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Navigating Human Immunodeficiency Virus and Primary Care Concerns Specific to the Transgender and Gender-Nonbinary Population

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Human immunodeficiency virus (HIV) prevention and treatment remain critically important to outpatient care among transgender and gender-nonbinary individuals. Epidemiologically, trans men and trans women are significantly more likely to have HIV compared with all adults of reproductive age. Here, we provide an overview of unique primary care considerations affecting transgender and gender-nonbinary individuals, including screening and treatment of HIV and other sexually transmitted infections as well as cancer screening and fertility preservation options. We also seek to review current literature and clinical practice guidelines related to drug–drug interactions between antiretroviral therapy (ART) and gender-affirming hormonal therapy (GAHT). In short, integrase strand transfer inhibitor–based therapy is not expected to have significant drug interactions with most GAHT and is preferred in most transgender individuals, including those on GAHT. Clinicians should also remain aware of current GAHT regimens and consider tailoring ART and GAHT to reduce cardiovascular and other risk factors.

Keyword. gender-affirming hormone therapy; HIV; HIV antiretroviral therapy; transgender health.

CLINICAL VIGNETTE 1

A 17-year-old trans man (pronouns: they/them) asks for guidance regarding initiation of human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) or tenofovir alafenamide/emtricitabine (TAF/FTC). They were assigned female at birth. From age 14 to 16, they received leuprolide as a puberty blocker and they now receive weekly testosterone injections for gender-affirming hormonal therapy (GAHT). They are interested in fertility preservation. They became sexually active 1 year ago with 2 partners, who are both cisgender men. The patient prefers receptive anal sex and has engaged in condomless sexual activities. What are the considerations for HIV and sexually transmitted infection (STI) screening and prevention in this patient?

1. What is the prevalence of HIV among transgender and gender-nonbinary individuals in the United States (US)?

With improved recognition of transgender individuals and better insurance coverage of GAHT and surgery, providers are increasingly seeing individuals who identify as transgender or nonbinary [1, 2]. Medicare, for example, currently covers GAHT as part of Medicare Part D and does not exclude coverage for surgical gender-affirming therapy [3, 4].

Although population-level data remain sparse, recent surveys estimate 1.0 million to 1.4 million transgender individuals living in the US, or 0.4%–0.6% of the US population [5, 6]; estimates of people who identify as gender nonbinary remain uncertain [6, 7]. It is estimated that more than twice as many individuals identify as trans women compared with trans men [8].

In the US, the prevalence of HIV among all transgender individuals is estimated to be 9% compared with 0.4% of all US adults aged 15–49 years [9, 10]. HIV prevalence is higher among trans women than trans men. According to a 2019 systematic review and meta-analysis, the prevalence of HIV among trans women in the US is approximately 14%, compared with 3% of trans men [10]. Racial disparities in HIV prevalence are also apparent, with HIV prevalence ranging from 44% among Black trans women to 7% among White trans women. Among Hispanic trans women, the HIV prevalence is approximately 26% [10],

2. What are the recommendations for screening of HIV and other STIs among transgender and nonbinary individuals?

The 2021 Centers for Disease Control and Prevention (CDC) STI guidelines [1] recognize the diversity of gender-affirming surgical procedures and hormone use within the transgender community. The CDC therefore recommends that STI screening be based on overall risk assessment including patterns of sexual behaviors, STI symptoms, and current anatomy [11]. HIV screening should be offered to all transgender individuals at risk of infection. The CDC recommends HIV testing at least once for everyone aged 13–64 years. The frequency of repeat screening should be based on individual risk assessment. Providers should consider 3- to 6-month STI and HIV screening in all individuals engaged in high-risk activities including having multiple sexual partners, engaging in condomless sex, receptive anal intercourse, or illicit substance use [1].

Improved patient experiences and health outcomes may be promoted through an open and nonjudgmental clinical environment that facilitates disclosure of sexual orientation, gender identity, and sexual behaviors. Because transgender individuals are more likely to have a history of sexual trauma as well as prior maltreatment in medical environments [12], clinical practice guidelines recommend a trauma-informed approach that includes self-collection of specimens when possible for improved patient autonomy [13].

