

Pregnant People Who Have Not Achieved Viral Suppression on Antiretroviral Therapy

Updated: January 31, 2024

Reviewed: January 31, 2024

Panel's Recommendations
<ul style="list-style-type: none">Regular viral load monitoring is needed in pregnancy to quickly detect lack of viral suppression (AII). See Initial Evaluation and Continued Monitoring of HIV-Related Assessments During Pregnancy.To detect problems with viral suppression early, more frequent viral load monitoring (every 1–2 months) is recommended when individuals are receiving regimens associated with lower drug levels in the third trimester or drugs with limited or no pharmacokinetic (PK) data about use in pregnancy (AII). See Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive.When lack of suppression is identified, a thoughtful evaluation of potential contributing factors is needed, including barriers to adherence, drug resistance, drug-drug and drug-food interactions, PK changes in pregnancy that affect drug levels, and combinations of these factors. Viral suppression management should address each of these factors, if relevant (AII) (see Virologic Failure in the Adult and Adolescent Antiretroviral Guidelines). After these factors are addressed, repeat viral load monitoring within 2 to 4 weeks (AII).In general, adding a single antiretroviral drug to a virologically failing regimen is not recommended because this would rarely result in full virologic suppression and, therefore, may cause the development of resistance to one or more drugs in the regimen (BII).Consider consulting with an HIV treatment specialist when modifying ART due to inadequate viral suppression (BIII). Consultation is also available through the National Perinatal HIV hotline (1-888-448-8765).Discontinuing or briefly interrupting ART may lead to a rapid increase in HIV RNA, a decrease in CD4 T lymphocyte cell count, and an increase in the risk of perinatal HIV transmission and clinical progression. Therefore, this strategy is not recommended (AI). <p>Please see Intrapartum Care for People with HIV for guidance about use of intrapartum intravenous zidovudine prophylaxis and scheduled cesarean delivery for pregnant people who have not achieved viral suppression on ART.</p> <p>Rating of Recommendations: A = Strong; B = Moderate; C = Optional</p> <p>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</p>

Virologic suppression to undetectable levels is defined as a confirmed plasma HIV RNA level that is below the lower limits of detection of an ultrasensitive assay. Suppression of HIV RNA to undetectable levels should be achieved as rapidly as possible in pregnancy because viral load affects the risk of perinatal transmission, with the lowest risk associated with viral load <50 copies/mL.^{1,2} Baseline HIV RNA levels have been shown to affect the time to viral suppression in both pregnant and nonpregnant individuals, and no difference in time to viral response has been observed between pregnant and nonpregnant women.³⁻⁵

HIV RNA levels should be assessed regularly in pregnancy (see [Initial Evaluation and Continued Monitoring of HIV-Related Assessments During Pregnancy](#) for guidance on timing and frequency).

Physiologic changes that occur during pregnancy may result in lower levels of certain antiretrovirals (ARVs), resulting in loss of virologic control with the potential for perinatal transmission. To detect problems with viral suppression early, more frequent viral load monitoring (every 1–2 months) is recommended when individuals are receiving regimens associated with lower

drug levels in the third trimester or drugs with limited or no pharmacokinetic (PK) data about use in pregnancy (see [Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive](#)).

In the [Adult and Adolescent Antiretroviral Guidelines](#) for nonpregnant individuals, virologic failure is defined as the inability to achieve or maintain an HIV RNA level of <200 copies/mL (see [Virologic Failure](#)).⁶ Incomplete virologic response is defined as two consecutive HIV RNA level test results ≥200 copies/mL after 24 weeks on an ARV regimen in a patient who has not yet had documented virologic suppression on that regimen. Virologic rebound is defined as a confirmed HIV RNA level of ≥200 copies/mL after virologic suppression. During pregnancy or breastfeeding, any detectable viral load or, in some cases, a viral load >50 copies/mL is considered lack of viral suppression; these observations would indicate viral rebound if they occurred after viral suppression was achieved. If an HIV RNA level below the lower limit of detection of an ultrasensitive assay has not been achieved or viral rebound has occurred, causes of detectable viremia should be evaluated and addressed before considering a change in an ARV regimen.

