| **Author, year**  **Study** | **Study design** | **Number of centers, Country** | **Study duration Followup** | **Intervention** | **Inclusion criteria** | **Patient characteristics** | **N** | **Quality rating** | **Funding source** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Aaron, 201246 | Prospective cohort | 1 site  U.S. (Philadelphia, PA) | Through birth January 2000 through January 2011 | A. Any ART initiation during pregnancy (n=137)  B. NNRTI use (n=39)  C. PI use (n=117) | HIV-infected, pregnant, and older than age 17 years | Maternal age: mean, 28 years  Race/ethnicity: 74.7% African American; 25.3% other  Started medication in pregnancy: 74.9% | 183 | Fair | NR |
| Antiretroviral Pregnancy Registry, 201847 | Cohort (≈1,000 women prospectively included) | Multinational (69 countries), 75% U.S. and its territories | January 1989 through January 2018 | 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%) | Pregnant women exposed to antiretroviral drug for treatment of HIV and HBV infection and prevention of HIV infection (PrEP or postexposure prophylaxis) | Pregnancies enrolled in database (n=19,449):  Maternal age: median 28 years  Indication for ART at start of pregnancy: 89.4% HIV infected, 1.7% prophylaxis (HIV uninfected), 4.1% HBV monoinfected, 2.3% unknown, 2.4% missing  CD4 count at start of pregnancy: 30.9% ≥500 cells/mm3, 39.4% 200–499 cells/mm3, 14.1% <200 cells/mm3 | 9,336 | Fair | Cosponsored and cofunded by 26 pharmaceutical companies that manufacture drugs used in ART |
| Berard, 201748 Quebec Pregnancy Cohort | Prospective cohort | Database study (Quebec Drug Plan) Canada | From birth in 1998 to 2015 | A. No ART exposure (n=214,042) B. First-trimester ART exposure (n=198) | Age 15 and 45 years on the first day of gestation, continuously insured by the RAMQ drug plan for at least 6 months before the first day of gestation and during pregnancy, and have a singleton live birth | A vs. B Maternal age: 31.5 vs. 28.3 years (p<0.0001) Welfare recipient: 54% vs. 23% (p<0.0001) Infant gestational age: 38.2 vs. 38.8 weeks | 214,240 | Fair | Canadian Institutes of Health Research, Fonds de Antiretroviral la Recherche du Québec–Santé |
| Chagomerana, 201749 | Retrospective cohort | 1 hospital Malawi | Through birth Period April 2012 to November 2015 | A. ART (n=2,909) B. No ART (n=165) | HIV+ pregnant women who initiated ART before 27 weeks of gestation or did not receive ART and delivered after 27 weeks | A vs. B Maternal age: 27 to 30 vs. 26 years Gestation at delivery: 38 vs. 38 weeks | 3,074 | Fair | National Institutes of Health and a Gilead Training Fellowship |
| Chen, 201250 | Prospective cohort | 6 sites Botswana | May (1 site) or November (5 sites)  2009 through April 2011  28 days after delivery | 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) | All women who delivered live births or stillbirths at a gestational age of ≥20 weeks at 6 government facilities  in Botswana | A vs. B vs. C vs. D  Maternal age: median 32 vs. 29 vs. 27 vs. 27 years  Botswana nationality: 99% vs. 98% vs. 97% vs. 64%  Received antenatal care: 97% vs. 99% vs. 99% vs. 78% | 9,504 | Fair | Centers for Disease Control and Prevention, National Institutes of Health, Harvard University, Doris Duke Charitable  Research Foundation |
| Chiappini, 201351  EPPICC Study | Analysis from 8  cohort studies | 8 cohorts from 7 countries in Europe: U.K. and Ireland’s NSHPC and CHIPS; ITLR; Madrid Cohort of HIV-Infected Children; CoRISPE-Cat; “Victor Babes” Hospital Cohort, Bucharest, Romania; MoCHiV; ECS on HIV- Infected Pregnant Women and Their Children; ECS was considered as 2 studies | Up to 18 months Period 1996-  2010 | 1. 3 or more drugs (n=2,355) 2. 2 drugs (n=255) 3. 1 drug (n=681) 4. No therapy (n=1,933) | Children born to diagnosed HIV-infected mothers between January 1,1996 and June 30, 2010 at high risk for acquiring HIV infection whose mothers received antenatal and intrapartum antiretroviral drugs but had suboptimal viral suppression at delivery (defined as a detectable viral load [>50 copies/mL] documented in the last 8 weeks of pregnancy and/or at delivery), received only intrapartum antiretroviral drugs, and received no antenatal or intrapartum antiretroviral drugs | Maternal age: mean NR; 70% age ≥20 years Race/ethnicity: 29% white; 40% black; 3% other  Region or country: 37% Europe; 42% Africa Maternal CD4 count: mean NR; 53% ≥200 cells/mm3  Maternal viral load: mean NR; 27% ≥1,000 copies/mL  Gestational age: mean NR; 6% ≤32 weeks; 16% 33 to 36 weeks; 76% ≥37 weeks | 5,285  mother- infant pairs | Fair | European Union Seventh Framework Programme; Pediatric European Network or Treatment of AIDS Foundation |
