



Prevention of Mother to Child Transmission (MTCT) of HIV

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Overview

- The three-pronged strategy for the prevention of MTCT of HIV
- Recommendations on the use of antiretroviral drugs for the prevention of MTCT
- Recommendations on HIV and infant feeding
- Recommendations on MTCT research
- Activities Department RHR on MTCT



Estimated Rates of HIV Transmission

Breastfeeding 18m - 24m	Breastfeeding 6m	No breastfeeding	
5 to 10	5 to 10	5 to 10	During pregnancy
10 to 20	10 to 20	10 to 20	During labour
			Through breastfeeding
5 to 10	5 to 10		First 2m
5 to 10	1 to 5		After 2m
30 to 40	25 to 35	15 to 30	Overall



Three Integrated Strategies to Reduce Paediatric AIDS



Prevention of
unwanted
pregnancies



Prevention of
Mother to Child
Transmission
(PMTCT)

- . during late pregnancy
- . during labor
- . through breast-feeding



Primary
HIV
prevention in
parents to be



MTCT-Prevention Intervention

- Identification of HIV-positive women (Voluntary Counselling and Testing)
- Provision of antiretroviral regimens
- Counselling on infant feeding options
- Care and support
 - Psychosocial support to mother (and family)
 - Treatment of opportunistic infections
 - (*Access to antiretroviral drugs for treatment*)
- Support for HIV-negative women and their partners

