

## Prenatal Care, Antiretroviral Therapy, and HIV Management in People with Perinatal-Acquired HIV Infection

(Last updated December 30, 2021; last reviewed December 30, 2021)

Panel's Recommendations
<ul style="list-style-type: none"><li>• The management of prenatal care and general principles of antiretroviral therapy (ART) and HIV management do not differ between pregnant people with perinatally-acquired HIV (PHIV) and those with non-perinatally acquired HIV (<b>AII</b>).</li><li>• Using the same guiding principles that are used for heavily ART-experienced adults, optimal ARV regimens should be selected based on resistance testing, ART treatment history, and pill burden (<b>AII</b>).</li><li>• 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 (<b>AIII</b>).</li><li>• Pregnant people with PHIV warrant enhanced focus on adherence interventions during pregnancy and after delivery (<b>AII</b>).</li></ul>
<p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional</p> <p><b>Rating of Evidence:</b> 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>

With the availability of potent antiretroviral therapy (ART), morbidity and mortality have significantly declined in individuals with HIV, including those with perinatally-acquired HIV (PHIV). Most of the women with PHIV have reached childbearing age, and many are becoming pregnant. A significant number of these pregnancies are unplanned.<sup>1-3</sup> The components of prenatal care and general principles of ART and HIV management do not differ between pregnant people with PHIV and those with non-perinatally acquired HIV (NPHIV), who acquired HIV through other routes of transmission. However, the reproductive health care needs and the prevention of perinatal transmission in people with PHIV pose unique challenges. Adherence to ART is often a major challenge for people with PHIV. In addition, because most of them are still adolescents and young adults, they may be at higher risk of certain pregnancy complications, such as preterm delivery, small-for-gestational-age (SGA) infants, low birth weight, and preeclampsia.<sup>4-9</sup> However, in some studies, the risk of premature delivery tends to be similar among women with PHIV and women with NPHIV after adjusting for age.<sup>10</sup>

Because women with PHIV have extensive ART experience,<sup>8</sup> optimal antiretroviral (ARV) regimens should be selected using the same guiding principles as for ART-experienced adults; in particular, the ARV regimen should be selected on the basis of resistance testing, pill burden, and the patient's specific ART history and preferences. Because individuals who acquired HIV perinatally have the potential to develop complex drug-resistance mutation patterns, clinicians may consider performing phenotypic resistance testing when resistance testing is indicated during pregnancy. Regimens that optimize dosing intervals and minimize pill burden should be considered. Regimens should be constructed using ARV drugs that are recommended for use in pregnancy whenever possible. However, in many cases, the presence of extensive drug resistance may warrant the use of ARV

drugs for which there is limited experience in pregnancy; consultation with experts in HIV and pregnancy is recommended in such cases.

People with PHIV experience prolonged HIV infection, have received multiple ARV regimens—including suboptimal monotherapy or dual-therapy regimens received as children—and are more likely to harbor drug-resistant virus. As many as 30% to 70% of pregnant women with PHIV have evidence of HIV drug resistance.<sup>8,11–13</sup> Despite these factors, many studies have shown that the risk of perinatal transmission does not appear to be increased in this population, as long as these women receive appropriate prenatal management and achieve viral suppression.<sup>8,13–18</sup> However, in an analysis of data from SMARTT PHACS (Surveillance Monitoring for ART Toxicities Study—Pediatric HIV/AIDS Cohort Study) that included 2,123 births from 2007 to 2015, pregnant women with PHIV had a higher perinatal HIV transmission rate (1.1%; 95% confidence interval [CI], 0.3% to 4.3%) than pregnant women with NPHIV (0.4%; 95% CI, 0.2% to 1.0%); this higher rate was associated with a greater likelihood of detectable maternal viral load at delivery.<sup>19</sup> Women with PHIV are more likely to have detectable viral loads at delivery, lower CD4 T lymphocyte counts, and genotypic drug resistance than women with NPHIV; these factors can have implications during labor and delivery.<sup>8,13,16,19,20</sup> Several studies have suggested that pregnant women with PHIV are more likely to have a cesarean delivery in order to prevent HIV transmission; cesarean deliveries are most commonly indicated in these women due to a lack of viral load suppression.<sup>11,16</sup> Cesarean delivery in these young people raises concerns for increased risk of adverse obstetric outcomes if repeated cesarean deliveries are required for future pregnancies.

