

Women with HIV

(Last updated June 3, 2021; last reviewed June 3, 2021)

Key Considerations and Recommendations

- Antiretroviral therapy (ART) is recommended for all people living with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners without HIV (AI).
- When prescribing antiretroviral (ARV) drugs for women with HIV, clinicians should consider that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives (AII) and hormone replacement therapy (BIII). Consult Tables 21a, 21b, 21d, and 21e for detailed recommendations and a summary of available data when selecting ARV and hormone combination therapy (AIII).
- Clinicians should consider the possibility of weight gain in women when initiating or changing ART, because women in general and Black women in particular experience greater weight gain with ART over time than men (AI).
- A pregnancy test should be performed for women of childbearing potential before initiation of ART, and choice of ART should be guided by recommendations from the [Perinatal Guidelines](#) (AIII).
- When selecting or evaluating an ARV regimen for women with HIV of childbearing potential, consider the regimen's effectiveness, the woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and fetus (AII).
- During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy to reduce the risk of transmission to the fetus and newborn (AI).
- When selecting an ARV combination regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on use during pregnancy for each agent. The risks and benefits of ARV use during pregnancy should be discussed with all individuals of childbearing potential (AIII), and clinicians should consult the most current [Perinatal Guidelines](#) when designing a regimen (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

This section focuses on some unique clinical and therapeutic issues to consider and basic principles to follow when caring for cisgender women living with HIV. In this section, cisgender are defined as women who were assigned female at birth and who identify themselves as women. Some topics discussed in this section—such as contraception, drug-drug interactions between antiretroviral (ARV) drugs and hormonal therapy, and pregnancy—also apply to transgender men (men assigned female at birth), and individuals assigned female at birth who identify as nonbinary (gender identities that are not exclusively feminine or masculine) or gender fluid (gender identity is not fixed). See [Transgender People with HIV](#) for more information on the specific HIV care needs of these individuals. Clinicians who care for pregnant patients should consult the current [Perinatal Guidelines](#) for a more in-depth discussion on treating pregnant patients and guidance on managing these patients.

Sex Difference Considerations in Antiretroviral Therapy

In general, studies to date have not shown sex differences in virologic responses to antiretroviral therapy (ART).¹⁻⁵ However, there are limited data showing that pharmacokinetics (PKs) for some ARV drugs may differ between men and women, possibly because of variations in factors such as body weight, plasma volume, gastric emptying time, plasma protein levels, cytochrome P450 activity, drug transporter function, and excretion activity.⁶⁻⁹

Adverse Effects

Several studies with older ARV drugs have suggested that sex may influence the frequency, presentation, and severity of some ARV-related adverse events. Most notably, women are more likely to develop severe symptomatic hepatotoxicity with nevirapine^{10, 11} and lactic acidosis with prolonged use of zidovudine (ZDV), stavudine, and didanosine.¹²

Some studies have investigated how metabolic complications that are associated with the use of ARV drugs differ between women and men. At 96 weeks after initiation of ART, women with HIV were less likely to have decreases in limb fat but more likely to have decreases in bone mineral density (BMD) than men with HIV.^{13, 14} Women have an increased risk of osteopenia, osteoporosis, and fractures, particularly after menopause, and this risk is exacerbated by HIV and some ARV drugs.¹⁵⁻¹⁸ ARV regimens that contain tenofovir disoproxil fumarate (TDF), ritonavir-boosted protease inhibitors (PI/r), or both are associated with a significantly greater loss of BMD than regimens that contain other nucleoside reverse transcriptase inhibitors (NRTIs) and raltegravir (RAL).¹⁹⁻²² Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to TDF for patients who are at risk of osteopenia or osteoporosis. Recommendations for the management of bone disease in people with HIV have been published.²³

