| **Study author, year** | **Intervention** | **HIV transmission** | **Adverse events** |
| --- | --- | --- | --- |
| Aaron, 201246 | A. Any ART initiation during pregnancy (n=137)  B. NNRTI use (n=39)  C. PI use (n=117) | NR | 1. SGA, 10th percentile: aOR, 1.47 (95% CI, 0.60 to 3.58); 3rd percentile: aOR, 4.64 (95% CI, 0.81 to 26) 2. SGA, 10th percentile: aOR, 0.28 (95% CI, 0.10 to 0.75); 3rd percentile: 0.16 (95% CI, 0.03 to 0.91) 3. SGA, 10th percentile: aOR, 1.68 (95% CI, 0.79 to 3.55); 3rd percentile: aOR, 2.73 (95% CI, 0.83 to 9.00) |
| Antiretroviral Pregnancy Registry, 201847 | Preferred initial treatment drugs in U.S.:  A. ABC (1,131; 12%)  B. 3TC (5,008; 54%)  C. TDF (3,535; 38%)  D. FTC (2,785; 30%)  E. ATV (1,279; 14%)  F. RTV (3,155; 34%)  G. DRV (456; 5%)  H. RAL (291; 3%)  Alternative initial treatment drugs in U.S.:  I. ZDV (4,178; 45%)  J. LPV (1,418; 15%)  K. EFV (1,023; 11%)  L. RPV (297; 3%) | NR | Congenital abnormalities  First-trimester exposed vs. unexposed, unadjusted OR (our analysis):  A. 1.04 (0.72 to 1.52)  B. 1.26 (0.98 to 1.63)  C. 0.77 (0.59 to 1.01)  D. 0.85 (0.64 to 1.13)  E. 0.77 (0.52 to 1.15)  F. 0.74 (0.56 to 0.97)  G. 0.88 (0.48 to 1.61)  H. 1.14 (0.58 to 2.24)  I. 1.38 (1.08 to 1.77)  J. 0.74 (0.50 to 1.09)  K. 0.84 (0.55 to 1.29)  L. 0.36 (0.11 to 1.12) |
| Berard, 201748 Quebec Pregnancy Cohort | A. No ART exposure (n=214,042) B. First-trimester ART exposure (n=198) | NR | A vs. B Any major congenital malformation: aOR, 0.59 (95% CI, 0.33 to 1.06) Nervous system major malformation: aOR, 0.21 (95% CI, 0.03 to 1.83) Circulatory system major malformation: aOR, 0.75 (95% CI, 0.31 to 1.85) Digestive system major malformation: aOR, 0.80 (95% CI, 0.14 to 4.40) Urinary system major malformation: aOR, 0.14 (95% CI, 0.02 to 1.12) Musculoskeletal major malformation: aOR, 0.59 (95% CI, 0.21 to 1.68) Specific malformations for which there was a statistically significant difference between groups:  Small intestine: aOR, 10.32 (95% CI, 2.85 to 37.38)  Other digestive congenital malformations (excluding tongue, mouth, pharynx, esophagus, intestines, gall bladder, bile ducts, liver): aOR, 6.83 (95% CI, 2.18 to 21.35)  *OR adjusted for HIV diagnosis in the 6 months before and during pregnancy, maternal age, place of residence and welfare status, hospitalizations and emergency department visits, physician and specialist visits, number of other medication use and number of prescribers, maternal diabetes, hypertension, and asthma.* |
| Chagomerana, 201749 | A. ART (n=2,909) B. No ART (n=165) | NR | Overall preterm birth: 24% (731/3,074) A vs. B Preterm birth: 31% (690/2,219) vs. 33% (41/124); aRR, 1.14 (95% CI, 0.84 to 1.55) Extremely to very preterm (27–32 weeks) birth: 6% (133/2,219) vs. 13% (16/124); aRR, 2.33 (95% CI, 1.39 to 3.92) |
| Chen, 201250 | A. Continued HAART during pregnancy (n=2,189)  B. Initiated HAART during pregnancy (n=1,101)  C. Initiated ZDV during pregnancy (n=4,625)  D. No ART (n=1,234) | NR | A vs. (B or C or D)  Preterm delivery: 26.5% (543/2,050) vs. 22.7% (1,515/6,676); aOR, 1.2 (95% CI, 1.1 to 1.4)  SGA: 26.1% (562/2,151) vs .15.6% (1,067/6,840); aOR, 1.8 (95% CI, 1.6 to 2.1)  Stillbirth: 6.3% (1,38/2,189) vs. 4.1% (283/6,960); aOR, 1.5 (95% CI, 1.2 to 1.8)  A vs. B  SGA: 26.1% (562/2,151) vs. 21.6% (237/1,095); aOR, 1.3 (95% CI, 1.0 to 1.5)  B vs. C  Preterm delivery: 19.8% (177/892) vs. 14.2% (533/3,762); aOR, 1.4 (95% CI, 1.2 to 1.8)  SGA: 21.5% (200/930) vs. 14.2% (542/3,811); aOR, 1.5 (95% CI, 1.2 to 1.9)  Stillbirth: 4.7% (44/936) vs. 1.7% (64/3,827); aOR, 2.5 (95% CI, 1.6 to 3.9) |
| Chiappini, 201351  EPPICC Study | A. 3 or more drugs (n=2,355)  B. 2 drugs (n=255)  C. 1 drug (n=681)  D. No therapy (n=1,933) | A. 2.8% (65/2,355); aOR, 0.36 (95% CI, 0.23 to 0.57); p<0.001  B. 1.2% (3/255); aOR, 0.12 (95% CI, 0.04 to 0.40); p<0.001  C. 3.1% (21/681); aOR, 0.33 (95% CI, 0.19 to 0.55); p<0.005  D. 14.3% (158/1,107); aOR, 1 reference | NR |