Evidence from studies is conflicting as to whether women with PHIV have higher rates of preterm and SGA infants than women with NPHIV.<sup>21–23</sup> Several studies have demonstrated no associations between perinatally-acquired HIV status and preterm birth, SGA infants, or low birth weight.<sup>8,13,21,22,24</sup> Other studies with smaller sample sizes have reported conflicting results:

- A case series reported high rates of preterm birth (31%) among women with PHIV.<sup>11</sup>
- Jao et al. reported a fourfold increased risk for SGA births among women with PHIV compared to those with NPHIV.<sup>9</sup>
- Munjal et al. reported earlier gestational age at delivery and lower average birth weights in infants born to women with PHIV compared to those with NPHIV.<sup>16</sup>

Women with PHIV also have poor rates of retention in care and viral suppression for up to 2 years postpartum.<sup>25</sup> In a retrospective analysis of 37 pregnancies among women with PHIV and 40 pregnancies among age-matched women with NPHIV who delivered during the same time period, the viral load declines achieved during pregnancy in women with PHIV were not sustained during postpartum follow-up, in contrast to the age-matched comparison group. Another study found that, during 4 years of follow-up postpartum, there were four deaths due to AIDS-related complications among women with PHIV but none among the women with NPHIV.<sup>16</sup> Although genotypic mutations were more common in women with PHIV, loss of viral suppression that resulted in postpartum disease progression was more likely to be related to adherence difficulties, highlighting the need for adherence interventions after delivery.

Psychosocial challenges in PHIV may be magnified by the presence of a lifelong chronic illness, high rates of depression,<sup>26</sup> and, frequently, the loss of one or both parents. Attention to developmentally appropriate adherence counseling is critical. A systematic review and meta-analysis of 50 eligible studies on ART adherence in individuals with HIV aged 12 years to 24 years old

reported 62.3% adherence overall among youth with HIV. Youth from U.S. studies had the lowest average rate of adherence at 53%.<sup>27</sup> In a 2014 study of 1,596 people with PHIV who were living in New York City, only 61% were virally suppressed. The authors attributed poor ART adherence to social, behavioral, and developmental factors.<sup>28</sup> A history of depression also has been associated with nonadherence to ART among pregnant women with PHIV.<sup>29,30</sup> Focused attention on diagnosis and treatment of depression during the preconception period may lead to better medication adherence. Self-motivation and social support were key to achieving medication adherence in a study of adolescents with HIV in the United Kingdom.<sup>31</sup>

Studies have noted reduced rates of retention in care and viral suppression among pediatric and adolescent persons with HIV who are transitioning to adult health care.<sup>32</sup> Among adolescents with PHIV, pregnancy may create additional complications in the transition from pediatric/adolescent HIV care to adult care due to the complexity of navigating an adult health care system with multiple providers. However, pregnancy also may be an opportune time for a young person to transition to adult care. There is a need to identify, develop or adapt, and implement culturally sensitive and women- and patient-centered interventions for improving HIV care continuum outcomes of pregnant and postpartum people with HIV.<sup>33</sup> Coordination of care across multiple disciplines, including HIV primary care, OB/GYN, and perinatal case management, is advised.<sup>34</sup> Integration of reproductive health counseling and family planning services—including consistent counseling on condom use, sexually transmitted infection testing and prevention, optimal pregnancy spacing, and developmentally appropriate skill building to support disclosure—as indicated, is recommended.

