Prepregnancy Counseling and Care for People of Childbearing Age with HIV

Updated: January 31, 2024
Reviewed: January 31, 2024

Panel's Recommendations
• Discuss reproductive desires and plans with all people with HIV who are of childbearing potential on an ongoing basis throughout the course of their care (AIII). • Provide information about effective and appropriate contraceptive methods to people who do not currently desire pregnancy (AI). Offer all contraceptive methods or refer for contraceptive services. Individuals with HIV can use all available contraceptive methods (e.g., pill, patch ring, injection, implant); however, the presence of other medical co-morbidities and drug–drug interactions between hormonal contraceptives, antiretroviral (ARV) drugs, and other medications should be considered (see Table 3) (AII). This information may help support shared decision-making about acceptable contraception options for people not currently desiring pregnancy. • During prepregnancy counseling, provide information on safer sex and ask about the use of alcohol, nicotine products, and other substances. Provide or refer to evidence-based interventions for substance use disorder, including medication-assisted treatment for opioid use disorder (e.g., methadone, buprenorphine), and counsel people on how to manage health risks (e.g., by accessing a syringe services program) when indicated (AII). • Provide education and counseling about interventions to prevent perinatal HIV transmission, including antiretroviral therapy (ART). Explain that people with HIV should attain maximum viral suppression before attempting conception for their own health, to prevent sexual HIV transmission to partners without HIV (AI), and to minimize the risk of *in utero* HIV transmission to the infant (AI). When fully suppressive ART is started before pregnancy and undetectable viral load is maintained throughout pregnancy and at delivery, the risk of HIV transmission to the infant is extremely low (<1%). • For people with HIV who are considering or planning a pregnancy, begin to provide patient-centered, evidence-based counseling to support shared decision-making about infant feeding (AIII) (see Infant Feeding for Individuals with HIV in the United States). Information and plans for infant feeding should be reviewed throughout pregnancy and again after delivery. • When selecting or evaluating an ARV regimen for people of childbearing potential with HIV, consider a regimen's effectiveness, changes in ARV pharmacokinetics in the second and third trimesters of pregnancy, a person's hepatitis B status, and the possible adverse outcomes for the pregnant person and their fetus (AII). See Teratogenicity and Recommendations for Use of Antiretroviral Drugs During Pregnancy: Overview for more information. The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission emphasizes the importance of counseling and shared decision-making regarding all ARV regimens for people with HIV (AIII).
Rating of Recommendations: A = Strong; B = Moderate; C = Optional *Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Overview

The Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists (ACOG), and other national organizations recommend offering all people of childbearing potential comprehensive family planning and the opportunity to receive prepregnancy counseling and care as a component of routine primary medical care. The purpose of prepregnancy care is to improve the health of each person before conception by identifying risk factors for adverse outcomes for the pregnant person and their fetus, tailoring education and counseling to individual

needs, and treating or stabilizing medical conditions to optimize outcomes for the pregnancy and the fetus/newborn.[1,2] Prepregnancy care is not something that occurs in a single clinical visit; rather, it requires integrating ongoing care and interventions into primary care to address people's needs during the different stages of reproductive life. Integrating comprehensive family planning and prepregnancy care into routine health care visits can help people with HIV reach their desired reproductive outcomes by supporting them to make informed decisions about their fertility and contraceptive use that are aligned with their preferences and reproductive goals.[3-6] Providers should initiate and document a nonjudgmental conversation with all people of reproductive age about their reproductive desires because they may be reluctant to bring up the subject themselves.[7-11]

A meta-analysis of 50 studies found a 42% prevalence of fertility desire among people with HIV. In a pooled analysis, fertility desire was associated with being on antiretroviral therapy (ART), male sex, age younger than 30, being married or cohabitating, a secondary education or higher, and being childless.[12] In a retrospective study among 255 women with HIV, 69 (27.1%) reported an intended pregnancy. Those with intended pregnancies were more likely to be older, White, married, privately insured, and college educated. They were less likely than those with unintended pregnancies to use tobacco, alcohol, opiates, or cocaine during pregnancy, more likely to disclose their HIV status to the father of the baby by delivery, and more likely to receive less effective contraception (e.g., condoms) postpartum. In a multivariate analysis, pregnancy intendedness was an important predictor of nondetectable viral load at pregnancy entry but not at delivery.[13] Pregnancy intentions may not be binary and may change over time, thus underscoring the need for health care providers to engage in ongoing discussions to support dynamic pregnancy intentions.[11]

Health care providers who routinely care for people of reproductive age with HIV play an important role in promoting prepregnancy health and informed reproductive decisions. However, even among providers who offer primary care to people with HIV, the delivery of comprehensive reproductive counseling often falls short of the current guidelines.[14-16]

The fundamental principles of prepregnancy counseling and care are outlined in the CDC Preconception Care Work Group's Recommendations to Improve Preconception Health and Health Care. In addition to the general components of prepregnancy counseling and care that are appropriate for all people of reproductive age, people with HIV have specific needs that should be addressed.[17-20]

- Discuss reproductive options; actively assess their pregnancy intentions on an ongoing basis throughout the course of care; and, when appropriate, make referrals to HIV and reproductive health specialists, including experts in reproductive endocrinology and infertility when necessary. The HIV status of one or both parents should not be a reason to withhold standard of care infertility treatment and assist individuals and couples in reaching their desired reproductive outcomes.
- Offer all people who currently do not desire pregnancy a full range of contraceptive methods to help them achieve their fertility goals. People with HIV can use all available contraceptive methods, including hormonal contraception (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs); see Medical Eligibility Criteria for Contraceptive Use and the updated summary chart.[21] Providers should be aware of the presence of other medical co-morbidities and potential interactions between antiretroviral (ARV) drugs, hormonal contraceptives, and other medications that could lower contraceptive efficacy or increase the risk of such adverse effects as blood clots (see Table 3 below).

- Offer emergency contraception as appropriate, including emergency contraceptive pills and IUDs (see the ACOG Practice Bulletin on Emergency Contraception). Emergency contraceptive pills that contain estrogen and progestin and those that only contain levonorgestrel (LNG) may have interactions with ARV drugs that are similar to the ones observed with combined oral contraceptives.[22] AIDS Clinical Trials Group (ACTG) 5375 showed that doubling the dose of LNG from 1.5 mg to 3 mg in women receiving efavirenz (EFV)-based ART helped overcome the drug–drug interaction with this ARV.[23,24] No data are available on potential interactions between ARV drugs and ulipristal acetate, a progesterone receptor modulator; however, ulipristal acetate is metabolized predominantly by cytochrome P450 (CYP) 3A4, so interactions may occur (see the HIV Drug Interaction Checker).
- Use the prepregnancy period to modify the ARV regimen for people who are contemplating pregnancy to optimize virologic suppression and minimize potential adverse effects (see Recommendations for Use of Antiretroviral Drugs During Pregnancy and Table 7). Recognize that individuals with perinatally acquired HIV may have special needs (e.g., psychosocial support, adherence support)[25] (see Prenatal Care, Antiretroviral Therapy, and HIV Management in People with Perinatally Acquired HIV Infection).
- Recognize that transgender and gender-diverse people who were assigned female sex at birth may have special needs.[26] For transgender men attempting pregnancy, the use of testosterone may induce hypothalamic–pituitary–gonadal suppression, leading to decreased ovulation.[27]
- Recognize that the primary treatment goal for people with HIV who are planning a pregnancy should include sustained suppression of plasma viral load below the limit of detection before conception for their own health, to minimize the risk of perinatal HIV transmission, and to prevent sexual HIV transmission to a partner without HIV (see Reproductive Options When One or Both Partners Have HIV). Inform individuals who are considering or planning pregnancy that with ART started before pregnancy and an undetectable viral load maintained throughout pregnancy and delivery, their risk of HIV transmission to the infant is extremely low (<1%).[28,29]
- Explain that people with HIV who take ART as prescribed and who achieve and maintain an undetectable viral load will not transmit HIV through sex, commonly known as Undetectable = Untransmittable or U=U. For more information, see Let's Stop HIV Together.
- Encourage individuals to disclose their HIV status to their partner or co-parent before pregnancy if doing so is safe. However, this disclosure should not be a requirement of assisting couples in achieving pregnancy.
- Encourage sexual partners to receive HIV counseling and testing so that they can seek HIV care if they have HIV or seek advice about HIV prevention, including pre-exposure prophylaxis (PrEP), if they do not have HIV (see Pre-exposure Prophylaxis (PrEP) to Reduce the Risk of Acquiring HIV During Periconception, Antepartum, and Postpartum Periods).
- Ask about the use of alcohol, tobacco, and other substances. Provide or refer to evidence-based interventions for substance use disorder, including medication-assisted treatment for opioid use disorder (e.g., methadone, buprenorphine), and counsel people on how to manage health risks (e.g., access to a syringe services program). A 2019 analysis[30] reported that overall, 39% of women with HIV of reproductive age reported current drinking and 10% reported binge drinking. Compared to non-drinkers, binge drinkers were less likely to adhere to ART or be virally suppressed and more likely to smoke and use drugs. Between 2007 and 2019, marijuana use during pregnancy among women with HIV increased from 7.1% to 11.7%, whereas alcohol and opioid use were unchanged. Postpartum alcohol (44.4%), marijuana (13.6%), and concomitant

