Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Maternal HIV Testing and Identification of Perinatal HIV Exposure

(Updated November 14, 2017; Last reviewed November 14, 2017)

### Panel's Recommendations

- HIV testing is recommended as standard of care for all sexually active women, and should be a routine component of preconception care (AII).
- All pregnant HIV-negative women in the United States should be tested as early as possible during each pregnancy (AII).
- Repeat HIV testing in the third trimester is recommended for pregnant women with initial negative HIV antibody tests who are known to be at risk of acquiring HIV, who are receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year, who are incarcerated, or who reside in jurisdictions with elevated HIV incidence (see Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings and [http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf](http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) (AII).
- Expedited HIV testing at the time of labor or delivery should be performed for any woman with undocumented HIV status; testing should be available 24 hours a day, and results available within 1 hour (AII). If results are positive, intrapartum and infant postnatal antiretroviral (ARV) drug prophylaxis should be initiated immediately, pending results of supplemental HIV testing (AII) see [Perinatal Guidelines](http://www.cdc.gov) for guidance.
- Women who have not been tested for HIV before or during labor should undergo expedited HIV antibody testing during the immediate postpartum period (or their newborns should undergo expedited HIV antibody testing) (AII). If results in mother or infant are positive, an appropriate infant antiretroviral (ARV) drug regimen should be initiated immediately, and the mothers should not breastfeed unless supplemental HIV testing is negative (AII). Infants with initial positive HIV viral tests (RNA, DNA) should have their ARV regimen modified, if necessary, to a three-drug combination of ARV drugs at treatment dosages (antiretroviral therapy) (see [Antiretroviral Management of Exposed Infants](http://www.cdc.gov)).
- Results of maternal HIV testing should be documented in the newborn’s medical record and communicated to the newborn’s primary care provider (AIII).
- HIV testing to determine HIV status is recommended for infants and children in foster care and adoptees for whom maternal HIV status is unknown (AIII).

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

### Rating of Evidence: I = One or more randomized trials in children† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion

† Studies that include children or children and adolescents, but not studies limited to post-pubertal adolescents
Preconception Counseling and Care for Women of Childbearing Age Living with HIV  
(Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

- Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care (AII).
- Provide information about effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy (AI).
- During preconception counseling, include information on safer sexual practices and elimination of alcohol, tobacco, and other drugs of abuse; if elimination is not feasible, appropriate treatment (e.g., methadone) and prevention (e.g., access to syringe services program) should be provided (AII).
- All women living with HIV who are contemplating pregnancy should be receiving antiretroviral therapy (ART), and have a plasma viral load below the limit of detection prior to conception (AII).
- When selecting or evaluating ART for women of childbearing age living with HIV, consider a regimen’s effectiveness, a woman’s hepatitis B status, teratogenic potential of the drugs in the ART regimen, and possible adverse outcomes for the mother and fetus (AII).
- HIV infection does not preclude the use of any contraceptive method; however, drug-drug interactions between hormonal contraceptives and ART should be considered (AII).

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

Reproductive Options for Couples with the Same or Differing HIV Status  
(Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

For Couples Who Want to Conceive When One or Both Partners are Living with HIV:
- Expert consultation is recommended so that approaches can be tailored to couples’ specific needs (AIII).
- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).
- Partners living with HIV infection should attain maximum viral suppression before attempting conception to prevent HIV sexual transmission (AI) and, for women living with HIV, to minimize the risk of HIV transmission to the infant (AII).
- For couples with differing HIV status, when the woman is living with HIV, assisted insemination at home or in a provider’s office with a partner’s semen during the peri-ovulatory period is recommended as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV (AII).
- For couples with differing HIV status, when the man is living with HIV, the use of donor sperm from a man who is HIV-uninfected can be used as a conception strategy that eliminates the risk of HIV transmission to the partner without HIV (BIII).
- For couples with differing HIV status, when the partner living with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom limited to the 2 to 3 days before and the day of ovulation (peak fertility) is an approach to conception with very low risk of sexual HIV transmission to the partner without HIV (BII).
- For couples with differing HIV status who attempt conception via sexual intercourse without a condom (despite counseling) when the partner living with HIV has not been able to achieve viral suppression or when the viral suppression status is not known, administration of antiretroviral pre-exposure prophylaxis (PrEP) to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV (AI). Couples should still be counseled to limit sex (without condoms) to the period of peak fertility (AII).
- For couples with differing HIV status who attempt conception (sexual intercourse without a condom limited to peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear whether administering PrEP to the partner without HIV further reduces the risk of sexual transmission (CIII).

