Chapter 13
HIV Infection in Transgender Persons

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Introduction

Transgender persons are disproportionately affected by HIV compared to the general population. In this chapter, we hope to shed light on the true burden of HIV on this marginalized population. We will review the factors that contribute to the high prevalence of HIV among transgender persons, in particular, high-risk sexual behaviors and substance abuse. Additionally, we will discuss the unique socioeconomic and psychosocial barriers that predispose this population to poor outcomes related to HIV prevention and treatment. We will also explain the contribution of transphobia in healthcare systems to the poor outcomes across the continuum of HIV care. This chapter will highlight challenges for transgender persons living with HIV, and attempt to offer solutions to overcome some of the obstacles. The choice of antiretroviral therapy with concomitant use of gender-affirming therapies will be discussed in detail.

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Epidemiology

Global HIV Prevalence

HIV was first recognized in a small group of men who have sex with men (MSM) in 1981. Since then, the epidemic has grown globally. As of 2016, the number of people worldwide estimated to be infected with the virus is approximately 36.7 million for a global prevalence of approximately 0.8% [1]. Certain populations with higher burdens of disease have been well characterized throughout the literature focusing both on geography (sub-Saharan Africa, Southeast Asia, Latin America, and the United States) and on sexual identity and behaviors (MSM, sex workers, intravenous drug users (IVDU), and prisoners).

In the United States, the CDC estimates that there are over 1.1 million people living with HIV, with 1 in 7 of those unaware of their diagnosis [2]. While the overall number of annual infections is thought to have declined by 18% from 2008 to 2014, there were still 39,782 new infections reported to the CDC in 2016 alone. The most highly affected group is MSM, who accounted for 67% of new infections in 2016. Furthermore, African-American MSM made up a disproportionate share of that number.

As the acceptance of the transgender community grows in the US and worldwide, there is an increasing need to understand the burden of HIV on these individuals. To date, studies of HIV in the transgender population are limited, but the picture they paint is dire.

Challenges in Assessing HIV Prevalence in Transgender Individuals

While it is clear that, compared to the general population, prevalence of HIV infection is increased in the transgender community, it is not as well characterized as in other populations. This is due to logistical difficulties in studying this at-risk population. Cross-sectional population-based studies are severely limited because most national agencies do not collect gender identity information. Even when gender identity information is collected, there is risk of inaccuracy in the recording of the correct gender identity [2]. Due to this limitation, there is a reliance on convenience and snowball sampling to identify and study transgender populations, while acknowledging their inherent flaws. Sample sizes are typically small, resulting in insufficient power from which to make significant conclusions. Furthermore, researchers frequently target locations where transgender individuals are known to congregate. These locations include bars, clubs, and healthcare facilities that target sexual and gender minority populations. This may lead to sampling from a subgroup with a different level of risk than the general transgender population.

There are significant behavioral differences between transmen and transwomen that lead to different prevalence between these two populations. As such, they must be studied separately. In fact, the majority of research to date has been in transwomen, and only recently have there been studies focusing on the transmale population. This is likely due to the perception of transwomen's heightened risk of HIV acquisition due to sexual behaviors including number of partners and sexual practices similar to MSM. Recent, small studies show that HIV risk may also be elevated in certain groups of transmen who have sex with men, and additional studies are necessary to better characterize prevalence and risk factors in this group [3, 4].

HIV Prevalence in Trans-women

The majority of studies of prevalence in transwomen are limited to small geographic regions, mainly major urban areas such as Boston, Chicago, Los Angeles, San Francisco, and New York City, with a few additional studies at the state or regional level. Given the limited sample areas, the true burden of disease is likely underestimated. Based on a 2008 nationwide meta-analysis, the demonstrated prevalence of positive HIV testing in transwomen is 27.7%, while HIV positive status was self-reported by only 11.8% of transwomen [5]. The prevalence in this population is higher than the prevalence of HIV infection in MSM in the US, which was reported to be 15.35% (95% CI 14.82–15.98%) in 2010 [6].

In a more recent review, Poteat et al. published a broad range of self-reported HIV prevalence in transwomen of 2.0–29.9% [7]. They also found that laboratory-confirmed HIV prevalence was even higher in certain community samples in San Francisco and New York City, 35.0 and 40.1%, respectively. In a 2013 review, Baral et al. found that transwomen ages 15–49 were at significantly increased risk of HIV infection in both the US (OR = 34.21% (95% CI 31.22–37.48)) and worldwide (OR = 48.78% (95% CI 31.19–76.28)), as compared to the general population [8]. They also found a similar prevalence of 21.7% (95% CI 18.4–25.1) in the US population studied, while the worldwide prevalence was 19.1% (95% CI 17.4–20.7). While these results are startling, there are large variances when considering subpopulations, particularly by race and geographic region.

Outside of the areas already mentioned, the southeastern region of the United States has been greatly affected by HIV in both MSM and transfemale populations. Self-reported prevalence in this region is as high as 60% in locations such as Atlanta, GA [9]. In this study, the majority of participants (83.7%) were African-American with HIV prevalence as high as 63%. Even more concerning is that 40% of the participants were either not taking antiretroviral therapy or had poor adherence.

On a global scale, prevalence varies widely by region and, in some areas, by country. In sub-Saharan Africa, overall HIV prevalence in transwomen is approximately 25%. Higher prevalence is seen in various areas, for example, prevalence in

Lesotho is 59%, Gambia is 50%, and Senegal is 39% [10]. The transfemale population in many South American countries is also affected with HIV prevalence as high as 33.5% (95% CI 28.3–38.8) in Argentina and 33.1% (95% CI 26.7–39.4) in Brazil. Other South American countries are similarly though not quite as strongly affected [8]. Prevalence varies widely among countries in Asia. Reported HIV prevalence in transwomen in Pakistan is 2.2%, Cambodia is 5.9%, Thailand is 12.5%, Indonesia is 26.1%, and in India as high as 43.7% [8, 11]. While prevalence varies widely by both global region and individual country, it is clear that there is a significant burden of disease throughout the transfemale population worldwide.

HIV Prevalence in Trans-men

Owing to the assumption of lower risk and prevalence of HIV in transmen as compared to transwomen, there is a paucity of evidence on burden of disease and risk factors in this population. To date, research has focused predominantly on transwomen.

A study of transgender individuals in Ontario, Canada found elevated HIV risk factors in transmen who have sex with men. While there were no self-reported HIV diagnoses in this population, rates of testing in the prior year were only 18%. Rates of ever receiving an HIV test were less than 50%. The result of HIV testing was not recorded as part of the study, so true HIV prevalence was not calculated [12]. In the US, a study in Boston, MA identified a number of factors leading to increased HIV risk in the transmen who have sex with men including: having three or more sexual partners in the prior 6 months, condomless anal or vaginal sex with a cisgender male in the prior 6 months, and lifetime sexually transmitted infection (STI) diagnosis. In this study, the rate of HIV testing in the prior 6 months was only 40% [13]. Unfortunately, the result of HIV testing was not included in this study either. In a San Francisco, California-based study, HIV infection rates between transmen and transwomen receiving care in STI clinics from 2006 to 2009 were comparable at 10 and 11%, respectively [14]. A 2006–2010 study of HIV in transgender individuals in New York City, 6% of new diagnoses were among transmen [15].

These studies highlight the need for additional research to fully define the prevalence of HIV in the transmale population and develop risk-reduction strategies for this population.

Risk Factors for HIV Transmission

Transgender persons are at increased risk for acquisition of HIV infection owing to an intersection of various behavioral and biological factors. These factors include types of sexual activity, trading sex for money, shelter, drugs, higher rates of

incarceration, social and societal stigma, as well as higher rates of depression, drug use, and other factors.

The greatest risk factor for HIV transmission in transwomen is unprotected receptive anal intercourse [5]. From a purely virologic perspective, efficiency of HIV transmission is dependent on properties of the virus itself as well as the method of exposure. When considering sexual routes of transmission, receptive anal intercourse is the most efficient method of viral transmission with a significantly higher per act risk than receptive vaginal intercourse or insertive intercourse of any type [16]. Additionally, risk may be further increased by the presence of other STIs including chlamydia, gonorrhea, syphilis, and herpes simplex infection [17]. When considering risk of HIV transmission in receptive neovaginal intercourse, there is insufficient research to quantify risk.

From a behavioral standpoint, there are a variety of reasons why transwomen are more likely to participate in unprotected receptive anal intercourse. For some transwomen, there may be external pressure from a committed sex partner to engage in unprotected intercourse in order to maintain the relationship. Studies show that transwomen experience pressure to engage in unprotected intercourse for fear of being replaced with a cisgender partner [18]. For other individuals, participating in unprotected sex with men may provide affirmation of their chosen gender [19]. Some transwomen who engage in sex work are coerced into engaging in unprotected sex because clients may offer extra compensation for condomless sex acts. This extra money can be necessary to meet basic needs or to improve access to gender-affirming therapies (i.e., hormonal therapy) [20].

Because stigma and discrimination by employers make obtaining and/or keeping a job difficult for transwomen, sex work is common among these individuals. Rates of ever participating in sex work are as high as 75% in transwomen in Tijuana, Mexico [21], and 68% in black transwomen in Atlanta, GA [22]. When other sources of income are unavailable, transwomen may turn to sex work to meet their basic needs. In addition to leading to higher numbers of unprotected sex acts, sex work also leads to a higher number of sexual partners, which also increases risk for transmission of HIV and other STIs.

Increased HIV prevalence is independently tied to prevalence of other STIs. In a 2016 study in Cambodia, HIV prevalence was significantly greater for individuals with STIs in the prior 12 months. Risk was even greater in individuals who had a genital ulceration or sore at the same time, as compared to those who did not [11]. The reason for the increased prevalence is two-fold: the same behaviors that increase risk of STIs also increase the risk of HIV transmission, and active STIs independently increase the risk of HIV infection by increasing local inflammation and recruiting additional CD4 cells susceptible to HIV infection to the area [23].

Historically, incarceration has been considered a risk factor for HIV infection. The first case of AIDS in an incarcerated individual was reported in 1983, just 1 year after the first reports of AIDS in MSM [24]. High rates of HIV in prisoners are likely not related to HIV infection while incarcerated, but rather the concentration of substance abusers and sex workers who are imprisoned or pass through the prison system. A 1997 estimate put the percentage of the HIV positive population

of the US who passed through the prison system in that year at 20–26% [16]. Transgender individuals are at risk of incarceration given the high rates of substance use and sex work as previously described. In a 2012 cross-sectional study of transwomen in Chicago, IL and Los Angeles, CA, Brennan et al. demonstrate that incarceration was associated with increased risk of HIV infection in this population [25]. Using a convenience sample from the National Transgender Discrimination Survey, Reisner et al. found that 19.3% of transwomen in the sample had been incarcerated. They also showed that the risk of having ever been incarcerated was significantly higher in Black transwomen as compared to their Caucasian counterparts (ARR 3.26 (95% CI 2.24–4.75)) [26].