| Duryea, 201552 | Retrospective cohort | Single site Texas, U.S. | Through birth Period January 1984 to April 2014 | A. ART with PI (n=597) B. ART without PI (n=230) C. No ART (n=177) | All HIV+ women who delivered at the institution (University  of Texas Southwestern Medical Center, Dallas) during the study period | Maternal age at delivery: 25 to 28 years (p<0.001) Race/ethnicity: black 64% to 69%, Hispanic 19%, white 11% to 16% Gestational age at presentation for prenatal care: 12 to 24 weeks (p<0.001) CD4 count at presentation: 456 to 557 cells/mm3 (p<0.001) CD4 count at delivery: 505 to 565 cells/mm3 (p=0.349) Duration of diagnosis: 1 to 2 years (p<0.001) | 1,004 | Fair | NR |
| Floridia, 201353  Italian Group on Surveillance on Antiretroviral Treatment in Pregnancy | Prospective cohort | Unclear  Italy | Through birth Period 2001 to 2011 | Various cART regimens | HIV-positive pregnant women with data from the Italian National Programme on Surveillance on Antiretroviral Treatment in Pregnancy | Mean maternal age at conception: 32.3 years Ethnicity: 66% white, 29% African, 4% other  CD4 count at first trimester: 464 cells/mm3  HIV RNA at first trimester: 3.0 copies/mL, log10  HCV coinfection: 22%  HBV coinfection: 11%  Treatment-naive before pregnancy: 36%  Diagnosis of HIV during current pregnancy: 24.6%  Week of first ART in pregnancy: 10.4  Mode of HIV acquisition: 73.1% sexual, 13.6% PWID  Maternal ART at first trimester: 55.3% NRTI, 20.4% NNRTI, 27.8% PI | 1,257 | Fair | Italian Medicines Agency |
| French Perinatal Cohort Study ANRS-EPF  Mandelbrot, 201561 | Prospective cohort, no control | 90 sites  France (but majority from sub-Saharan Africa) | Pre- conception to postpartum Period 2000 to 2011 | cART 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% | All HIV-1+ women enrolled in the French Perinatal Cohort delivering in metropolitan France between 2000 and 2011 that received HAART (regimen containing ≥3 drugs or 1 drug other than a NRTI) during pregnancy. Women who received only reverse-transcriptase inhibitor monotherapy or dual therapy were excluded. However, women who switched from a combination therapy to monotherapy or dual therapy were included, as were the small number of women who received monotherapy with RTV-boosted PIs.  Breastfeeding women were excluded. | N=8,678  Age: <25 years 8.7%, 25 to 34 years 56.5%, >34 years 34.8%  Geographic origin: metropolitan France 16.6%, sub-Saharan Africa 71.6%, other 11.8%  HIV diagnosis before conception: 80.4%  Timing of ART initiation: before conception 47.2% (n=4,095), 1st trimester 8.2% (n=713), 2nd trimester 32.3% (n=2,803), 3rd trimester 12.3% (n=1,067)  Initial ART regimen during pregnancy: triple NRTI 5.9%, PI-based 76.1%, NNRTI-based 15.8%, 3 classes 1.2%, other 1.0% Last ART regimen during pregnancy: ZDV monotherapy 0.4%, dual NRTI 1.1%, triple NRTI 3.1%, PI-based 81.2%, NNRTI-based 10.9%, 3 classes 1.3%, other 2.0%  Maintained initial ART regimen throughout pregnancy: 71.4%  Last viral load before delivery (copies/mL): <50 68.0%, undetectable (50 to 400) 5.9%, 50 to 399 15.2%, ≥400 10.9%  CD4 count before delivery (cells/mm3):  <200 9.0%, 200 to 349 21.0%, 350 to 499 28.0%, ≥500 42.0%  Delivery mode: vaginal 42.7%, emergency Caesarean 22.0%, planned Caesarean 35.3% | Eligible: 8,678  mother- infant pairs  HIV status of child determ-ined: 8,075  mother- infant pairs | Fair | Agence Nationale de Recherche sur le SIDA et les Hepatites Virales |
