Considerations related to postnatal HIV transmission and infant feeding

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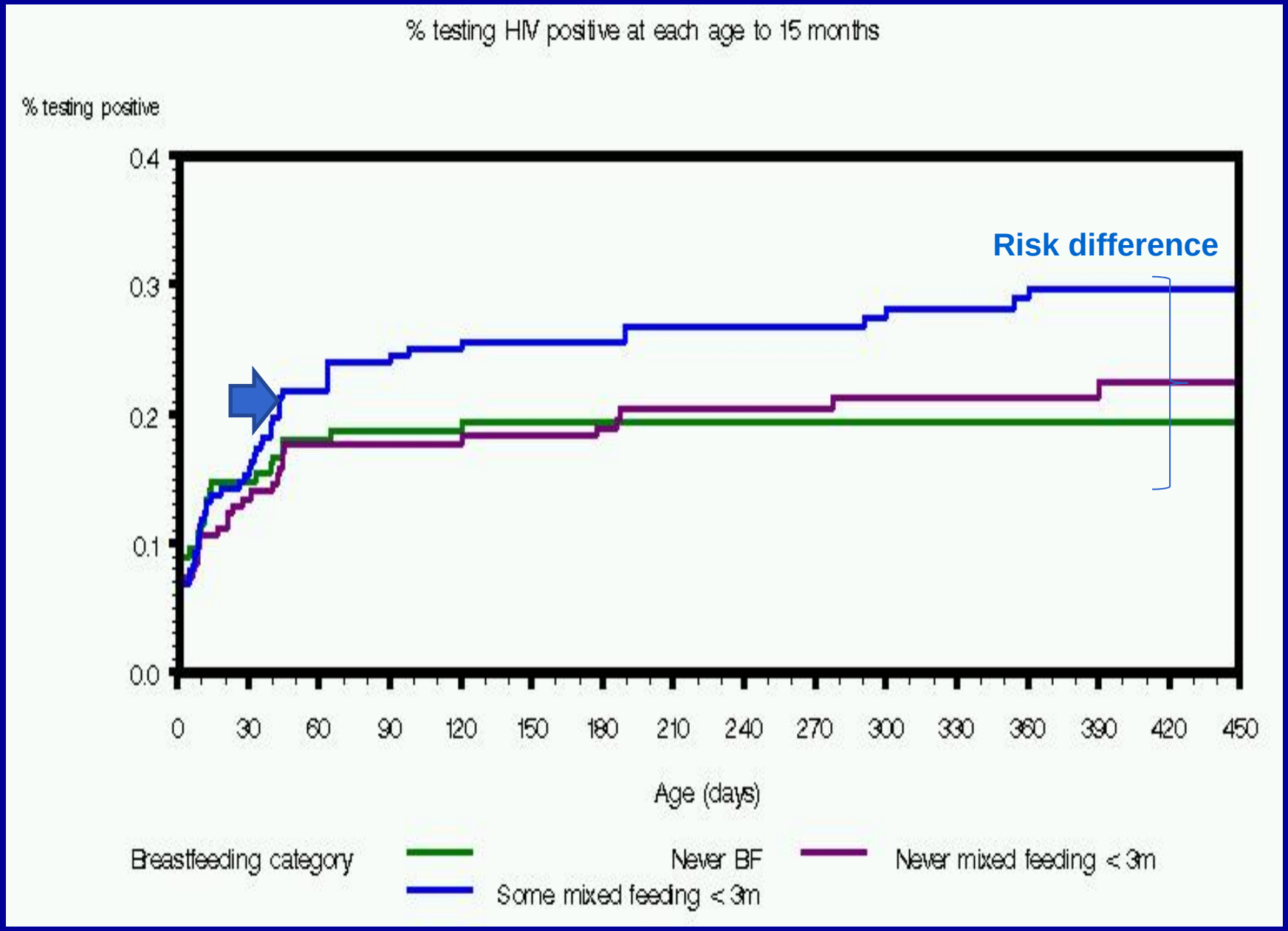
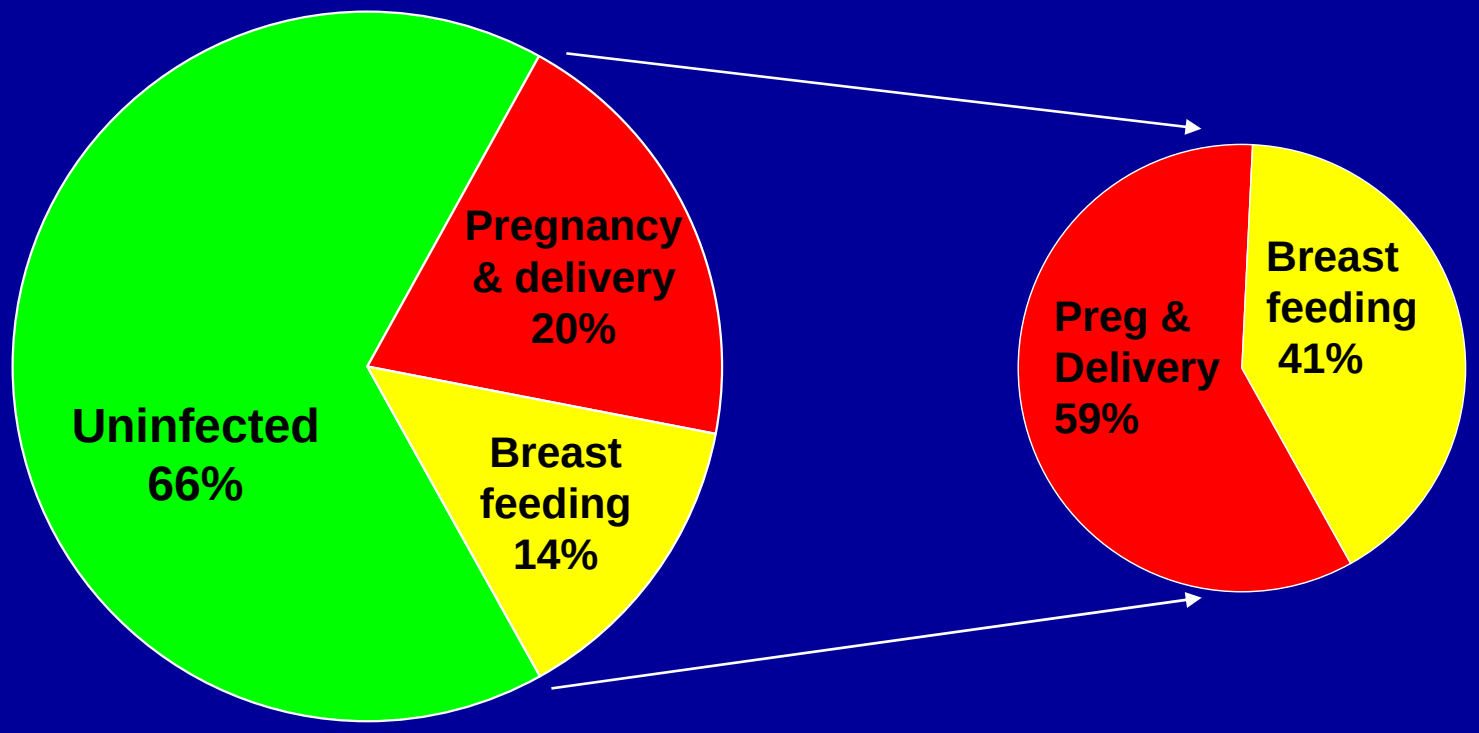

% testing HIV positive at each age to 15 months
% testing positive
0.4
0.3
0.2
0.1
0.0
Risk difference
0
30
60
90
120
150
180
210
240
270
300
330
360
390
420
450
Age (days)
Breastfeeding category
Never BF
Never mixed feeding < 3m
Some mixed feeding < 3m

Study design considerations

1. Comparison population
2. Repeated PCR testing
3. Follow-up past the completion of breastfeeding
4. Appropriate adjustment for censoring

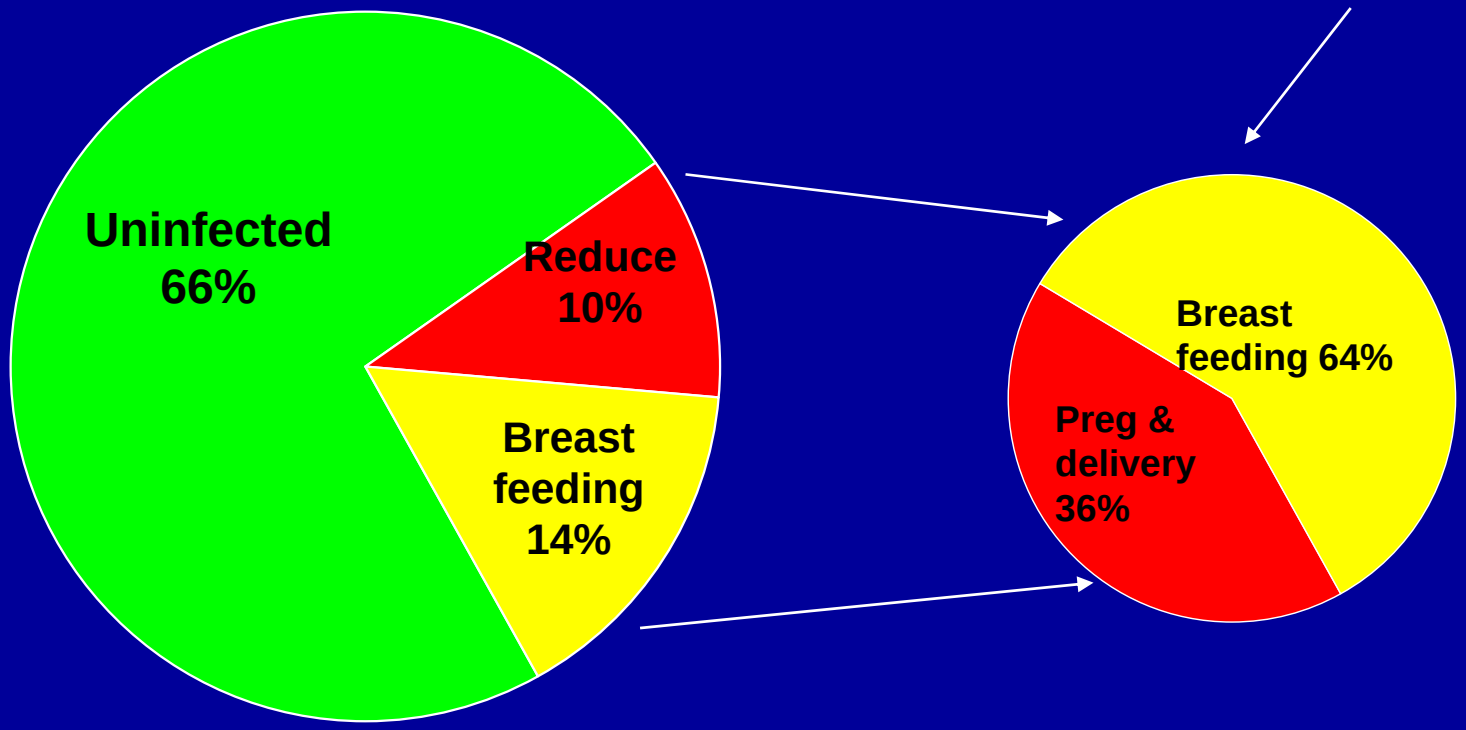
Transmission rates among breast-fed infants born to HIV-infected mothers