alcohol and marijuana (10%) use were common; marijuana use increased from 10.2% in 2006 to 23.7% in 2019, whereas postpartum alcohol use was unchanged.[31]

- Counsel on maintaining a healthy diet and healthy weight before and during pregnancy.
- Counsel people who are contemplating pregnancy to take a daily multivitamin that contains 400 mcg of folic acid to help prevent neural tube defects (NTDs). Individuals with a history of having a child with NTDs, with a family history of NTDs, or on certain anti-epileptic medications, especially valproic acid, are candidates for receiving a higher dose (1,000–4,000 mcg) of folic acid. Higher doses of folate may also be considered for people receiving trimethoprim/sulfamethoxazole who are trying to conceive (see Special Considerations in Pregnancy in *Pneumocystis* Pneumonia).
- Optimize the health of people with HIV prior to pregnancy (e.g., ensure appropriate folate intake, test for all sexually transmitted infections and treat as indicated, consider the teratogenic potential of all prescribed medications, and consider switching to safer medications).
- Educate and counsel about the risk factors for perinatal HIV transmission, the strategies to reduce those risks, and the potential effects HIV or taking ARV drugs during pregnancy may have on the course of pregnancy and health outcomes for the pregnant person and fetus.
- Support shared decision-making about ART. Educate and counsel on the factors that affect the selection of ARVs for people who are trying to conceive, are pregnant, or are postpartum. For more information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy: Overview.
- Consider the following factors when prescribing ART to people of childbearing potential: the regimen's effectiveness, changes in ARV pharmacokinetics (PK) in the second and third trimesters of pregnancy, an individual's hepatitis B virus (HBV) status, possible adverse outcomes for the pregnant person and their fetus, and the likelihood of developing drug resistance.[32-34]
- Provide patient-centered, evidence-based counseling to support shared decision-making about infant feeding (see Infant Feeding for Individuals with HIV in the United States). Information about and plans for infant feeding should be reviewed throughout pregnancy and again after delivery.
- Evaluate and manage ART-associated adverse effects (e.g., hyperglycemia, anemia, hepatotoxicity) that may affect health outcomes for the pregnant person and fetus.
- Administer all vaccines as indicated (see CDC's Recommended Immunization Schedule and ACOG Maternal Immunization Practice Advisory 2022), which includes vaccination for influenza, pneumococcus, HBV, tetanus, and SARS-CoV-2.[35] All people, including those with HIV, should receive Tdap (tetanus, diphtheria, and pertussis) vaccination during each pregnancy, typically between 27 and 36 weeks of gestation but preferably as early in this time window as possible.
- Ask pregnant people whether they feel safe at home and offer assistance or referrals for those experiencing intimate partner violence (IPV) or requesting assistance.

Drug–Drug Interactions Between Hormonal Contraceptives and Antiretroviral Therapy

Data on drug interactions between ARVs and hormonal contraceptives primarily come from drug labels and several studies on the PK and pharmacodynamics among the different forms of contraception and ARVs.[22,36-59] The contraceptive effectiveness of the LNG IUD is largely through local (i.e., intrauterine) release of LNG, not through systemic absorption. CDC's U.S. Medical Eligibility Criteria for Contraceptive Use lists the LNG IUD as category 1 (no restrictions) in drug interactions with all ARVs in women who already have an IUD and category 1/2 (benefits outweigh risk) for those initiating the use of an IUD.

Hormonal contraceptives can be used with ARVs in people with HIV without other contraindications. The contraception effect is usually attributable to the progestin component of contraceptives. Drug interactions that decrease concentrations of the progestin component may affect contraceptive efficacy. An alternative or additional contraceptive method may be recommended when drug interactions are known. For people receiving darunavir/ritonavir (DRV/r)-based ART, an alternative or additional contraception may be considered because the area under the curve (AUC) for oral contraceptive hormones may be decreased.[60] Cobicistat-boosted protease inhibitors (PIs) are contraindicated with drosperinone-containing hormonal contraceptives due to the potential for hyperkalemia.[54] Depot medroxyprogesterone acetate (DMPA) can be used without restriction because of its relatively higher dose than other progesterone-based contraception, and limited studies have shown no significant interaction between DMPA and ARVs.[37,39,49,61]

Several studies have shown that the use of EFV decreases the effectiveness of hormonal implants and hormonal vaginal rings. Although contraceptive implants (e.g., etonogestrel [ENG], LNG) generally can be used in people who are receiving ARVs, both PK and clinical data suggest that these implants have decreased efficacy when used with EFV-based regimens.[47,62-64] LNG implants are not available in the United States. A PK evaluation reported that the geometric mean ratios of LNG concentrations (patients taking EFV-based ART vs. ART-naive patients) were 0.53 at 24 weeks and 0.43 at 48 weeks. Three pregnancies occurred in the EFV group (15%) between Week 36 and Week 48, whereas no pregnancies occurred in the ART-naive or nevirapine (NVP) groups.[51]

In a study of 570 women with HIV in Eswatini, formerly known as Swaziland, who had LNG implants (i.e., Jadelle), none of the women on NVP- or lopinavir/ritonavir-based regimens (n = 208 and n = 13, respectively) became pregnant, whereas 15 women on EFV (n = 121; 12.4%) became pregnant.[47] A prospective study in seven African countries collected data from 5,153 women with HIV who were followed for 1 to 3 years. During the follow-up period, 40% used injectables, 14% used oral contraceptives, and 9% of the women used implants (mostly LNG); 31% of these women took ART during the follow-up period, mostly NVP-containing (75%) or EFV-containing (15%) regimens. Among women who were not using contraception, pregnancy rates were 13.2 per 100 person-years for those who were on ART and 22.5 per 100 person-years for those who were not on ART. Implants greatly reduced the incidence of pregnancy among women on ART (adjusted hazard ratio [aHR] 0.06; 95% confidence interval [CI], 0.01–0.45) and women who were not on ART (aHR 0.05; 95% CI, 0.02–0.11). Injectables and oral contraceptives also reduced pregnancy risk but to lesser degrees. A potential lesser degree of effectiveness of these methods may be due to their greater dependence on user action, as compared to longer acting methods. ART use did not significantly diminish contraceptive effectiveness, although all methods showed nonsignificant reduced contraceptive effectiveness when people used EFV concurrently.[65]