| Duryea, 201552 | A. ART with PI (n=597) B. ART without PI (n=230) C. No ART (n=177) | NR | Preterm birth (<37 weeks): A. 14% (82/597); 1 reference B. 13% (31/230); 0.9 (95% CI, 0.5 to 1.5) C. 21% (37/177); 1.0 (95% CI, 0.5 to 2.0) SGA (<10th percentile): 4% to 10% depending on ART regimen: A. 19% (116/597); 1 reference B. 23% (54/230); 1.3 (95% CI, 0.8 to 1.9) C. 22% (39/177); 1.1 (95% CI, 0.6 to 2.0) |
| Floridia, 201353  Italian Group on Surveillance on Antiretroviral Treatment in Pregnancy | Various cART regimens | Data on transmission available for 868 infants, of which 4 were HIV positive (0.5% [95% CI, 0.0 to 0.9]) | Birth defects (Antiretroviral Pregnancy Registry criteria):  Overall: 3.3% (42/1,257) for exposure at any time to ART during pregnancy  Exposure to any ART during the first trimester: prevalence 3.2% (95% CI, 1.9 to 4.5) (23 cases with defects) vs. initial exposure to ART after the first trimester: prevalence 3.4% (95% CI, 1.9 to 4.9) (19 cases)  By drug:  No associations found between major birth defects and first-trimester exposure to any ART: OR, 0.94 (95% CI, 0.51 to 1.75)  NRTI: OR, 0.95 (95% CI, 0.51 to 1.76)  NNRTI: OR, 1.20 (95% CI, 0.56 to 2.55)  PI: OR, 0.92 (95% CI, 0.43 to 1.95)  Also, no associations found for individual drugs  Stillbirth: 0.8% (10/1,257)  Death within 2 weeks of delivery: 4 (different from the 4 infants with HIV, and none had birth defects). Reasons: 2 deaths from complications from prematurity and 2 deaths from neonatal sepsis  Preterm delivery (<37 weeks): 20.9%  Very preterm delivery (<32 weeks): 2.5%  Low birth weight (<2,500 g): 22.1%  Very low birth weight (<1,500 g): 2.5% |
| French Perinatal Cohort Study  ANRS-EPF  Mandelbrot, 201561 | ART comparing starting at different times and viral loads  A. Preconception  B. 1st trimester  C. 2nd trimester  D. 3rd trimester  Other interventions: Intrapartum ZDV 96.0%  Neonatal antiretroviral prophylaxis: 91.6% ZDV monotherapy, 7.5% other  Neonatal single dose NVP: 4.2% | Overall mother-to-child HIV transmission: 0.7% (56/8,075) (95% CI, 0.5 to 0.9)  A vs. B vs. C vs. D  Mother-to-child HIV transmission based on timing of ART initiation: 0.2% (6/3,505) vs. 0.4% (3/709) vs. 0.9% (24/2,810) vs. 2.2% (23/1,051); p<0.001  Mother-to-child HIV transmission based on viral load (copies/mL) near delivery: <50, 0.3 (95% CI, 0.1 to 0.4); undetectable >50, 0.2 (95% CI <0.1 to 1.2); 50 to 399, 1.5 (95% CI, 0.9 to 2.4); ≥400, 2.8 (95% CI, 1.8 to 4.2), p<0.001; aOR, 4.0 (95% CI, 1.9 to 8.2) | A vs. B vs. C vs. D  Live born: 99.1% (4,055/4,095) vs. 99.2% (707/713) vs. 99.1% (2,772/2,803) vs. 99.6% (1,062/1,067)  Median birth weight (g): 3,020 vs. 3,065 vs. 3,018 vs. 3,040  Median length at birth (cm): 48.0 vs. 48.0 vs. 48.0 vs. 49.0  Median head circumference (cm): 34.0 vs. 34.0 vs. 34.0 vs. 34.0  5-Minute APGAR 8–10: 96.4% (3,776/4,095) vs. 97.3% (659/713) vs. 97.3% (2,618/2,803) vs. 97.7% (1,017/1,067)  Gestational age at delivery:  <32 weeks: 4.0% (164/4,095) vs. 3.2% (23/713) vs. 3.6% (100/2,803) vs. 0.7% (7/1,067)  32 to 36 weeks: 13.4% (549/4,095) vs. 12.8% (91/713) vs. 12.0% (336/2,803) vs. 11.6% (124/1,067)  ≥37 weeks: 82.6% (3,382/4,095) vs. 84.0% (599/713) vs. 84.4% (2,367/2,803) vs. 87.7% (936/1,067)  Stillbirth: 1.0% (38/4,095) vs. 0.8% (6/713) vs. 0.9% (25/2,803) vs. 0.4% (4/1,067)  Death before HIV diagnosis: 0.5% (22/4,095) vs. 0.6% (4/713) vs. 0.5% (15/2,803) vs. 0.3% (3/1,067) |
| French Perinatal Cohort Study ANRS-EPF C01/C011  Sibiude, 201272 | A. ZDV monotherapy (n=2,975)  B. NRTI dual therapy (n=1,664)  C. cART therapy (n=6,738)  Substudy:  D. Boosted PI (n=1,066)  E. Nonboosted PI (n=187) | NR | Full cohort, A vs. B vs. C  Premature birth: 9.6% vs.11.3% vs. 14.7%; B vs. A: aOR, 1.24 (95% CI, 0.96 to 1.60); C vs. A: aOR, 1.69 (95% CI, 1.38 to 2.07)  Substudy, D vs. E  Premature birth: 14.4% vs. 9.1%; aHR, 2.03 (95% CI, 1.06 to 3.89)  Gestational diabetes: 2.9% vs. 1.6%; p=0.46 |
