

Estimates re. postnatal transmission in infants, uninfected at birth, by feeding practice and time periods

	Population (Maternal CD4 count, ART or ARV intervention, feeding practice, interval period)	Postnatal Transmission estimate for specified interval	Ref.	Comment
1	< 200 None EBF 0-5m	9.0%	14	Based on PEPI control arm (<200, BF - EBF recommended but not assessed). 6 week transmission = 10.7. Cumulative transmission at 6 mo = 21.9. Assumed additional BF transmission = 11.2%. Assume EBF assoc. with 20% risk reduction in this group.
2	> 200 None EBF 0-5m	3.0%	4,5,18	Populations in referenced populations included mothers with CD4 counts <200 which would increase transmission rate in infants. Iliff = 5.1 per 100 child years (2.5%/6m); Coovadia=4.04%; SPECTRUM estimates 6m transmission with RF=20% and EBF=23%, difference=3%.
3	< 200 ART EBF 0-5m	1.6%	1,2	DREAM reported 0.8%. Tonwe-Gold (<250 or clinical) point prevalence @ 1m=1% and 6m=3.3%. Postnatal transmission in cohort assessed=1.9%. No breastfeeding type reported, though assume to be MBF. BF for ~5.4m. Assume EBF assoc. with 15% risk reduction in this group.
4	> 200 ARV EBF 0-5m	1.5%	7	BANS reported 1.8%. No breastfeeding type reported, though assume to be MBF. Assume EBF assoc. with 15% risk reduction in this group.
5	< 350 None EBF 0-5m	6.0%	12	Kesho Bora. Maternal CD4 200-350 and short course ARVs, postnatal transmission=4.2%. EBF supported but not differentiated in data analysis. Increase total transmission to reflect infants of mothers (~15%) with CD4<200.
6	> 350 None EBF 0-5m	1.8%	12	Kesho Bora. Among all infants ever breastfed and born to mothers on short course ARV only, 6wk=4.5% and 6m=8.8%. Diff=4.3%. This includes infants of mothers with CD4 counts 200-350. In infants of mothers with CD4 counts 350-500 diff=2.5%. Allow for lower risk of infants of mothers with CD4>500 and also assume EBF assoc with 25% risk reduction.
7	< 350 ART EBF 0-5m	1.5%	1, 12	DREAM reported cumulative 1.8% <u>in all</u> . CD4 not stated and including those FF. (BF group had less postnatal transmission than FF). Kesho Bora. 200-350 and mothers on triple ARVs, diff =1.9%. Assume EBF assoc. with 15% risk reduction in this group.
8	> 350 ARV EBF 0-5m	1.2%	12	Kesho Bora. Among all infants ever breastfed and born to mothers on triple ARVs, 6wk=3.0% and 6m=5.0%. Diff=2.0%. Among all infants born to mothers with CD4>350 and on triple ARVs, 6wk=2.9% and 6m=4.1%. Diff=1.2%.
9				
10	Unknown None EBF 0-5m	4.0%	4, 5	Populations in referenced populations included mothers with CD4 counts <200. Iliff = 5.1 per 100 child years (2.5%/6m); Coovadia=4.04%
11	< 200 None MBF 0-5m	12.0%	14	Based on PEPI control arm (<200, BF - EBF recommended but not assessed). 6 week transmission = 10.7. Cumulative transmission at 6 mo = 21.9. Assumed additional BF transmission = 11.2%. Assume most mothers were MBF and therefore assoc. only 5% risk increase in this group. Cf #1 above, this infers a 25% risk differential between EBF and MBF in infants of mothers with CD4<200 and no intervention