In the absence of interventions



With short course AZT+NVP

Breastfeeding responsible for 64% of infections



Denominator = all infants born to HIV-infected mothers

Denominator = infants who are **infected**

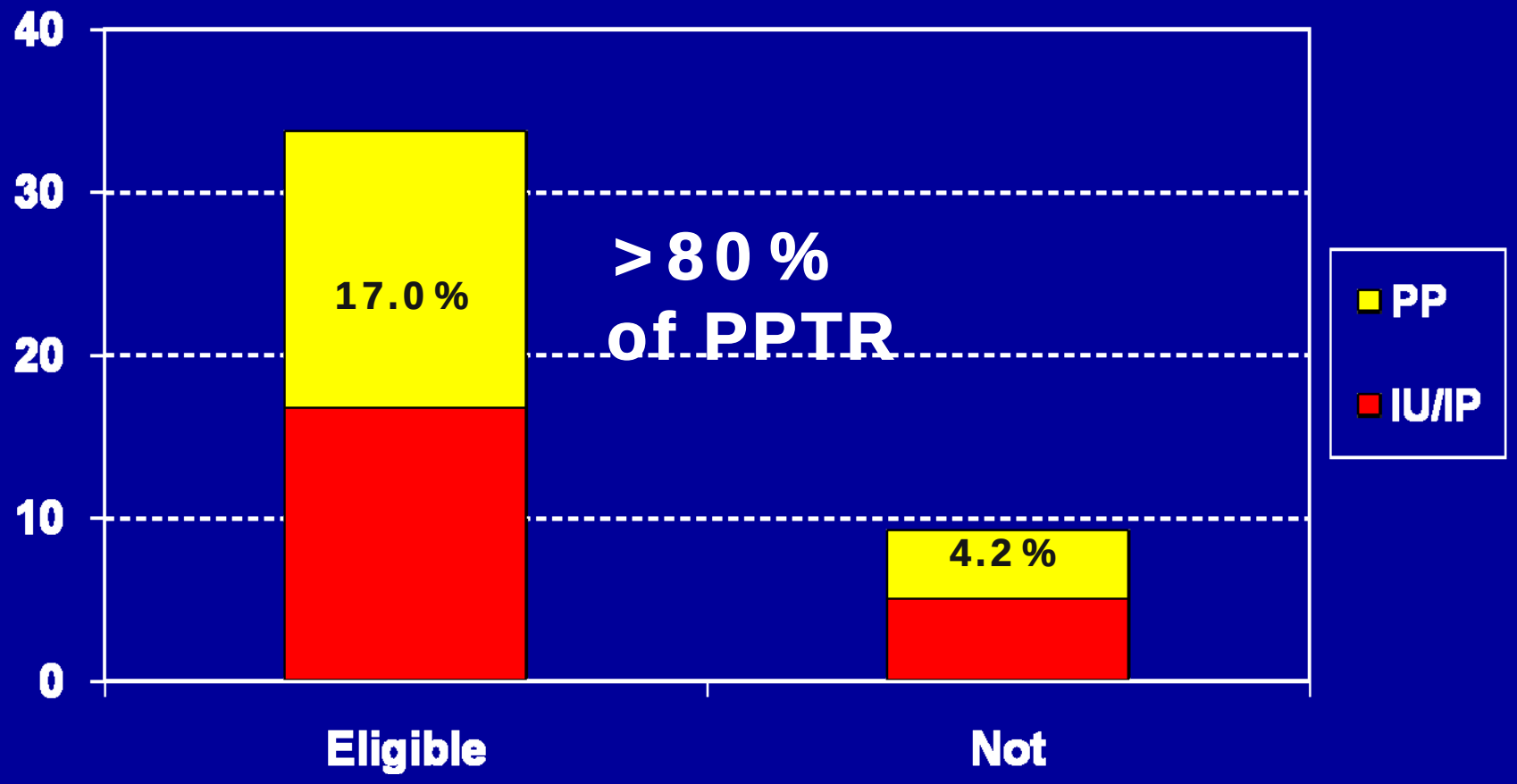
Interpreting results depending on study population

Postnatal transmission will be influenced by:

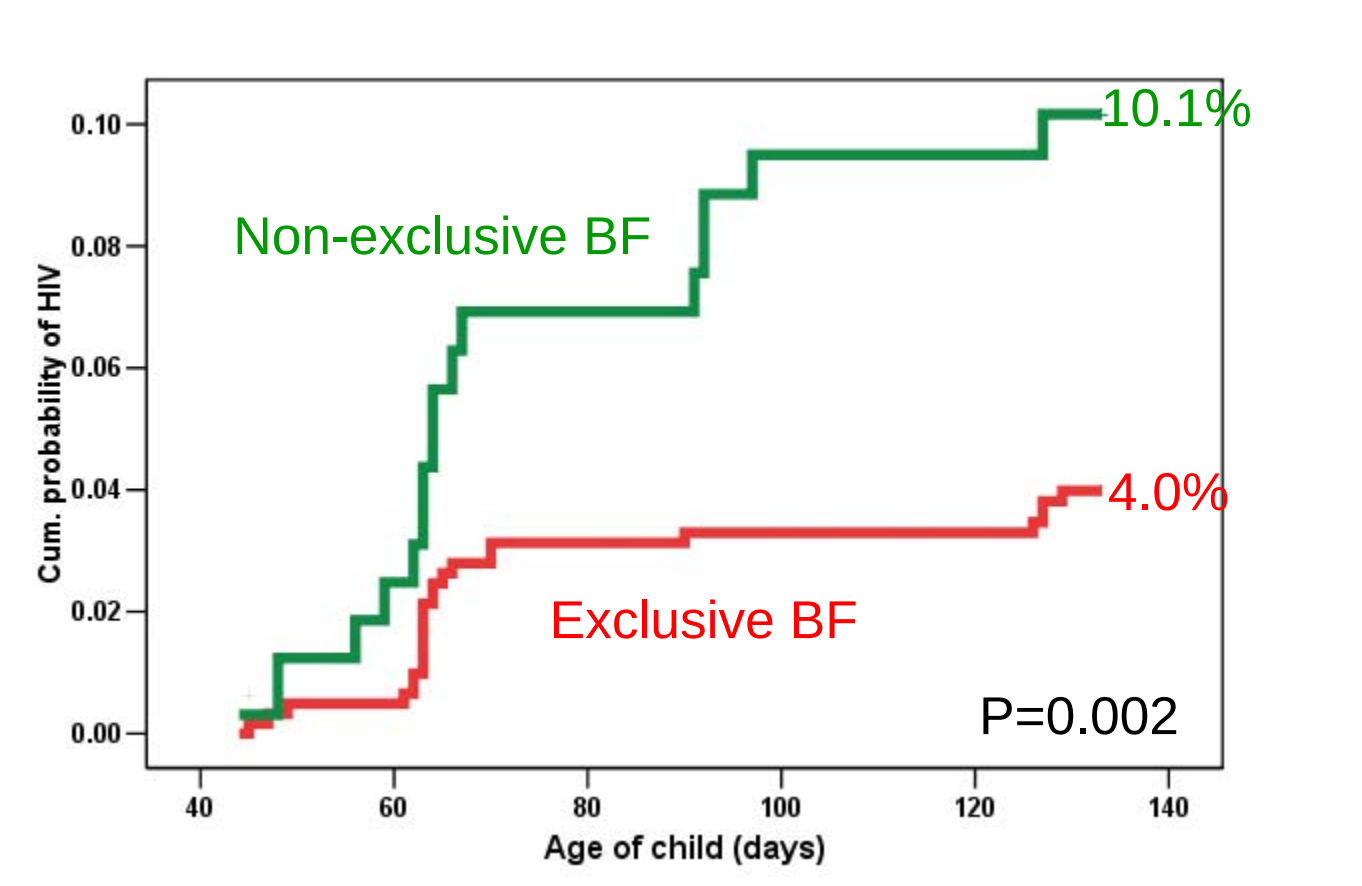
- Quality of breastfeeding
- Duration of breastfeeding
- Use of antiretrovirals
- Severity of maternal disease

Comparisons across contexts not possible without information on these parameters

Most postnatal HIV transmission occurs among women who meet current criteria for HAART



Benefits of exclusive breastfeeding on early postnatal transmission through 4 months



Increased transmission due to non-exclusive BF:
(as time-dependent) Relative Hazard 3.5 (95% CI: 1.7–7.2)

