Infant Feeding in the context of HIV: Revised WHO Principles and Recommendations 2010

Investing in maternal and child survival

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UNICEF/WHO/UNAIDS recommendations (2007) on HIV and infant feeding

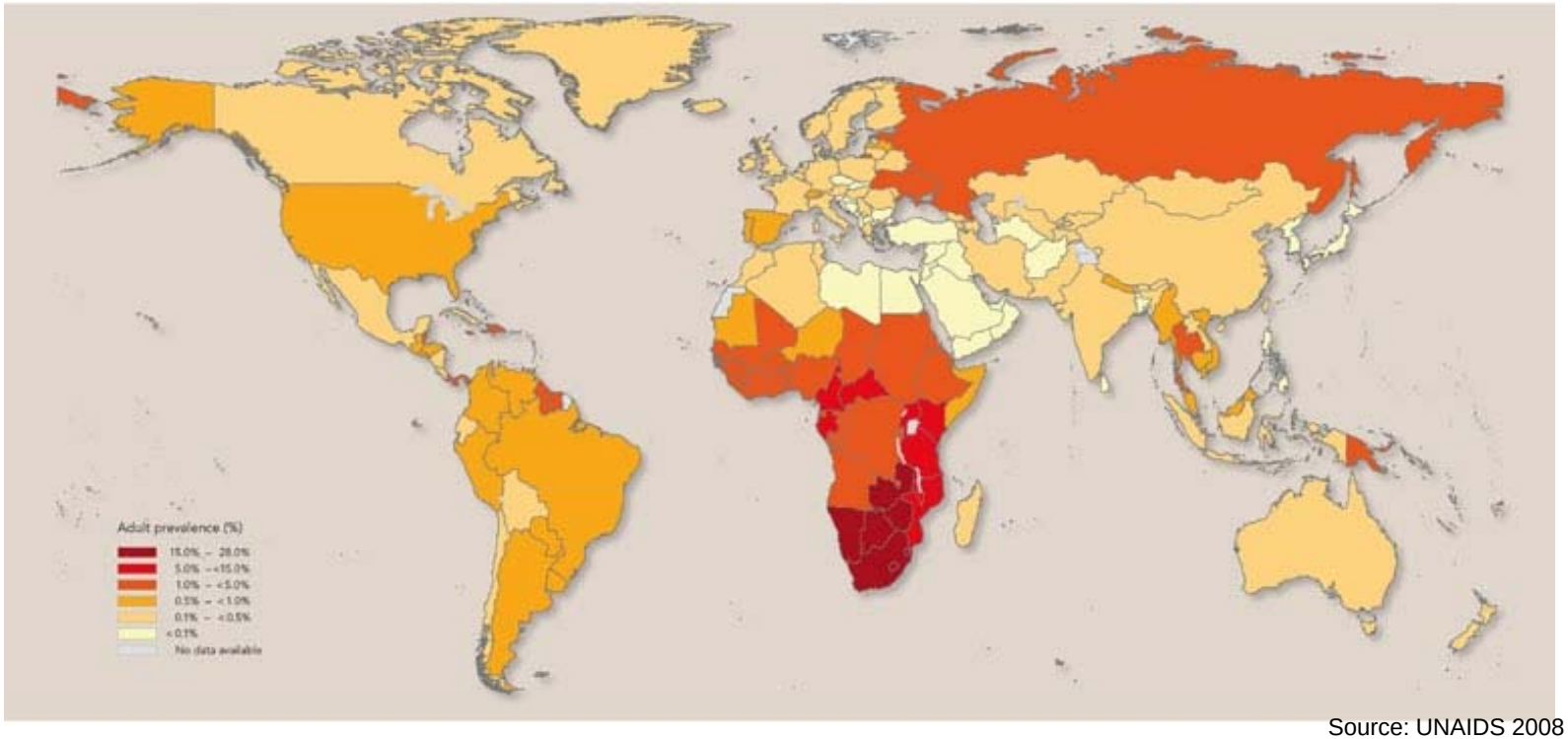
- Exclusive breastfeeding is recommended for HIV-infected mothers for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time.
- At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed

