HIV-free survival in infants

ARV and breastfeeding or replacement feeding: What is the best strategy?

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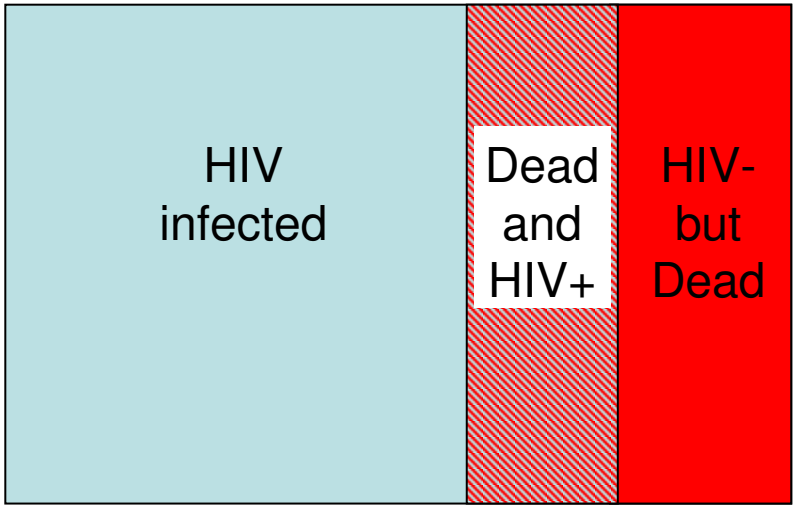
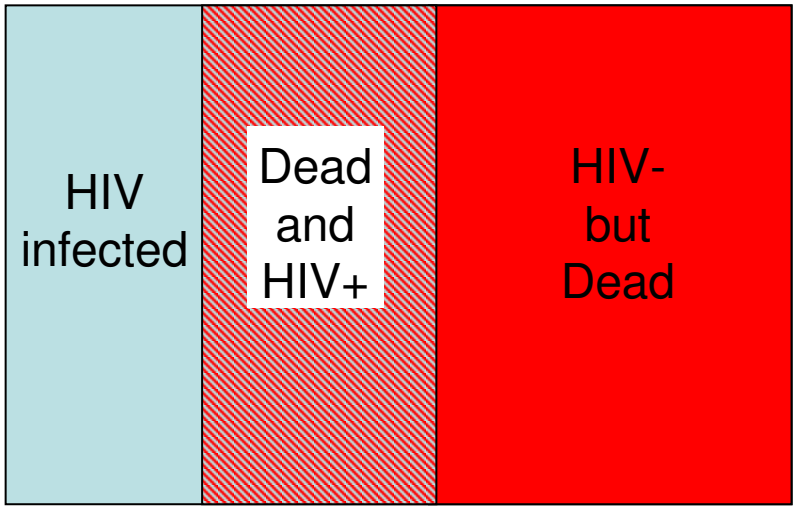
HIV free survival

- HIV infection treated as equivalent to death
- Estimated at 18 months
- Only consider children who are HIV-negative at birth

Infant feeding and HIV free survival



Breast feeding increases HIV-transmission but reduces mortality from other causes



Replacement (formula) feeding reduces HIV-transmission but increases mortality from other causes

Strategic options

Anti-retroviral interventions:

- Lifelong triple therapy to mothers (ART)
- Triple antiretrovirals to mothers only while breastfeeding (ARV)
- Daily nevirapine to infants while breastfeeding (ARV)

Feeding options:

- Exclusive breastfeeding (E)
- Continued breastfeeding (C)
- Replacement feeding (R)

Compare different combinations of these options in successive periods 0 to 6 months; 6 to 12 months; 12 to 18 months

Difficulty in assessing influence of infant feeding on HIV FS

We are concerned with HIV-free survival in those born HIV-negative

Most studies measure HIV-free survival in those born HIV-positive or HIV-negative

Difficult to measure survival in all possible combinations of feeding and ART

Difficulty with estimating mortality from studies

Study conditions generally better than local settings;

Better advice and monitoring of infant feeding in studies;

Background (non-HIV) mortality varies among countries;

Comparisons within cohorts possible but difficult to apply outside of study.