For patients initiating or changing antiretroviral therapy (ART), HIV RNA is expected to decline fairly quickly, ideally achieving at least a 10-fold ($1 \log_{10}$) drop within 4 weeks. With the use of integrase strand transfer inhibitors (INSTIs) as part of an ARV regimen, the decline may be even faster (e.g., a decrease of approximately 100-fold [$2 \log_{10}$] in HIV RNA levels can be expected by week 2 of therapy).^{6,7} In the United Kingdom, a multicenter, retrospective observational study of women initiating ART during pregnancy found that higher baseline viral load was the only independent factor associated with faster first-phase HIV RNA half-life decay, and that lower viral load on day 14 after starting ART was associated with an increased likelihood of achieving an undetectable plasma viral load by 36 weeks gestation.⁸

Situations in which virologic suppression is not achieved (i.e., viral load is detectable) remain a common problem for pregnant people in the United States and globally. For example, a report from the HIV Outpatient Study noted that among 119 pregnancies between 2005 and 2015, 33 women (27.7%) were not virally suppressed (HIV RNA >500 copies/mL) at the end of pregnancy.⁹

Evaluating Factors Contributing to Detectable Viremia

Lack of virologic suppression is frequently associated with inadequate adherence. Other potential causes of detectable viremia include drug–drug interactions and lack of attention to food requirements with some ARV agents (e.g., rilpivirine [RPV], darunavir) that affect adequate drug absorption; concomitant administration or inadequate spacing of vitamins or foods containing calcium or iron (e.g., dolutegravir, bictegravir, raltegravir, elvitegravir; see [Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy](#)); and overall poor tolerability of the ARV drug, exacerbated by nausea and vomiting associated with pregnancy or hyperemesis gravidarum.

Barriers to adherence should be addressed when the viral load does not decline as expected (see [Adherence to the Continuum of Care](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)). A systematic review and meta-analysis of ART adherence during and after pregnancy in low-, middle-, and high-income countries (27% of studies were from the United States) found that only 73.5% of pregnant women achieved adequate (>80%) ART adherence.¹⁰ Factors that can contribute to suboptimal adherence in pregnancy include depression and other mental health disorders, barriers to HIV seropositive status disclosure, adverse drug reactions, a history of intimate partner violence,

substance use, a lack of prior experience with taking ART, and a lack of knowledge about the role of ART in preventing perinatal transmission.¹¹⁻¹³ Other factors that have been associated with lack of viral suppression in pregnancy, and are likely associated with difficulties with adherence, include unintended pregnancy and social and economic vulnerabilities (e.g., living in the United States for less than 5 years with no family/friends' support, neighborhood exposures to crime), as well as poor engagement in prenatal care.¹⁴⁻¹⁶

A retrospective study of 318 pregnant women addressed the risk of a viral rebound **to HIV RNA >50 copies/mL** in pregnancy among women who received ART for ≥ 4 weeks and who had had one or more prior undetectable viral load test result. Nineteen women (6%) had **a** viral rebound (HIV RNA >50 copies/mL) within 1 month before delivery; 6 of these 19 women had viral loads above 1,000 copies/mL. Significant predictors of viral rebound included cocaine use and testing positive for hepatitis C virus RNA.¹⁷ Viral load testing is currently recommended at 34 to 36 weeks gestation for delivery planning; providers may consider repeat testing subsequently in selected patients who are at increased risk for viral rebound. Risk for viral rebound may be greater in people receiving regimens with PK concerns for lower drug levels in late pregnancy (e.g., cobicistat-boosted regimens and RPV) (see [Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs and People Taking Antiretrovirals When They Become Pregnant](#)).

The lack of virologic suppression by late pregnancy may indicate virologic failure, but it may also represent inadequate time on ART for people who initiated ART in pregnancy. Among 1,070 ART-naive pregnant women with HIV who participated in the prospective cohort study International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT) P1025, initiating **three-drug ART at >32 weeks gestation (with a protease inhibitor– or non-nucleoside inhibitor–based regimen or a nucleoside transcriptase inhibitor–only regimen)** also was associated with a significantly higher risk of having a viral load >400 copies/mL at delivery.¹⁸ A recent cross-sectional analysis of 10,052 pregnant women with HIV receiving antenatal care in public facilities in South Africa reported that failure to achieve viral suppression (HIV RNA <50 copies/mL) was associated primarily with late registration for antenatal care and late initiation of ART.¹⁹ In the French Perinatal Cohort of 14,630 women with HIV and delivering from 2000 to 2017, both HIV RNA level at delivery and timing of ART initiation were independently associated with risk of perinatal transmission of HIV.¹

Pregnant people with acute HIV generally have high viral loads and may take longer than nonpregnant people to achieve viral suppression (see [Early \[Acute and Recent\] HIV Infection](#)).

