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Outline of presentation

- Will present assumptions around breastfeeding and HIV transmission and for each assumption will consider what facts there are available to either justify, refute or qualify the assumption
- We will consider what research questions still need to be answered to allow us to examine some of the assumptions more carefully



Breastmilk of HIV infected women contains HIV virus and breastfeeding is therefore dangerous for infants of HIV infected women –

therefore no HIV infected women should breastfeed



Breastfeeding by HIV infected women does carry a risk for HIV transmission but the risk depends on many factors

Facts:

- In 1992 based on results from studies with very unequal numbers of breastfed and formula fed babies and with ELISA measurements at 18-24 months, Dunn et al estimated the additional risk of MTCT of HIV was 14% (CI: 7-22%) – no qualification of when tx occured
- Recently 2 large studies (Kenya, South Africa) with over 100 breastfed and 100 formula fed infants and with frequent PCR testing confirmed finding but showed it was a cumulative risk over 24 months not a one off risk.
- It was also clear from these studies that the risk was associated with mixed breastfeeding

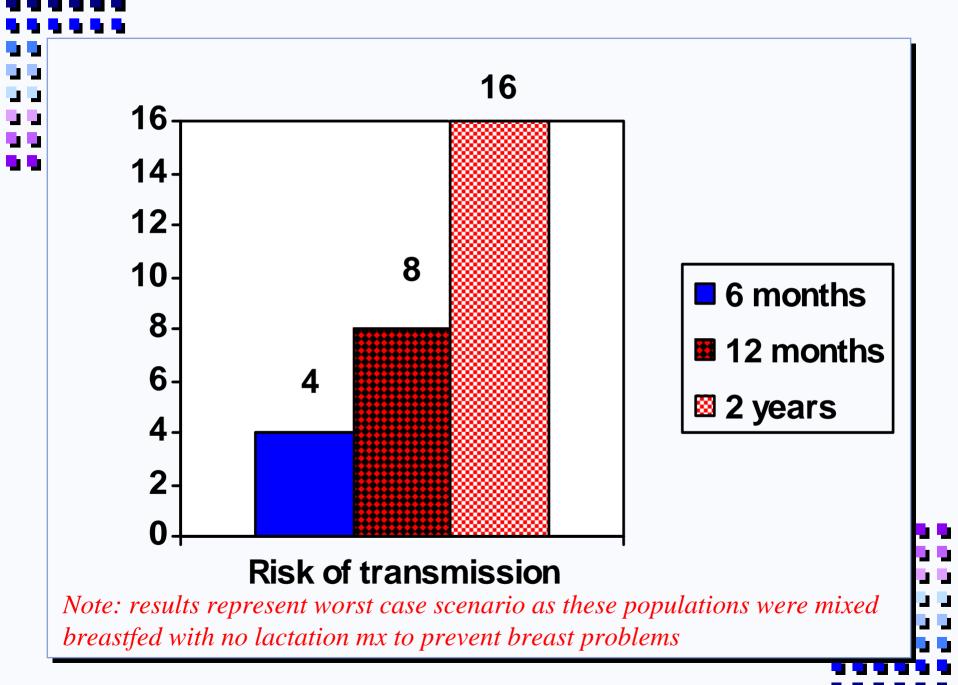
Breastfeeding and HIV International Transmission Study – BHITS

- 3442 children uninfected at 4 weeks of age, of whom 231 became infected
- Estimated rate of BF transmission was 8.0 per 100 child-years of breastfeeding = 0.74%/mth of BF ie 6 months of breastfeeding carries a risk of about 4-5%

Transmission and duration of BF – BHITS

Risk was <u>roughly constant over 24</u> <u>months</u>

 Transmission related to nonexclusive breastfeeding (mixed breastfeeding)





What is the risk if women practiced exclusive breastfeeding for at least 3 months

Risk of HIV infection over time in 157 children never breastfed; 118 EBF; and 276 mixed breastfeeders **40 35 30 25 ■** Never brf **20 Excl brf 15** Mixed Brf **10 Birth** 6 Mths 12 mths 15 mths Durban, South Africa



- ·Breast health
- GI factors

Immune factors

Facts:

Apart from mixed breastfeeding and prolonged durations of breastfeeding what other factors make breastfeeding risky for HIV transmission?