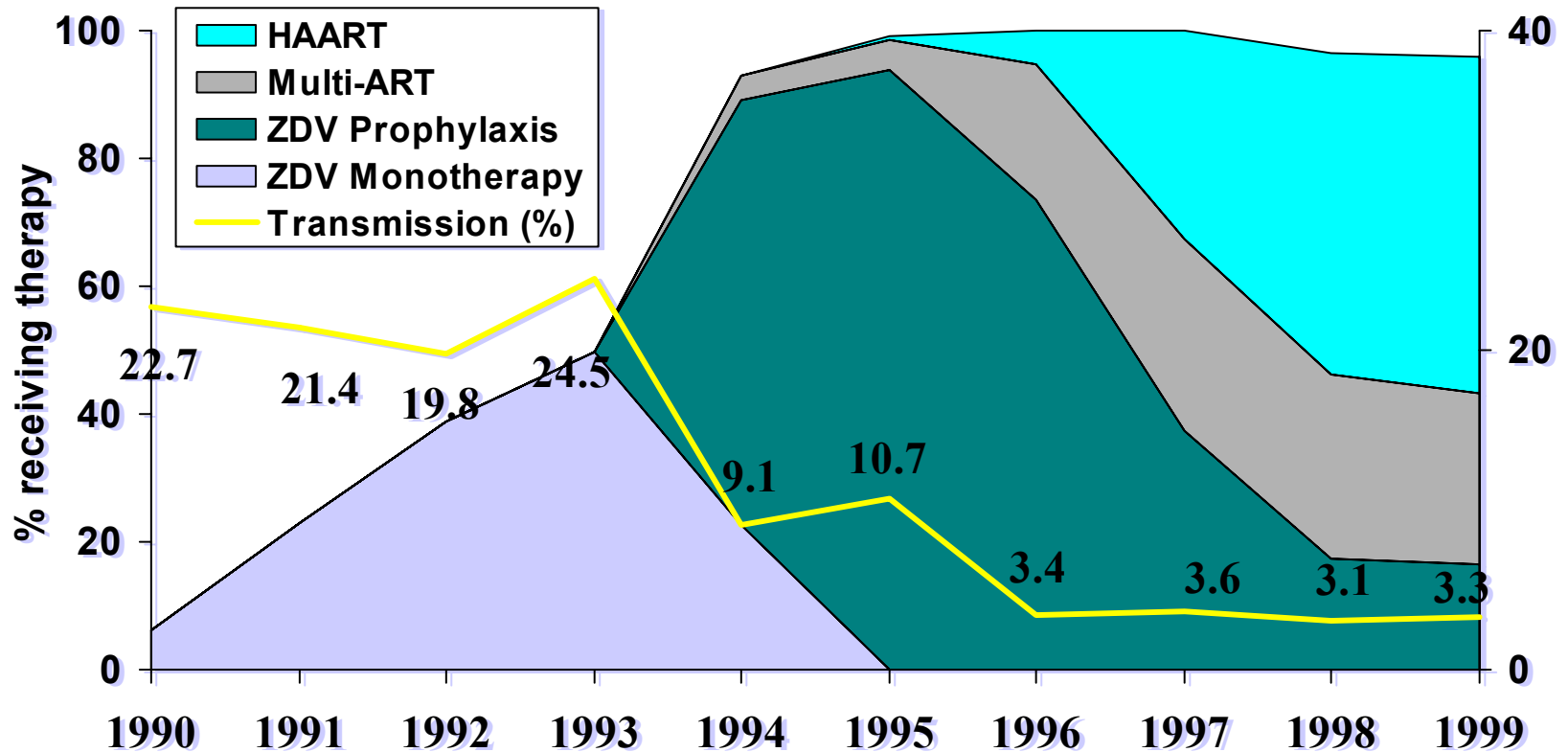


Interventions Known to Reduce HIV Transmission of HIV

- Use of antiretroviral regimens during pregnancy, delivery and/or postnatally
- Elective Caesarean section
- Replacement feeding



ARV Use and HIV Transmission (WITS, USA)



Source: Blattner, Durban 2000, LbOr4



Proven ARV Regimens

- 1994: PACTG 076
 - Intensive ZDV regimen: 68% reduction in risk
 - Impractical in developing countries
 - Superseded by combination therapies for mother
- 1998 CDC Thai regimen
 - Short course ZDV (from 36 wks): 50% reduction
 - “Standard” in resource-limited settings
 - Also effective in breast feeding populations (37% reduction in risk)



Proven ARV Regimens

- 1999: PETRA Study
 - Combination ZDV + 3TC
 - Arm A (36w + 1 w postnatal) 54% reduction in risk
 - Arm B (Labour + 1 w postnatal) 39% reduction in risk
- 1999 HIVNET 012
 - Nevirapine (1x mother & 1x infant) 48% reduction in risk
- 2000: SAINT Study
 - PETRA Arm B 10% transmission
 - Nevirapine 13% transmission



Proven ARV Regimens

- Perinatal HIV-Prevention Trial Thailand
- ZDV only, non-breastfeeding population
 - Long - long (28w mother, 6w infant) 7% transmission
 - Long - short (28w mother, 3d infant) 6% transmission
 - Short - long (35w mother, 6w infant) 8% transmission
 - Short - short (35w mother, 3d infant) 11% transmission

Source: Lallemand, *NEJM* 2000



WHO Recommendation on ARV Regimens (October 2000)

- ARV regimens starting early in pregnancy more effective than those starting in late pregnancy or during labour
- Available data demonstrate safety of short course regimens
- Some concerns about mitochondrial disease in infants exposed to ZDV or ZDV+3TC
- Benefits outweigh risks



Drug Resistance

- NVP-resistance observed in 20-25% mothers
- Spread of resistant virus in population?
 - Unlikely since replicating virus reverts to dominance of wild type once selective pressure of NVP removed
- Disease progression?
 - Unlikely (for reasons above)
- Efficacy of NVP in subsequent pregnancy?
 - Unlikely (as above), of less public health importance
- Impact on future treatment options?



WHO Recommendation on ARV Regimens (October 2000)