- **Rapid cessation of breastfeeding and modified cows milk as a replacement feed dropped as recommendations**

If prevention of mother-to-child transmission of HIV were the only priority then …

- Give all HIV-infected mothers antiretroviral drugs, and,
- Stop all breastfeeding

Geographical distribution of HIV burden, 2007

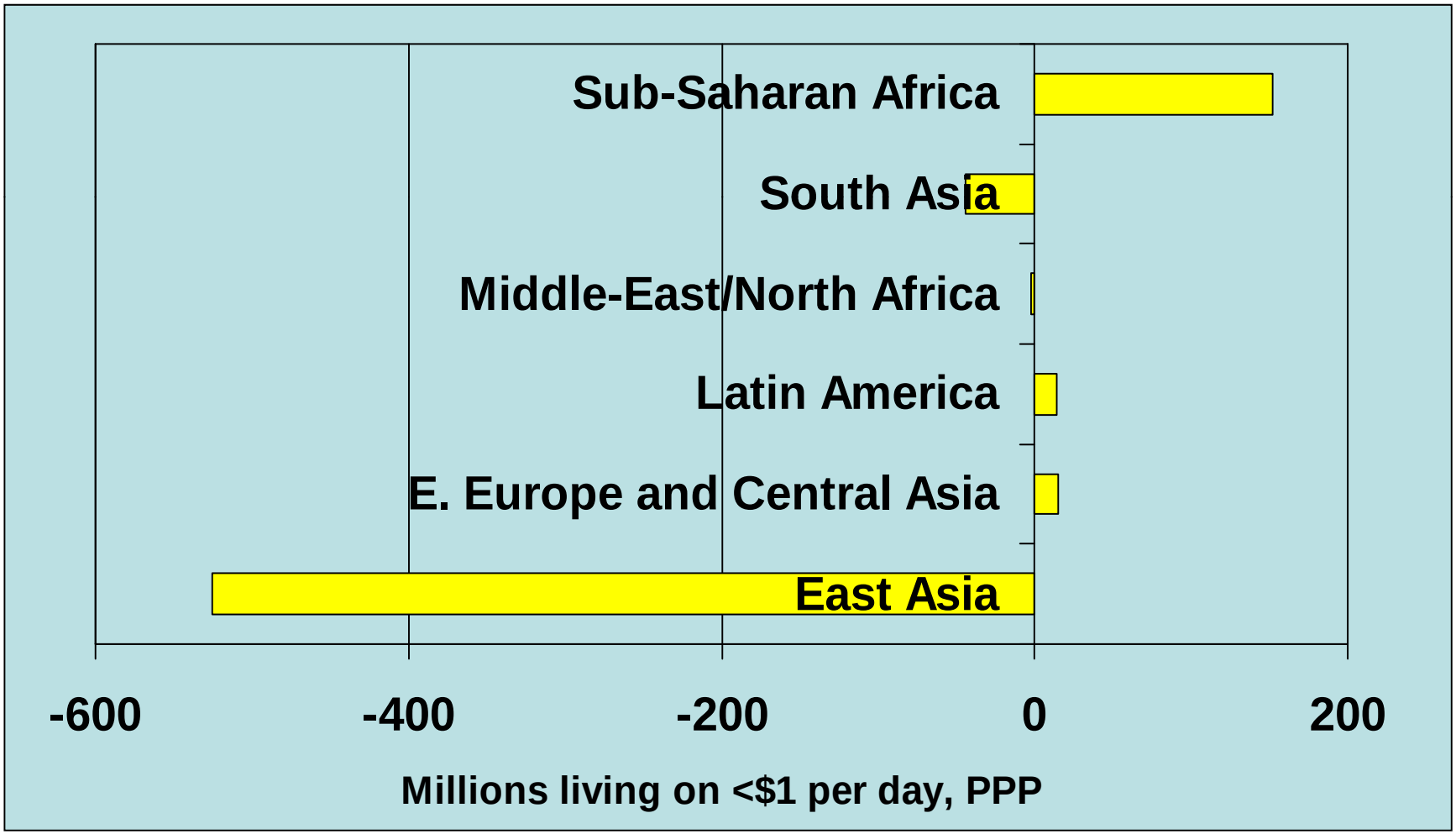


Source: UNAIDS 2008

- 19 of 20 countries with highest PMTCT burden are in sub-Saharan Africa
- 68 countries share 97% of global maternal and child deaths
- 12 reported an increase in child mortality rates between 1990 and 2006
  - All 12 in Africa
  - 8 high HIV prevalence countries
  - All have high or very high maternal mortality