The concept of weaning: definitions and their implications

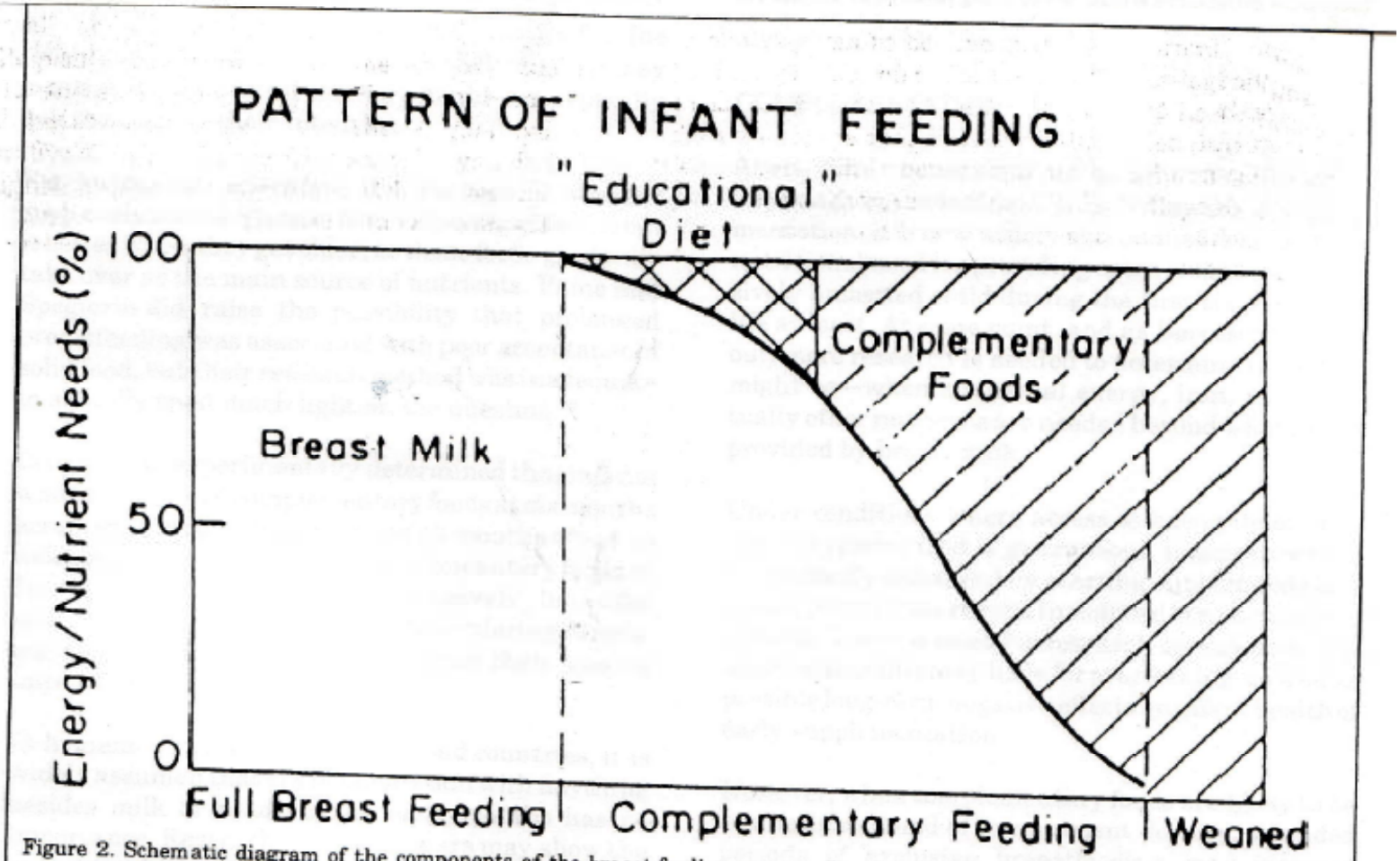
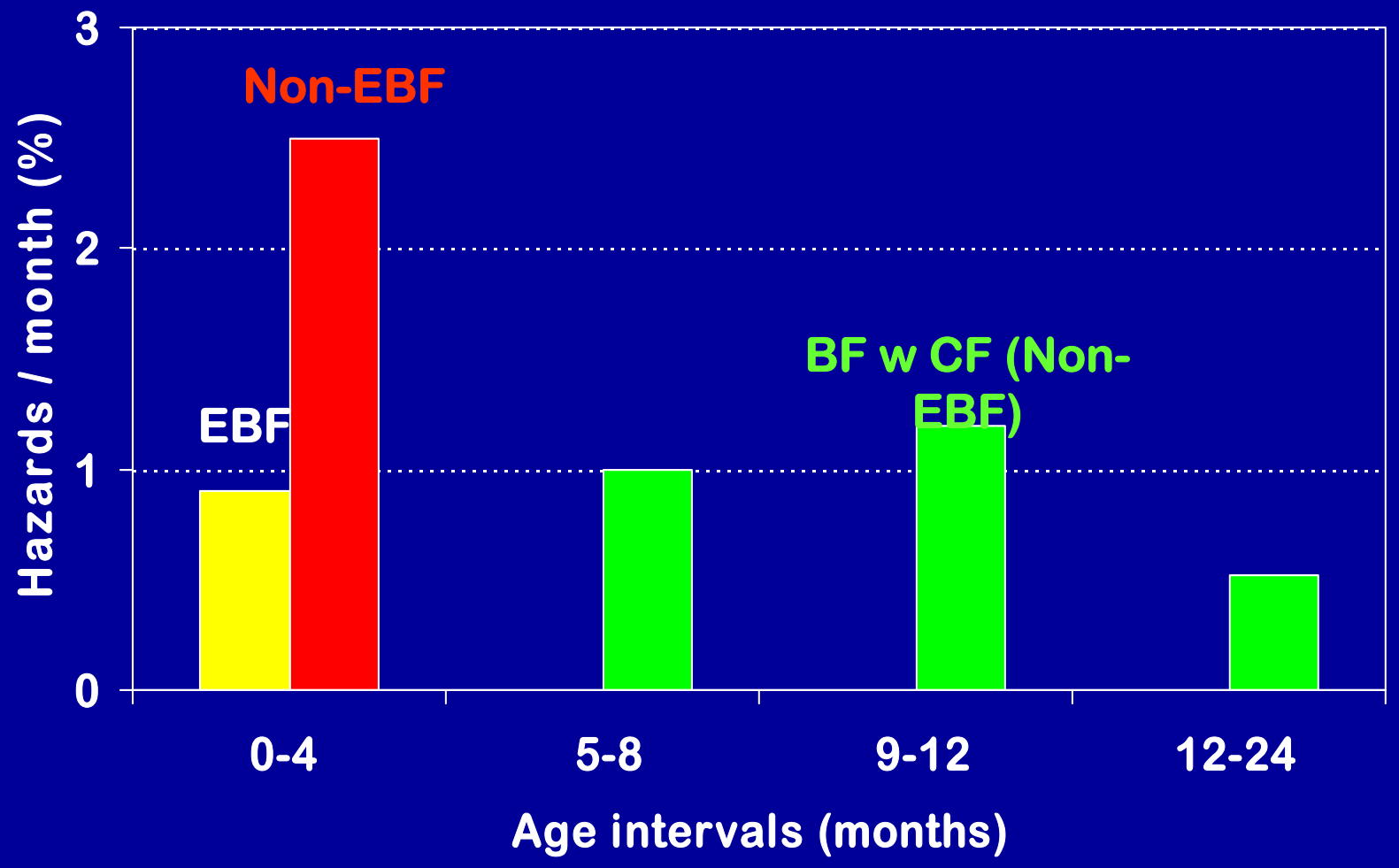


Figure 2. Schematic diagram of the components of the breast-feeding process. Reprinted with permission. Greinter T: Sustained breastfeeding, complementation and care. Food Nutr Bull 16:317, 1995. (See text for explanation of the numbers.)

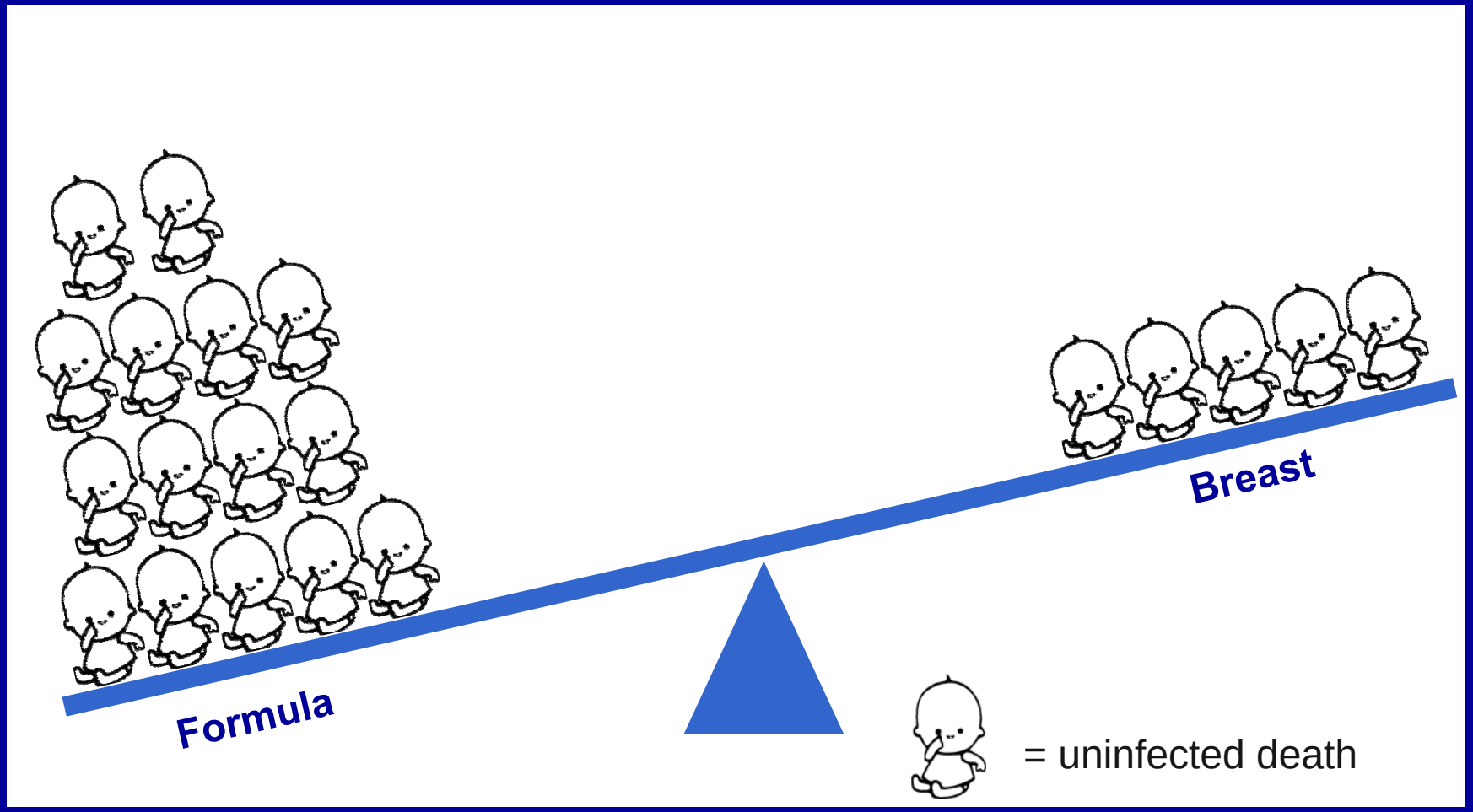
Greiner T. J Human Lactation 1996; 12: 123-128

Age-specific hazard rates of postnatal HIV transmission per month of breastfeeding in control group

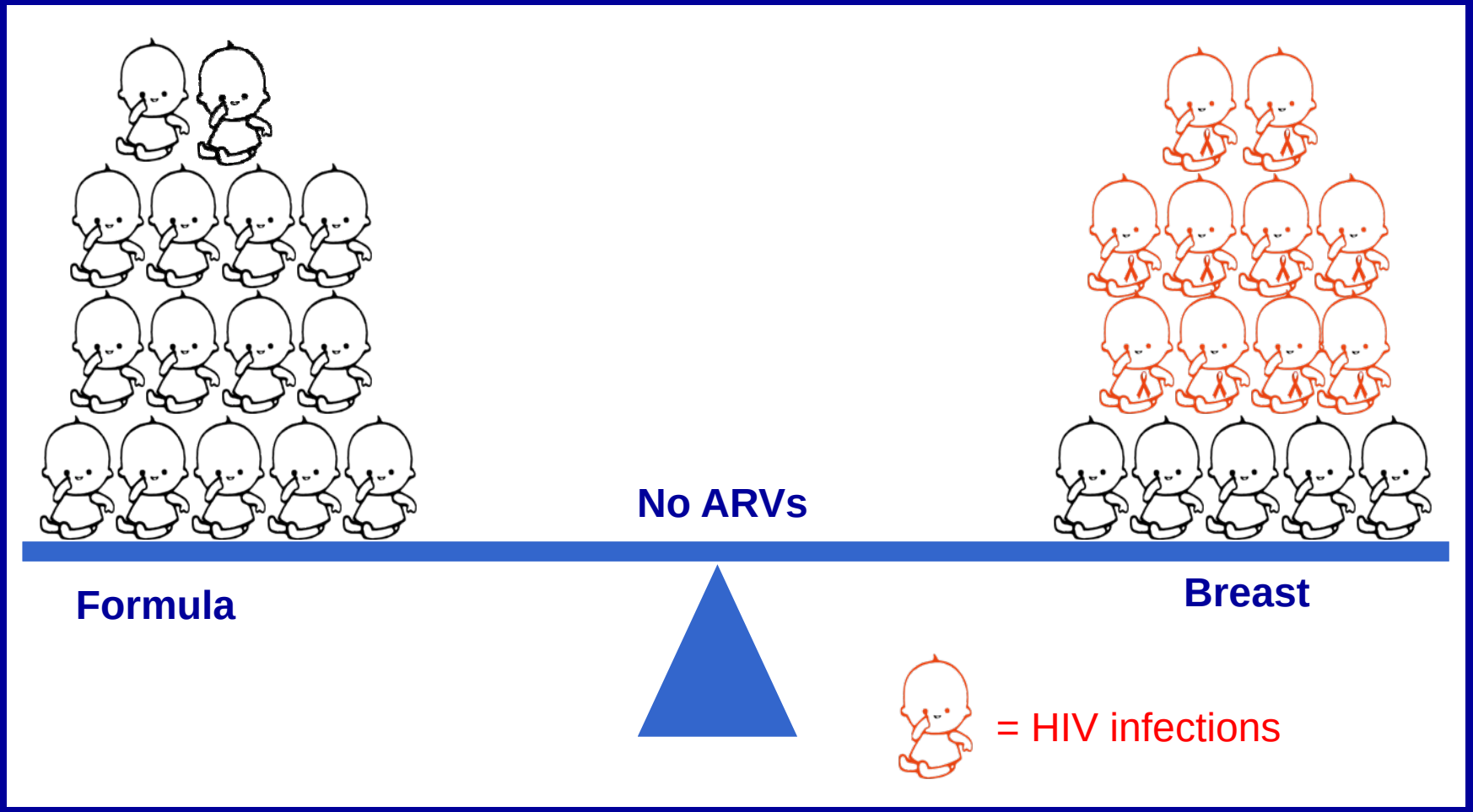


What to include in models?

