PREPREGNANCY COUNSELING AND CARE

Updated: June 12, 2025
Reviewed: June 12, 2025

Panel's Recommendations
• When there is childbearing potential, HIV care should include discussions about reproductive desires and plans on an ongoing basis throughout the course of care **(AIII).** • Provide information about effective and appropriate contraceptive methods when pregnancy is not currently desired **(AI).** Offer all contraceptive methods or refer for contraceptive services. All available contraceptive methods (e.g., pill, patch, ring, injection, implant) can be used with HIV; 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 when pregnancy is not currently desired. • Assess knowledge about partner HIV status and the need to screen partner(s) for HIV and sexually transmitted infections; provide testing or refer for services as needed **(AII).** Discuss whether HIV status has been disclosed to sexual partner(s); discuss options for pre-exposure prophylaxis when indicated **(AII)** (see Reproductive Options When One or Both Partners Have HIV and Pre-exposure Prophylaxis to Prevent HIV During Periconception, Antepartum, and Postpartum Periods). • Provide education and counseling about interventions to prevent perinatal HIV transmission, including antiretroviral therapy (ART). Explain that maximum viral suppression of HIV should be attained before attempting conception for personal 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%). • When pregnancy with HIV is being considered or planned, begin to provide patient-centered, evidence-based counseling to support shared decision-making about infant feeding **(AIII)** (see Preventing HIV Transmission During Infant Feeding). Information and plans for infant feeding should be reviewed throughout pregnancy and again after delivery. • When selecting or evaluating an ARV regimen and there is the potential for pregnancy, consider a regimen's effectiveness, changes in ARV pharmacokinetics in the second and third trimesters of pregnancy, hepatitis B status, possible drug–drug interactions with other needed medications, and the possible adverse outcomes for maternal and fetal health **(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 treating 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 comprehensive family planning and the opportunity to receive prepregnancy counseling and care as a component of routine primary medical care when there is the potential for pregnancy. The purpose of prepregnancy care is to improve health before conception by identifying risk factors for maternal and

fetal adverse outcomes, 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 needs during the different stages of reproductive life. Integrating comprehensive family planning and prepregnancy care into routine HIV health care visits can help patients 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.[7-12]

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, being younger than 30, being married or cohabitating, having a secondary education or higher, and being childless.[13] 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.[14] 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 HIV care, the delivery of comprehensive reproductive counseling often falls short of the current guidelines.[15-17]

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 and in ACOG's Prepregnancy Counseling guidance. 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.[18-21]

- Discuss reproductive options; routinely assess ~~their~~ pregnancy intentions 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.
- When pregnancy is not currently desired, offer a full range of contraceptive methods to help achieve fertility goals. In the context of HIV, all available contraceptive methods, including hormonal contraception (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs) can be used; see Medical Eligibility Criteria for Contraceptive Use.[22] 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.[23] 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.[24,25] 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).
- When pregnancy is being contemplated, use the prepregnancy period to modify the ARV regimen to optimize virologic suppression and minimize potential adverse effects (see Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Table 7). In the context of perinatally acquired HIV, there may be more difficulty maintaining viral suppression, a greater likelihood of multidrug-resistant virus, and there may be a benefit to providing additional psychosocial and/or adherence support[26] (see Prenatal Care, Antiretroviral Therapy, and HIV Management When HIV Was Perinatally Acquired).
- Recognize that patients whose self-expression is less common may have special needs.[27] For example, the use of testosterone may induce hypothalamic–pituitary–gonadal axis suppression, leading to decreased ovulation.[28]
- Recognize that the primary HIV treatment goal when pregnancy is being planned should include sustained suppression of plasma HIV viral load below the limit of detection before conception for personal 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). When pregnancy is being considered or planned, counseling should include that with ART started before pregnancy and an undetectable viral load maintained throughout pregnancy and delivery, the risk of HIV transmission to the infant is extremely low (<1%).[29,30]
- 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 disclosure of HIV status to partners or co-parents 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 Prevent 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 on how to manage health risks (e.g., access to a syringe services program). A 2019 analysis[31] 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.[32]
- Counsel on maintaining a healthy diet and healthy weight before and during pregnancy.