| French Perinatal Cohort Study ANRS-EPF C01/C011  Sibiude, 201471 | cART | NR | Overall birth defects prevalence (EUROCAT classification): .4% (575/13,124) (95% CI, 4.0 to 4.7)  Overall birth defects prevalence (MACDP classification): 7.0% (914/13,124) (95% CI, 6.5 to 7.4)  Premature delivery (<37 weeks): 14.5% (1,901/13,124)  Low birth weight (<2,500 g): 16.2% (2,127/13,124)  After adjustment for potential confounders, and by drug:  Significant association found between exposure to ZDV in the first trimester and CHD: 2.3% (74/3,267); aOR, 2.2 (95% CI, 1.3 to 3.7)  Significant association found between exposure to ddl and head and neck defects: 0.5%; aOR, 3.4 (95% CI, 1.1 to 10.4)  Significant association found between exposure to IDV and head and neck defects: 0.9%; aOR, 3.8 (95% CI, 1.1 to 13.8)  Significant association found between exposure to EFV and neurological defects (MACDP classification): n=4; aOR, 3.0 (95% CI, 1.1 to 8.5); but not significant using the EUROCAT classification: aOR, 2.1 (95% CI, 0.7 to 5.9)  No association found between birth defects and LPV or RTV (with a power >85%) nor for NVP, tenofovir, D4T, ABC (with a power >70%) |
| French Perinatal Cohort Study ANRS-EPF C01/C011  and nested PRIMEVA ANRS 135 RCT  Sibiude, 201570 | A. ZDV exposure (n=3,262)  B. No ZDV exposure (n=9,626) | Overall mother-to-child HIV transmission: 1.3% (169/12,888) | A vs. B  CHD: 1.5% vs. 0.77%; aOR, 2.2 (95% CI, 1.5 to 3.2)  CHD, boys: aOR, 2.1 (95% CI, 1.2 to 3.7  CHD, girls: aOR, 2.0 (95% CI, 1.2 to 3.2); p=0.89 for interaction  Echocardiography (based on RCT data only): girls more likely than boys to show LV shortening fraction at 1 month (p=0.3 for interaction); no significant differences for other measures at 1 month or 1 year |
| Fowler, 201644  PROMISE  trial | A. ZDV-based ART (ZDV, 3TC, LPV/r)  B. Tenofovir-based ART (tenofovir, FTC, LPV/r)  C. ZVD alone (ZDV plus intrapartum single-dose NVP with 6 to 14 days of tenofovir and FTC postpartum)  All infants received NVP from birth.  During period 1 (April 2011 to September 2012), women without HBV were assigned only to ZDV alone or ZDV-based ART, but starting in October 2012, due to additional data on tenofovir, women were assigned to any regimen regardless of HBV status (period 2 = October 2012 to October 2014) | Periods 1 and 2, A vs. B vs. C  Rate of transmission: 0.5% (7/1,385) vs. 0.6% (2/325) vs. 1.8% (25/1,386), difference A and B vs. C: -1.3 percentage points (repeated CI, -2.1 to -0.4)  Gestational age at trial entry <34 weeks: 0.5% (6/1,230) vs. 0.4% (1/274) vs. 1.3% (16/1,229), difference A and B vs. C: -0.8 percentage points (repeated CI, -1.6 to -0.1)  Gestational age at trial entry ≥34 weeks: 0.6% (1/154) vs. 2.0% (1/51) vs. 5.7% (9/157), difference A and B vs. C: -4.8 percentage points (repeated CI, -8.9 to -0.6)  CD4 count at trial entry, 350–499 cells/mm3: 0.7% (4/592) vs. 0.7% (1/136) vs. 2.8% (16/577), difference A and B vs. C: -2.1 percentage points (repeated CI, -3.7 to -0.5)  CD4 count at trial entry, ≥500 cells/mm3: 0.4% (3/793) vs. 0.5% (1/189) vs. 1.1% (9/809),  difference A and B vs. C: -0.7 percentage points (repeated CI, -1.6 to 0.2)  Viral load at trial entry, <1,000 copies/mL: 0.4% (1/253) vs. 0% (0/57) vs. 0% (0/299), difference A and B vs. C: 0.3 percentage points (repeated CI, -0.4 to 1.0)  Viral load at trial entry, ≥1,000 copies/mL: 0.5% (6/1,129) vs. 0.7% (2/268) vs. 2.3% (25/1,083), difference A and B vs. C: -1.7 percentage points (repeated CI, -2.8 to -0.7) | Periods 1 and 2 A vs. C  Maternal any grade ≥2 adverse event: 21.1% (318/1,505) vs. 17.3% (261/1,510), p=0.008  Maternal grade ≥2 abnormal blood chemical value: 5.8% (88/1,505) vs. 1.3% (19/1,505), p<0.001  Any adverse pregnancy outcome: 40.0% (563/1,407) vs. 27.5% (389/1,414), p<0.001  Low birth weight, <2,500 g: 23.0% (306/1,332) vs. 12.0% (161/1,347); p<0.001  Preterm delivery, <37 weeks: 20.5% (288/1,406) vs. 13.1% (185/1,411); p<0.001  Any severe adverse pregnancy outcome: 7.1% (99/1,385) vs. 5.9% (83/1,399); p=0.22  Very preterm delivery, <34 weeks: 3.1% (44/1,406) vs. 2.6% (37/1,411); p=0.43  Infant death through week 1: 1.2% (17/1,419) vs. 2.0% (28/1,532); p=0.13 Period 2  A vs. B  Maternal any grade adverse event: 15.8% (61/385) vs. 15.8% (60/380); p>0.99  Maternal abnormal blood chemistry value: 4.7% (18/385) vs. 2.9% (11/380); p=0.26  Any adverse pregnancy outcome: 37.5% (123/328) vs. 34.7% (111/320), p=0.46  Low birth weight, <2,500 g: 20.4% (65/319) vs. 16.9% (51/301); p=0.30 Preterm delivery, <37 weeks: 19.7% (68/346) vs. 