In a retrospective study among 1,152 women with HIV using either EFV or NVP and ENG or LNG implants, 115 pregnancies occurred, yielding a pregnancy incidence rate of 6.32 (5.27–7.59), with a rate of 9.26 and 4.74 among ENG and LNG implant users, respectively. Pregnancy incidence rates did not differ between EFV- and NVP-based regimens (incidence rate ratio [IRR] = 1.00; 95% CI, 0.71–1.43). No pregnancies were recorded among women on PI-based regimens. Pregnancy rates of EFV- and NVP-containing regimens were similar at 6.41 (4.70–8.73) and 6.44 (5.13–8.07), respectively. Pregnancy rates differed by implant type with LNG implant users half as likely to become pregnant as ENG implant users (IRR = 0.51; 95% CI, 0.33–0.73; $P > 0.01$).[66] A study of 42 women in Malawi (30 women with HIV on EFV and LNG, and 12 women without HIV on LNG) showed that EFV users had lower LNG concentrations that non-EFV users, and one-third of the EFV/LNG users had LNG concentrations <180 pg/mL, which is the suggested minimum level for efficacy. No pregnancies were reported over 60 women-years of follow-up.[67]

In a non-randomized, open label, parallel group, longitudinal pharmacokinetic study among Ugandan women aged 18 to 45, participants with HIV who were on EFV 600 mg received double-dose 300-mg LNG implants and were compared to women without HIV who received standard-dose 150-mg LNG implants. Plasma LNG concentration was quantified more than 48 weeks after implant insertion. LNG AUC from 0 to 24 weeks was 34% lower among women taking 300-mg LNG plus ART versus women taking 150-mg LNG (geometric mean 9,998 vs. 15,231 pg•week/mL, respectively). Double-dose LNG implants did not completely overcome the drug–drug interaction with EFV[58]; therefore, prescribing double-dose LNG implants is not recommended to overcome this drug–drug interaction. Since ovulatory activity was noted among women taking 300-mg LNG plus ART, another contraceptive method that does not interact with EFV is needed.

Genetic contributions also may influence observed drug–drug interactions between contraceptives and ARVs. In a study of 19 women not on ART (control group), 19 women on EFV, and 19 women on NVP, all received ENG implants. Women in the EFV group with CYP2B6 516 G>T had 43% lower ENG minimum plasma concentration (C_{min}) and 34% lower AUC from 0 to 24 hours postdose ($AUC_{0–24}$) at 24 weeks. For women on NVP, those with NR1I2 63396 C>T had lower ENG C_{min} and 37% lower $AUC_{0–24}$ at 24 weeks.[55] A PK study reported that EFV reduced the median ENG level by at least 93% in CYP2B6 slow metabolizers versus 75% in normal and intermediate metabolizers. EFV reduced median ethinyl estradiol (EE) concentration by 75% in slow metabolizers and 41% in normal and intermediate metabolizers among women using hormonal vaginal ring contraceptives.[68]

Tuberculosis Treatment, Antiretrovirals, and Contraception

Other medications, such as concomitant tuberculosis (TB) treatment and ARVs, may also have drug–drug interactions with contraceptives. A PK study of DMPA among women with HIV/TB coinfection who received EFV-based HIV treatment and rifampicin-based TB treatment showed that among 42 evaluable women, 5 women (11.9%; 95% CI, 4.0% to 25.6%) had medroxyprogesterone acetate (MPA) <0.1 ng/mL at Week 12, the level above which ovulation is prevented; of these women, 1 had MPA <0.1 ng/mL at Week 10. The median clearance of MPA was higher in women on EFV compared with women with HIV who were not on ART, thus leading to subtherapeutic concentrations of MPA in 12% of women at Week 12.[69] After performing PK modeling with DMPA and ART, the authors of this study suggested redosing DMPA more frequently,[70] such as every 8 to 10 weeks. In a PK study of the interaction between DMPA, EFV, rifampicin, and isoniazid (INH) during treatment for HIV and tuberculosis, there were no associations between either CYP2B6 or N-acetyltransferase 2 genotype and MPA C_{min} at Week 12. The study was not designed to distinguish inductive effects of rifampicin from possible inhibitory effects of INH on MPA clearance.

Nevertheless, the authors recommended that more frequent DMPA dosing may be appropriate for women receiving all these medications.[71]

Long-Acting Cabotegravir

In a secondary analysis of 85 cisgender women enrolled in HPTN 077, compared to women reporting no hormonal contraception (n = 6), oral contraceptive use (n = 18) was associated with lower long-acting cabotegravir (CAB-LA) peak concentration but was not associated with other PK parameters, suggesting this association is not likely to be clinically significant. No other hormonal contraceptive type (injectable, implants, and other) was associated with significant differences in CAB-LA PK parameters.[72]

Vaginal Ring

A new contraceptive vaginal ring containing segesterone/EE (Annovera) has recently been approved by the U.S. Food and Drug Administration. No available drug–drug interaction studies with this contraceptive vaginal ring and ARV and CYP inducers/inhibitors are known. The contraceptive may possibly be metabolized in the same way as ENG and EE in the NuvaRing (see Table 3 below).[57]

Table 3

Because data are limited on pregnancy rates among people on different hormonal contraceptives and ARVs, some of the dosing recommendations in Table 3 are based on consensus expert opinion. Whenever possible, the recommendations are based on available data regarding PK interactions between ARVs and combined hormonal methods, DMPA, and LNG and ENG implants. The smallest decrease in PK for which an alternative method was recommended was a 14% decrease in norethindrone (with DRV/r). The Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission does not recommend any change in EE dose in people who are receiving etravirine (EE increased 22%) or rilpivirine (EE increased 14%).

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

Note: All recommendations in this table are based on consensus expert opinion. Additional information can be found in the Centers for Disease Control and Prevention Update to U.S. Medical Eligibility Criteria for Contraceptive Use, 2016: Updated Recommendations for the Use of Contraception Among Women at High Risk for HIV Infection.[73]

