

Maternal-infant HIV care: To breast feed or not to breast feed

Douglas Watson, M.D.
University of Maryland School of Medicine
13 June 2012



Infant feeding and transmission of HIV

- About 10-18% additional risk of transmission from breastfeeding
 - Risk highest in early infancy but continues throughout breastfeeding
 - Risk associated with
 - Maternal plasma viral load
 - Mastitis
 - **Maternal CD4**
 - **Milk viral load**
 - **Maternal ART: ~80% reduction**
 - **Infant NVP: > 70% reduction(?)**
- } *Probably highly related to adherence*

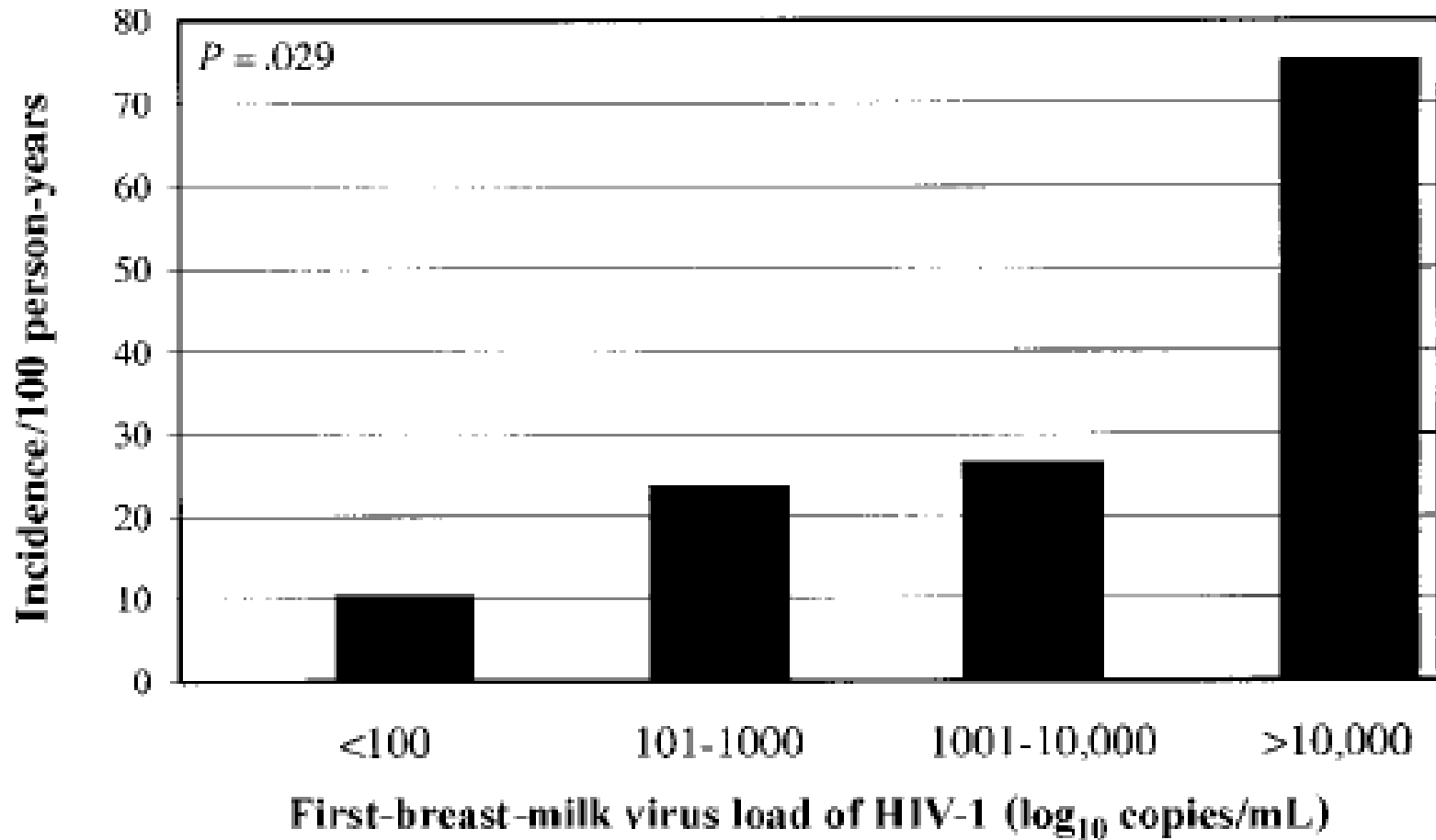


Figure 1. First-breast-milk load of human immunodeficiency virus type 1 (HIV-1)—and incidence of mother-to-child transmission.

Rousseau CM. JID 2003; 187:741–7

Infant feeding: First 6 months

- Types of breast feeding:
 - **Exclusive breast feeding** (EBF): *nothing* other than breast milk for first 6 months
 - **Mixed feeding**
 - **Partial breast feeding** (PBF): breast + non-milk liquids (water, teas, etc)
 - **Mixed milk feeding** (MMF): breast + non-human milks +/- solids
- **Breast milk substitute feeding** (BMS)
 - No breast milk
 - **Exclusive formula feeding** (EFF)
 - Other feeding methods
 - Other animal milks (may be diluted & fortified) +/- solids
 - With or without solids

