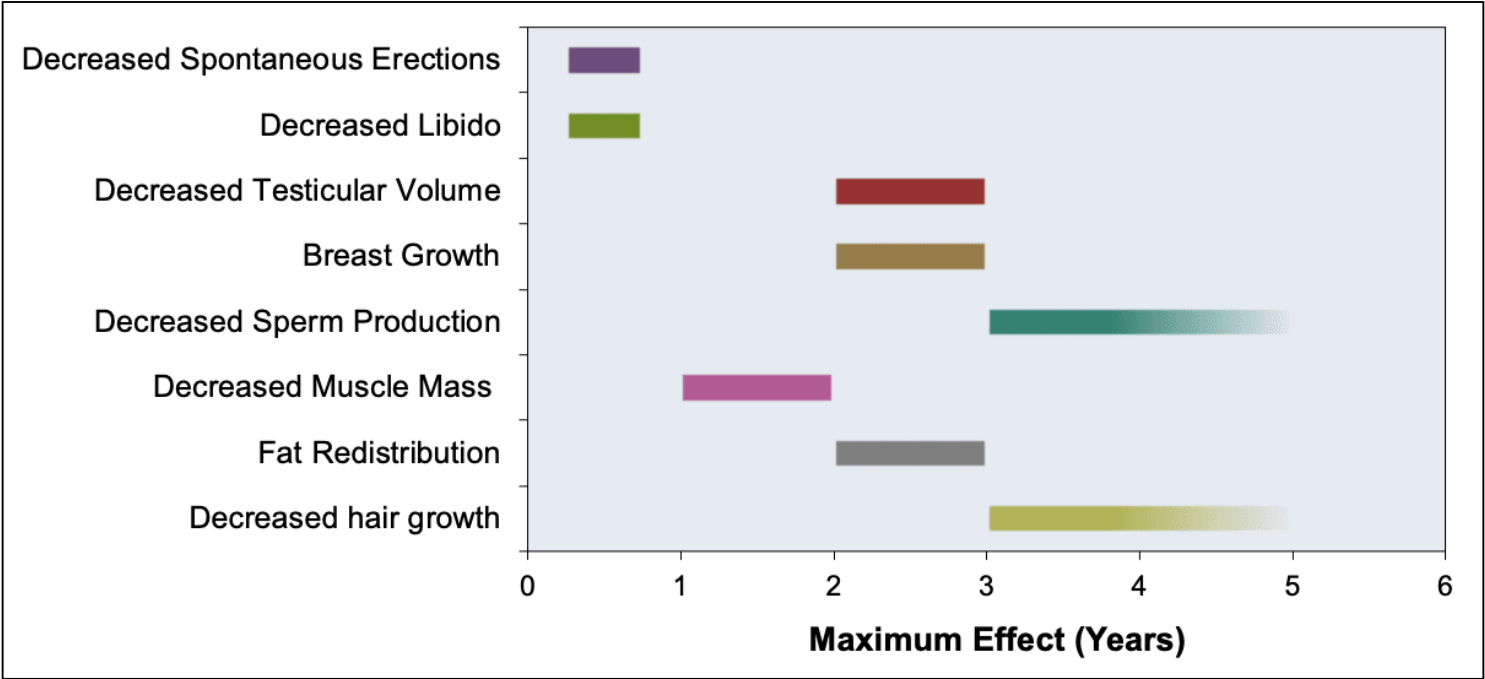
Source: Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017;102:3869-3903.