Weight Gain and Antiretroviral Therapy

Weight gain after initiation of ART, especially in people with advanced HIV, can be a sign of a return to better health. However, as discussed below, recent and emerging data from clinical trials and longitudinal cohort studies suggest sex differences in ARV-associated weight gain across all classes of ART among treatment-naïve individuals, particularly with the use of certain integrase strand transfer inhibitors (INSTI)-based regimens (dolutegravir [DTG] and bictegravir [BIC]). In a pooled analysis of eight randomized controlled trials with ARV-naïve people with HIV initiating treatment, at follow-up, female sex was associated with 1.5 times the odds of $\geq 10\%$ weight gain compared to male sex (17.4% versus 12.2%), with Black females significantly more likely to experience $\geq 10\%$ weight gain than non-Black females (19.7% versus 12.4%).²⁴ At 144 weeks of follow-up in the ADVANCE study, a 12.3-kg weight gain was recorded among women receiving TAF/emtricitabine (FTC)/DTG compared to 7.4 kg and 5.5 kg in TDF/FTC/DTG and TDF/FTC/efavirenz (EFV), respectively.²⁵ In addition to women being more likely to experience weight gain with ARV initiation, the pattern of weight gain differs between men and women. In the ADVANCE study, women gained more fat than lean body mass than men, with weight gain concentrated in the limbs and trunk at 96 weeks of follow-up. ARV-associated weight gain similarly has been observed among virologically suppressed women switching to an INSTI-based regimen.^{26, 27} In the Women's Interagency HIV Study, virologically suppressed women who switched to an INSTI-based ART or had an INSTI added to their regimen ($n = 234$) gained an average of 4.2 kg in body weight at the 2-year follow-up compared with 0.2 kg in women remaining on non-INSTI ART ($n = 884$).²⁷ Mean change in percent body fat (1.7% versus 0.3%) and body circumference measures were also greater in the INSTI group than in the non-INSTI group. Investigators did not detect a difference in weight gain by individual INSTI.

All these data indicate that ARV-associated weight gain should be a factor to consider when initiating or changing ART, particularly in Black women. To date, it remains unclear whether switching to a non-INSTI-based regimen results in the reversal of weight gain. It should be noted that although randomized controlled trials and observational studies suggest that individuals receiving INSTI-based regimens experience greater weight gain than those receiving comparator regimens, significant uncertainty continues as to whether INSTIs are causing weight gain or whether the comparator drugs are suppressing weight gain. For example, a recent analysis in the ADVANCE trial demonstrated that the greater weight gain observed in DTG- versus EFV-treated participants was dependent primarily on CYP2B6 polymorphisms associated with slow EFV metabolism (and presumably higher EFV levels). Among those with rapid EFV metabolism genotypes, no evidence was found for a difference between DTG- and EFV-treated participants.²⁸ The underlying mechanisms for this weight gain and their impact on cardiovascular disease, diabetes, pregnancy-related outcomes, and age-related comorbidities among women with HIV is currently unknown.

Adherence to Antiretroviral Therapy

Multiple observational studies have found that women are more likely than men to have suboptimal adherence to ART. Defining adherence as missing no dose of ART in the prior three days, the Centers for Disease Control and Prevention analyzed data from the nationally representative Medical Monitoring Project

(n = 12,394) by race and gender.²⁹ Race comparisons by gender indicated that women had consistently lower ART adherence than men of the same race. Adherence rates were 94% for white men compared with 88% for white women; 93% for Latino men compared with 88% for Latina women; and 89% for Black men compared with 87% for Black women. A Canadian study followed 4,534 individuals (including 904 women) for a median of 65.9 months and found that a significantly lower proportion of women relative to men were optimally adherent (57.0% versus 77.1%).³⁰ In the analysis adjusted for ethnicity and injection drug use, female sex remained associated independently with suboptimal adherence. Women with HIV face multifactorial barriers to adherence. However, increasing access to social services—such as food, housing, and transportation—has been associated with improved ART adherence, as have social support and good patient-provider relationships.^{31,32} Another analysis of 6,186 women from the Medical Monitoring Project found that women age 50 and older were more likely to be adherent to ART than women younger than 50.³³ However, menopausal symptoms have been associated significantly with suboptimal ART adherence in cross-sectional³⁴ and longitudinal studies³⁵ of older women with HIV. It also was noted that although 68.8% of older women with HIV experienced symptoms of menopause, only 17% received treatment for these symptoms. It is plausible that treating menopausal symptoms may improve ART adherence among older women with HIV.³⁵

Antiretroviral Therapy Considerations in Adults and Adolescents with HIV Who Are of Childbearing Potential

All adults and adolescents with HIV who are of childbearing potential should be offered comprehensive reproductive and sexual health counseling and care as part of routine primary medical care. Topics for discussion should include safe sex practices, reproductive desires and options for conception, the HIV status of sexual partner(s), the use of effective contraception to prevent unplanned pregnancy, and maintaining viral suppression to optimize health in preparation for pregnancy. Counseling also should include discussion of special considerations pertaining to ARV use when using hormonal contraceptives, when trying to conceive, and during pregnancy (see the [Perinatal Guidelines](#)). Clinicians should discuss intentions regarding pregnancy with all persons of childbearing potential, and a pregnancy test should be performed before initiating ART (AIII).

