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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Lessons from International Clinical Trials of Short-Course Antiretroviral Regimens for Prevention of Perinatal Transmission of HIV (Last updated July 31, 2012; last reviewed July 31, 2012)

A number of regimens have been identified that are effective in reducing perinatal transmission in resource-limited countries (see Table 3). In many cases, direct comparison of results from trials of these regimens is not possible because the studies involved diverse patient populations residing in different geographic locations, infected with diverse viral subtypes, and with different infant feeding practices. However, some generalizations are relevant to understanding use of antiretroviral (ARV) drugs for prevention of perinatal transmission in both resource-limited and resource-rich countries.

Combination antenatal prophylaxis taken over a longer duration is more effective than a short-course single-drug regimen in reducing perinatal transmission.

The use of ARV drugs to prevent transmission is highly effective, even in HIV-infected women with advanced disease.[1, 2] Efficacy has been demonstrated for a number of short-course ARV regimens, including those with zidovudine alone; zidovudine plus lamivudine; single-dose nevirapine; and single-dose nevirapine combined with either short-course zidovudine or zidovudine/lamivudine.[3-12] In general, combination regimens are more effective than single-drug regimens in reducing perinatal transmission. In addition, for prevention of perinatal transmission, administration of ARV drugs during the antepartum, intrapartum, and postpartum periods is superior to administration of ARV drugs only during the antepartum and intrapartum periods or intrapartum and postpartum periods.[4, 13, 14]

Almost all trials in resource-limited countries have included oral intrapartum prophylaxis, with varying durations of maternal antenatal and/or infant (and sometimes maternal) postpartum prophylaxis. Perinatal transmission is reduced by regimens with antenatal components starting as late as 36 weeks' gestation and lacking an infant prophylaxis component.[9-11] However, longer duration antenatal ARV prophylaxis (starting at 28 weeks' gestation) is more effective than shorter duration ARV prophylaxis (starting at 36 weeks' gestation), suggesting that a significant proportion of *in utero* transmission occurs between 28 and 36 weeks' gestation.[12] Analyses from the European National Study of HIV in Pregnancy and Childhood have shown that efficacy is increased with even longer duration antenatal ARV prophylaxis (starting before 28 weeks' gestation), with each additional week of a triple-drug regimen corresponding to a 10% reduction in risk of transmission after adjustment for viral load, mode of delivery, and sex of the infant.[15] More prolonged infant post-exposure prophylaxis does not appear to substitute for longer duration maternal ARV prophylaxis.[12]

No trials have directly compared the efficacy of zidovudine plus single-dose nevirapine with a triple-drug ARV regimen for prevention of *in utero* transmission in women with higher CD4 T-lymphocyte (CD4-cell) counts. In African women with CD4-cell counts ranging from 200 to 500 cells/mm^3, the Kesho Bora trial compared a triple-ARV drug prophylaxis regimen with zidovudine plus single-dose nevirapine prophylaxis, both started at 28 weeks' gestation or later. The women in the triple-drug arm continued the drugs until breastfeeding ceased, but those in the zidovudine/single-dose nevirapine arm did not receive postnatal prophylaxis. Although the rate of postnatal transmission was significantly lower in the triple-drug arm than in the zidovudine/single-dose nevirapine arm without postnatal prophylaxis, the rates of transmission at birth were similar in women randomized to a triple-drug regimen (1.8%) and women randomized to antepartum zidovudine/single-dose nevirapine (2.5%); for women with CD4-cell counts from 350 to 500 cells/mm^3, the rate of infection at birth was 1.7% in each arm.[16] However, the study was not powered to address equivalence between regimens in preventing *in utero* infection in women with higher CD4-cell counts and the drugs in both arms were administered antepartum for only 6 weeks.

Regimens that do not include maternal ARV prophylaxis during pregnancy have been evaluated because some women may lack antenatal care and present for prenatal care for the first time when they go into labor.