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

Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States  
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Antepartum Care (Last updated November 14, 2017; last reviewed November 14, 2017)

General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

### Panel’s Recommendations

- **Panel’s Recommendations**
  - Initial evaluation of pregnant women living with HIV should include assessment of HIV disease status and plans to initiate, continue, or modify antiretroviral therapy (ART) (AII). The National Perinatal HIV Hotline (888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
  - All pregnant women living with HIV should receive ART, initiated as early in pregnancy as possible, to prevent perinatal transmission regardless of plasma HIV RNA copy number or CD4 T lymphocyte count (AI). Maintenance of a viral load below the limit of detection throughout pregnancy and lifetime of the individual living with HIV is recommended (AII).
  - To minimize the risk of perinatal transmission, antiretroviral (ARV) drugs should be administered at all time points, including antepartum and intrapartum to the woman as well as postnatally to the neonate (AI).
  - The known benefits and potential risks of all medication use, including ARV drug use during pregnancy and postpartum, should be discussed with all women living with HIV (AIII).
  - The importance of adherence to ARV drug regimens should be emphasized in patient counseling (AII).
  - ARV drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AIII).
  - In pregnant women not already receiving ART, ART should be initiated before results of drug-resistance testing are available because earlier viral suppression has been associated with lower risk of transmission. If ART is initiated before results are available, the regimen should be modified, if necessary, based on resistance assay results (BIII).
  - Coordination of services among prenatal care providers, primary care and HIV specialty care providers, and when appropriate, mental health and drug abuse treatment services, intimate partner violence support services, and public assistance programs is essential to help ensure that women living with HIV adhere to their ARV drug regimens (AII).
  - Providers should also initiate counseling during pregnancy about key intrapartum and postpartum considerations, including mode of delivery, maternal lifelong HIV therapy, family planning and contraceptive options, infant feeding, infant ARV prophylaxis, timing of infant diagnostic testing, and neonatal circumcision (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

### Teratogenicity (Last updated November 14, 2017; last reviewed November 14, 2017)

### Panel’s Recommendations

- **All cases of antiretroviral (ARV) drug exposure during pregnancy should be reported to the Antiretroviral Pregnancy Registry (see http://www.APRegistry.com) (AIII).**
- Based on the preponderance of studies indicating no difference in rates of birth defects for first-trimester compared with later ARV drug exposures, women can be counseled that antiretroviral therapy during pregnancy generally does not increase the risk of birth defects (BIII).

**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
**Combination Antiretroviral Drug Regimens and Maternal and Neonatal Outcomes**

*(Last updated November 14, 2017; last reviewed November 14, 2017)*

<table>
<thead>
<tr>
<th>Panel's Recommendations</th>
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<tr>
<td>• Clinicians should be aware of a possible small increased risk of preterm delivery in pregnant women receiving antiretroviral therapy; however, given the clear benefits of such regimens for both a woman’s health and the prevention of perinatal transmission, HIV treatment should not be withheld for fear of altering pregnancy outcomes <em>(AII)</em>.</td>
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**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

**Recommendations for Use of Antiretroviral Drugs during Pregnancy: Overview** *(Last updated October 19, 2017; last reviewed October 19, 2017)*

<table>
<thead>
<tr>
<th>Panel’s Recommendations</th>
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<tbody>
<tr>
<td>• Multiple factors must be considered when choosing an antiretroviral (ARV) drug regimen for a pregnant woman, including comorbidities, convenience, adverse effects, drug interactions, resistance testing results, pharmacokinetics (PK), and experience with use in pregnancy <em>(AIII)</em>.</td>
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<tr>
<td>• In general, the same regimens as recommended for treatment of non-pregnant adults should be used in pregnant women if appropriate drug exposure is achieved in pregnancy, unless there are known adverse effects for women, fetuses, or infants that outweigh benefits <em>(AII)</em>.</td>
</tr>
<tr>
<td>• In most cases, women who present for obstetric care on fully suppressive ARV regimens should continue their current regimens <em>(AIII)</em>.</td>
</tr>
<tr>
<td>• PK changes in pregnancy may lead to lower plasma levels of drugs and necessitate increased dosages, more frequent dosing, or boosting <em>(AII)</em>.</td>
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**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
Panel’s Recommendations

**Pregnant Women Living with HIV Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive)**

- Antiretroviral therapy (ART) should be recommended to all pregnant women living with HIV to reduce the risk of perinatal transmission of HIV and to optimize the health of the mother (AI). Initiation of ART as soon as HIV is diagnosed during pregnancy is recommended based on data demonstrating that earlier virologic suppression is associated with lower risk of transmission (AII).
- Antiretroviral (ARV) drug-resistance studies should be performed to guide selection of regimens in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL) unless drug-resistance studies have already been performed (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AI). If ART is initiated before the results of the drug-resistance assays are available, the ARV regimen should be modified, if necessary, based on the resistance assay results (BIII).
- The choice of regimen should be informed by current adult treatment guidelines, what is known about the use of specific drugs in pregnancy, and the risk of teratogenicity (see Table 6 and Table 9) and maternal factors such as nausea, vomiting, and comorbid conditions. ART regimens that are preferred for the treatment of pregnant women living with HIV who are ARV-naive include: a dual nucleoside reverse transcriptase inhibitor combination (abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine or lamivudine) and either a ritonavir-boosted protease inhibitor (atazanavir/ritonavir or darunavir/ritonavir) or an integrase strand transfer inhibitor (raltegravir) (see Table 6) (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