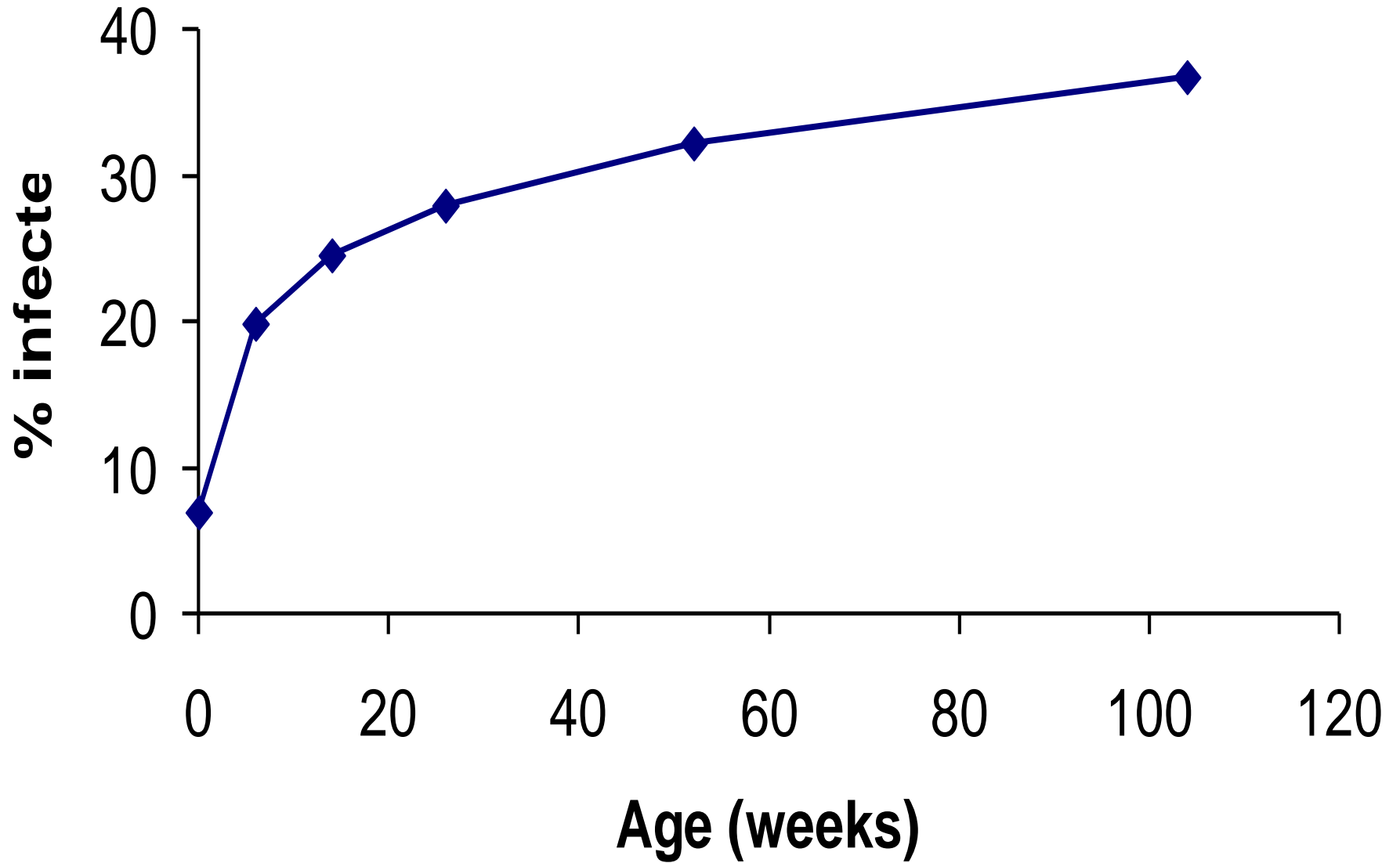
Infant feeding: After 6 months

- After 6 months infants need appropriate complementary foods
 - + Breast milk = ***Complementary breast feeding***
 - + Formula = ***Complementary formula feeding***
 - No breast or formula “***Not breast fed***”

“Complementary breast feeding” is NOT “mixed feeding”- the infant > 6 month can tolerate and needs complementary foods

The incidence of HIV transmission goes down after 6 months despite infants getting complementary foods

HIV infection rate in breastfed infants (Nduati, et al., JAMA 2000)



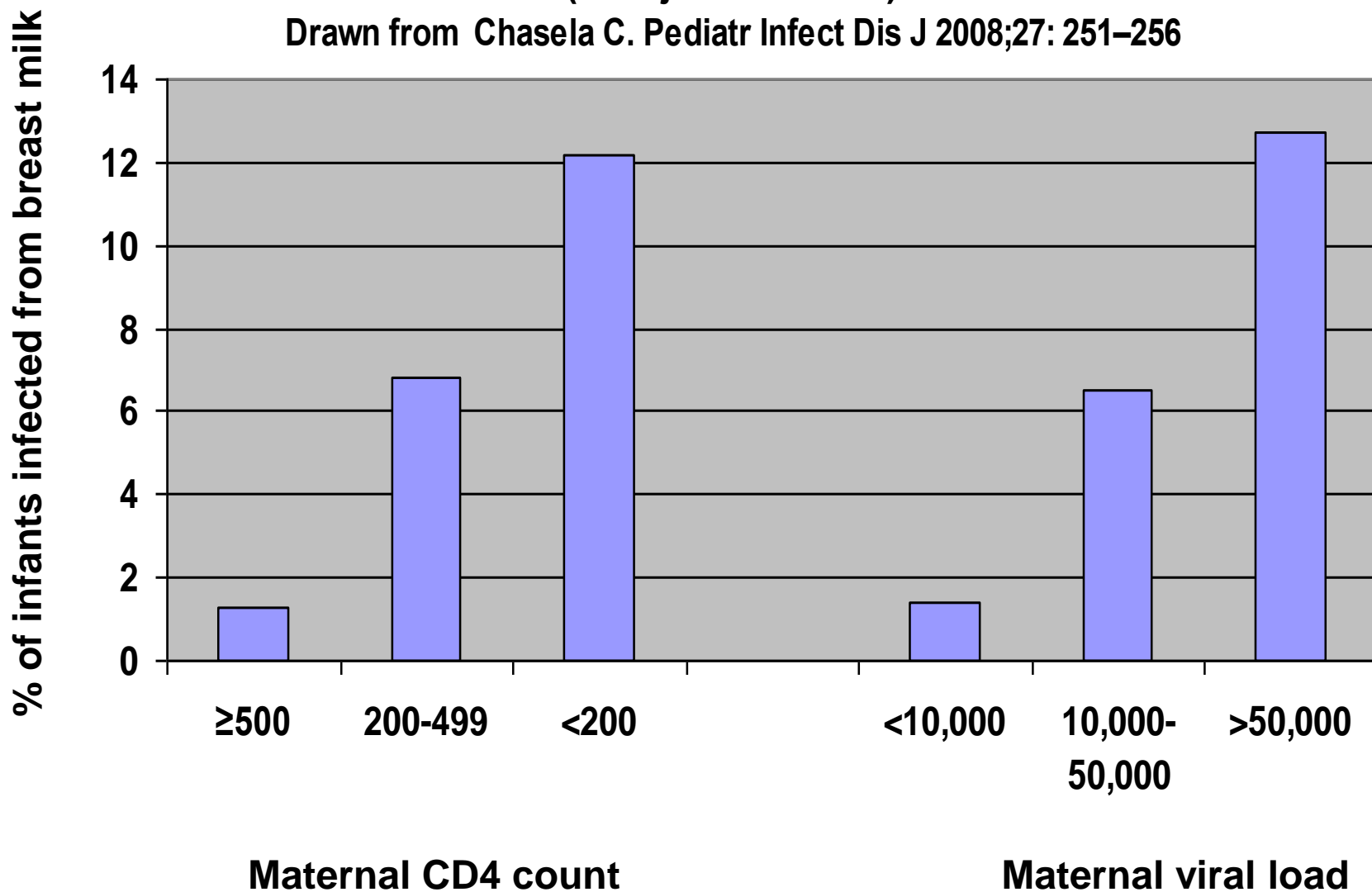
HIV transmission after 6 weeks and mortality according to feeding type

Piwoz, et al 15th International AIDS Conference, 2004

Feeding type	N	Postnatal transmission %	Adjusted hazard ratio death or HIV	95% CI for death or HIV
Breast only	156	6.9	1	
Breast + non-milk liquids	490	8.5	1.4	0.71-2.78
Breast + non-human milk or solids	1409	14.1	2.02	1.07-3.82

Risk of infection from breastmilk according to maternal CD4 or viral load in Blantyre, Lilongwe, Dar es Salmam, and Lusaka (unadjusted results)

Drawn from Chasela C. *Pediatr Infect Dis J* 2008;27: 251–256



To breast feed or not to breast feed: which is safest?