Changes in World Poverty 1981-2001

73.7 million more people in SSA in poverty since 1987

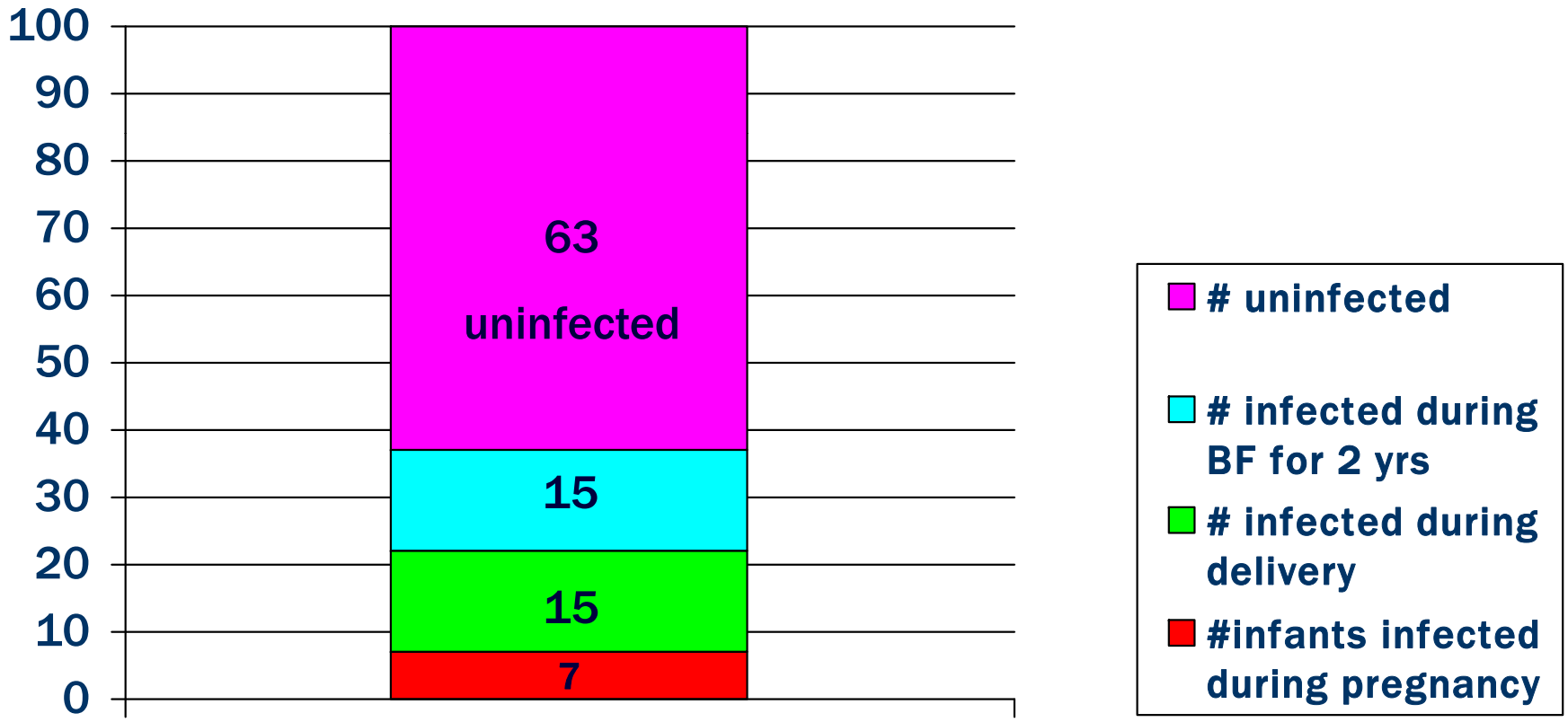


Chen and Ravallion 2004

UNDP. Human Development Report. 2006

- More than 1.1 billion people worldwide do not have access to clean water,
- 2.6 billion do not have adequate sanitation and
- Diarrhoea due to a lack of clean water kills five times more children than HIV/AIDS.