STI screening recommendations should consider what organs are present and if they are at risk for infection based on sexual practices. Trans women who have undergone vaginoplasty (creation of a neovagina) through either penile inversion or colovaginoplasty do not have a cervix, and therefore screening for cervical human papillomavirus (HPV) is inappropriate in this population [13]. However, inverted penile skin is susceptible to infection with syphilis, herpes simplex virus, and HPV; therefore, the presence of lesions or STI symptoms should prompt a physical examination and appropriate diagnostic testing. Use of an anoscope rather than a speculum may be more appropriate for pelvic examination postvaginoplasty [13]. For trans men who retain a cervix, the CDC recommends that genital STI testing include a cervical swab [1]. Providers should also be cognizant of difficulties with speculum examination in trans men due to narrowing of the introitus and vaginal atrophy from testosterone use, as well as possible history of sexual trauma, and self-taken vaginal swabs may be offered instead. Recommendations for management of confirmed STIs do not differ between transgender and non-transgender individuals [13].

For transgender individuals with HIV, STI screening should be conducted at least annually and include antibody tests for syphilis and hepatitis C (HCV), as well as nucleic acid amplification tests (NAAT) for gonorrhea, chlamydia, and trichomoniasis, as appropriate [1]. NAATs performed on self-collected vaginal, pharyngeal, and rectal swabs as well as urine specimens have similar sensitivities and specificities to provider-collected samples [13, 14]. All transgender individuals at risk of HIV should also be screened for hepatitis B (HBV) infection, which will help guide antiretroviral therapy (ART) selection [15–17]. Discontinuing lamivudine-, emtricitabine-, or tenofovir (TFV)–based regimens for treatment or prevention of HIV also increases the risk of hepatitis B flares and hepatic dysfunction. Those who are not immunized should commence a course of the HBV vaccine [15, 17].

3. Should TDF/FTC or TAF/FTC be recommended for HIV PrEP among high-risk transgender and/or nonbinary individuals?

The US Food and Drug Administration (FDA) approved the use of TDF/FTC for HIV PrEP in all high-risk individuals, including trans women, trans men, and nonbinary individuals regardless of GAHT use [18, 19]. TAF/FTC has only been approved for use in cisgender men and trans women due to concerns about reduced TAF tissue concentrations in natal vaginal tissue [20, 21]. However, a phase 1 randomized study comparing TAF/FTC and TDF/FTC co-formulations in healthy volunteers found that median TFV concentrations in vaginal tissue were approximately 6-fold higher with TAF/FTC compared with TDF/FTC [22]. A clinical trial to evaluate the safety and efficacy of TAF/FTC in HIV prevention in cisgender women is currently planned [23].

For trans women and nonbinary individuals on estrogen therapy, 2 small studies from the US and Thailand report that feminizing GAHT may lead to lower plasma and rectal tissue concentrations of tenofovir when taking TDF/FTC for PrEP [24, 25]. A 2019 pharmacokinetic study from the US also found a 32% reduction in plasma TFV and FTC trough concentrations among trans women taking PrEP and feminizing GAHT, compared to cisgender men. Increased renal clearance of TFV and FTC was proposed as a possible causal mechanism [26]. Finally, the multinational Preexposure Prophylaxis Initiative (iPrEx) study found that TDF/FTC was ineffective in preventing HIV among trans women based on an intention-to-treat analysis due to very low adherence overall. However, those trans women who had sufficient concentrations of TFV in their blood were not found to be at increased risk of acquiring HIV [27]. These findings highlight the importance of counseling patients on feminizing GAHT about daily PrEP adherence as well as avoidance of on-demand 2-1-1 dosing schedules. Providers can also reassure patients that concurrent use of GAHT and PrEP has not been found to impact serum estrogen concentrations [25, 26].