Antiretroviral Regimen Considerations for Individuals Who Are Trying to Conceive or Who Cannot Use Effective Contraception

EFV is teratogenic in nonhuman primates.³⁶ However, a meta-analysis that included data from 23 studies found no evidence for an increased risk of birth defects in infants born to women who received EFV during the first trimester compared with infants born to women who received other ARV drugs during the first trimester (pooled relative risk [RR] 0.78; 95% confidence interval [CI], 0.56–1.08).³⁷ Recently, Zash et al. reported on the outcomes of a large birth surveillance study in Botswana. Among 7,959 deliveries for women who were taking EFV around the time of conception, three neural tube defects (NTDs) (0.04%; 95% CI, 0.01% to 0.11%) were reported, which is similar to the rate of NTDs that was observed among infants born to 89,372 women without HIV (0.08%; 95% CI, 0.06% to 0.10%).³⁸ These data on more than 7,900 periconception exposures to EFV from Botswana are sufficient to rule out a threefold or greater increased risk of NTDs with the use of EFV. EFV can be used in individuals of childbearing potential who are not using effective contraception or who are contemplating pregnancy. Individuals who become pregnant while on EFV-containing regimens should continue their current regimens (BIII).

Preliminary data from the birth outcomes surveillance study in Botswana raised concern of an increased risk of NTDs (0.9%) in infants born to women who were receiving DTG at the time of conception.^{39,40} Folate fortification of grains in the geographic area of this study was not mandatory and was uncommon. Folate prescribed before conception was low (0.1% to 0.2%) among the study participants. (Zash et al. NEJM 2019) Updated results from the same study have shown that the prevalence of NTDs in 3,591 infants who were exposed to DTG at the time of conception is substantially lower than initial estimates at 0.19% (95%

CI, 0.09, 0.40).⁴¹ The difference in prevalence of NTDs between those who received DTG at conception and those who received non-DTG-containing regimens at conception was 0.09% (95% CI, -0.03, 0.30), and between DTG at conception and women without HIV was 0.12% (95% CI, 0.01, 0.32). Although these differences suggest a higher risk for NTDs (1.9/1,000 in those on DTG-containing regimens at conception versus 1.1/1,000 in those on non-DTG-containing regimens at conception), they were not statistically significant, and the Panel considers this risk to be very low. Because folic acid is known to prevent NTDs in the general population, all pregnant women and women who might conceive should take at least 400 mcg of folic acid daily (AI).

Before initiating an INSTI-based regimen in a person of childbearing potential, clinicians should review the [What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient](#) section and the [Perinatal Guidelines](#) for information to consider when choosing an ARV regimen. The key recommendations are listed below:

- **For individuals who are trying to conceive**, the Panel recommends initiating one of the following regimens, which are designated as *Preferred* regimens during pregnancy in the [Perinatal Guidelines](#): a dual NRTI-inhibitor combination (ABC plus lamivudine [3TC] or TDF plus either FTC or 3TC) and either a PI/r (atazanavir/r or darunavir[DRV]/r) or an INSTI (DTG or RAL) (AIII). Clinicians should discuss the risks and benefits of using DTG with patients to allow them to make an informed decision. The decision to recommend DTG as a *Preferred* ARV is based on a very small increased risk of NTDs compared to other ARV drugs and other advantages of DTG, which include once-daily dosing being generally well tolerated. Moreover, DTG-based regimens are associated with rapid, durable viral load suppression, which is important for maternal health and the prevention of perinatal HIV transmission. Data are insufficient to recommend BIC at this time. The use of long-acting injectable (LAI) cabotegravir (CAB) with rilpivirine (RPV) has not been studied in pregnancy and currently is not recommended in individuals who are trying to conceive (AIII).
- **For individuals who are not planning to conceive but who are sexually active and not using contraception**, consider a regimen's effectiveness and tolerability, the available data on potential teratogenicity, and the person's preferences (e.g., pill burden) when choosing between regimens that are recommended for initial therapy (see [Table 6](#)). Clinicians should refer to the [Perinatal Guidelines](#) for recommendations.