Regimens that include only intrapartum and postpartum drug administration also have been shown to be effective in reducing perinatal transmission.[3-5] However, without continued infant post-exposure prophylaxis, intrapartum pre-exposure prophylaxis alone with nucleoside reverse transcriptase inhibitor drugs (zidovudine/lamivudine) is not effective in reducing transmission.[4] The SAINT trial demonstrated that intrapartum/postpartum zidovudine/lamivudine and single-dose intrapartum/newborn nevirapine are similar in efficacy and safety.[5]

Combination infant ARV prophylaxis is recommended in the United States for infants whose mothers have not received antenatal ARV drugs.

In some situations, it may be impossible to administer maternal antepartum and intrapartum therapy and only infant prophylaxis may be an option. In the absence of maternal therapy, the standard infant prophylaxis regimen of 6 weeks of zidovudine was effective in reducing HIV transmission compared with no prophylaxis, based on epidemiologic data in resource-rich countries.[17] A trial in Malawi in breastfeeding infants demonstrated that adding 1 week of zidovudine therapy to infant single-dose nevirapine reduced risk of transmission by 36% compared with infant single-dose nevirapine alone.[6]

To define the optimal infant prophylaxis regimen in the absence of maternal antepartum ARV drug administration in a formula-fed population of infants such as in the United States, the NICHD-HPTN 040/P1043 (NCT00099359) multicountry (Argentina, Brazil, South Africa, and the United States) clinical trial enrolled 1,735 formula-fed infants born to HIV-infected mothers who did not receive ARV drugs during the current pregnancy before labor (if women presented early enough, intravenous intrapartum zidovudine was given).[18] The study compared 3 infant ARV regimens: standard 6 weeks of zidovudine alone versus 6 weeks of zidovudine plus 3 doses of nevirapine given in the first week of life (first dose birth to 48 hours; second dose 48 hours after first dose; third dose 96 hours after second dose) versus 6 weeks of zidovudine plus lamivudine and nelfinavir given from birth through age 2 weeks. The study demonstrated that the combination regimens reduced risk of intrapartum transmission by approximately 50% compared with infant prophylaxis with zidovudine alone (see Table 3). Based on these data, combination ARV prophylaxis is now recommended in the United States for infants whose mothers have not received antenatal ARV drugs (see Infant Antiretroviral Prophylaxis).

Adding single-dose intrapartum nevirapine is not recommended for women in the United States who are receiving standard recommended antenatal ARV prophylaxis.

Several studies in formula-fed and breastfed populations in resource-limited countries have found that adding maternal/infant single-dose nevirapine to a maternal short-course zidovudine or zidovudine/lamivudine regimen increased efficacy compared with the short-course regimen alone.[14, 19, 20] Whether single-dose nevirapine provides any additional efficacy when combined with the standard recommended combination ARV prophylaxis regimens used in the United States was evaluated in PACTG 316, a clinical trial conducted in the United States, Europe, Brazil, and the Bahamas. This study demonstrated that for nonbreastfeeding women in resource-rich countries, the addition of single-dose nevirapine did not offer significant benefit in the setting of combination ARV prophylaxis throughout pregnancy and very low viral load at the time of delivery.[21] Thus, adding single-dose intrapartum nevirapine is not recommended for women in the United States who are receiving standard recommended antenatal ARV prophylaxis (see Intrapartum Care).

Breastfeeding by HIV-infected women is not recommended in the United States.

Breastfeeding by HIV-infected women (including those receiving ARV drugs) is not recommended in the United States where replacement feeding is affordable, feasible, acceptable, sustainable, and safe and the risk of infant mortality due to diarrheal and respiratory infections is low. A number of studies have evaluated the use of maternal or infant ARV prophylaxis during breastfeeding to reduce postnatal transmission (see Table 3). Observational data and randomized clinical trials have demonstrated that infant prophylaxis (primarily