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	
Efavirenz (EFV)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, and ENG Implants	If efficacy is of primary importance, consider an alternative method (or a reliable method of barrier contraception in addition to this method).
Dosing Recommendation/Clinical Comment for DMPA[a]	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No effect on EE concentrations • ↓ active metabolites of norgestimate; LNG AUC ↓ 83% and norelgestromin AUC ↓ 64%[40] • ENG (in COC) C_{24h} ↓ 61%[46] • ENG ↓ 79%; EE ↓ 59%[57] DMPA • No effect on DMPA levels[37,39] • DMPA AUC ↓ 33-35% when coadministered with EFV, rifampin, and INH. More frequent DMPA dosing may be appropriate.[69] ENG Implant • ENG ↓ below the level necessary to prevent pregnancy (90 pg/mL) in 60% of people on EFV[74] • ↓ 49% ENG concentration[56] • ENG AUC ↓ 63% to 82%[64,75] LNG Implant • ↓ 61% LNG concentration[56] • LNG AUC ↓ 47%[51] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[66] • LNG AUC ↓ 40–73% over 30 months of use[67] • Doubling the dose of LNG implant from 150 mg to 300 mg did not overcome the decrease in LNG concentration.[58]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	LNG Emergency Contraception (Oral Dosing) • LNG (emergency contraception) AUC ↓ 58%[22] • C_{max} was 51% higher with 3 mg LNG (24.9 ng/mL) compared to 1.5 mg (15.1 ng/mL), and the 48-hour concentration was 66% higher (0.6 vs. 0.3 ng/mL, respectively). Dose adjustment of LNG EC from 1.5 mg to 3 mg helped to overcome the drug–drug interaction in women receiving EFV-based ART.[23] Vaginally Administered ENG/EE (Vaginal Ring) • ENG ↓ 93% in CYP2B6 slow metabolizers and ↓ 75% in normal and intermediate metabolizers[68] • EE ↓ 75% in slow metabolizers and ↓ 41% in normal and intermediate metabolizers[68] Changes in ARV Levels and/or Effects on HIV *COC* • No effect on EFV concentrations[40] • EFV C_{12h} ↓ 22%; under therapeutic threshold in 3 of 16 subjects[46] *DMPA* • No effect on HIV disease progression[37,76,77] • No effect on EFV concentrations[37] LNG Implant • No effect on HIV disease progression[51]
Clinical Studies	COC • No difference in pregnancy rates[65] • Pregnancy rate was 13% higher in women using COCs and EFV than in women using COCs alone.[63,78] • Progesterone >3 ng/mL (a surrogate for ovulation) in 3 of 16 women[79] • No ovulations[40] DMPA • No increase in pregnancies[37,63,65,77] • Low endogenous progesterone, consistent with no ovulation[37,39,77] ENG Implant • Pregnancy rate higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception[63] • Presumptive ovulation in 5%[75] LNG Implant • 12% pregnancy rate[47] • 15% pregnancy rate[51]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	• Pregnancy rate higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception[63] • No increase in pregnancy rate[65]
Justification/Evidence for Recommendation	For COCs, some studies suggest higher pregnancy rate and ovulation rate and decreased progestin levels. EFV may decrease, but clinical significance is unclear. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. Also, no effect on HIV disease progression or EFV levels. More frequent DMPA dosing may be appropriate for women receiving rifampicin, INH, and EFV. For implants, some studies suggest higher pregnancy rate and decreased hormone levels. For vaginally administered ENG/EE, PK evaluation showed that ENG levels were 79% lower and EE levels were 59% lower in participants on EFV than in controls after 21 days.[57]
Etravirine (ETR)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↑ 22%[80] No significant effect on NE[80]
Clinical Studies	COC • No ovulations[80]
Justification/Evidence for Recommendation	For COCs, one study found no ovulations and no significant change in progestin levels. No data on POPs
Nevirapine (NVP)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 29%[81]; no change in EE AUC[82] NE AUC ↓ 18%[81] ENG (in COC) C_{24h} ↓ 22%[46] DMPA • No significant change[37] LNG Implant • LNG AUC ↑ 35%[51]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	• ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[66] Changes in ARV Levels and/or Effects on HIV *COC* • No significant effect on NVP levels[79,81,83] *DMPA* • No effect on HIV disease progression[37,76,77,84] *LNG Implant* • No effect on HIV disease progression[51,85]
Clinical Studies	COC • No increase in pregnancy rate[63,65,78,86,87] • No ovulations[79,82,87] DMPA • No increase in pregnancy rates[63,65,77,86] • Low serum progesterone, consistent with no ovulation[37] ENG Implant • No increase in pregnancy rate[63] LNG Implant • No increase in pregnancy rate[47,51,63,65,85]
Justification/Evidence for Recommendation	For COCs, evidence does not show effects on pregnancy rate or ovulations. Evidence demonstrated a small decrease in progestin levels. No effect on NVP levels. For DMPA, evidence does not show effects on pregnancy rate, ovulation, or DMPA levels. No effect on HIV disease progression. For implants, evidence does not show effects on pregnancy rate or HIV disease progression.
Rilpivirine (Oral RPV)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↑ 14%[45] No significant change on NE[45] Changes in ARV Levels and/or Effects on HIV *COC* • No change in RPV levels compared to historical controls[45]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Clinical Studies	COC • No change in progesterone[45]
Justification/Evidence for Recommendation	For COCs, evidence does not show effects on ovulation or progestin levels. No change in RPV levels. No data on POPs
Doravirine (DOR)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	No clinically significant interaction with EE and LNG[88]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data
Ritonavir (RTV)–Boosted Protease Inhibitors (PIs)	
Atazanavir/Ritonavir (ATV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 19%[89] Norgestimate AUC ↑ 85%[89] POP • NE AUC ↑ 50%[90] Vaginally Administered ENG/EE • ENG ↑ 71% • EE ↓ 38%[57]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, increase in progestin levels seen in only one study. Using a COC with at least 35 mcg/day may decrease breakthrough bleeding. For POPs, increase in progestin levels seen in only one study RTV inhibits CYP3A4, which may increase contraceptive hormone levels.
Darunavir/Ritonavir (DRV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, and ENG Implants	If efficacy is of primary importance, can consider an alternative method (or a reliable method of barrier contraception in addition to this method)
Dosing Recommendation/Clinical Comment for DMPA[a]	No additional contraceptive protection is needed.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 44%[60] NE AUC ↓ 14%[60]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, small decrease in progestin levels No data on POPs
Lopinavir/Ritonavir (LPV/r)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	EE AUC ↓ 55%[36] NE AUC ↓ 17% Patch • EE AUC ↓ 45%[36] • Norelgestromin AUC ↑ 83%[36] DMPA • DMPA AUC ↑ 46%[49] ENG Implant • ENG AUC ↑ 52%[75] Changes in ARV Levels and/or Effects on HIV *Patch* • LPV/r ↓ 19%[36] *DMPA* • No effect on HIV disease progression[49] • No change in LPV/r levels[49]
Clinical Studies	COC • Trend of increased pregnancy rate, but CIs overlap[63] Patch • Low serum progesterone consistent with no ovulations (n = 8)[36] DMPA • No pregnancies and no ovulations[49] • Trend of increased pregnancy rate, but CIs overlap[63] ENG Implant • No increase in pregnancy rate[63]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	LNG Implant • No increase in pregnancy rate[47,63]
Justification/Evidence for Recommendation	For COCs, nonsignificant increase in pregnancy rate. Small decrease in progestin level. For patch, no ovulations, and progestin levels increased For DMPA, evidence shows no effect on pregnancy rate or ovulations. Progestin levels increased. For implants, evidence shows no effect on pregnancy rate. Progestin levels increased.
Cobicistat (COBI)-Boosted Protease Inhibitors (PIs)	
Atazanavir/Cobicistat (ATV/c)	
Dosing Recommendation/Clinical Comment for COC/P/R	**Contraindicated** with drospirenone-containing hormonal contraceptives due to potential for hyperkalemia
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 2.3-fold[54] No change in LNG concentration 25% decrease in EE C24[53]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No data on POPs
Darunavir/Cobicistat (DRV/c)	
Dosing Recommendation/Clinical Comment for COC/P/R	Clinical monitoring is recommended when DRV/c is used in combination with drospirenone-containing COCs as a result of the potential for hyperkalemia.
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 1.6-fold EE AUC ↓ 30%[54]
Clinical Studies	N/A
Justification/Evidence for Recommendation	No data on POPs
Protease Inhibitors (PIs) without Ritonavir (RTV)	
Atazanavir (ATV)	
Dosing Recommendation/Clinical Comment for COC/P/R	Prescribe oral contraceptive that contains no more than 30 mcg of EE or recommend alternative contraceptive method.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Dosing Recommendation/Clinical Comment for POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • EE AUC ↑ 48%[91] • NE AUC ↑ 110%[91]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, increased concentrations of estrogen and progestin, but the only data available are from the product label. No data on POPs
CCR5 Antagonist	
Maraviroc (MVC)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No significant effect on EE or LN[92]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin. No clinical data. No data on POPs
Integrase Strand Transfer Inhibitors (INSTIs)	
Bictegravir/Emtricitabine/Tenofovir Alafenamide (BIC/FTC/TAF)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	No significant drug interactions with EE or norgestimate
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data
Dolutegravir (DTG)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No significant effect on ENG implants[74] • No significant effect on norgestimate or EE • No change in DTG AUC[50]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin. No clinical data. No data on POPs
Elvitegravir/Cobicistat (EVG/c)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • Norgestimate AUC ↑ 126% • EE AUC ↓ 25%[93,94]
Clinical Studies	N/A
Justification/Evidence for Recommendation	When administered as the four-drug regimen EVG/c/FTC/TDF, increases in progestin and a small decrease in EE were observed. No clinical data. No data on POPs
Raltegravir (RAL)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	COC • No change in EE • Norgestimate AUC ↑ 14%[95]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE and a small increase in progestin. No clinical data. No data on POPs.
Long-Acting Cabotegravir (CAB-LA)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG Implants	No additional contraceptive protection needed
Effect on Contraceptive Drug Levels and Contraceptive's Effects on ART and HIV	Oral contraceptive use was associated with ↓ CAB-LA C_{max} compared to women not on any hormonal contraception (GMR 0.75; 90% CI, 0.59–0.93; $P = 0.033$). However, oral contraceptive use did not result in significant differences in other CAB-LA PK parameters.
Clinical Studies	N/A
Justification/Evidence for Recommendation	Although oral contraceptive use was associated with lower CAB-LA peak concentration, no other PK parameters seen suggesting the association is not likely to be clinically significant.