| French Perinatal Cohort Study ANRS-EPF C01/C011  Sibiude, 201272 | See above | See above | See  Period 1990 to 2009 | 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) | All HIV-1+ women enrolled in the French Perinatal Cohort between 1990 and 2009  Substudy cohort:  Singleton births from 2005 through 2009 for mothers enrolled in the CO1 component of the cohort, which recorded more detailed data | A vs. B vs. C  Maternal age: median NR; 65% vs. 63% vs. 57% ages 25 to 34 years  Maternal geographic origin France: 28% vs. 31% vs. 19%  Africa: 51% vs. 53% vs. 63%  Other: 21% vs. 16% vs. 17%  D vs. E  Maternal age: median NR; 83% vs. 84% ages 25 to 39 years  Maternal geographic origin: Europe: 11% vs. 14%  Africa or Caribbean: 88% vs. 83%  Other: 1% vs. 3% | 13,271 | See above | French Agence Nationale de Recherche sur le SIDA |
| French Perinatal Cohort Study ANRS-EPF C01/C011  Sibiude, 201471 | Prospective cohort | 90 centers  France (but majority from sub-Saharan Africa) | 2 years  Period 1994 to 2010 | cART | Same as Sibiude 2012 | Same as Sibiude 2012  Median maternal age: 31 years  Origin sub-Saharan Africa: 61%  PWID: 2%  Exposed to ART in the first trimester: 42% (5,388) | 13,124 | See above | See above |
| French Perinatal Cohort Study ANRS-EPF C01/C011  and nested PRIMEVA ANRS  135 RCT  Sibiude, 201570 | Cohort combining prospectively collected observational data and retrospective analysis of data from an RCT | Same as Sibiude 2014 | Up to 24 months Period 1994 to 2010 | A. ZDV exposure (n=3,262)  B. No ZDV exposure (n=9,626) | Same as Sibiude 2014 | Maternal age: mean NR; 60% ages 25 to 34 years  Race/ethnicity: NR  Maternal geographic origin: 22% France; 61% Africa | 12,888 | See above | Agence Nationale de Recherche sur le SIDA et les Hepatites Virales |
| Fowler, 201644  PROMISE  trial | RCT, open label | 14 sites in 7 countries (India, Malawi, South Africa, Tanzania, Uganda, Zambia, Zimbabwe) | Through 6 to  14 days postpartum (antepartum period)  Period 2011 to 2014 | A. ZDV-based ART (ZDV, 3TC, LPV/r)  B. Tenofovir-based ART (tenofovir, FTC, LPV/r)  C. ZDV alone (ZDV plus intrapartum single-dose NVP with 6 to 14 days of TDF-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 TDF, women were assigned to any regimen regardless of HBV status (period 2 = October 2012 to October 2014) | CD4 count of ≥350 cells/mm3 (or a country-specific threshold for initiating triple-drug ART, if that threshold was higher), gestation of ≥14 weeks and not in labor, no previous use of triple-drug ART, no clinical or immune-related indication for triple-drug ART, a hemoglobin level of at least 7.5 g/dL, an absolute neutrophil count of at least 750 cells/mm3, an ALT of <2.5 times the upper limit of the normal range, an estimated creatinine clearance of >60 mL/min, and no serious pregnancy complications. Receipt of 1 or 2 antiretroviral agents for the prevention of mother-to-child transmission in previous pregnancies and for ≤30 days during the current pregnancy before enrollment was permitted. Key exclusion criteria were active tuberculosis or receipt of tuberculosis treatment within 30 days before trial entry, HBV infection requiring HBV treatment (patients who did not require HBV treatment could enroll), a structural or conduction heart defect, or a fetus with a serious congenital malformation. | Median age: 26 years  Race/ethnic group: 97% black African, 3% Indian, <0.5% other  Median CD4 count: 530 cells/mm3  Median viral load: 3.9 log10 copies/mL  WHO clinical stage 1: 97% Gestational age: 26 weeks  Region or country: 47% East Africa, 33% South Africa, 17% Southern Africa, 3% India | Enrolled 3,529  mother- infant pairs Analyzed: 3,490  mother- infant pairs | Fair | The National Institute of Allergy and Infectious Diseases of the National Institutes of Health, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the National Institute of Mental Health, and some study drugs were donated by pharmaceutical companies |