18.5% (62/335); p=0.77  Any severe adverse pregnancy outcome: 4.3% (14/322) vs. 9.2% (29/314); p=0.02  Very preterm delivery, <34 weeks: 2.6% (9/346) vs. 6.0% (20/335); p=0.04 Infant death through week 1: 0.6% (2/346) vs. 4.4% (15/341); p=0.001  Period 2  B vs. C  Maternal any grade adverse event: 15.8% (60/380) vs. 15.0% (59/393); p=0.77  Maternal abnormal blood chemistry value: 2.9% (11/380) vs. 0.8% (3/392); p=0.03  Any adverse pregnancy outcome: 34.7% (111/320) vs. 27.2% (91/334); p=0.04  Low birth weight, <2,500 g: 16.9% (51/301) vs. 8.9% (28/315); p=0.004  Preterm delivery, <37 weeks: 18.5% (62/335) vs. 13.5% (46/341); p=0.09  Any severe adverse pregnancy outcome: 9.2% (29/314) vs. 6.7% (22/329); p=0.25  Very preterm delivery, <34 weeks: 6.0% (20/335) vs. 3.2% (11/341); p=0.10 Infant death through week 1: 4.4% (15/341) vs. 3.2% (11/349); p=0.43 |
| Kakkar, 201554  CMIS Mother-Infant cohort | A. Boosted PI (n=144)  B. Unboosted PI (n=220)  C. Other treatment (n=166)  D. No treatment (n=59) | NR | A vs. B  Preterm delivery: 19.3% vs. 10.8%; aOR, 2.17 (95% CI, 1.05 to 4.51)  C vs. B  Preterm delivery: 8.8% vs. 10.8%; aOR, 0.67 (95% CI, 0.27 to 1.63)  D vs. B  Preterm delivery: 25% vs. 10.8%; aOR, 1.50 (95% CI, 0.33 to 6.78) |
| Knapp, 201255  IMPAACT Groups Protocol P1025 | Various cART regimens  A. Congenital anomaly (n=61)  B. No congenital anomaly (n=1,051) | 0.63% (7/1,112) | Congenital anomalies (MACDP guidelines):  Overall: 5.5% (61/1,112 infants), prevalence 5.49/100 live births (95% CI, 4.22 to 6.99), including 80 anomalies: cardiovascular (n=33), musculoskeletal (n=15), renal (n=9), genitourinary (n=6), craniofacial (n-4), and central nervous system (n=2)  Preterm birth (<37 weeks): 17% (191/1,112)  Low birth weight (<2,500 g): 14% (153/1,112)  EFV, 1st-trimester exposure: OR, 2.84 (95% CI, 1.13 to 7.16)  No other significant aORs for other drugs or timing of exposure |
| Kreitchmann, 201456  LILAC Study | At least 28 days in 3rd trimester:  A. HAART + PI (888; 59%)  B. HAART no PI (410; 27%)  C. Non-HAART (134; 9%)  D. No ARV (80; 5%)  Total N=1,512 | NR | Receiving ART at conception vs. no ART at conception, preterm delivery  <37 weeks: 1.53 (95% CI, 1.11 to 2.09) |
| Li, 201657 | A. Initiated ZDV during pregnancy (1,768; 53%)  B. Initiated HAART during pregnancy (512; 15%)  C. Continued HAART from before pregnancy (582; 18%)  D. No ART (452; 14%) | NR | HAART vs. ZDV started during pregnancy, preterm delivery: 34 to 37 weeks: 0.85 (95% CI, 0.70 to 1.02); p=0.14  <34 weeks: 0.87 (95% CI, 0.60 to 1.25); p=0.45 |
| Lopez, 201259 | A. HAART entire pregnancy (n=226)  B. HAART 2nd half of pregnancy only (n=72)  C. PI during pregnancy (n=178)  D. No HAART (n=221) | NR | Spontaneous preterm birth:  A vs. D: aOR, 0.55 (95% CI, 0.20 to 1.51)  B vs. D: aOR, 0.55 (95% CI, 0.18 to 1.68)  C vs. D: aOR, 1.95 (95% CI, 0.87 to 4.38)  Iatrogenic preterm birth:  A vs. D: aOR, 3.42 (95% CI, 0.80 to 14.63)  B vs. D: aOR, 6.16 (95% CI, 1.42 to 26.8)  C vs. D: aOR, 0.44 (95% CI, 0.18 to 1.10) |
| Lu, 201460  CPHSP Study | A. Complete antiretroviral prophylaxis (n=251)  B. Incomplete antiretroviral prophylaxis (n=336)  C. No antiretroviral prophylaxis (n=58) | A. 1% (3/251)  B. 2% (8/336)  C. 67% (39/58) | NR |
| Moodley, 201662 | A. Dual ART (AZT/NVP; n=974)  B. Triple ART (D4T/3TC/NVP; n=907)  C. Fixed-dose ART (EFV/TDF-FTC; n=1,666)  D. No ART (n=148) | NR | Stillbirth:  A vs. D: aOR, 0.08 (95% CI, 0.04 to 0.16)  B vs. D: aOR, 0.20 (95% CI, 0.11 to 0.38)  C vs. D: aOR, 0.18 (95% CI, 0.10 to 0.34)  Preterm birth:  A vs. D: aOR, 0.20 (95% CI, 0.08 to 0.51)  B vs. D: aOR, 0.21 (95% CI, 0.08 to 0.55)  C vs. D: aOR, 0.31 (95% CI, 0.11 to 0.90)  Low birth weight:  A vs. D: aOR, 0.06 (95% CI, 0.02 to 0.18)  B vs. D: aOR, 0.09 (95% CI, 0.03 to 0.24)  C vs. D: aOR, 0.12 (95% CI, 0.04 to 0.37)  SGA:  A vs. D: aOR, 0.37 (95% CI, 0.10 to 1.45)  B vs. D: aOR, 0.29 (95% CI, 0.08 to 1.07)  C vs. D: aOR, 0.35 (95% CI, 0.07 to 0.87) |