**Pregnant Women Living with HIV Who Are Currently Receiving Antiretroviral Therapy**

- In general, women living with HIV receiving antiretroviral therapy (ART) who present for pregnancy care generally should continue their ART during pregnancy, provided the regimen is tolerated and effective in suppressing viral replication (HIV viral load less than lower limits of detection of the assay) (AII).
- Certain drugs should not be continued in pregnant women because of toxicity risk ( stavudine, didanosine, and treatment-dose ritonavir, which are also recommended for non-pregnant individuals). Additionally, consider replacing certain drugs that have low drug exposure in pregnancy associated with potential increase in virologic failure (i.e., elvitegravir/cobicistat). These drugs should be replaced with ARVs recommended in pregnancy (see Table 6) (BIII). More frequent virologic monitoring is warranted when an antiretroviral (ARV) regimen is altered during pregnancy (CIII).
- HIV ARV drug-resistance testing should be performed to assist in the selection of active drugs when changing ARV regimens in pregnant women on therapy with virologic failure and HIV RNA levels >1,000 copies/mL (AI). In individuals with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered (BII) (see Lack of Viral Suppression).

**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
Panel’s Recommendations

- Obtain an accurate history of all prior antiretroviral (ARV) regimens used for treatment of HIV disease or prevention of transmission, including virologic efficacy, tolerance of the medications, results of prior resistance testing, and problems with adherence (AIII).

- Choose and initiate a combination antiretroviral therapy (ART) regimen based on results of prior resistance testing, prior ARV use, concurrent medical conditions, and current recommendations for ART in pregnancy, avoiding drugs with potential known adverse effects for the mother or fetus/infant (AII).

- If HIV RNA is above the threshold for resistance testing (i.e., >500–1,000 copies/mL), ARV resistance studies should be performed prior to starting an ARV drug regimen (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy) (AI).

- In general, ART should be initiated prior to receiving results of current ARV resistance studies because longer ART has been associated with reduced transmission rates compared to shorter treatment periods (BIII). ART should be modified based on the results of the resistance assay, if necessary (AIII).

- If the ART regimen results in insufficient viral suppression, repeat resistance testing and assess other considerations including adherence and drug interactions (BIII).

- Consider consulting with an HIV treatment specialist about the choice of ART regimen to initiate in women who previously received ARV drugs or to modify ART in those who are not fully suppressed (BIII).

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
## Monitoring of the Woman and Fetus During Pregnancy

### Panel’s Recommendations

- **Plasma HIV RNA levels** of pregnant women with HIV should be monitored at the initial visit (AI); 2 to 4 weeks after initiating (or changing) antiretroviral (ARV) drug regimens (BI); monthly until RNA levels are undetectable (BIII); and then at least every 3 months during pregnancy (BIII). HIV RNA levels also should be assessed at approximately 34 to 36 weeks’ gestation to inform decisions about mode of delivery (see [Transmission and Mode of Delivery](#)) and to inform decisions about optimal treatment of the newborn (see [Antiretroviral Management of Newborns](#) (AII)).

- **CD4 T lymphocyte (CD4) cell count** should be monitored at the initial antenatal visit (AI) and every 3 to 6 months during pregnancy (BIII). Monitoring of CD4 cell count can be performed every 6 months in patients on combination antiretroviral therapy (ART) with consistently suppressed viral load who have CD4 counts well above the threshold for opportunistic infection risk (CIII).

- HIV drug-resistance studies should be performed before starting ARV regimens in all ARV-naive pregnant women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) unless they have recently been tested for ARV resistance (AIII). HIV drug-resistance studies should be performed before modifying the ARV regimens of patients with detectable HIV RNA levels that are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) or who have suboptimal virologic response to ARV drugs started during pregnancy; however, **therapy should not be delayed while waiting for resistance testing results** (AII). If ART is initiated before the results of the drug-resistance assays are available, the ARV regimen should be modified, if necessary, based on the resistance assay results (BIII).

- Monitoring for complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving (AII).

- Women taking ART during pregnancy should undergo standard glucose screening at 24 to 28 weeks’ gestation (AII). Some experts suggest earlier glucose screening for women receiving ongoing protease inhibitor (PI)-based regimens initiated before pregnancy, similar to recommendations for women with risk factors for glucose intolerance (BIII). For further information on PIs, see [Combination Antiretroviral Drug Regimens and Pregnancy Outcome](#).

- An ultrasound, performed as soon as possible, is recommended to confirm gestational age and, if scheduled cesarean delivery is necessary, to guide the timing of the procedure (see [Transmission and Mode of Delivery](#)) (AII).