In the US, African-American race is associated with increased risk of HIV transmission, particularly in the southern states, an association that does not spare the transgender community. The high seroprevalence in this population increases the likelihood of exposure to the virus [4, 7]. In a San Francisco-based study, African-American race was the single largest risk factor for HIV infection (AOR 5.81 (95% CI 2.82–11.96)) [27]. In addition to high seroprevalence in this population, African-American race is associated with added discrimination that leads to accumulation of HIV risk factors already discussed, including: unemployment, incarceration, sex work, and abuse [22]. This is particularly important when considered within the context of prevalence of racial groups within the transgender community. African-American comprise 16% of the transgender population as compared to 13% of the general US population. While the majority of the transgender population is composed of Non-Hispanic Whites (55%), African-American are overrepresented within the transgender community as compared to the general population. This serves to further highlight the increased burden of HIV disease in the African-American minority [28].

Social and mental disorders are common among transgender individuals and lead to increased HIV risk. A 2017 study in sub-Saharan Africa found an elevated odds ratio (OR 1.48 (95% CI 1.21–1.81)) for HIV infection in transwomen and cis-MSM who also had positive depression screens [10]. Poteat et al. identified mental health as one of the most common syndemic factors with HIV infection [7]. In 2016, a study of transwomen in Chicago, IL and Boston, MA showed that 41.5% of participants had one or more mental health or substance dependence disorder. The most common diagnoses identified were major depressive episode, suicidality, generalized anxiety disorder, posttraumatic stress disorder, alcohol dependence, and non-alcohol psychoactive substance use [29].

Substance use is a well-described risk factor for HIV infection, especially IV drug use through sharing of needles [30]. While education and needle exchange programs have decreased the frequency of transmission via this modality, there continue to be new outbreaks of HIV in this subpopulation in different localities throughout the world [31]. This increased risk translates also to transgender individuals. In a study of Black and Latina transwomen in Chicago, IL, Houston, TX and Los Angeles County, CA, as many as 16% reported ever injecting illicit drugs in their lifetime [32]. In a San Francisco study, nonhormonal injection drug use was associated with increased adjusted odds ratio of HIV infection (AOR 2.69 (95% CI

1.56–4.62)) [27]. When considering hormone injection, there is conflicting evidence of HIV transmission risk. A Cambodian study showed increased risk of HIV infection in transwomen who injected gender-affirming hormones (AOR 4.4 (95% CI 1.1–17.3)) [11], but significant increased risk was not seen in the group of transwomen in San Francisco mentioned previously (AOR 1.67 (95% CI 0.94–2.97)). The risk from sharing needles for hormone injection is an area that deserves further scrutiny.

It should now be clear that the prevalence of HIV in transwomen is high, owing to a complex risk profile for HIV infection. Risk factors include sexual behaviors especially condomless anal intercourse, any psychoactive substance use, injection drug use, Black/African-American race, employment status, sex work, mental health, and social and societal stigma. These disparities will be described in greater detail later on. Furthermore, there is lack of recognition of elevated risk in transmen who have sex with men. Both transmen and transwomen should be rigorously screened for HIV and other STIs, and be targeted for appropriate education, prevention, and care.

HIV-Related Health Disparities in Transgender People

We established the high prevalence of HIV infection among adult transgender persons and outlined the contributing factors leading to this high prevalence in Sect. 14.1. Despite the high HIV prevalence, transgender persons are less likely to exercise prevention modalities for HIV or know their HIV status. Those living with HIV also experience poorer health outcomes across the HIV care continuum. Studies have shown that HIV positive transgender persons are less likely to be linked to care, retained in care, receive and adhere to antiretroviral therapy (ART) or achieve sustainable HIV viral suppression compared to HIV positive cisgender persons [33–36].

There are multiple factors contributing to health disparities in transgender persons, many of which are discussed in detail in earlier chapters of this book. Health disparities among transgender persons are important and preventable contributors to higher rates of HIV infection, and are major contributing factors to relatively poor outcomes in those who become infected with HIV.

What follows is a non-exhaustive list of factors contributing to HIV-related health disparities among transgender persons. These factors act together, many simultaneously occurring, or syndemic, to contribute to the higher rate of HIV infection and to potentially lead to poorer health outcomes associated with HIV infection in transgender persons [36–38]. We have grouped these factors into three categories: socioeconomic factors, psychosocial and behavioral factors, and social and healthcare-related stigmatization. It is important to acknowledge the interplay between these categories and how one feeds on the other to place the transgender person in a disadvantageous and marginalized group with major impacts on health including HIV-related health and outcomes.

Socio-Economic Factors

Poverty and economic inequality are contributing factors in the HIV epidemic [39]. Poverty leads to development of socially marginalized communities and HIV hot spots and increases the individual's chance of risky behavior [39, 40]. **Minimal legal employment opportunities** and poverty have both been identified as risk factors for sexually transmitted infections including HIV among the transgender population [39, 41, 42]. In a survey conducted in Massachusetts between 2007 and 2009, it was found that the transgender adult respondents were 3.2 times more likely to be unemployed and 3.1 times more likely to be living at less than or equal to 100% poverty than non-transgender adults [43]. Another survey submitted as a report in 2013 by Human Rights Campaign (HRC) Deputy Communications Director called *A Broken Bargain: Discrimination, Fewer Benefits, and More Taxes for LGBT Workers* concluded that the rate of unemployment in the transgender workers surveyed was twice as much as cisgender worker, it was also discovered that many who worked were underemployed and were more likely to have an annual household income under $10,000. Poverty and minimal legal employment opportunities contribute to the high prevalence of **unstable housing** in transgender persons as well [41, 44, 45]. Transwomen who have unstable housing or are homeless have higher rates of substance use and risky sexual behaviors, especially unprotected serodiscordant receptive anal intercourse [41]. Housing instability also contributes to poor HIV-related health outcomes [44]. In an attempt to escape poverty and unstable housing, many transwomen engage in HIV risk behaviors, including **sex work** [41]. Economic inequality and discrimination specific to transgender people are important contributing factors to transgender women's engagement in sex work to earn money [27, 41]. Another noteworthy socioeconomic factor impacting HIV prevalence and outcomes in transgender minorities—especially Latinas in United States—is immigration **documentation status**. Legal authorization to live in the US is not only a barrier for HIV testing and treatment but also a key risk factor for HIV infection [46]. In a study of transgender Latinas between 18- and 29-years-old, it was found that "obtaining legal documentation to live in the United States can protect against HIV infection risk among undocumented transgender Latinas by affirming their identity, making it easier to avoid controlling sexual partners, and providing access to greater employment opportunities and public services" [46].

Psychosocial and Behavioral Factors

Minority stress theory suggests that sexual minorities, including transgender persons, suffer increased prevalence of more health problems due to social stressors, most notably due to the impact of stigma on various aspects of life [47]. The collective impact of stressors can be a potential contributing factor to higher rates of

mental illness in this population [37, 47]. Multiple studies have shown that transgender persons have higher risks of depression and anxiety, and between 26.0 and 43.0% attempt suicide in their lifetime [27, 48, 49]. There is a syndemic relationship between mental health and other health outcomes including HIV infection. Studies have shown a higher rate of HIV prevalence in individuals receiving mental health services in the US [37, 50]. According to Substance Abuse and Mental Health Services Administration (SAMHSA) in 2014, the rate of **substance use disorders** in general population was 8.4%. The rate of substance use disorders in transgender persons is much higher, with estimates between 25 and 28% [51, 52]. The National Survey on Drug Use and Health (NSDUH) in 2015 reported that sexual minority adults including transgender persons were more likely to have used alcohol, illicit drugs, marijuana, or misused pain relievers in the past year [53]. The relationship between substance use disorder and HIV infection is well established. Illicit drug use can increase risk of HIV infection via the sharing of needles or other paraphernalia. Illicit drug use also increases risky sexual behavior due to impaired judgment. There are multiple common links between mental health, substance abuse, and HIV infection and the co-occurrence of this triad is so common that many agencies and healthcare centers focus on comprehensive services located in one setting to address all three components in an attempt to improve linkage, retention, and health outcomes associated with these challenging illnesses. Another psychosocial and behavioral factor that impacts the transgender person's approach to both testing and treatment of HIV is **mistrust of social services and healthcare providers**. This has been shown to be due to either conspiracy beliefs [37, 54], in response to transphobia within the healthcare system, or in some cases due to gender insensitivity and forced care [55].

Social and Healthcare-Related Stigmatization and Transphobia

Transphobia in healthcare settings has a major impact on the transgender person's medical experience and leads to decreased access to HIV-related prevention and care [56, 57]. Transphobia is exaggerated in HIV-infected transgender persons due to collection of stigmatized social identities, namely, HIV status and gender identity [5, 57]. Transgender women of color are most affected by this stigmatization [5]. Transphobia in the delivery of social and healthcare services may, in extreme cases, manifest as denial of services by providers [46, 58–60]. HIV-related stigma also impacts organization of care as evidenced by low levels of engagement of transgender persons in healthcare research [57, 61]. Figure 13.1 is adopted from an article on the topic by Dr. Ashley Lacombe-Duncan who argues that the intersectional analysis of the depicted factors helps to understand and improve this experience of social exclusion [57]. **Societal stigma** and **internalized stigma** have also been shown as factors associated with HIV vulnerability and lower

