

Table 1

**Risk of Vertical Transmission of HIV with cART**

<b>Ref</b>	<b>Location</b> * Indicates breastfeeding population	<b>Study Group</b>	<b>Study design</b>	<b>Years</b> (data collection, if available, or publication)	<b>Data</b> BF= breastfeeding; VL= viral load; (c)ART= (combined) antiretroviral therapy; VT= vertical transmission (of HIV)
1	United Kingdom and Ireland	National Study of HIV in Pregnancy and Childhood (NSHPC)	National surveillance data	2000-2011	<ul style="list-style-type: none"> <li>12,486 HIV-exposed infants delivered from 2000-2011 in the UK/Ireland.</li> <li>VT declined from 2.1% in 2000-2001 (17/816, 95% CI: 1.2-3.3%) to 0.46% in 2010-2011 (9/1975, 95% CI: 0.21-0.86).</li> <li>VT was 0.09% (6/6345) with undetectable VL (&lt;50 copies/ml) near delivery, and 0.05% (2/3859) with undetectable VL on cART.</li> <li>With preconception cART: 93% had undetectable VL at delivery (1894/2045), 5% were virally suppressed (50-399 copies/mL; 101/2045), and 2% had ≥400 copies/mL (50/2045).</li> <li>With preconception cART: overall VT was 0.19% (4/2105), and VL was detectable (n = 3) or missing (n = 1) for transmitting mothers.</li> <li>No transmissions occurred among those with preconception cART and undetectable VL at delivery (n=1894).</li> </ul>
2	France	French Perinatal Cohort	Prospective cohort	2000-2011	<ul style="list-style-type: none"> <li>8075 HIV-exposed infants delivered from 2000-2011.</li> <li>VT was 0.2% (6/3505) with preconception cART, vs. 0.4% (3/709), 0.9% (24/2810), and 2.2% (23/1051) for those starting during the first, second, or third trimester (P &lt; .001).</li> </ul>
3	United States	Ponce Family and Youth Clinic of the Grady Health Systems	Retrospective chart review	2005-2012	<ul style="list-style-type: none"> <li>In review of all perinatal HIV cases treated in a regional referral center Atlanta, GA during this period, 24/27 (89%) were delivered by mothers with detectable VL.</li> <li>Of those perinatally infected infants who delivered in the setting of undetectable VL, each had additional risk factors: prolonged rupture of membranes of unknown duration, placental abruption, and preterm delivery after third trimester VL &gt; 100,000.</li> <li>Clear risk factors for VT: insufficient cART and/or prenatal care, illicit drug use</li> </ul>
4	United States	IMPAACT	Prospective cohort	2002-2011	<ul style="list-style-type: none"> <li>In this multicenter study, 671 ART-naïve women started cART during pregnancy and 13.1% had a detectable VL at delivery.</li> <li>91.4% (117/128), 87.7% (399/455) and 76.1% (67/88) starting in first, second and third trimesters, respectively, achieved undetectable VL by delivery (P = 0.003).</li> <li>The only case of VT (0.2%) in this cohort had third trimester initiation, nonadherence to cART, and VL &gt; 1000 near delivery.</li> </ul>
5	Malawi, Mozambique, Tanzania, Rwanda, Botswana, Uganda, and Kenya*	DREAM, Mitra, Mitra Plus, AMATA, Mima Bana, Kisumu	Systematic review	2001-2009	<ul style="list-style-type: none"> <li>In 8 high quality clinical trials, up to 6 months of exclusive BF while on cART was associated with 0-1% postnatal VT.</li> </ul>

Table 1 (continued)