| Mor, 201763 | A. Infants born before 1996 (n=80) B. Infant born after 1997 (HAART introduced; n=716) | Mother-to-child HIV transmission:  Overall: 3.1% (25/796)  A vs. B: 16.3% (13/80) vs. 1.7% (12/716); p<0.01  Transmission with HAART and vaginal delivery: 1.5%  Transmission with HAART and Caesarean delivery: 0.6%  Variables on mother-to-child HIV transmission  HAART vs. no HAART during pregnancy: aOR, 0.4 (95% CI, 0.1 to 0.8)  Infant ART prophylaxis: aOR, 0.2 (95% CI, 0.1 to 0.5) | NR |
| Pintye, 201765  Partners PrEP Study and Partners Demonstration Project | A. TDF-containing 3-drug ART (n=208) B. Non-TDF–containing 3-drug ART (n=214) | NR | A vs. B Pregnancy loss: 14% (17/208) vs. 9% (7/214); aOR, 1.05 (95% CI, 0.75 to 1.46) Pregnancy loss, <20 weeks: 11% (13/208) vs. 7% (6/214); aOR, 1.02 (95% CI, 0.73 to 1.40) Pregnancy loss, >20 weeks: 2% (4/208) vs. 1% (1/214); aOR, 1.04 (95% CI, 0.95 to 1.13) Neonatal death: 1% (3/208) vs. 2% (4/214); aOR, 1.01 (95% CI, 0.96 to 1.06) Preterm birth: 6% (10/208) vs. 10% (20/214); aOR, 0.85 (95% CI, 0.74 to 1.02) *OR adjusted for study cohort, maternal age, time since HIV diagnosis, HIV RNA at first pregnancy visit, and year pregnancy occurred* |
| Ramokolo, 201766  PWTCT Study | A. Postconception ART (n=780) B. Preconception ART (n=616) C. ZDV prophylaxis (n=873) D. No ART (n=330) | NR | A vs. B vs. C vs. D Preterm delivery: A vs. B: aOR, 1.7 (95% CI, 1.1 to 2.5); A vs. C: aOR, 1.4 (95% CI, 0.9 to 2.0); A vs. D: aOR, 1.9 (95% CI, 1.1 to 3.1) Low birth weight: A vs. B: aOR, 0.9 (95% CI, 0.6 to 1.3); A vs. C: aOR, 0.8 (95% CI, 0.6 to 1.1); A vs. D: aOR, 1.1 (95% CI, 0.8 to 1.6) SGA: A vs. B: aOR, 0.9 (95% CI, 0.6 to 1.3); A vs. C: aOR, 0.7 (95% CI, 0.5 to 1.0); A vs. D: 0.7 (95% CI, 0.4 to 1.1) Underweight for age: A vs. B: aOR, 1.1 (95% CI, 0.7 to 1.6); A vs. C: aOR, 1.1 (95% CI, 0.8 to 1.6); A vs. D: aOR, 1.4 (95% CI, 0.9 to 2.2) |
| Sartorius, 201345  Kesho Bora Trial | A. Triple ART, CD4 <200 cells/mm3 (n=118)  B. ZDV plus single-dose NVP, CD4 >500 cells/mm3 (n=128)  C. Triple ART, CD4 200 to 500 cells/mm3 (n=412)  D. ZDV plus single-dose NVP, CD4 200 to 500 cells/mm3 (n=412)  Note: >70% breastfed | NR | A vs. B vs. C vs. D  Severe maternal anemia (hemoglobin <8 g/dL), cumulative incidence:  At delivery: 0.14 (95% CI, 0.09 to 0.22) vs. 0.05 (95% CI, 0.03 to 0.11) vs.  0.09 (95% CI, 0.06 to 0.12) vs. 0.08 (95% CI, 0.06 to 0.11); p=0.51  6 months postpartum: 0.30 (95% CI, 0.23 to 0.39) vs. 0.10 (95% CI, 0.06 to 0.16) vs. 0.16 (95% CI, 0.13 to 0.20) vs. 0.17 (95% CI, 0.14 to 0.21); p=0.44  12 months postpartum: 0.33 (95% CI, 0.26 to 0.41) vs. 0.11 (95% CI, 0.06 to 0.17) vs. 0.18 (95% CI, 0.14 to 0.21) vs. 0.19 (95% CI, 0.16 to 0.23); p=0.71  18 months postpartum: 0.34 (95% CI, 0.27 to 0.42) vs. 0.11 (95% CI, 0.06 to 0.17) vs. 0.18 (95% CI, 0.15 to 0.22) vs. 0.21 (95% CI, 0.17 to 0.25); p=0.36  C vs. D: aHR, 0.78 (95% CI, 0.54 to 1.11) |
| Short, 201368 | A. ZDV (n=65)  B. Dual NRTI (n=7)  C. Triple NRTI (n=5)  D. Short-term cART (n=59)  E. Preconception cART (n=131)  F. New continuous cART (n=56) | NR | A vs. B vs. C vs. D vs. E vs. F  Preterm delivery rate: 6.2% vs. 0% vs. 0% vs. 25.4% vs. 9.9% vs. 17.9%  D vs. A: aOR, 5.00 (95% CI, 1.49 to 16.79) |
| SMARTT and PHACS Studies  Nozyce, 201464 | Any maternal cART regimen containing at least 3 antiretroviral drugs from at least 2 drug classes, analyzed by assessment scale:  WPPSI-III (n=369)  WASI (n=452)  WIAT-II-A (n=451)  Other intervention: Neonatal prophylaxis defined as antiretroviral drugs used during the first 8 weeks of life | NR | Mean cognitive and academic scores were significantly below population norms (p=0.01 to p<0.001), with the exception of the WASI VIQ (p=0.48); data from figure  There were no significant differences in adjusted mean scores for any cognitive or academic outcome when comparing different cART regimens or specific drugs or cumulative duration of prenatal cART exposure |
| PHACS Study  Lipshultz, 201558 | A. HIV-exposed uninfected (n=417)  B. HIV unexposed controls (n=98) | NR | A vs. B, adjusted mean difference z-score  LV ejection fraction: 0.04 (95% CI, 0.14 to 0.21)  LV M-mode shortening fraction: 0.06 (95% CI, 0.26 to 0.15)  LV stress–velocity index: 0.12 (95% CI, 0.11 to 0.35)  LV M-mode end diastolic short axis dimension: 0.07 (95% CI, 0.15 to 0.29)  LV M-mode end diastolic postwall thickness: 0.05 (95% CI, 0.25 to 0.15)  LV M-mode end diastolic septal thickness: 0.06 (95% CI, 0.25 to 0.13)  LV M-mode mass: 0.02 (95% CI, 0.23 to 0.19)  LV M-mode end systolic wall stress: 0.02 (95% CI, 0.29 to 0.25)  LV M-mode thickness-to-dimension ratio: 0.07 (95% CI, 0.26 to 0.12) |