## References

1. Kenny J, Williams B, Prime K, Tookey P, Foster C. Pregnancy outcomes in adolescents in the UK and Ireland growing up with HIV. *HIV Med.* 2012;13(5):304-308. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22136754>.
2. Brogly SB, Ylitalo N, Mofenson LM, et al. *In utero* nucleoside reverse transcriptase inhibitor exposure and signs of possible mitochondrial dysfunction in HIV-uninfected children. *AIDS.* 2007;21(8):929-938. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17457086>.
3. Badell ML, Lindsay M. Thirty years later: pregnancies in females perinatally infected with human immunodeficiency virus-1. *AIDS Res Treat.* 2012;2012:418630. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22970353>.
4. Ganchimeg T, Ota E, Morisaki N, et al. Pregnancy and childbirth outcomes among adolescent mothers: a World Health Organization multicountry study. *BJOG.* 2014;121 Suppl 1:40-48. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24641534>.
5. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980–2010: age-period-cohort analysis. *BMJ.* 2013;347:f6564. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24201165>.
6. Witt WP, Cheng ER, Wisk LE, et al. Preterm birth in the United States: the impact of stressful life events prior to conception and maternal age. *Am J Public Health.* 2014;104 Suppl 1:S73-80. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24354830>.
7. Jao J, Agwu A, Mhango G, et al. Growth patterns in the first year of life differ in infants born to perinatally vs. nonperinatally HIV-infected women. *AIDS.* 2015;29(1):111-116. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25562495>.
8. Badell ML, Kachikis A, Haddad LB, Nguyen ML, Lindsay M. Comparison of pregnancies between perinatally and sexually HIV-infected women: an observational study at an urban hospital. *Infect Dis Obstet Gynecol.* 2013;2013:301763. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24106419>.
9. Jao J, Sigel KM, Chen KT, et al. Small for gestational age birth outcomes in pregnant women with perinatally acquired HIV. *AIDS.* 2012;26(7):855-859. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/22313958>.
10. Lundberg P, Andersson R, Machado ES, Costa TPD, Hofer CB. Pregnancy outcomes in young mothers with perinatally and behaviorally acquired HIV infections in Rio de Janeiro. *Braz J Infect Dis.* 2018;22(5):412-417. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/30339778>.
11. Williams SF, Keane-Tarchichi MH, Bettica L, Dieudonne A, Bardeguez AD. Pregnancy outcomes in young women with perinatally acquired human immunodeficiency virus-1. *Am J Obstet Gynecol.* 2009;200(2):149 e141-145. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/18973871>.

12. Cruz ML, Santos E, Benamor Teixeira Mde L, et al. Viral suppression and resistance in a cohort of perinatally-HIV infected (PHIV+) pregnant women. *Int J Environ Res Public Health*. 2016;13(6). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27338425>.
13. Lazenby GB, Mmeje O, Fisher BM, et al. Antiretroviral resistance and pregnancy characteristics of women with perinatal and nonperinatal HIV infection. *Infect Dis Obstet Gynecol*. 2016;2016:4897501. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27413359>.
14. Phillips UK, Rosenberg MG, Dobroszycki J, et al. Pregnancy in women with perinatally acquired HIV-infection: outcomes and challenges. *AIDS Care*. 2011;23(9):1076-1082. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21562997>.
15. Calitri C, Gabiano C, Galli L, et al. The second generation of HIV-1 vertically exposed infants: a case series from the Italian Register for paediatric HIV infection. *BMC Infect Dis*. 2014;14:277. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24885649>.
16. Munjal I, Dobroszycki J, Fakioglu E, et al. Impact of HIV-1 infection and pregnancy on maternal health: comparison between perinatally and behaviorally infected young women. *Adolesc Health Med Ther*. 2013;4:51-58. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24600295>.
17. Millery M, Vazquez S, Walther V, Humphrey N, Schlecht J, Van Devanter N. Pregnancies in perinatally HIV-infected young women and implications for care and service programs. *J Assoc Nurses AIDS Care*. 2012;23(1):41-51. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/21820325>.
18. Patel K, Karalius B, Powis K, et al. Trends in post-partum viral load among women living with perinatal HIV infection in the USA: a prospective cohort study. *Lancet HIV*. 2020;7(3):e184-e192. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/31870676>.
19. 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://www.ncbi.nlm.nih.gov/pubmed/29742647>.
20. Byrne L, Sconza R, Foster C, Tookey PA, Cortina-Borja M, Thorne C. Pregnancy incidence and outcomes in women with perinatal HIV infection. *AIDS*. 2017;31(12):1745-1754. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28590327>.
21. Hleyhel M, Tubiana R, Rouzioux C, et al. Pregnancies in women who acquired HIV perinatally. Presented at: Conference on Retroviruses and Opportunistic Infections 2017. Seattle, WA.
22. Jao J, Kacanek D, Williams P, et al. Birth weight and preterm delivery outcomes of perinatally vs. non-perinatally HIV-infected pregnant women in the U.S.: results from the PHACS SMARTT study and IMPAACT P1025 protocol. *CID*. [In Press]. 2017.
23. Jao J, Kacanek D, Yu W, et al. Neurodevelopment of HIV-exposed uninfected infants born to women with perinatally acquired HIV in the United States. *J Acquir Immune Defic Syndr*. 2020;84(2):213-219. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/32032301>.