using daily infant nevirapine) during breastfeeding significantly decreases risk of postnatal transmission in breast milk and that maternal triple-drug prophylaxis during breastfeeding likewise decreases postnatal infection.[1, 16, 22-27] Maternal prophylaxis with triple-drug regimens may be less effective than infant prophylaxis when the maternal triple regimen is first started postpartum or late in pregnancy because it takes several weeks to months before full viral suppression in breast milk is achieved.[26, 28] Importantly, although significantly lowering the risk of postnatal infection, neither infant nor maternal postpartum ARV prophylaxis completely eliminates the risk of HIV transmission through breast milk. Therefore, breastfeeding is not recommended for HIV-infected women in the United States (including those receiving combination ARV drug regimens). Finally, both infant nevirapine prophylaxis and maternal triple-drug prophylaxis during breastfeeding may be associated with development of ARV drug resistance in infants who become infected despite prophylaxis.[29-32] Three studies have found multiclass drug resistance in breastfeeding infants who became infected despite maternal triple-drug prophylaxis.[30-33]

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child Transmission of HIV (page 1 of 9)

Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
PACTG 076 United States, France[34] Formula feeding	ZDV vs. placebo	Long (from 14 weeks) IV IP	Long (6 weeks), infant only	• MTCT at 18 months was 8.3% in ZDV arm vs. 25.5% in placebo arm (68% efficacy).
CDC short-course ZDV trial Thailand[11] Formula feeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	• MTCT at 6 months was 9.4% in ZDV arm vs. 18.9% in placebo arm (50% efficacy).
DITRAME (ANRS 049a) trial Ivory Coast, Burkina Faso[10, 35] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	Short (1 week), mother only	• MTCT was 18.0% in ZDV arm vs. 27.5% in placebo arm at 6 months (38% efficacy) and 21.5% vs. 30.6% at 15 months (30% efficacy). • MTCT was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).
CDC short-course ZDV trial Ivory Coast[9, 10] Breastfeeding	ZDV vs. placebo	Short (from 36 weeks) Oral IP	None	• MTCT was 16.5% in ZDV arm vs. 26.1% in placebo arm at 3 months (37% efficacy). • MTCT was 22.5% in ZDV arm vs. 30.2% in placebo arm in pooled analysis at 24 months (26% efficacy).

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Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
PETRA trial South Africa, Tanzania, and Uganda[4] Breastfeeding and formula feeding	AP/IP/PP ZDV + 3TC vs. IP/PP ZDV + 3TC vs. IP-only ZDV + 3TC vs. placebo	Short (from 36 weeks) Oral IP	Short (1 week), mother and infant	• MTCT was 5.7% at 6 weeks for AP/IP/PP ZDV + 3TC, 8.9% for IP/PP ZDV + 3TC, 14.2% for IP-only ZDV + 3TC, and 15.3% for placebo (efficacy compared with placebo: 63%, 42%, and 0%, respectively). • MTCT was 14.9% at 18 months for AP/IP/PP ZDV + 3TC, 18.1% for IP/PP ZDV + 3TC, 20.0% for IP-only ZDV + 3TC, and 22.2% for placebo (efficacy compared with placebo: 34%, 18%, and 0%, respectively).
HIVNET 012 trial Uganda[3] Breastfeeding	sdNVP vs. ZDV	No AP ARV Oral IP: sdNVP vs. oral ZDV	sdNVP within 72 hours of birth, infant only vs. ZDV (1 week), infant only	• MTCT was 11.8% in NVP arm vs. 20.0% in ZDV arm at 6–8 weeks (42% efficacy); 15.7% in NVP arm vs. 25.8% in ZDV arm at 18 months (41% efficacy).
SAINT trial South Africa[5] Breastfeeding and formula feeding	sdNVP vs. ZDV + 3TC	No AP ARV Oral IP: sdNVP vs. ZDV + 3TC	sdNVP within 48 hours of birth, mother and infant vs. ZDV + 3TC (1 week), mother and infant	• MTCT was 12.3% in sdNVP arm vs. 9.3% in ZDV + 3TC arm at 8 weeks (difference not statistically significant, $P = 0.11$).
Perinatal HIV Prevention Trial (PHPT-1) Thailand[12] Formula feeding	Four ZDV regimens with different durations of AP and infant PP administration, no placebo	Long (from 28 weeks), short (from 36 weeks) Oral IP	Long (6 weeks), short (3 days), infant only	• Short-short arm stopped at interim analysis (10.5%). MTCT was 6.5% in long-long arm vs. 4.7% in long-short arm and 8.6% in short-long arm at 6 months (no statistical difference). *In utero* transmission was significantly higher with short vs. long maternal therapy regimens (5.1% vs. 1.6%).