Reproductive Options for Couples with Differing HIV Status

Couples with differing HIV status should be informed of options to prevent sexual transmission of HIV while attempting conception. Interventions include screening and treating both partners for sexually transmitted infections and using ART to maximally suppress and maintain the viral load of the partner with HIV. For couples with different HIV serostatus, if the partner with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom allows conception with effectively no risk of sexual HIV transmission to the partner without HIV.⁴²⁻⁴⁴ If the partner with HIV has not achieved sustained viral suppression or viral suppression status is unknown, or if concerns exist that the partner with HIV may be inconsistently adherent to ART during the periconception period, administration of ARV pre-exposure prophylaxis (PrEP) to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV (AI). Timing condomless sex to coincide with ovulation (peak fertility) is an approach that can optimize the probability of conception.

Hormonal Contraception

Safe and effective reproductive health and family planning services to prevent unplanned pregnancies and perinatal transmission of HIV are essential components of care for individuals with HIV of childbearing potential. These individuals should receive ongoing counseling on reproductive issues. Individuals who do not desire pregnancy currently but are sexually active or considering initiating sexual activities should be offered effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Individuals

with HIV can use all available contraceptive methods (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs)⁴⁵, after consideration of potential drug-drug interactions as discussed in the next section.

Drug-Drug Interactions

Interactions between ARV drugs and hormonal contraceptives may reduce contraceptive efficacy. However, most data are generated from healthy-volunteer, short-duration PK studies, and clinical data regarding interactions between ARV drugs and hormonal contraceptives in women with HIV are limited. The magnitude of change in drug concentrations that may reduce contraceptive efficacy or increase the risk of adverse effects is not known for all forms of contraceptives, making the clinical implications of some ARV-hormone drug interactions challenging to interpret.

Concerns about PK interactions between hormonal contraceptives and ARV drugs should not prevent clinicians from prescribing hormonal contraceptives for individuals on ART who prefer a contraceptive method. However, an alternative or additional effective contraceptive method is recommended when significant interactions occur between hormonal contraceptives and ARV drugs (see Tables 21a, 21b, 21d, and 21e). A summary of ARVs with known interactions with hormonal contraceptives is described below:

Combination contraceptives containing ethinyl estradiol and progestins, including combined oral contraceptives (COCs), transdermal patches, and intravaginal rings:^{46, 47}

- EFV significantly decreases progestin concentrations from both COCs and intravaginal rings, which may increase the risk of contraceptive failure. EFV did not reduce oral ethinyl estradiol exposure in one small study, but it did reduce exposure when combined with an intravaginal ring, which may increase the risk of intermenstrual bleeding (spotting), particularly with ultra-low and low-dose estrogen-containing contraceptives.
- Elvitegravir boosted with cobicistat (EVG/c), and cobicistat- or ritonavir-boosted PIs decrease ethinyl estradiol levels, which may increase the risk of intermenstrual bleeding (spotting), particularly with ultra low and low-dose estrogen-containing contraceptives. However, these ARV regimens also increase progestin exposure, which preserves contraceptive effectiveness.
- Cobicistat- and ritonavir-containing regimens should be avoided with drospirenone-containing products because of an increased risk of hyperkalemia.
- Fostemsavir (FTR) increases ethinyl estradiol exposure, which may increase risk of thromboembolic events. Product labeling recommends a maximum dose of ethinyl estradiol 30 mcg per day when combined with FTR.⁴⁸

Progestin only pills:^{46, 47}

- EFV significantly decreases concentrations of oral progestin pills, including emergency contraception, which may increase the risk of contraceptive failure.
- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure. The combination may be used without dose adjustment; monitor for progestin-related adverse effects.

Injectable Contraceptives (depot-medroxyprogesterone):

- One study of EFV-based ART plus depo-medroxyprogesterone acetate (DMPA) did not find a significant reduction in medroxyprogesterone acetate (MPA) exposure. No change in DMPA dose or frequency is necessary.⁴⁹
- For women receiving both rifampin and EFV for the treatment of tuberculosis (TB) and HIV, some experts suggest administering DMPA every 8 to 10 weeks, instead of every 12 weeks. This recommendation is based on the results of one study of 42 women with HIV and TB in South Africa that found 12% of participants with MPA concentrations below the level of contraceptive effectiveness at Week 12.⁵⁰ One study of EFV-based ART plus DMPA did not find a significant reduction in MPA exposure.⁴⁹

Progestin-Releasing Contraceptive Implants.^{46, 47}

- EFV significantly decreases progestin concentrations released from a contraceptive implant. Cohort studies have found that women receiving EFV-based ART and contraceptive implants have a higher rate of unintended pregnancies than women receiving other ART combinations.^{51, 52}
- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure, but the combination may be used without dose adjustment.