[a] Because the hormonal levels achieved with DMPA are substantially higher than the levels that are required for contraception, any small reduction in hormonal level attributed to ARV drugs is unlikely to reduce contraceptive effectiveness.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Key to Symbols:

↑ = increase
↓ = decrease

Key: ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{12h} = concentration at 12 hours postdose; C_{24h} = concentration at 24 hours postdose; CAB-LA = long-acting cabotegravir; CI = confidence interval; $C_{max;}$ = minimum plasma concentration; COBI = cobicistat; COC = combined oral contraceptives; COC/P/R = COC/patch/ring; CYP = cytochrome P450; DMPA = depot medroxyprogesterone acetate; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EC = emergency contraception; EE = ethinyl estradiol; EFV = efavirenz; ENG = etonogestrel; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; GMR = geometric mean ratio; INH = isoniazid; INSTI = integrase strand transfer inhibitor; LNG = levonorgestrel; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NE = norethindrone; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; POP = progesterone-only oral contraceptive pills; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Sources: Panel on Antiretroviral Guidelines for Adults and Adolescents; Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV; Table 24a, Table 24b, and Table 24d

1

References

1. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 762: prepregnancy counseling. *Obstet Gynecol*. 2019;133(1):e78-e89. Available at: https://pubmed.ncbi.nlm.nih.gov/30575679.

2. Elwood C, Kennedy VL, Loutfy M, et al. The Canadian HIV pregnancy planning guidelines: what pregnancy care providers need to know about HIV transmission and pre-conception considerations. *J Obstet Gynaecol Can*. 2021;43(7):884-887. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33272875.

3. Salters K, Loutfy M, de Pokomandy A, et al. Pregnancy incidence and intention after HIV diagnosis among women living with HIV in Canada. *PLoS One*. 2017;12(7):e0180524. Available at: https://pubmed.ncbi.nlm.nih.gov/28727731.

4. Aebi-Popp K, Mercanti V, Voide C, et al. Neglect of attention to reproductive health in women with HIV infection: contraceptive use and unintended pregnancies in the Swiss HIV Cohort Study. *HIV Med*. 2018;19(5):339-346. Available at: https://pubmed.ncbi.nlm.nih.gov/29336516.

5. Sutton MY, Zhou W, Frazier EL. Unplanned pregnancies and contraceptive use among HIV-positive women in care. *PLoS One*. 2018;13(5):e0197216. Available at: https://pubmed.ncbi.nlm.nih.gov/29771940.

6. Dude AM, Miller ES, Garcia PM, Yee LM. Unintended pregnancy and viral suppression in pregnant women living with HIV. *Am J Obstet Gynecol MFM*. 2021;3(2):100300. Available at: https://pubmed.ncbi.nlm.nih.gov/33359637.

7. Rahangdale L, Stewart A, Stewart RD, et al. Pregnancy intentions among women living with HIV in the United States. *J Acquir Immune Defic Syndr*. 2014;65(3):306-311. Available at: https://pubmed.ncbi.nlm.nih.gov/24525467.

8. Matthews LT, Beyeza-Kashesya J, Cooke I, et al. Consensus statement: supporting safer conception and pregnancy for men and women living with and affected by HIV. *AIDS Behav*. 2018;22(6):1713-1724. Available at: https://pubmed.ncbi.nlm.nih.gov/28501964.

9. Cohn SE, Haddad LB, Sheth AN, et al. Parenting desires among individuals living with human immunodeficiency virus in the United States. *Open Forum Infect Dis*. 2018;5(10):ofy232. Available at: https://pubmed.ncbi.nlm.nih.gov/30302356.

10. Skerritt L, de Pokomandy A, O'Brien N, et al. Discussing reproductive goals with healthcare providers among women living with HIV in Canada: the role of provider gender and patient comfort. *Sex Reprod Health Matters*. 2021;29(1):1932702. Available at: https://pubmed.ncbi.nlm.nih.gov/34165395.

11. Skerritt L, Kaida A, O'Brien N, et al. Patterns of changing pregnancy intentions among women living with HIV in Canada. *BMC Womens Health*. 2021;21(1):350. Available at: https://pubmed.ncbi.nlm.nih.gov/34615492.

12. Yan X, Du J, Ji G. Prevalence and factors associated with fertility desire among people living with HIV: a systematic review and meta-analysis. *PLoS One*. 2021;16(3):e0248872. Available at: https://pubmed.ncbi.nlm.nih.gov/33735265.

13. Murphy EM, Keller JM, Powell AM, et al. Women living with human immunodeficiency virus with intended and unintended pregnancy: characteristics and patient outcomes. *J Womens Health (Larchmt)*. 2023;32(4):445-451. Available at: https://pubmed.ncbi.nlm.nih.gov/36602512.

14. Gokhale RH, Bradley H, Weiser J. Reproductive health counseling delivered to women living with HIV in the United States. *AIDS Care*. 2017;29(7):928-935. Available at: https://pubmed.ncbi.nlm.nih.gov/28114813.

15. Tanner AE, Chambers BD, Philbin MM, et al. The intersection between women's reproductive desires and HIV care providers' reproductive health practices: a mixed methods analysis. *Matern Child Health J*. 2018;22(9):1233-1239. Available at: https://pubmed.ncbi.nlm.nih.gov/30008042.

16. Teodoro N, Fu A, Ohly NT, et al. Long-acting reversible contraception knowledge, attitudes and use among HIV-infected and -uninfected women and their providers. *Contraception*. 2019;100(4):269-274. Available at: https://pubmed.ncbi.nlm.nih.gov/31226320.

17. Lampe MA. Human immunodeficiency virus-1 and preconception care. *Matern Child Health J*. 2006;10(5 Suppl):S193-195. Available at: https://pubmed.ncbi.nlm.nih.gov/16832609.

18. Aaron EZ, Criniti SM. Preconception health care for HIV-infected women. *Top HIV Med*. 2007;15(4):137-141. Available at: https://pubmed.ncbi.nlm.nih.gov/17721000.

19. Anderson J. Women and HIV: motherhood and more. *Curr Opin Infect Dis*. 2012;25(1):58-65. Available at: https://pubmed.ncbi.nlm.nih.gov/22156896.

20. Jones D, Chakhtoura N, Cook R. Reproductive and maternal healthcare needs of HIV infected women. *Curr HIV/AIDS Rep*. 2013;10(4):333-341. Available at: https://pubmed.ncbi.nlm.nih.gov/23918674.