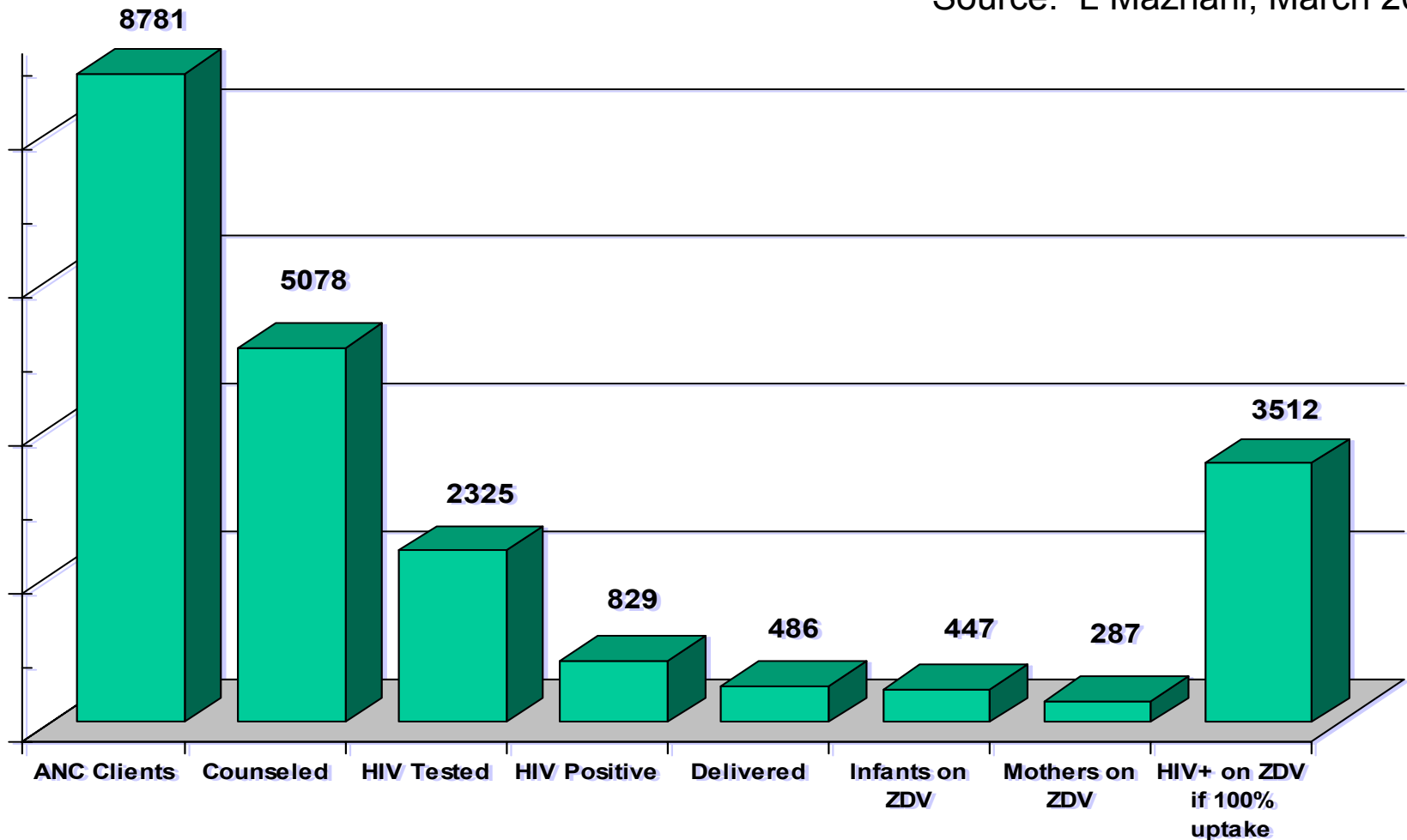
- The benefits of decreasing MTCT of HIV greatly outweigh concerns related to development of drug resistance
- The choice of ARV regimen should be determined according to local circumstances on the grounds of costs and practicality, particularly as related to the availability and quality of antenatal care.



Cascade of HIV+ Mothers

Botswana (April 1999 - February 2000)

Source: L Mazhani, March 2000





Universal Nevirapine ?

- Calls for systematic use of Nevirapine to all pregnant mothers in areas of high HIV prevalence
- Major cost and difficulty in providing voluntary counselling and testing in antenatal care
- Could reach much larger numbers of infected women and ultimately save more infants from HIV infection



Universal Nevirapine ?