Pregnant people with perinatally acquired HIV may also face additional barriers to adherence and virologic suppression. Several studies from the United States and Europe have demonstrated that among pregnant people, perinatally acquired HIV is a risk factor for detectable viral load near the time of delivery and a higher perinatal transmission rate than non-perinatally acquired HIV.^{20,21} If needed, ARV regimens should be optimized in consultation with HIV treatment experts, and other possible contributing factors should be considered (see [Prenatal Care, Antiretroviral Therapy, and HIV Management in People with Perinatally Acquired HIV Infection](#)).

Managing Lack of Viral Suppression

A three-pronged approach is indicated for evaluating and managing pregnant people on ART who have lack of suppression of HIV RNA, taking time on treatment into account. The approaches include the following—

- Assessing adherence, tolerability, correct dosing, or potential problems with absorption (e.g., nausea/vomiting, use of gastroesophageal reflux disease medications, coadministration of prenatal vitamins and iron with INSTIs,^{22,23} lack of attention to food requirements); Ordering ARV drug-resistance tests should be considered before changing regimens if plasma HIV RNA levels >200 copies/mL while on the current regimen. For people with confirmed HIV have RNA levels >200 copies/mL but <500 copies/mL, drug-resistance testing may be unsuccessful but should still be considered; *and*
- Considering modifying the ARV regimen (see [People with HIV Who Are Taking Antiretroviral Therapy When They Become Pregnant](#), [Table 7. Situation-Specific Recommendations for Use of Antiretroviral Drugs in Pregnant People and Nonpregnant People Who Are Trying to Conceive](#), and [Virologic Failure](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)) *and*
- Repeating viral load monitoring within 2 to 4 weeks after relevant factors contributing to detectable viral load are addressed.

Evaluation of and support for adherence during pregnancy are critical to achieving and maintaining maximal viral suppression. Pre-pregnancy counseling and family planning services should be promoted and accessible to reduce unintended pregnancy, help those with HIV achieve their childbearing aspirations, *and provide an important opportunity to support ART adherence*. Early attention to the special need for adherence support among immigrant communities affected by HIV and other communities with adverse neighborhood exposures is also critical to achieving and maintaining maximal viral suppression. In a retrospective cohort study at a Texas community center, group prenatal care for pregnant women with HIV, as compared to individual care, showed promise in achieving viral suppression by the time of delivery (adjusted odds ratio 2.29; 95% confidence interval [CI], 0.94–5.55; $P = 0.068$).²⁴ Other possible interventions include adherence education, treating problems that may interfere with drug absorption (e.g., vomiting), ensuring that a patient is taking ART in accordance with food requirements (see [Table 14. Antiretroviral Drug Use in Pregnant People with HIV: Pharmacokinetic and Toxicity Data in Human Pregnancy and Recommendations for Use in Pregnancy](#)), and directly observing drug administration in the home or hospital setting.²⁵

When considering altering an ARV regimen because viral suppression targets have not been reached, resistance testing should be performed while the pregnant person is still taking their current regimen (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)). Resistance testing generally can be performed when HIV RNA levels are >500 copies/mL. For HIV RNA >200 to <500 copies/mL, drug-resistance testing may be unsuccessful but should still be considered. The results can be used to select a new ARV regimen with a greater likelihood of suppressing viral replication to undetectable levels. For patients with current or prior INSTI exposure, INSTI resistance testing in addition to standard genotype testing should be obtained.

The [Adult and Adolescent Antiretroviral Guidelines](#) offer specific regimen modifications for situations in which viral suppression has not been achieved or where there has been a rebound of viral load (see [Virologic Failure](#)).

In addition, when poor adherence is the reason that the patient has not achieved or maintained virologic suppression, it is unclear whether adding a new drug to the existing regimen will improve adherence. *In general, adding a single ARV drug to a virologically failing regimen is not recommended because this would rarely result in full virologic suppression and, therefore, may risk the development of resistance to one or more drugs in the regimen.*

Before modifying an ARV regimen, consultation with a specialist in clinical care for ARV-experienced adults is recommended (e.g., the [National Perinatal HIV](#) hotline at 1-888-448-8765). This is particularly important in cases where a drug regimen must be modified due to resistance or adverse effects. Regimen simplification may be considered to promote better adherence.