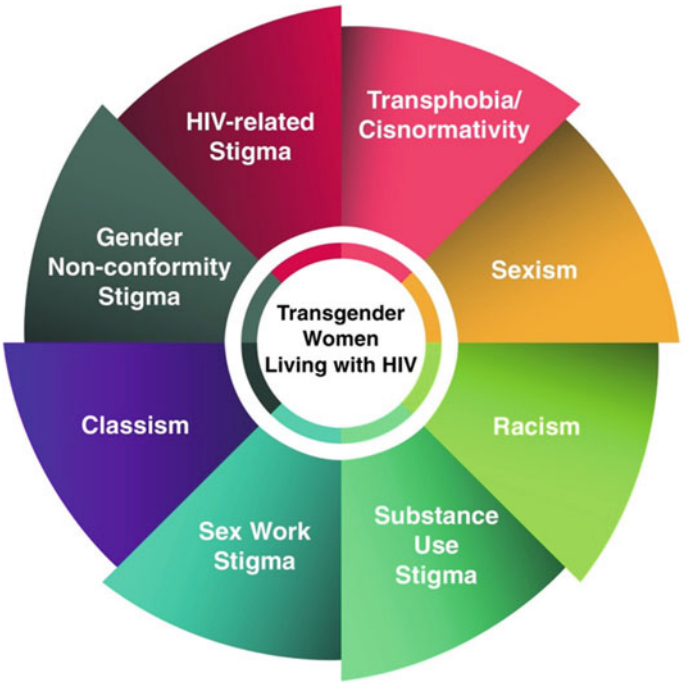


Fig. 13.1 Intersecting stigmas influencing access to HIV-related health care for transgender women—adapted from Lacombe-Duncan perspective published [57]

engagement and retention rates in HIV-related care [41, 62]. Adequate **social and tangible support** is an important factor contributing to effective and enduring engagement in HIV care as well [37, 63]. Tangible support is defined as "having persons available to help out and offer practical assistance in times of need" [37], and has shown to impact linkage and adherence in HIV-infected individuals [63, 64]. Studies show that compared to cisgender men and women, transwomen have the lowest degree of tangible social support [37, 63]. **Family-based stigma and rejection** seem to be important contributors to the reduced support system of transgender persons and contributes significantly to rates of homelessness, substance use, depression, and suicide attempt in this population [65]. In a secondary analysis of the 2015 data from the National Transgender Discrimination Survey of 3458 individuals who self-identified as transgender or gender nonconforming, health risks by reported family support were examined. Odds of drug and alcohol use to cope with transgender-related discrimination was significantly increased with increasing level of family rejection even after controlling for age, race, and other socioeconomic factors [65]. Suicide attempts were reported in 42.3% of the sample [65]. The researchers concluded that "Family rejection related to gender identity is an understudied interpersonal stressor that may negatively affect health outcomes for transgender and gender nonconforming individuals" [65].

Summary

In conclusion, as listed above, there are multiple, interwoven, co-occurring factors that work together to create a perfect storm of HIV-related health disparities in transgender persons. The approach to prevent new HIV infections and to improve the health outcomes for those already infected is multifaceted. Any solution must include interventions to deal with socioeconomic disadvantages, such as addressing the housing insecurity [45] and implementing anti-discrimination laws to name a few. Psychosocial and behavioral factors should address resilience building and empowerment [57] as well as supporting and expanding healthcare systems that provide mental health, substance use, and HIV services in a transgender friendly environment, with providers that are trained to provide culturally sensitive, unbiased care to this population in a comprehensive manner.

Special Programs of National Significance (SPNS) in transgender care by the Health Resources and Services Administration (HRSA) in the United States is an example of a multifaceted approach implemented and studied to improve the HIV-related health outcomes. HRSA funded this project from 2012 to 2017. The funds supported multiple demonstration projects at different clinical sites to design, implement, and evaluate novel interventions to improve HIV care outcomes in transgender women of color, who, as pointed out before, are the most affected by the HIV epidemic in transgender community in both the US and internationally [8, 66]. The funded demonstration projects used different interventions including community outreach, transcompetency training, transcompetent HIV medical care, non-HIV trans-related healthcare services, social network engagement, and establishment of community advisory boards among others [66]. The interventions of this initiative addressed many of the barriers discussed above for the HIV-infected transgender community. The outcome results of this project may give us a road map toward better understanding and caring for transgender persons along the HIV care continuum from prevention strategies to effective, sustainable interventions toward HIV control in those infected.

Screening Transgender Persons for HIV and Other STIs

As discussed previously, many of the behaviors that increase the risk of HIV infection in transgender persons also increase the risk of sexually transmitted infections (STIs) such as multiple sexual partners, condomless intercourse, sex work, mental health, and substance abuse disorders. Data on STI prevalence in the transgender population are limited. There are a number of small studies in various countries that show elevated rates [67–71]. Although all transgender persons in the US can be affected, non-White transgender individuals carry a disproportionate burden of STIs [72].

Formal guidelines for STI testing in asymptomatic transgender persons are lacking. The CDC recommends testing based on anatomy and sexual behaviors as assessed by the clinician, but does not put forth any formal recommendations for routine screening for asymptomatic STIs in transgender persons [73]. The WHO does recommend routine screening for asymptomatic STIs in transwomen and transmen who have sex with men, although the strength of these recommendations vary depending on the organism being tested and the modality used [74].

As previously discussed, transwomen, transmen who have sex with men, and MSM tend to participate in similar sexual behaviors [5, 75, 76]. Given the similarities in risk between these groups, it is reasonable to apply STI screening guidelines based on sexual practices rather than identity. As such, at least yearly screening for asymptomatic STIs should be done as follows: syphilis, HIV in those who have had more than one partner since their most recent HIV test, urethral gonorrhea and chlamydia in those who have had insertive intercourse in the prior year, rectal gonorrhea and chlamydia in those who have had receptive anal intercourse in the prior year, and pharyngeal gonorrhea and chlamydia in those who have had receptive oral intercourse in the prior year [73]. This testing is recommended regardless of condom usage. In accordance with CDC guidelines, the preferred testing modality for urethral gonorrhea and chlamydia testing is by urine nucleic acid amplification test (NAAT). For pharyngeal and rectal testing, NAAT of swab specimens from pharynx and rectal area is the test of choice [77]. Those patients who have known exposures or present with symptoms consistent with an STI should also be tested. Additionally, it is recommended to test every 3–6 months in patients with increased risk, including those who have multiple sexual partners, or who have partners with multiple sexual partners [73].

Viral hepatitis can also be transmitted via sexual behaviors. The CDC recommends one-time screening for hepatitis B in all MSM, followed by vaccination if not immune. Those tested positive should be referred to a provider who is experienced in the treatment of hepatitis B. Due to the high risk of sexually transmitted hepatitis C infection in patients with HIV infection, screening is recommended in patients who are newly diagnosed with HIV, and in those with chronic HIV infection [78]. Cost-effective screening in asymptomatic HIV positive individuals relies on two screening methods. Liver function testing (LFT) is cost-effective and recommended at least every 6 months. In areas where prevalence of hepatitis C is greater than 1.25 cases/100 person-years, LFTs should be checked every 3 months. Both should be coupled with yearly hepatitis C antibody serologies in asymptomatic patients [79]. Screening is also recommended in patients who have ever used IV drugs as this is the predominant method of transmission [80]. To our knowledge there have been no studies to date of prevalence of viral hepatitis in transgender persons but given the similarities in risk in transwomen and transmen who have sex with men as compared to MSM, we recommend following the guidelines for MSM in these groups.

The most effective means of prevention of hepatitis A and hepatitis B is immunization. Immunization for hepatitis A is recommended for MSM, people who use IV drugs, and anyone with chronic liver disease in whom there is no

documentation of immunity. Hepatitis B vaccination is part of the recommended childhood vaccination schedule in the US since 1994. For those born prior to 1994, the recommendation for immunization is for high-risk populations including MSM, people who use IV drugs, and anyone with multiple sexual partners unless there is confirmed documentation of immunity. Again, given the similar risk profile in transwomen and transmen who have sex with men, we recommend immunization for hepatitis A and hepatitis B for both of these groups. Consideration for immunization should also be given for transmen who use IV drugs or have multiple sexual partners, regardless of whether or not they have sex with men [81].

In summary, while recommendations specific to transgender persons are minimal and evidence is severely limited, both worldwide and in the US, we believe that testing for HIV and other STIs remains a very important part of the primary care of transgender individuals. These groups are at high risk for acquisition of HIV and other STIs due to a high prevalence of risky sexual behaviors. All patients with signs and symptoms concerning for infection with HIV or STIs should be tested. In addition, screening for asymptomatic STIs in transwomen, transmen who have sex with men, and other transmen with identified risk factors should be performed at least yearly and more frequently in those with significantly increased risk. Screening and treatment of asymptomatic infection will lead to improvement in the health of this special population and lead to a decrease in transmission of these diseases.

HIV Prevention, Pre-exposure Prophylaxis, and Nonoccupational Post-exposure Prophylaxis in Transgender Persons

What is Pre-exposure Prophylaxis (PrEP)?

Traditionally, HIV prevention has focused on abstinence from sex, condom usage during sexual acts, needle exchange programs, and postexposure prophylaxis (PEP) following high risk exposures with antiretroviral medications, and more recently, treatment as prevention in those who are HIV infected as a means to decrease transmission. One of the newest developments in HIV prevention is the introduction of pre-exposure prophylaxis (PrEP). A co-formulation of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) in a fixed-dose combination pill that is taken once a day by individuals at high risk of HIV infection is currently the only United States Food and Drug Administration (FDA) drug approved for PrEP. It is intended to be used in conjunction with safer sexual practices. Studies of additional drugs and formulations are currently underway, and other options for PrEP may be available in the future [82].

TDF/FTC was approved by the FDA for PrEP in 2012 based on favorable data from two large, randomized, double-blind, placebo-controlled clinical trials:

Pre-exposure prophylaxis for HIV prevention (iPrEx) and antiretroviral prophylaxis for HIV prevention in heterosexual men and women (Partners PrEP Trial) [83]. The Centers for Disease Control and Prevention (CDC) quickly endorsed the use of PrEP but stipulated that it required consistent usage. They recommended usage as part of a larger package of preventative services including risk-reduction education, access to condoms, and interventions for prevention, early diagnosis, and treatment of other STIs [84]. The CDC did not publish formal guidelines for the usage of PrEP until 2014 [85]. Early adoption was slow, but education of providers and strategic advertising has increased the number of at-risk persons on PrEP, with the goal to decrease the number of new HIV infections.

Efficacy

Large, randomized, double-blind, placebo-controlled clinical trials have proven efficacy of PrEP in MSM and serodiscordant heterosexual couples [86, 87]. While efficacy was not studied specifically in the transgender population, transwomen were included in the iPrEx trial. A 2015 subgroup analysis of this group of transwomen showed that PrEP is efficacious in transwomen if they are adherent to the daily regimen. There were a total of 339 transwomen included in the iPrEx trial. In the modified intent-to-treat analysis, there were a total of 21 seroconversions in transwomen, 11 of which were in the treatment group. Of those 11 seroconversions, however, none had detectable drug levels in plasma or peripheral blood mononuclear cells at the time of their seroconversion. Incidence of HIV infection in transwomen was 0 (95% CI not calculable) if drug was detected, as compared to 4.9/100 PY (95% CI 0-0.8) if drug was not detected [88]. The overall results from the trial showed a relative risk reduction of 92% (95% CI 70–99; $p < 0.001$) in all study participants who had detectable drug levels [86].