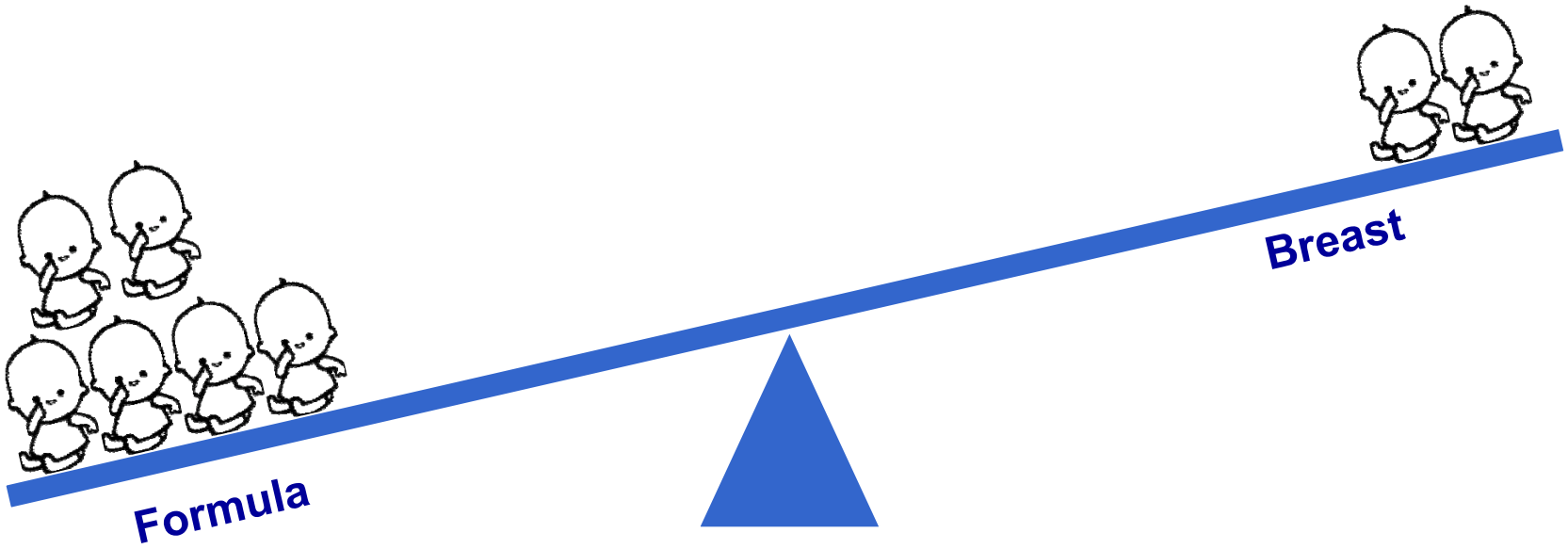
Why HIV upset everything ….



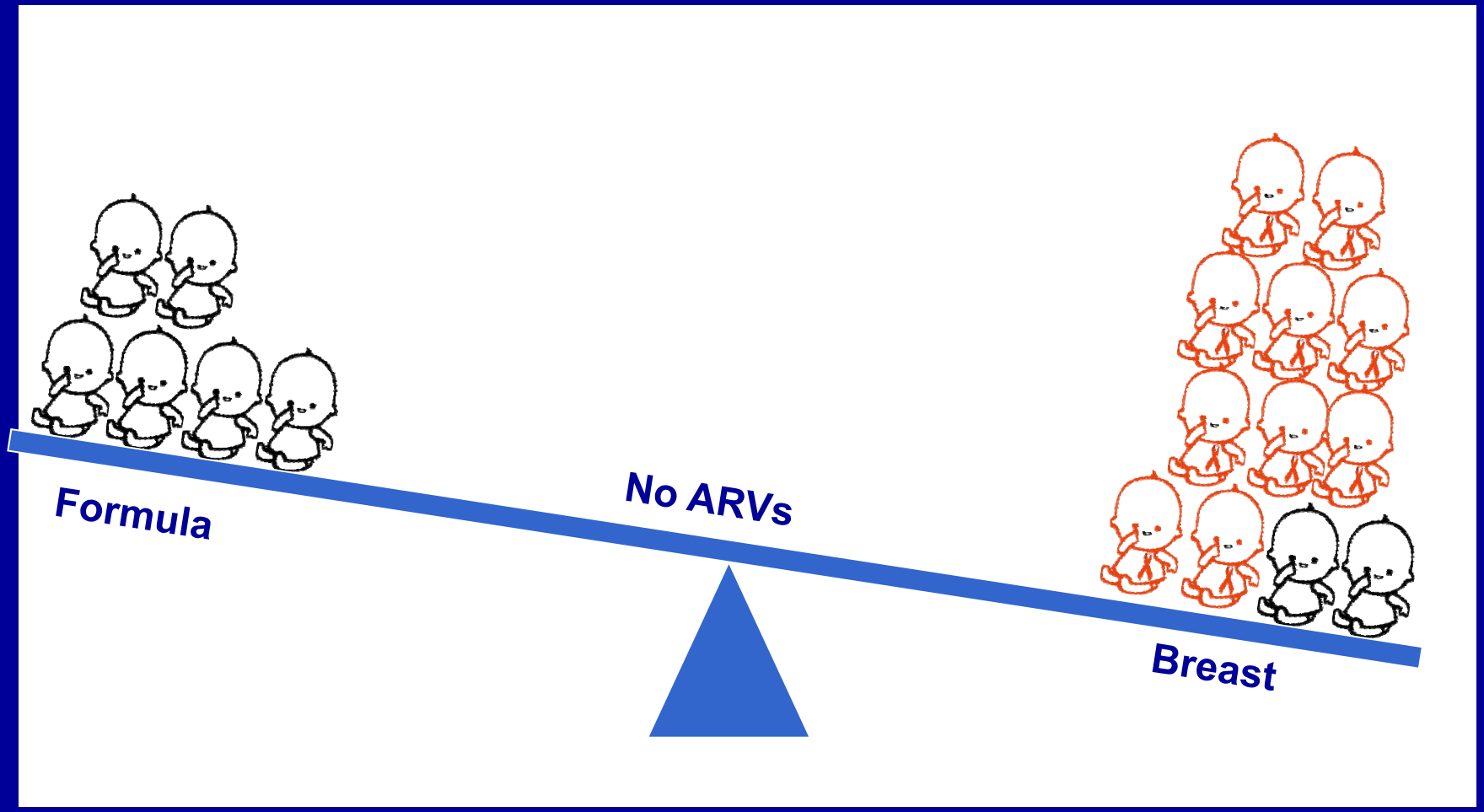
In high mortality settings, a delicate balance



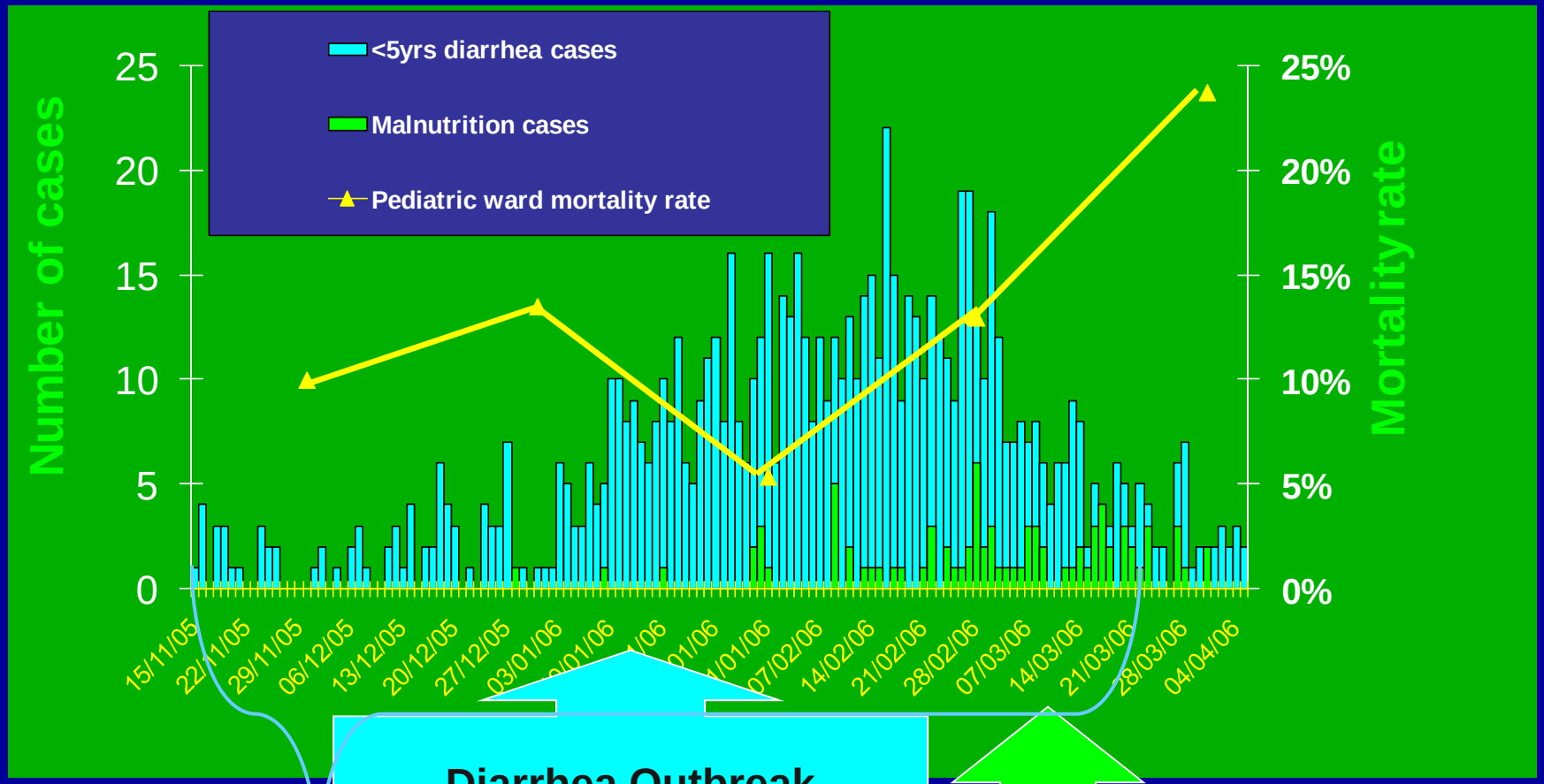
Why the “double standard” ...