- Amniocentesis should be performed on women living with HIV only after initiation of an effective ART regimen and, ideally, when HIV RNA levels are undetectable (BIII). In women with detectable HIV RNA levels in whom amniocentesis is deemed necessary, consultation with an expert should be considered (BIII).

### 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**
### Antiretroviral Drug Resistance and Resistance Testing in Pregnancy (Last updated November 14, 2017; last reviewed November 14, 2017)

**Panel’s Recommendations**

- HIV drug-resistance studies should be performed in women living with HIV whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 to 1,000 copies/mL) before:
  - starting antiretroviral (ARV) regimens in all ARV-naive pregnant women unless they have already been tested for ARV resistance (AIII).
  - initiating antiretroviral therapy (ART) in ARV-experienced pregnant women.
  - modifying ART regimens for women entering pregnancy while receiving ARV drugs or who have suboptimal virologic response to ARV drugs started during pregnancy (AII).
- ART should be initiated in pregnant women prior to receiving results of ARV-resistance studies; ART should be modified, if necessary, based on the results of the resistance assay (BIII).
- If an integrase strand transfer inhibitor (INSTI) is being considered for an ART-naive patient and INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay (BIII).
- Documented zidovudine resistance does not affect the indications for use of intrapartum zidovudine (BII).
- Choice of ARV regimen for an infant born to a woman with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist, preferably before delivery (see Antiretroviral Management of Newborns) (AIII).
- Pregnant women living with HIV should be given ART to maximize suppression of viral replication, which is the most effective strategy for preventing development of resistance and minimizing risk of perinatal transmission (AII).
- All pregnant and postpartum women should be counseled about the importance of adherence to prescribed ARV medications to reduce the potential for development of resistance (AII).

**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

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### Lack of Viral Suppression (Last updated November 14, 2017; last reviewed November 14, 2017)

**Panel’s Recommendations**

- Because maternal antenatal viral load correlates with risk of perinatal transmission of HIV, suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible (AII).
- If an ultrasensitive HIV RNA assay indicates failure of viral suppression (after an adequate period of treatment):
  - Assess adherence and perform tests for resistance if HIV RNA level is > 500 copies/mL (AII).
  - Consult an HIV treatment expert and consider possible antiretroviral regimen modification (AIII).
- Scheduled cesarean delivery at 38 weeks' gestation is recommended for pregnant women living with HIV who have HIV RNA levels >1,000 copies/mL near the time of delivery (AII).

**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
Stopping Antiretroviral Drugs during Pregnancy  (Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

• If an antiretroviral (ARV) drug regimen must be stopped during pregnancy (e.g., for severe toxicity), all ARV drugs should be stopped simultaneously and antiretroviral therapy should be reinitiated as soon as possible (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

HIV/Hepatitis B Virus Coinfection  (Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

• All pregnant women living with HIV should be screened during the current pregnancy for hepatitis B virus (HBV) and unless they are known to have HIV/HBV coinfection and for hepatitis C virus (HCV) infection unless they are known to have HIV/HCV coinfection (see HIV/Hepatitis C Virus Coinfection) (AIII).

• All pregnant women living with HIV who screen negative for HBV (i.e., HBV surface antigen-negative, HBV core antibody-negative, and HBV surface antibody-negative) should receive the HBV vaccine series (AII).

• Women with chronic HBV infection who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV because they are at increased risk of complications from coinfection with other viral hepatitis infections. If they screen negative for HAV antibody, they should receive HAV vaccine, which is safe to use in pregnancy (AIII).

• All pregnant and postpartum women with HIV/HBV coinfection should receive antiretroviral therapy (ART). Antepartum ART in pregnant women with HIV/HBV coinfection should include tenofovir disoproxil fumarate (TDF) plus lamivudine or emtricitabine (AII). If women with HIV/HBV are virally suppressed on a tenofovir alafenamide (TAF) plus lamivudine or emtricitabine-based ART and become pregnant, they can be offered the choice of continuing that ART regimen or switching TAF to TDF in their ART regimen (BIII).

• Pregnant women with HIV/HBV coinfection receiving antiretroviral (ARV) drugs should be counseled about signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of ARV drugs and at least every 3 months thereafter during pregnancy (BIII).

• Women with chronic HBV should be counseled on the importance of continuing anti-HBV medications indefinitely, both during and after pregnancy. If ARV drugs that include anti-HBV activity are discontinued in women with HIV/HBV coinfection, frequent monitoring of liver function tests for potential exacerbation of HBV infection is recommended, with prompt re-initiation of treatment for HBV if a flare is suspected (BIII).

• Decisions concerning mode of delivery in pregnant women with HIV/HBV coinfection should be based on standard obstetric and HIV-related indications alone; HIV/HBV coinfection does not necessitate cesarean delivery, if not otherwise indicated (see Intrapartum Care) (AIII).