Risk of HIV Transmission to Sexual Partner

Despite their contraceptive benefits, concerns exist that certain types of hormonal contraception may increase the risk of HIV transmission. Oral contraceptive use in people on ART does not increase the risk of HIV transmission, although the data are limited.⁵³ Also, no evidence indicates an increased risk of transmission with contraceptive implants.⁵⁴ However, in a prospective study from Africa, injectable contraceptives were found to be associated with a significantly increased risk of HIV-1 transmission from women (who were not on ART) to their male partners. Higher HIV-1 RNA concentrations in endocervical secretions were detected in women with HIV who were using injectable contraceptive methods than in those who were not receiving any hormonal contraceptives, offering a potential mechanism for increased HIV-1 transmission risk.⁵⁵ A World Health Organization expert group reviewed all available evidence regarding hormonal contraception use and HIV transmission to a partner without HIV and recommended that individuals with HIV can continue to use all existing hormonal contraceptive methods without restriction.⁵⁵ Further research is needed to determine definitively whether hormonal contraceptive use is an independent risk factor for transmission of HIV, particularly in the setting of ART. Regardless, the potential association between hormonal contraception use and HIV transmission in the absence of ART underscores the importance of ART-induced viral suppression to reduce transmission risk.

IUDs appear to be a safe and effective contraceptive option for individuals with HIV.⁵⁷⁻⁵⁹ Although studies have focused primarily on IUDs that do not contain hormones (e.g., copper IUDs), several small studies have found that levonorgestrel-releasing IUDs are also safe and are not associated with increased genital tract shedding of HIV.⁶⁰⁻⁶⁴

Pregnancy

All women with HIV should receive ART early in pregnancy, regardless of their viral load or CD4 T lymphocyte (CD4) cell count, for their own health and for the prevention of perinatal HIV transmission and transmission of HIV to sexual partners. ARV drugs reduce the risk of perinatal HIV transmission by decreasing maternal viral load in blood and genital secretions.⁶⁵⁻⁶⁷ Clinicians who are caring for pregnant adults and adolescents with HIV should review the [Perinatal Guidelines](#).

Antiretroviral Regimen Considerations

In general, the recommendations for the use of ART in pregnant women are the same as those for women who are not pregnant. As in nonpregnant individuals, genotypic drug-resistance testing is recommended for all people who are pregnant before initiating ARV drugs (**AIII**) and for those with detectable HIV RNA while on ART (**AI**). However, ART initiation should not be delayed pending genotypic drug-resistance test results. The ARV regimen can be modified, if necessary, once the resistance test results are available (**BIII**). Unique considerations that influence recommendations on the ARV drugs to use during pregnancy include the following:

- Potential ARV-associated adverse effects for pregnant women, fetuses, and infants, including potential interactions with other medications women may already be receiving;
- Need for strict adherence to the prescribed ARV regimen to avoid drug resistance, optimize health outcomes, and minimize the risk of perinatal transmission; and

- Limited long-term outcome data for infants who were exposed to ARV drugs *in utero*, especially for newer ARV drugs.

Clinicians should review the [Perinatal Guidelines](#) for ARV drug recommendations for individuals who recently have received an HIV diagnosis or those who become pregnant while on ART. **Selection of ARV drugs for women who are pregnant should be individualized according to specific ARV history, the results of drug-resistance assays, and the presence of comorbidities, as well as the individual's preferences for balancing known and unknown risks and benefits of an ARV regimen.** Because of data suggesting decreased drug levels during pregnancy and associated loss of virologic suppression, cobicistat-containing regimens, including EVG/c or DRV/c, are not recommended for initiation during pregnancy.⁶⁸ A pregnant woman who has a suppressed plasma viral load on one of these regimens could continue the regimen with frequent viral load monitoring (e.g., every month). Alternatively, an alternative regimen can be used for the duration of the pregnancy. The use of LAI CAB with RPV has not been studied in pregnancy. In clinical trials, participants who became pregnant were switched from LAI CAB and RPV to an alternative oral ARV regimen throughout the remainder of their pregnancies.⁶⁹ Women who become pregnant while on therapy will need close oversight and their pregnancy outcomes should be reported to the [Antiretroviral Pregnancy Registry](#). The registry collects observational data regarding exposure to U.S. Food and Drug Administration–approved ARV drugs during pregnancy to assess potential teratogenicity.