**Figure 8 Time to Maximum Feminizing Effects with Gender-Affirming Hormone Therapy in Transgender Women**

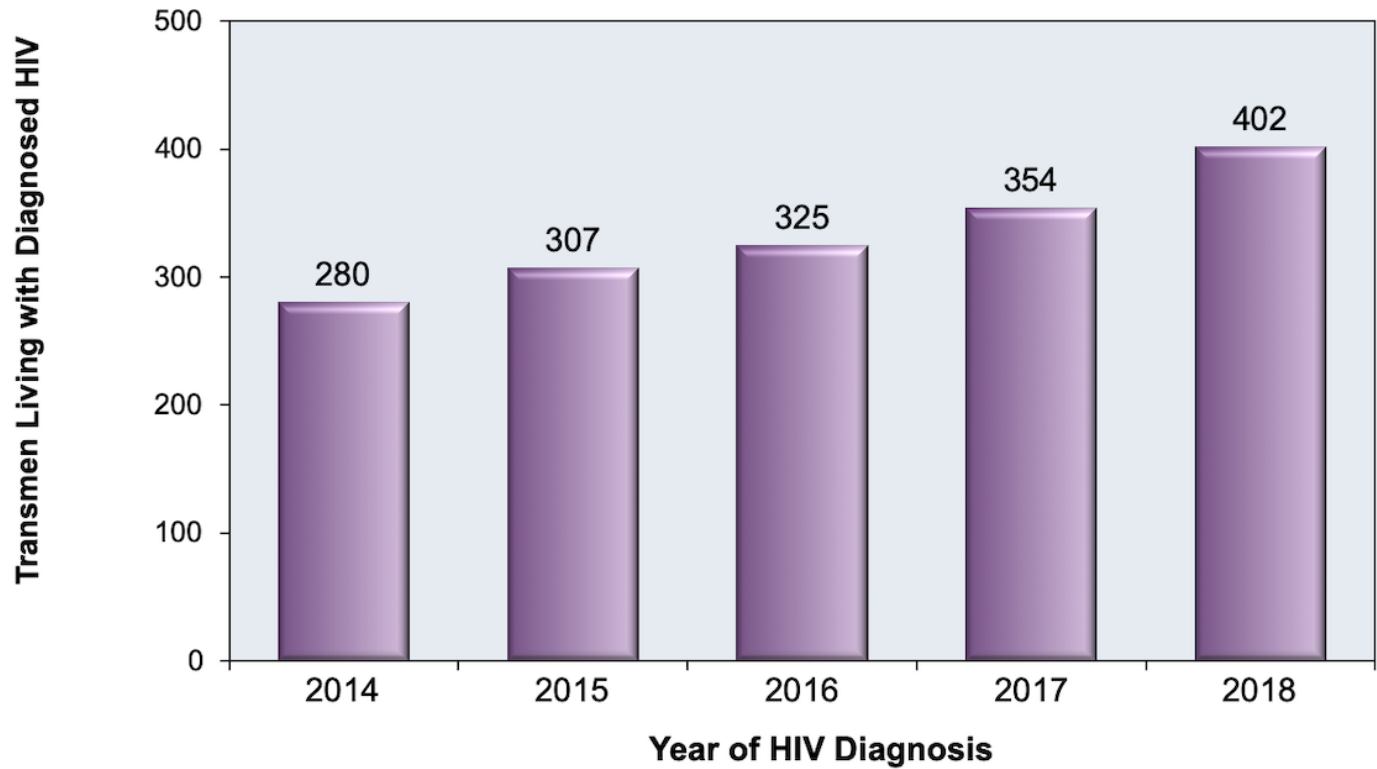
This figure shows the approximate time for maximal effects with gender-affirming hormone therapy in transgender women. The time for maximal effect on softening of skin is not known. The time to maximal effect for decreased sperm production and for decreased hair growth is greater than 3 years.

Source: Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017;102:3869-3903.