While evidence shows that PrEP is highly efficacious, there are concerns that individuals on PrEP may become infected with a viral strain that is resistant to one or both of the antiretroviral drugs used in PrEP. To date, there are only two documented cases of patients—both MSM—with verified medication adherence becoming infected with a strain of HIV that is at least partially resistant to both of the antiviral agents in PrEP. In both of these cases, there is evidence that each patient became infected with HIV virus with transmitted resistance mutations against both TDF and FTC [89, 90].

Barriers to Use of PrEP in Transgender Persons

The most important barriers to widespread use of PrEP in high-risk transgender persons center around awareness of PrEP, access to PrEP-related services, and challenges with adherence due to factors described in the HIV-related disparities

section of this chapter. For example, fear of stigma in healthcare centers, mental illness, housing instability, distrust of healthcare services, and fear of interaction of PrEP with medications used for gender-affirming therapy [91].

While many of these disparities have been addressed previously, it is important to consider the interaction of PrEP with gender-affirming hormonal therapy. For transwomen, there is substantial concern about taking other medications that may interact with and decrease efficacy of their hormonal regimen. This may lead to a direct decrease in PrEP adherence. The subgroup analysis of transwomen in iPrEx showed a decreased likelihood to have detectable ARV drug levels in transwomen on hormones as compared to those not on hormonal therapy [88]. Furthermore, in the previously cited San Francisco survey transwomen expressed outright lack of interest in taking a PrEP regimen if it would interfere with hormonal therapy [91].

Although there are studies underway to evaluate the interactions of PrEP and gender-affirming hormonal therapy in transwomen, to date there have been no prospective studies of interactions between TDF/FTC and gender-affirming hormonal therapy in transwomen or transmen [92]. There have, however, been studies of TDF and FTC in combination with hormonal contraceptive therapy. While estrogens and progestins are extensively metabolized in the liver, TDF and FTC are prodrugs that are converted to their active forms intracellularly. They undergo minimal biotransformation via the CYP system and are primarily excreted unchanged in the urine. A 2009 study of TDF concurrently administered with norgestimate ethinyl estradiol showed no change in hormone levels while taking TDF [93]. A 2016 review of the pharmacology of PrEP in transwomen failed to identify any theoretical or experimental evidence of drug interactions between TDF/FTC and estradiol, progestins, or spironolactone; however, there is still ample room for prospective study in this area [94].

Who Should Receive PrEP?

To date, the study of PrEP has not focused on the transgender population leading to a lack of representation in the current CDC and World Health Organization (WHO) guidelines. While recognizing these limitations, it is still reasonable to extrapolate indications for use in transgender individuals based on the risk factors for HIV transmission that are shared among transwomen, MSM, and transmen who have sex with men.

The WHO recommends initiation of oral PrEP in all individuals with substantial risk of HIV infection, which they define as an incidence of greater than 3 per 100 person-years [95]. The CDC guideline is somewhat more narrow, and is based on provider assessment of risk factors for each patient in the context of HIV prevalence within their community or demographic [85]. As mentioned previously, this guideline does not specifically mention transgender persons, making it necessary for clinicians to extrapolate how to apply these guidelines to transgender persons without a large body of empiric evidence. It is reasonable to apply these guidelines

to transwomen and transmen who have sex with men with consideration of the specific HIV risk factors that we have discussed earlier in this chapter.

Based on the recommendations for MSM, we propose that PrEP should be used in transmen and transwomen without acute or chronic HIV infection, who are not in a monogamous partnership with a known HIV negative partner, who have had any male sexual partner in the past 6 months, and/or who have one or more significant risk factors, which include any condomless anal sex in the past 6 months, any vaginal sex with one or more partners of unknown HIV status who are at substantial risk of HIV infection (defined as illicit drug use or a bisexual male partner), any STI diagnosis within the past 6 months, any IV drug use with sharing of injection or drug preparation equipment in the past 6 months, been in a methadone, buprenorphine, or suboxone treatment program in the past 6 months, or in an ongoing relationship with an HIV positive partner. The CDC also recommends screening for increased risk based on use of alcohol and non-injection illicit substances (alcohol use before sexual activity, amyl nitrite, stimulants, etc.) which may affect sexual risk behaviors, although they do not formally recommend PrEP use based on these risk factors alone [85].

FDA drug labeling identifies one absolute contraindication for TDF/FTC use as PrEP: unknown or positive HIV-1 status. Additionally, because of renal clearance of the drugs, patients with a calculated creatinine clearance less than 60 mL/min should not be started on PrEP. Because TDF has been associated with bone mineral density loss, any pathologic fracture or risk factors for osteoporosis and bone loss should be considered relative contraindications to PrEP [96].

How to Appropriately Prescribe PrEP in Transgender Persons

The goal of PrEP is to reduce morbidity, mortality, and cost of HIV infection by decreasing acquisition of the disease. To this end, the CDC has recommended a number of subgoals: prescribing safe and effective medication regimens, educating patients on their regimen to maximize use, provide support with medication adherence, provide HIV risk reduction and prevention services to minimize HIV exposure, and monitor for HIV infection, medication toxicities, and risk behaviors [85].

At present, there are no formal guidelines for prescribing PrEP to transgender patients. The prescribing and care of transgender PrEP patients should be comparable to the care of cisgender PrEP patients, with modifications made based on the biologic sex of the patient, their individual risk factors, and special consideration to barriers and adherence as discussed previously.

For patients who are deemed to have elevated risk for HIV infection and who would benefit from PrEP use, there are a number of steps that must be taken to identify individuals who may be harmed from initiation of PrEP. First, counseling

on PrEP use and misuse should be given to clarify any misconceptions and to assess the likelihood of adherence with therapy. For transwomen and transmen on gender-affirming hormone therapy, concerns about possible interaction with PrEP drugs should be discussed [97]. Drug interactions between antiretroviral therapy and gender-affirming hormone therapy will be discussed in detail later in this chapter. After making the decision that PrEP would be appropriate and acceptable to a transgender patient, HIV testing should be performed and negative results confirmed prior to initiation of therapy. The CDC recommends a negative HIV test (preferably point of care fourth-generation antigen–antibody test) within 1 week before initiating therapy. Risk of recent HIV infection and possibility of acute HIV infection should also be assessed. Patients who have a recent potential exposure (e.g., condom breakage during sex with an HIV positive partner, condomless sex for money, injection drug use with shared equipment, etc.) may require more rigorous screening prior to initiation of PrEP, especially in the setting of nonspecific signs or symptoms of viral infection. In these patients, it is reasonable to repeat testing at a later date and/or consider performing HIV RNA testing to rule out acute HIV infection. Only after a negative HIV test has been confirmed should a 30-day prescription for TDF/FTC be provided [85, 98].

In addition to HIV testing, other baseline laboratory testing should be performed and confirmed prior to initiating therapy. Urinalysis and calculated creatinine clearance should be assessed to rule out chronic kidney disease that would make PrEP contraindicated. STI screening (gonorrhea, chlamydia, and syphilis) should be performed and infections treated given shared infection risk and increased risk of HIV transmission with active STI infection [17]. Hepatitis A, B (HBsAg, anti-HBs, anti-HBc IgG or total), and C serologies, and liver enzymes should be checked as there is risk of co-infection with these viruses. Chronic hepatitis B infection deserves special consideration as TDF and FTC are also effective against hepatitis B virus, and discontinuation of these medications in HIV-infected patients has resulted in reactivation of the disease. For those with positive hepatitis B antigen, quantitative HBV DNA should be tested and the patient should be referred to a clinician familiar with treatment of hepatitis B [99].

Following initiation of PrEP, patients should follow-up at 30 days for assessment of medication tolerability and adherence. Repeat renal function testing can be sent at this time in patients with borderline renal function at baseline. Risk-reduction counseling should also be reinforced at this visit, as well as any other patient concerns [98]. HIV testing is not necessary during this visit unless there is concern for acute HIV infection that was previously unrecognized. If all is well, a 60-day refill of PrEP can be given.

At the next follow-up, the patient should be assessed for signs and symptoms of acute HIV infection. Regardless of the presence of symptoms, HIV testing should be repeated. Again, medication tolerability and adherence should be assessed. Support should be given for medication adherence and risk-reduction behaviors [85, 98].

After the initial period, patients should return at least every 3 months for assessment of signs and symptoms of acute HIV infection and repeat HIV testing,

assessment of signs or symptoms of other STIs (gonorrhea, chlamydia, and syphilis) with testing as appropriate, assessment of medication tolerability and adherence, support with medication adherence and risk-reduction counseling, and refill of PrEP prescription. In addition, calculated creatinine clearance, urinalysis, and STI testing should be performed every 6 months. Finally, need to continue PrEP for HIV prevention should be reassessed at least once a year, but can be assessed at each visit [85, 98].

Prescribing PrEP at this point, where the only option is combination of Tenofovir and Emtricitabine, does not require comprehensive knowledge of HIV medicine and can be performed by any provider with a reasonable amount of education in PrEP prescribing practices. This is important because a study of barriers to PrEP acceptability in transwomen found that adding additional appointments and medical monitoring to an already busy schedule would decrease tolerability [91]. Transwomen reported greater willingness to take PrEP if it was included in their usual transgender care [97]. This bundling of trans-related services may not only increase the willingness to take PrEP, but also increase knowledge of and access to PrEP for transgender persons by offering it in a trans-friendly environment with gender-affirming policies and procedures [100].

Appropriate Discontinuation of PrEP

In patients on PrEP, there are several important indications for discontinuation of PrEP. These include new HIV infection, calculated creatinine clearance less than 50 mL/min while on PrEP, failure to comply with HIV testing requirements, and those no longer at risk for HIV infection [85].

PrEP should be immediately discontinued for any patient who tests positive for HIV infection while on PrEP. Supplemental testing should be sent in accordance with the CDC recommended HIV testing algorithm [101]. Assessment of interruptions in therapy or adherence should be performed and documented. Consultation with a clinician experienced in HIV care should be obtained for consideration of initiation of full antiretroviral treatment with at least three antiretroviral medications. Only if supplementary testing does not confirm infection should PrEP be resumed [102].

In patients who fail to comply with HIV testing requirements, who are poorly compliant with regular follow-up, or who have ongoing poor adherence with the PrEP medication regimen, clinicians should identify and discuss barriers and possible modifications that would improve compliance with care. The risk versus benefits of continuing PrEP in the setting of poor adherence should also be discussed. Consideration should be given to discontinuing PrEP if patients continue to have poor adherence with testing and medications despite attempts at barrier modification [85, 102].