- Study in Nairobi (Nduati, et al JAMA 2001) randomly assigned HIV-infected mothers to:
 - Breast feed with advice to exclusively breast feed
 - Formula feed with formula and training provided by study

Outcome of breast versus formula study

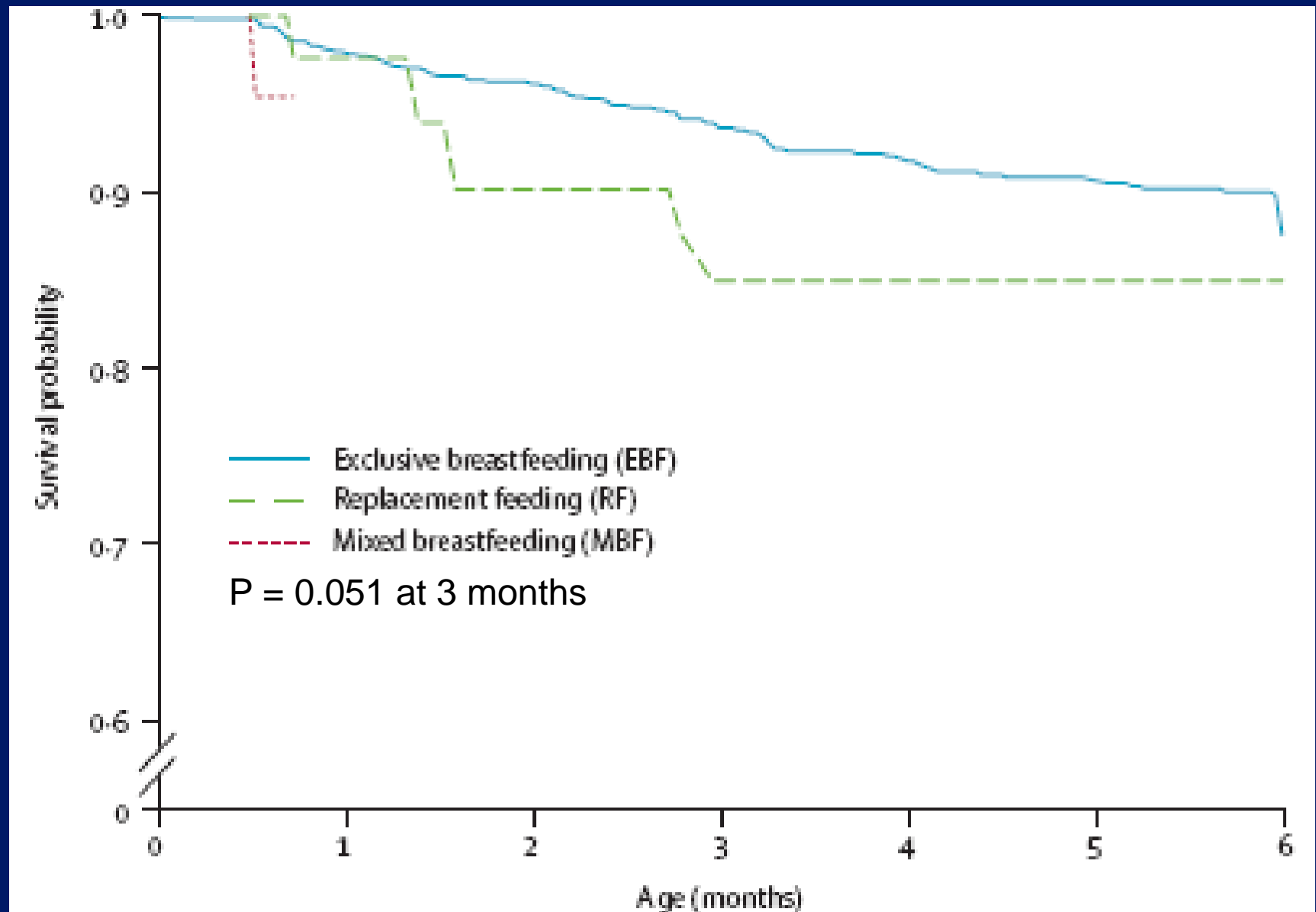
- HIV infection
 - Breast 36.7%
 - Formula 20.5%
- Death by 2 years of age
 - Breast 24.4%
 - Formula 20.0% (no significant difference)
- Death or HIV infection
 - Breast 42%
 - Formula 30%

Limitations of breast versus formula study

- *Study provided formula and training*
- *Reasonably clean municipal water*
- These conditions may not be easy to duplicate!
- Whether these results apply to the *individual mother and infant* has to be determined according to *individual circumstances*
- There is no one “right” answer- we must help each family discover what is best for them

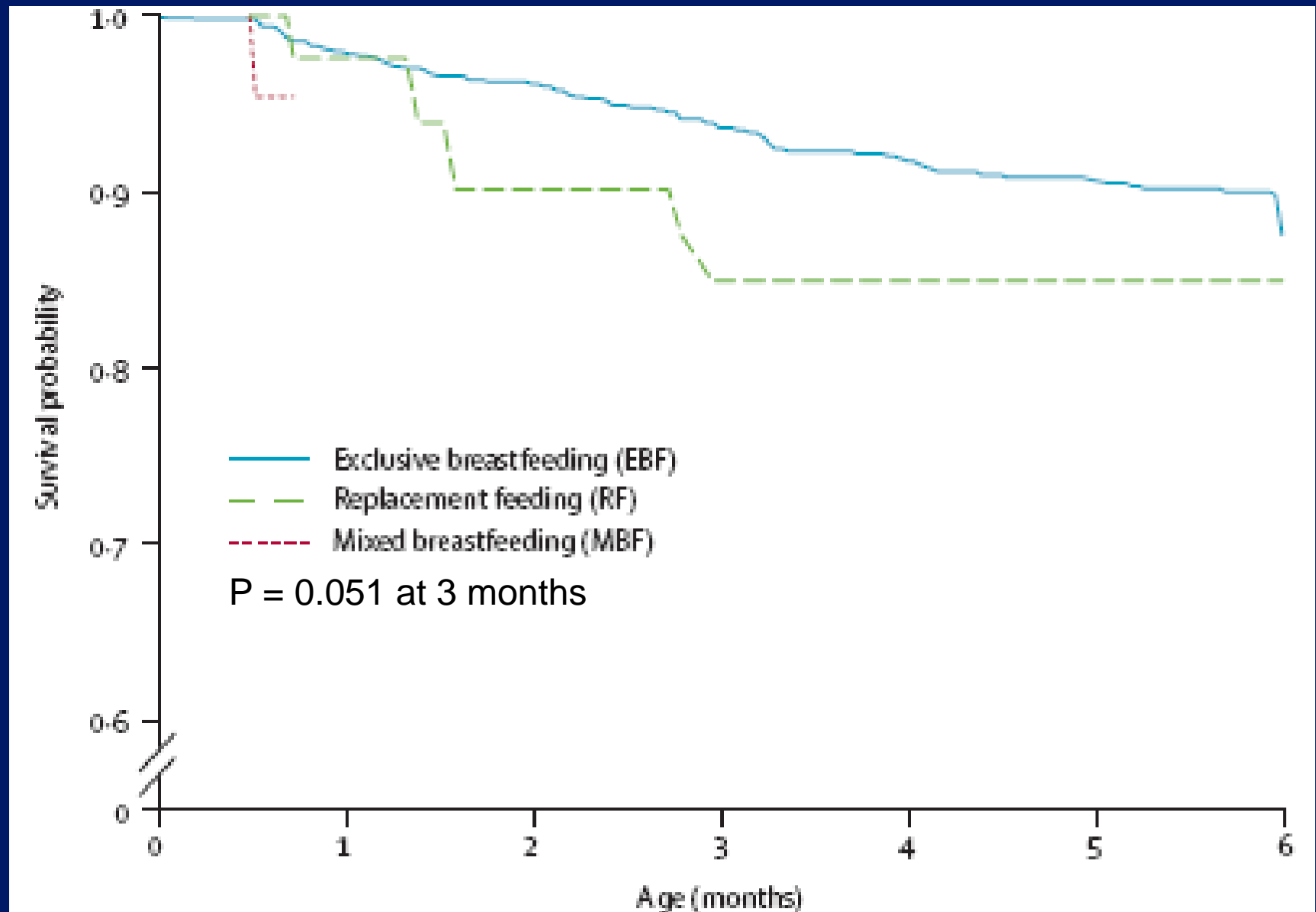
Survival of HIV-exposed infants, self-selected to breastfeeding versus program-supplied formula in KwaZulu Natal (multiple sites)