- Pro

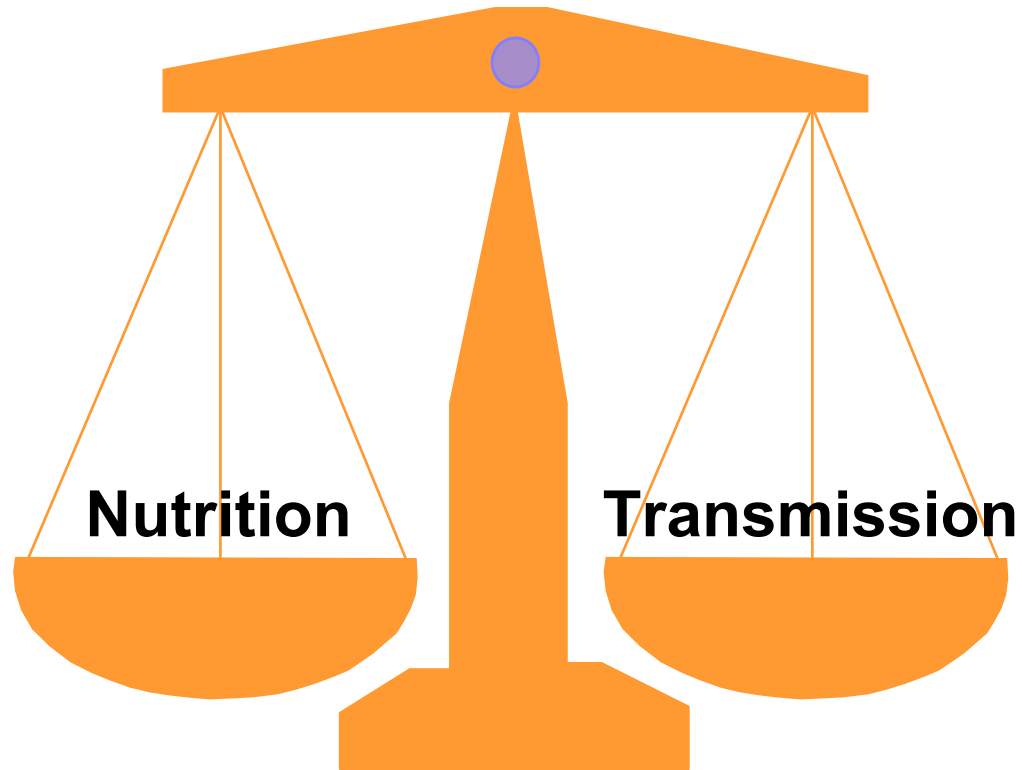
- Coverage
- Cost
- Ethical to insist on VCT (Voluntary Counselling and Testing) before NVP?
- HIV emergency requires special measures

- Against

- Objective is not just to prevent intrapartum transmission
- Even in high prevalence areas, majority are not infected with HIV. Will miss opportunity for primary prevention
- Cannot make best infant feeding choice
- May undermine VCT services
- Greater chance to see rare side effects



Breastfeeding and HIV Transmission





The Dilemma Remains

- Without breastfeeding HIV transmission is reduced, but:
 - Increased infant mortality and morbidity?
 - Increased stigma?
 - Undermine BF promotion among HIV-negative and unknown HIV status?
- Exclusive breastfeeding
 - Lower transmission risk than mixed feeding? Feasible?
- Increased mortality in HIV (+) women who breastfeed?



Benefits of Breast Feeding in General Population

- Large body of literature demonstrating that breast is best and highlighting the increased morbidity and mortality associated with early use of breast milk substitutes
- Most research has combined exclusive and mixed breast feeding compared to not breast feeding when assessing outcomes
- Exclusive breast feeding is rare across cultures