Transmission assumptions

Consider transmission and mortality in three successive 6 month periods

Provision of ART, ARV or nothing depends on mothers CD4 cell counts

Consider two CD4 cell cut-offs: 200/µl or 350/µl

Transmission estimates

Infant feeding practice

Maternal CD4 +/- ART/ARV intervention	EBF 0-5m	MBF 0-5m	CBF 6-11m	CBF 12-18m	RF
<200, no ART	9%	12%	10%	10%	0%
>200, no PN ARVs	3%	5%	4.5%	4.5%	0%
<200, ART	1.6%	1.9%	1.5%	1.5%	0%
>200, PN ARVs	1.5%	1.8%	1.2%	1.2%	0%
<350, no ART	6%	7.5%	7%	7%	0%
>350, no PN ARVs	1.8%	2.5%	2.5%	2.5%	0%
<350, ART	1.5%	1.8%	1.6%	1.6%	0%
>350, PN ARVs	1.2%	1.4%	1.4%	1.4%	0%
Unknown, no ARVs	4%	5%	5%	5%	0%

EBF-exclusive breastfeeding, MBF-mixed breastfeeding, CBF-continued breastfeeding, RF-replacement feeding

Mortality assumptions

Infant mortality risk does not depend on what happens to the mother

Survival benefit of BF decreases with time

Infant mortality after infection:

- No increase in first six months
- 15% increase in second six months
- 30% increase in third six months

Reported Hazard ratios for cumulative mortality at 12 months:

- FF *versus* BF = 6.1 (Uganda)
- MBF versus EBF = 2.4
- EBF versus FF = 6 (first six months); 2 (second six months)

Mortality estimates

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

* estimates reduced from those reported in literature to allow for mortality in infants who become HIV infected at birth

EBF-exclusive breastfeeding, MBF-mixed breastfeeding, CBF-continued breastfeeding, RF-replacement feeding

Use estimates of transmission and mortality to estimate HIV-free survival at 18 months

Monte-Carlo model allowing for uncertainty in the estimates and allowing for competing transmission and mortality

Assume that of the mothers

15% have CD4 < 200;