- the "..roots of the crisis in water can be traced to poverty, inequality, and unequal power relationships, as well as flawed water management policies …".

MTCT in 100 HIV+ mothers by timing of transmission



HIV free survival

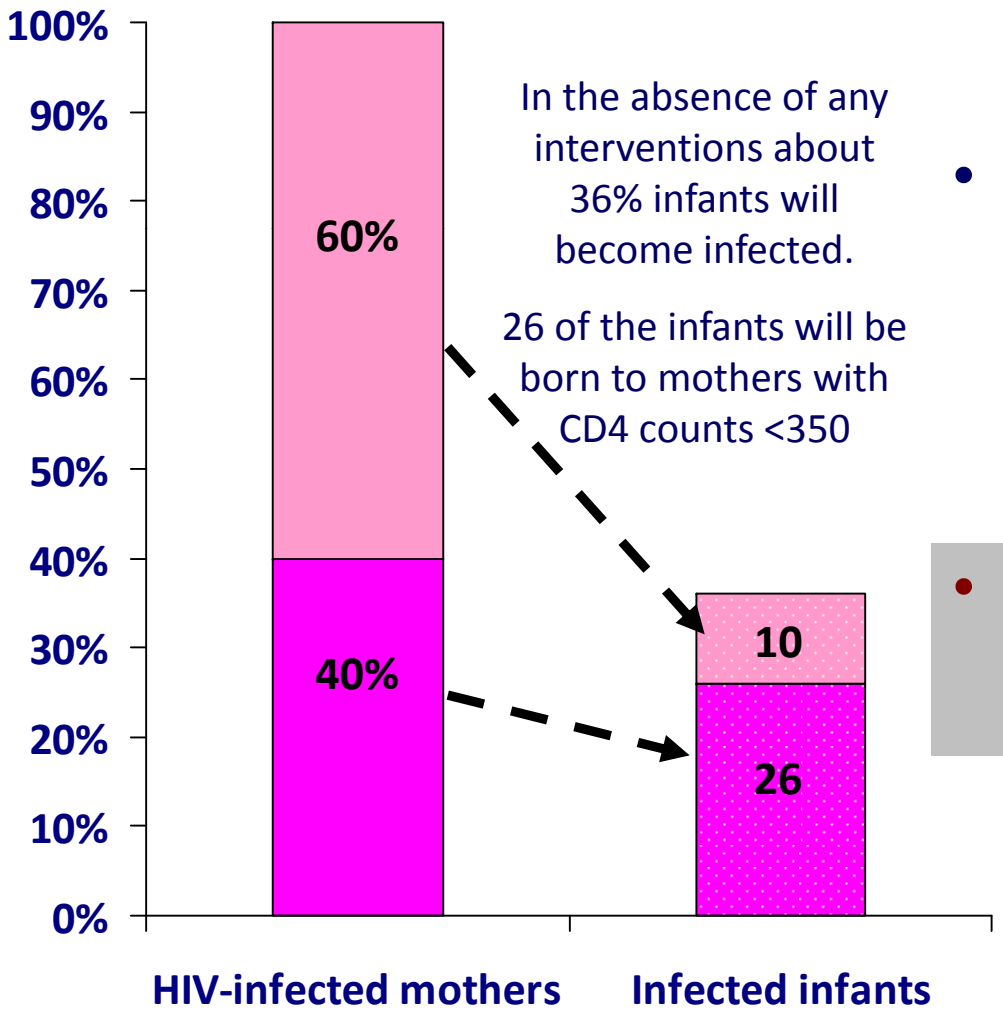
- To have children of mothers known to be HIV-infected survive while remaining HIV uninfected is the top priority