21. Centers for Disease Control and Prevention. U S. medical eligibility criteria for contraceptive use, 2016: updated recommendations for the use of contraception among women at high risk for HIV infection. *MMWR*. 2020;69(RR-4):405-410. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6914a3.htm.

22. Carten ML, Kiser JJ, Kwara A, et al. Pharmacokinetic interactions between the hormonal emergency contraception, levonorgestrel (Plan B), and Efavirenz. *Infect Dis Obstet Gynecol*. 2012;2012:137192. Available at: https://pubmed.ncbi.nlm.nih.gov/22536010.

23. Scarsi KK, Smeaton LM, Podany AT, et al. PK of dose-adjested emergency contraception with EFV-based ART in ACTH 5375. Presented at: Conference on Retroviruses and Opportunistic Infections. 2021. Virtual.

24. Scarsi KK, Smeaton LM, Podany AT, et al. Pharmacokinetics of dose-adjusted levonorgestrel emergency contraception combined with efavirenz-based antiretroviral

therapy or rifampicin-containing tuberculosis regimens. *Contraception*. 2023;121:109951. Available at: https://pubmed.ncbi.nlm.nih.gov/36641094.

25. Byrne L, Sconza R, Foster C, et al. Pregnancy incidence and outcomes in women with perinatal HIV infection. *AIDS*. 2017;31(12):1745-1754. Available at: https://pubmed.ncbi.nlm.nih.gov/28590327.

26. American College of Obstetricians Gynecologists' Committee on Gynecologic Practice, American College of Obstetricians Gynecologists' Committee on Health Care for Underserved Women. Health care for transgender and gender diverse individuals: ACOG committee opinion, number 823. *Obstet Gynecol*. 2021;137(3):e75-e88. Available at: https://pubmed.ncbi.nlm.nih.gov/33595253.

27. Taub RL, Ellis SA, Neal-Perry G, et al. The effect of testosterone on ovulatory function in transmasculine individuals. *Am J Obstet Gynecol*. 2020;223(2):229 e221-229 e228. Available at: https://pubmed.ncbi.nlm.nih.gov/32044312.

28. Mandelbrot L, Tubiana R, Le Chenadec J, et al. No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clin Infect Dis*. 2015;61(11):1715-1725. Available at: https://pubmed.ncbi.nlm.nih.gov/26197844.

29. Sibiude et al. Zero vertical transmissions from over 5000 pregnant women with undetectable HIV in France. Presented at: Conference on Retroviruses and Opportunistic Infections. 2022. Virtual. Available at: https://www.eatg.org/hiv-news/croi-2022-zero-vertical-transmissions-from-over-5000-pregnant-women-with-undetectable-hiv-in-france.

30. Frazier EL, Esser MB, McKnight-Eily LR, et al. Alcohol use among HIV-positive women of childbearing age, United States, 2013–2014. *AIDS Care*. 2021;33(8):1024-1036. Available at: https://pubmed.ncbi.nlm.nih.gov/32808534.

31. Yee LM, Kacanek D, Brightwell C, et al. Marijuana, opioid, and alcohol use among pregnant and postpartum individuals living with HIV in the US. *JAMA Netw Open*. 2021;4(12):e2137162. Available at: https://pubmed.ncbi.nlm.nih.gov/34860242.

32. Cotter AM, Garcia AG, Duthely ML, et al. Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth? *J Infect Dis*. 2006;193(9):1195-1201. Available at: https://pubmed.ncbi.nlm.nih.gov/16586354.

33. Tuomala RE, Shapiro DE, Mofenson LM, et al. Antiretroviral therapy during pregnancy and the risk of an adverse outcome. *N Engl J Med*. 2002;346(24):1863-1870. Available at: https://pubmed.ncbi.nlm.nih.gov/12063370.

34. Stek AM. Antiretroviral medications during pregnancy for therapy or prophylaxis. *Curr HIV/AIDS Rep*. 2009;6(2):68-76. Available at: https://pubmed.ncbi.nlm.nih.gov/19358777.

35. Murthy N, Wodi AP, Bernstein H, et al. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older - United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(7):229-233. Available at: https://pubmed.ncbi.nlm.nih.gov/35176010.

36. Vogler MA, Patterson K, Kamemoto L, et al. Contraceptive efficacy of oral and transdermal hormones when co-administered with protease inhibitors in HIV-1-infected women: pharmacokinetic results of ACTG trial A5188. *J Acquir Immune Defic Syndr*. 2010;55(4):473-482. Available at: https://pubmed.ncbi.nlm.nih.gov/20842042.

37. Cohn SE, Park JG, Watts DH, et al. Depo-medroxyprogesterone in women on antiretroviral therapy: effective contraception and lack of clinically significant interactions. *Clin Pharmacol Ther*. 2007;81(2):222-227. Available at: https://pubmed.ncbi.nlm.nih.gov/17192768.

38. Hoyt MJ, Storm DS, Aaron E, Anderson J. Preconception and contraceptive care for women living with HIV. *Infect Dis Obstet Gynecol*. 2012;2012:604183. Available at: https://pubmed.ncbi.nlm.nih.gov/23097595.

39. Nanda K, Amaral E, Hays M, et al. Pharmacokinetic interactions between depot medroxyprogesterone acetate and combination antiretroviral therapy. *Fertil Steril*. 2008;90(4):965-971. Available at: https://pubmed.ncbi.nlm.nih.gov/17880953.

40. Sevinsky H, Eley T, Persson A, et al. The effect of efavirenz on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy HIV-negative women. *Antivir Ther*. 2011;16(2):149-156. Available at: https://pubmed.ncbi.nlm.nih.gov/21447863.

41. Robinson JA, Jamshidi R, Burke AE. Contraception for the HIV-positive woman: a review of interactions between hormonal contraception and antiretroviral therapy. *Infect Dis Obstet Gynecol*. 2012;2012:890160. Available at: https://pubmed.ncbi.nlm.nih.gov/22927715.

42. Tseng A, Hills-Nieminen C. Drug interactions between antiretrovirals and hormonal contraceptives. *Expert Opin Drug Metab Toxicol*. 2013;9(5):559-572. Available at: https://pubmed.ncbi.nlm.nih.gov/23425052.

43. Landolt NK, Phanuphak N, Ubolyam S, et al. Efavirenz, in contrast to nevirapine, is associated with unfavorable progesterone and antiretroviral levels when co-administered with combined oral contraceptives. *J Acquir Immune Defic Syndr*. 2012;62(5):534-539. Available at: https://pubmed.ncbi.nlm.nih.gov/23187949.

44. Atrio J, Stanczyk FZ, Neely M, et al. Effect of protease inhibitors on steady-state pharmacokinetics of oral norethindrone contraception in HIV-infected women. *J Acquir Immune Defic Syndr*. 2014;65(1):72-77. Available at: https://pubmed.ncbi.nlm.nih.gov/24025339.

45. Crauwels HM, van Heeswijk RP, Buelens A, et al. Lack of an effect of rilpivirine on the pharmacokinetics of ethinylestradiol and norethindrone in healthy volunteers. *Int J Clin Pharmacol Ther*. 2014;52(2):118-128. Available at: https://pubmed.ncbi.nlm.nih.gov/24161160.

46. Landolt NK, Phanuphak N, Ubolyam S, et al. Significant decrease of ethinylestradiol with nevirapine, and of etonogestrel with efavirenz in HIV-positive women. *J Acquir Immune Defic Syndr*. 2014;66(2):e50-52. Available at: https://pubmed.ncbi.nlm.nih.gov/24608892.