• Within 12 hours of birth, infants born to women with HBV infection should receive hepatitis B immune globulin and the first dose of the HBV vaccine series (AI).
### Panel's Recommendations

- All pregnant women living with HIV should be screened during the current pregnancy for hepatitis B virus (HBV) unless they are known to have HIV/HBV coinfection and for hepatitis C virus (HCV) infection unless they are known to have HIV/HCV coinfection (see [HIV/Hepatitis B Virus Coinfection section](https://aidsinfo.nih.gov/guidelines) (AIII).

- All pregnant women living with HIV and/or HCV who screen negative for HBV infection (i.e., HBV surface antigen-negative and HBV core antibody-negative) and lack HBV immunity (i.e., HBV surface antibody-negative) should receive the HBV vaccine series (AII).

- Women with chronic HCV infection who have not already received the hepatitis A virus (HAV) vaccine series should be screened for immunity to HAV because they are at increased risk of complications from coinfection with other viral hepatitis infections (AIII). If they screen negative for HAV antibody, they should receive HAV vaccine, which is safe to use in pregnancy (AIII).

- If considering initiation or continuation of HCV treatment in a pregnant woman with HIV coinfection, consultation with an expert in HIV and HCV is strongly recommended (AIII).

- Recommendations for antiretroviral (ARV) drug use during pregnancy are the same for women living with HIV whether they have chronic HCV or not (AIII).

- Pregnant women with HIV/HCV coinfection receiving ARV drugs should be counseled about signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of ARV drugs and at least every 3 months thereafter during pregnancy (BIII).

- Decisions concerning mode of delivery in pregnant women with HIV/HCV coinfection should be based on standard obstetric and HIV-related indications alone; HCV coinfection does not necessitate cesarean delivery, if not otherwise indicated (see [Intrapartum Care](https://aidsinfo.nih.gov/guidelines) (AIII).

- Infants born to women with HIV/HCV coinfection should be evaluated for HCV infection (AIII). The specific type and timing of assays for HCV in children should be performed after consultation with an expert in pediatric HCV infection (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.
HIV-2  (Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

- HIV-2 infection should be considered in pregnant women who are from—or have partners from—countries in which the disease is endemic and who have positive results on an HIV-1/HIV-2 antibody or HIV-1/HIV-2 antigen/antibody immunoassay. They should be tested with a supplemental HIV-1/HIV-2 antibody differentiation assay. If they have only HIV-2 infection, the test will show negative HIV-1 antibodies and positive HIV-2 antibodies (AII).
- Pregnant women with HIV-1/HIV-2 coinfection should be treated as per guidelines for HIV-1 monoinfection, but using antiretroviral drugs that are active against HIV-2 (see below).
- No randomized clinical trials have been performed to address when to start treatment or what the optimal treatment is for HIV-2 infection (AIII). A regimen with two nucleoside reverse transcriptase inhibitors and certain boosted protease inhibitors or integrase strand transfer inhibitors is recommended for all pregnant women with HIV-2 infection (AIII).
- Non-nucleoside reverse transcriptase inhibitors and enfuvirtide are not active against HIV-2 and should not be used (AIII).
- All infants born to mothers with HIV-2 infection should receive the 6-week zidovudine prophylactic regimen (BIII).
- In the United States, where safe infant formula is readily available, breastfeeding is not recommended for infants of mothers with HIV-2 infection (AII).

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

The Management of Prenatal Care and General Principles of Antiretroviral Therapy and HIV Management in Women with Perinatal HIV Infection  (Last updated November 14, 2017; last reviewed November 14, 2017)

Panel’s Recommendations

- The management of prenatal care and general principles of antiretroviral therapy (ART) and HIV management do not differ between pregnant women with perinatally acquired HIV and those who acquired HIV infection postnatally. With effective ART and prenatal management, the risk of perinatal transmission does not appear to be increased in women who acquired HIV perinatally compared with those who acquired HIV infection postnatally (AII).
- Using the same guiding principles that are used for heavily ART-experienced adults, optimal ART regimens should be selected based on resistance testing, prior ART history, and pill burden (AII).
- Consultation with experts in HIV and pregnancy is recommended when the presence of extensive drug resistance warrants the use of antiretroviral drugs for which there is limited experience in pregnancy (AIII).
- Pregnant women with perinatally acquired HIV warrant enhanced focus on adherence interventions during and after delivery (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
### Panel’s Recommendations

- When acute retroviral syndrome is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction with a routine HIV antibody screening test or an antigen/antibody immunoassay test (see Acute and Recent (Early) HIV Infection in the Adult and Adolescent Antiretroviral Guidelines and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) (AII).

- Repeat HIV testing in the third trimester is recommended for pregnant women with initial negative HIV antibody tests who are known to be at risk of acquiring HIV, who are receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year, who are incarcerated, or who reside in jurisdictions with elevated HIV incidence (see Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings and http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf) (AII).

- All pregnant women with acute or recent HIV infection should start antiretroviral therapy (ART) as soon as possible to prevent perinatal transmission, with the goal of suppressing plasma HIV RNA to below detectable levels (AII).