Finally, patients who are no longer at risk of HIV infection can safely discontinue PrEP. However, the subpopulation of PrEP patients who are chronically

infected with hepatitis B deserves special consideration. Acute flares of hepatitis B due to reactivation have been triggered by discontinuation of TDF/FTC in patients infected with HIV. To date, there have been no reports of acute flares of hepatitis B in individuals without HIV infection who have discontinued PrEP. However, patients should be monitored by a clinician experienced in hepatitis B management so that prompt recognition and appropriate treatment can be initiated [85].

Nonoccupational Post-exposure Prophylaxis for HIV

It is possible, even likely, that transgender patients will approach their provider with concerns regarding known or possible sexual, injection drug use, or other nonoccupational exposure to HIV infection. While safe sexual practices, safe injection drug practices, and PrEP are the preferred methods of risk reduction for HIV acquisition, postexposure prophylaxis for HIV (PEP) is a viable option to reduce the risk of HIV infection in the appropriate setting.

Postexposure prophylaxis for HIV has been used for years but due to ethical considerations has never been studied in prospective randomized controlled clinical trials. PEP is divided into occupational and nonoccupational uses. Occupational PEP (oPEP) is defined as the practice of providing antiretroviral therapy (ART) to healthcare workers who sustain exposure to blood or body fluids from a known HIV-infected patient to reduce the risk of infection. Nonoccupational PEP (nPEP) is defined as the practice of providing ART after exposure to blood, genital secretions, and other body fluids that might contain HIV to reduce the likelihood of infection [103].

A 1997 case–control study of the use of single drug oPEP with the drug zidovudine represents the best efficacy data for the use of PEP. That study showed an 81% reduction in the odds of HIV transmission among healthcare workers with percutaneous exposure to HIV (95% CI = 48–97%) [104]. Formal 2005 CDC guidelines for the use of oPEP are available and should be referred to in the event of HIV exposure in the healthcare setting [105]. The quality of evidence for nPEP is poor and relies almost entirely on observational and case studies. Despite the limited data for use of nPEP, the CDC produced 2005 guidelines for its use and released an update in 2016, which is the basis of our discussion here [106].

Determining the appropriateness of use of nPEP is based primarily on three factors: demonstrated HIV negative status of the exposed individual, risk of HIV acquisition, and time since exposure. PEP is indicated only for HIV-uninfected people, and it is possible that the potentially exposed person may have undiagnosed HIV infection. As such, all potentially exposed individuals should be screened for HIV infection with a rapid third-generation Ab or fourth-generation Ag/Ab test within 1 hour if available. In the event that results of HIV testing are unavailable during the initial evaluation, it is reasonable to assume HIV negative status pending results of the test so as not to delay initiation of therapy. If results are subsequently positive for HIV infection, PEP should be discontinued [106]. Patients should then

be referred to an experienced HIV provider for initiation of ART. When screening for HIV during the initial evaluation, patient should also be screened for other STIs including gonorrhea, chlamydia, and syphilis, which should be treated if infection is present [107]. Other testing at the initial evaluation should include CBC, BUN, creatinine, LFTs, and pregnancy test if applicable.

For patients who are confirmed to be HIV negative—or those with pending results—it is important to assess the risk of HIV acquisition based on the type of exposure. Nonoccupational PEP is indicated for high risk exposures. High risk exposures are defined as exposure of vagina, rectum, eye, mouth, other mucosal membranes, non-intact skin, or percutaneous contact to blood, semen, vaginal secretions, rectal secretions, breast milk, or body fluid visibly contaminated with blood. Conversely, there is negligible risk of HIV transmission through exposure of the prior mentioned sites to urine, nasal secretions, saliva, sweat, or tears unless visibly contaminated with blood, and nPEP is not recommended for these low exposures [106]. Although not part of the CDC recommendations, the New York State Department of Health defines an intermediate risk exposure group and recommends case-by-case evaluation. This group is defined as oral–vaginal, oral–rectal, and both receptive and insertive penile–oral contact with or without ejaculation. nPEP is not necessary in this group unless additional risk factors are present, such as know high HIV viral load in the source patient, oral mucosa that is not intact, blood exposure, or presence of genital ulcerative disease or other STI. Patients can be safely counseled that nPEP is not necessary for exposures from kissing, oral–oral contact without mucosal damage, human bites without blood, exposure to solid bore needles, and mutual masturbation without skin breakdown or blood exposure [107].

Animal models demonstrate that efficacy of PEP is time dependent. PEP is less effective the longer the amount of time that has elapsed since exposure to HIV, and is unlikely to be effective if initiated more than 72 h following exposure [108]. For this reason, during the initial evaluation, it is important to verify a time line of potential exposure, and to counsel patients on the diminishing returns of therapy when significant time has passed since exposure.

Nonoccupational PEP can be initiated in individuals who are determined or assumed to be HIV negative pending test results, who have experienced a high risk exposure, and who have been exposed within the previous 72 h. For those in whom nPEP is indicated, counseling regarding medication side effects, duration of therapy, and importance of adherence should be provided. The preferred regimen for nPEP with a calculated creatinine clearance greater than 60 is a three-drug regimen containing fixed-dose combination TDF/FTC 300–200 mg with either raltegravir 400 mg twice a day or dolutegravir 50 mg once daily. For those patients with a calculated creatinine clearance less than 60, TDF/FTC can be replaced with zidovudine and lamivudine with doses adjusted based on creatinine clearance. Raltegravir and dolutegravir do not require adjustment for level of renal function. Duration of therapy with either regimen for nPEP is 28 days [106]. Regardless of whether or not nPEP is indicated, patients should be counseled on HIV

risk-reduction behaviors. They should also be referred to a provider experienced in HIV care for follow-up.

Nonoccupational PEP necessitates close follow-up for assessment of medication adherence and toxicities. Patients should be reevaluated in 3 days, either in person or by phone and then weekly while taking nPEP. Repeat serum liver enzymes, BUN, creatinine, and CBC should be checked at weeks 2 and 4. HIV testing should be repeated on week 4. If HIV testing remains negative at 4 weeks, patients can return at week 12 for final HIV testing [107]. If negative at week 4, it is reasonable to consider initiation of PrEP in patients who are eligible based on the previously described criteria. Patients who refuse PrEP or in whom PrEP is not indicated, can be discharged from care if week 12 HIV testing is negative.

Summary

In summary, PrEP is a safe, effective method of HIV prevention that has the potential to decrease the blight of HIV in at-risk transgender persons. While it has not been extensively studied in the trans-population, subgroup analysis from studies that included trans as part of other groups shows benefit in transwomen and transmen who have sex with men. Limited studies show that while knowledge of PrEP in the trans-population is low, when educated on its benefits there is significant interest as well as high acceptability. While further study of PrEP in the trans-population is warranted, incorporation into regular transgender care—including education on the lack of interaction between PrEP and gender-affirming hormone therapy—would likely increase acceptability of and adherence to the regimen by bypassing barriers to care in this unique population. For those patients not receiving PrEP who experience a known HIV exposure, nPEP is a viable option to reduce the risk of HIV acquisition.

Approach to New HIV Infection in Transgender Persons

Due to the high prevalence of HIV in the transgender population, it is important that clinicians who treat transgender persons be aware of the natural history of HIV and methods of diagnosis. It is also vital that clinicians are aware of appropriate counseling and linkage to care with an experienced HIV practitioner. Furthermore, clinicians should have a high suspicion for acute HIV infection for patients who present with history of risk behaviors or known exposure and symptoms of the acute retroviral syndrome.

Natural History and Methods of Diagnosis of HIV Infection

The natural history of HIV infection is inoculation followed by an acute retroviral syndrome that can be mild and disregarded by the recently infected person or severe enough to lead to seeking medical care in some. What follows if undiagnosed is a chronic, relatively asymptomatic period during which CD4+ T cells are depleted that finally culminates in symptomatic severe immunodeficiency. This final stage of infection is known as the acquired immune deficiency syndrome (AIDS). The estimated mean time of progression from infection to AIDS without treatment is approximately 11 years [109].

The natural history of the disease informs laboratory testing algorithms for HIV infection. Following infection, there is an "eclipse" period lasting approximately 7–10 days in which virus is undetectable in blood [110]. After this period, PCR for viral RNA becomes positive. At approximately 14 days there is sufficient circulating viral p24 antigen to be detected by currently available fourth-generation immunoassays. Detectable levels of antibodies to the virus appear only after 20–45 days [111]. The delay between infection and detectability is called the "window period," in which HIV antibody testing may be falsely negative.

The most recent recommendations from the CDC favor screening for HIV with a highly sensitive and specific fourth-generation immunoassay that tests for the presence of p24 antigen in addition to HIV-1/2 antibodies. It is also acceptable to use a third-generation HIV-1/2 antibody immunoassay if the fourth-generation test is not available; however, clinicians should be aware that there is a longer window period—up to 3 months—with this test owing to the lack of testing for the p24 antigen [112].

Patients may also present with signs and symptoms consistent with the acute retroviral syndrome. The symptoms are nonspecific, present in 50–90% of acutely infected individuals and may include one or more of the following: fever, malaise, lymphadenopathy, rash, headache, arthralgias, and myalgias. Atypical findings (encephalitis, nerve palsies, chest pain, acute renal insufficiency, pancytopenia, etc.) may also be present alone or as part of a syndrome [113]. Patients with high risk behaviors or known exposure, who present with any of these symptoms, should be suspected of acute HIV infection. In those suspected of acute HIV infection, testing with fourth-generation antigen/antibody testing should be performed promptly. A negative fourth-generation test in this setting should be followed by virologic testing for HIV RNA. Alternatively, it is reasonable to test with a third-generation antibody test with concurrent HIV RNA testing [112].

Following a positive result on a screening test, patients should be informed that they have a preliminary positive result, and confirmatory testing should be sent to a certified laboratory. Confirmatory testing consists of an HIV-1/2 differentiation immunoassay, Western blot, or indirect immunofluorescence assay. It is important to be aware that the fourth-generation antigen/antibody testing can be positive earlier than the confirmatory testing in some patients with acute infection. In the

setting of a positive antigen/antibody test and negative confirmatory test, HIV RNA testing should be sent to verify the presence or absence of HIV infection [112].

HIV Diagnosis Counseling in Transgender Persons

Though the stigma surrounding HIV-infected individuals has declined over time, there remains considerable stigma attached to HIV infection, because of the history of HIV and the AIDS crisis. In the case of transgender patients, this stigma is even stronger, and a new diagnosis often places significant stress on patients. Following a positive test result, all patients must be provided with the result of their test. They should also be provided with appropriate diagnosis counseling to address specific concerns regarding the diagnosis as well as emotional and social support. Patients should be counseled regarding the consequences of a positive test, what discrimination they may face, and what resources are available for support [114]. This is of particular importance in transgender persons because they already face significant stigma as a result of their gender identity [10]. In addition, they should be informed of the reportable nature of the disease and the need for both retrospective and prospective partner notifications.