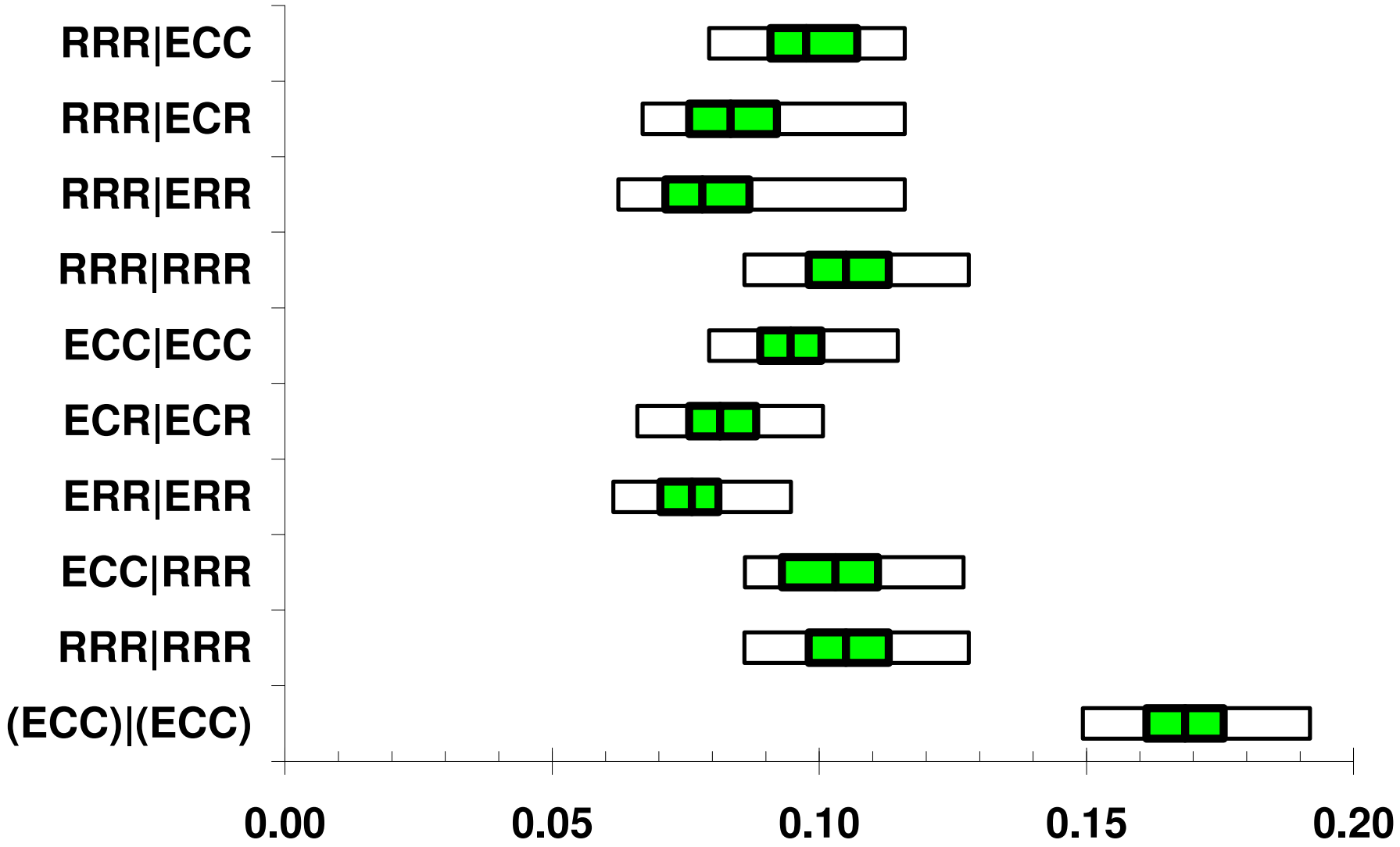
40% have CD4 < 350

Scenarios

	Below cut-off (CD4 200 or 350)				Above cut-off (CD4 200 or 350)			
Scenario	Intervention	0-5m	6-11m	12-18m	Intervention	0-5m	6-11m	12-18m
1	ART (maternal)	RF	RF	RF	ARV (infant phxs)	EBF	CBF	CBF
2	ART (maternal)	RF	RF	RF	ARV (infant phxs)	EBF	CBF	RF
3	ART (maternal)	RF	RF	RF	ARV (infant phxs)	EBF	RF	RF
4	ART (maternal)	RF	RF	RF	None	RF	RF	RF
5	ART (maternal)	EBF	CBF	CBF	ARV (infant phxs)	EBF	CBF	CBF
6	ART (maternal)	EBF	CBF	RF	ARV (infant phxs)	EBF	CBF	RF
7	ART (maternal)	EBF	RF	RF	ARV (infant phxs)	EBF	RF	RF
8	ART (maternal)	EBF	CBF	CBF	ARV (infant phxs)	RF	RF	RF
9	None	RF	RF	RF	None	RF	RF	RF
10	None	EBF	CBF	CBF	None	EBF	CBF	CBF