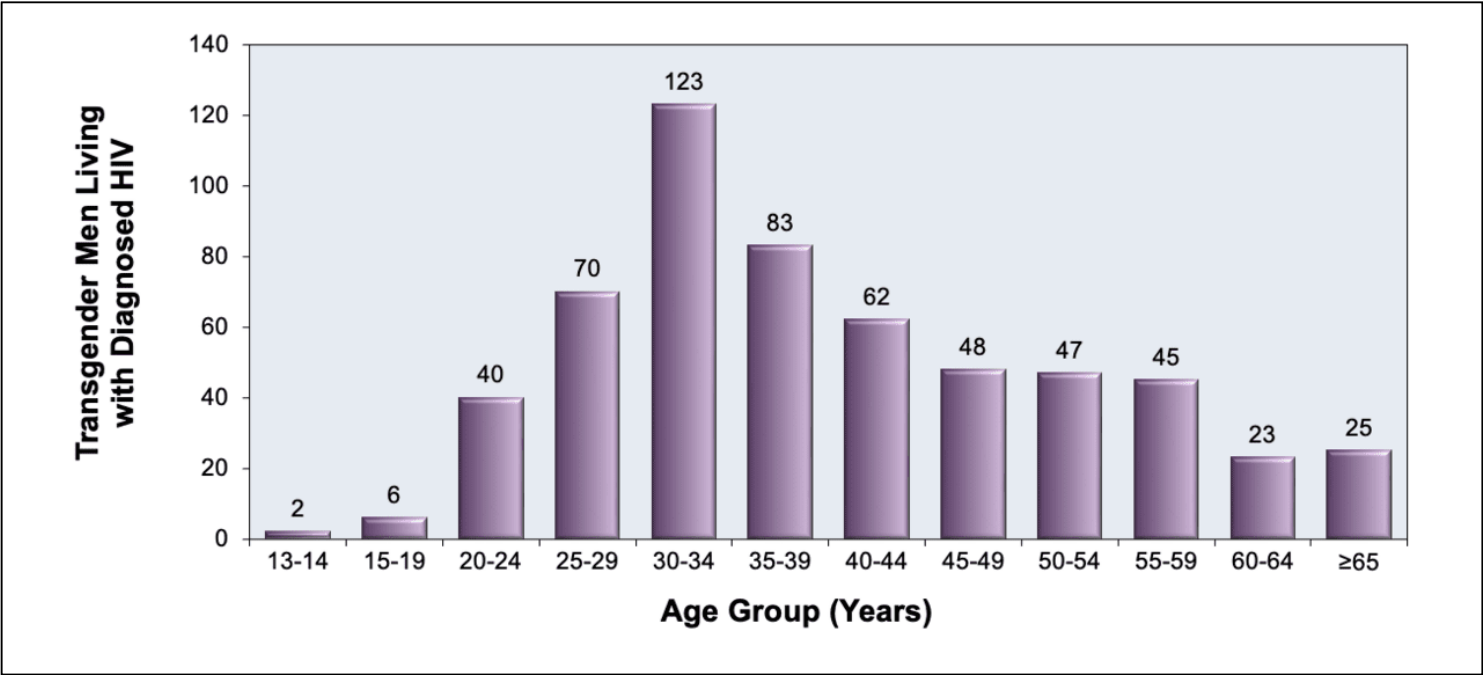
**Figure 9 (Image Series) - Transgender Men and HIV Epidemiology, United States (Image Series) -  
Figure 9 (Image Series) - Transgender Men and HIV Epidemiology, United States  
Image 9A: Transgender Men Living with Diagnosed HIV, 2017-2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



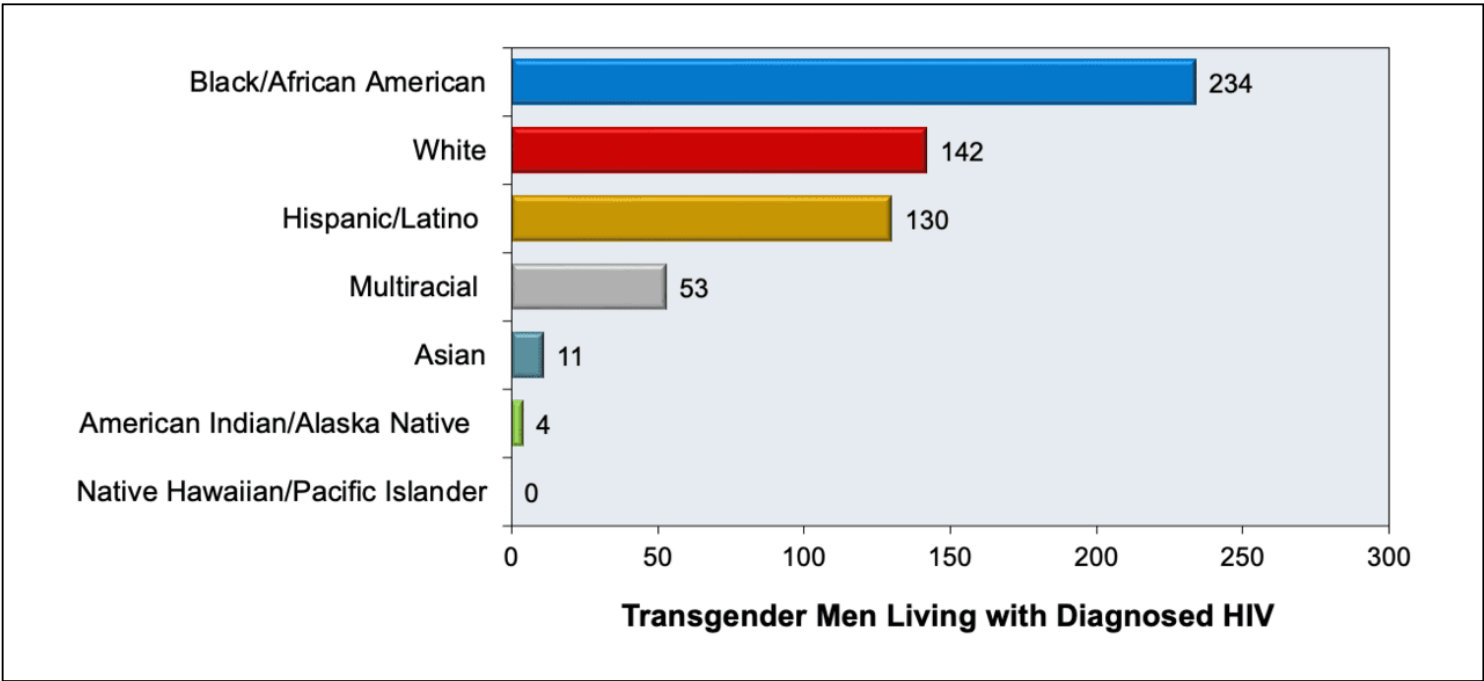
**Figure 9 (Image Series) - Transgender Men and HIV Epidemiology, United States**  
**Image 9B: Transgender Men Living with Diagnosed HIV, by Age Group, 2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