In addition to psychosocial counseling, patients with a new diagnosis should be counseled regarding the medical implications of the diagnosis and their need for establishment of ongoing care. As previously described, there are numerous factors (fear of discrimination, lack of financial means, homelessness, etc.) that lead to decreased access to medical care or low willingness to use the healthcare system among the transgender population. Patients should be counseled on the chronic and treatable nature of HIV if they remain in care [112]. Patients should also be counseled on methods to prevent/reduce disease transmission, including abstinence and correct, consistent condom use. Finally, it is of the utmost importance to link newly diagnosed patients to a provider experienced in HIV care for initiation of antiretroviral therapy.

Partner Notification in Transgender Persons

Partner notification is vital to link potentially exposed or infected partners to testing resources and treatment to prevent further spread of infection. Patients should be encouraged to notify sexual partners regarding their diagnosis. This also applies to any partners with whom they have shared needles or injection equipment, either for injectable drugs or hormone injections [112, 114]. The area of partner notification for HIV in transgender persons has not been rigorously studied.

Theoretically, the fear of being replaced by an alternate partner, loss of housing, and the high prevalence of sex work that we have discussed in prior sections may create barriers to willingness to notify partners. A study of both transwomen and

MSM in Lima, Peru showed that only 52.5% of persons with either HIV or other STI infection would notify their partner. Likeliness to notify was higher in stable partners, but lower in casual and commercial partners. In qualitative analysis of the study, the examiners found that likeliness to notify partners of HIV infection was lower in all groups. The reported reasons were fears of interpersonal violence, social exclusion, and societal stigma [115]. This area is deserving of further study, given the high prevalence of HIV in this population.

We recommend encouraging patients to disclose their diagnosis with any sexual partners who may have been exposed. As part of that process, we recommend psychosocial assessment to determine if there are any barriers to or risks of partner notification for individual patients. Assessment should include screening for housing status, domestic abuse, sex work, and number of both stable and casual or commercial partners. Any identified barriers should also be intervened upon as necessary as they may also be associated with a decreased likelihood to enter into regular medical care. In the event that a patient is unwilling to notify their partner, information should be forwarded to a local partner notification service, if available, for confidential notification and linkage to testing. Furthermore, any partners who may have been exposed in the prior 72 h should be considered for postexposure prophylaxis [112]. Assessment of need for and providing nonoccupational post-exposure prophylaxis for HIV has been discussed previously in this chapter.

Referral to an Experienced HIV Provider

As previously stated, it is of paramount importance that patients newly diagnosed with HIV infection are referred to an experienced HIV provider. HIV medicine remains a quickly evolving field and the medications used in management are numerous, complex, and frequently have interactions with other medications. As such, it is outside the scope of a practitioner to manage HIV without appropriate credentials and expertise, or without the assistance of an experienced HIV provider. We recommend that clinicians find and maintain a network of local HIV providers and HIV resources.

There are numerous barriers to HIV care for transgender persons including number of medical appointments, negative healthcare experiences related to stigma, and concern for drug–drug interactions with a prioritization for gender-affirming therapies over HIV treatment, which will be described in upcoming sections. When possible, HIV care should be coupled with transgender care to circumvent these obstacles. Centers that are able should utilize an on-site HIV provider for co-management of HIV and transgender care [116]. While there are no prospective trials, an on-site comprehensive care approach may increase adherence with follow-up and treatment, while simultaneously increasing tolerability for patients. When it is not feasible to have an HIV provider on-site, it is important to use other methods to keep an open dialog between transgender persons and HIV providers to address patient concerns including any conflicts in treatment plans.

In the US, the American Academy of HIV Medicine credentials providers, and maintains a directory of certified HIV providers which can be found at https://providers.aahivm.org/referral-link-search?reload=timezone.

HIV Cascade of Care for Transgender

The HIV care continuum or cascade of care describes the number of people who are living with HIV at each stage of care, starting from all infected persons and moving toward those who are diagnosed, linked to care, and achieve viral suppression. This model for HIV care was developed in order to monitor the progress of testing, linkage, and treatment of HIV [117]. As of 2016, the World Health Organization (WHO) estimates that there are over 36.7 million individuals living with HIV worldwide, yet only 25.5 million are aware of their diagnosis. Of those who are diagnosed with HIV, only 19.5 million are on ART, with approximately 16 million achieving viral suppression [118]. In 2013, the WHO set a goal to diagnose 90% of HIV-infected persons, treat 90% of those diagnosed, and achieve viral suppression in 90% of those treated by the year 2020. This is referred to as "90-90-90." Figure 13.2 shows the estimated number of people at each level of HIV care continuum in 2016, with the area in red representing the remaining population needed to reach the 90-90-90 goal.

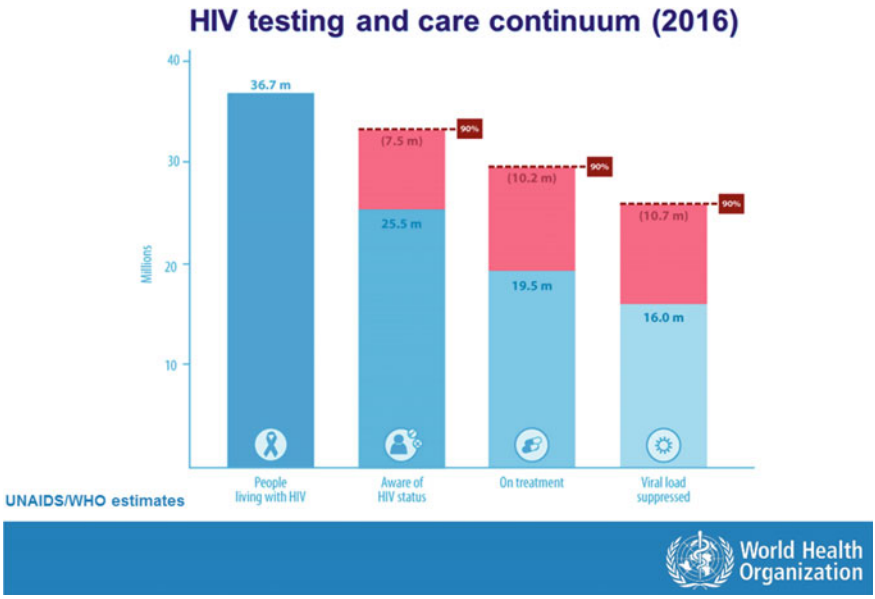
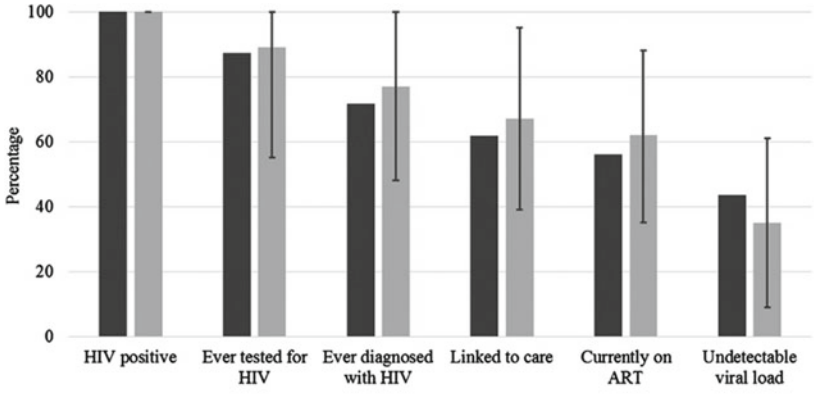


Fig. 13.2 The global estimate for the HIV cascade of care according to the World Health Organization [118]

While there is evidence that HIV greatly impacts the transgender community, the cascade of care for the transgender community is not clearly understood on a global level. The reason for this gap in knowledge is possibly due to lack of a systematic method to record and share information on gender identity in most health systems. For example, often times, transwomen are grouped together with MSM making it even more difficult to interpret the disaggregated data [119]. Thus, the care continuum among the transgender community may be underreported. To date, there have been small region-specific studies analyzing the HIV care continuum among transgender communities in Rio de Janeiro, Brazil and San Francisco, United States of America.

Jalil et al. studied a sample of 345 transwomen living in Rio de Janeiro, Brazil from 2015 to 2016. Of the 345 transwomen, 141 had HIV (40.9%), with 77.5% of HIV-infected individuals aware of their diagnosis. Approximately 62.2% of individuals were on antiretroviral therapy (ART), with only 35.4% achieving viral suppression (Fig. 13.3) [119]. A second study was conducted among 314 transwomen living in San Francisco in 2010, with a HIV prevalence of 39%. Of those who were HIV positive, 77% were linked to care, yet only 65% were on ART, of which 44% achieved viral suppression [45].

These studies, although scant, help fill in some of the gaps in understanding the true global cascade of care among the transgender community. These findings show evidence that there is a high prevalence of HIV in the transgender community, with modest use of ART, and lower than desired rates of virologic suppression. These findings emphasize the need to implement policies aimed at improving access to testing, linkage to care, and providing services to ensure retention in care among the transgender population [45, 118–120]. More studies are needed both globally and in



The HIV care continuum among HIV-positive transgender women in Rio de Janeiro, Brazil ($N = 141$). Crude percentages in dark grey, respondent-driven sampling weighted population estimates in light grey, error bars represent 95% confidence intervals for population estimates.

* $N = 138$ for denominator with undetectable viral load due to missing data.

Fig. 13.3 The HIV cascade of care among transwomen in Rio de Janeiro, Brazil, as adopted from Jalil et al. [119]

the United States to shed light on the epidemiologic characteristics of HIV infection in transgender people.

Choice of Antiretroviral Therapy in Transgender Persons

Goals of Therapy

The goals of antiretroviral therapy (ART) have evolved over the course of the past three decades. In 1987, the United States Food and Drug Administration (FDA) approved the first antiretroviral drug, zidovudine (AZT), a nucleoside reverse-transcriptase inhibitor (NRTI). The use of one medication, however, was not effective at maintaining viral suppression and led to resistance [121]. Over the years that followed, more medications were approved by the FDA, with the introduction of protease inhibitors (PIs) in 1995. By 1997, effective combination therapy to achieve sustained virologic suppression with NRTIs and PIs became the standard of care [122–124]. To date, there are now over 30 drugs approved for use in HIV treatment [125].