12	> 200 None MBF 0-5m	5.0%	11,18	MASHI reported mothers with total neutrophil count >1000 and median CD4 366, in BF (+ZDV) group 1mo transmission = 4.6. Cumulative transmission at 7 mo = 9.0. Assumed additional BF transmission = 4.4%. SPECTRUM estimates 6m transmission with RF=20% and MBF=26%, difference=6%.
13	< 200 ART MBF 0-5m	1.9%	2	Tonwe-Gold (<250 or clinical) point prevalence @ 1m=1% and 6m=3.3%. Postnatal transmission in cohort assessed=1.9%. No breastfeeding type reported, though assume to be MBF. BF for ~5.4m. Mma Bana reported 2% in one arm of mothers with CD4 count >200 receiving triple ARVs and <1% in the comparison arm with different regimen.
14	> 200 ARV MBF 0-5m	1.8%	7	BANS reported 1.8%. No breastfeeding type reported, though assume to be MBF.
15	< 350 None MBF 0-5m	7.5%	12	Kesho Bora. Maternal CD4 200-350 and short course ARVs, postnatal transmission=4.2%. EBF supported but not differentiated in data analysis. Increase total transmission to reflect infants of mothers (~15%) with CD4<200.
16	> 350 None MBF 0-5m	2.5%	12	Kesho Bora. Among all infants ever breastfed and born to mothers on short course ARV only, 6wk=4.5% and 6m=8.8%. Diff=4.3%. This includes infants of mothers with CD4 counts 200-350. In infants of mothers with CD4 counts 350-500 diff=2.5%. Allow for lower risk of infants of mothers with CD4>500.
17	< 350 ART MBF 0-5m	1.8%	1,12,23	DREAM reported cumulative 1.8% in all. CD4 not stated and including those FF. (BF group had less postnatal transmission than FF). Kesho Bora. 200-350 and mothers on triple ARVs, diff =1.9%. Mma Bana reported <1% postnatal transmission with triple ARVs
18	> 350 ARV MBF 0-5m	1.4%	7,12,23	BANS reported 1.8% in infants of mothers with CD4>250. Kesho Bora. Among all infants ever breastfed and born to mothers on triple ARVs, 6wk=3.0% and 6m=5.0%. Diff=2.0%. Among all infants born to mothers with CD4>350 and on triple ARVs, 6wk=2.9% and 6m=4.1%. Diff=1.2%. Mma Bana reported <1% postnatal transmission with triple ARVs
19				
20	Unknown None MBF 0-5m	5.0%	3	BHITS reported 0.79% per month. Over 6 months=4.74. Some of these may have been EBF. Therefore increase to 5%
21	< 200 None CBF 6-11m	10.0%		Based on #11 above and moderate to allow for increasing GI maturity and decreased breast milk intake by infant
22	> 200 None CBF 6-11m	4.5%	8	Based on #12 above and moderate to allow for increasing GI maturity and decreased breast milk intake by infant
23	< 200 ART CBF 6-11m	1.5%	8	See #13. Total at 12m=6.4% which included about 3% peripartum transmission, 1.9% MBF 0-5m.
24	> 200 ARV CBF 6-11m	1.6%		Based on #14 above. Hypothetically, if ARV extended and moderated transmission risk to allow for increasing GI maturity and decreased breast milk intake by infant
25	< 350 None CBF 6-11m	7.0%	3, 12	Based on #20 and #15 above to reflect increased risk in infants of mothers with CD4 counts <350 and also moderating effect of increasing age and decreased breast milk intake
26	> 350 None CBF 6-11m	2.5%		Based on #16 above and moderated transmission risk to allow for increasing GI maturity and decreased breast milk intake by infant.
27	< 350 ART CBF 6-11m	1.6%	1,12,23	Based on #17 above and moderated transmission risk to allow for increasing GI maturity and decreased breast milk intake by infant.
28	> 350 ARV CBF 6-11m	1.4%	7	Based #18 above.
29				
30	Unknown None CBF 6-11m	5.0%		Based on #20 above.
31	< 200 None CBF 12-18m	10.0%		As #21 above
32	> 200 None CBF 12-18m	4.5%		As #22 above

33	< 200 ART CBF 12-18m	1.5%		As #23 above
34	> 200 ARV CBF 12-18m	1.6%		As #24 above
35	< 350 None CBF 12-18m	7.0%		As #25 above
36	> 350 None CBF 12-18m	2.5%		As #26 above
37	< 350 ART CBF 12-18m	1.6%		As #27 above
38	> 350 ARV CBF 12-18m	1.4%		As #28 above
39				
40	Unknown None CBF 12-18m	5.0%		As #30 above
41	< 200 None RF 0-5m	0%		
42	> 200 None RF 0-5m	0%		
43	< 200 ART RF 0-5m	0%		
44	> 200 ARV RF 0-5m	0%		
45	< 350 None RF 0-5m	0%		
46	> 350 None RF 0-5m	0%		
47	< 350 ART RF 0-5m	0%		
48	> 350 ARV RF 0-5m	0%		
49				
50	Unknown None RF 6-11m	0%		