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6	South Africa, Malawi, Tanzania, Uganda, Zambia, Zimbabwe and India*	PROMISE	Randomized controlled trial	2006-2011	<ul style="list-style-type: none"> <li>Postnatal VT (n=2431) after 6, 9 and 12 months of BF with maternal cART was 0.3% (95% CI 0.1-0.6), 0.5% (95% CI 0.2-0.8) and 0.6% (95% CI 0.4-1.1), respectively.</li> </ul>
7	Botswana*	Mma Bana	Randomized controlled trial	2006-2008	<ul style="list-style-type: none"> <li>730 women initiated cART from 26-34 weeks:</li> <li>At enrollment: 13.6% had VL <math>\leq</math> 1000, 19.6% had VL <math>\geq</math> 100,000 and 23.3% had AIDS.</li> <li>At 6 months postpartum, &gt;90% had achieved and maintained viral suppression (&lt;400 copies/mL) during pregnancy and BF.</li> <li>Total VT was 1.1% (8/709), with 0.3% postnatal transmissions (2/709).</li> <li>Of the two postnatal transmitting mothers, one postnatal had undetectable VL at delivery but subsequent "adherence issues" (by pill count or self-report); the other had VL &gt; 170,000 at enrollment and delivered at 32 weeks with a detectable VL.</li> </ul>
8	Malawi*	BAN	Randomized controlled trial	2004-2010	<ul style="list-style-type: none"> <li>849 infants BF for 28 weeks while mothers took cART:</li> <li>Grade 3 or 4 adverse events included: 0.4% transaminitis (3), 19.6% anemia (166), 0.5% leukopenia (4), 1.1% thrombocytopenia (9), and 0.1% hypersensitivity rash (1).</li> <li>These infants did not have an increased rate of events compared to 668 controls with just 1 week of postpartum maternal prophylaxis (RR 1.1; 95% CI 0.86-8.45).</li> </ul>
9	Tanzania*	Kilombero and Ulanga Antiretroviral Cohort (KIULARCO)	Prospective cohort	2013-2016	<ul style="list-style-type: none"> <li>215 women started ART before delivery, and continued it while exclusively BF for <math>\geq</math> 5 months:</li> <li>During BF, 91% of mothers had VL &lt; 1000 copies/mL, with 75% &lt; 100 copies/mL.</li> <li>Two infants (1%) were infected from BF: one mother had high VL (144,111 copies/mL) one month postpartum, and the other mother stopped ART during BF.</li> <li>There was no VT through BF among mothers with suppressed VL in this cohort</li> </ul>
10	Mozambique, Malawi, Kenya, South Africa, Tanzania, Uganda, Zimbabwe, and India*	HPTN046 trial, Kisumu, BAN, DREAM, Mitra Plus, Vicente Ferrer HIV Cohort Study (VFHCS)	Systematic review and meta-analysis	2003-2010	<ul style="list-style-type: none"> <li>Meta-analysis of 6 studies, including 3 cohorts embedded in RCTs and 3 observational studies, published 2009-2012, comprising 2109 BF infants with mothers on cART:</li> <li>In pooled analysis, postpartum VT after 6 months of BF was 1.08% (95% CI 0.32-1.85), with range 0.24% (1/413; 95% CI 0.0%-1.40%) to 3.10% (4/127; 95% CI 1.20%-7.80%).</li> <li>Limited or absent maternal VL or adherence data, routine initiation of cART late in pregnancy for majority of participants, many BF without viral suppression, rare preconception cART only in the setting of advanced HIV/AIDS, and infants did not receive current standard-of-care prophylaxis.</li> <li>Very low quality evidence (GRADE profile) with "very serious" risk of bias, "very serious" inconsistency (I2=66.4%), "serious" indirectness, "not serious" imprecision.</li> </ul>