If maternal HIV RNA is $\geq 1,000$ copies/mL (or unknown) near delivery, intravenous infusion of ZDV during labor is recommended, regardless of the mother's antepartum regimen and resistance profile and the mode of infant delivery (**AI**). Administration of combination ART should continue during labor and before a cesarean delivery (oral medications can be administered with sips of water during this time).

Clinicians who are treating pregnant individuals with HIV are strongly encouraged to report cases of prenatal exposure to ARV drugs (either administered alone or in combination) to the [Antiretroviral Pregnancy Registry](#).

Postpartum Management

Following delivery, clinical, immunologic, and virologic follow-up should continue as recommended for nonpregnant adults and adolescents. Breastfeeding is not recommended for women in the United States who have confirmed HIV because safer [infant-feeding alternatives](#) are available. Maternal ART should be continued after delivery. For more information regarding postpartum management of HIV, refer to the [Perinatal Guidelines](#).

Several studies have demonstrated that adherence to ART may decline during the postpartum period.⁷⁰⁻⁷² Clinicians should address ART adherence at each postpartum clinic visit, including an evaluation of specific factors that facilitate adherence or that present a barrier to adherence. Clinicians may recommend an intervention to improve adherence (see [Adherence to the Continuum of Care](#)).

Clinicians should discuss future reproductive plans and timing, the risks and benefits of conceiving on specific ARV medications, and the use of appropriate contraceptive options to prevent unintended pregnancy. If a long-acting reversible contraceptive, such as an implant or IUD, is desired by the patient, it should be inserted before hospital discharge or during the postpartum visit.

HIV and Menopause

The population of people with HIV is aging; thus, the number of women with HIV who are experiencing menopause is increasing. The median age of menopause in the general U.S. population is 52.5 years.⁷³ Evidence suggests that women with HIV are reaching menopause at earlier ages than those who do not have HIV.^{74,75} However, other confounding factors may affect age of menopause in women with HIV, such as sociodemographic factors, illicit drug use, hepatitis C coinfection, smoking, and possibly ART.

A Canadian study of 229 women with HIV reported that the average age of menopause was 48 years, which was three years younger than the general Canadian population. Lower level of education and hepatitis C coinfection were associated independently with menopause at <45 years of age.⁷⁶ In another study of 667 women with HIV in Rio de Janeiro, Brazil, 24% reached menopause during the observational period and 27% had early menopause (<45 years of age). The median age of menopause was also 48 years of age. Age at menarche <11 years, cigarette smoking, chronic hepatitis C, and CD4 count <50 cell/mm³ were associated significantly with an earlier age of natural menopause.⁷⁷

Defining the relationship between HIV and menopausal symptoms, mental health, and depression is complicated due to overlapping symptoms from HIV itself, effects of ART, other comorbidities, and substance use. Some studies suggest that women with HIV experience a greater burden of menopausal symptoms, including vasomotor symptoms, sexual dysfunction, and mood changes.^{74, 75, 78} Other studies did not find differences between women with HIV and those without HIV.^{79, 80} Menopausal symptoms also have been associated with reduced adherence to ART and poor cognitive performance.^{34, 35, 81, 82}

No studies have shown evidence of estrogen deficiency (i.e., menopause) affecting CD4 cell count, plasma HIV viral loads, or response to ART.^{83, 84} Two small studies showed no difference in plasma levels of tenofovir and RAL between pre- and post-menopausal women.^{85, 86}

The use of hormone replacement therapy (HRT) is low among women with HIV.³⁵ Data are limited on drug-drug interactions between ART and estradiol as part of HRT, and drug interaction data with ethinyl estradiol cannot be extrapolated to the estrogens used for HRT because of differences in metabolism. Drug interactions between HRT and ART are possible, particularly regimens containing cobicistat, ritonavir, PIs, or some non-nucleoside reverse transfer inhibitors. See the drug-drug interaction Tables [21a](#), [21b](#), [21d](#), and [21e](#) for predicted interactions and clinical recommendations.

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