

HIV-2 Infection and Pregnancy

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Panel's Recommendations

- HIV-2 infection should be considered in pregnant women who are from—or who have partners who are from—countries in which the virus 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 be negative for HIV-1 antibodies and positive for HIV-2 antibodies **(AII)**.
- Pregnant women with HIV-2 should be treated as per guidelines for HIV-1 mono-infection but using antiretroviral (ARV) drugs that are active against HIV-2. Non-nucleoside reverse transcriptase inhibitors and enfuvirtide are not active against HIV-2 and **should not be used (AIII)**.
- 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 (NRTIs) and integrase strand transfer inhibitors or certain boosted protease inhibitors is recommended for all pregnant women with HIV-2 infection **(AIII)**.
- Dolutegravir (irrespective of trimester), raltegravir, darunavir/ritonavir, or lopinavir/ritonavir plus a dual-NRTI backbone of abacavir plus lamivudine (3TC), or tenofovir disoproxil fumarate (TDF) plus emtricitabine or 3TC are recommended for treating HIV-2 mono-infection in pregnant women and in women trying to conceive **(AIII)**. Zidovudine (ZDV) plus 3TC can be used as an alternative dual-NRTI backbone. See Updated Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy in [Recommendations for Use of Antiretroviral Drugs During Pregnancy](#) and [Appendix C: Antiretroviral Counseling Guide for Health Care Providers: Pregnant Women and Women who are Trying to Conceive](#).
- As with HIV-1, the possibility of hepatitis B virus/HIV-2 coinfection should be considered when choosing an ARV regimen to treat HIV-2 **(AI)** (see [Hepatitis B Virus/HIV Coinfection](#)).
- All infants born to women with HIV-2 infection (who do not have HIV-1 infection) should receive the 4-week ZDV prophylactic regimen **(BIII)**.
- In the United States, where safe infant formula is readily available, breastfeeding **is not recommended** for infants born to mothers with HIV-2 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 infection is endemic in West African countries, including the Ivory Coast, Ghana, Cape Verde, The Gambia, Mali, Senegal, Liberia, Guinea, Burkina Faso, Nigeria, Mauritania, Sierra Leone, Guinea-Bissau, Niger, Sao Tome, and Togo. It is also endemic in Angola, Mozambique, and in parts of India.¹⁻⁴ It also occurs in countries such as France and Portugal, which have large numbers of immigrants from these regions.⁵

HIV-2 remains rare in the United States. According to the National HIV Surveillance System, there were 327,700 diagnoses of HIV in the United States from 2010 to 2017, of which 198 (0.06%) met the criteria for HIV-2 (HIV-2 mono-infection, n = 102; dual HIV-1 and HIV-2, n = 11; probable but unconfirmed HIV-2, n = 85).⁶ Among these cases, 99 women had diagnoses of confirmed or probable HIV-2, and nine of these women had evidence of pregnancy at or after their diagnosis. No perinatal HIV-2 transmissions were reported. HIV-2 infection should be suspected in pregnant women who are from—or who 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 immunoassay. If they have only HIV-2 infection, the test will be negative for HIV-1 antibodies and positive for HIV-2 antibodies. In rare instances, a woman may have dual infection with HIV-1 and HIV-2, and both tests will be positive.

In 2014, the Centers for Disease Control and Prevention (CDC) released a new HIV testing algorithm. The first step in that algorithm is performing an HIV-1/HIV-2 antigen/antibody combination assay on serum or plasma (e.g., Abbott Architect HIV Ag/Ab combo assay, BioRad GS Combo Ag/Ab EIA, Alere Determine).⁷ This test does not distinguish between HIV-1 antibodies and HIV-2 antibodies. Specimens that are reactive on this test must be tested with a Food and Drug Administration (FDA)-approved antibody assay to distinguish HIV-1 antibodies from HIV-2 antibodies. The FDA-approved HIV-2 antibody supplemental test Geenius (Bio-Rad Laboratories) is used as part of the CDC-recommended HIV laboratory testing algorithm.

Viral load assays for HIV-2 are not commercially available, but they may be available under research protocols. The [University of Washington](#)⁸ and the [New York State Department of Health, Wadsworth Center](#)⁹ also offer HIV-2 viral load assays. [The University of Washington accepts specimens forwarded from laboratories, such as Quest Diagnostics.](#) All HIV-2 cases should be reported to the HIV surveillance program of the state or local health department, which can arrange for additional confirmatory testing for HIV-2 by the CDC.¹⁰ No validated HIV-2 genotype or phenotype resistance assays are available in the United States. HIV-2 genotypic resistance assays are available for research use only at the University of Washington. European experts developed a rule set and an automated tool for HIV-2 drug resistance analyses that is freely [available online](#).¹¹

HIV-2 has a longer asymptomatic phase than HIV-1, with a slower progression to AIDS. However, without effective antiretroviral therapy (ART), HIV-2 will progress to AIDS and death in the majority of individuals over time.¹² The most common mode of HIV-2 transmission is through heterosexual sex. HIV-2 is less infectious than HIV-1, with a five-fold lower rate of sexual transmission and 20-fold to 30-fold lower rate of vertical transmission.^{3, 13, 14} Several studies confirm that rates of perinatal transmission of HIV-2 are low with and without interventions (0% to 4%), which may be a result of reduced plasma viral loads and less cervical viral shedding in women with HIV-2 than in women with HIV-1.¹⁵⁻¹⁸ HIV-2 also can be transmitted through breastfeeding. HIV-2 infection does not protect against HIV-1, and dual infection, which carries the same prognosis as HIV-1 mono-infection, can occur.¹⁹