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Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
PACTG 316 trial Bahamas, Belgium, Brazil, France, Germany, Italy, Spain, Sweden, Switzerland, United Kingdom, United States[21] Formula feeding	sdNVP vs. placebo among women already receiving ZDV alone (23%) or ZDV + other ARV drugs (77% combination therapy)	Nonstudy ARV regimen Oral IP: placebo vs. sdNVP + IV ZDV	Placebo vs. sdNVP within 72 hours of birth + nonstudy ARV drugs (ZDV), infant only	• 77% of women received dual- or triple-combination ARV regimens during pregnancy. • Trial stopped early because of very low MTCT in both arms: 1.4% in sdNVP arm vs. 1.6% in placebo arm (53% of MTCT was *in utero*).
Perinatal HIV Prevention Trial (PHPT-2) Thailand[19] Formula feeding	ZDV alone vs. ZDV + maternal and infant sdNVP vs. ZDV + maternal sdNVP	ZDV from 28 weeks Oral IP: ZDV alone or ZDV + sdNVP	ZDV for 1 week with or without sdNVP, infant only	• ZDV-alone arm was stopped because of higher MTCT than the NVP-NVP arm (6.3% vs. 1.1%). In arms in which the mother received sdNVP, MTCT rate did not differ significantly between the infant receiving or not receiving sdNVP (2.0% vs. 2.8%).
DITRAME Plus (ANRS 1201.0) trial Ivory Coast[14] Breastfeeding and formula feeding	Open label, ZDV + sdNVP	ZDV from 36 weeks Oral IP: ZDV plus sdNVP	sdNVP + ZDV for 1 week, infant only	• MTCT was 6.5% (95% CI, 3.9%–9.1%) at 6 weeks; MTCT for historical control group receiving short ZDV (98% breastfed) was 12.8%.
DITRAME Plus (ANRS 1201.1) trial Ivory Coast[14] Breastfeeding and formula feeding	Open label, ZDV + 3TC + sdNVP	ZDV + 3TC from 32 weeks (stopped at 3 days PP) Oral IP: ZDV + 3TC + sdNVP	sdNVP + ZDV for 1 week, infant only	• MTCT was 4.7% (95% CI, 2.4%–7.0%) at 6 weeks; MTCT for historical control group receiving short ZDV (98% breastfed) was 12.8%.
NVAZ trial Malawi[6] Breastfeeding	Neonatal sdNVP vs. sdNVP + ZDV	No AP or IP ARV (latecomers)	sdNVP with or without ZDV for 1 week, infant only	• MTCT was 15.3% in sdNVP + ZDV arm and 20.9% in sdNVP-only arm at 6–8 weeks. MTCT rate at 6–8 weeks among infants who were HIV uninfected at birth was 7.7% and 12.1%, respectively (36% efficacy).
Postnatal NVP + ZDV trial Malawi[7] Breastfeeding	Neonatal sdNVP vs. sdNVP + ZDV	No AP ARV Oral IP: sdNVP	sdNVP with or without ZDV for 1 week, infant only	• MTCT was 16.3% in NVP + ZDV arm and 14.1% in sdNVP-only arm at 6–8 weeks (difference not statistically significant). MTCT rate at 6–8 weeks among infants who were HIV uninfected at birth was 6.5% and 16.9%, respectively.