Over the decades since the availability of effective antiretroviral therapies, the pendulum has moved frequently on the appropriate timing for the initiation of therapy. Previously, CD4-guided treatment was the standard of care for the initiation of therapy, based on CD4 counts of 200 or 350 [126, 127]. Currently, the most updated recommendation is treatment for all HIV-infected individuals, regardless of CD4 count. This recommendation is based on two major studies, the Strategic Timing of Antiretroviral Therapy (START) as well as the Strategies for Management of Antiretroviral Therapy (SMART). In the START trial, a multicontinental study, 4685 HIV positive adults with a CD4 count >500 were randomized to start therapy immediately or to defer until CD4 count <350. The primary endpoints were AIDS-related events, non-AIDS-related events, or death from any cause. The primary endpoints occurred in 42 individuals in the immediate imitations group, in contrast to 96 patients in the deferred-initiation group, with a hazard ratio of 0.43. The conclusion of this study was that the initiation of ART regardless of CD4 count provided a net benefit as compared to deferring treatment to a certain CD4 count [128].

Antiretroviral therapy has revolutionized the care of all HIV-infected individuals, with the main goal of suppressing HIV RNA to undetectable levels in order to enhance the immune function of infected individuals and prevent the clinical progression of HIV disease [129]. By suppressing viral load and increasing CD4 count, ART decreases the morbidity and mortality associated with HIV, as well as decreases the risk of transmission of HIV [130]. In addition to reducing opportunistic infections, the SMART trial proved that ART decreases the incidence of death secondary to HIV-related comorbid conditions [131]. In the SMART trial, 5472 participants were randomly assigned to receive ART regardless of CD4 count

or to defer therapy until CD4 count was <250. This study concluded that immediate ART decreased the risk of opportunistic disease, and death from any cause including cardiovascular, renal, and hepatic disease. Further studies have also shown that the introduction of ART has also reduced the incidence of infection-related cancers, such as Kaposi sarcoma and lymphoma [128, 132]. There have also been studies that have shown that ART decreases the risk of non-AIDS defining malignancies, such as liver, breast, colorectal, and lung cancer [133].

Multiple clinical studies have made evident these life-sustaining goals of ART. Walensky et al. examined how treatment has influenced survival benefits. Through the use of national surveillance data, efficacy data, and probability models, it was concluded that as of 2006 ART has saved at least 3 million years of life in the United States [134]. In 2010, the HIV Cohorts Analyzed Using Structural Approaches to Longitudinal data (HIV-CASUAL) Collaboration Study included 62,760 HIV-infected individuals from five European countries [135]. During the follow-up period of 3 years, there were approximately 2039 deaths. When comparing individuals on therapy to those who were not, it was demonstrated that ART halved the mortality rate of HIV positive patients [135].

Based on these landmark studies, ART is recommended for all individuals living with HIV, regardless of gender identity, sexual orientation, age, and race. These life-sustaining goals are universal and apply to transgender persons as well.

Treatment as Prevention

In addition to improving the health of infected individuals, another major benefit of ART is that it plays a major role in the prevention of HIV transmission. The lower the concentration of the HIV virus in an individual's blood and genital secretions, the decreased is the likelihood of transmission to others, including sexual partners, intravenous (IV) drug users sharing needles, and mother to child transmission during pregnancy and breastfeeding [136].

The results from the 2011 HIV Prevention Trials Network (HPTN052) confirmed the notion that treatment can be used to prevent transmission of HIV. This study was conducted in nine countries and included 1763 discordant couples, in which one partner was HIV positive and the other partner was seronegative. A large majority of the individuals in the study were heterosexual, with CD4 counts ranging from 350 to 550. The partners who were HIV positive were randomly assigned to receive ART immediately or to wait until the CD4 count declined to 250. The final analysis revealed 39 cases of HIV transmission, with 28 cases being linked to the infected partner, with only one occurring in the early-therapy group. This study provided evidence that early initiation of ART reduced the risk of transmission to seronegative partner by 96% [137]. This landmark study promoted the universal importance of treatment as a means of prevention.

There have, however, been very limited studies that have analyzed the effect of treatment as a means of HIV prevention in the transgender community. Historically,

it has been difficult to engage the transgender community in clinical trials and research, due to barriers we have previously described [138]. More studies are needed in order to better target transgender-specific interventions in the goal of treatment as prevention.

Preferred ARV Regimen in Transgender Persons

The choice of antiretroviral therapy for transgender individuals does not differ from non-transgender individuals, as long as consideration is given to drug–drug interaction for those concomitantly on hormone or other gender-affirming therapy. Below, we discuss first-line recommendations for preferred therapy and later discuss considerations regarding hormone therapy.

The HIV life cycle can be categorized into seven separate steps: (1) binding, (2) fusion, (3) reverse transcription, (4) integration, (5) replication, transcription, and translation, (6) assembly, and (7) budding and maturation. There are currently six classes of antiviral medications, each with different mechanisms of action directed to inhibit the HIV life cycle. When drugs from different groups are combined, the HIV virus can be disrupted at multiple stages of replication, as seen in Fig. 13.4 [139].

Chemokine receptor inhibitors (CCR5) such as maraviroc inhibit the binding or attachment of the HIV virus to the cell. Fusion or entry inhibitors (EI), such as enfuvirtide (T-20) inhibit the fusion of the HIV envelope and CD4 membrane and thus prevent HIV from entering the cell. Nucleoside reverse-transcriptase inhibitors (NRTIs) act as competitive substrate inhibitors of reverse transcriptase, with examples including zidovudine (AZT), emtricitabine (FTC), lamivudine (3TC), and abacavir (ABC). Nucleotide reverse-transcriptase inhibitors also act as competitive inhibitors of reverse transcriptase, with tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) being the most commonly prescribed drugs. Non-nucleoside reverse-transcriptase inhibitors (NNRTIs) act as noncompetitive inhibitors of reverse transcriptase. This class of medication can be classified as first-generation drugs, which include nevirapine (NVP) and efavirenz (EFV), and second-generation drugs, which include etravirine (ETR) and rilpivirine (RPV) [140]. Integrase nuclear strand transfer inhibitors (INSTIs) inhibit the enzyme integrase, blocking the insertion of viral DNA into the DNA of the host CD4 cell. Examples include elvitegravir (EVG) and dolutegravir (DTG). Protease inhibitors (PIs) competitively inhibit the cleavage of the Gag-Pol polyproteins in HIV-infected cells, which inhibit the maturation and budding of the virus. Example of PIs includes darunavir (DRV) and atazanavir (ATV) [141].

Since the advent of AZT in 1987, there have been multiple studies to assess the most appropriate drug regimen to suppress HIV viral load. Clinical studies have proven that monotherapy is associated with high rates of virological failure, and is thus not recommended [121, 142]. In 1997, in a double-blinded study, 97 HIV-infected individuals were randomized to receive monotherapy, dual therapy, or

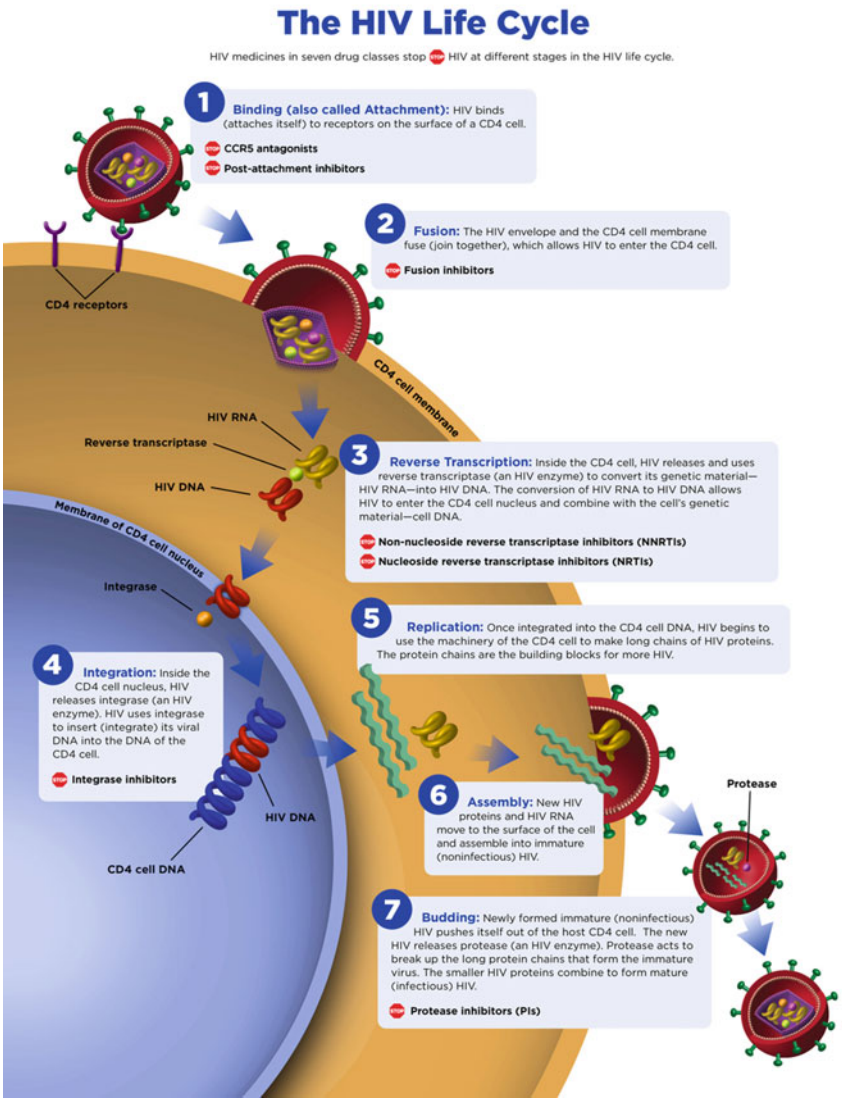


Fig. 13.4 The HIV life cycle and the targets for the six classes of drugs [139]

triple therapy. The three-drug group experienced the greatest decline in viral load over the longest period of time. Since this landmark study, the preferred recommendation for ART includes the combination of three or more ARV drugs from two classes [124]. As of 2016, the World Health Organization (WHO) recommends starting two NRTIs plus a NNRTI or an INSTI [143]. The 2016 International Antiviral Society-USA (IAS-USA) and the 2017 U.S Department of Health and

Human Services (USDHHS) guidelines recommend integrase-based regimens as initial therapy for most people with HIV. Under certain clinical situations, alternative regimens such as combinations of NRTIs with a boosted PI or a NNRTI may be more appropriate [144, 145].