- In women with acute HIV infection, baseline genotypic resistance testing should be performed simultaneously with initiation of ART, and the regimen should be adjusted, if necessary, to optimize virologic response (AII).

- In women with acute HIV infection, a ritonavir-boosted protease-inhibitor-based regimen or a dolutegravir-based regimen with tenofovir disoproxil fumarate/emtricitabine should be initiated (AII) (see Table 6).

- When acute HIV infection is diagnosed during pregnancy or breastfeeding, given the high risk of transmission to the infant, consultation with a pediatric HIV specialist regarding appropriate infant management and antiretroviral prophylaxis regimen is strongly recommended (see Infant Management section) (AII).

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**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
Intrapartum Care  

Panel’s Recommendations

- Women should continue taking their antepartum combination antiretroviral therapy (ART) on schedule as much as possible during labor and before scheduled cesarean delivery (AIII).
  - Intravenous (IV) zidovudine:
    - Should be administered to women living with HIV with HIV RNA >1,000 copies/mL (or unknown HIV RNA) near delivery (AI),
    - Is not required for women receiving ART regimens who have HIV RNA ≤50 copies/mL during late pregnancy and near delivery and no concerns regarding adherence to the ART regimen (BII).
    - May be considered for women with HIV RNA between 50 and 999 copies/mL. There are inadequate data to determine whether administration of IV zidovudine to women with HIV RNA levels between 50 and 999 copies/mL provides any additional protection against perinatal transmission. However, some experts would administer IV zidovudine to women with RNA levels in this range, as the transmission risk is slightly higher when HIV RNA is in the range of 50 and 999 copies/mL compared to <50 copies/mL (CII).
  - Scheduled cesarean delivery at 38 weeks’ gestation (compared to 39 weeks for most indications) is recommended for women who have HIV RNA >1,000 copies/mL near delivery (see Transmission and Mode of Delivery) (AI).
- Women who present in labor with unknown HIV status should undergo expedited antigen/antibody HIV testing (AII).
  - If the results are positive, an HIV-1/HIV-2 antibody differentiation test and an HIV-1 RNA assay should be done as soon as possible and maternal (IV zidovudine)/infant (combination antiretroviral [ARV] prophylaxis) ARV drugs should be initiated pending results of the differentiation test (AII).
  - If the maternal HIV differentiation test is positive or the HIV RNA suggests acute infection, infant ARV drugs should be managed as discussed in the Antiretroviral Management of Newborns section (AI).
  - If the maternal HIV differentiation test is negative and acute HIV infection has been reasonably excluded with a negative HIV RNA test, the maternal and infant ARV drugs should be stopped (AIII). Women with positive initial testing should not initiate breastfeeding until HIV infection is definitively ruled out (see Postpartum Care) (AII).

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
# Transmission and Mode of Delivery

**Panel’s Recommendations**

- Scheduled cesarean delivery at 38 weeks’ gestation to minimize perinatal transmission of HIV is recommended for women with HIV RNA levels >1,000 copies/mL or unknown HIV levels near the time of delivery, irrespective of administration of antepartum antiretroviral therapy (ART) (AII).

- Scheduled cesarean delivery performed solely for prevention of perinatal transmission in women receiving ART with HIV RNA ≤1,000 copies/mL is not routinely recommended due to the low rate of perinatal transmission in this group (AII).

- In women with HIV RNA levels ≤1000 copies/mL, if scheduled cesarean delivery or induction is indicated, it should be performed at the standard time for obstetrical indications (AII).

- In women with an HIV RNA >1,000 copies/mL or unknown HIV RNA level who present in spontaneous labor or with ruptured membranes, there is insufficient evidence to determine whether cesarean reduces the risk of perinatal HIV transmission. Management of women originally scheduled for cesarean delivery because of HIV infection who present in labor must be individualized at the time of presentation (BII). In these circumstances, consultation with an expert in perinatal HIV (e.g., telephone consultation with the National Perinatal HIV/AIDS Clinical Consultation Center at (888) 448-8765) may be helpful in rapidly developing an individualized delivery plan.

- In women on ART with HIV RNA ≤1,000 copies/mL, duration of ruptured membranes is not associated with an increased risk of perinatal transmission, and vaginal delivery is recommended (BII).

**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
Panel’s Recommendations

- Artificial rupture of membranes (ROM) performed in the setting of antiretroviral therapy (ART) and virologic suppression is not associated with increased risk of perinatal transmission and can be performed for standard obstetric indications (BII).