Finally, discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA, a decrease in CD4 T lymphocyte cell count, and an increase in the risk of perinatal transmission and clinical progression.²⁶⁻²⁸ Therefore, this strategy **is not recommended** in the setting of virologic failure.

References

1. Sibiude J, Le Chenadec J, Mandelbrot L, et al. Update of perinatal human immunodeficiency virus type 1 transmission in France: zero transmission for 5,482 mothers on continuous antiretroviral therapy from conception and with undetectable viral load at delivery. *Clin Infect Dis.* 2023;76(3):e590-e598. Available at: <https://pubmed.ncbi.nlm.nih.gov/36037040>.
2. Townsend CL, Byrne L, Cortina-Borja M, et al. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000–2011. *AIDS.* 2014;28(7):1049-1057. Available at: <https://pubmed.ncbi.nlm.nih.gov/24566097>.
3. Read PJ, Mandalia S, Khan P, et al. When should HAART be initiated in pregnancy to achieve an undetectable HIV viral load by delivery? *AIDS.* 2012;26(9):1095-1103. Available at: <https://pubmed.ncbi.nlm.nih.gov/22441248>.
4. Rachas A, Warszawski J, Le Chenadec J, et al. Does pregnancy affect the early response to cART? *AIDS.* 2013;27(3):357-367. Available at: <https://pubmed.ncbi.nlm.nih.gov/23079802>.
5. Kourtis AP, Wiener J, King CC, et al. Effect of pregnancy on response to antiretroviral therapy in HIV-infected African women. *J Acquir Immune Defic Syndr.* 2017;74(1):38-43. Available at: <https://pubmed.ncbi.nlm.nih.gov/27787340>.
6. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. 2023. Available at: <https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/whats-new>.
7. Rahangdale L, Cates J, Potter J, et al. Integrase inhibitors in late pregnancy and rapid HIV viral load reduction. *Am J Obstet Gynecol.* 2016;214(3):385 e381-387. Available at: <https://pubmed.ncbi.nlm.nih.gov/26928154>.
8. Alagaratnam J, Peters H, Francis K, et al. An observational study of initial HIV RNA decay following initiation of combination antiretroviral treatment during pregnancy. *AIDS Res Ther.* 2020;17(1):41. Available at: <https://pubmed.ncbi.nlm.nih.gov/32660502>.
9. Patel M, Tedaldi E, Armon C, et al. HIV RNA suppression during and after pregnancy among women in the HIV outpatient study, 1996 to 2015. *J Int Assoc Provid AIDS Care.* 2018;17:2325957417752259. Available at: <https://pubmed.ncbi.nlm.nih.gov/29357772>.
10. Nachega JB, Uthman OA, Anderson J, et al. Adherence to antiretroviral therapy during and after pregnancy in low-income, middle-income, and high-income countries: a systematic review and meta-analysis. *AIDS.* 2012;26(16):2039-2052. Available at: <https://pubmed.ncbi.nlm.nih.gov/22951634>.

