**Supplementary Material**

**Studies included in the review of mother to child transmission probabilities**

Review of data since the last 2015 review included published literature, reviewed by Pub Med search, personal files, and conference presentations (CROI and IAS 2016-2018). Cohort and observational data as well as clinical trials were included. Criteria for inclusion included: 1) provision of data on timing of diagnostic testing to be able to distinguish peripartum and postpartum transmission timing; 2) delineation of type of maternal antepartum antiretroviral (ARV) regimen; 3) if mother received antiretroviral therapy (ART), timing of initiation (before/during pregnancy); 4) when available, data on HIV RNA levels and transmission if the mother was receiving ART during pregnancy and timing of RNA measurement was near delivery; 5) when available, data on duration of maternal ART and transmission.

The search terms included: “incident/acute HIV in pregnancy” (37 papers identified), “incident/acute HIV during breastfeeding” (5 papers identified), and “mother to child HIV transmission” (949 papers identified); 991 papers and 7 abstracts were identified, 86 of which underwent full review, yielding 24 relevant new publications and 3 abstracts (1-27).

*Peripartum HIV transmission* was measured by infant HIV status generally at 4-6 weeks of age, although some studies reported data at 2 weeks or as late as 3 months. In formula-fed infants, this reflects in utero and intrapartum transmission; in breast-fed infants this reflects in utero, intrapartum and early postpartum transmission. The cumulative number of infections was divided by the cumulative number of HIV-exposed infants for an average peripartum transmission rate for each ARV category.

*Postpartum HIV transmission* was measured by transmission rates in breastfed infants who were uninfected at 4-6 weeks and subsequently found to be infected. The age at which postpartum transmission was measured differed between studies; in the 2015 review, the data primarily reflected 6-month data, because most studies were reporting on interventions that ceased at 6 months. However, since guidelines now recommend ART for all pregnant and breastfeeding women, ART no lower stops at 6 months, and the more recent studies report on postnatal transmission for longer durations on ART, through 12-18 months. Monthly postnatal transmission probabilities were calculated by dividing the cumulative postnatal transmission percent measured over a particular time interval by the number of months in that time period after subtracting the number of months when the “baseline” transmission was measured (because early postpartum transmission would have already been included in the “peripartum” 4-6 week transmission rate). For example, if peripartum transmission was measured at 6 weeks and cumulative transmission was measured again at 6 months, the transmission rate at 6 months was subtracted from the 6-week transmission rate, and divided by 4.5 months (the period during which breastfeeding had occurred in the infant after 6 weeks). Thus, if transmission at 6 weeks was 4% and at 6 months was 8%, then 4% of transmission was attributed to breastfeeding and was divided by 4.5 months (the time period between the 6-week and 6-month measurement), giving a postnatal transmission rate of 0.89% per month of breastfeeding. The weighted average for the particular PMTCT regimen category was calculated based on the study sample size.

*Incident infection* refers to newly acquired infections in pregnant or lactating women. Methods used to identify such women varied between studies, in some cases reflecting seroconversion from HIV-negative to positive and in a few studies reflecting the use of specific assay values.

Studies to evaluate postpartum transmission for the “*no prophylaxis*” category included studies of infants whose mothers received no ARV during pregnancy and postnatally or had received very short course (<4 weeks) zidovudine (AZT) or AZT/lamivudine (3TC) antepartum regimens. Studies to evaluate postpartum transmission for the “*single-dose nevirapine (sdNVP) prophylaxis*” category included studies in which infants had received sdNVP prophylaxis and no further infant or maternal prophylaxis was given.

Studies to evaluate postpartum transmission with *AZT/NVP* included studies in which extended infant prophylaxis was given; this included when the mother had received antepartum AZT/intrapartum sdNVP or in a few cases when the mother had not received AZT/sdNVP (e.g., the Breastfeeding and Nutrition (BAN) study was postnatal infant prophylaxis alone) (28).

*Duration of antepartum ART* was defined by the study; only studies that included mothers starting ART during pregnancy were included for evaluation of duration of ART and transmission. The category of < or >4 weeks was analyzed (included as “ART start near delivery” for the Spectrum model), but only a four studies (one new) reported this timeline.