- When pregnancy is being contemplated, counsel to take a daily multivitamin that contains 400 mcg of folic acid to help prevent neural tube defects (NTDs). When there is a history of having a child with NTDs, there is a family history of NTDs, or when certain anti-epileptic medications, especially when using valproic acid, a higher dose (1,000–4,000 mcg) of folic acid can be prescribed. 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 in the Adult and Adolescent Opportunistic Guidelines.
- 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; consider switching to safer medications; encourage cessation of tobacco, alcohol, and other substances; optimize management of chronic health conditions).
- 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 maternal and fetal health outcomes.
- Support shared decision-making about ART. Educate and counsel on the factors that affect the selection of ARVs when trying to conceive, during pregnancy, or during postpartum. For more information, see Recommendations for Use of Antiretroviral Drugs During Pregnancy: Overview.
- Consider the following factors when prescribing ART and there is the possibility of pregnancy: the regimen's effectiveness, changes in ARV pharmacokinetics (PK) in the second and third trimesters of pregnancy, hepatitis B virus (HBV) status, possible adverse maternal and fetal health outcomes,, and the likelihood of developing drug resistance.[33-35]
- Provide patient-centered, evidence-based counseling to support shared decision-making about infant feeding (see Preventing HIV Transmission During Infant Feeding). 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 maternal and fetal health outcomes.
- Administer all vaccines as indicated (see CDC's Recommended Immunization Schedule and ACOG's Maternal Immunization Practice Advisory, 2022), which includes vaccination for influenza, pneumococcus, HBV, tetanus, and SARS-CoV-2.[36] Tdap (tetanus, diphtheria, and pertussis) vaccination should be performed during each pregnancy, including pregnancies impacted by HIV, typically between 27 and 36 weeks of gestation but preferably as early in this time window as possible.
- Ask about safety at home and offer assistance or referrals to those experiencing intimate partner violence 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.[37-39] 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 the context of 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. When using darunavir/ritonavir-based ART, an alternative or additional contraception may be considered because the area under the curve (AUC) for oral contraceptive hormones may be decreased.[40] Cobicistat-boosted protease inhibitors are contraindicated with drosperinone-containing hormonal contraceptives due to the potential for hyperkalemia.[41] 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.[42-45]

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 when using ARVs, both PK and clinical data suggest that these implants have decreased efficacy when used with EFV-based regimens.[46-49] 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.[50]

Tuberculosis Treatment, Antiretrovirals, and Contraception

Other medications, such as concomitant tuberculosis (TB) treatment with EFV, may also have drug–drug interactions with contraceptives. PK studies of HIV/TB coinfection when using EFV-based HIV treatment and rifampicin-based TB treatment show increased metabolism of DMPA and levonorgestrel emergency contraception, suggesting that redosing DMPA more frequently or doubling the dose of emergency contraception may be required for effective contraception.[25,51-54]

Vaginal Ring

For the ENG/EE contraceptive vaginal ring (NuvaRing), PK evaluation showed that ENG levels were 79% lower and EE levels were 59% lower in participants on EFV-based ART regimens compared with the control group.[56] A newer contraceptive vaginal ring containing segesterone/EE (Annovera) also is approved by the U.S. Food and Drug Administration, but no drug–drug interaction studies with this contraceptive ring and ARVs have been reported to date. The segesterone and EE in the Annovera vaginal ring may be metabolized in the same way as ENG and EE in the NuvaRing (see Table 3 below).[56]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives

Table 3 provides a summary of drug interactions between antiretroviral (ARV) agents and hormonal contraceptives, with recommendations for contraceptive dosing and additional contraceptive protection. Because data are limited on pregnancy rates when using 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 pharmacokinetic interactions between ARVs and combined hormonal methods, depot medroxyprogesterone acetate, and levonorgestrel and etonogestrel implants.