Table 2

**Impact of Breastfeeding on Infant Health in High Income Countries**

Ref	Location	Study design	Years (data collection, if available, or publication)	Data
11	International	National surveillance data	2014	<p>BF= breastfeeding; (c)ART= (combined) antiretroviral therapy; SIDS= sudden infant death syndrome; NEC= necrotizing enterocolitis</p> <ul style="list-style-type: none"> <li>• Under-5 child mortality is 6.5/1000 in the US, vs. 83.1/1000 livebirths in Sub-Saharan Africa</li> <li>• Gastrointestinal and respiratory infections are leading causes of child mortality in low-income-countries, but not in high-income-countries.</li> <li>• In the US 83% of under-5 child deaths occur in the first year of life, a similar proportion to low-income-countries.</li> </ul>
12	United States	National surveillance data	2013	<ul style="list-style-type: none"> <li>• Infant mortality (5.96/1000 livebirths) is predominantly from complications of prematurity (36.1%) (eg. NEC, sepsis), and SIDS (6.7%).</li> <li>• Preterm infants disproportionately bear the mortality burden, as they comprise 11.4% of livebirths, but 66.4% of deaths.</li> <li>• Infant mortality per 1,000 livebirths was 11.11 for non-Hispanic blacks vs. 5.06 for non-Hispanic whites, largely attributed to disparities in death from prematurity and SIDS (3 and 2 times higher mortality, respectively).</li> </ul>
13	United States	Prospective cohort and retrospective review	2007-2010	<ul style="list-style-type: none"> <li>• 18.6% of HIV-exposed infants are preterm (n=1869), with highest rates of spontaneous preterm delivery among those with pre-conception cART (OR 1.59, 95% CI 1.10-2.30).</li> <li>• Preterm birth occurred among 155 of 748 women (21%) with first-trimester exposure to cART and among 155 of 924 women (17%) with initial exposure to cART during the second or third trimester (P = .043, by the Fisher exact test).</li> <li>• Very preterm birth occurred among 3% of those with first-trimester exposure and among 1% of those with later exposure to combination regimens (P = .005, by the Fisher exact test), with risk up to 4 times greater with PI containing ART regimens, adjusted analysis (adjusted OR, 4.17; 95% CI, 1.70–10.26; P = .003), compared with no combination regimen in the first trimester.</li> </ul>
14	United States	Prospective cohort	2001-2011	<ul style="list-style-type: none"> <li>• Of 183 HIV-exposed infants, 31.2% were small for gestational age <math>\leq</math>10th percentile, with 12.6% weighing <math>\leq</math>3rd percentile.</li> </ul>
15	France	Prospective cohort	2005-2009	<ul style="list-style-type: none"> <li>• HIV-exposed infants (n=1,377) were twice as likely as the general population to be premature, with rates highest among those with pre-conception treatment.</li> </ul>
16	High Income Countries	Confounder-adjusted meta-analyses	2016	<ul style="list-style-type: none"> <li>• 11 studies showed 35% reduction (95% CI 14–51) in type 2 diabetes;</li> <li>• 23 high-quality studies with <math>\geq</math> 1500 participants showed 13% lower overweight/obesity (95% CI 6–19);</li> <li>• 29 studies on asthma showed 9% (95% CI 2–15) reduction;</li> <li>• 18 studies on childhood leukemia showed 19% (95% CI 11–27) reduction; and,</li> <li>• 16 studies showed child intelligence quotient (IQ) increased by 3.4 points (95% CI 2.3–4.6).</li> </ul>
17	Israel	Case-control	1995-2003	<ul style="list-style-type: none"> <li>• Among 6198 preterm infants (&lt;37 weeks), BF significantly decreased urosepsis (OR 0.314, 95% CI 0.140–0.707, P&lt;0.009).</li> </ul>

Table 2. (continued)

**Impact of Breastfeeding on Infant Health in High Income Countries**

Ref	Location	Study design	Years (data collection, if available, or publication)	Data
18	High Income Countries	Systematic review and meta-analysis	2007	<p>BF= breastfeeding; (c)ART=(combined) antiretroviral therapy; SIDS= sudden infant death syndrome; NEC= necrotizing enterocolitis</p> <ul style="list-style-type: none"> <li>• 4 randomized-controlled trials demonstrate BF decreases NEC 58% (95% CI 4-82).</li> <li>• In 23 studies, comprising 4,251 cases and 58,055 controls, "the overall risk of SIDS was twice as great for bottle-fed infants compared to [BF] infants." (OR 2.11; 95% CI 1.66-2.68).</li> <li>• BF prevents gastroenteritis (OR 0.36, 95% CI 0.18-0.74, P=0.005) and hospitalization for respiratory infections (RR 0.28, 95% CI 0.14-0.54).</li> <li>• Sub-analysis of 6 high-quality studies showed BF decreased SIDS by 36% (95% CI 19-49), adjusted summary odds ratio [SOR]: 0.64 [95% confidence interval (CI): 0.51-0.81].</li> </ul>
19	United Kingdom	Systematic review and economic model	2013	<ul style="list-style-type: none"> <li>• A model of the impact of BF on preterm infants (n=51,703, the number born in the index year) demonstrated 190 fewer deaths from sepsis and NEC if the infants were BF vs. formula-fed while in the NICU.</li> </ul>
20	High Income Countries	Meta-analysis	1995-2009	<ul style="list-style-type: none"> <li>• The multivariable pooled estimate revealed decreased SIDS with any BF (OR 0.55, 95% CI: 0.44-0.69).</li> <li>• SIDS risk is lowest with exclusive BF (OR 0.27; 95% CI, 0.27-0.31).</li> </ul>
21	United States	Monte Carlo simulation and cost-analysis	2016	<ul style="list-style-type: none"> <li>• An estimated 721 excess pediatric deaths/year were attributed to suboptimal BF in the US, mostly from SIDS (n = 492) and NEC (n = 190).</li> <li>• Increased uptake of BF decreased this estimate from 911 excess deaths in 2010.</li> </ul>
22	United States	National surveillance data	2014	<ul style="list-style-type: none"> <li>• Acute lower respiratory and gastrointestinal infections caused 476 US infant deaths (12/100,000 livebirths).</li> <li>• 275 deaths of children &lt; 15 years old from sepsis.</li> </ul>
23	United States	Umbrella review	2016	<ul style="list-style-type: none"> <li>• Acute otitis media, which affects <input type="checkbox"/>80% under 3 years, is decreased by 40-50% with BF (OR 0.50, 95% CI 0.36-0.70).</li> </ul>
24	United States	National surveillance data	2014	<ul style="list-style-type: none"> <li>• Mortality from perinatal HIV is extremely low: there was 1 death among 1,995 children &lt; 13 with perinatal HIV, 0.05/100 child-years.</li> </ul>
25	United States	National surveillance data and population-based surveys	2014-2015	<p>Healthy People 2020 Objectives:</p> <ul style="list-style-type: none"> <li>• 81.1% of US women initiate BF; target 81.9%</li> <li>• 51.8% are BF at 6 months; target 60.6%</li> <li>• 30.7% are BF at 1 year; target 34.1%</li> <li>• Exclusively BF at 3 months: 44.4%; target 46.2%</li> <li>• Exclusively BF at 6 months: 22.3%; target 25.5%</li> <li>• Reduce proportion of BF newborns who receive formula supplementation in first two days of life: 17.1%; target 14.2%</li> <li>• Increase proportion of livebirths occurring in facilities providing recommended lactation care: 18.3%; target 8.1%</li> </ul>