24. Agwu AL, Jang SS, Korthuis PT, Araneta MR, Gebo KA. Pregnancy incidence and outcomes in vertically and behaviorally HIV-infected youth. *JAMA*. 2011;305(5):468-470. Available at: <https://pubmed.ncbi.nlm.nih.gov/21285423/>.
25. Meade CM, Hussen SA, Momplaisir F, Badell M, Hackett S, Sheth AN. Long term engagement in HIV care among postpartum women with perinatal HIV infection in the United States. *AIDS Care*. 2018;30(4):488-492. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29254363>.
26. Mellins CA, Brackis-Cott E, Dolezal C, Abrams EJ. Psychiatric disorders in youth with perinatally acquired human immunodeficiency virus infection. *Pediatr Infect Dis J*. 2006;25(5):432-437. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16645508>.
27. Kim SH, Gerver SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. *AIDS*. 2014;28(13):1945-1956. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24845154>.
28. Xia Q, Shah D, Gill B, Torian LV, Braunstein SL. Continuum of care among people living with perinatally acquired HIV infection in New York City, 2014. *Public Health Rep*. 2016;131(4):566-573. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27453601>.
29. Sheth SS, Coleman J, Cannon T, et al. Association between depression and nonadherence to antiretroviral therapy in pregnant women with perinatally acquired HIV. *AIDS Care*. 2015;27(3):350-354. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25616659>.
30. Angrand RC, Sperling R, Roccobono K, Osborne LM, Jao J. Depression in perinatally HIV-infected pregnant women compared to non-perinatally HIV-infected and HIV-uninfected pregnant women. *AIDS Care*. 2018;30(9):1168-1172. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29776314>.
31. Kim SH, McDonald S, Kim S, Foster C, Fidler S. Importance of self-motivation and social support in medication adherence in HIV-infected adolescents in the United Kingdom and Ireland: a multicentre HYPNet Study. *AIDS Patient Care STDS*. 2015;29(6):354-364. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25825814>.
32. Hatfield-Timajchy K, Brown JL, Haddad LB, Chakraborty R, Kourtis AP. Parenting among adolescents and young adults with human immunodeficiency virus infection in the United States: challenges, unmet needs, and opportunities. *AIDS Patient Care STDS*. 2016;30(7):315-323. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27410495>.
33. Momplaisir FM, Storm DS, Nkwihoreze H, Jayeola O, Jemmott JB. Improving postpartum retention in care for women living with HIV in the United States. *AIDS*. 2018;32(2):133-142. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29194122>.
34. Anderson EA, Momplaisir FM, Corson C, Brady KA. Assessing the Impact of perinatal HIV case management on outcomes along the HIV care continuum for pregnant and postpartum women living with HIV, Philadelphia 2005–2013. *AIDS Behav*. 2017;21(9):2670-2681. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28176167>.