| Kakkar, 201554  CMIS Mother-Infant Cohort | Retrospective cohort | Canada (Montreal) | Period 1988 to 2011 | A. Boosted PIs (n=144)   1. B. Unboosted PI (n=220) 2. C. Other treatment (n=166) 3. D. No treatment (n=59) | CMIS mother-child cohort of all HIV- positive pregnant women presenting to Centre Hospitalier Universitaire Sainte-Justine with attendance for at least 2 antenatal obstetric visits and singleton live births, at gestational age of 24 weeks or older | A vs. B vs. C vs. D  Maternal age: median NR; 60% vs. 63% vs. 66% vs. 62% ages 25 to 35 years  Race/ethnicity: 79% vs. 63% vs. 66% vs.  64% black; 15% vs. 28% vs. 26% vs. 34%  Caucasian; 5% vs. 9% vs. 9% vs. 2% other | 525  mother- infant pairs | Fair | Fonds de Recherche du Quebec-Santé |
| Knapp, 201255  IMPAACT Groups Protocol P1025 | Case-control | Multiple sites International | Through birth Period 2002 to 2007 | Various cART regimens  A. Congenital anomaly (n=61)  B. No congenital anomaly (n=1,051) | Singleton children born to HIV-infected mothers enrolled in P1025 trial | Maternal age at enrollment, ≤24 years: 33%  Maternal age at enrollment, 25 to 34 years: 53%  Maternal age at enrollment, ≥35 years: 15%  HIV diagnosis prior to pregnancy: 69%  Earliest ART use during pregnancy: 47% first trimester, 52% second trimester  HIV RNA near labor and delivery <400 copies/mL: 76% | 1,112 | Fair | National Institutes of Health, National Institute of Allergy and Infectious Diseases |
| Kreitchmann, 201456  LILAC Study | Prospective cohort | Multisite  Latin America and Caribbean | Through birth Period 2002 to 2011 | At least 28 days in 3rd trimester:   1. A. HAART + PI (888; 59%) 2. B. HAART no PI (410; 27%) 3. C. Non-HAART (134; 9%) 4. D. No ART (80; 5%)   Total N=1,512 | Pregnant women who were enrolled in the NISDI Perinatal and LILAC protocols with first pregnancy after study enrollment, and either a live birth or a stillbirth | Maternal age: mean 28.2 years  Maternal education: mean 8.0 years  Race/ethnicity: 91.4% Hispanic/Latino; 70% non-Hispanic/Latino; 58% white; 20.4% black; 21.6% other races | 1,563 | Fair | National Institute of Child Health and Human Development |
| Li, 201657 | Prospective cohort | 10 sites Tanzania | 18 months November 2004 to September 2011 | 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%) | HIV-infected pregnant women who had uninfected HIV-exposed infants at birth | Maternal age: median 30 years  Race/ethnicity: NR | 3,314 | Fair | U.S. President's Emergency Plan for AIDS Relief |
| Lopez, 201259 | Retrospective cohort (case control) | 1 site  Spain (Barcelona) | January 1986  to June 2010 Through birth | 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) | HIV-infected pregnant women who consecutively attended and delivered in a university referral hospital in Barcelona, Spain, covering an urban area of about 1 million inhabitants between January 1986 and June 2010. Inclusion criteria were singleton pregnancy and delivery beyond 22 weeks. Women with active PWID during pregnancy were excluded | HIV infected only:  Maternal age: mean 30 years  8% Black; other race/ethnicity NR  Low education level: 50%  Prior preterm delivery: 8% | 519 | Fair | NR |
| Lu, 201460  CPHSP Study | Retrospective cohort, no control | Canada (Ontario) | Through birth Period 1996 to 2008 | A. Complete antiretroviral prophylaxis (n=251)  B. Incomplete antiretroviral prophylaxis (n=336)  C. No antiretroviral prophylaxis (n=58) | Data from women delivering 1996 to 2008 in the Ontaria group of the CPHSP | Maternal age: NR  Maternal race/ethnicity: 63% black; 26% white  Maternal region or country: 52% Africa; 30% Canada  Caesarean delivery: 43%  Screen-detected HIV during pregnancy: NR; 13% were considered late diagnoses (diagnosed at or after delivery) | 645  mother- child pairs | Fair | None reported |
| Moodley, 201662 | Retrospective cross sectional analysis | Single center South Africa | July to December 2011 and January to June 2014 | 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) | Women with viable pregnancies delivering a neonate weighing ≥500 g and whose birth outcomes were recorded in the maternity register | NR | 3,695 | Fair | NR |