Table 3

**Impact of Breastfeeding on Maternal Health in High Income Countries**

Ref	Location	Study design	Years (data collection, if available, or publication)	Data BF= breastfeeding
26	United States	Secondary analysis of prospective cohorts	1994-2005	<ul style="list-style-type: none"> <li>Among 139,681 parous participants in the Women's Health Initiative, women who had lactated were less likely to be obese, hypertensive, diabetic or hyperlipidemic than those who had not, with direct dose-response observed.</li> </ul>
27	United States	Secondary analysis of prospective cohort	1986-2002	<ul style="list-style-type: none"> <li>In the Nurses' Health Study of 89,326 parous women over 1,350,965 years of follow-up demonstrated that 2 years of cumulative lifetime BF reduced myocardial infarction by 23% (95% CI 6–38%, p-value=0.02), with 34% reduction (HR 0.66, 95% CI, 0.49-0.89) in first 30 years after last delivery.</li> </ul>
28	United States	Secondary analysis of prospective cohort	1991-2005	<ul style="list-style-type: none"> <li>Women who never BF are more likely to develop hypertension than those who BF <math>\geq 6</math> months (HR 1.29, 95% CI: 1.20-1.40).</li> </ul>
29	United States, Italy, Canada, Australia, Poland, China, and Sweden	Meta-analysis	1992-2013	<ul style="list-style-type: none"> <li>Analysis of 8,981 women with endometrial cancer and 17,241 control women demonstrated that ever having BF was associated with an 11% reduction in risk of endometrial cancer (pooled OR 0.89, 95% CI 0.81-0.98).</li> </ul>
30	United Kingdom	Cross-sectional analysis of population-based survey	1996-2001	<ul style="list-style-type: none"> <li>BMI decreased 1% per 6 months of BF among 740,628 British women.</li> </ul>
31	United States, Germany, Australia, and China	Systematic review and meta-analysis	1989-2008	<ul style="list-style-type: none"> <li>Meta-analysis demonstrates 32% lower risk of type 2 diabetes (OR 0.68, 95% CI 0.57–0.82), with risk decreasing ~11% per 3 months of BF.</li> </ul>
32	High Income Countries	Systematic review and meta-analysis	2015	<ul style="list-style-type: none"> <li>Meta-analysis of 72 studies showed 19% decrease in breast carcinoma (pooled OR 0.81, 95% CI 0.77-0.85, p&lt;.001) with any BF compared to never BF, and after fine adjustment of international data for parity and other confounders risk was reduced 7% (OR 0.93, 95% CI 0.89–0.97).</li> <li>35 studies on ovarian cancer demonstrated 26% reduction with any BF (OR 0.74, 95% CI 0.68–0.80, p&lt;.001), and 18% reduction in finely adjusted sub-analysis of international data (OR 0.82, 95% CI 0.75–0.89).</li> </ul>
33	International	Systematic review and meta-analysis	1960-2010	<ul style="list-style-type: none"> <li>Among parous women, BF has a stronger inverse association with hormone/triple-negative breast cancer (OR 0.78; 95% CI 0.66–0.91) than BF alone.</li> <li>Meta-analysis shows a protective effect of ever BF against hormone receptor-negative breast cancers, which are more common in younger women and generally have a poorer prognosis than other subtypes of breast cancer.</li> <li>Because black women have elevated baseline risk of hormone-and-triple-negative breast cancers, BF decreases their risk by 19%.</li> </ul>