An analysis of peripartum transmission by *maternal viral load near delivery* in women receiving ART was also performed, with a focus on “high viral load” >1,000 copies/mL criteria, although some studies reported on different viral load thresholds (>50, >400 copies/mL). Of 11 studies allowing comparison of peripartum transmission with viral load >1,000 copies/mL, 8 were from resource-rich, formula-feeding countries. These estimates were not used in the revised Spectrum model due to limited data availability from low-middle income or breastfeeding settings to inform the model, and viral load data were not viewed as being readily available in low-middle income countries.

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**Appendix Table 1. Retention in care at delivery.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study** | **Setting** | **# At risk** | **# Retained in care** | **% In care at delivery** | **% On ART**  **pre-conceptiona** |
| **Studies directly reporting on retention near delivery:** | | | | | |
| Abrams (2018) | Swaziland | 983 | 692 | 70% | 0% |
| Deschamps (2018) | Haiti | 883 | 657 | 74% | 42% |
| Oyeledun (2017) | Nigeria | 247 | 208 | 84% | 0% |
| Schnack (2016) | Uganda | 124 | 79 | 64% | 0% |
| **Studies from which retention near delivery was inferredb:** | | | | | |
| Chan (2016) | Malawi | 456 | 381 | 84% | 11% |
| Erlwanger (2017) | Malawi | 997 | 902 | 90% | 0% |
| Hauser (2018) | Malawi | 478 | 417 | 87% | 0% |
| Kim (2015) | Malawi | 1302 | 998 | 77% | 30% |
| Tweya (2014) | Malawi | 2930 | 2491 | 85% | 0% |
| **Pooled estimate:** | | | | | |
| **Total** |  | **8400** | **6825** | **81%** |  |
| **ANC:** antenatal care  **a**The pooled estimate of retention in care at delivery was 77% for the 3 studies that included any ART use prior to pregnancy and 83% for the six studies that did not include any ART use prior to pregnancy.  **b** These studies did not directly report retention at delivery; however, these studies did report retention in care at month X among women who were registered in antenatal care. If median gestational age at antenatal care enrollment was specified for an ART-naïve cohort, this information was used to approximate time of ART start. If median time on ART and/or gestational age at enrollment were not specified, it was assumed that women were registered in antenatal HIV care three months prior to delivery based on the average time on ART in pregnancy reported from the included studies. If the proportion retained in care was reported at month X and month X aligned with expected time of delivery based on gestational age at ANC enrollment and/or time on ART prior to delivery, then this proportion was taken to represent the % in care at delivery. | | | | | |

**Appendix Table 2. Retention in care through 24 months postpartum.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **2a. Retention in care at 6-10 weeks postpartum** | | | | |
| **Study** | **Setting** | **# At riska** | **# In care** | **% In care** |
| Asbjornsdottir (2017) | Mozambique | 1,576 | 851 | 54% |
| Dzangare (2016) | Zimbabwe | 118 | 96 | 81% |
| Etoori (2018) | Swaziland | 496 | 396 | 80% |
| Hauser (2018) | Malawi | 417 | 360 | 75% |
| Joseph (2016) | Uganda | 686 | 499 | 73% |
| Odeny (2018) | Kenya | 747 | 571 | 76% |
| Sarko (2017)b | Nigeria | 168 | 14 | 8% |
| Schwartz (2015) | South Africa | 50 | 48 | 96% |
|  |  |  |  |  |
| **Pooled estimate** |  | **4,258** | **2,835** | **67%** |
| **2b. Retention in care at ~6m postpartumc** | | | | |
| **Study** | **Setting** | **# At riska** | **# In care** | **% In care** |
| Abrams (2018) | Swaziland | 692 | 558 | 81% |
| Asbjornsdottir (2017) | Mozambique | 1,576 | 504 | 32% |
| Chan (2016) | Malawi | 381 | 368 | 85% |
| Erlwanger (2017) | Zimbabwe | 902 | 849 | 85% |
| Etoori (2018) | Swaziland | 496 | 351 | 71% |
| Ford (2017) | Zimbabwe | 385 | 327 | 85% |
| Foster (2017) | Zimbabwe | 138 | 113 | 82% |
| Harrington (2018) | Malawi | 291 | 235 | 81% |
| Koole (2014) | Malawi | 586 | 498 | 85% |
| Muhumuza (2017) | Uganda | 2,169 | 1,609 | 74% |
| Musomba (2017) | Uganda | 856 | 830 | 97% |
| Nance (2017) | Tanzania | 374 | 220 | 59% |
| Olwedo (2016) | Uganda | 277 | 177 | 64% |
| Oyeledun (2017) | Nigeria | 208 | 146 | 69% |
| Sarko (2017)d | Nigeria | 149 | 10 | 7% |
| Tweya (2014) | Malawi | 2,491 | 2,403 | 82% |
|  |  |  |  |  |
| **Pooled estimate** |  | **12,853** | **9,198** | **77%** |