| Mor, 201763 | Cohort | Multisite Israel | Through birth Period 1985 to 2011 | A. Infants born before 1996 (n=80) B. Infant born after 1997 (HAART introduced; n=716) | All HIV-infected women who delivered in Israel and were local citizens between January 1988 and December 2011 | A vs. B  Maternal age: 27.6 vs. 30.4 years (p=0.001)  Mother born in Ethiopia: 87.5% vs. 81.7%  HIV transmission route: endemic country 88.6% vs. 82.6%, drug use 1.3% vs. 5.3%, heterosexual 10.1% vs. 12.1%  Previous HIV-infected child(ren): 12.0% vs. 9.9%  Mother did not receive HAART during pregnancy: 90.0% vs. 46.8% (p=0.001)  Caesarian delivery: 11.2% vs. 44.4% (p=0.001)  Mother did not receive ART during labor: 95.0% vs. 55.8%  Infant did not receive ART after birth: 80.0% vs. 19.9% (p=0.001)  Breastfed: 1.3% vs. 1.0% | 796 infants born to HIV-infected mothers | Fair | No funding received |
| Pintye, 201765  Partners PrEP Study and Partners Demonstration Project | Cohort | Kenya and Uganda | Partners  PrEP: 2008 through 2012 Partners Demonstration Project: 2012–2016 | A. TDF-containing 3-drug ART (n=208) B. Non-TDF–containing 3-drug ART (n=214) | Women who were HIV-infected at enrollment in Partners PrEP or Partners Demonstration Projects and became pregnant during the study period | A vs. B Maternal age 24.7 vs. 26.6 years Years of education: 8 vs. 7 years Timing of ART initiation: 39.2% vs. 26.4% before pregnancy; 20.6% vs. 13.0% first trimester; 40.2% vs. 60.6% second or third trimester | 422 preg-nancies | Fair | National Institutes of Health, University of Washington Center for AIDS Research, University of Washington Global Center for Integrated Health of Women, Adolescents, and Children |
| Ramokolo, 201766  PMTCT Program | Cross- sectional cohort | 580 sites South Africa | Through 4–8 weeks postpartum Period October 2012 to May 2013 | A. Postconception ART (n=780) B. Preconception ART (n=616) C. ZDV prophylaxis (n=873) D. No ART (n=330) | Mother-infant pairs attending immunization services at 1 of 580 primary health facilities offering immunization services consecutively or systematically enrolled, regardless of maternal HIV status | A vs. B vs. C vs. D Maternal age: 3.1% vs. 1.8% vs. 7.0% vs. 5.2% <20 years; 28.5% vs. 10.0% vs. 36.2% vs. 34.9% ages 20–25 years; 27.2% vs. 23.3% vs. 26.1% vs. 24.5% ages 26–29 years; 29.8% vs. 35.2% vs. 19.1% vs. 20.7% ages 30–35 years; 14.6% vs. 29.8% vs. 11.6% vs. 14.7% >35 years Education less than 7th grade: 15.1% vs. 16.9% vs. 21.8% vs. 22.1% Black race: 98.2% vs. 97.3% vs. 96.2% vs. 97.5% | 2,599 (HIV exposed infants only) | Fair | Centers for Disease Control and Prevention; South African National Health Scholarship Programme |
| Sartorius, 201345  Kesho Bora Trial | RCT | Africa (3 countries) | January 2005 and August 2008  Duration: 28 weeks of pregnancy until 12 to 24 months after delivery | A. Triple ART, CD4 <200 (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 | HIV-infected women had to reside and plan to continue living in the study area until 2 years postdelivery, have no contraindication to receive ART, and no evidence of clinically significant conditions (obstetric, cardiac, respiratory including active tuberculosis, hepatic, gastrointestinal, endocrine, renal, hematologic, psychiatric, neurologic, or allergic) that may interfere with study interventions | A vs. B vs. C vs. D  Maternal age: 28 vs. 26 vs. 27 vs. 27 years  Secondary education or higher: 36% vs. 40% vs. 52% vs. 49% | 1,072 | Fair | NR |
| Short, 201368 | Retrospective analysis | 1 site  U.K. (London) | Period 1996 to 2010 | A. ZDV (n=65)   1. B. Dual NRTI (n=7) 2. C. Triple NRTI (n=5) 3. D. Short-term cART (n=59)   E. Preconception cART (n=131)  F. New continuous cART (n=56) | HIV-positive pregnant women managed by a single, multidisciplinary team at St Mary’s Hospital | Maternal age: median 32 years  Race: 78% black African; other races NR  Maternal history of any AIDS-defining illness: 11.5%  Median gestational age: 13 weeks | 331 | Fair | NR |