Coovadia HM, et al. *Lancet* 2007; 369: 1107–16



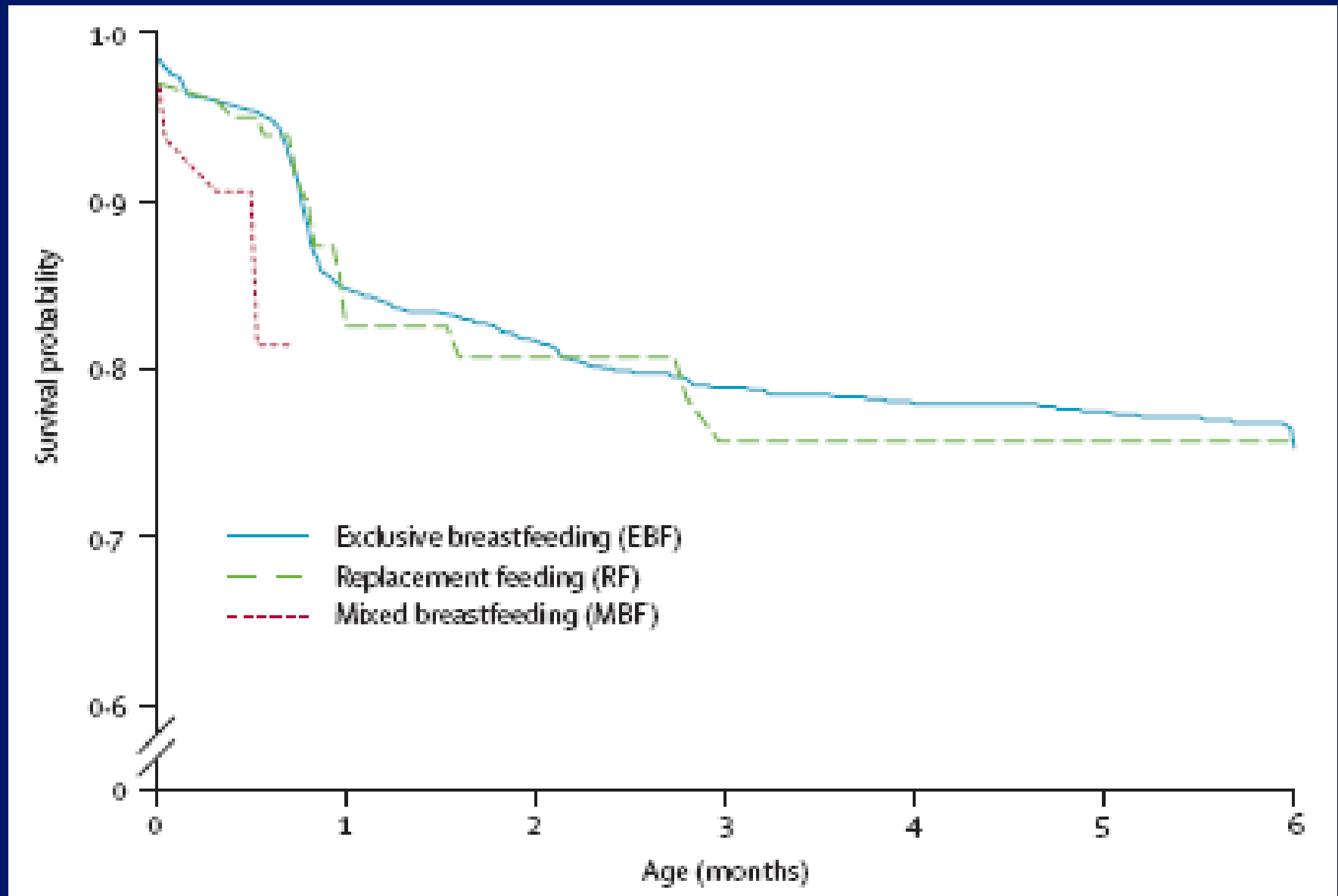
Survival of HIV-exposed infants, self-selected to breastfeeding versus program-supplied formula in KwaZulu Natal (multiple sites)

Coovadia HM, et al. *Lancet* 2007; 369: 1107–16



HIV-free survival of HIV-exposed infants, self-selected to breastfeeding versus program-supplied formula in KwaZulu Natal (multiple sites)

Coovadia HM, et al. *Lancet* 2007; 369: 1107–16



Mashi study (Botswana)

Thior, I et al, JAMA 296:794 (2006)

Mothers: ZDV from 34 weeks & randomized +/- SD NVP

Infants: Randomized +/- SD NVP and randomized formula + placebo *versus* breast + ZDV for 6 months

	Formula feed + placebo	Breast feed + ZDV	Difference CI and p value
HIV+ at 7 months	5.6%	9.0%	-6.4- -0.4 p = 0.04
Mortality at 7 months	9.3%	4.9%	p = 0.003
HIV infection or mortality at 18 months	13.9%	15.1%	-5.3-2.9% p = 0.60

Breast versus formula: nonrandomized experience in rural Uganda

J.Kagaayi, et al. AIDS 2008, Abstract MOPE0499

- Mothers offered formula or breastfeeding
- Different antenatal/intrapartum regimens according to need for HAART; non-HAART got ZDV + SD NVP +/- 3TC
- Mortality at 12 months:
 - Breast: **0.19**/1000 person-weeks
 - Formula: **0.41**/1000 person-weeks
- HIV-free survival at 12 months:
 - Breast: 74.3%
 - Formula: 76.6%
 - P = 0.84

Can a substitute feeding program work: PIH program in Rwanda

- Rural setting
- ARVs according to Rwanda guidelines then current (maternal ART if < 350 , otherwise WHO short course)
- Mothers given formula, complementary foods after 6 months, stove, fuel, bottles, containers, and training including home visits
- Daily DOT of maternal and infant ARVs
- 96% HIV-free survival at 12 months (greater than Rwanda national infant survival)

Problems experienced by programs providing breast milk substitute (BMS)