11. Yee LM, Crisham Janik M, Dorman RM, et al. Relationship between intimate partner violence and antiretroviral adherence and viral suppression in pregnancy. *Sex Reprod Healthc.* 2018;17:7-11. Available at: <https://pubmed.ncbi.nlm.nih.gov/30193723>.
12. Mills JC, Pence BW, Edmonds A, et al. The impact of cumulative depression along the HIV care continuum in women living with HIV during the era of universal antiretroviral treatment. *J Acquir Immune Defic Syndr.* 2019;82(3):225-233. Available at: <https://pubmed.ncbi.nlm.nih.gov/31335585>.
13. Brittain K, Mellins CA, Remien RH, et al. Impact of HIV-status disclosure on HIV viral load in pregnant and postpartum women on antiretroviral therapy. *J Acquir Immune Defic Syndr.* 2019;81(4):379-386. Available at: <https://pubmed.ncbi.nlm.nih.gov/30939530>.
14. Dude AM, Miller ES, Garcia PM, Yee LM. Unintended pregnancy and viral suppression in pregnant women living with HIV. *Am J Obstet Gynecol MFM.* 2021;3(2):100300. Available at: <https://pubmed.ncbi.nlm.nih.gov/33359637>.
15. Momplaisir FM, Nassau T, Moore K, et al. Association of adverse neighborhood exposures with HIV viral load in pregnant women at delivery. *JAMA Netw Open.* 2020;3(11):e2024577. Available at: <https://pubmed.ncbi.nlm.nih.gov/33156348>.
16. Premkumar A, Yee LM, Benes L, Miller ES. Social vulnerability among foreign-born pregnant women and maternal virologic control of HIV. *Am J Perinatol.* 2020;38(8):753-758. Available at: <https://pubmed.ncbi.nlm.nih.gov/33368072>.
17. Boucoiran I, Albert AYK, Tulloch K, et al. Human immunodeficiency virus viral load rebound near delivery in previously suppressed, combination antiretroviral therapy-treated pregnant women. *Obstet Gynecol.* 2017;130(3):497-501. Available at: <https://pubmed.ncbi.nlm.nih.gov/28796673>.
18. Katz IT, Leister E, Kacanek D, et al. Factors associated with lack of viral suppression at delivery among highly active antiretroviral therapy-naïve women with HIV: a cohort study. *Ann Intern Med.* 2015;162(2):90-99. Available at: <https://pubmed.ncbi.nlm.nih.gov/25599347>.
19. Woldesenbet SA, Kufa T, Barron P, et al. Viral suppression and factors associated with failure to achieve viral suppression among pregnant women in South Africa. *AIDS.* 2020;34(4):589-597. Available at: <https://pubmed.ncbi.nlm.nih.gov/31821189>.
20. Byrne L, Sconza R, Foster C, et al. Pregnancy incidence and outcomes in women with perinatal HIV infection. *AIDS.* 2017;31(12):1745-1754. Available at: <https://pubmed.ncbi.nlm.nih.gov/28590327>.
21. Goodenough CJ, Patel K, Van Dyke RB, Pediatric HIV AIDS Cohort Study. Is there a higher risk of mother-to-child transmission of HIV among pregnant women with

- perinatal HIV infection? *Pediatr Infect Dis J.* 2018;37(12):1267-1270. Available at: <https://pubmed.ncbi.nlm.nih.gov/29742647>.
22. Bordes C, Leguelinel-Blache G, Lavigne JP, et al. Interactions between antiretroviral therapy and complementary and alternative medicine: a narrative review. *Clin Microbiol Infect.* 2020;26(9):1161-1170. Available at: <https://pubmed.ncbi.nlm.nih.gov/32360208>.
23. Federspiel J, Bukhari MJ, Hamill MM. Interactions between highly active antiretroviral therapy and over-the-counter agents: a cautionary note. *BMJ Case Rep.* 2021;14(1). Available at: <https://pubmed.ncbi.nlm.nih.gov/33408101>.
24. McKinney J, Jackson J, Sangi-Haghpeykar H, et al. HIV-adapted group prenatal care: assessing viral suppression and postpartum retention in care. *AIDS Patient Care STDS.* 2021;35(2):39-46. Available at: <https://pubmed.ncbi.nlm.nih.gov/33571047>.
25. McCabe CJ, Goldie SJ, Fisman DN. The cost-effectiveness of directly observed highly-active antiretroviral therapy in the third trimester in HIV-infected pregnant women. *PLoS One.* 2010;5(4):e10154. Available at: <https://pubmed.ncbi.nlm.nih.gov/20405011>.
26. Deeks SG, Wrin T, Liegler T, et al. Virologic and immunologic consequences of discontinuing combination antiretroviral-drug therapy in HIV-infected patients with detectable viremia. *N Engl J Med.* 2001;344(7):472-480. Available at: <https://pubmed.ncbi.nlm.nih.gov/11172188>.
27. Lawrence J, Mayers DL, Hullsieck KH, et al. Structured treatment interruption in patients with multidrug-resistant human immunodeficiency virus. *N Engl J Med.* 2003;349(9):837-846. Available at: <https://pubmed.ncbi.nlm.nih.gov/12944569>.
28. Strategies for Management of Antiretroviral Therapy Study Group, El-Sadr WM, Lundgren JD, et al. CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med.* 2006;355(22):2283-2296. Available at: <https://pubmed.ncbi.nlm.nih.gov/17135583>.