In low mortality settings, HIV makes a larger contribution to the balance of risks



Diarrhea Outbreak in Francistown, Botswana, 11/05-4/06



Diarrhea Outbreak

Tracy Creek, CROI 2007

Heavy rains began in Nov 05 until Mar 06

Kwashiorkor & Marasmus outbreak in March

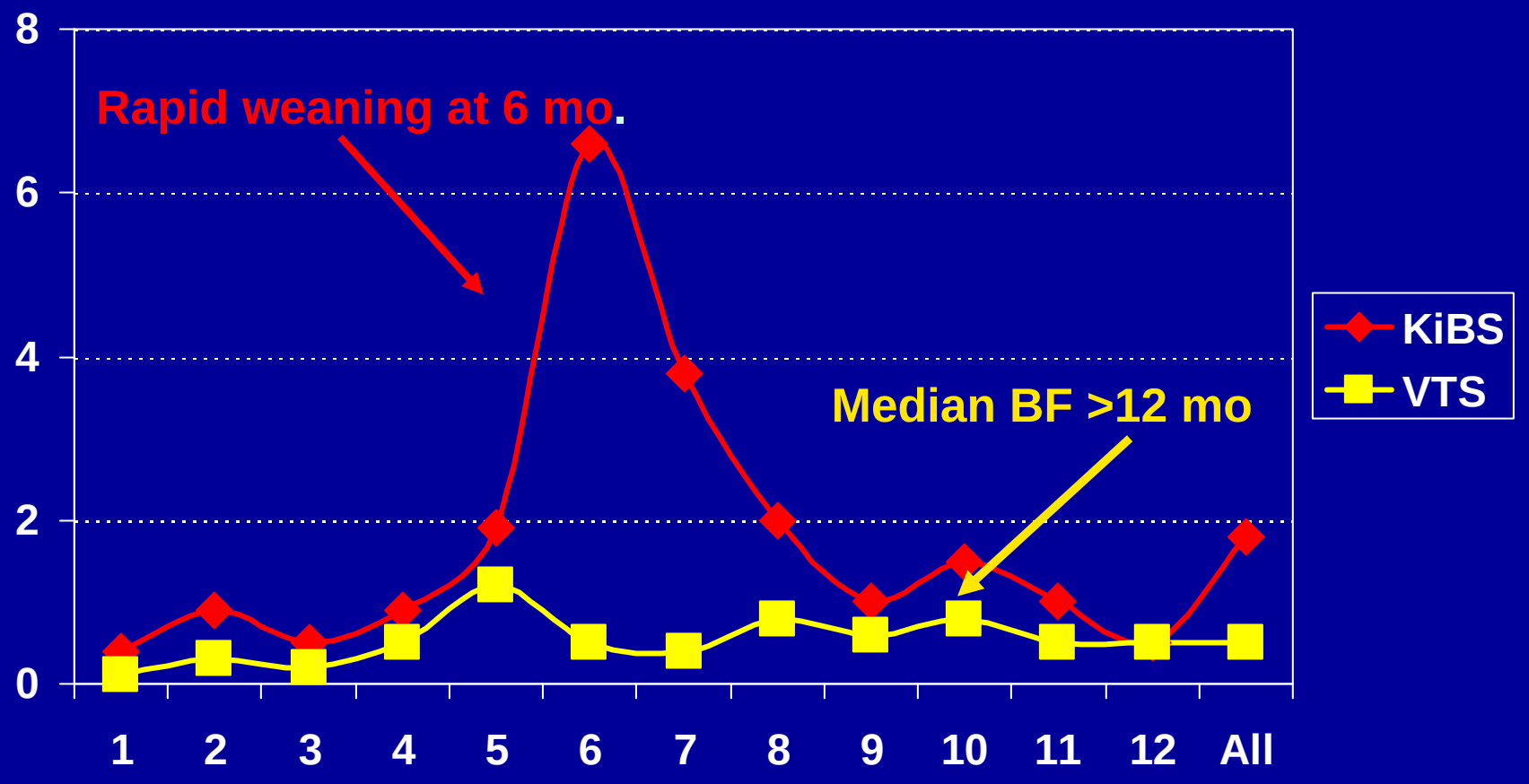
CDC case study of diarrhea outbreak in Botswana, Feb-Mar 2006

N	153
Age	97% < 2 years
HIV infected	18%
Death	22% (33/153)