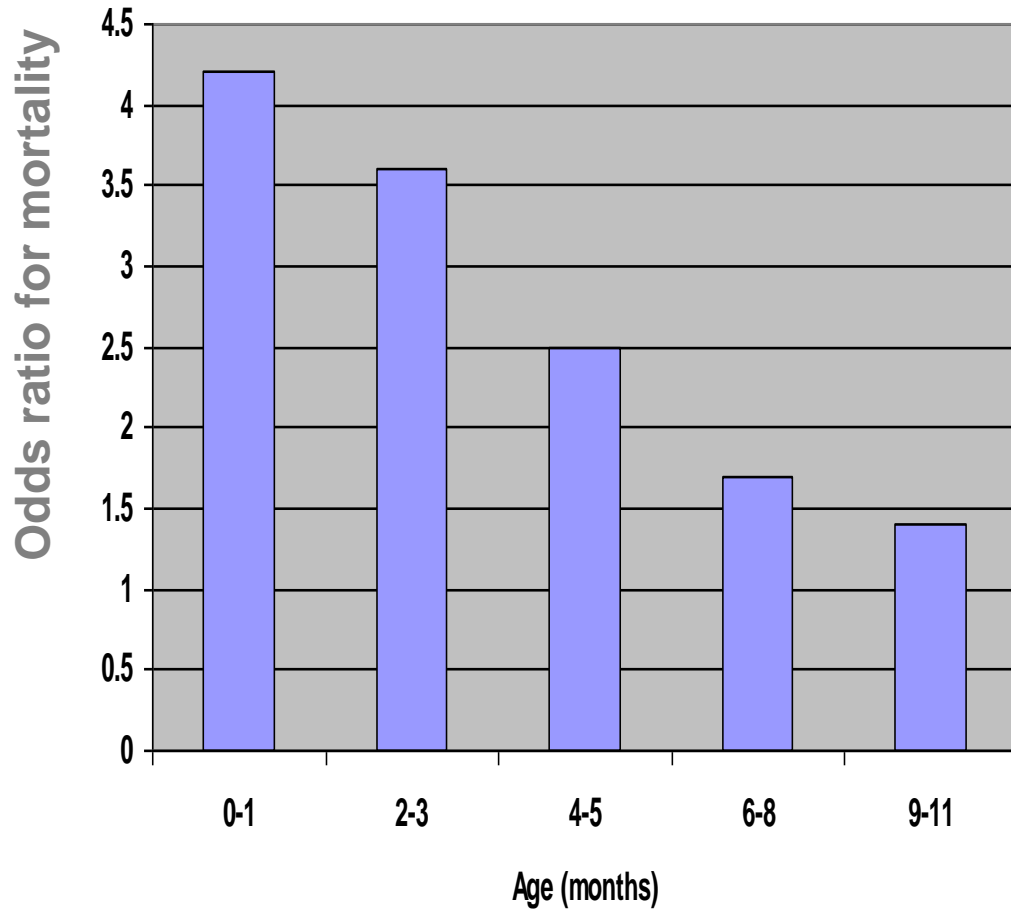
- Poor quality counseling
- Not all mothers accept BMS; stigma
- Many mothers continue breast + BMS (i.e. mixed feeding, putting child at risk for HIV and diarrhea/malnutrition)
- Difficulty sustaining supply
 - Program runs out
 - Family runs out before scheduled visit or misses visit
 - Diversion of product
- Improper preparation, storage, feeding
- “Spillover” effect on breastfeeding in HIV negative mothers

Early weaning of HIV-exposed infant?

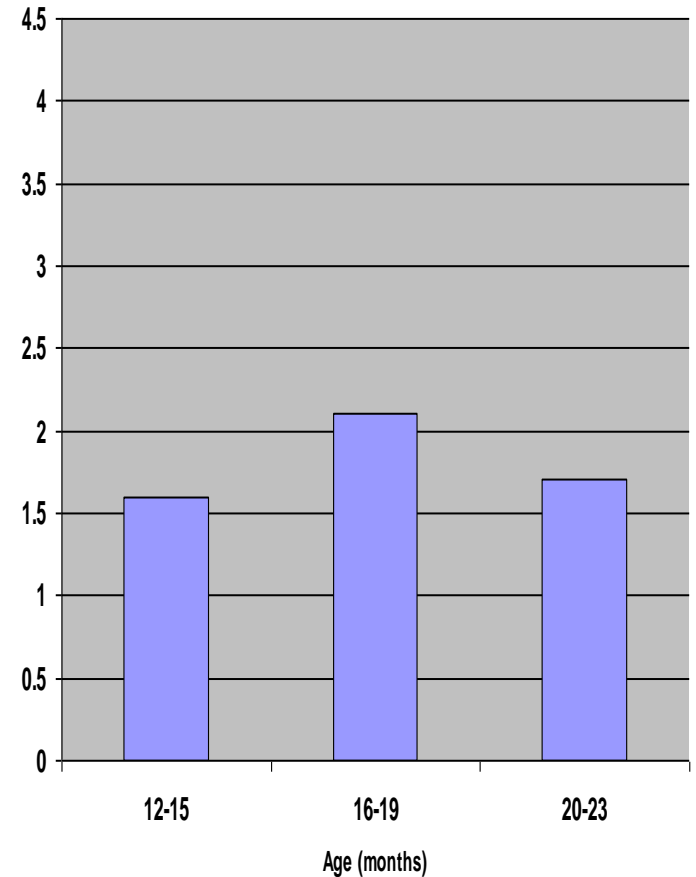
- Increased morbidity & mortality soon after early weaning of HIV-exposed infants (several studies)
- Randomized controlled trial in Lusaka, Zambia of weaning exposed infants at 4 months *with provision of formula & training* did not show benefit in HIV-free survival
 - Poor weight gain immediately after early weaning
 - Mortality especially high in early-weaned infants who were HIV-infected

Mortality in non-breastfed infants compared to breastfed infants (not HIV-exposed), pooled from multiple studies