4. Do legal guardians need to consent for initiation of HIV PrEP in transgender youth (<18 years old)?

In 2018, the FDA officially approved TDF/FTC for HIV prevention in adolescents, lifting a major barrier to PrEP use. Initiation and continuation of HIV PrEP may or may not require guardian consent depending on local policies. Notably, many states have

laws authorizing testing and treatment of minors for STIs and, in many cases, HIV, without parental notice or consent. PrEP providers should become familiar with local statutes and regulations before initiating PrEP to minors without parental or guardian consent [28]. Providers should also be cognizant of inadvertent disclosure via parental insurance claims when discussing PrEP. Currently, all GAHT, including the use of gonadotropin-releasing hormone (GnRH) receptor agonists for puberty suppression, requires parental or legal guardian consent if a youth is under age 18 [29, 30].

CLINICAL VIGNETTE 2

A 50-year-old trans woman (pronouns: she/her) is referred for infectious disease consultation with a new diagnosis of HIV infection. She has been on GAHT with oral 17β-estradiol and spironolactone for 10 years and has not had gender-affirming surgery. Her past medical history is significant for primary hypertension and diabetes. What are the key considerations for selection of ART in the setting of concomitant GAHT? What are the considerations for healthcare maintenance, including cancer screening?

1. What are the recommendations for ART initiation in transgender or gender-nonbinary individuals with HIV?

The US Department of Health and Human Services (HHS) does not provide specific ART recommendations for transgender or nonbinary individuals, or patients on GAHT [31]. Current guidelines for selection of initial ART regimens for treatment-naive patients living with HIV prioritize an integrase strand transfer inhibitor (INSTI) in combination with 1 or 2 nucleoside reverse transcriptase inhibitors (NRTIs). Additional considerations include review of potential drug–drug interactions, particularly for individuals on GAHT, which may preclude usage of some ART drugs as outlined below. In some instances, GAHT can be associated with elevated cardiovascular risk factors and osteopenia; clinicians and patients on GAHT should consider ART regimens that will not increase the risk of these adverse effects [31].

2. What are the most common GAHT regimens?

Feminizing Hormone Therapy

Feminizing GAHT for trans women and nonbinary individuals includes a combination of estrogens (eg, oral/sublingual, transdermal, or parenteral) and antiandrogens (eg, spironolactone or finasteride) to promote female secondary sex characteristics including breast development, body fat redistribution, and decreased facial and body hair [32]. To date, no randomized controlled trials have compared various regimens. Current guidance is available from the seventh version of the *Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People* published by the World Professional Association for Transgender Health (WPATH) [33, 34].

Estrogen therapy is initiated at a low dose and titrated upward based on patient preference and clinical response. For individuals wishing to achieve serum estrogen concentrations comparable to those in premenopausal cisgender women, a target estradiol range of 100–200 pg/mL and a serum testosterone concentration <50 ng/dL is recommended [35]. Progesterone may also be used to help promote breast growth, improve mood, and increase libido [36] (Table 1).

Compared to oral formulations, transdermal estrogens provide more stable bioavailability, have reduced thrombotic risk by avoiding first-pass metabolism, and are preferred in patients with a history of unprovoked thrombosis or clotting disorders [37, 38]. However, estrogen patches are more expensive than oral estrogen and not covered by some insurance [32, 33].

In addition to estrogen, antiandrogens are often used as part of feminization therapy to lower testosterone concentrations and/or inhibit the effects of testosterone on target tissues; commonly utilized antiandrogens include spironolactone and 5-α reductase inhibitors (finasteride), used together or alone [32, 33, 39]. The potential adverse effects of these medication are described in Table 2 [40].

Masculinizing Hormone Therapy

Testosterone therapy is the mainstay of masculinizing therapy for trans men and nonbinary individuals and is commonly delivered topically (eg, patches and gels), subcutaneously, or intramuscularly. New oral and intranasal testosterone formulations

Table 1.   Estrogen and Progesterone Preparations in Feminizing Gender-Affirming Hormonal Therapy

Preparation	Route	Initial Dose	Maximum Dose	Comments
Estradiol	Oral/sublingual	2–4 mg/day	8 mg/day	Recommend BID dosing if >2 mg/day
Estradiol	Transdermal	100 µg (1 patch)	400 µg/day, twice weekly	Patches are normally replaced every 3–5 days
Estradiol valerate	IM	20 mg every 2 weeks	40 mg every 2 weeks	May divide into weekly injections
Estradiol cypionate	IM	2 mg every 2 weeks	5 mg every 2 weeks	May divide into weekly injections
Medroxyprogesterone acetate	Oral	2.5 mg nightly	10 mg nightly	May cause weight gain and irritability; increased CVD risk seen in postmenopausal cisgender women
Micronized progesterone	Oral	100 mg/day	100–200 mg/day	May have positive or negative effects on mood

Abbreviations: BID, twice daily; CVD, cardiovascular disease; IM, intramuscular.