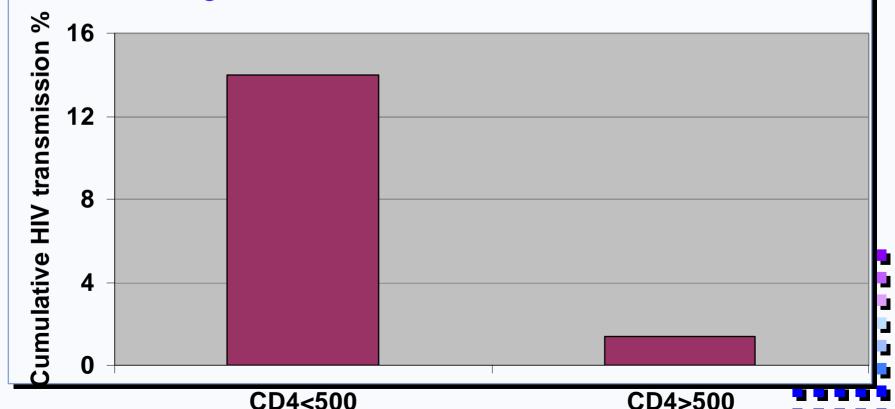


Current understanding of risk factors

- Prolonged breastfeeding
- Mixed breastfeeding
- High plasma viral load, low CD4

Risk factors for postnatal transmission: Maternal immune status

HIV transmission from 6w-24mths in W.Africa by maternal baseline CD4 count





- Prolonged breastfeeding
- Mixed breastfeeding
- High plasma viral load, low CD4
- Seroconversion during lactation
- Mastitis
- Cracked bleeding nipples, abscesses
- Sub-clinical mastitis (raised Na/K ratio)
- High viral load in breastmilk
- Oral thrush in infant



By reducing/eliminating these risk factors breastfeeding can be made safer



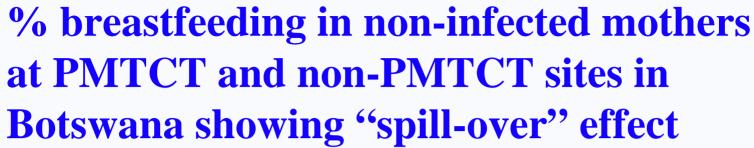
- Exclusive breastfeeding up to 6 mths
- Shorter duration 6 months??
- Encourage condom use during lactation period
- Good lactation management (attachment, positioning) to avoid mastitis

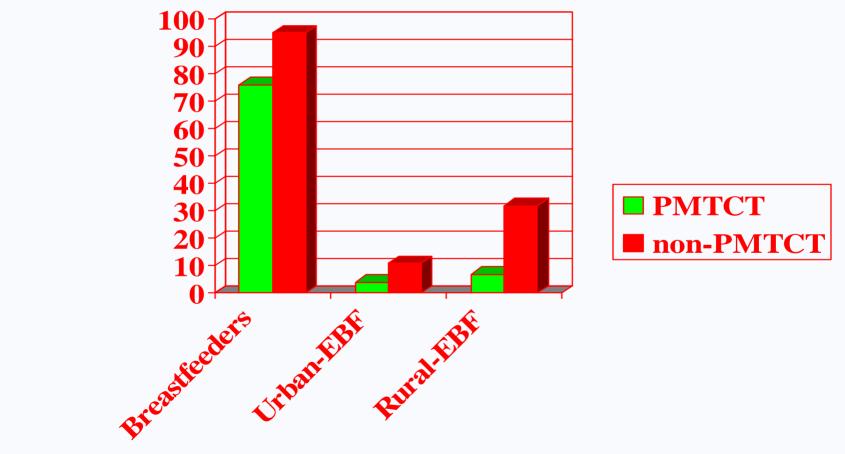


- No feeding from breast with cracked bleeding nipples or abscesses (express milk from affected side and continue feeding from unaffected side)
- Prompt treatment of oral thrush
- Heat treatment of expressed breastmilk
- Anti-retrovirals to infant during breastfeeding period