Table 3 (continued)

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Ref	Location	Study design	Years (data collection, if available, or publication)	Data BF= breastfeeding
34	United States	Retrospective case-control with Arizona state surveillance data	2003-2007	<ul style="list-style-type: none"> <li>Among 1466 singleton infant deaths, short interpregnancy intervals significantly increased mortality and preterm birth, even after adjusting for confounders.</li> <li>Mortality risk was increased with short birth intervals (aOR 1.68, 95% CI 1.09–2.59, <math>p &lt; .05</math>) vs. the optimal interval (18–23 months); infant mortality is 76 % higher for interpregnancy interval &lt;6 months and 38 % higher for 12–17 months.</li> <li>After adjusting for confounders, short intervals increased risk for subsequent preterm birth: aOR 4.44 (95% CI, 3.35–5.89, <math>p &lt; .01</math>), and small for gestational age: aOR 1.96 (95% CI 1.45–2.66, <math>p &lt; .01</math>).</li> </ul>
35	Latin America; United States	Retrospective cohort study	1985-1997; 1989-1997	<ul style="list-style-type: none"> <li>Among 456,889 Latin American women, maternal death was more likely with interpregnancy interval &lt;6 months (aOR 2.5; 95% CI 1.2-5.4)</li> <li>A second pregnancy within 12 months postpartum significantly increased the risk of placental abruption by 52% and 111% among women whose first births were vaginal and cesarean, respectively. Interpregnancy intervals &lt;12 months were associated with 70% increased risk of placenta previa for women with a prior cesarean first birth (n= 156,475; RR 1.7, 95% ci 0.9-3.1).</li> </ul>
36	Brazil, Philippines, and Zimbabwe	Meta-analysis	1982-2004	<ul style="list-style-type: none"> <li>Subsequent pregnancies are also affected, as birth intervals &lt;18 months are independently associated with SGA (aOR 1.51), prematurity (aOR 1.58), and infant mortality (aOR 1.83).</li> </ul>
37	United States	Monte Carlo simulation and cost-analysis	2016	<ul style="list-style-type: none"> <li>Approximately 2,605 maternal deaths per year are attributed to suboptimal initiation and duration of BF.</li> </ul>
38	United States	National surveillance data	2015	<p>Examples of Racial and Ethnic Health Disparities:</p> <ul style="list-style-type: none"> <li>% of pregnancies that are unintended: Black (69%), Hispanic (56%), White (42%)</li> <li>% of livebirths that are premature: Black (17%), Hispanic (12%), White (10%)</li> <li>Maternal deaths per 100,000 livebirths: Black (26), Hispanic (5), White (7)</li> <li>Breast cancer deaths per 100,000 population: Black (31), Hispanic (15), White (22)</li> <li>Diabetes-related deaths per 100,000 population: Black (33), Hispanic (13), White (24)</li> </ul>
39	United States	Secondary analysis of observational study data	1993-2010	<p>In confounder-adjusted analysis of the Women's Health Initiative Observational Study data:</p> <ul style="list-style-type: none"> <li>Ever BF had a 23% lower risk of stroke than never BF (adjusted hazard ratio=0.77; 95% confidence interval 0.70–0.83).</li> <li>Stroke risk was most decreased with BF among non-Hispanic black women (adjusted hazard ratio=0.52; 95% confidence interval 0.37–0.71).</li> <li>Breastfeeding for a relatively short duration (1–6 months) was associated with a 19% lower risk of stroke (adjusted hazard ratios=0.81; 95% confidence interval 0.74–0.89).</li> </ul>

## Works Cited for Supplemental Tables

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