Table 2. Antiandrogen Preparations in Feminizing Gender-Affirming Hormonal Therapy

Preparation	Route	Initial Dose	Maximum Dose	Comments
Spironolactone	Oral	50 mg twice daily	200 mg twice daily	May start at 25 mg daily based on medical history (eg, history of hyperkalemia, orthostasis)
Finasteride	Oral	1 mg daily	5 mg daily	Consider in individuals with male-pattern baldness
Dutasteride	Oral	0.5 g daily	0.5 mg daily	Blocks type 1 isoenzyme in pilosebaceous unit

are also commercially available. For trans men on testosterone therapy, experts recommend titrating dosages to maintain serum testosterone concentrations in the male physiologic range of 300–700 ng/dL, with dose adjustments based on desired masculinization and adverse effects [35].

Starting doses of subcutaneous or intramuscular testosterone cypionate or enanthate range from 20 to 50 mg weekly, titrated up until desired effects are obtained [41]. Some guidelines suggest a maximum dose of 200 mg every 2 weeks to minimize adverse cardiovascular and psychological effects [42, 43]. Recent studies show that subcutaneous testosterone is associated with less injection site pain compared to intramuscular injections with some added benefits, including less variability in serum concentrations (Table 3) [44, 45].

Puberty-Blocking Agents

GnRH receptor agonists suppress puberty in transgender youth and may lower lifetime rates of suicide and suicidality [46], increase time to explore gender identity, and prevent development of sex characteristics that are difficult or impossible to reverse (such as voice changes in trans women) [47, 48]. When puberty blockers are utilized, they are often started when the child reaches at least Tanner stage 2 or 3 [49].

GnRH receptor agonists (eg, leuprolide and histrelin) are synthetic analogues of natural GnRH and suppress pubertal changes in adolescents by downregulating GnRH receptors, thereby decreasing pituitary luteinizing hormone and follicle-stimulating hormone production as well as androgen/estradiol from the ovaries or testes. The typical starting dose is leuprolide 3.75 mg intramuscularly monthly, which can be titrated based on effect. Histrelin can also be delivered via time-release implants (Table

4) and is FDA approved for 12 months with annual replacement (but may last longer in some individuals) [50].

3. What drug–drug interactions exist between GAHT and HIV ART?

Feminizing Hormone Therapy

Concerns about drug–drug interactions among individuals on HIV ART and GAHT are common and may impact ART adherence. One study found that 40% of trans women with HIV did not take ART as prescribed due to such concerns [51]. A full list of potential drug–drug interactions involving GAHT and HIV ART is provided by the HHS and summarized below [31]. While interactions can be present, taking ART is not contraindicated among individuals on GAHT, nor vice versa.

INSTIs and NRTIs.

HHS guidelines currently recommend an INSTI-based regimen containing bictegravir (BIC) or dolutegravir (DTG) as first-line therapy for everyone, including individuals on GAHT [31]. INSTIs and NRTIs are not considered to have significant interactions with feminizing GAHT. Small studies suggest that TFV concentrations may decrease in trans women on GAHT who are taking TDF/FTC for treatment or prevention of HIV, but the clinical significance of this is unknown [25, 26, 52].

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs).