Recommended Antiretroviral Therapy for Pregnant Women with HIV-2

Pregnant women with HIV-2 should be treated according to the guidelines for patients with HIV-1 mono-infection, though clinicians should make sure that the chosen antiretroviral (ARV) regimen is also appropriate for treatment of HIV-2. Once treatment is started, ART should be continued postpartum, as is recommended for all patients with HIV-1. A systematic review analyzed data collected from 1996 to 2012 on treatment outcomes among nonpregnant patients with HIV-2. The review reported a heterogeneity of treatment outcomes among patients who initiated ART, especially in resource-limited settings.²⁰ Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and enfuvirtide are not active against HIV-2 and **should not be used** for treatment or prophylaxis.^{21, 22} The integrase strand transfer inhibitors (INSTIs) raltegravir (RAL), elvitegravir, dolutegravir (DTG), and bictegravir are effective against HIV-2.^{23, 24} Although DTG may be able to rescue a failing RAL-based regimen in a person with HIV-2, a study has reported the emergence of DTG resistance mutations in people with HIV-2.²⁵ The CCR5 antagonist maraviroc appears to be active against some strains of HIV-2, although there are no approved assays to determine HIV-2 co-receptor tropism.^{26, 27} HIV-2 drug resistance has been documented with various ARV drugs.^{28, 29} Among 47 ART-naïve persons with HIV-2, ultradeep sequencing showed that three people displayed plasma viruses with a resistance-associated mutation (RAM) above the 20% detection threshold, with a prevalence of transmitted drug resistance for nucleoside reverse transcriptase inhibitors (NRTIs) of 7.9% (95% confidence interval, 0.0% to 16.5%). No RAM above the 20% detection

threshold was found for protease inhibitors (PIs) or INSTIs.³⁰

HIV-2 has variable susceptibility to PIs, with lopinavir (LPV), saquinavir, and darunavir (DRV) having the most activity.³¹

The care of pregnant women with HIV-2 mono-infection has been based on expert opinion. A regimen with two NRTIs and an INSTI or a ritonavir-boosted PI currently is recommended for all pregnant women with HIV-2. The following regimens can be used to treat HIV-2, based on the available efficacy and safety data on these drugs from clinical trials of pregnant women with HIV-1:

- DTG (irrespective of trimester), RAL, DRV/r, or LPV/r plus a dual-NRTI backbone of abacavir plus lamivudine (3TC), or tenofovir disoproxil fumarate (TDF) plus emtricitabine or 3TC are the recommended regimens for treating HIV-2 mono-infection in pregnant women and women trying to conceive. See Updated Panel Recommendations Regarding the Use of Dolutegravir in Pregnancy in [Recommendations for Use of Antiretroviral Drugs During Pregnancy](#) and [Appendix C: Antiretroviral Counseling Guide for Health Care Providers: Pregnant Women and Women who are Trying to Conceive](#).
- Zidovudine (ZDV) plus 3TC can be used as an alternative dual-NRTI backbone.
- NNRTIs **should not be used** because they are not active against HIV-2.

When monitoring the plasma viral loads and CD4 T lymphocyte (CD4) cell counts in pregnant women with HIV-2, clinicians should follow the guidelines outlined for people with HIV-1 (see [Monitoring of the Woman and Fetus During Pregnancy](#)). However, disease progression can occur in the setting of undetectable HIV-2 plasma viral load. Patients who have HIV-2 plasma viral loads that are below the limits of detection should still have routine CD4 counts and clinical monitoring (see [Plasma HIV-1 RNA \(Viral Load\) and CD4 Count Monitoring](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)).

There are no data to address whether treatment should be continued after pregnancy in women with HIV-2 mono-infection. To date, no randomized trials have addressed the question of an optimal treatment strategy for HIV-2 infection, although clinical trials are underway. The [Adult and Adolescent Antiretroviral Guidelines](#) recommend that all patients with HIV-2 should be treated using the guidelines provided for patients with HIV-1.

All infants born to mothers with HIV-2 (who do not have HIV-1) should receive a 4-week ZDV prophylaxis regimen, see [Table 8](#) and [Table 9](#). The possible risks and benefits of ARV prophylaxis should be discussed with the mothers. As noted above, rates of perinatal transmission of HIV-2 are low with and without interventions, and it is unclear whether infants born to women with undetectable HIV-2 viral loads will benefit from ARV prophylaxis. However, monitoring maternal HIV-2 plasma viral loads and receiving the results in a timely manner can be difficult, as plasma samples must be sent to the University of Washington or the New York State Department of Health. Therefore, the Panel recommends that all infants born to mothers with HIV-2 receive prophylaxis. The use of ZDV prophylaxis is recommended in this clinical situation because nevirapine lacks activity against HIV-2.

There are no data on the impact of scheduled cesarean delivery on HIV-2 perinatal transmission. The risk to infants from breastfeeding is lower for HIV-2 than for HIV-1, but breastfeeding should be avoided in the United States and other countries where safe infant formula is readily available.¹⁶

Infants born to mothers with HIV-2 should be tested for HIV-2 infection with HIV-2-specific virologic assays at time points similar to those used for HIV-1 testing, see [Diagnosis of HIV Infection in Infants and Children](#).³² Quantitative HIV-2 plasma RNA viral load testing for clinical care is available from the University of Washington⁸ and the New York State Department of Health.⁹ Antibody testing of infants (e.g., with the Bio-Rad Laboratories Multispot HIV-1/HIV-2 test) can also be performed at age 18 months to confirm clearance of HIV-2 antibodies.

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