| SMARTT study of the and PHACS cohort and P1025 study of the IMPAACT cohort  Rough, 201867 | A. TDF-FTC + LPV/r (128; 8%)  B. ZDV + 3TC + LPV/r (954; 59%)  C. TDF-FTC + ATV/r (539; 33%) | NR | Preterm delivery, aOR:  A vs. B: 0.90 (95% CI, 0.60 to 1.33)  C vs. B: 0.69 (95% CI, 0.51 to 0.94)  A vs. C: 1.14 (95% CI, 0.75 to 1.72)  Very preterm delivery, unadjusted OR:  A vs. B: 0.85 (95% CI, 0.34 to 2.13)  C vs. B: 1.04 (95% CI, 0.60 to 1.83)  A vs. C: 0.82 (95% CI, 0.31 to 2.17)  Low birth weight, aOR:  A vs. B: 1.13 (95% CI, 0.78 to 1.64)  C vs. B: 0.80 (95% CI, 0.60 to 1.09)  A vs. C: 1.45 (95% CI, 0.96 to 2.17)  Very low birth weight, unadjusted OR:  A vs. B: 0.41 (95% CI, 0.06 to 3.06)  C vs. B: 0.89 (95% CI, 0.40 to 2.00)  A vs. C: 0.49 (95% CI, 0.07 to 3.57)  Stillbirth—Fetal loss was undefined, included stillbirth (likely also included spontaneous abortion and fetal demise)  Unadjusted OR (our analysis) for initial drug regimen:  A vs. B: 2.51 (95% CI, 0.50 to 13)  A vs. C: 4.26 (95% CI, 0.60 to 31)  B vs. C: 1.70 (95% CI, 0.34 to 8.45)  Neonatal death—within 14 days of live birth  Unadjusted OR (our analysis) for initial drug regimen:  A vs. B. 2.47 (95% CI, 0.10 to 61)  A vs. C: 1.40 (95% CI, 0.06 to 34)  B vs. C: 0.56 (95% CI, 0.04 to 9.04) |
| SMARTT and PHACS Studies  Siberry, 201269 | A. TDF-containing ART (n=449) B. non-TDF–containing ART (n=1,580) | NR | A vs. B Low birth weight (n=1,302): 19.5% vs. 19,1%; aOR, 0.73 (95% CI, 0.48 to 1.11) SGA (n=1,148): 8.3% vs. 8.6%; aOR, 0.96 (95% CI, 0.60 to 1.52) |
| SMARTT and PHACS Studies  Watts, 201375 | Various maternal cART regimens | NR | Overall:  Preterm birth (<37 weeks): 18.6% (346/1,869)  Spontaneous preterm birth (occurred after preterm labor or membrane rupture, without other complications): 10.2% (191/1,869)  Very preterm delivery: 2.1% (37/1,799)  SGA (birth weight <10% for gestational age): 7.3% (135/1,861)  First trimester exposure:  Association of first-trimester exposure to PI-based cART and preterm birth: aOR, 1.55 (95% CI, 1.16 to 2.07)  Association of first-trimester exposure to PI-based cART and spontaneous preterm birth: aOR, 1.59 (95% CI, 1.10 to 2.30)  No association of first-trimester exposure to PI-based cART and SGA: aOR, 0.79 (95% CI, 0.49 to 1.26)  No associations for regimens containing NNRTI or ≥3 NRTIs during the first trimester  Exposure overall (no significant associations):  PI-based cART and preterm birth: aOR, 1.49 (95% CI, 0.83 to 2.67)  PI-based cART and spontaneous preterm birth: aOR, 1.41 (95% CI, 0.66 to 2.99)  NNRTI-based cART and preterm birth: aOR, 1.28 (95% CI, 0.62 to 2.66) NNRTI-based cART and spontaneous preterm birth: aOR, 1.53 (95% CI, 0.62 to 3.81)  ≥3 NRTI-based cART and preterm birth: aOR, 1.04 (95% CI, 0.50 to 2.14)  ≥3 NRTI-based cART and spontaneous preterm birth: aOR, 0.88 (95% CI,  0.34 to 2.29) |
| SMARTT and PHACS Studies  Williams, 201576 | A. Any ART (n=1,219)  B. Any HAART (n=1,025)  C. NNTRI (n=214)  D. NRTI (n=1,211)  E. PI (n=887)  F. No ART exposure of any kind (n=1,298 to 2,303 depending on comparison)  All exposure was during first trimester | NR | Any CA:  A vs. F: aOR, 1.20 (95% CI, 087 to 1.67)  B vs. F: aOR, 1.35 (95% CI, 0.98 to 1.87)  C vs. F: aOR, 0.97 (95% CI, 0.54 to 1.74)  D vs. F: 1.19 (95% CI, 0.86 to 1.65)  E vs. F: 1.39 (95% CI, 1.00 to 1.92)  For specific drugs, there was no significant difference in risk of CA for exposed vs. unexposed except:  ddl plus D4T: aOR, 8.19 (95% CI, 1.53 to 43)  ATV sulfate: aOR, 1.95 (95% CI, 1.24 to 3.05)  RTV when used as a booster: aOR, 1.56 (95% CI, 1.11 to 2.20) |