Some NNRTIs interact with estrogens as they are both metabolized by the cytochrome P450 (CYP450) system. Older

Table 3. Testosterone Preparations in Masculinizing Gender-Affirming Hormonal Therapy

Preparation	Route	Initial Dose	Maximum Dose	Comments
Testosterone cypionate	IM/SQ	50 mg weekly or 100 mg every 2 weeks	100 mg weekly or 200 mg every 2 weeks	SQ route preferred due to less variable serum concentrations. Suspended in cottonseed oil (for allergy consideration)
Testosterone enanthate	IM/SQ	50 mg weekly or 100 mg every 2 weeks	100 mg weekly or 200 mg every 2 weeks	SQ route preferred due to less variable serum concentrations. Suspended in sesame seed oil (for allergy consideration)
Testosterone intranasal (Natesto)	Intranasal	11 mg (2 pumps, 1 in each nostril), 3 times per day	11 mg, 3 times per day	Total of 6 pumps per day
Testosterone gel 1%	Topical	20 mg every morning	100 mg every morning	Comes in pump or packet form
Testosterone gel 1.62%	Topical	20.25 mg every morning	103.25 mg every morning	Comes in pump or packet form
Testosterone patch	Topical	1–2 mg every evening	8 mg every evening	Comes in 2-mg and 4-mg patches
Testosterone undecanoate (Jatenzo)	Oral	158 mg twice per day	396 mg twice per day	FDA approved in 2019

Abbreviations: FDA, Food and Drug Administration; IM, intramuscular; SQ, subcutaneous.

Table 4. Gonadotropin-Releasing Hormone Receptor Agonists Used in Puberty Suppression

Preparation	Route	Initial Dose	Maximum Dose	Comments
Leuprolide acetate	IM	3.75 mg monthly	11.25 mg monthly	3-month depots are also available
Histrelin acetate	SQ implant	65 µg/day for 12 months	65 µg/day for 12 months	Each implant contains 50 mg to last 1 year

Abbreviations: IM, intramuscular; SQ, subcutaneous.

NNRTIs, such as efavirenz (EFV), etravirine, and nevirapine, can lower plasma estrogen concentrations by inducing estrogen metabolism, thereby requiring higher doses of estradiol. Newer-generation NNRTIs such as doravirine and rilpivirine appear to have a more favorable drug interaction profile [53].

There is also evidence that estrogen can induce metabolism of some NNRTIs [54]. The Interaction between the use of Feminizing hormone therapy and Antiretroviral agents Concomitantly among Transgender women (iFACT) study measured the plasma concentrations of EFV and estradiol in 20 Thai trans women with newly diagnosed HIV initiating ART with TDF/FTC/EFV [52]. As expected, a significant 36% reduction was seen in estrogen concentrations in the presence of ART. However, EFV trough concentrations also dropped by 9% in the presence of GAHT, though the clinical significance of this was unknown [55].

Protease Inhibitors (PIs) and Pharmacologic Enhancers.

Pharmacologic enhancers (eg, ritonavir or cobicistat) and some PIs can also interact with estrogen through both induction and inhibition of the CYP450 system [31]. Serum estrogen concentrations should be monitored and GAHT doses adjusted based on desired concentrations and clinical effects when there is concomitant administration of NNRTIs, PIs, or pharmacologic enhancers [34].

Masculinizing Hormone Therapy

There are limited data on drug interactions between testosterone and ART. Available data suggest that serum testosterone concentrations may increase when given with pharmacologic enhancers. Serum testosterone concentrations should therefore be monitored frequently in patients on concomitant pharmacologic enhancers [31].

Puberty-Blocking Agents

Recent reviews suggest that drug interactions between GnRH receptor agonists and currently used ART are unlikely [56]. GnRH receptor agonists such as leuprolide are metabolized through intravascular and extravascular hydrolysis of the C-terminal amino acids, rather than hepatically, followed by excretion in the urine [57].

4. What are current guidelines for healthcare maintenance and cancer screening for transgender and nonbinary individuals?

Cancer Screening.