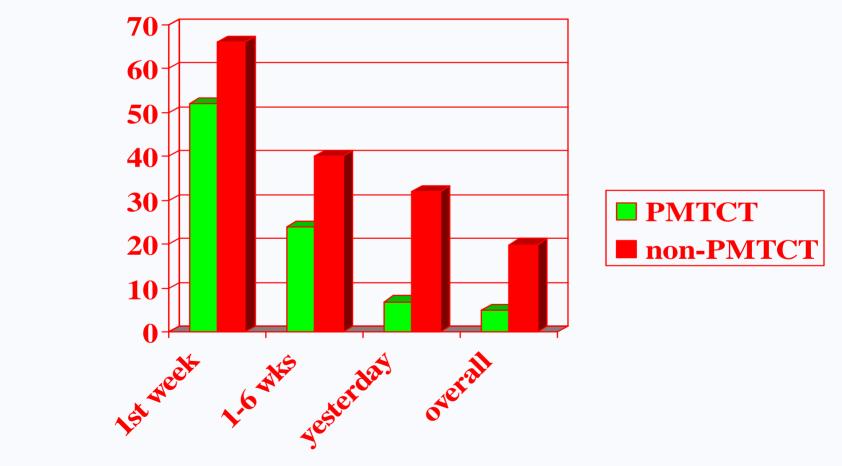
To ensure exclusive breastfeeding occurs – health workers need to be committed to improving breastfeeding practices.

This is only possible if free formula is not distributed and effort is put into promoting BFHI and good breastfeeding practices.





% Exclusive Breastfeeding in uninfected mothers at PMTCT and non-PMTCT sites in Botswana showing "spill-over" effect



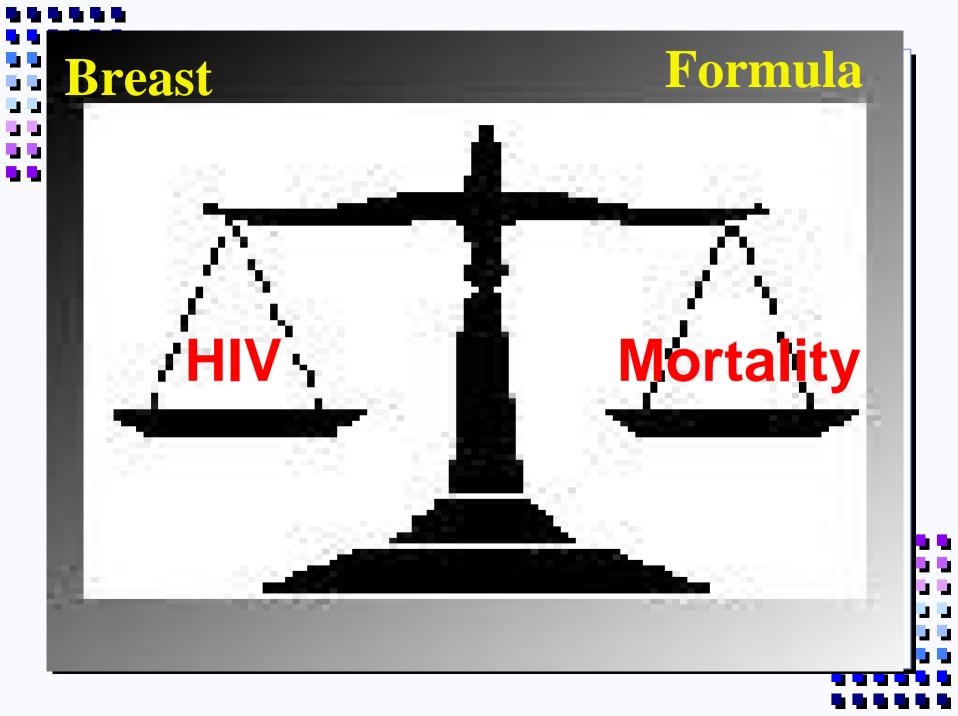
Assumption:

 Because of the risk of HIV transmission through breastfeeding, all HIV infected women should replace breastfeeding (usually with formula feeding) – this implies that there is no risk associated with formula feeding

Facts:

There are risks associated with not breastfeeding and these will obviously vary according to different socio-economic conditions