- The success of PMTCT activities , including cost-effectiveness, needs to be measured in terms of HIV-free survival and not just transmissions averted

HIV transmission through breastfeeding

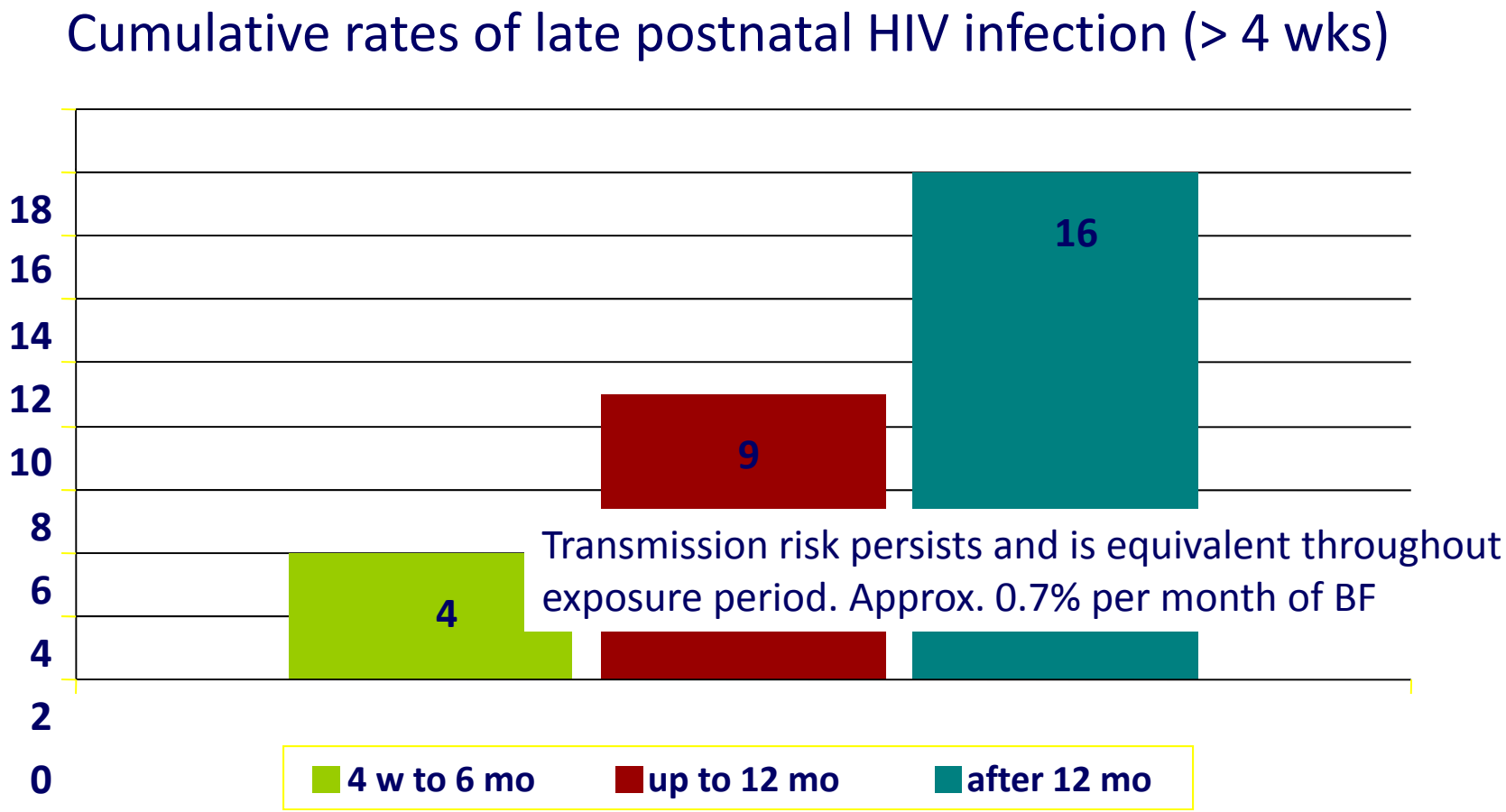
- Maternal health
- Duration of breastfeeding (vs. early cessation)
- Type of breastfeeding
- Breast health
  - Mastitis and subclinical mastitis
  - Cracked and/or bleeding nipples