No standardized cancer screening recommendations exist for transgender or nonbinary individuals. Some clinical practice guidelines suggest that cancer screening should be based on whether the body part meets criteria for screening [58]. For trans women and nonbinary individuals on feminizing GAHT, breast cancer screening should be performed according to age-appropriate recommendations after the patient has been on feminizing GAHT for at least 5 years [59]. For women at average risk of breast cancer, this includes a mammogram every 2 years between the ages of 50 and 74, with younger ages recommended if a first-degree relative was affected by breast cancer [60]. Breast cancer screening in trans women on GAHT can be done via mammography, ultrasound, or magnetic resonance imaging (MRI). However, in patients who received free silicone for breast augmentation, contrast-enhanced breast MRI may be more appropriate [61]. There are currently no distinct guidelines for breast cancer screening for trans men; mammography is not routinely performed following gender-affirming bilateral mastectomy. However, breast cancer risk persists if breast tissue is left following contouring surgery. Trans men who do not have mastectomy should have routine mammogram screening based on recommendations for cisgender women [58].

Trans men and nonbinary persons who retain a cervix should undergo the same cervical cancer screening as cisgender women (every 3 years from ages 21 to 29, and every 3–5 years for those between 30 and 65 years). For those who are unable or unwilling to undergo a pelvic examination for cervical Papanicolaou (Pap) testing, an alternative may be vaginal self-swab testing for high-risk HPV [62]. Although routine screening for anal HPV and anal cancer has yet to be adopted nationally, some state and local guidelines do recommend annual anal Pap smears for all people living with HIV [63]. The CDC recommends the 9-valent HPV vaccination to all individuals as part of childhood immunization, and up to age 26 years as well as some adults aged 27–45 years who have not received the vaccine, after speaking with their provider about the possible benefits of vaccination [64].

For trans women and nonbinary individuals with a prostate, most experts recommend prostate cancer screening in accordance with guidelines for cisgender men. For trans women on estrogen therapy, the prostate volume is reduced and prostate-specific antigen concentrations will be lower [65]; therefore, some experts have recommended adjusting the upper limit of normal to 1.0 ng/mL in trans women receiving GAHT [66].

Cardiovascular Disease (CVD).

Cardiovascular disease is among the leading causes of death among transgender individuals on GAHT, with trans women having a 2- to 3-fold risk of CVD compared to all other groups [67, 68]. This includes higher rates of both myocardial infarction and stroke [67, 69]. In a study of nearly 1000 Dutch trans women on GAHT, cardiovascular mortality due to ischemic heart disease was found to be 64% higher among trans women compared to the age-adjusted general population. Use of high-dose oral ethinyl estradiol, which is no longer routinely used due to increased risk of venous thromboembolism (VTE), was independently associated with a 3-fold increase in cardiovascular death [67]. However, the study did not control for other independent CVD risk factors more prevalent among trans women, including tobacco use, making the relative contribution of GAHT unclear [67].

To reduce cardiovascular risk among trans women, the Endocrine Society recommends the use of oral, transdermal, or intramuscular 17β-estradiol for feminizing GAHT. Oral ethinyl estradiol and conjugated estrogens are not recommended due to elevated VTE risk [35]. The University of California, San Francisco *Transgender Care and Treatment Guidelines* also recommend that trans women with CVD risk factors or established CVD use the transdermal route of estrogen rather than oral estradiol to lower CVD risk [70]. For those individuals on progesterone, use of micronized progestin rather than medroxyprogesterone acetate has been shown to decrease the risk of thromboembolism, at least among postmenopausal cisgender women [71]. Among trans men, testosterone use has also been associated with an increased risk of erythrocytosis and the development of blood clots, particularly during the first year of GAHT [72]. For all individuals on GAHT, healthcare providers should carefully explain the risk of thromboembolic events and evaluate for the presence of other CVD risk factors, particularly smoking, to provide a holistic risk-reduction approach [73].

Bone Health.

Some experts recommend obtaining bone density evaluation in all transgender individuals beginning at age 65 years and considering bone density evaluation in trans women aged 50–64 years who have osteoporosis risk factors or who are postorchiectomy and have been off estrogen therapy for at least 5 years [34, 74]. Since TDF use has been associated with reductions in bone mineral density, TDF should be used with caution in transgender people with established osteoporosis or risk factors for it [75, 76].