We need to remember that a similar balance of risks is associated with mode of delivery - vaginal delivery carries more risk for HIV transmission however we don't automatically recommend c/s in resource poor settings because there are risks attached to this intervention similar scenario exists in terms of not breastfeeding - cannot simply recommend it because there are substantial risks associated with formula feeding



Risks: HIV Infection with brf

vs Mortality with avoidance of brf: *Global Figures*

Babies infected through 300 000 p.a breastfeeding (UNAIDS)

Mortality from 1 500 000 p.a. avoidance of breastfeeding (UNICEF)



what are the risks of not breastfeeding?



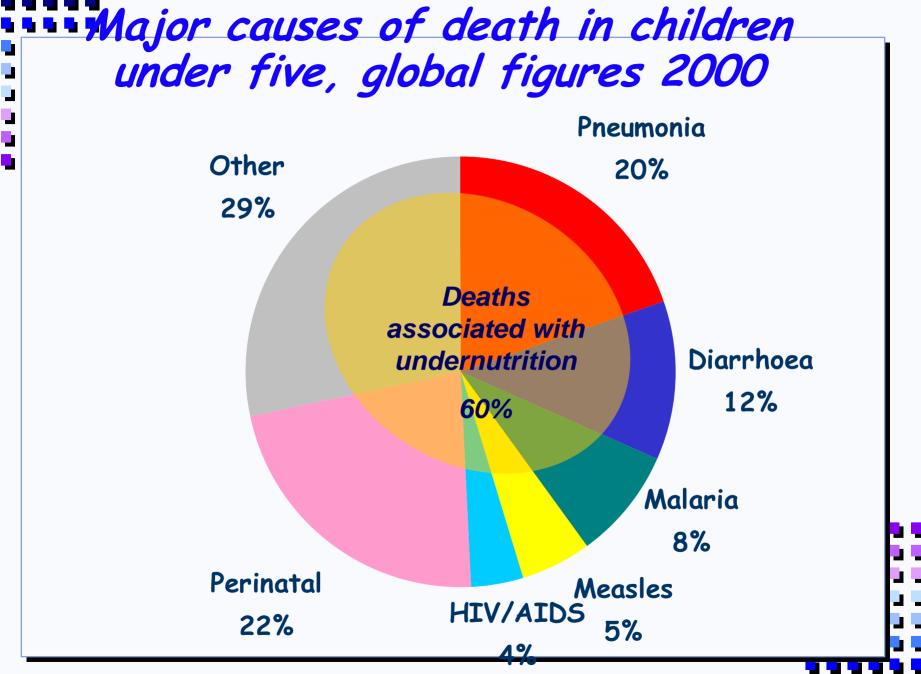
Not breastfeeding – results in loss of benefits of breastfeeding:

- 1. Optimum nutrition until 6 months
- 2. Protection from infectious diseases
- 3. Cognitive development
- 4. Bonding and psycho-social benefits
- 5. Delays maternal fertility
- 6. Decreased maternal ovarian and breast cancer

Economic Benefits of Breastfeeding in USA

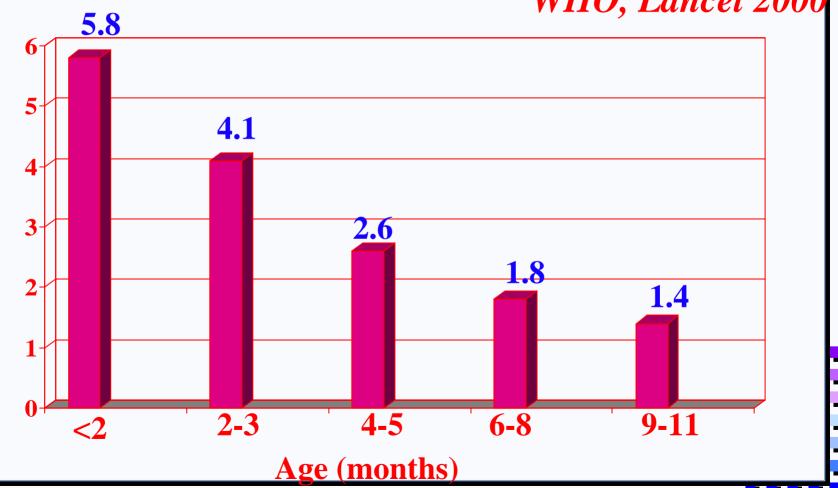
\$3.6 billions could be saved from the Rx of OM, GE, and NEC by merely increasing breastfeeding rates from the current 29% (at 6 mths) to 50%.