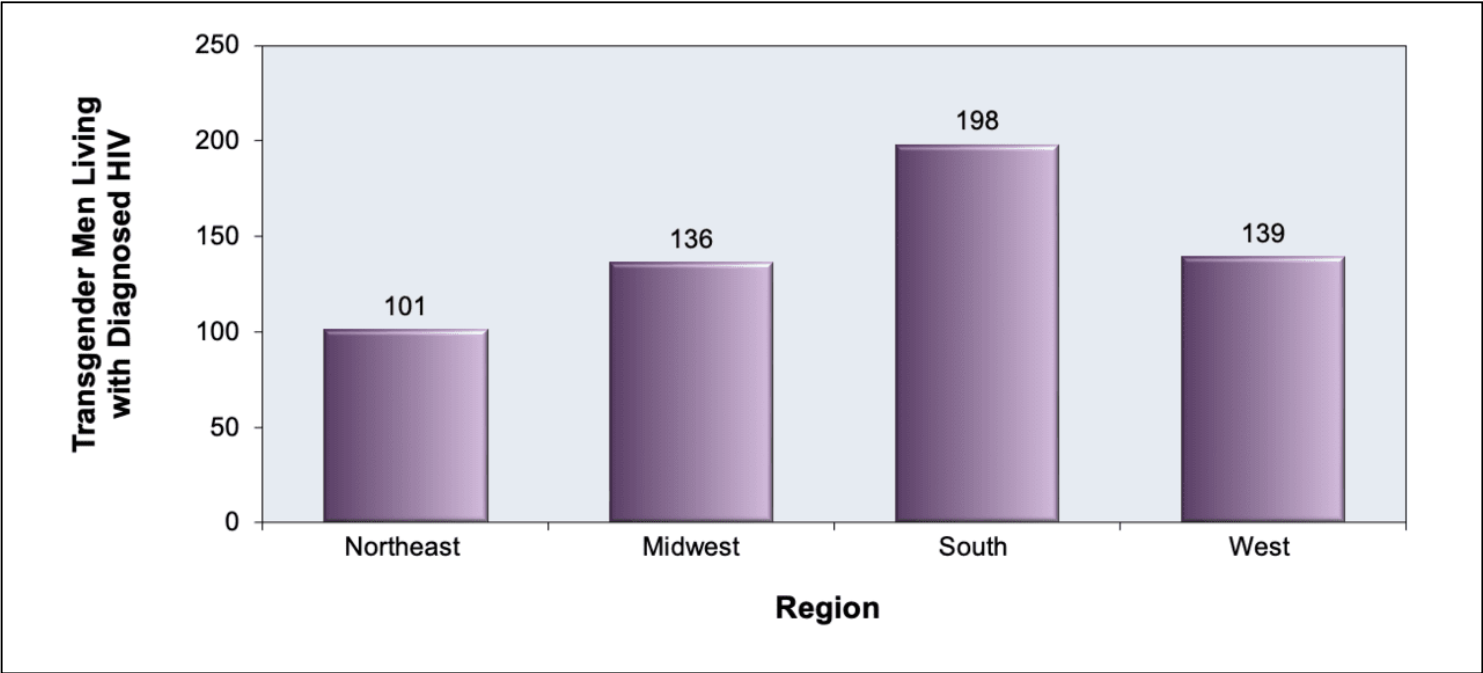
**Figure 9 (Image Series) - Transgender Men and HIV Epidemiology, United States**  
**Image 9C: Transgender Men Living with Diagnosed HIV, by Race/Ethnicity, 2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.