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child Transmission of HIV (page 4 of 9)

Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
Post-exposure Infant Prophylaxis South Africa[8] Breastfeeding and formula feeding	Neonatal sdNVP vs. ZDV for 6 weeks	No AP or IP ARV	sdNVP vs. ZDV for 6 weeks	• For formula-fed infants only, MTCT was 14.3% in sdNVP arm vs. 14.1% in ZDV arm at 6 weeks (not significant, P = 0.30). For breastfed infants only, MTCT was 12.2% in sdNVP arm and 19.6% in ZDV arm (P = 0.03).
Mashi Botswana[20, 36] Breastfeeding and formula feeding	Initial: short-course ZDV with/without maternal and infant sdNVP and with/without breastfeeding Revised: short-course ZDV + infant sdNVP with/without maternal sdNVP and with/without breastfeeding; women with CD4 T-lymphocyte (CD4-cell) counts <200 cells/mm^3 receive combination therapy	1st randomization ZDV from 34 weeks Oral IP: ZDV + either sdNVP vs. placebo	2nd randomization Breastfeeding + ZDV (infant) 6 months + sdNVP, infant only vs. Formula feeding + ZDV (infant) 4 weeks + sdNVP, infant only	• Initial design: In formula-feeding arm, MTCT at 1 month was 2.4% in maternal and infant sdNVP arm and 8.3% in placebo arm (P = 0.05). In breastfeeding + infant ZDV arm, MTCT at 1 month was 8.4% in sdNVP arm and 4.1% in placebo arm (difference not statistically significant). • Revised design: MTCT at 1 month was 4.3% in maternal + infant sdNVP arm and 3.7% in maternal placebo + infant sdNVP arm (no significant difference; no interaction with mode of infant feeding). • MTCT at 7 months was 9.1% in breastfeeding + ZDV arm and 5.6% in formula-feeding arm; mortality at 7 months was 4.9% in breastfeeding + ZDV arm vs. 9.3% in formula-feeding arm; HIV-free survival at 18 months was 15.6% breastfeeding + ZDV arm vs. 14.2% formula-feeding arm.

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Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
SWEN Uganda, Ethiopia, India[23] Breastfeeding	sdNVP vs. NVP for 6 weeks	No AP ARV Oral IP: sdNVP	Infant sdNVP vs. NVP for 6 weeks	• Postnatal infection in infants uninfected at birth: - MTCT at 6 weeks was 5.3% in sdNVP arm vs. 2.5% in extended NVP arm (risk ratio 0.54, $P = 0.009$). - MTCT at 6 months was 9.0% in sdNVP arm vs. 6.9% in extended NVP arm (risk ratio 0.80, $P = 0.16$). • HIV-free survival was significantly lower in extended NVP arm at both 6 weeks and 6 months of age.
PEPI-Malawi Trial Malawi[22] Breastfeeding	sdNVP + ZDV for 1 week (control) vs. two extended infant regimens (NVP or NVP/ZDV) for 14 weeks	No AP ARV Oral IP: sdNVP (if mother presents in time)	Infant sdNVP + ZDV for 1 week (control) vs. control + NVP for 14 weeks vs. control + NVP/ZDV for 14 weeks	• Postnatal infection in infants uninfected at birth: - MTCT at age 6 weeks was 5.1% in control vs. 1.7% in extended NVP (67% efficacy) and 1.6% in extended NVP/ZDV arms (69% efficacy). - MTCT at age 9 months was 10.6% in control vs. 5.2% in extended NVP (51% efficacy) and 6.4% in extended NVP/ZDV arms (40% efficacy). • No significant difference in MTCT between the extended prophylaxis arms; however, more hematologic toxicity with NVP/ZDV.
MITRA Tanzania[25] Breastfeeding	Infant 3TC for 6 months (observational)	ZDV/3TC from 36 weeks through labor	Maternal ZDV/3TC for 1 week; infant 3TC for 6 months	• MTCT at age 6 months was 4.9% (postnatal MTCT between ages 6 weeks and 6 months was 1.2%).