Not breastfeeding was associated with 8.5-fold increased risk of mortality

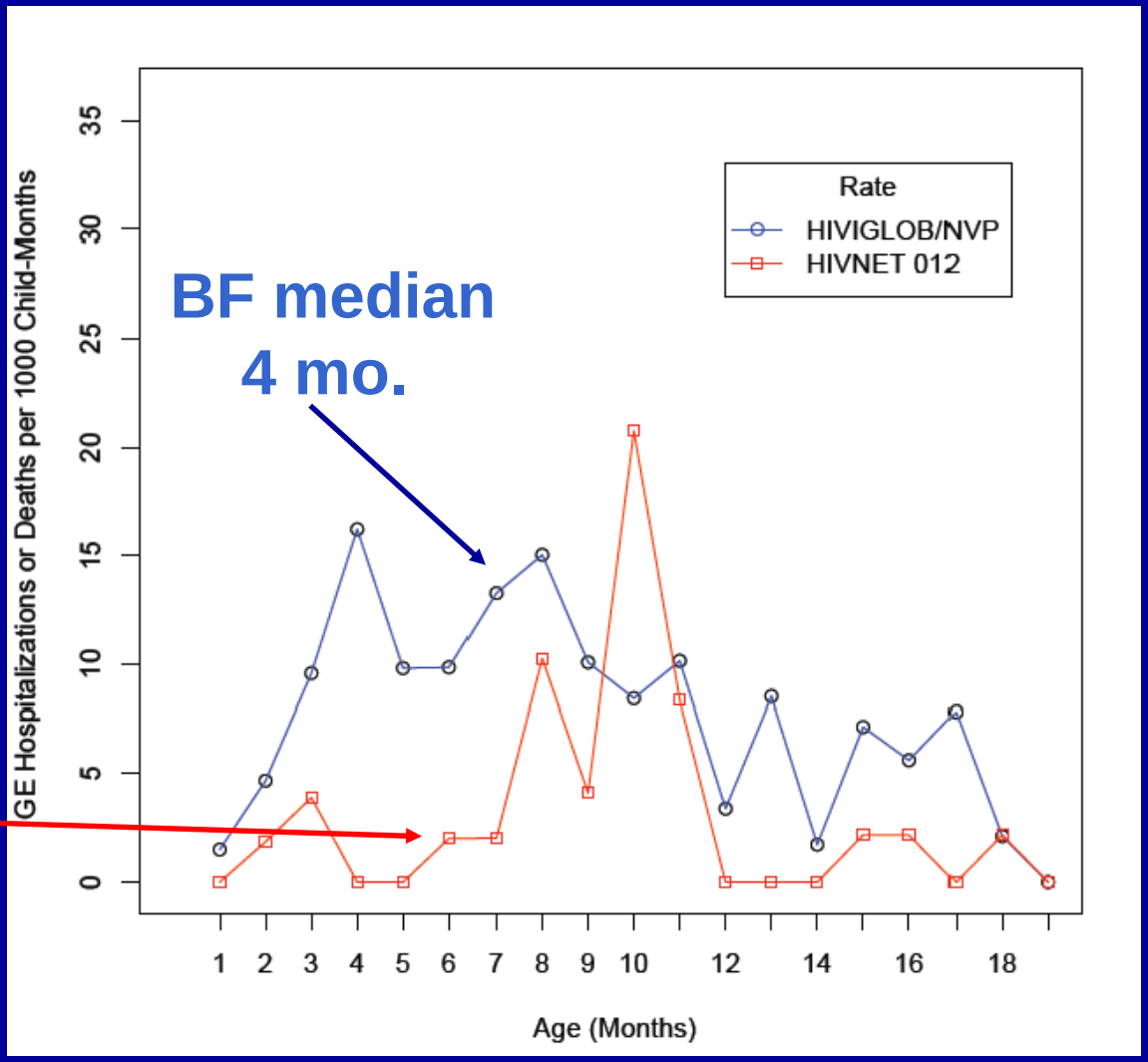
Tracy Creek, CROI 2007

Kisumu, Kenya



Thomas T, Masaba R, van Eijk A, et al. **CROI Los Angeles** 2007

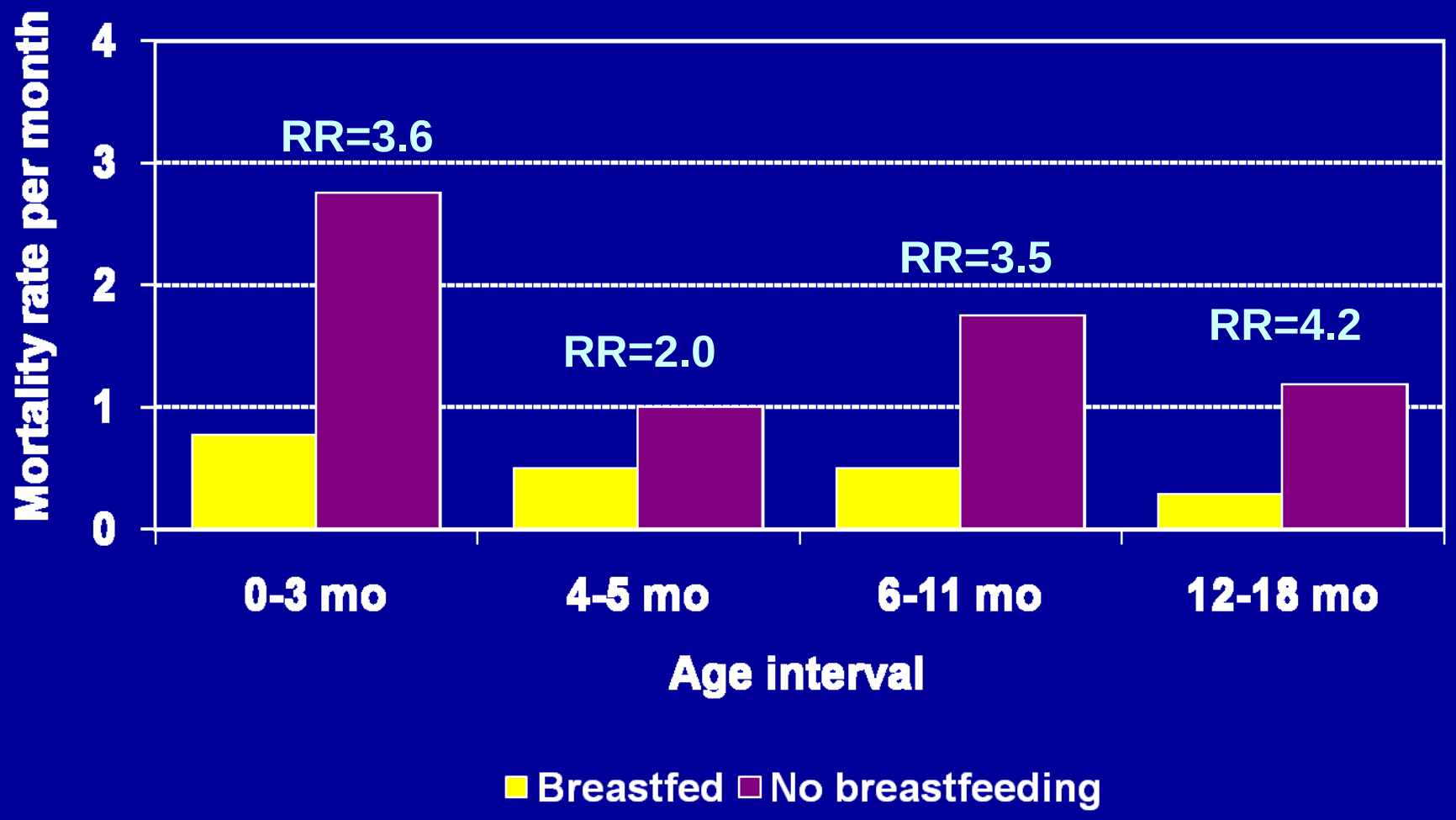
Kampala, Uganda



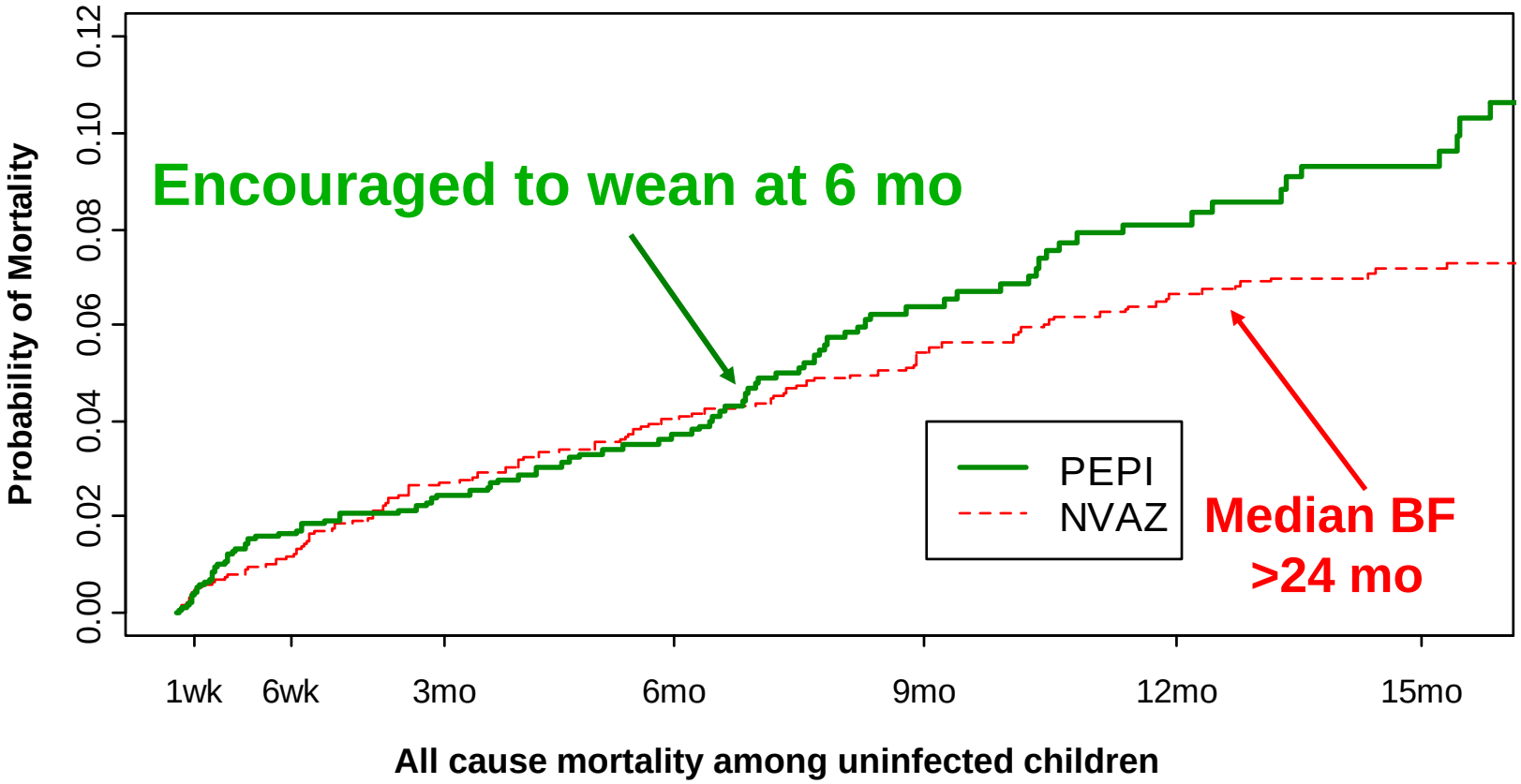
BF median
9 mo.

Onyango-Makumbi C, Bagenda D, Mwatha A, et al. ***J Acquir Immune Defic Syndr.*** 2009 Sep 25. [Epub ahead of print]

Not breastfeeding was associated with 2 to 4-fold increases in uninfected child mortality at all ages to 18 months in ZEBS

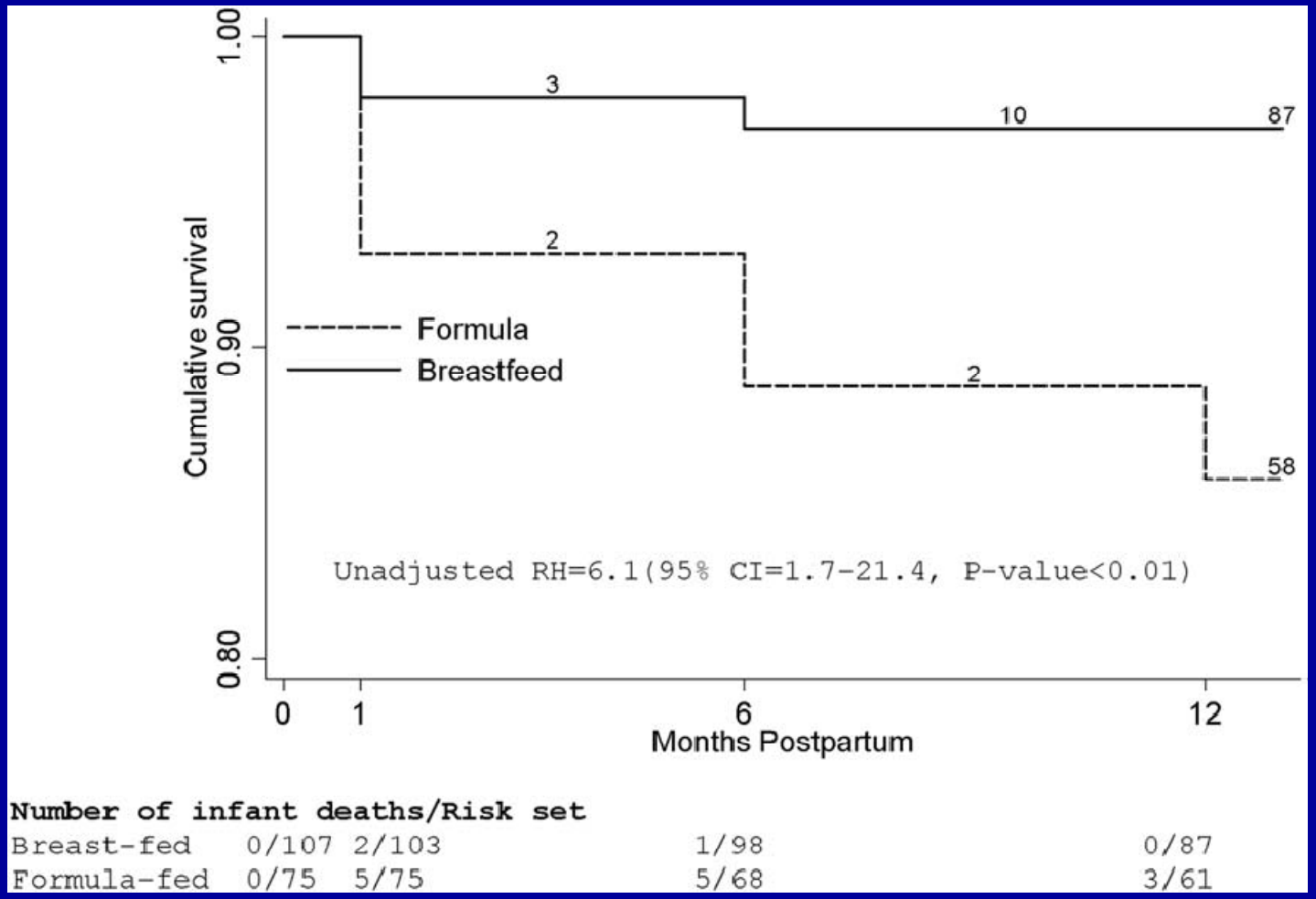


Blantyre, Malawi



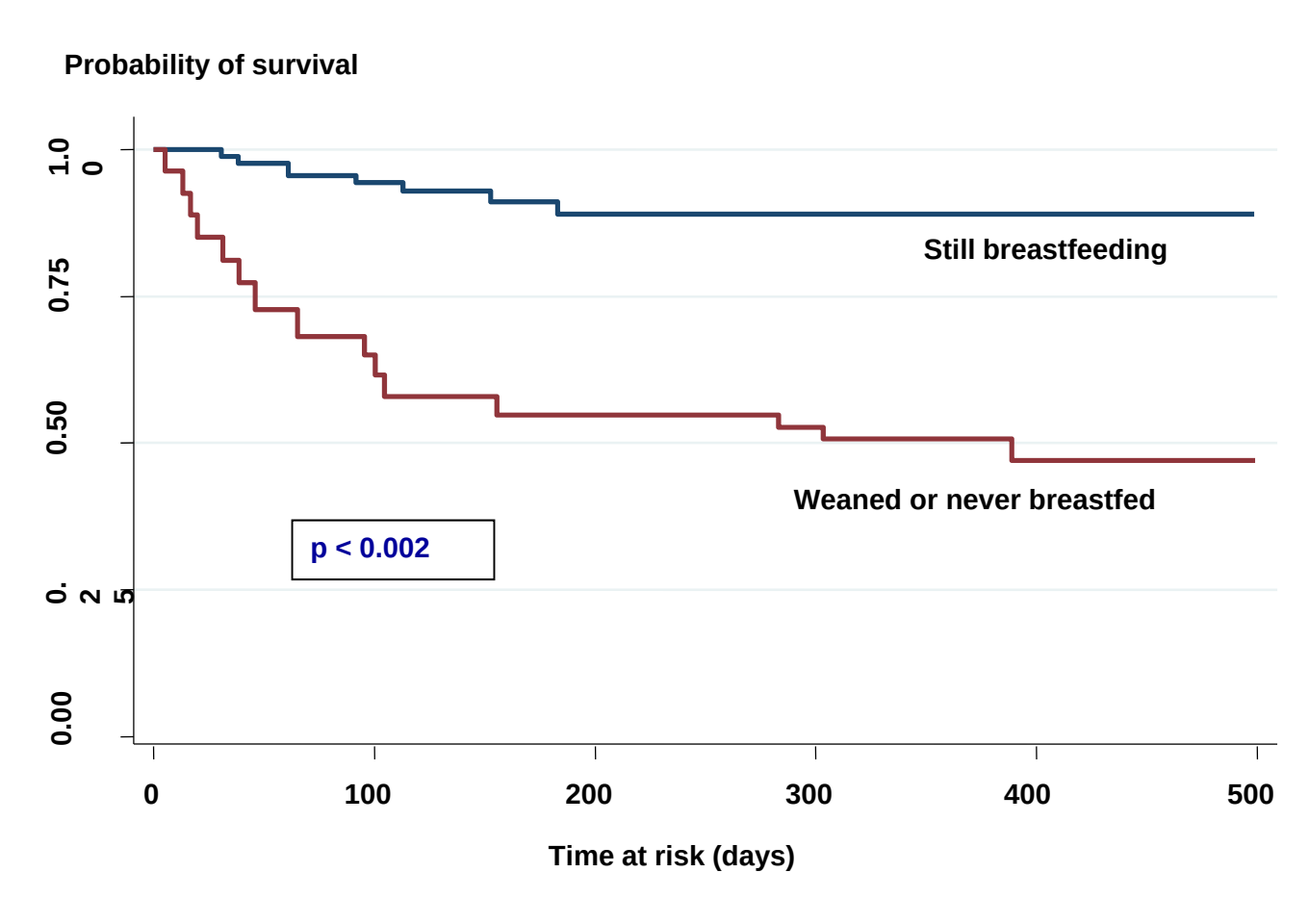
Kafulafula G, Hoover DR, Taha T, et al.
J Acquir Immune Defic Syndr. 2009 (in press)

Increased mortality with abstinence from breastfeeding in a program in rural, Rakai, Uganda