**Figure 9 (Image Series) - Transgender Men and HIV Epidemiology, United States**  
**Image 9D: Transgender Men Living with Diagnosed HIV, by Region, 2021**

Source: Centers for Disease Control and Prevention. Diagnoses of HIV infection in the United States and dependent areas, 2021. HIV Surveillance Report, 2021; vol. 34. Published May 2023.

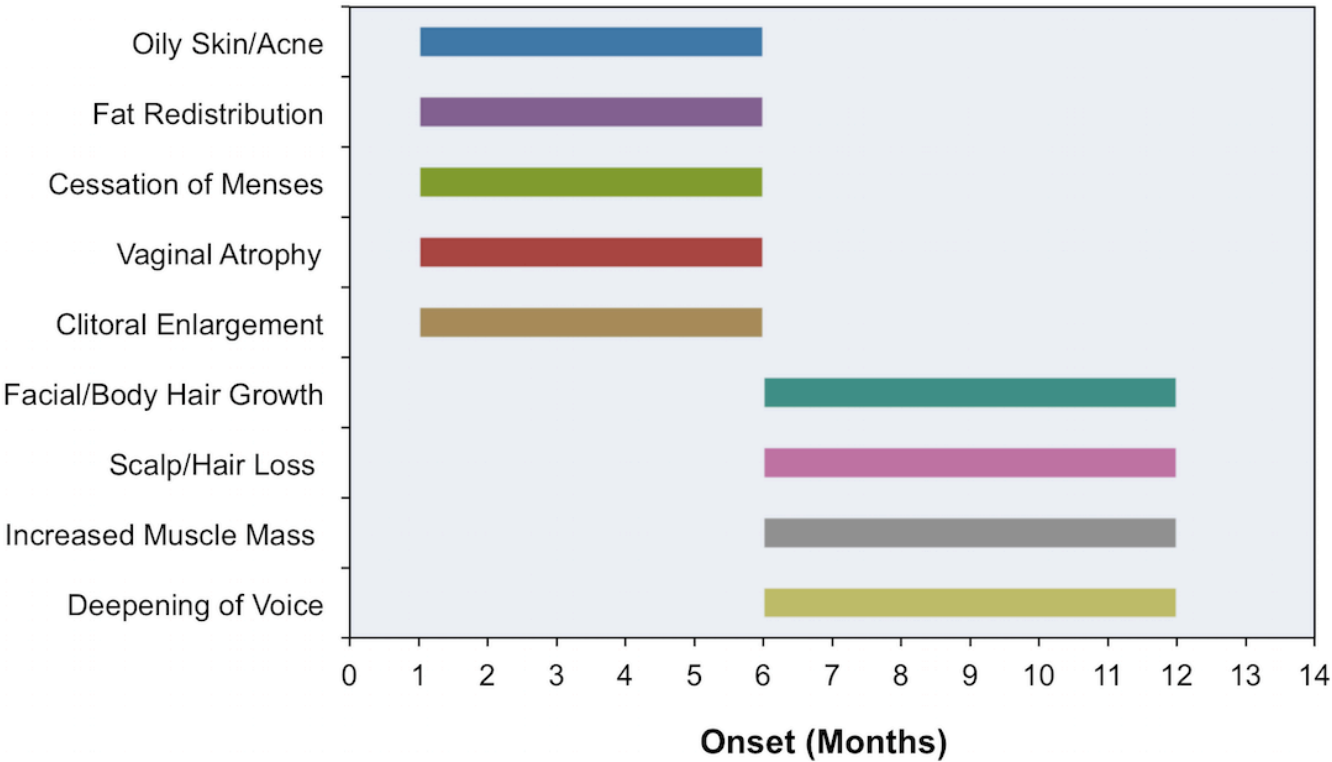




**Figure 10 Onset of Masculinizing Effects with Gender-Affirming Hormone Therapy in Transgender Men**

This figure shows approximate time for onset of certain masculinizing features associated with onset of use of testosterone in transgender men.

Source: Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017;102:3869-3903.



**Figure 11 Time to Reach Maximal Masculinizing Effects with Gender-Affirming Hormone Therapy in Transgender Men**

This figure shows approximate time to reach maximal effect with certain masculinizing features associated with onset of use of testosterone in transgender men.

Source: Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017;102:3869-3903.