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child Transmission of HIV (page 6 of 9)

Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
Kisumu Breastfeeding Study (KiBS) Kenya[27] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4-cell count >250 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4-cell count >250 cells/mm^3) for 6 months; infant sdNVP	• MTCT at age 6 months was 5.0% (postnatal MTCT between ages 7 days and 6 months was 2.6%).
MITRA-PLUS Tanzania[24] Breastfeeding	Maternal triple-drug prophylaxis (observational)	ZDV/3TC/NVP (NFV if CD4-cell count >200 cells/mm^3) from 34 weeks through labor	Maternal ZDV/3TC/NVP (NFV if CD4-cell count >200 cells/mm^3) for 6 months; infant ZDV/3TC for 1 week	• MTCT at age 6 months was 5.0% (postnatal MTCT between ages 6 weeks and 6 months was 0.9%), not significantly different from 6 months infant prophylaxis in MITRA.
Kesho Bora Multi-African[16] Breastfeeding primarily	Antepartum ZDV/sdNVP with no postnatal prophylaxis vs. maternal triple-drug prophylaxis in women with CD4-cell counts of 200–500 cells/mm^3	Arm 1: ZDV/3TC/LPV/r Arm 2: ZDV + sdNVP From 28 weeks through labor	Arm 1: Maternal ZDV/3TC/LPV/r for 6 months; infant sdNVP + ZDV for 1 week Arm 2: Maternal ZDV/3TC for 1 week (no further postnatal prophylaxis); infant sdNVP + ZDV for 1 week (no further postnatal prophylaxis)	• MTCT at birth was 1.8% with maternal triple-drug prophylaxis Arm 1 and 2.5% with ZDV/sdNVP Arm 2, not significantly different. In women with CD4-cell counts 350–500 cells/mm^3, MTCT at birth was 1.7% in both arms. • MTCT at age 12 months was 5.4% with maternal triple-drug prophylaxis Arm 1 and 9.5% with ZDV/sdNVP (with no further postnatal prophylaxis after 1 week) Arm 2 (P = 0.029).
Mma Bana Botswana[1] Breastfeeding	Maternal triple-drug prophylaxis (compares 2 regimens) in women with CD4-cell counts >200 cells/mm^3	Arm 1: ZDV/3TC/ABC Arm 2: ZDV/3TC/LPV/r From 26 weeks through labor	Arm 1: Maternal ZDV/3TC/ABC for 6 months; infant sdNVP + ZDV for 4 weeks Arm 2: Maternal ZDV/3TC/LPV/r for 6 months; infant sdNVP + ZDV for 4 weeks	• MTCT at age 6 months overall was 1.3%: 2.1% in ZDV/3TC/ABC Arm 1 and 0.4% in ZDV/3TC/LPV/r Arm 2 (P = 0.53).

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Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
BAN Malawi[26, 37] Breastfeeding	Postpartum maternal triple-drug prophylaxis vs. infant NVP in women with CD4-cell counts ≥250 cells/mm^3	No AP drugs IP regimens: Arm 1 (control): ZDV/3TC + sdNVP Arm 2: ZDV/3TC + sdNVP Arm 3: ZDV/3TC + sdNVP	Arm 1 (control): Maternal ZDV/3TC for 1 week; infant sdNVP + ZDV/3TC for 1 week Arm 2: Control as above, then maternal ZDV/3TC/LPV/r for 6 months Arm 3: Control as above, then infant NVP for 6 months	• Postnatal infection in infants uninfected at age 2 weeks: - MTCT at age 28 weeks was 5.7% in control Arm 1; 2.9% in maternal triple-drug prophylaxis Arm 2 (P = 0.009 vs. control); 1.7% in infant NVP Arm 3 (P <0.001 vs. control). - MTCT at age 48 weeks was 7.0% in control Arm 1; 4% in maternal triple-drug prophylaxis Arm 2 (P = 0.0273 vs. control); 4% in infant NVP Arm 3 (P = 0.0027 vs. control). • No significant difference between maternal triple-drug prophylaxis Arm 2 and infant NVP Arm 3 (P = 0.12 at 28 weeks and P = 0.426 at 48 weeks).