**Appendix Table 2. Retention in care through 24 months postpartum (cont).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **2c. Retention in care at ~12m postpartume** | | | | |
| **Study** | **Setting** | **# At riska** | **# In care** | **% In care** |
| Akama (2018) | Kenya | 156 | 123 | 79% |
| Atanga (2017) | Cameroon | 211 | 182 | 86% |
| Deschamps (2018) | Haiti | 657 | 474 | 54% |
| Domercant (2017) | Haiti | 3,390 | 1,681 | 50% |
| Erlwanger (2017) | Zimbabwe | 902 | 753 | 76% |
| Ford (2017) | Zimbabwe | 382 | 302 | 79% |
| Gamell (2017) | Tanzania | 109 | 92 | 66% |
| Haas (2016) | Malawi | 26,658 | 20,475 | 77% |
| Kamuyango (2014) | Malawi | 189 | 185 | 98% |
| Karajeanes (2017) | Mozambique | 8,316 | 5,946 | 72% |
| Llenas-Garcia (2016) | Mozambique | 303 | 124 | 41% |
| CDC MMWR (2013) | Malawi | 2,949 | 2,267 | 77% |
| Muhumuza (2017) | Uganda | 2,169 | 1,447 | 67% |
| Mwapasa (2017) | Malawi | 384 | 274 | 71% |
| Myer (2018) | South Africa | 192 | 136 | 71% |
| Olwedo (2016) | Uganda | 277 | 114 | 41% |
| Phiri (2017) | Malawi | 437 | 261 | 60% |
| Schwartz (2015) | South Africa | 45 | 33 | 73% |
| Tweya (2014) | Malawi | 2,491 | 2,315 | 79% |
|  |  |  |  |  |
| **Pooled estimate** |  | **50,217** | **37,184** | **74%** |
| **2d. Retention in care at ~18m postpartumf** | | | | |
| **Study** | **Setting** | **# At riska** | **# In care** | **% In care** |
| Bobrow (2016) | Rwanda | 575 | 458 | 80% |
| Etoori (2018) | Swaziland | 455 | 262 | 58% |
| Mikitu (2016) | Ethiopia | 346 | 268 | 78% |
| Muhumuza (2017) | Uganda | 2,169 | 1,345 | 62% |
|  |  |  |  |  |
| **Pooled estimate** |  | **3,545** | **2,333** | **66%** |
| **2e. Retention in care at ~24m postpartumg** | | | | |
| **Study** | **Setting** | **# At riska** | **# In care** | **% In care** |
| Haas (2016) | Malawi | 25,849 | 18,306 | 71% |
| Karajeanes (2017) | Mozambique | 8,316 | 4,915 | 59% |
| Phiri (2017) | Malawi | 432 | 169 | 39% |
|  |  |  |  |  |
| **Pooled estimate** |  | **34,597** | **23,390** | **68%** |
| **a** When reported, deaths andclinic transfers were censored from the number at risk at each time point.  **b** The pooled estimate with removal of the Sarko (2017) study as an outlier is 69%.  **c** Pooled retention in care at ~6 months included data reported between the window of 3-8 months postpartum.  **d** The pooled estimate with removal of the Sarko (2017) study as an outlier is unchanged at 78%  **e** Pooled retention in care at ~12 months included data reported between the window of 9-14 months postpartum.  **f** Pooled retention in care at ~18 months included data reported between the window of 15-20 months postpartum.  **g** Pooled retention in care at ~24 months included data reported between the window of 21-16 months postpartum. | | | | |

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