- The following should generally be avoided because of a potential increased risk of transmission, unless there are clear obstetric indications:
  - Artificial ROM in the setting of viremia (BIII)
  - Routine use of fetal scalp electrodes for fetal monitoring (BIII)
  - Operative delivery with forceps or a vacuum extractor (BIII)

- The ART regimen a woman is receiving should be taken into consideration when treating excessive postpartum bleeding resulting from uterine atony:
  - In women who are receiving a cytochrome P450 (CYP) 3A4 enzyme inhibitor (e.g., a protease inhibitor, cobicistat), methergine should be used only if no alternative treatments for postpartum hemorrhage are available and the need for pharmacologic treatment outweighs the risks. If methergine is used, it should be administered in the lowest effective dose for the shortest possible duration (BIII).
  - In women who are receiving a CYP3A4 enzyme inducer such as nevirapine, efavirenz, or etravirine, additional uterotonic agents may be needed because of the potential for decreased methergine levels and inadequate treatment effect (BIII).

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
## Panel’s Recommendations

- Antiretroviral therapy (ART) is currently recommended for all individuals living with HIV to reduce the risk of disease progression and to prevent HIV sexual transmission (AI).

- Plans for modifying ART after delivery should be made in consultation with the woman and her HIV care provider, ideally before delivery, taking into consideration the preferred regimens for non-pregnant adults (AIII).

- Because the immediate postpartum period poses unique challenges to antiretroviral (ARV) adherence, arrangements for new or continued supportive services should be made before hospital discharge (AII).

- Contraceptive counseling should start during the prenatal period; a contraceptive plan should be developed prior to hospital discharge (AIII).

- Women with a positive rapid HIV antibody test during labor require immediate linkage to HIV care and comprehensive follow-up, including confirmation of HIV infection (AII).

- Prior to hospital discharge, the woman should be given ARV medications for herself and her newborn to take at home (AIII).

- Infant feeding counseling, including a discussion of potential barriers to formula feeding, should begin in the prenatal period and this information should be reviewed after delivery (AIII).

- Breastfeeding is not recommended for women in the United States with confirmed or presumed HIV infection, because safe alternatives are available (AI).

### 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
Panel’s Recommendations

- All newborns perinatally exposed to HIV should receive postpartum antiretroviral (ARV) drugs to reduce the risk of perinatal transmission of HIV (AI).
- Newborn ARV regimens—at gestational-age-appropriate doses—should be initiated as close to the time of birth as possible, preferably within 6 to 12 hours of delivery (AII).
- The selection of a newborn ARV regimen should be determined based on maternal and infant factors that influence risk of HIV transmission (AIII). The uses of ARV regimens in newborns include:
  - **ARV Prophylaxis**: The administration of one or more ARV drugs to a newborn without confirmed HIV infection to reduce the risk of HIV acquisition.
  - **Empiric HIV Therapy**: The administration of a three-drug combination ARV regimen to newborns at highest risk of HIV acquisition. Empiric HIV therapy is intended to be preliminary treatment for a newborn who is later confirmed have HIV but also serves as prophylaxis against HIV acquisition for those newborns who are exposed to HIV in utero, during the birthing process or during breastfeeding and who do not acquire HIV.
  - **HIV Therapy**: The administration of a three-drug combination ARV regimen at treatment dosages (antiretroviral therapy [ART]) to newborns with confirmed HIV infection (see Diagnosis of HIV Infection).
- For newborns whose mothers have received ART during pregnancy with sustained viral suppression near delivery and for whom there are no concerns related to maternal adherence, a 4-week zidovudine ARV prophylaxis regimen can be used (BII).
- Newborns at higher risk of HIV acquisition should receive a combination ARV regimen (ARV prophylaxis or empiric HIV therapy based on clinician assessment of risk), including those born to women with HIV who:
  - Have not received antepartum or intrapartum ARV drugs (AI), or
  - Have received only intrapartum ARV drugs (AI), or
  - Have received antepartum ARV drugs but have not achieved viral suppression near delivery (AII), or
  - Have primary or acute HIV infection during pregnancy (AI), or
  - Have primary or acute HIV infection during breastfeeding (AII).
- Newborns of women with unknown HIV status who test positive on expedited testing performed during labor or shortly after birth should initiate an ARV regimen (ARV prophylaxis or empiric HIV therapy based on clinician assessment of risk) (AII). If supplemental testing is negative, the ARV regimen can be discontinued (AII).
- For newborns with confirmed HIV, ART should be initiated (AI).
- In the United States, the use of ARV drugs other than zidovudine, lamivudine, and nevirapine cannot be recommended for any indication in premature newborns (<37 weeks gestational age) because of lack of dosing and safety data (BIII).
- Providers with questions about ARV management of perinatal HIV exposure should consult the National Perinatal HIV Hotline (1-888-448-8765), which provides free clinical consultation on all aspects of perinatal HIV, including newborn care (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.
Diagnosis of HIV Infection in Infants and Children  *(Last updated November 14, 2017; last reviewed November 14, 2017)*

Panel’s Recommendations

- Virologic assays (i.e., HIV RNA and HIV DNA nucleic acid tests) that directly detect HIV must be used to diagnose HIV infection in infants and children younger than 18 months with perinatal and postnatal HIV exposure; HIV antibody tests should not be used *(AII)*.
  - RNA or DNA polymerase chain reaction (PCR) testing are recommended equally for most patients; RNA PCR is recommended for known maternal non-subtype B virus *(AII)*.