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Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
HPTN 046 South Africa, Tanzania, Uganda, Zimbabwe[33] Breastfeeding	Postpartum prophylaxis of breast milk transmission of HIV with 6 weeks vs. 6 months of infant NVP	AP drugs allowed if required for maternal health	All infants received daily NVP from birth through age 6 weeks. Arm 1: Daily infant NVP from 6 weeks through 6 months of age Arm 2: Daily infant placebo from 6 weeks through age 6 months of age	• In infants uninfected at age 6 weeks, the 6-month infant HIV infection rate was 1.1% (0.3%–1.8%) in the extended NVP Arm 1 and 2.4% (1.3%–3.6%) in the placebo Arm 2 ($P = 0.048$). • At infant randomization at age 6 weeks, 29% of mothers in each arm were receiving a triple-drug ARV regimen for treatment of HIV. • For mothers receiving triple-drug ARV regimens at the time of randomization, in infants uninfected at age 6 weeks, the 6-month infant HIV infection rate was 0.2% and not statistically different between extended NVP Arm 1 (0.5%) and placebo Arm 2 (0%). • For mothers with CD4-cell counts >350 cells/mm^3 who were not receiving triple-drug ARV regimens, in infants uninfected at age 6 weeks, the 6-month infant HIV infection rate was 0.7% (0%–1.5%) in the extended NVP Arm 1 and 2.8% (1.3%–4.4%) in the placebo Arm 2 ($P = 0.014$).

Table 3. Results of Major Studies on Antiretroviral Prophylaxis to Prevent Mother-to-Child Transmission of HIV (page 9 of 9)

Study Location(s) Mode of Infant Feeding	Antiretroviral (ARV) Drugs	Antepartum and Intrapartum	Postpartum	Mother-to-Child Transmission (MTCT) Rate and Efficacy
NICHD-HPTN 040/PACTG 1043 trial Argentina, Brazil, South Africa, United States[18] Formula feeding	Infant prophylaxis with 6 weeks ZDV vs. 6 weeks infant ZDV plus three doses of NVP in first week of life vs. 6 weeks infant ZDV plus 2 weeks of 3TC/NFV	No AP drugs If mother presented early enough, IV ZDV during labor through delivery	Arm 1 (control): Infant ZDV for 6 weeks Arm 2: Control as above plus NVP with first dose within 48 hours of birth, second dose 48 hours later, and third dose 96 hours after the second dose Arm 3: Control as above, plus 3TC and NFV from birth through 2 weeks of age	• IP HIV transmission among infants with negative HIV test at birth: 4.8% (3.2%–7.1%) ZDV (Arm 1) vs. 2.2% (1.2%–3.9%) in ZDV plus NVP (Arm 2) (P = 0.046 compared with Arm 1) vs. 2.4% (1.4%–4.3%) in ZDV plus 3TC/NFV (Arm 3) (P = 0.046 compared with Arm 1). • Overall HIV transmission rates, including *in utero* infection: 11.0% (8.7%–14.0%) ZDV (Arm 1) vs. 7.1% (5.2%–9.6%) in ZDV plus NVP (Arm 2) (P = 0.035 compared with Arm 1) vs. 7.4% (5.4%–9.9%) in ZDV plus 3TC/NFV (Arm 3) (P = 0.035 compared with Arm 1). • Grade 3 or 4 neutropenia more frequent in ZDV/3TC/NFV Arm 3, 70 infants, compared with ZDV alone Arm 1, 33 infants, or ZDV/NVP Arm 2, 32 infants (P <0.001).

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, AP = antepartum, ARV = antiretroviral, CDC = Centers for Disease Control and Prevention, CI = confidence interval, IP = intrapartum, IV = intravenous, LPV/r = lopinavir/ritonavir, MTCT = mother-to-child transmission, NFV = nelfinavir, NVP = nevirapine, PP = postpartum, sd = single-dose, ZDV = zidovudine

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