Nutrition Research Report no.13 March 2001, Jon Weimer, USDA

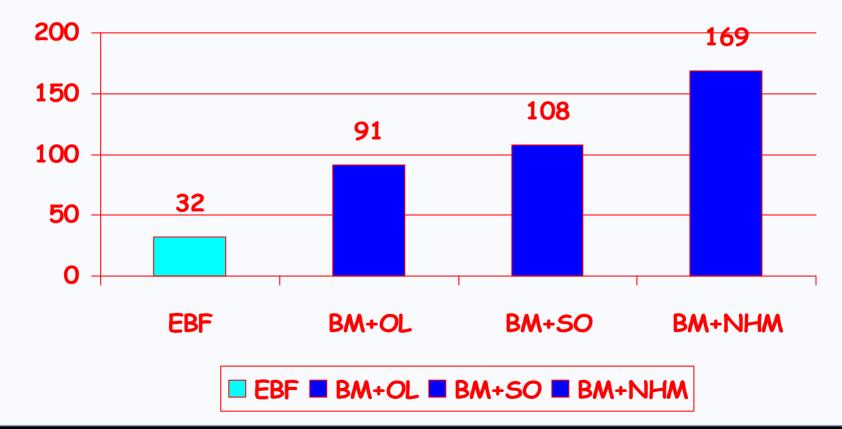


Not breastfeeding increases mortality

RR of infectious disease mortality among non-breastfed infants WHO, Lancet 2000

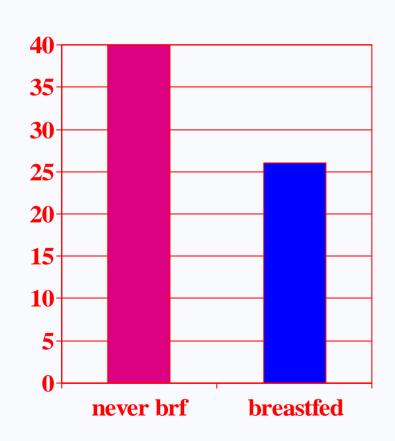


Increasing levels of replacement of breastmilk in the first 3 months is associated with increasing risk of mortality in Zimbabwean study of HIV infected women



Adjusted HR for BM+NHM (non-human milk) vs EBF = 4.5

Not breastfeeding in the first 2 months significantly increases morbidity in infants born to HIV infected women *Durban VITA/breastfeeding study*



% of infants who had an illness episode in the first 2 months

Coutsoudis et al. in press, Acta Paediatr, Aug 2003.

Even early cessation of breasfeeding has been associated with increased morbidity Zambia Exclusive Breastfeeding Study

(personal communication, L Kuhn not to be quoted)

Infants randomised to:

EBF for 4 mths and then rapid weaning or

EBF for 4 months and gradual weaning:

Early results:

Infants in group that was rapidly weaned had:

- increased diarrhoea and ARI
- significant growth failure

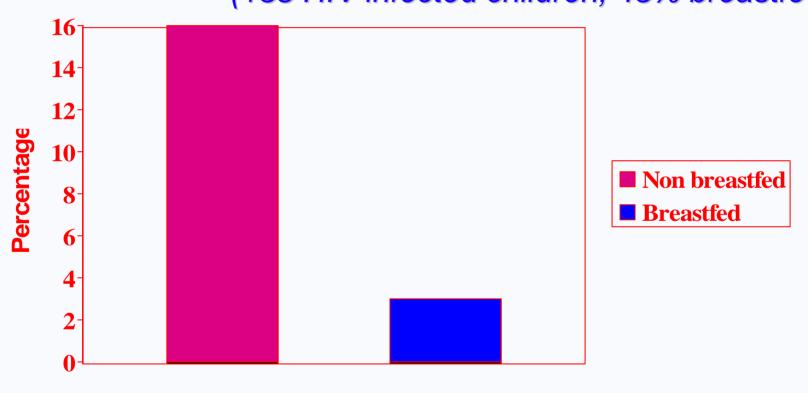
Assumption:

 Decisions on replacement feeding, only need to be made for the negative HIV infants – what about those born HIV positive – an assumption is made that they should be fed with formula milk Facts:

The number of children born HIV infected in resource poor settings is about 20% and in those resource poor settings which have instituted the nevirapine regimen to reduce PMTCT this % will drop to about 12% - still a substantial number worth considering before subjecting them to the risks of formula feeding.

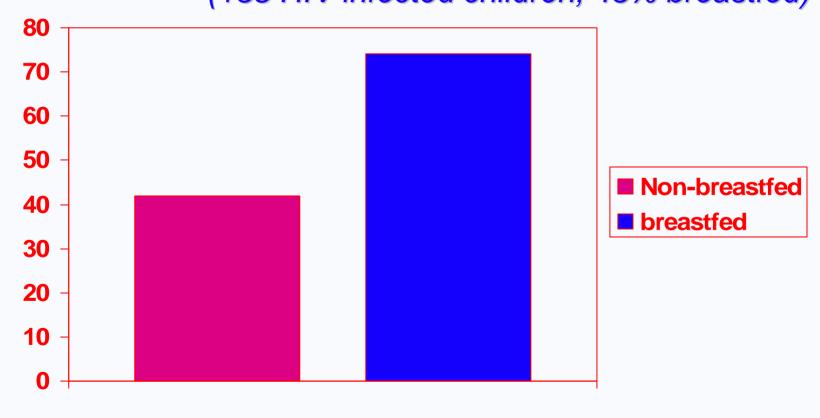
HIV infected children who were not breastfed had significantly more recurrent diarrhoea

Frederick et al, Los Angeles Study 1997 (138 HIV infected children, 43% breastfed)



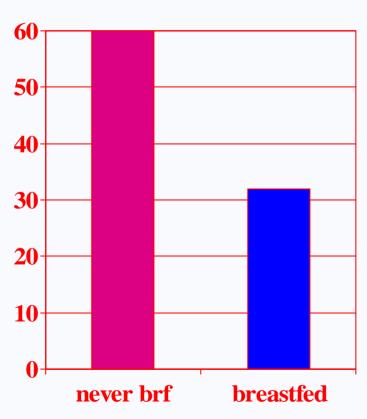
HIV infected children who were not breastfed progressed to AIDS more quickly

Frederick et al, Los Angeles Study 1997 (138 HIV infected children, 43% breastfed)



HIV infected children who were not breastfed had significantly more morbidity

*Durban breastfeeding study**



% of infants who had 3 or more morbidity episodes

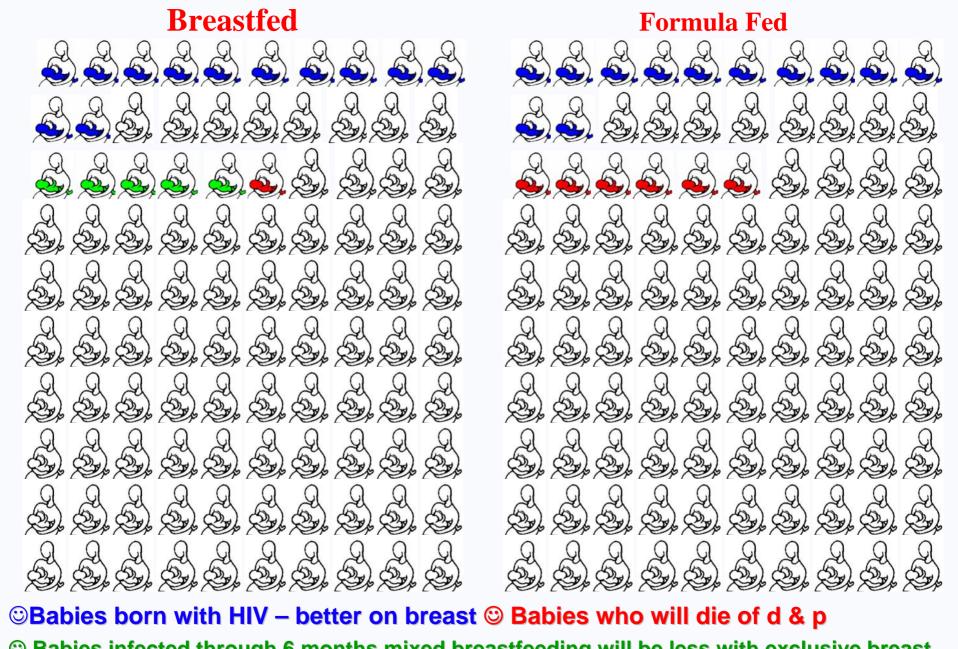
Coutsoudis et al. in press, Acta Paediatr, Aug 2003