From WHO Collaborative Study Team, *Lancet* 2000; 355: 451–55

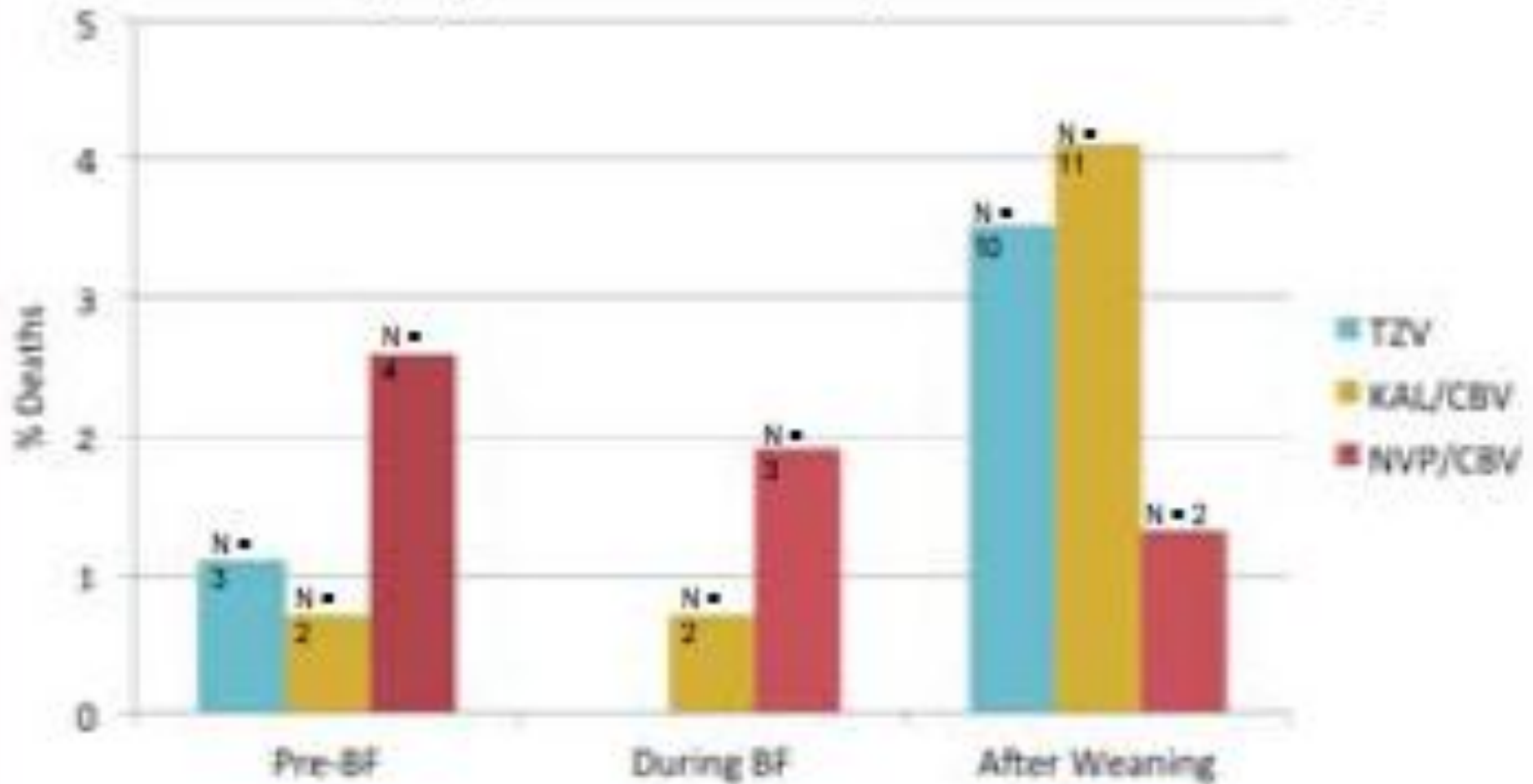


Brazil, Pakistan, Philippines

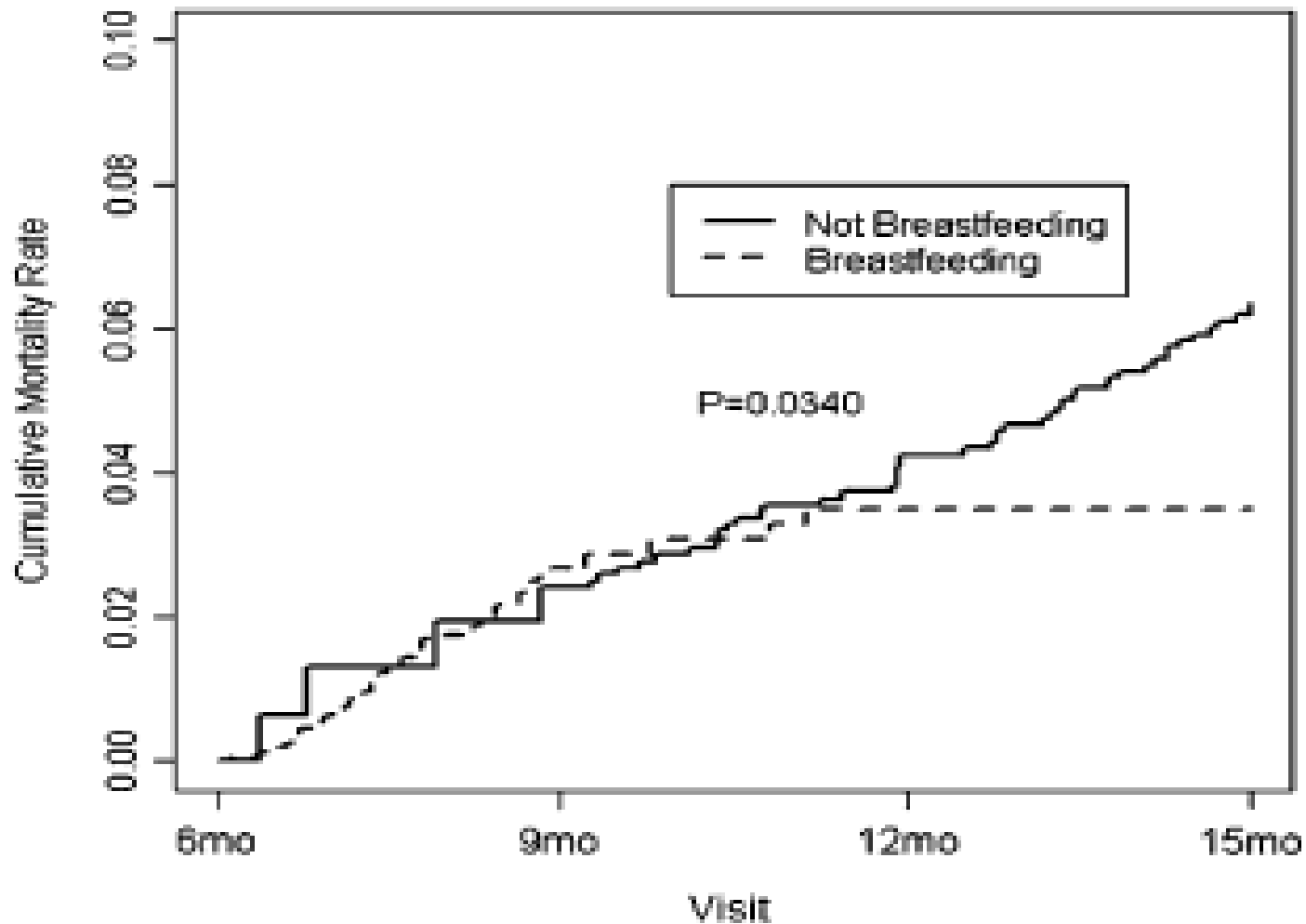


Senegal, Ghana, Gambia,
Pakistan, Philippines

Infant Mortality, by Maternal Study Arm and Feeding Status



Infant mortality in Mma Bana study. Pregnant women with CD4 > 200 randomized to AZT/3TC/ABC or AZT/3TC/LPV/r; women with CD4 < 200 all got AZT/3TC/NVP. Advised to wean at 6 months (most did). Shapiro R., CROI 2011.



Cumulative mortality according to feeding type in HIV-exposed, uninfected infants in Malawi in the Pepi study.
 Morbidity and malnutrition more common in non-BF at 6-9, 9-12, and 12-15 months.
 Taha TE Clinical Infectious Diseases 2011.

Summary of substitute feeding of HIV-exposed infants

- RCT of EBF versus formula showed net increase in HIV-free survival
 - In relatively middle class population in Nairobi
- Cohort studies show no net benefit in HIV-free survival (i.e. 1 child killed for every one saved from infection)
 - South Africa, Botswana, Uganda, Zimbabwe
 - All of these provided formula
- Increased morbidity and mortality with early weaning
- RCT of weaning to formula at 4 month in Lusaka: no net benefit in HIV-free survival

Even though studies provided formula and did not provide maternal ART or daily infant NVP, there was no net benefit in most African settings. Without formula but with ARVs, we can expect BF to be much favored

Summary of WHO 2010/2012 recommendations for ARVs in pregnant women with CD4 > 350 and WHO class 1 and 2 and their infants

	Option A	Options B and B+
Pregnancy	AZT at 14 weeks	ART at 14 weeks (AZT/3TC or TDF/3TC) + (EFV or LPV/r)
Labor	AZT/3TC/NVP (NVP X 1 + AZT/3TC 2 tabs X 1 then 1 tab every 12 hours)	Continue ART
Maternal postpartum	AZT/3TC X 1 week	Option B: Breastfeeding: ART until 1 week after weaning Non-breastfeeding: discontinue ART after delivery
		Option B+: Continue ART life-long
Infant (BF)	NVP daily until 1 week after weaning	NVP (or AZT) X 6 weeks
Infant (non-BF)	NVP (or AZT) X 6 weeks	NVP (or AZT) X 6 weeks