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.[57]

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 the Contraceptive's Effects on ART and HIV	**COC** • No effect on EE concentrations • ↓ active metabolites of norgestimate; LNG AUC ↓ 83% and norelgestromin AUC ↓ 64%[58] • ENG (in COC) C_{24h} ↓ 61%[59] • ENG ↓ 79%; EE ↓ 59%[56] **DMPA** • No effect on DMPA levels[42,43] • DMPA AUC ↓ 33% to 35% when coadministered with EFV, rifampin, and INH. More frequent DMPA dosing may be appropriate.[54] **ENG Implant** • ENG ↓ below the level necessary to prevent pregnancy (90 pg/mL) in 60% receiving EFV[60] • ↓ 49% ENG concentration[61] • ENG AUC ↓ 63% to 82%[49,62] **LNG Implant** • ↓ 61% LNG concentration[61] • LNG AUC ↓ 47%[50] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[63]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	• LNG AUC ↓ 40% to 73% over 30 months of use[64] • Doubling the dose of LNG implant from 150 mg to 300 mg did not overcome the decrease in LNG concentration.[65] **LNG Emergency Contraception (Oral Dosing)** • LNG (emergency contraception) AUC ↓ 58%[23] • C_{max} was 51% higher with 3 mg LNG (24.9 ng/mL) than with 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.[24] **Vaginally Administered ENG/EE (Vaginal Ring)** • ENG ↓ 93% in CYP2B6 slow metabolizers and ↓ 75% in normal and intermediate metabolizers[66] • EE ↓ 75% in slow metabolizers and ↓ 41% in normal and intermediate metabolizers[66] **Changes in ARV Levels and/or Effects on HIV** *COC* • No effect on EFV concentrations[58] • EFV C_{12h} ↓ 22%; under therapeutic threshold in 3 of 16 participants[59] *DMPA* • No effect on HIV disease progression[42,67,68] • No effect on EFV concentrations[42] **LNG Implant** • No effect on HIV disease progression[50]
Clinical Studies	**COC** • No difference in pregnancy rates[69] • Pregnancy rate was 13% higher in women using COCs and EFV than in women using COCs alone.[48,70] • Progesterone >3 ng/mL (a surrogate for ovulation) in 3 of 16 women[71] • No ovulations[58] **DMPA** • No increase in pregnancies[42,48,68,69] • Low endogenous progesterone, consistent with no ovulation[42,43,68] **ENG Implant** • Pregnancy rate was higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception.[48] • Presumptive ovulation in 5%[62]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	LNG Implant • 12% pregnancy rate[47] • 15% pregnancy rate[50] • Pregnancy rate was higher with EFV compared with no ART but still lower with implants than with other hormonal methods of contraception.[48] • No increase in pregnancy rate[69]
Justification/Evidence for Recommendation	For COCs, some studies suggest higher pregnancy rate and ovulation rate and decreased progestin levels. EFV levels 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.[56]
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 the Contraceptive's Effects on ART and HIV	EE AUC ↑ 22%[72] No significant effect on NE[72]
Clinical Studies	**COC** • No ovulations[72]
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 the Contraceptive's Effects on ART and HIV	EE AUC ↓ 29%[73]; no change in EE AUC[74] NE AUC ↓ 18%[73] ENG (in COC) C_{24h} ↓ 22%[59] **DMPA** • No significant change[42]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