The global recommendation for ART may vary depending on cost, availability of medications, and an individual's comorbidities [146]. The exact timing of medication initiation has also been debated throughout the years. As described earlier, according to all three guidelines published by US DDHS, IAS-USA, and WHO, presently it is recommended to start ART as soon as possible after diagnosis, regardless of CD4 count [147]. Acknowledging the guidelines and multiple studies that have proven that early initiation of ART improves short- and long-term outcomes and decreases morbidities and mortalities due to HIV infection, we need to point out that there are many other factors that may delay the initiation of ART like availability, affordability, some acute illnesses, and patient acceptance, to name a few.

Interactions with Hormonal Therapies

Both ART and hormone therapy (HT) can improve the quality of life for transgender persons, yet drug–drug interactions need to be assessed and taken into account before drugs are prescribed. Studies have reported HT use in anywhere from 27 to 93% of transwomen [146]. Studies have also shown that up to 40% of transwomen were not taking ART because of concerns regarding drug interactions with HT [33]. Thus, it is imperative for both providers and patients to discuss drug–drug interactions and any concerns and barriers patients may have to treatment.

Masculinizing hormone therapy consists of testosterone, which is available in oral (testosterone undecanoate), parenteral (testosterone enanthate or cypionate or undecanoate), and transdermal forms (gel or patch). Testosterone is metabolized in the liver by glucuronosyltransferases and sulfotransferases [148]. Testosterone has been used safely with ART with no reported drug interactions. This evidence is based on studies in which testosterone, prescribed for reasons such as hypogonadism and erectile dysfunction, was used concomitantly with ART without any evidence of drug interactions [149–151].

Feminizing hormone therapy consists of three classes of medications: estrogen, antiandrogens, and gonadotropin-releasing hormone (GnRH) agonists. Estrogen is available in oral (17 beta-estradiol valerate), transdermal (estradiol patch), and parenteral routes (estradiol valerate, estradiol cypionate). Antiandrogen, examples including spironolactone, finasteride, and cyproterone acetate, acts as competitive inhibitor of the androgen receptor and inhibit testicular steroidogenesis. GnRH agonists inhibit gonadotropin secretion and suppress testicular testosterone production, and include leuprolide and goserelin [152].

To date, we are not aware of any clinical studies examining the interaction of feminizing hormone therapy in transgender persons and antiretroviral therapy.

There have been many studies, however, that have analyzed the interactions of oral contraceptives containing estrogen and progesterone with ART. These studies can be extrapolated to understand the potential interactions between feminizing hormone therapy and ART. It is important to use caution when applying these studies to transgender women, who would have to take estrogen doses 3–4 times that of what is recommended for contraceptive purposes [153].

When discussing drug interactions, it is important to understand how each drug is metabolized. Estradiol is metabolized via hydroxylation into catechol estrogens through the cytochrome P450 enzymes and is a P-glycoprotein/ABCB1 substrate. In the liver, estradiol is metabolized into 2-hydroxyestradiol by CYP1A2, CYP3A4, and CYP2CP and also metabolized into estrone by CYP2CP, CYP2C19, and CYP2C8 via 17β-hydroxy dehydrogenation [154]. Thus, any medication that may affect the aforementioned cytochrome enzymes can result in a drug interaction.

Ritonavir and cobicistat are strong inhibitors of cytochrome P450 enzymes, especially CYP3A4, and due to this property are used rather commonly as a booster of other ART, mostly PIs and some integrase inhibitors. Due to the same CYP inhibitory properties, these boosters may increase the levels of estradiol when used concomitantly [146, 153]. On the other hand, some NNRTIs can induce the CYP3A4 system. Thus, the levels of estradiol, a CYP3A4 substrate, may be decreased when combined with these NNRTIs [153]. Thus, for the transgender person who is prescribed these medications as part of their ART, hormone levels need to be monitored and adjusted accordingly. Table 13.1 is adapted from a comprehensive literature review by Radix et al. published in 2016 and summarizes the interaction of most currently available ART with ethinyl estradiol which is the most commonly used estrogen in oral contraceptives.

NRTIs do not impact the cytochrome P450 system. They are converted intracellularly by hydrolysis through non-CYP enzymes. Thus, this class of medications is not expected to have any effect on the metabolism of hormonal therapy or hormone levels. Clinical studies have confirmed this and to date, no clinically significant drug interactions have been reported between currently used NRTIs and hormonal therapy [94]. Further studies have identified that zidovudine combined with contraceptive therapy has no effect on CD4 count and viral load [155]. No interactions have been noted between estradiol and the chemokine receptor inhibitors such as maraviroc [153]. INSTIs, such as raltegravir and dolutegravir, are also substrates of BCRP/ABCG2 enzymes. There have also been no described drug interactions with this class of medication and estradiol.

In some instances, estradiol may impact ART level with potential to cause virologic failure. There are some studies that point to decrease efficacy of amprenavir, unboosted fosamprenavir, and stavudine when used with ethinyl estradiol [146, 156]. These medications are not part of preferred ART regimen anymore and their use in the US and worldwide are limited. Considering the possible interaction outlined above, their concomitant use with feminizing hormones should be discouraged.

Conjugated equine estrogens are not recommended for feminizing hormone therapy because of the toxicities associated with its use, including thrombogenicity

Table 13.1 Interactions between antiretroviral therapy and ethinyl estradiol

Effect on ethinyl estradiol levels (AUC)	Antiretroviral	Change
Increase	Atazanavir [72]	AUC ↑ 48%
	Etravirine [89]	AUC ↑ 22%
	Fosamprenavir [72]	Cmin ↑ 32%
	Rilpivirine [72, 90]	AUC ↑ 0–14%, Cmax ↑ 17%
Decrease	Atazanavir/ritonavir [72, 84]	AUC ↓ 19%, Cmax ↓ 16% and Cmin ↓ 37%
	Darunavir/ritonavir [86]	AUC ↓ 44%, Cmin ↓ 62%, Cmax ↓ 32%
	Fosamprenavir/ritonavir [84]	AUC ↓ 37%, 28% ↓ Cmax and 34%
	Lopinavir/ritonavir [72, 87]	AUC ↓ 42%, Cmax ↓ 41% ↓ 58%
	Nevirapine [72, 88]	AUC ↓ 29%
	EVG/c/TDF/FTC [72]	AUC ↓ 25%, Cmin ↓ 44%
	Tipranavir/ritonavir [72]	AUC ↓ 37–48%
No effect	Dolutegravir [72, 97]	
	Efavirenz [94]	
	Maraviroc [91]	
	Raltegravir [72, 92]	
	Tenofovir [94]	
	Zidovudine [95]	
No data	Abacavir	
	Atazanavir/cobicistat	
	Darunavir/cobicistat	

Adapted from a literature review by Radix et al. JIAS 2016 [146]

and cardiovascular risk [157]. Yet, this class of medication has been used in the past for feminizing hormone therapy and there are cases in which it still may be used. Thus, understanding any drug interactions with ART is imperative. Conjugated equine estrogen is an inhibitor of CYP1A2 and a major substrate of CYP3A4. Conjugated estrogen can interact with NNRTIs, which are CYP3A4 inducers. Thus, NNRTIs may decrease the concentration of the conjugated estrogen. There are no reported drug interactions between this class of medications and boosted or non-boosted PIs, entry inhibitors, or NRTIs [158].

Antiandrogens, such as spironolactone, undergo extensive hepatic metabolism including deacetylation by esterases followed by glucuronidation [94]. There are no known drug interactions between antiandrogens and boosted or non-boosted PIs, NRTIs, NNRTIs, or INSTIs. The metabolism and transport effects of GnRH are unknown. GnRH agonists are known to be QTc-prolonging agents, and this therapy

needs to be monitored when combined with ritonavir and NNRTIs, another QTc-prolonging agent.

To summarize, it is important to note that antiretroviral therapy is not a contraindication for hormone therapy. Masculinizing hormone therapy can safely be combined with ART. Combination of some feminizing hormone therapy with some antiretroviral agents, however, requires close follow-up, as estradiol may interact with boosted PIs and NNRTIs. QTc needs to also be monitored when GnRH agonists are combined with boosted PIs and NNRTIs. It is encouraging to point out that to date there is no evidence of drug interaction between available unboosted integrase inhibitors (raltegravir, dolutegravir, and bictegravir) and gender-affirming medications. Considering that integrase-based regimens for treating HIV infection are currently preferred in most cases, it may be reasonable to use integrase-inhibitor-based therapy as a first choice, when possible, for transgender persons who are also on hormone therapy. Hormone therapy is best provided in the context of HIV care. Providers should use treatment with hormones as a means to discuss antiretroviral therapy and link patients to care [146].

Adherence

Importance of Adherence and Development of Resistance

Medication adherence is of utmost importance for viral suppression. Lack of medication adherence is directly linked to the development of drug resistance. Skipping medications allows the virus to multiply and increases the risk of viral mutations leading to drug resistance. Mutated virus may not be inhibited by ART, and will continue to replicate despite therapy. This in turn leads to treatment failure. Drug-resistant HIV can be spread to other people, and thus infected individuals may have drug resistance before even starting ART [159].

Multiple studies have shown that transgender women have lower adherence to medication compared to non-transgender males and non-transgender females [160]. Baguso et al. analyzed 295 individuals living with HIV in San Francisco. The study concluded that 72.4% of cisgender men and 23.1% of cisgender women achieved viral suppression, compared to only 4.5% of transgender women [161]. The conclusions from this study are also in agreement with Wiewel et al. who compared adherence among transgender persons compared with MSM in New York City from 2006 to 2011. Transgender women were likely to be linked to care, but less likely to adhere to medication and achieve viral suppression as compared to MSM [162].

There are many barriers to engage and retain HIV-infected transgender persons in care, which may explain the lower level of adherence to ART. These barriers and health disparities were discussed in earlier sections.

Conclusion

As we have shown throughout this chapter, prevalence of HIV is significantly increased in the transgender community as compared to both the general population and MSM. This is particularly true in transwomen and transmen who have sex with men. In addition, transgender persons suffer from the intersection of multiple socioeconomic, psychosocial, and behavioral disparities including transphobia in health care, which lead to poor performance at all levels of HIV cascade of care. It is important that providers who care for transgender patients be aware of the prevalence of HIV, risk factors for acquisition of HIV infection, and the barriers that these individuals face in obtaining and remaining in care. Additionally, providers must be aware of the options for HIV prevention, including the use of PrEP in high risk individuals. Finally, it is important to reiterate the greater acceptability of obtaining HIV care commensurately with transgender care, and the ability to improve outcomes when care is obtained together. With improved recognition of the barriers that transgender patients face, increased preventative services based on risk factors, and systematic improvement in the manner in which HIV and transgender care is delivered, it should be possible to reduce the prevalence of HIV in the transgender community and improve the HIV-related health outcomes of this at-risk population.

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