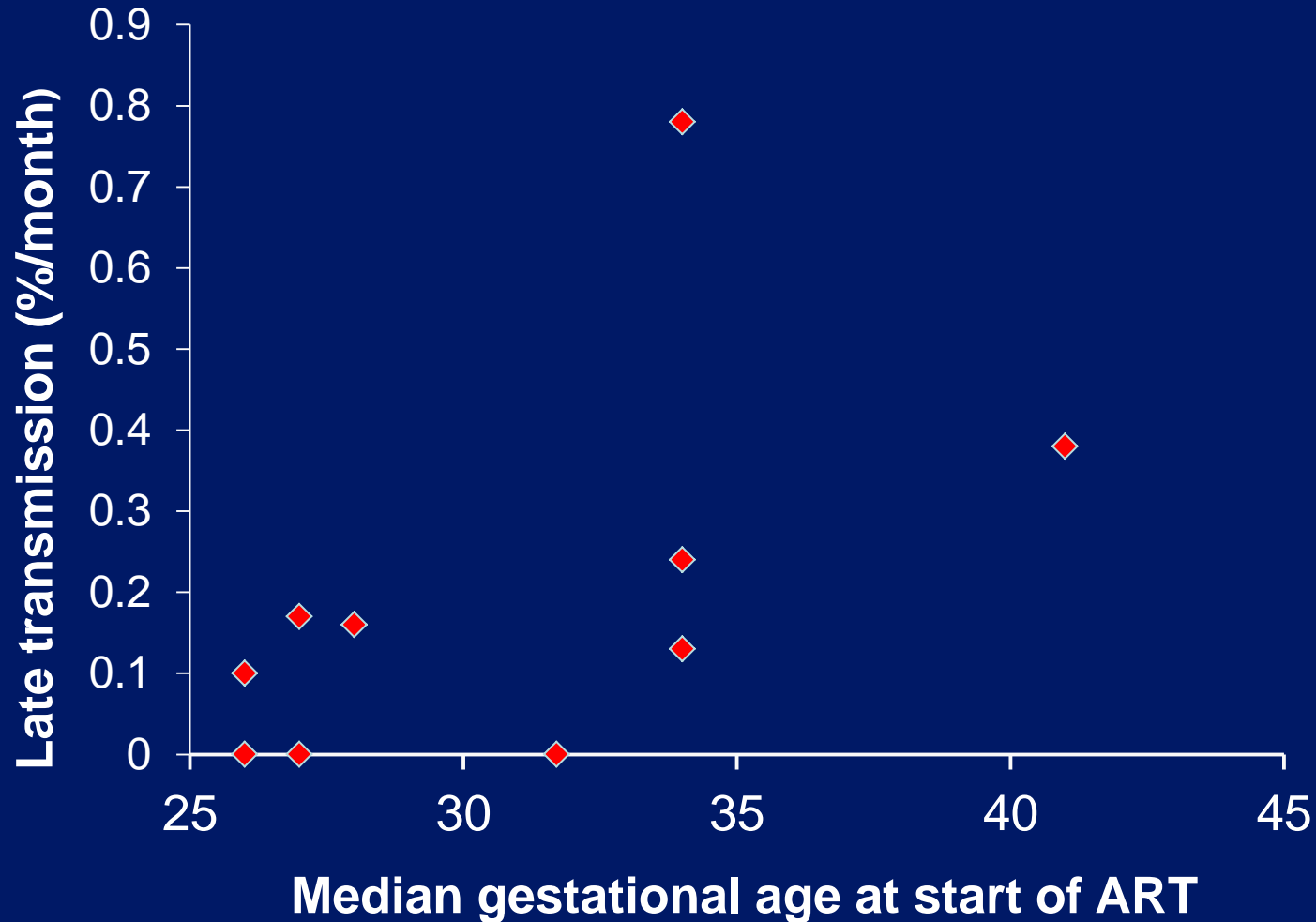
Summary of studies of **infant ARV** for preventing post-natal HIV transmission

- Randomized, controlled trials show benefit
 - SWEN (6 weeks NVP)
 - Pepi-Malawi (14 weeks NVP ± AZT)
 - HPTN 046 (6 wk vs 6 months NVP)
- Other studies suggest 3TC effective, AZT not effective
- BAN: randomized, controlled study of *postnatal* maternal ART, daily infant NVP, or control

Summary of studies of **maternal ART** for preventing post-natal HIV transmission

- Multiple cohort studies and trials show low rate of transmission- *roughly 1/5th of expected*
- Some studies had no cases of transmission
- Transmission risk appears to be related to *how early* maternal ART started
- ABC/AZT/3TC may be less effective than LPV/r/AZT/3TC
- Causes of failure not well described

Late HIV transmission (between 6 weeks - ~ 6 months) to infants from mothers starting HAART at different gestational ages in multiple cohort or randomized studies



Maternal HAART or infant NVP to prevent postnatal HIV transmission: The BAN Study

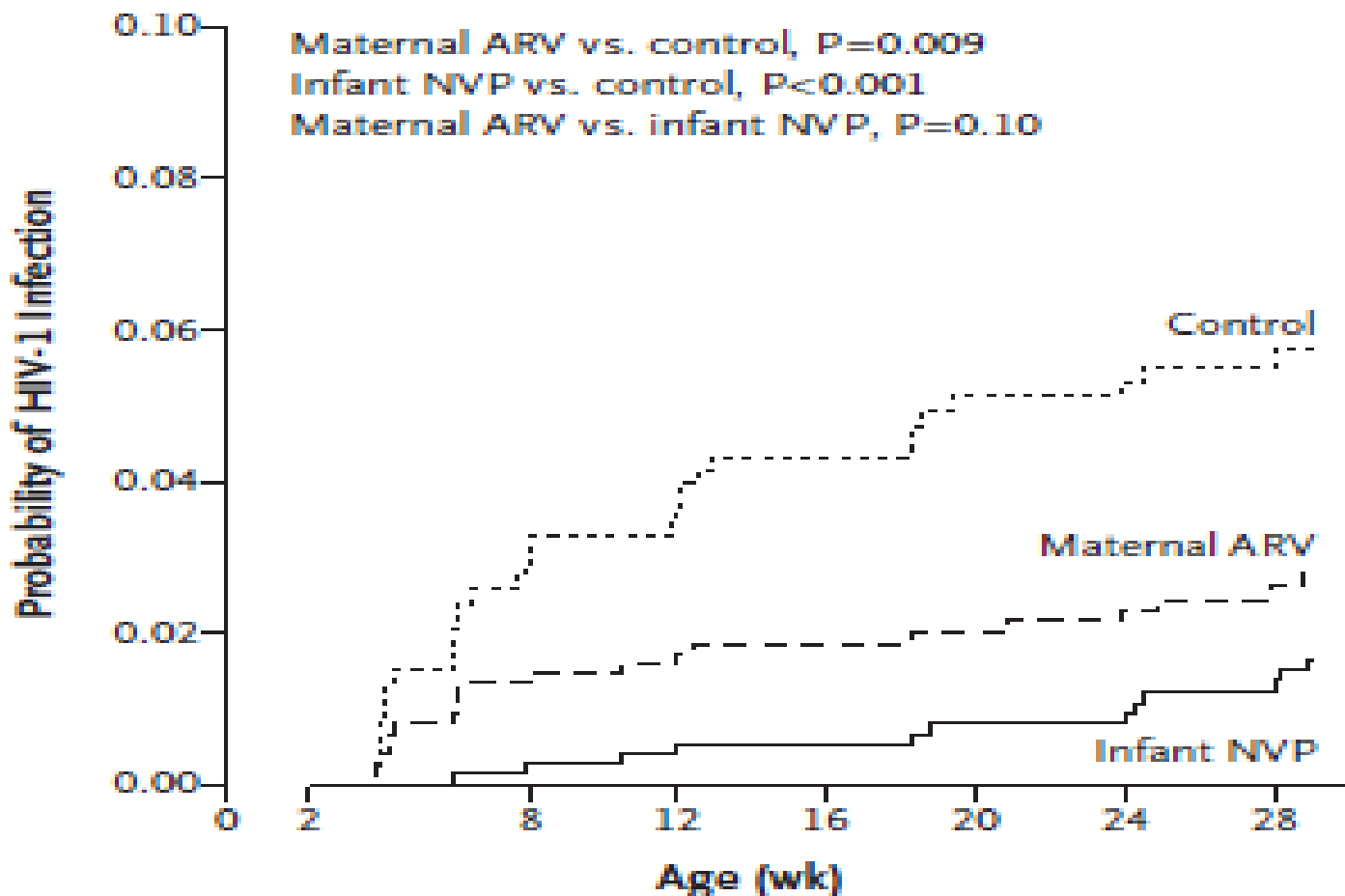
- 2637 mother-infant pairs in Malawi with maternal CD4 >250
- NO ARV PRIOR TO LABOR
- Intrapartum SD NVP plus ZDV/3TC then maternal ZDV/3TC for 1 week
- 4.9% PCR+ at birth
- Randomized in first week of life to maternal HAART, infant NVP, or control for 24 weeks, then rapid weaning
- Study not powered to measure difference between maternal HAART and infant NVP (p = 0.07 for HIV+ or death)