| SMARTT and PHACS Studies  Williams, 201677 | A. Any HAART exposure (n=2,211)  B. NNTRI exposed (n=395)  C. NRTI (n=1,907)  D. PI (n NR)  E. No ART exposure of any kind (n=469) | NR | Adverse event cases:  A vs. E: aRR, 0.98 (95% CI, 0.82 to 1.16)  B vs. E: aRR, 0.98 (95% CI, 0.81 to 1.18)  C vs. E: aRR, 1.15 (95% CI, 0.73 to 1.82)  D vs. E: aRR, 1.01 (95% CI, 0.86 to 1.17)  Differences for specific drug/event combinations:  HAART, metabolic cases: aRR, 0.60 (95% CI, 0.44 to 0.82)  PIs, metabolic cases: aRR, 0.69 (95% CI, 0.52 to 0.92)  ZDV exposure, metabolic cases: aRR, 1.61 (95% CI, 1.01 to 2.58)  LPV exposure, metabolic cases: aRR, 0.46 (95% CI, 0.31 to 0.69)  LPV (1st trimester), metabolic cases: aRR, 0.39 (95% CI, 0.20 to 0.78)  RTV (as booster), metabolic cases: aRR, 0.59 (95% CI, 0.43 to 0.81)  RTV (1st trimester), metabolic cases: aRR, 0.61 (95% CI, 0.40 to 0.95)  NRTIs, impaired growth: aRR, 0.48 (95% CI, 0.24 to 0.96)  Neurodevelopmental impairment:  HAART: aRR, 0.47 (95% CI, 0.27 to 0.83)  NNRTIs: aRR, 0.38 (95% CI, 0.14 to 1.04)  3TC: aRR, 0.36 (95% CI, 0.36 to 1.02)  ZVD + 3TC: aRR, 0.71 (95% CI, 0.41 to 1.17)  3TC (1st trimester): aRR, 0.64 (95% CI, 0.35 to 1.18) |
| Snijdewind, 201873  ATHENA cohort | A. PI-based (928; 67%)  B. NNRTI-based (438; 31%)  C. Both or NRTI (12; 1%) | NR | Preterm delivery  Unadjusted OR:  A. 1 (reference)  B. 1.30 (95% CI, 0.95 to 1.77); p=0.11  C. 1.15 (95% CI, 0.41 to 3.19); p=0.78  Low birth weight  Unadjusted OR:  A. 1 (reference)  B. 1.19 (95% CI, 0.88 to 3.97); p=0.26  C. 1.47 (95% CI, 0.54 to 3.97); p=0.45  SGA  Unadjusted OR:  A. 1 (reference)  B. 1.04 (95% CI, 0.80 to 1.16); p=0.76  C. 2.51 (95% CI, 1.16 to 5.53); p=0.02  aOR:  A. 1 (reference)  B. 0.95 (95% CI, 0.71 to 1.27); p=0.73  C. 2.11 (95% CI, 0.98 to 4.57); p=0.06 |
| Tookey, 201674  NSHPC Study | LPV/r | 2003 to 2007  Overall: 18/1,633 (1.1% [95% CI, 0.6 to 1.6])  LPV/r initiation:  Before conception: 2/6,333 (0.6% [95% CI, 0.2% to 2.2%])  1st trimester: 0/33 (0%)  2nd trimester: 8/858 (0.9% [95% CI, 0.5% to 4.1%])  3rd trimester: 8/376 (2.1% [95% CI, 1.1% to 4.1%])  2008 to 2012  Overall: 12/2,406 (0.5% [95% CI, 0.2% to 0.8%])  LPV/r initiation:  Before conception: 2/635 (0.3% [95% CI, 0.1% to 1.1%])  1st trimester: 0/77 (0%)  2nd trimester: 5/1,397 (0.4% [95% CI, 0.2% to 0.8%])  3rd trimester: 5/264 (1.9% [95% CI, 0.8% to 4.4%]) | Infant mortality: 0.5% (24/4,762) Gestational age:  <32 weeks: 2.5% (112/4,762)  32 to 36 weeks: 10.4% (473/4,762)  ≥37 weeks: 87% (3971/4,762)  Birth weight:  <1,500 g: 2.3% (101/4,762)  1,500 to 2,499 g: 12.4% (545/4,762)  ≥2,500 g: 85.3% (3,749/4,762)  Any CA: 2.9% |
| Zash, 201679 | A. TDF-FTC-EFV at conception (n=165) B. Other 3-drug ART at conception (n=2,006) C. TDF-FTC-EFV during pregnancy (n=1,054) D. Other 3-drug ART during pregnancy (n=2,172) | NR | Initiated ART at conception A vs. B Stillbirth: 4.9% (8/165) vs. 6.4% (128/2,006); aOR, 0.4 (95% CI, 0.1 to 2.9) Preterm birth: 28% (47/165) vs. 31% (631/2,006); aOR, 0.9 (95% CI, 0.3 to 2.9) Very preterm birth: 10% (17/165) vs. 12% (236/2,006); aOR, 0.9 (95% CI, 0.1 to 8.0) SGA, Botswana norms: 8% (14/165) vs. 24% (476/2,006); aOR, 0.4 (95% CI, 0.1 to 1.4) SGA, WHO norms: 13% (22/165) vs. 32% (636/2,006); aOR, 0.3 (95% CI, 0.1 to 1.0) Any adverse outcome (any stillbirth, preterm birth, and/or SGA): 33% (55/165) vs. 51% (1,030/2,006); aOR, 0.5 (95% CI, 0.1 to 1.2) Initiated ART during pregnancy C vs. D Stillbirth: 1.7% (18/1,054) vs. 3.2% (70/2,172); aOR, 0.6 (95% CI, 0.3 to 1.3) Preterm birth: 18.2% (192/1,054) vs. 20.7% (450/2,172); aOR, 0.7 (95% CI, 0.5 to 1.1) SGA, Botswana norms: 11.9% (125/1,054) vs. 21.1% (459/2,172); aOR, 0.4 (95% CI, 0.3 to 0.6) SGA, WHO norms: 19.2% (202/1,054) vs. 27.7% (602/2,172); aOR, 0.5 (95% CI, 0.4 to 0.7) Any adverse outcome (any stillbirth, preterm birth, and/or SGA): 27% (287/1,054) vs. 41% (880/2,172); aOR, 0.4 (95% CI, 0.3 to 0.6) |