47. Perry SH, Swamy P, Preidis GA, et al. Implementing the Jadelle implant for women living with HIV in a resource-limited setting in sub-Saharan Africa: concerns for drug interactions leading to unintended pregnancies. *AIDS*. 2014;28(5). Available at: https://pubmed.ncbi.nlm.nih.gov/24401645.

48. Thurman AR, Anderson S, Doncel GF. Effects of hormonal contraception on antiretroviral drug metabolism, pharmacokinetics and pharmacodynamics. *Am J Reprod Immunol*. 2014;71(6):523-530. Available at: https://pubmed.ncbi.nlm.nih.gov/24521428.

49. Luque AE, Cohn SE, Park JG, et al. Depot medroxyprogesterone acetate in combination with a twice-daily lopinavir-ritonavir-based regimen in HIV-infected women showed effective contraception and a lack of clinically significant interactions, with good safety and tolerability: results of the ACTG 5283 study. *Antimicrob Agents Chemother*. 2015;59(4):2094-2101. Available at: https://pubmed.ncbi.nlm.nih.gov/25624326.

50. Song IH, Borland J, Chen S, et al. Dolutegravir has no effect on the pharmacokinetics of oral contraceptives with norgestimate and ethinyl estradiol. *Ann Pharmacother*. 2015;49(7):784-789. Available at: https://pubmed.ncbi.nlm.nih.gov/25862012.

51. Scarsi KK, Darin KM, Nakalema S, et al. Unintended pregnancies observed with combined use of the levonorgestrel contraceptive implant and efavirenz-based antiretroviral therapy: a three-arm pharmacokinetic evaluation over 48 weeks. *Clin Infect Dis*. 2016;62(6):675-682. Available at: https://pubmed.ncbi.nlm.nih.gov/26646680.

52. Nanda K, Stuart GS, Robinson J, et al. Drug interactions between hormonal contraceptives and antiretrovirals. *AIDS*. 2017;31(7):917-952. Available at: https://pubmed.ncbi.nlm.nih.gov/28060009.

53. Elliot ER, Bisdomini E, Penchala SD, et al. Pharmacokinetics (PK) of ethinylestradiol/levonorgestrel co-administered with atazanavir/cobicistat. *HIV Res Clin Pract*. 2019:1-10. Available at: https://pubmed.ncbi.nlm.nih.gov/31335301.

54. Majeed SR, West S, Ling KH, et al. Confirmation of the drug-drug interaction potential between cobicistat-boosted antiretroviral regimens and hormonal contraceptives. *Antivir Ther*. 2020;24(8):557-566. Available at: https://pubmed.ncbi.nlm.nih.gov/31933482.

55. Neary M, Chappell CA, Scarsi KK, et al. Effect of patient genetics on etonogestrel pharmacokinetics when combined with efavirenz or nevirapine ART. *J Antimicrob Chemother*. 2019;74(10):3003-3010. Available at: https://pubmed.ncbi.nlm.nih.gov/31299074.

56. Patel RC, Stalter RM, Thomas KK, et al. A pharmacokinetic and pharmacogenetic evaluation of contraceptive implants and antiretroviral therapy among women in Kenya and Uganda. *AIDS*. 2019;33(13):1995-2004. Available at: https://pubmed.ncbi.nlm.nih.gov/31306173.

57. Scarsi KK, Cramer YS, Rosenkranz SL, et al. Antiretroviral therapy and vaginally administered contraceptive hormones: a three-arm, pharmacokinetic study. *Lancet HIV*. 2019;6(9):e601-e612. Available at: https://pubmed.ncbi.nlm.nih.gov/31498109.

58. Cirrincione LR, Nakalema S, Chappell CA, et al. Effect of double-dose levonorgestrel subdermal implant in women taking efavirenz-based antiretroviral therapy: the DoubLNG pharmacokinetic study. *Contraception*. 2023;122:109975. Available at: https://pubmed.ncbi.nlm.nih.gov/36787829.

59. Nakalema S, Chappell CA, Pham M, et al. Pharmacokinetics of levonorgestrel and etonogestrel contraceptive implants over 48 weeks with rilpivirine- or darunavir-based antiretroviral therapy. *J Antimicrob Chemother*. 2022;77(11):3144-3152. Available at: https://pubmed.ncbi.nlm.nih.gov/36059130.

60. Sekar VJ, Lefebvre E, Guzman SS, et al. Pharmacokinetic interaction between ethinyl estradiol, norethindrone and darunavir with low-dose ritonavir in healthy women. *Antivir Ther*. 2008;13(4):563-569. Available at: https://pubmed.ncbi.nlm.nih.gov/18672535

61. Weinberg A, Park JG, Bosch R, et al. Effect of depot medoxyprogesterone acetate on immune functions and inflammatory markers of HIV-infected women. *J Acquir Immune Defic Syndr*. 2016;71(2):137-145. Available at: https://pubmed.ncbi.nlm.nih.gov/26413850.

62. Leticee N, Viard JP, Yamgnane A, et al. Contraceptive failure of etonogestrel implant in patients treated with antiretrovirals including efavirenz. *Contraception*. 2012;85(4):425-427. Available at: https://pubmed.ncbi.nlm.nih.gov/22036046.

63. Patel RC, Onono M, Gandhi M, et al. Pregnancy rates in HIV-positive women using contraceptives and efavirenz-based or nevirapine-based antiretroviral therapy in Kenya: a retrospective cohort study. *Lancet HIV*. 2015;2(11):e474-482. Available at: https://pubmed.ncbi.nlm.nih.gov/26520927.

64. Chappell CA, Lamorde M, Nakalema S, et al. Efavirenz decreases etonogestrel exposure: a pharmacokinetic evaluation of implantable contraception with antiretroviral therapy. *AIDS*. 2017;31(14):1965-1972. Available at: https://pubmed.ncbi.nlm.nih.gov/28692531.

65. Pyra M, Heffron R, Mugo NR, et al. Effectiveness of hormonal contraception in HIV-infected women using antiretroviral therapy. *AIDS*. 2015;29(17):2353-2359. Available at: https://pubmed.ncbi.nlm.nih.gov/26544706.

66. Pfitzer A, Wille J, Wambua J, et al. Contraceptive implant failures among women using antiretroviral therapy in western Kenya: a retrospective cohort study. *Gates Open Res*. 2019;3:1482. Available at: https://pubmed.ncbi.nlm.nih.gov/32051928.

67. Tang JH, Davis NL, Corbett AH, et al. Effect of efavirenz on levonorgestrel concentrations among Malawian levonorgestrel implant users for up to 30 months of concomitant use: a subanalysis of a randomized clinical trial. *Contracept X*. 2020;2:100027. Available at: https://pubmed.ncbi.nlm.nih.gov/33364598.

68. Haas DW, Cramer YS, Godfrey C, et al. Pharmacogenetic interactions between antiretroviral drugs and vaginally administered hormonal contraceptives. *Pharmacogenet Genomics*. 2020;30(3):45-53. Available at: https://pubmed.ncbi.nlm.nih.gov/32106141.

69. Mngqibisa R, Kendall MA, Dooley K, et al. Pharmacokinetics and pharmacodynamics of depot medroxyprogesterone acetate in African women receiving treatment for human

immunodeficiency virus and tuberculosis: potential concern for standard dosing frequency. *Clin Infect Dis*. 2020;71(3):517-524. Available at: https://pubmed.ncbi.nlm.nih.gov/31504342.

70. Francis J, Mngqibisa R, McIlleron H, et al. A semimechanistic pharmacokinetic model for depot medroxyprogesterone acetate and drug-drug interactions with antiretroviral and antituberculosis treatment. *Clin Pharmacol Ther*. 2021;110(4):1057-1065. Available at: https://pubmed.ncbi.nlm.nih.gov/34151439.