	LNG Implant • LNG AUC ↑ 35%[50] • ↑ pregnancy incidence rate among women using LNG or ENG implants, more among ENG users[63] **Changes in ARV Levels and/or Effects on HIV** *COC* • No significant effect on NVP levels[71,73,75] *DMPA* • No effect on HIV disease progression[42,67,68,76] *LNG Implant* • No effect on HIV disease progression[50,77]
Clinical Studies	**COC** • No increase in pregnancy rate[48,69,70,78,79] • No ovulations[71,74,79] **DMPA** • No increase in pregnancy rates[48,68,69,78] • Low serum progesterone, consistent with no ovulation[42] **ENG Implant** • No increase in pregnancy rate[48] **LNG Implant** • No increase in pregnancy rate[47,48,50,69,77]
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[b] RPV)	
Dosing Recommendation/Clinical Comment for COC/P/R, POPs, DMPA[a], ENG or LNG Implants	No additional contraceptive protection is needed.
Effect on Contraceptive Drug Levels and the Contraceptive's Effects on ART and HIV	EE AUC ↑ 14%[80] No significant change on NE[80] **Changes in ARV Levels and/or Effects on HIV** *COC* • No change in RPV levels compared with historical controls[80] **ENG or LNG Implants** • ENG and LNG concentrations not altered with RPV-based ART[38]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Clinical Studies	**COC** • No change in progesterone[80]
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 the Contraceptive's Effects on ART and HIV	No clinically significant interaction with EE and LNG[81]
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 the Contraceptive's Effects on ART and HIV	EE AUC ↓ 19%[82] Norgestimate AUC ↑ 85%[82] **POP** • NE AUC ↑ 50%[83] **Vaginally Administered ENG/EE** • ENG ↑ 71% • EE ↓ 38%[56]
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 or LNG 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 the Contraceptive's Effects on ART and HIV	EE AUC ↓ 44%[40] NE AUC ↓ 14%[40] **ENG or LNG Implants** • Progestin concentrations higher with DRV/r-based ART but no related adverse effects[38]
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 the Contraceptive's Effects on ART and HIV	EE AUC ↓ 55%[84] NE AUC ↓ 17% **Patch** • EE AUC ↓ 45%[84] • Norelgestromin AUC ↑ 83%[84] **DMPA** • DMPA AUC ↑ 46%[44] **ENG Implant** • ENG AUC ↑ 52%[62] **Changes in ARV Levels and/or Effects on HIV** *Patch* • LPV/r ↓ 19%[84] *DMPA* • No effect on HIV disease progression[44] • No change in LPV/r levels[44]
Clinical Studies	**COC** • Trend of increased pregnancy rate, but CIs overlap[48] **Patch** • Low serum progesterone[84] consistent with no ovulations (n = 8) **DMPA** • No pregnancies and no ovulations[44] • Trend of increased pregnancy rate, but CIs overlap[48] **ENG Implant** • No increase in pregnancy rate[48] **LNG Implant** • No increase in pregnancy rate[47,48]

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Justification/Evidence for Recommendation	For COCs, nonsignificant increase in pregnancy rate and 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 the Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 2.3-fold[41] No change in LNG concentration 25% decrease in EE C24[85]
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 the Contraceptive's Effects on ART and HIV	Drospirenone AUC ↑ 1.6-fold EE AUC ↓ 30%[41]
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.
Dosing Recommendation/Clinical Comment for POPs, DMPA[a], ENG Implants	No additional contraceptive protection is needed.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Effect on Contraceptive Drug Levels and the Contraceptive's Effects on ART and HIV	**COC** • EE AUC ↑ 48%[86] • NE AUC ↑ 110%[86]
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 the Contraceptive's Effects on ART and HIV	**COC** • No significant effect on EE or LN[87]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE or progestin concentrations. 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 the 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 the Contraceptive's Effects on ART and HIV	**COC** • No significant effect on ENG implants[60] • No significant effect on norgestimate or EE • No change in DTG AUC[88]
Clinical Studies	N/A

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

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 the Contraceptive's Effects on ART and HIV	**COC** • Norgestimate AUC ↑ 126% • EE AUC ↓ 25%[89,90]
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 the Contraceptive's Effects on ART and HIV	**COC** • No change in EE • Norgestimate AUC ↑ 14%[91]
Clinical Studies	N/A
Justification/Evidence for Recommendation	For COCs, no change in EE concentrations and a small increase in progestin concentrations. 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 is needed.
Effect on Contraceptive Drug Levels and the Contraceptive's Effects on ART and HIV	Oral contraceptive use was associated with lower CAB-LA C_{max} than for 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 differences in other PK parameters were observed, suggesting that the association is not likely to be clinically significant.

Table 3. Drug Interactions Between Antiretroviral Agents and Hormonal Contraception

Entry and Attachment Inhibitors	
Fostemsavir (FTR)	
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 the Contraceptive's Effects on ART and HIV	Temsavir (the active moiety of FTR) increased EE concentrations by 40% but had no effect on NE concentrations. EE dose should not exceed 30 µg or equivalent.[92] FTR did not impact progestin. Progestin-only and nonhormonal contraceptives will not be affected by FTR.
Clinical Studies	N/A
Justification/Evidence for Recommendation	No clinical data

[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.

[b] No data are available for long-acting RPV.

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; C12h = concentration at 12 hours postdose; C24h = concentration at 24 hours postdose; CAB-LA = long-acting cabotegravir; CI = confidence interval; Cmax; = maximum 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; FTR = fostemsavir; 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; Adult and Adolescent Antiretroviral Guidelines; Table 24a, Table 24b, and Table 24d.

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