| Zash, 201778 | A. TDF-FTC-EFV (n=2,472) B. TDF-FTC-NVP (n=760) C. TDF-FTC-LPV/r (n=231) D. ZDV-3TC-NVP (n=1,365) E. ZDV-3TC-LPV/r (n=167) | NR | Preterm birth A. 21.4% (529/2,472), reference B. 19.1% (145/760); RR, 0.88 (95% CI, 0.75 to 1.04); aRR, 0.88 (95% CI, 0.75 to 1.05) C. 23.8% (55/231); RR, 1.11 (95% CI, 0.87 to 1.41); aRR, 1.12 (95% CI, 0.88 to 1.43) D. 24.8% (338/1,365); RR, 1.15 (95% CI, 1.02 to 1.30); aRR, 1.14 (95% CI, 1.01 to 1.29) E. 29.3% (49/167); RR, 1.36 (95% CI, 1.07 to 1.74); aRR, 1.36 (95% CI, 1.06 to 1.75) Very preterm birth (<32 weeks) A. 4.1% (101/2,472), reference B. 5.1% (39/760); RR, 1.25 (95% CI, 0.87 to 1.79); aRR, 1.23 (95% CI, 0.84 to 1.80) C. 5.2% (12/231); RR, 1.26 (95% CI, 0.71 to 2.27); aRR, 1.36 (95% CI, 0.76 to 2.45) D. 5.9% (80/1,365); RR, 1.43 (95% CI, 1.07 to 1.90); aRR, 1.44 (95% CI, 1.07 to 1.95) E. 9.0% (15/167); RR, 2.19 (95% CI, 1.30 to 3.67); aRR, 2.21 (95% CI, 1.29 to 3.79) SGA (<10th percentile) A. 16.9% (419/2,472), reference B. 24.9% (189/760); RR, 1.44 (95% CI, 1.24 to 1.68); aRR, 1.44 (95% CI, 1.24 to 1.68) C. 27.7% (64/231); RR, 1.62 (95% CI, 1.29 to 2.03); aRR, 1.56 (95% CI, 1.25 to 1.97) D. 28.2% (385/1,365); RR, 1.65 (95% CI, 1.46 to 1.86); aRR, 1.66 (95% CI, 1.46 to 1.87) E. 20.4% (34/167); RR, 1.19 (95% CI, 0.87 to 1.63); aRR, 1.13 (95% CI, 0.82 to 1.56) Very SGA (<3rd percentile) A. 7.1% (176/2472), reference B. 11.2% (85/760); RR, 1.55 (95% CI, 1.21 to 1.98); aRR, 1.52 (95% CI, 1.18 to 1.94) C. 13.4% (31/231); RR, 1.87 (95% CI, 1.31 to 2.67); aRR, 1.81 (95% CI, 1.26 to 2.59) D. 12.9% (176/1,365); RR, 1.80 (95% CI, 1.47 to 2.19); aRR, 1.76 (95% CI, 1.44 to 2.16) E. 12.6% (21/167); RR, 1.75 (95% CI, 1.15 to 2.67); aRR, 1.70 (95% CI, 1.10 to 2.62) Stillbirth A. 2.4% (59/2,472), reference B. 2.9% (22/760); RR, 1.21 (95% CI, 0.75 to 1.97); aRR, 1.15 (95% CI, 0.70 to 1.89) C. 4.3% (10/231); RR, 1.81 (95% CI, 0.94 to 3.50); aRR, 1.81 (95% CI, 0.94 to 3.50) D. 6.1% (83/1,365); RR, 2.55 (95% CI, 1.84 to 3.53); aRR, 2.31 (95% CI, 1.64 to 3.26) E. 3.6% (6/167); RR, 1.51 (95% CI, 0.66 to 3.44); aRR, 1.53 (95% CI, 0.67 to 3.49) Neonatal death A. 1.2% (29/2,472), reference B. 1.7% (13/760); RR, 1.46 (95% CI, 0.77 to 2.80); aRR, 1.57 (95% CI, 0.81 to 3.06) C. 1.7% (4/231); RR, 1.50 (95% CI, 0.53 to 4.24); aRR, 1.60 (95% CI, 0.56 to 4.76) D. 2.1% (28/1,365); RR, 1.82 (95% CI, 1.09 to 3.04); aRR, 1.94 (95% CI, 1.13 to 3.33) E. 4.2% (7/167); RR, 3.64 (95% CI, 1.62 to 8.17); aRR, 4.01 (95% CI, 1.78 to 9.11) |

**Abbreviations:** 3TC=lamivudine; ABC=abacavir; aHR=adjusted hazard ratio; ANRS-EPF=French Agence Nationale de Recherche sur le SIDA-Enquête Périnatale Française; aOR=adjusted odds ratio; APGAR=Appearance, Pulse, Grimace, Activity, Respiration; aRR=adjusted risk ratio; ART=antiretroviral therapy; ATV=atazanavir; CA=congenital abnormality; cART=combination antiretroviral therapy; CD4=cluster of differentiation 4; CHD=congenital heart defect; CI=confidence interval; CMIS=Centre Maternel et Infantile sur le SIDA; CPHSP=Canadian Perinatal HIV Surveillance Program; D4T=stavudine; ddl=didanosine; DRV=darunavir; EFV=efavirenz; EPPICC=European Pregnancy and Paediatic HIV Cohort Collaboration; EUROCAT=European Surveillance of Congenital Anomalies; FTC=emtricitabine; HAART=highly-active antiretroviral therapy; HBV=hepatitis B virus; IMPAACT=International Maternal Pediatric Adolescent AIDS Clinical Trials; IND=indinavir; LILAC=Perinatal and Longitudinal Study in Latin American Countries; LPV=lopinavir; LPV/r=lopinavir/ritonavir; LV=left ventricle; MACDP=Metropolitan Atlanta Congenital Defects Program; NNRTI=nonnucleoside reverse transcriptase inhibitors; NR=not reported; NRTI=nucleoside reverse transcriptase inhibitor; NSHPC=National Study of HIV in Pregnancy and Childhood; NVP=nevirapine; OR=odds ratio; PHACS=Pediatric HIV/AIDS Cohort Study; PI=protease inhibitor; PRIMEVA-ANRS=Protease Inhibitor Monotherapy Evaluation-French Agence Nationale de Recherche sur le SIDA; PROMISE=Promoting Maternal and Infant Survival Everywhere; PWTCT=Prevention of Mother to Child Transmission Program; RAL=raltegravir; RCT=randomized, controlled trial; RNA=ribonucleic acid; RTV=ritonavir; SGA=small size for gestational age; SMARTT=Surveillance Monitoring for Antiretroviral Treatment Toxicities; TDF=tenofovir disoproxil fumarate; U.S.=United States; VIQ=verbal intelligence quotient; WASI=Wechsler Abbreviated Scale of Intelligence; WHO=World Health Organization; WIAT-II-A=Wechsler Individual Achievement Test, 2nd Edition; WPPSI-III=Wechsler Preschool and Primary Scale of Intelligence, 3rd Edition; ZDV=zidovudine.