Maternal health and child outcomes



- Strong relationship between maternal health and both HIV transmission risk and also child survival
- ~40% HIV-infected mothers have CD4 counts <350 but account for 80% transmissions (26/36) and 80% HIV-associated 'maternal mortality'
- **Maternal ART improves child survival independent of the effect on transmission**

The risk of HIV transmission through breastmilk over 24 months



Infant infections by feeding mode – VTS study

	HR	p	95% CI
EBF	1.0		
BM + fluid/food	1.56	0.308	0.66-3.69
BM + solids	10.87	0.018	1.51-78.00
BM+FF (@12wks)	1.82	0.057	0.98-3.36

Coovadia H. Lancet 2007

Infant infections by feeding mode – Zvitambo

Zvitambo Vitamin A trial

4495 HIV-infected mothers + 2870 infants uninfected at 6 wks
(feeding data on 2060 infants)

Postnatal transmission

Exclusive BF	Predominant BF	Mixed BF
5.1	6.7	10.5
100 child yrs	100 child yrs	100 child yrs

WHO recommendations

- Last revised 2006/2007
  - 'HIV and Infant Feeding Update' - ISBN 978 92 4 159596 4
- 2009/2010 revisions considered …
  - New research evidence
  - Accumulated programmatic experience
  - Public health implications
- Overall aim – to improve HIV free survival of infants born to mothers known to be HIV-infected

Strength of recommendations

Strong recommendations can be interpreted as:

- Most individuals should receive the intervention;
- Most well informed individuals would want the recommended course of action and only a small proportion would not;
- Could unequivocally be used for policy making.

Weak recommendations can be interpreted as:

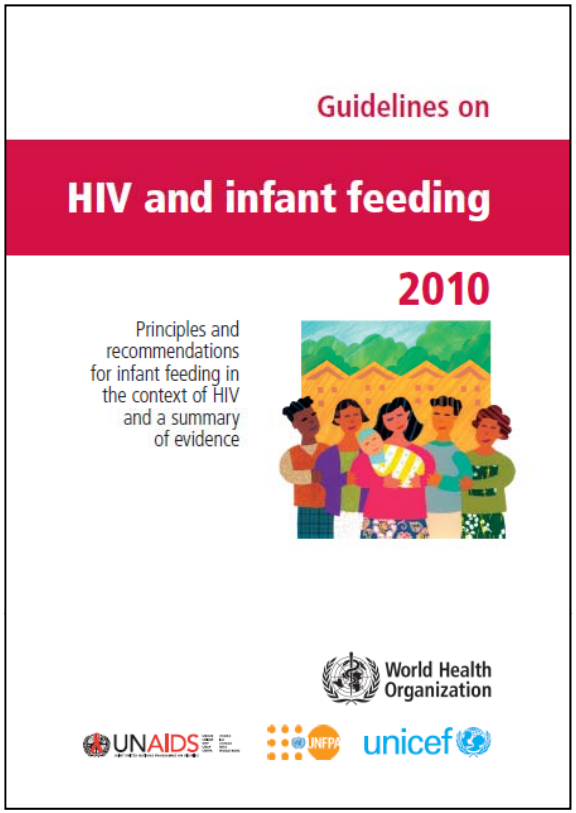
- The majority of well informed individuals would want the suggested course of action, but an appreciable proportion who would not;
- Widely varying values and preferences;
- Policy making will require extensive debates and involvement of many stakeholders.