| SMARTT and PHACS Studies  Nozyce, 201464 | Prospective cohort | Multisite  U.S. | Up to 13 years  Period 2007 to 2012 | Any maternal cART regimen containing ≥3 antiretroviral drugs from ≥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 | All children enrolled in the SMARTT Static cohort (HIV-exposed) who completed a valid, age-appropriate measure of cognition and/or academic achievement in English and had information regarding in utero and neonatal ART exposure | Male: 49% to 52%  Ethnicity: 75% to 77% black, 19% to 25% Hispanic  Preterm birth (<37 weeks): 17% to 21%  Low birth weight (<2,500 g): 18% to 20%  Household annual income ≤$20,000: 59% to 69%  Caregiver with less than a high school education: 32% to 34%  First viral load during pregnancy >400 copies/mL: 60% to 72%  Last viral load prior to delivery >400 copies/mL: 19% to 33% | 739 | Fair | Eunice Kennedy Shriver National Institute of Child Health and Human Development; National Institute on Drug Abuse; National Institute of Allergy and Infectious Diseases; Office of AIDS Research; National Institute of Mental Health; National Institute of Neurological Disorders and Stroke; National Institute on Deafness and Other Communication Disorders; National Heart, Lung, and Blood Institute; National Institute of Dental and Craniofacial Research; and the National Institute on Alcohol Abuse and Alcoholism; Harvard University and Tulane University and National Institutes of Health |
| PHACS Study  Lipshultz, 201558 | Same as Nozyce 2014 | Same as Nozyce 2014 | Mean 4 years  Period 2007 to 2012 | A. HIV-exposed uninfected (n=417)  B. HIV-unexposed controls (n=98) | SMARTT enrolled children with echocardiography and unexposed controls | A vs. B  Maternal age: 28 vs. 26 years  Race: 62% vs. 70% black; 30% vs. 26% white; 9% vs. 4% other; 39% vs. 22% Hispanic  Child age at time of echocardiography: 4.0 vs. 4.8 years | 515 | Same as Nozyce 2014 | National Institutes of Health |
| SMARTT, study of the PHACS cohort and P1025 study of the IMPAACT cohort  Rough, 201867 | Cohort | 2 multisite cohorts  U.S. | Period 2007 to 2016 for Dynamic cohort of the SMARTT study and 2002 to 2013 for the P1025 study | A. TDF-FTC + LPV/r (128; 8%)  B. ZDV + 3TC + LPV/r (954; 59%)  C. TDF-FTC + ATV/r (539; 33%) | All infants with an observed birth outcome in the SMARTT or P1025 study, when the first ART regimen that their mothers used during pregnancy was one of the following: TDF-FTC + LPV/r, ZDV + 3TC + LPV/r, or TDF-FTC + ATV/r | A vs. B vs. C  Maternal age: 39.1% vs. 37.2% vs. 25.2% ≤24 years, 52.3% vs. 49.6% vs. 54.4% 25–34 years, 8.6% vs. 13.1% vs. 20.2% ≥35 years  Race: 11.7% vs. 7.1% vs. 8.2% non-Hispanic white, 63.3% vs. 64.0% vs. 67.7% non-Hispanic black, 23.4% vs. 27.0% vs. 22.3% Hispanic, 0.8% vs. 1.2% vs. 1.7% other  First CD4 count in pregnancy: 23.4% vs. 20.3% vs. 18.6% <250 cells/mm3, 36.7% vs. 39.9% vs. 38.0% 250–500 cells/mm3, 36.7% vs. 38.3% vs. 41.7% >500 cells/mm3  First viral RNA in pregnancy: 47.7% vs. 29.5% vs. 51.4% <400 copies/mL, 25.8% vs. 37.8% vs. 25.4% 400–10,000 copies/mL, 25.8% vs. 32.0% vs. 22.6% >10,000 copies/mL  Timing of regimen initiation: 45.3% vs. 11.6% vs. 49.2% before pregnancy, 14.1% vs. 12.1% vs. 15.2% first trimester, 40.6% vs. 76.3% vs. 35.6% second or third trimester | 1,621 | Fair | Same as Nozyce 2014 |
| SMARTT and PHACS Studies  Siberry, 201269 | Prospective cohort | Multisite U.S. | Through infant growth at 1 year Period through January 2011 | A. TDF-containing ART (n=449) B. non-TDF–containing ART (n=1,580) | Data collected in the SMARTT of the PHACS network, restricted primary models to consider only those exposed in utero to combination antiretroviral regimens with vs. without TDF | Race/ethnicity: black 66%, Latino 33% Caesarian delivery: 54% Gestational age: <32 weeks 3%, 32–37 weeks 17%, ≥37 weeks 76% Maternal CD4 count <250 cells/mm3 at delivery: 15% HBV+: 2% | 2,029 | Same as Nozyce 2014 | Same as Nozyce 2014 |