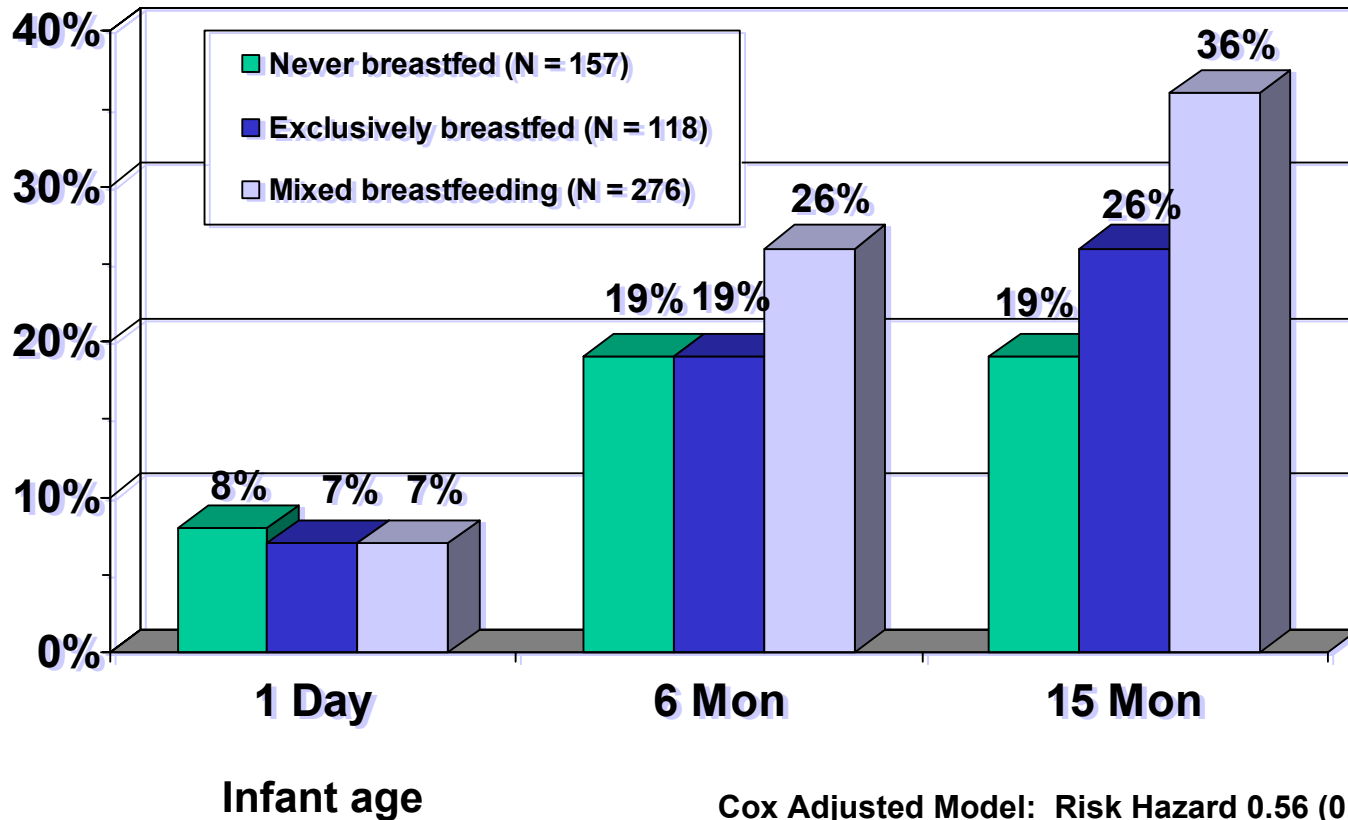


Clinical Risk Factors for HIV Transmission Through Breastfeeding

- Younger maternal age
- Lower parity
- Seroconversion during lactation
- Duration of breastfeeding
- Clinical and subclinical mastitis, breast abscesses
- Possible protective effect of exclusive breastfeeding through 3 months of age



Method of Infant Feeding and HIV Transmission in Breastfed Children



Cox Adjusted Model: Risk Hazard 0.56 (0.22-1.42)

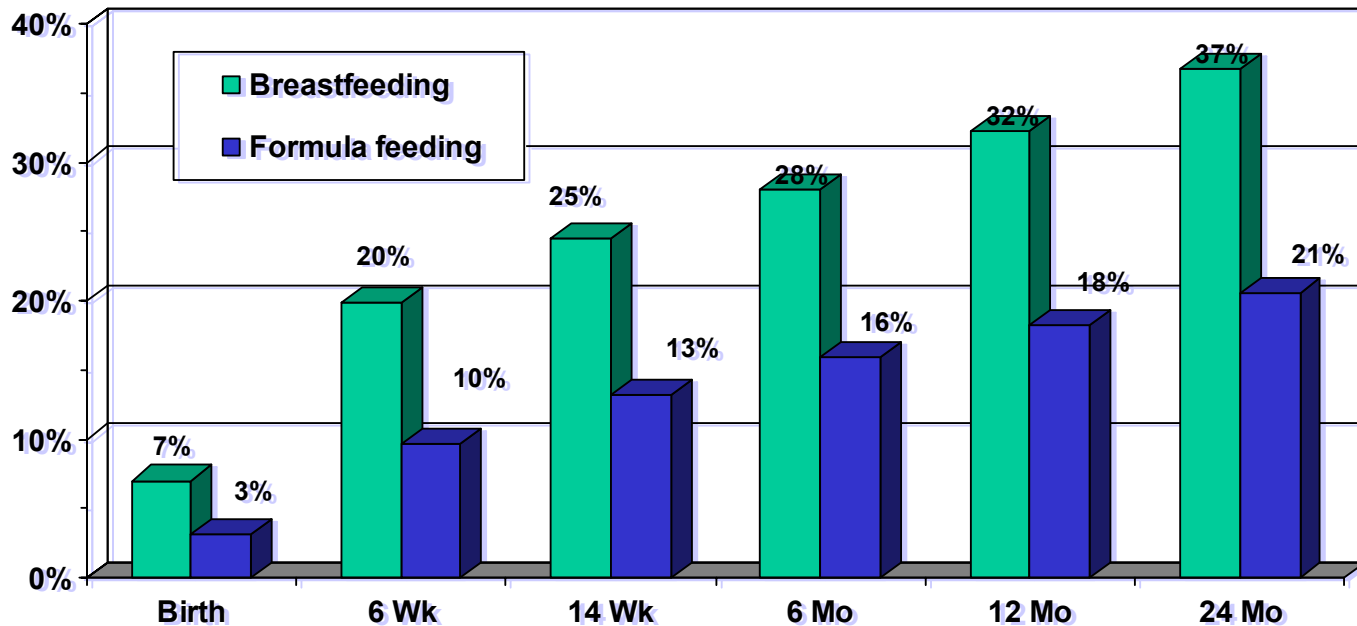
Coutsoudis A. XIII AIDS Conf, July 2000, Durban S Africa (LbOr6)