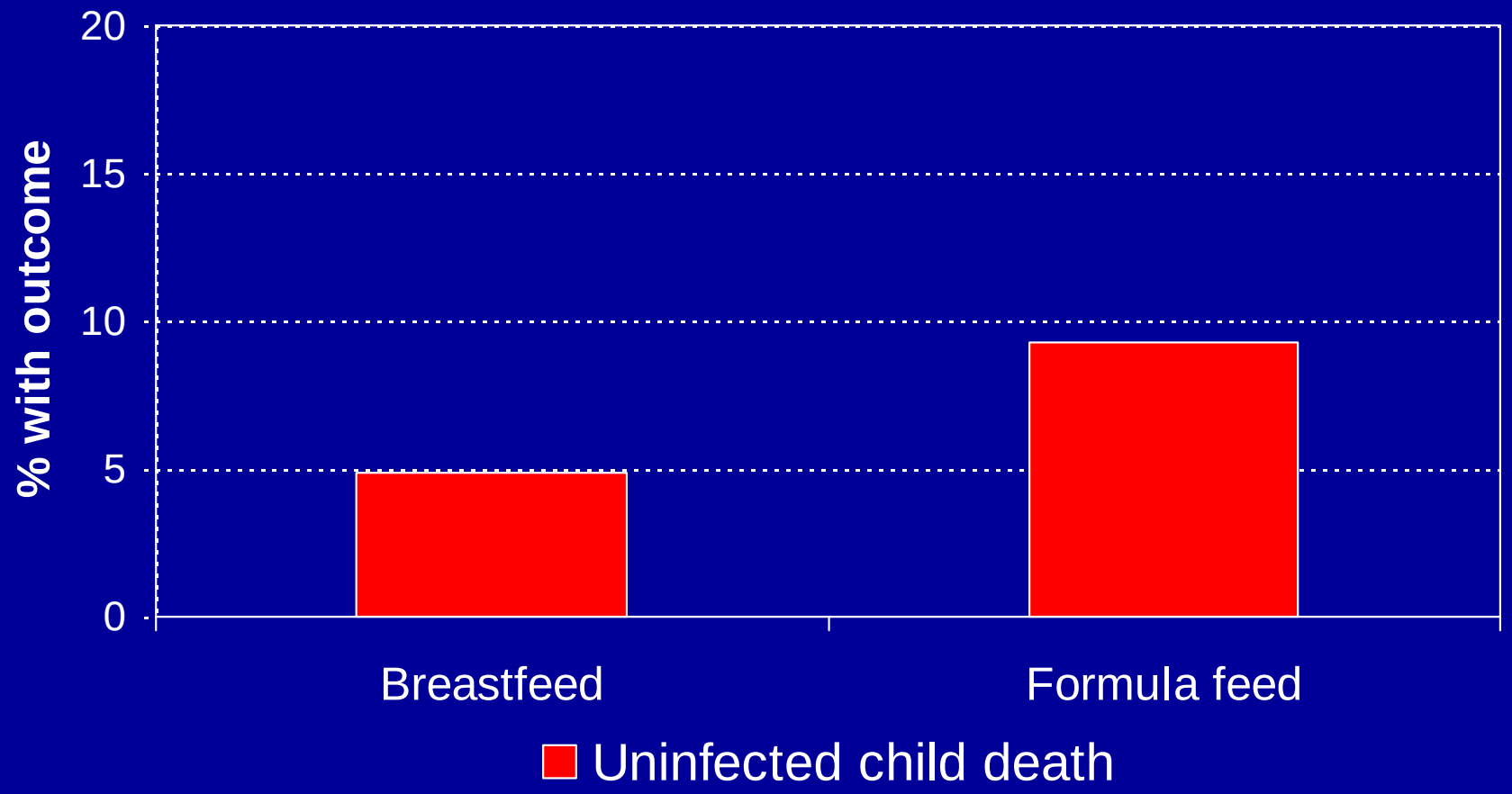
Kagaayi J, Gray RH, Brahmbhatt H. et al. **PLoS ONE** 2008; December 3: e3877

Tororo and Busia Districts in rural Uganda



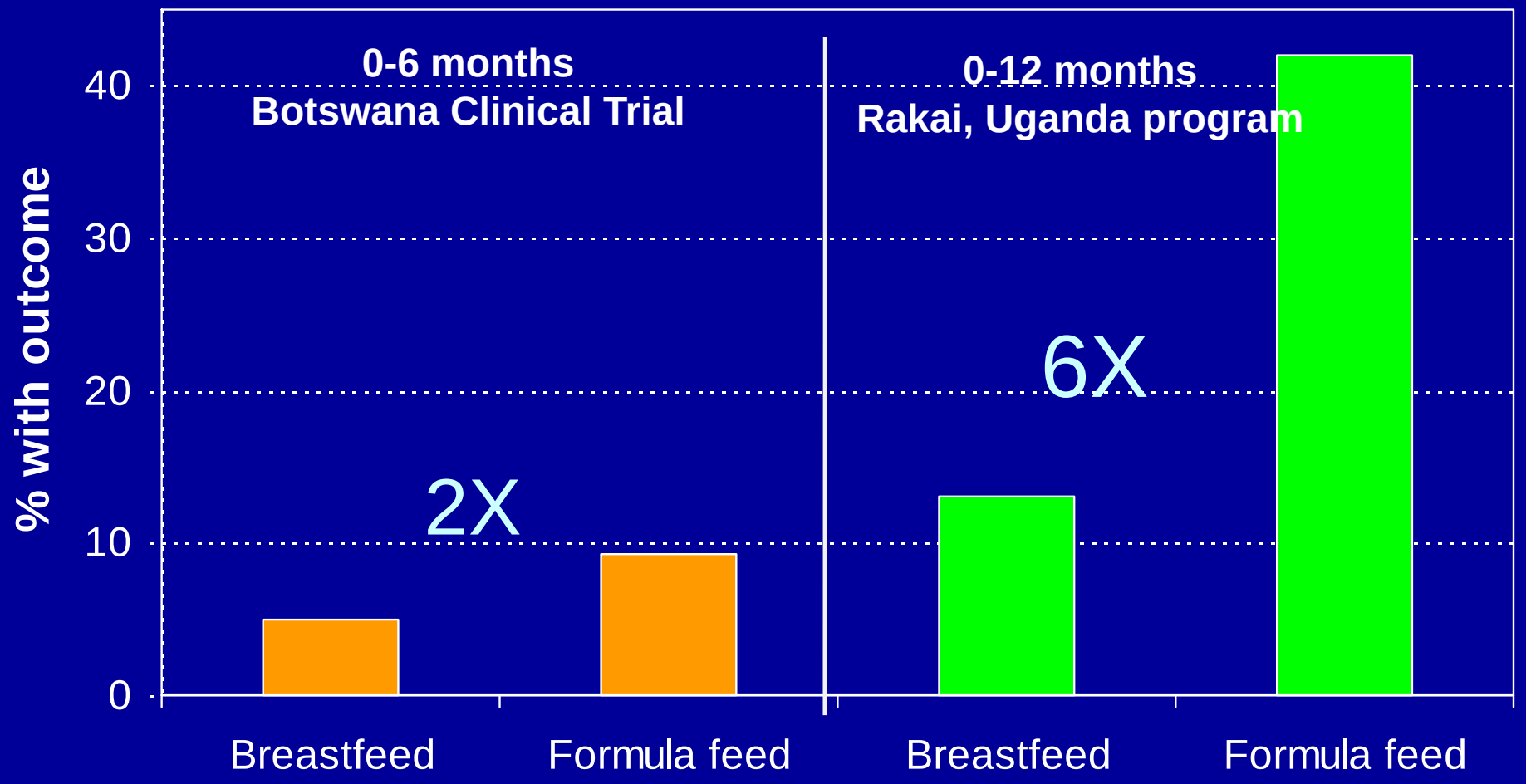
Homsy J, Moore D, Barasa A, et al. ***J Acquir Immune Defic Syndr.*** 2009 Sep 25. [Epub ahead of print]

Increased mortality with abstinence from breastfeeding in a **clinical trial** in urban Botswana



Thior I, Lockman S, Smeaton LM et al. ***JAMA*** 2006; 296: 794-805

Adverse effects of abstinence from breastfeeding are greater in programs than in clinical trials



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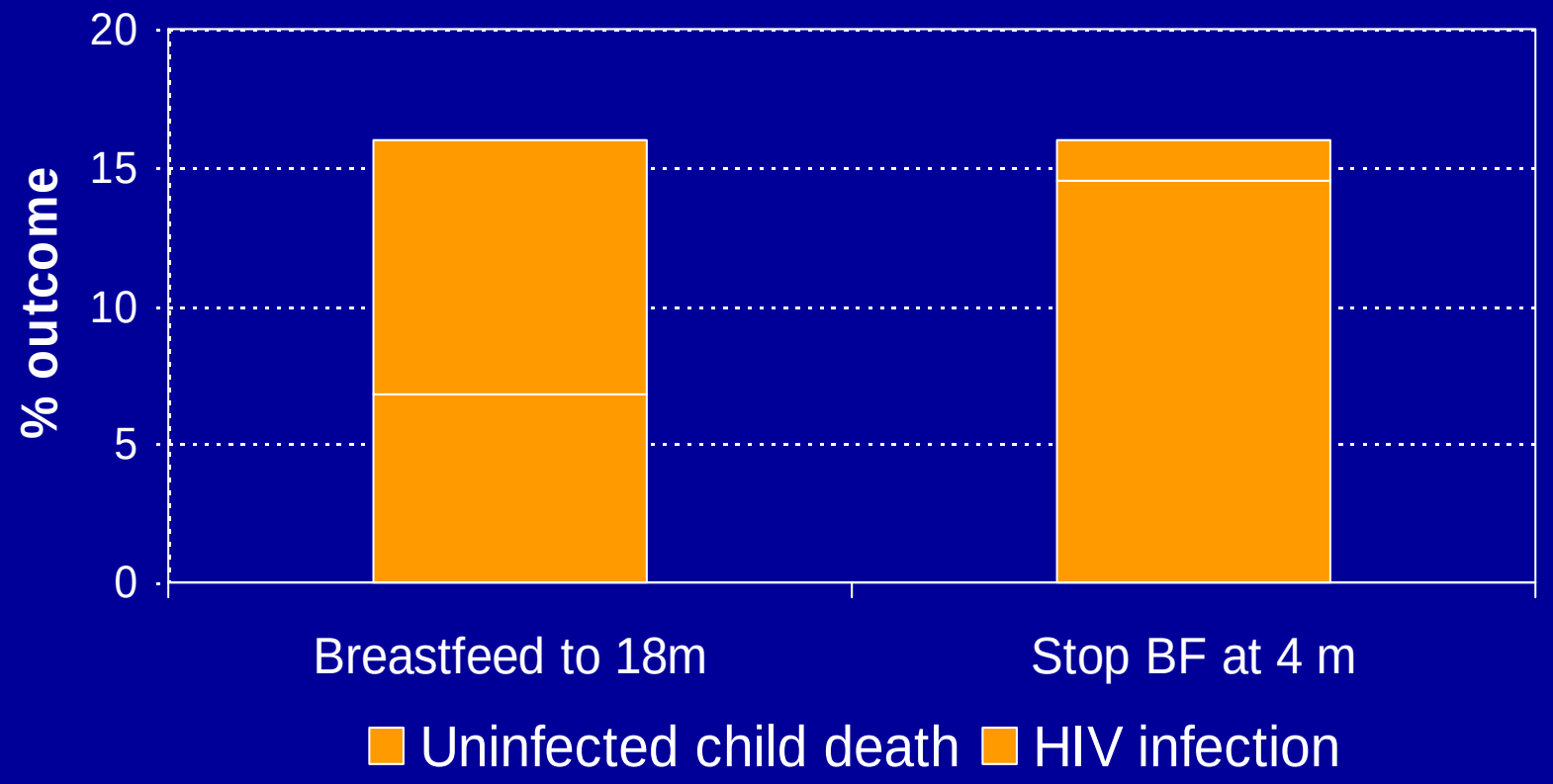
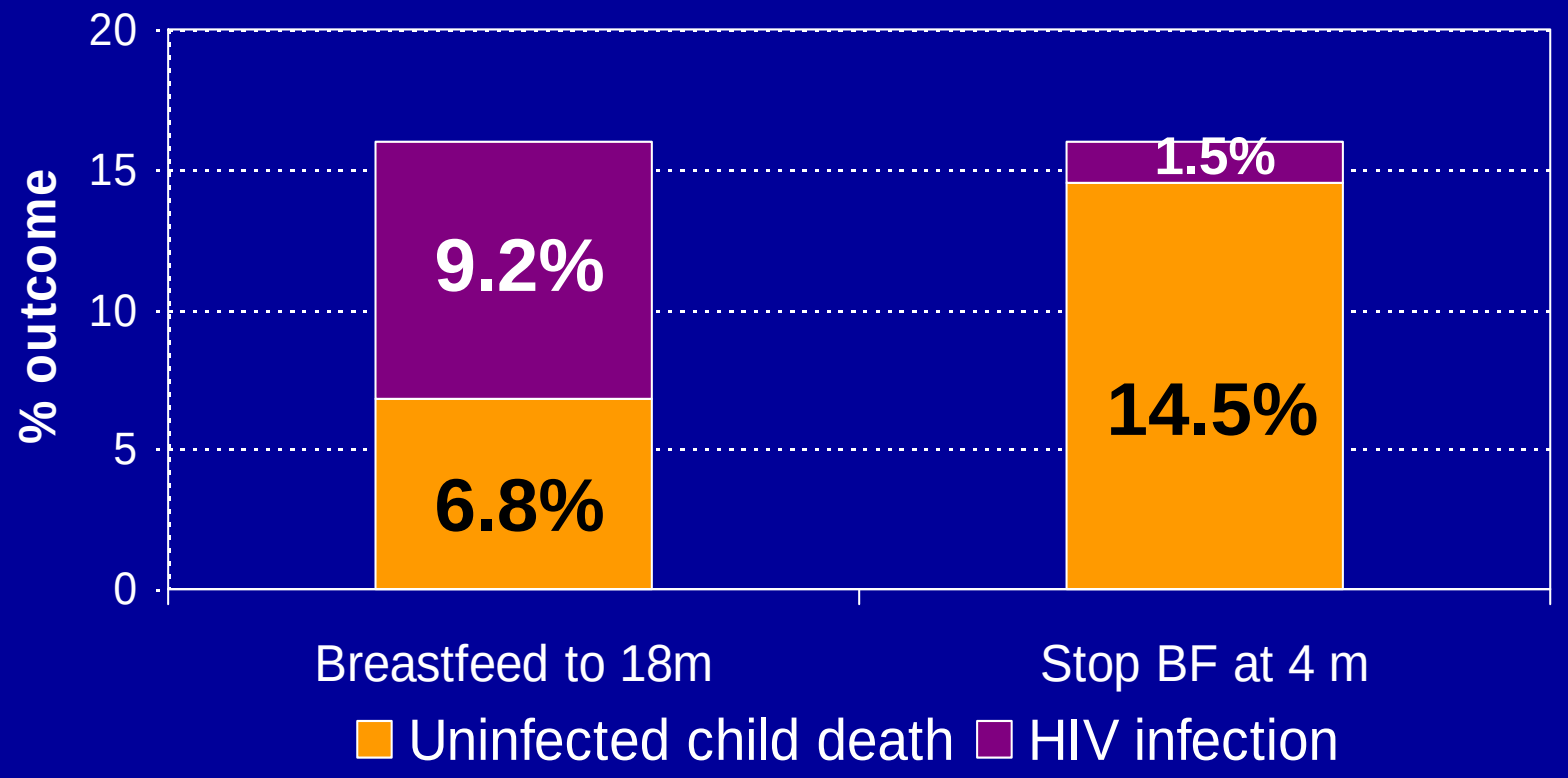
Kagaayi J, Gray RH, Brahmbhatt H. et al. **PLoS ONE** 2008; Dec 3: e3877