71. Haas DW, Mngqibisa R, Francis J, et al. Pharmacogenetics of interaction between depot medroxyprogesterone acetate and efavirenz, rifampicin, and isoniazid during treatment of HIV and tuberculosis. *Pharmacogenet Genomics*. 2022;32(1):24-30. Available at: https://pubmed.ncbi.nlm.nih.gov/34369424.

72. Blair CS, Li S, Chau G, et al. Brief report: hormonal contraception use and cabotegravir pharmacokinetics in HIV-uninfected women enrolled in HPTN 077. *J Acquir Immune Defic Syndr*. 2020;85(1):93-97. Available at: https://pubmed.ncbi.nlm.nih.gov/32452972.

73. Tepper NK, Curtis KM, Cox S, Whiteman MK. Update to U.S. medical eligibility criteria for contraceptive use, 2016: updated recommendations for the use of contraception among women at high risk for HIV infection. *MMWR Morb Mortal Wkly Rep*. 2020;69(14):405-410. Available at: https://pubmed.ncbi.nlm.nih.gov/32271729.

74. Bishop IJ, Gertz AM, Simon B, et al. Etonogestrel concentrations among contraceptive implant users in Botswana using and not using dolutegravir-based antiretroviral therapy. *Contraception*. 2020;102(3):174-179. Available at: https://pubmed.ncbi.nlm.nih.gov/32387328.

75. Vieira CS, Bahamondes MV, de Souza RM, et al. Effect of antiretroviral therapy including lopinavir/ritonavir or efavirenz on etonogestrel-releasing implant pharmacokinetics in HIV-positive women. *J Acquir Immune Defic Syndr*. 2014;66(4):378-385. Available at: https://pubmed.ncbi.nlm.nih.gov/24798768

76. Polis CB, Curtis KM. Use of hormonal contraceptives and HIV acquisition in women: a systematic review of the epidemiological evidence. *Lancet Infect Dis*. 2013;13(9):797-808. Available at: https://pubmed.ncbi.nlm.nih.gov/23871397.

77. Watts DH, Park JG, Cohn SE, et al. Safety and tolerability of depot medroxyprogesterone acetate among HIV-infected women on antiretroviral therapy: ACTG A5093. *Contraception*. 2008;77(2):84-90. Available at: https://pubmed.ncbi.nlm.nih.gov/18226670.

78. Clark RA, Theall K. Population-based study evaluating association between selected antiretroviral therapies and potential oral contraceptive failure. *J Acquir Immune Defic Syndr*. 2004;37(1):1219-1220. Available at: https://pubmed.ncbi.nlm.nih.gov/15319685.

79. Landolt NK, Phanuphak N, Ubolyam S, et al. Efavirenz, in contrast to nevirapine, is associated with unfavorable progesterone and antiretroviral levels when coadministered with combined oral contraceptives. *J Acquir Immune Defic Syndr*. 2013;62(5):534-539. Available at: https://pubmed.ncbi.nlm.nih.gov/23187949.

80. Scholler-Gyure M, Kakuda TN, Woodfall B, et al. Effect of steady-state etravirine on the pharmacokinetics and pharmacodynamics of ethinylestradiol and norethindrone. *Contraception*. 2009;80(1):44-52. Available at: http://ac.els-cdn.com/S0010782409000262/1-s2.0-S0010782409000262-main.pdf?_tid=50ea57a0-6797-11e5-8db9-00000aab0f01&acdnat=1443633710_360a599a6e8d2fa152528b542d290cdb.

81. Mildvan D, Yarrish R, Marshak A, et al. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. *J Acquir Immune Defic Syndr*. 2002;29(5):471-477. Available at: https://pubmed.ncbi.nlm.nih.gov/11981363.

82. Stuart GS, Moses A, Corbett A, et al. Combined oral contraceptives and antiretroviral PK/PD in Malawian women: pharmacokinetics and pharmacodynamics of a combined oral contraceptive and a generic combined formulation antiretroviral in Malawi. *J Acquir Immune Defic Syndr*. 2011;58(2):e40-43. Available at: https://pubmed.ncbi.nlm.nih.gov/21921726.

83. Muro E, Droste JA, Hofstede HT, et al. Nevirapine plasma concentrations are still detectable after more than 2 weeks in the majority of women receiving single-dose nevirapine: implications for intervention studies. *J Acquir Immune Defic Syndr*. 2005;39(4):419-421. Available at: https://pubmed.ncbi.nlm.nih.gov/16010163.

84. Day S, Graham SM, Masese LN, et al. A prospective cohort study of the effect of depot medroxyprogesterone acetate on detection of plasma and cervical HIV-1 in women initiating and continuing antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2014;66(4):452-456. Available at: https://pubmed.ncbi.nlm.nih.gov/24798764.

85. Hubacher D, Liku J, Kiarie J, et al. Effect of concurrent use of anti-retroviral therapy and levonorgestrel sub-dermal implant for contraception on CD4 counts: a prospective cohort study in Kenya. *J Int AIDS Soc*. 2013;16:18448. Available at: https://pubmed.ncbi.nlm.nih.gov/23458102.

86. Myer L, Carter RJ, Katyal M, et al. Impact of antiretroviral therapy on incidence of pregnancy among HIV-infected women in sub-Saharan Africa: a cohort study. *PLoS Med*. 2010;7(2):e1000229. Available at: https://pubmed.ncbi.nlm.nih.gov/20161723.

87. Nanda K, Delany-Moretlwe S, Dube K, et al. Nevirapine-based antiretroviral therapy does not reduce oral contraceptive effectiveness. *AIDS*. 2013;27 Suppl 1:S17-25. Available at: https://pubmed.ncbi.nlm.nih.gov/24088680.

88. Khalilieh SG, Yee KL, Sanchez RI, et al. Doravirine and the potential for CYP3A-mediated drug-drug interactions. *Antimicrob Agents Chemother*. 2019;63(5):e02016-02018. Available at: https://pubmed.ncbi.nlm.nih.gov/30783000.

89. Zhang J, Chung E, Yones C, et al. The effect of atazanavir/ritonavir on the pharmacokinetics of an oral contraceptive containing ethinyl estradiol and norgestimate in healthy women. *Antivir Ther*. 2011;16(2):157-164. Available at: https://pubmed.ncbi.nlm.nih.gov/21447864.

90. DuBois BN, Atrio J, Stanczyk FZ, Cherala G. Increased exposure of norethindrone in HIV+ women treated with ritonavir-boosted atazanavir therapy. *Contraception*. 2015;91(1):71-75. Available at: https://pubmed.ncbi.nlm.nih.gov/25245190.

91. Atazanavir (Reyataz) [package insert]. Food and Drug Administration. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021567s044,206352s008lbl.pdf.

92. Abel S, Russell D, Whitlock LA, et al. Effect of maraviroc on the pharmacokinetics of midazolam, lamivudine/zidovudine, and ethinyloestradiol/levonorgestrel in healthy volunteers. *Br J Clin Pharmacol*. 2008;65 Suppl 1:19-26. Available at: https://pubmed.ncbi.nlm.nih.gov/18333862.

93. Stribild (elvitegravir, cobicitstat, emtricitabine, tenofovir disaproxil fumarate) [package insert]. Food and Drug Administration. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/203100s035lbl.pdf.

94. Genvoya (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) [package insert]. Food and Drug Administration. 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207561s025lbl.pdf.

95. Anderson MS, Hanley WD, Moreau AR, et al. Effect of raltegravir on estradiol and norgestimate plasma pharmacokinetics following oral contraceptive administration in healthy women. *Br J Clin Pharmacol*. 2011;71(4):616-620. Available at: https://pubmed.ncbi.nlm.nih.gov/21395656.