Nairobi RCT

Breastfeeding vs. Formula Feeding

Cumulative HIV Infection Rates



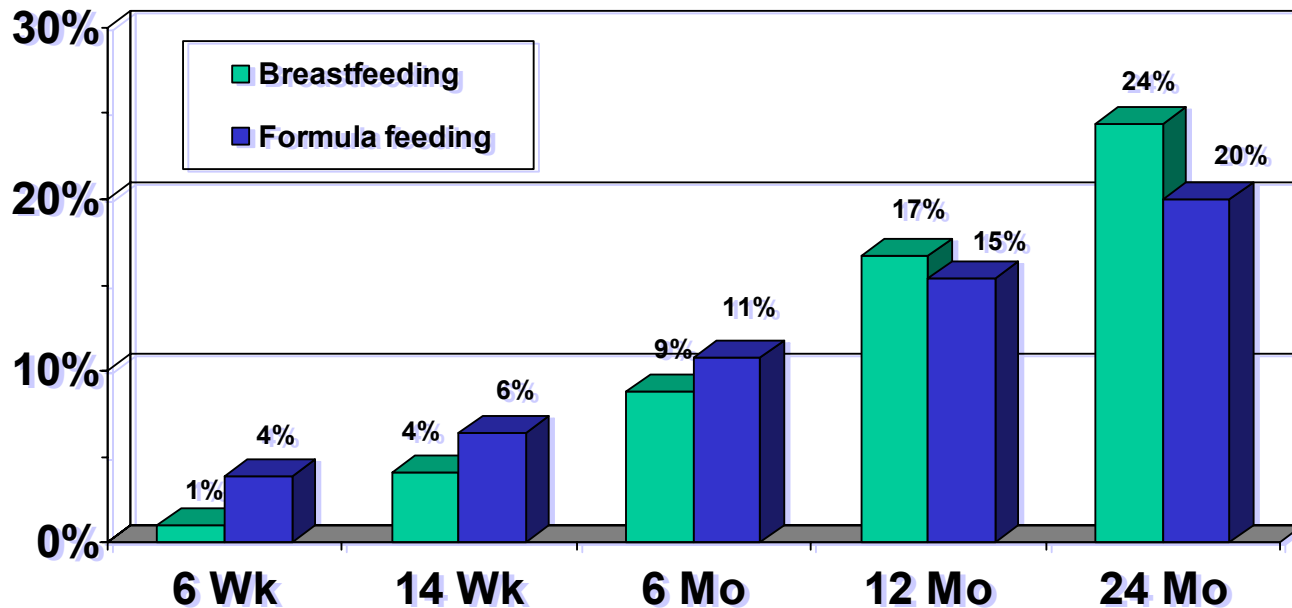
Nduati *et al*, *JAMA* 2000; 283:1167-74



Nairobi RCT

Breastfeeding vs. Formula Feeding

Cumulative Mortality Rates in Infants



Nduati *et al*, *JAMA* 2000; 283:1167-74



HIV and infant feeding

- October 2000: clarification of existing 1998 recommendations
 - Replacement feeding recommended when acceptable, feasible, affordable, sustainable and safe
 - There is a need to guide mother in choice in selecting the option most likely to suitable for her situation