Why did ZEBS find no benefit for HIV-free survival of stopping breastfeeding early?



Kuhn L, Aldrovandi G, Sinkala M, et al. ***New England Journal of Medicine*** 2008; 359:130-41

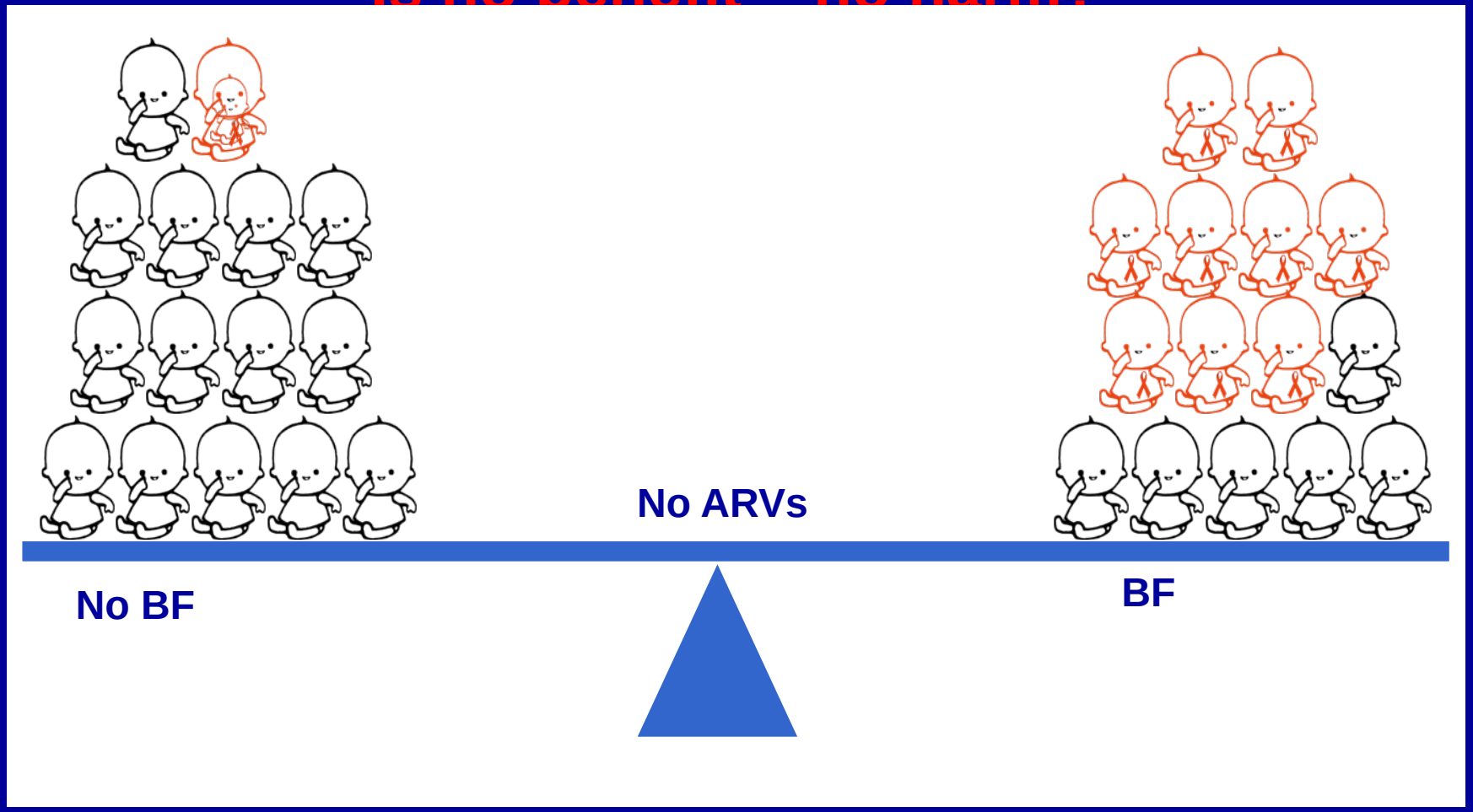
Mortality caused canceled out HIV transmission prevented



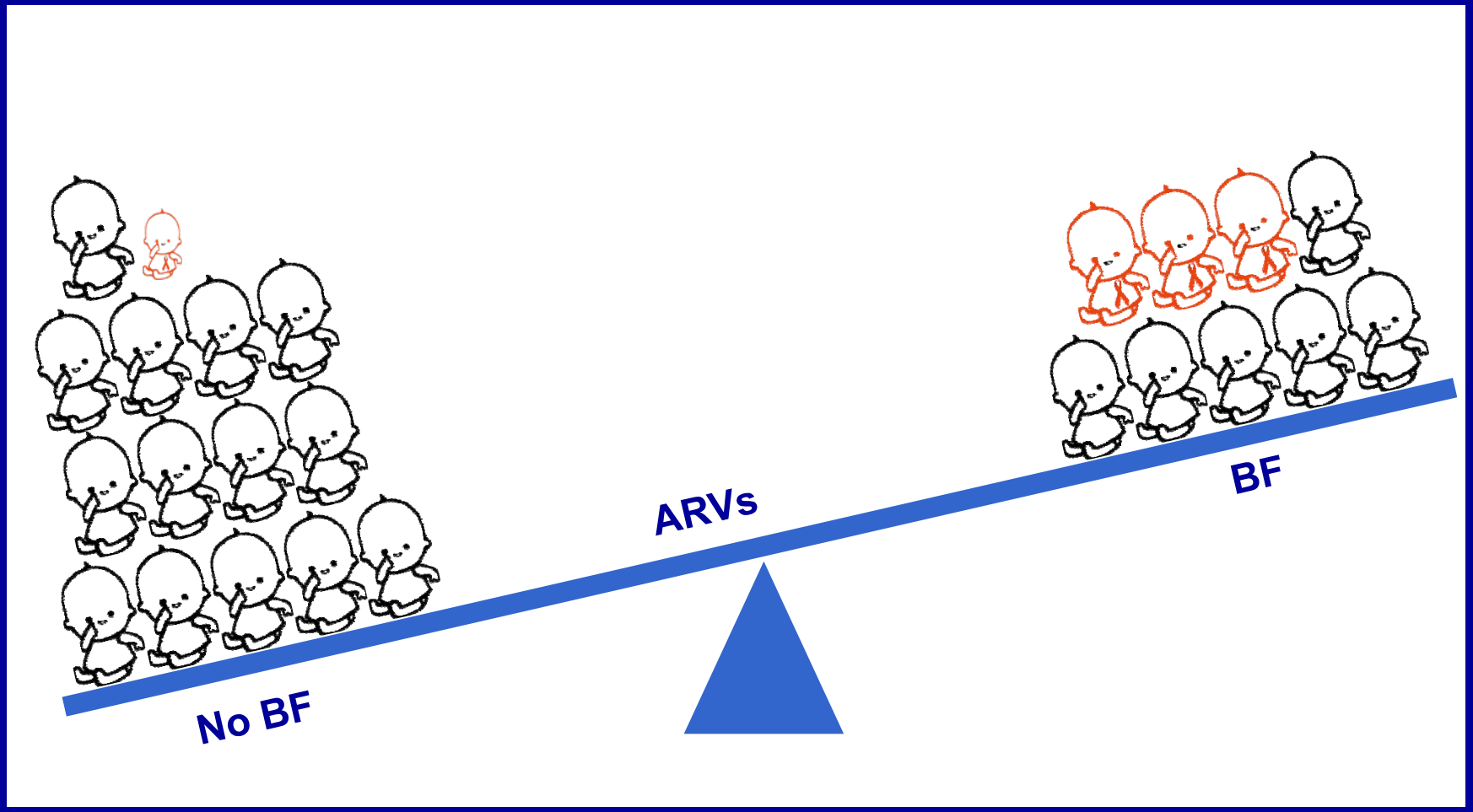
Kuhn L, Aldrovandi G, Sinkala M et al. ***PLoS One*** 2009; June 4: e6059

When no effective antiretroviral drugs, abstinence from BF may result in equivalent outcomes

Is no benefit = no harm?



With effective antiretroviral drugs, abstinence from BF results in worse outcomes



Importance of data on infant and young child mortality

- Intended and unintended reductions in breastfeeding increase mortality
- Focus only on HIV transmission can lead to erroneous conclusions of benefit when there is harm
- Focus only on HIV transmission can under-estimate benefits of interventions

Conclusion

- Mortality needs to be considered either combined with HIV transmission (HIV-free survival) or as an independent outcome