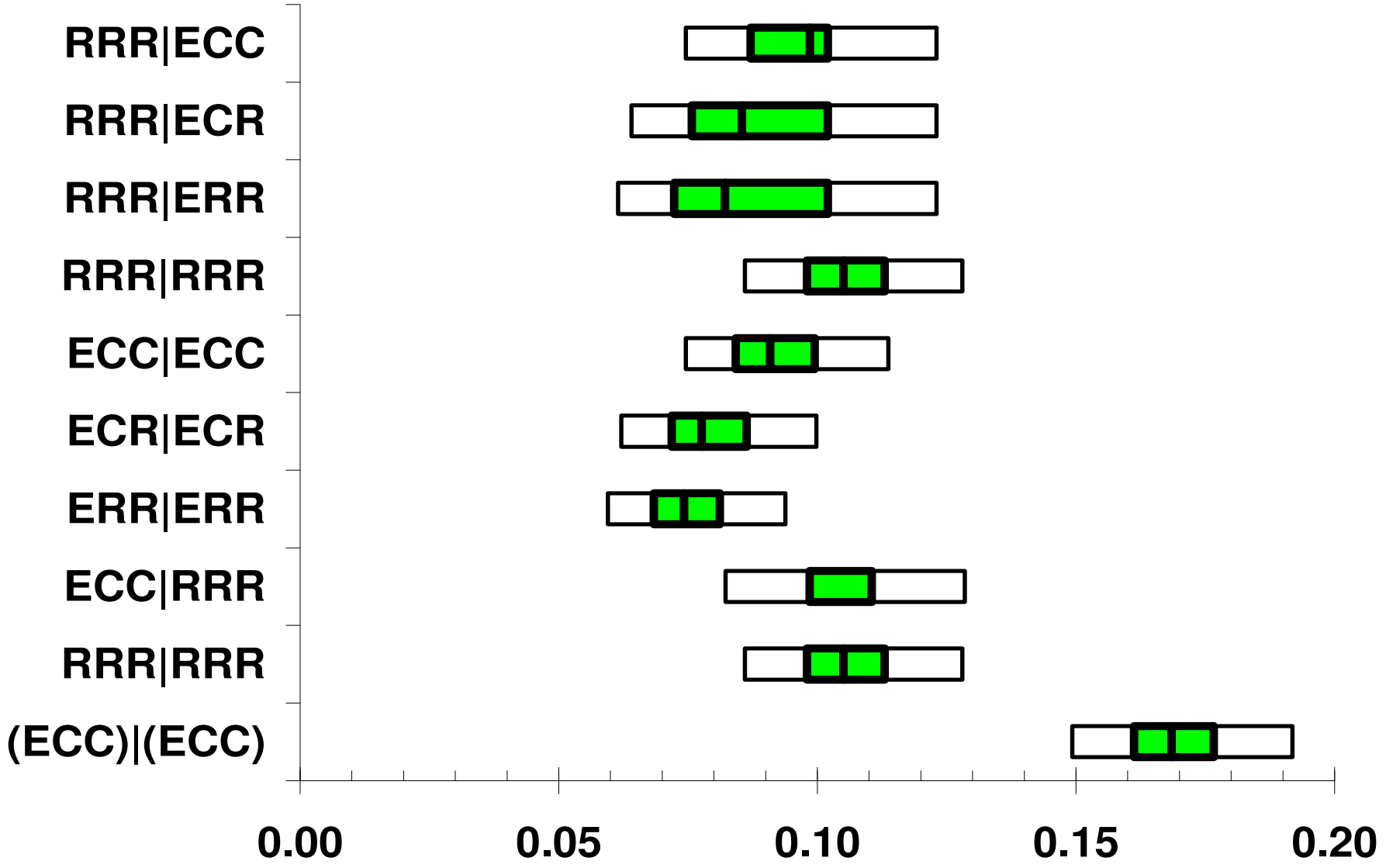
EBF-exclusive breastfeeding, MBF-mixed breastfeeding, CBF-continued breastfeeding, RF-replacement feeding

ART|ARV at 200/μL



Probability of being infected or dead at 18 months

ART|ARV at 350/μL



Probability of being infected or dead at 18 months

ART|ARV	200/ml	350/mL
RRR|ECC	0.098	0.099
RRR|ECR	0.083	0.085
RRR|ERR	0.078	0.082
RRR|RRR	0.105	0.105
ECC|ECC	0.095	0.091
ECR|ECR	0.081	0.078
ERR|ERR	0.076	0.074
ECC|RRR	0.103	0.095
RRR|RRR	0.105	0.105
(ECC)|(ECC)	0.168	0.168

Probability of being infected or dead at 18 months

Infants infected at birth

- Infants infected at birth are not included in the models
- Breastfeeding would not change their infection status but may improve their chances of surviving until they have the opportunity to start ART

Peltier, AIDS 2009

- Maternal ART or triple ARV if not eligible for ART
  - HIV Free survival at 9 months
    - 94% if FF
    - 95% if BF