HIV and infant feeding

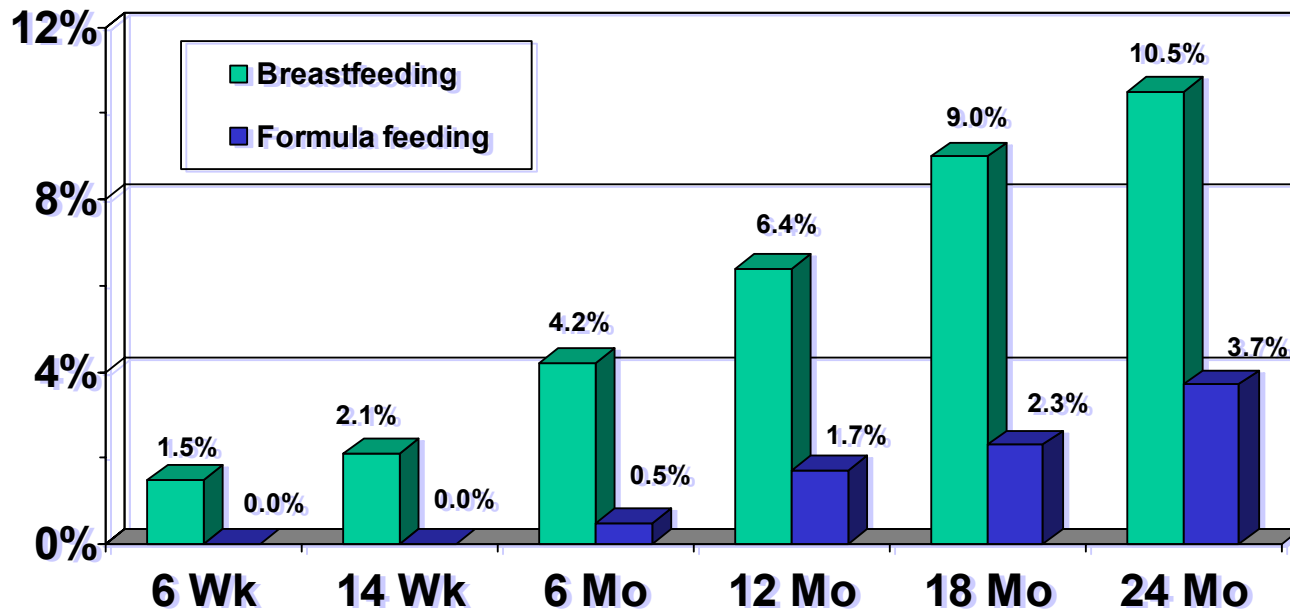
- If mother chooses to breastfeed, exclusive breastfeeding is recommended for the first months of life, and should be discontinued when an alternative form of feeding becomes feasible
- The mother should be supported in her choice



Nairobi RCT

Breastfeeding vs. Formula Feeding

Cumulative Mortality Rates in Mothers



R risk of death: 3.2 (1.3 - 8.1), P = 0.01

Nduati *et al*, *Lancet* 2001; 357: 1651-55



RHR Activities in MTCT Prevention

- HIV and infant feeding
 - Tool to standardise assessment of infant feeding patterns in the context of MTCT
 - Inventory of ongoing/planned studies in infant feeding and MTCT
 - Sponsoring individual case meta-analysis of mortality among HIV-infected mothers who breastfeed
 - Exploring other sources of relevant data



MTCT Prevention - The Future

- Access to ARV treatments rapidly accelerating
- MTCT-prevention as entry point to therapy
 - Will increase acceptability and uptake
 - Resolves ethical dilemma of giving prophylaxis for infant yet nothing for mother or father
- How best to provide ART?
 - Safety and effectiveness of MTCT and ART
 - Will ART reduce breast feeding transmission risk sufficiently?



References and Sources

- General information on the HIV epidemic and country reports
 - www.unaids.org
- Mother to Child Transmission of HIV
 - UNAIDS
 - www.unaids.org/publications/documents/mtct/index.html
 - Department of Reproductive Health and Research
 - www.who.int/reproductive-health/rtis/MTCT/index.htm