| SMARTT and PHACS Studies  Watts, 201375 | Prospective cohort | 22 sites  U.S. | Unclear Period 2007 to 2010 | Various maternal cART regimens | HIV-infected mothers and their children enrolled in SMARTT of the PHACS network. This analysis limited to singleton gestations with maternal enrollment on or before October 2010. | Mean maternal age at delivery: 27 years  Ethnicity: 65% black, 28% white, 7% other [34% Hispanic]  Annual household income <$20,000: 63%  CD4 count <200 cells/mm3: 13%  CD4 count 200 to 500 cells/mm3: 46%  CD4 count >500 cells/mm3: 36%  Antiretroviral regimen: 3% none, 7% monotherapy or dual therapy, 71% combination with PI (with or without NNRTI), 10% combination with ≥3 NRTIs, 9% combination with NNRTI (no PI)  First trimester use of cART: 40%  Second trimester use of cART: 63%  Third trimester use of cART: 76% | 1,869 | Same as Nozyce 2014 | Same as Nozyce 2014 |
| SMARTT and PHACS Studies  Williams, 201576 | Combined data from prospective and retrospective cohorts | Same as Nozyce 2014 | Period 2007-  2012 | A. Any ART (n=1,219)   1. 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 | Static (retrospective) cohort: Mothers or caregivers and their children younger than age 12 years who had detailed information on ART use during pregnancy and pregnancy outcomes  Dynamic (prospective) cohort: Pregnant women and their infants between 22 weeks of gestation and 1 week after delivery | Maternal age: mean NR; 13% >35 years Race/ethnicity: 66% black; 27% white; 0.5%  other; 33% Latino/Hispanic Caregiver not a high school graduate: 5% | 2,580 | Same as Nozyce 2014 | Same as Nozyce 2014 |
| SMARTT and PHACS Studies  Williams, 201677 | Same as Nozyce 2014 | Same as Nozyce 2014 | Period 2007 to 2012 | 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) | SMARTT cohort of children with adverse event trigger cases, defined as language impairment, metabolic abnormality, impaired growth, neurologic diagnosis, neurodevelopmental impairment, elevated blood lactate, chemistry or hematology toxicity, or hearing impairment | No adverse event vs. adverse event  Maternal age: mean NR; 33% vs. 33% <25 years  Infant characteristics  49% vs. 47% female  Race/ethnicity: 68% vs. 61% black; 26% vs.  32% white; 4% vs. 4% Puerto Rican; 1% vs.  1% other; 32% vs. 37% Hispanic  17% vs. 25% low birth weight  19% vs. 24% preterm birth (<37 weeks of gestation)  55% vs. 56% Caesarean delivery | 2,680 | Same as Nozyce 2014 | Same as Nozyce 2014 |
| Snijdewind, 201873  ATHENA Cohort | Retrospective cohort | 26 centers  The Netherlands | Period 1997 to 2015 | A. PI-based (928; 67%)  B. NNRTI-based (438; 31%)  C. Both or NRTI (12; 1%) | ATHENA cohort database; HIV-positive women age >18 years who gave birth to HIV- exposed and uninfected infants after a minimum 24 weeks of pregnancy; singleton births; includes women who started cART preconception as well as those who began postconception | Maternal age: median 29 years  Region of origin: 61.3% sub-Saharan Africa, 20.7% Western Europe, 16.5% other  Mode of delivery: 44.5% spontaneous labor, 13.6% elective Caesarean delivery, 6.8% emergency Caesarean delivery, 27.7% unknown  CD4 count: median 520 cells/mm3  HIV RNA: 79.1% ≤500 copies/mL  Infant birth weight: median 3,090 kg  Duration of pregnancy: 85.3% >37 weeks, 11.9% <37 weeks | 1,378 | Fair | Dutch Health Ministry |
| Tookey, 201674  NSHPC Study | Retrospective cohort, no control | U.K. and Ireland | Through birth Period 2003 to 2012 | LPV/r | NSHPC participants with pregnancies who were due to deliver | Maternal age: median 30 years  Maternal race/ethnicity: 15% white; 77% black; 8% other  Maternal region/country: 14% U.K./Ireland; 77%  Africa; 10% other | 4,118  mothers, 4,864  pregnan-cies | Fair | Health Protection Agency, National Screening Committee and the Welton Foundation, Medical Research Council, National Institute for Health Research, Biomedical Research Centre at Great Ormond Street Hospital for Children, National Health Service Foundation Trust, and University College London |