There is a definite balance of risks which will depend on an individual woman's situation

Even with a low infant mortality rate of 40/1000 in breastfed populations like SA, about 1/100 would die of D&P and not breastfeeding, according to the WHO meta-analysis would push this up 6 fold ie 6/100 – so even at this low IMR, risk of formula feeding mortality = risk of HIV transmission thru' 6 months of mixed breastfeeding (5%)

Most countries in developing world have IMRs in excess (Malawi 132; Kenya 76)



Babies infected through 6 months mixed breastfeeding will be less with exclusive breast

For most babies 6 months of exclusive breastfeeding will be the best option

If you answer no to any of these questions, formula feeding may not be the best option

- •Do you have easy access to clean safe water
- Do you have easy facilities to boil water
- •Do you have facilities to sterilise bottles etc.
- •Do you have a fridge with regular electricity
- •Do you have a guaranteed income of R150/month to spend on formula, bottles, teats, sterilising fluid etc.
- •Does your family know your status & will they support you to formula feed
- •Will it be acceptable to give f/feeds at night or when baby is crying in public
- •Do you have easy access to clinic/hospital if child gets diarrhea



HIV infected women who breastfeed are at risk for increased mortality



This assumption is based on one study which has not been validated by a subsequent large meta-analysis

BF and Maternal death - BHITS

- Nairobi (Nduati): Relative risk of death for mothers assigned to BF vs. FF: 3.2 (p=0.01)
- SA (Coutsoudis): No significant difference
 - Mortality
 - » 0.49% (2/410) ever BF
 - » 1.92% (3/156) never BF
 - Morbidity similar between those who BF >3mths vs. those who did not (p>0.1)
- BHITS: 4237 mothers included CD4 associated with mortality but feeding modality only significantly associated with mortality at 12 months and in fact breastfeeding mothers had a lower risk of mortality than mothers who did not breastfeed

Some Research Questions that still remain unanswered

- What is the risk of HIV Tx at 12 and 24 mths if women practice "safe" breastfeeding including exclusive breastfeeding for 6 mths & then continue breastfeeding
- Impact of lactation Mx, nutritional interventions, and antibiotic Rx on clinical and sub-clinical mastitis and thus on Tx risk
- Effect of breastfeeding replacement on infant morbidity and mortality
- Effect of "rapid" and early cessation of breastfeeding
- Effect of breastfeeding on maternal health
- Effect of antiretrovirals to mum, infant or both on Tx

Current Research Underway

- Effect of different breastfeeding patterns on HIV Tx –
 SA, Cote D'Ivoire, Zimbabwe, Tanzania
- Diffs between rapid cessation of breastfeeding at 4 months compared to gradual weaning off breastmilk at about 2 years - *Tanzania*
- HIVNET 027 Safety trial of ALVAC (canary pox) vaccine vs placebo given orally to infants during breastfeeding period *Uganda*
- HIVNET 046 trial of nvp vs placebo given to infants during the first 6 months of breastfeeding *multi-site*
- CDC study trial of HAART to mum vs NVP to infant during breastfeeding period and effect of nutritional support - Malawi

- In 1992 based on results from studies with very unequal numbers of breastfed and formula fed babies and with ELISA measurements at 18-24 months, Dunn et al estimated the additional risk of MTCT of HIV was 14% (CI: 7-22%) – no qualification of when tx occured
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