- Virologic diagnostic testing is recommended for all infants with perinatal HIV exposure at the following ages:
  - 14 to 21 days *(AII)*
  - 1 to 2 months *(AII)*
  - 4 to 6 months *(AII)*

- Additional virologic diagnostic testing at birth should be considered for infants at higher risk of perinatal HIV transmission *(AIII)* and at 2 to 4 weeks after cessation of antiretroviral prophylaxis *(BIII)*.

- A positive virologic test should be confirmed as soon as possible by a repeat virologic test on a second specimen *(AII)*.

- Definitive exclusion of HIV infection in non-breastfed infants is based on 2 or more negative virologic tests, with 1 obtained at age ≥1 month and 1 at age ≥4 months, or 2 negative HIV antibody tests from separate specimens obtained at age ≥6 months *(AII)*.

- Some experts confirm the absence of HIV infection at 12 to 18 months of age in children with prior negative virologic tests by performing an HIV antibody test to document loss of maternal HIV antibodies *(BIII)*.

- Since children aged 18 to 24 months with perinatal HIV exposure occasionally have residual maternal HIV antibodies, definitive exclusion or confirmation of HIV infection in children in this age group who are HIV antibody-positive should be based on an HIV nucleic acid test *(AII)*.

- Diagnostic testing in children with non-perinatal exposure only or children with perinatal exposure aged >24 months relies primarily on the use of HIV antibody (or antigen/antibody) tests; when acute HIV infection is suspected, additional testing with an HIV nucleic acid test may be necessary to diagnose HIV infection *(AII)*.

**Note:** The National Clinical Consultation Center provides consultations on issues related to the management of perinatal HIV infection (1-888-448-8765; 24 hours a day, 7 days a week).

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

**Rating of Evidence:** I = One or more randomized trials in children with clinical outcomes and/or validated endpoints; I* = One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies in children with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies in adults with long-term clinical outcomes with accompanying data in children from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = Expert opinion

† Studies that include children or children and adolescents, but not studies limited to post-pubertal adolescents
Panel's Recommendations

- A complete blood count and differential should be performed on newborns as a baseline evaluation (BIII).
- If hematologic abnormalities are identified in infants receiving prophylaxis, decisions on whether to continue infant antiretroviral (ARV) prophylaxis need to be individualized. Consultation with an expert in pediatric HIV infection is advised if early discontinuation of prophylaxis is considered (CIII).
- Decisions about the timing of subsequent monitoring of hematologic parameters in infants depend on baseline hematologic values, gestational age at birth, clinical condition of the infant, the zidovudine dose being administered, receipt of other ARV drugs and concomitant medications, and maternal antepartum therapy (CIII).
- Hemoglobin and neutrophil counts should be remeasured 4 weeks after initiation of prophylaxis for infants who receive combination zidovudine/lamivudine-containing ARV prophylaxis regimens (AI).
- Routine measurement of serum lactate is not recommended. However, measurement can be considered if an infant develops severe clinical symptoms of unknown etiology (particularly neurologic symptoms) (CIII).
- Virologic tests are required to diagnose HIV infection in infants aged <18 months (see Diagnosis of HIV Infection in Infants and Children) (AII).
- To prevent Pneumocystis jirovecii pneumonia (PCP), all infants born to women with HIV should begin PCP prophylaxis at ages 4 to 6 weeks, after completing their ARV prophylaxis regimen, unless there is adequate test information to presumptively exclude HIV infection (see the Pediatric Opportunistic Infections Guidelines) (AII).
- Health care providers should routinely inquire about breastfeeding and premastication; instruct caregivers living with HIV to avoid these practices, and advise on safer feeding options (AII).

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

Long-Term Follow-Up of Infants Exposed to Antiretroviral Drugs

Panel's Recommendations

- Children with in utero/neonatal exposure to antiretroviral (ARV) drugs who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction (CIII).
- It is important that the long-term medical record of a child without HIV includes information about in utero and neonatal ARV exposure (BIII).

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
**Guidance for Counseling and Managing Women Living with HIV in the United States Who Desire to Breastfeed**  
(Last updated March 27, 2018; last reviewed March 27, 2018)

<table>
<thead>
<tr>
<th>Panel's Recommendations</th>
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<tbody>
<tr>
<td>• Breastfeeding is not recommended for women living with HIV in the United States (AII).</td>
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<tr>
<td>• Women who have questions about breastfeeding or who desire to breastfeed should receive patient-centered, evidence-based counseling on infant feeding options (AIII).</td>
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<tr>
<td>• When women with HIV choose to breastfeed despite intensive counseling, they should be counseled to use harm-reduction measures to minimize the risk of HIV transmission to their infants (BIII).</td>
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**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

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