| Zash, 201679 | Cohort | 2 hospitals Botswana | Through birth Period May 2009 to April 2011 and April 2013 to April 2014 | A. TDF-FTC and EFV at conception (n=165) B. Other 3-drug ART at conception (n=2,006) C. TDF-FTC and EFV during pregnancy (n=1,054) D. Other 3-drug ART during pregnancy (n=2,172) | All women who delivered live-born or stillborn infants at 8 government maternity wards in Botswana  Excluded births that occurred before arrival at hospital and at gestational age <24 weeks | HIV infected, years 2009–2011 vs. 2013–2014: Maternal age: 28.9 vs. 30.2 years Any medical history: 17.4% vs. 19.5% Hypertension in pregnancy: 19.1% vs. 17.5% Anemia in pregnancy: 59.0% vs. 48.1% Primiparous 20.6% vs. 15.9% No prenatal care: 5.7% vs. 4.8% Unknown HIV status: 4.7% vs. 1.2% No ART during pregnancy: 16.1% vs. 12.3% Initiated ART <4 weeks prior to delivery: 24.7% vs. 17.0% Initiated ART <28 weeks gestational age: 22.0% vs. 59.8% Median CD4 count: 388 vs. 415 cells/mm3 | 32,583 births, 9,445 HIV- infected women | Fair | CDC, National Institutes of Health/National Institute of Allergy and Infectious Diseases |
| Zash, 201778 | Surveillance cohort | 8 government hospitals Botswana | Through birth Period August 2014 to August 2016 | 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) | All women who delivered live-born or stillborn infants at 8 government maternity wards in Botswana  Excluded births that occurred before arrival at hospital and at gestational age <24 weeks, and HIV- positive mothers with no ART exposure, unknown ART timing, or unknown ART exposure | Maternal age: median 31 years Primiparous: 14.8% Gestational age at antenatal care presentation: median 17 weeks Received no prenatal care: 3.3% Alcohol consumption or smoking during pregnancy: 8.1% Caesarean delivery: 23.7% ART prior to conception: 5,780 infants, breakdown below: TDF-FTC-EFV: 2,503 ZDV-3TC-NVP: 1,403 TDF-FTC-NVP: 775 Unspecified ART: 547 TDF-FTC-LPV/r: 237 ZDV-3TC-LPV/r: 169 Other 3-drug ART: 104 Nonstandard ART: 21 Changed or terminated ART: 21 ART after conception: 4,812 infants, breakdown below: TDF-FTC-EFV: 4,569 Other ART regimen: 129 Unspecified ART: 94 Changed or terminated ART: 14 ZDV monotherapy: 3 Nonstandard ART: 3 | 47,124 total births 11,932 HIV- exposed births 10,592 included in analysis | Fair | National Institutes of Health |

**Abbreviations:** 3TC=lamivudine; ABV=abacavir; ANRS-EPF=French Agence Nationale de Recherche sur le SIDA-Enquête Périnatale Française; ART=antiretroviral therapy; ATV=atazanavir; ATV/r=atazanavir/ritonavir; AZT=azidothymidine cART=combination antiretroviral therapy; CD4=cluster of differentiation 4; CDC=Centers for Disease Control and Prevention; CHIPs=Collaborative HIV Paediatric Study; CMIS=Centre Maternal et Infantile sur le SIDA; CPHSP=Canadian Perinatal HIV Surveillance Program; CoRISPE-Cat=Catalan Cohort of HIV-Infected Children; D4T=stavudine; DRV=darunavir; ECS=European Collaborative Study; EFV=efavirenz; EPPICC=European Pregnancy and Paediatric HIV Cohort Collaboration; FTC=emtricitabine; HAART=highly-active antiretroviral therapy; HBV=hepatitis B virus; HCV=hepatitis C virus; IMPAACT=International Maternal Pediatric Adolescent AIDS Clinical Trials; ITLR=Italian Register for HIV Infection in Children; LILAC=Perinatal and Longitudinal Study in Latin American Countries; LPV=lopinavir; LPV/r=lopinavir/ritonavir; MoCHiV=Swiss Mother and Child HIV Cohort Study; NIH=National Institutes of Health; NISDI=National Institute of Child Health and Human Development International Site Development Initiative; NNRTI=nonnucleoside reverse transcriptase inhibitors; NR=not reported; NRTI=nucleoside reverse transcriptase inhibitor; NSHPC=National Study of HIV in Pregnancy and Childhood; NVP=nevirapine; PHACS=Pediatric HIV/AIDS Cohort Study; PI=protease inhibitor; PrEP=pre-exposure prophylaxis; PROMISE=Promoting Maternal and Infant Survival Everywhere; PWID=persons who inject drugs; PWTCT=Prevention of Mother to Child Transmission Program; RAL=raltegravir; RAMQ=Régie de l'Assurance Maladie du Québec; RCT=randomized, controlled trial; RNA=ribonucleic acid; RPV=rilpivirine; RTV=ritonavir; SMARTT=Surveillance Monitoring for Antiretroviral Treatment Toxicities study; TDF=tenofovir disoproxil fumarate; U.K.=United Kingdom; U.S.=United States; 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.