Status at 28 weeks in infants who were HIV PCR negative at entry				
Arm	HIV PCR+ (%)	p vs control	HIV+ or death (%)	p vs control
Maternal ZDV/3TC/LPV/r	3.0	0.003	4.7	0.003
Infant NVP daily	1.8	< 0.0001	2.9	< 0.0001
Control	6.4	---	7.6	---

BAN: **Postpartum only** maternal ART vs daily infant NVP HIV infection in infants uninfected at birth

(All got ZDV/3TC/NVP in labor + 1 wk maternal/infant ZDV/3TC) (Chasela, NEJM 2010)

A HIV-1 Infection in HIV-1–Negative Infants at 2 Weeks



No. at Risk

Control	600	558	539	514	480	476	471
Maternal ARV	767	731	715	699	683	679	662
Infant NVP	785	752	741	727	710	706	687

HPTN 046: Randomized trial of daily infant NVP for 6 months versus 6 weeks.

Coovadia H, CROI 2011

- 1522 breastfeeding infants from SA, Zambia, TZ, Uganda who were PCR negative at 6 weeks of age
- All infants received daily NVP to 6 weeks at which point they enrolled and randomized to stop NVP or continue until 6 months of age
- Any maternal CD4 count (median ~545)
- 29% of women were taking ART at enrollment
- Most weaned at 6 months

HIV transmission (%) among infants who were PCR negative at 6 weeks of age in HPTN 046

Group	6 months	9 months	12 months
-------	----------	----------	-----------

MTCT after 6 weeks: All infants

NVP to 6 months	1.1	1.5	2.0
NVP to 6 weeks	2.4	2.9	3.0

MTCT after 6 weeks: Maternal CD4 < 350, not on ART

NVP to 6 months	4.8	7.5	8.9
NVP to 6 weeks	8.1	8.1	10.0

MTCT after 6 weeks: Maternal CD4 ≥ 350, not on ART

NVP to 6 months	0.7	0.9	1.5
NVP to 6 weeks	2.8	3.3	3.3

MTCT after 6 weeks: Mothers receiving ART

NVP to 6 months	0.5		
NVP to 6 weeks	0		

A **VIRAL LOAD** around term (~3-4 months after starting ART) is critical for identifying women at risk of MTCT during breastfeeding

Dilemma of late-presenting or unsuppressed woman

- Infant may already be infected: ARVs will not prevent infection and will select for resistance in some circumstances
- Distinguish between high-risk *delivery* and high-risk *pregnancy*
- For high-risk *delivery*:
 - Maternal 3 drugs in labor- ALWAYS
 - C/S helps
 - Infant on 3 ARVs, carefully selected and dosed to prevent resistance (AZT/3TC/NVP)

How well is infant feeding counseling work, and does feeding choice affect outcome?

Doherty T, et al. AIDS 2007

- Prospective study of 635 HIV+ women in SA
 - SD NVP for PMTCT
 - Counseling according to WHO 2001
 - Provided with free formula by choice
 - 55% had completed high school
- *Declared* feeding intent
 - 46% formula of which
 - 29% gave at least some breast milk
 - 73% experience formula stock-out
 - 49% breast of which
 - 13% were EBF at 12 weeks
 - 33% were formula feeding
- No difference in postnatal transmission rate according to feeding practice intent

Infant feeding counseling and outcome experience in S. Africa (continued)

- No socioeconomic correlate of feeding choice except disclosure (more formula)
- Among women declaring intent to formula feed, **HIV-free survival** associated with combination of:
 - Piped water
 - Fuel (electricity, gas, or paraffin)
 - Disclosure

Conditions needed to safely formula feed

Mothers known to be HIV-infected should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status, when specific conditions are met:¹

- a. safe water and sanitation are assured at the household level and in the community; and
- b. the mother, or other caregiver can reliably provide sufficient infant formula milk to support normal growth and development of the infant; and
- c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and
- d. the mother or caregiver can, in the first six months, exclusively give infant formula milk; and
- e. the family is supportive of this practice; and
- f. the mother or caregiver can access health care that offers comprehensive child health services.

HIV infant feeding and counseling tools- WHO 2000



***How well does this reflect the risk of HIV transmission to your patient?
How well does this reflect the risk of NOT breastfeeding?***

PACT INITIAL INFANT FEEDING QUESTIONNAIRE

Mother's name:

PACT #

Infant's name:

PACT #

Date:

Introductory messages

- Breast milk is the best nutrition for babies
- Babies that are not breastfed are more likely to suffer diarrhea, malnutrition, and death
- HIV medications can help prevent your baby from getting HIV while breastfeeding
- Formula feeding also prevents HIV and may be safe under certain conditions

Questions for mother

1. Does the mother wish to consider formula feeding? **Y N**
 - a. **Yes**- CONTINUE to question 2
 - b. **No**- STOP and counsel on safe breastfeeding
2. Can she formula feed without feeling she needs to put the baby to breast to disguise her status? **Y N**
3. Can the family afford or is there a guaranteed supply of infant formula for 12 months? **Y N**
4. Does she have time to prepare formula several times each day (or if not, do they have reliable refrigeration)? **Y N**
5. Does the family have a source of clean water and stove with fuel (electricity, gas, or paraffin) to boil water several times each day? **Y N**

Assessment

- N** **ONE OR MORE** answers to questions 1-5 above are **NO**.
Breastfeeding with maternal ART or daily infant NVP is safest
- Y** **ALL** answers to 1-5 above are **YES**. Formula feeding may be considered

Plan

- EBF** Exclusive breastfeeding plus maternal ART or daily infant NVP.
Counsel on Safe Breastfeeding of HIV-Exposed Infant
- EFF** Exclusive formula feeding. Counsel on Safe Formula Feeding of
HIV-Exposed Infant