5. Is fertility preservation an option for individuals on GAHT?

Although reproductive desire is high among transgender individuals, the use of fertility-preserving procedures is low. A 2018 survey of 409 Australian transgender individuals found that 33% of those who were not already parents hoped to have children [77]. Options for fertility preservation in transgender individuals are determined by pubertal status, underlying medical conditions, and stage of medical or surgical transition [3]. Cost is a common barrier for many transgender individuals interested in fertility preservation [78, 79].

In trans women, options for fertility preservation before GAHT include cryopreservation of semen or testicular tissue as well as embryo creation. For trans women who have already started GAHT, options include discontinuation of hormonal medication and sperm banking [3]. Although feminizing GAHT does reduce sperm counts, a small retrospective study suggests that mobile sperm counts may return to about half pretherapy concentrations following 3–6 months of GAHT discontinuation [80].

For trans men who have not yet begun GAHT, options for fertility preservation include oocyte, embryo, or ovarian tissue cryopreservation. For those who have already begun testosterone therapy but do not plan on having gender-affirming surgeries involving removal of the uterus or ovaries, oocyte or embryo cryopreservation (using partner or donor sperm) can also be performed following a 3- to 6-month period of testosterone cessation, though successful cases have been reported with <1 month of testosterone cessation [81, 82].

Pregnancy desires and contraception options should be discussed with all individuals. GAHT may not completely prevent ovulation or sperm production [32, 83]. Some gender-affirming surgeries, such as masculinizing chest surgery, do not impact fertility [84]. For those individuals at risk of pregnancy, appropriate contraception, the risk of teratogenicity associated with masculinizing GAHT, and potential adverse effects of certain ART regimens should also be discussed [85].

CONCLUSIONS

In this review, we explored the epidemiology of HIV among transgender individuals and considerations for STI and HIV screening and prevention. We provided an overview of unique primary care considerations affecting transgender and gender-nonbinary individuals including appropriate cancer screening. Among individuals with HIV, we summarized basic principles underlying GAHT usage and drug interactions with ART.

Returning to the first clinical vignette, this patient is a candidate for HIV PrEP based on high-risk sexual activities. TDF/FTC should be utilized, as TAF/FTC has not yet been approved for cisgender women or trans men; however, TAF/FTC could be considered if they only engage in receptive anal sex [21]. STI screening should be offered including HIV, syphilis, gonorrhea, chlamydia, trichomoniasis, HBV, and HCV tests. Whether this patient would need parental or guardian consent to start PrEP depends on where they live [86]. This patient would be a

candidate for oocyte or ovarian tissue cryopreservation if they have reached Tanner stage 2 or 3 and fertility preservation was desired.

In the second vignette, this 50-year-old trans woman with a new diagnosis of HIV should be started on a nonboosted INSTI-based regimen with NRTIs. Options may include BIC/TAF/FTC, DTG/TAF/FTC, or DTG/lamivudine [87]. Other NRTIs such as abacavir could be considered but may be avoided in individuals on GAHT due to increased CVD risk [88]. The patient should receive information about potential interactions between ART and GAHT to ensure informed decision making and improved adherence. Given the history of hypertension and diabetes, providers could consider transdermal estrogen to reduce CVD risk. Because this patient has been on estrogen therapy for 10 years, breast cancer screening with a mammogram every 2 years (as for cisgender women) should be offered, along with prostate cancer screening at 55 years of age after an informed discussion regarding the risks and benefits of prostate cancer screening [66]. Screening for anal cancer could be considered, though cervical cancer screening is not indicated in the absence of a cervix.

Gender-affirming approaches are critical to ensure holistic care for transgender and nonbinary individuals. This is particularly true for providers who offer HIV prevention and treatment services since HIV disproportionately impacts trans women and trans men, especially those of color. Providers should be aware of the indications and special considerations for STI and HIV screening and prevention, including HIV PrEP, among transgender patients. As GAHT becomes increasingly utilized, providers should also become familiar with common regimens, including interactions with HIV ART. Although concerns about drug interactions between ART and GAHT are common among transgender individuals, providers can reassure patients that there are few known interactions between GAHT and first-line HIV ART, particularly with the use of INSTI- and NRTI-based regimens.

Notes

Potential conflicts of interest. All authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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