Additional assumptions

1. EBF associated with 20% transmission risk reduction vs. MBF in settings where maternal CD4 count <200 and mother not on ART and no infant ARV intervention. Note in published literature, the protective effect of EBF vs. MBF re. transmission is about 40% or more;
2. When ART/ARV given then protective effect of EBF vs. MBF re. transmission is diminished to 15%;
3. Transmission estimates for infants born to mothers with CD4 counts <350 sometimes based on populations of mothers with CD4 count 200-350. In these settings, estimate increased to account for inclusion of higher risk group. Similarly, for estimates of risk in infants of mothers with CD4 >350, if based on data from mothers with CD4 350-500, then estimate decreased to account for inclusion of lower risk group;
4. In model, the denominator should change over each 6 month interval to reflect the number of infants infected in the preceding interval and therefore should not be considered in subsequent interval;
5. Transmission risk marginally decreased in later time periods (6-12 m and 12-18m) to reflect less BM consumption and increasing GI maturity.

Estimates re. Mortality in infants, uninfected at birth, by feeding practice

	Population (Infant feeding practice, interval period)	Mortality estimate for <u>uninfected</u> infants in specified interval	
		Based on research data	Applying relative risks from programme settings*
1	EBF 0-5m	1.5%	1.5%
2	MBF 0-5m	3.5%	3.5%
3	CBF 6-11m	2.0%	2.0%
4	CBF 12-18m	2.0%	2.0%
5	RF 0-5m	6.0%	7.5%
6	RF 6-12m	3.0%	4.0%
7	RF 12-18m	2.0%	3.0%

* estimates reduced from those reported in literature (24,25) to allow for mortality in infants who become HIV infected at birth

Assumptions

- In all populations, assume that infants uninfected at birth (no peripartum transmission). Mortality risk over any given interval the same irrespective of maternal CD4, +/- ART or other ARV prophylaxis interventions. Minimal data to estimate differential risks according to maternal health or access to ART. Two papers report $\times 3.5$ mortality among HIV-exposed infants (irrespective of feeding modality or infant HIV status) when maternal CD4 < 200 and $\times 4$ when mother dies. However, other paper from Uganda (Homsy, ref 9. did not see similar association though mothers generally on ART);
- In all MBF populations, assume that all infants uninfected at birth (no peripartum transmission). Mortality risk the same irrespective of maternal CD4, +/- ART or other ARV prophylaxis interventions. (see note above);
- In RF infants assume risk of death greatest in first 6 months, less in second 6 months and slightly less again between 12-18m. Assume programme conditions with a range of women taking this option, some of whom have safe conditions and some who do not and should not consider FF at all unless specific interventions e.g. to provide potable water;
- Ref. 17 (Mbori-Ngacha) The only paper that specifically disaggregated mortality in uninfected vs. all exposed infants. Mortality at 12 months in all infants born to HIV-infected mothers (all CD4 counts) including infants infected perinatally, if FF=15.4% vs. if BF=16.7% in all infants. Note that birth and 6 week transmission rates in FF arm were 3.1% and 9.7% respectively vs. in BF arm 7% and 19.9% respectively (?randomisation). Among uninfected infants, mortality at 24 m if FF =10 % and if BF=8.1%;
- Ref 11. (Thior - Botswana). Cumulative mortality at 7 months among all HIV-exposed infants (including those infected perinatally) if FF=9.3% vs. if BF=4.9%. Deaths in BF group more likely to be in HIV-infected infants and at older ages;
- Ref. 13. (Kagaayi - Rakai). Cumulative mortality at 12 months among all HIV-exposed infants (including those infected perinatally) if FF=18% vs. if BF=3%. HR 6.1;
- In general, protective effect (survival) decreases over time. Among 1223 child deaths (<2yrs) breastfeeding vs. no BF protected against death <2mth $\times 5.8$, 2-3mth $\times 4.1$, 4-5mth $\times 2.6$, 6-8mth $\times 1.8$, 9-11mth $\times 1.4$. In first six month protection against death from diarrhoea $\times 6$ and for pneumonia deaths $\times 2.4$. In second 6 months protection against diarrhoeal and respiratory deaths = 1.9 and 2.5 respectively;
- In another report, in 9,424 uninfected infants, risk of mortality in first 6 months in 'never BF' infants about $\times 10$ vs. predominant BF (Ghana, India and Peru) . In same report, risk of mortality in MBF about $\times 2.4$ vs. predominant BF. No difference between predominant and exclusive breastfeeding.

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