Revised WHO Recommendations on the use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants (2009)

- Eligibility criteria for ART
  - CD4 count <350, irrespective of clinical stage
  - Clinical stage 3 or 4, irrespective of CD4 count
- The 2009 recommendations … provide two alternative options for women who are not on ART and breastfeed:
  - 1) If a woman received AZT during pregnancy, daily NVP is recommended for her child from birth until the end of the breastfeeding period.

  or
  - 2) If a woman received a three-drug regimen during pregnancy, a continued regimen of triple therapy is recommended through the end of the breastfeeding period.
- ARV prophylaxis …. should continue until one week after all exposure to breast milk has ended.

Principles and Recommendations



- Principles define the values and context within which recommendations are implemented
- Recommendations reflect the best available evidence base

- 9 principles and 7 recommendations
  - Generally reinforced former principles and recommendations including:
    - Optimal feeding practices of infants of HIV uninfected mother or mothers of unknown HIV status
    - Feeding of infants already known to be HIV-infected
    - Protecting and promoting optimal infant feeding practices in general population
  - **2 significant changes from 2007**
    - Effective ARV interventions have transformed the 'landscape' for decisions re. infant feeding in HIV settings

2010 WHO Principles on HIV and infant feeding

1. Balancing HIV prevention with protection from other causes of child mortality;
2. Integrating HIV interventions into maternal and child health services;
3. Setting national recommendations for infant feeding in the context of HIV;
4. When antiretroviral drugs are not (immediately) available;
5. Informing mothers known to be HIV-infected about infant feeding alternatives;
6. Providing services to specifically support mothers to appropriately feed their infants;
7. Avoiding harm to infant feeding practices in the general population;
8. Advising mothers who are HIV uninfected or whose HIV status is unknown;
9. Investing in improvements in infant feeding practices in the context of HIV.

2010 WHO Recommendations on HIV and infant feeding

1. Ensuring mothers receive the care they need;
2. Which breastfeeding practices and for how long;
3. When mothers decide to stop breastfeeding;
4. What to feed infants when mothers stop breastfeeding;
5. Conditions needed to safely formula feed;
6. Heat-treated, expressed breast milk;
7. (Feeding) When the infant is HIV-infected.

Setting national recommendations for infant feeding in the context of HIV

National (or sub-national) health authorities should decide whether health services will principally counsel and support mothers known to be HIV-infected to:

- breastfeed and receive ARV interventions, **or,**
- avoid all breastfeeding,

as the strategy that will most likely give infants the greatest chance of HIV-free survival.

This decision should be based on international recommendations and consideration of the socio-economic and cultural contexts of the populations served by Maternal and Child Health services, the availability and quality of health services, the local epidemiology including HIV prevalence among pregnant women and main causes of infant and child mortality and maternal and child under-nutrition

… in settings where national authorities decide to promote and support BF and ARVs to improve HIV FS in exposed infants …

Which breastfeeding practices and for how long?

Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

When HIV-infected mothers decide to stop breastfeeding (at any time) they should do so gradually within one month

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- 12 months represents the duration for most HIV-infected mothers that capitalizes on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In the presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection vs. risk

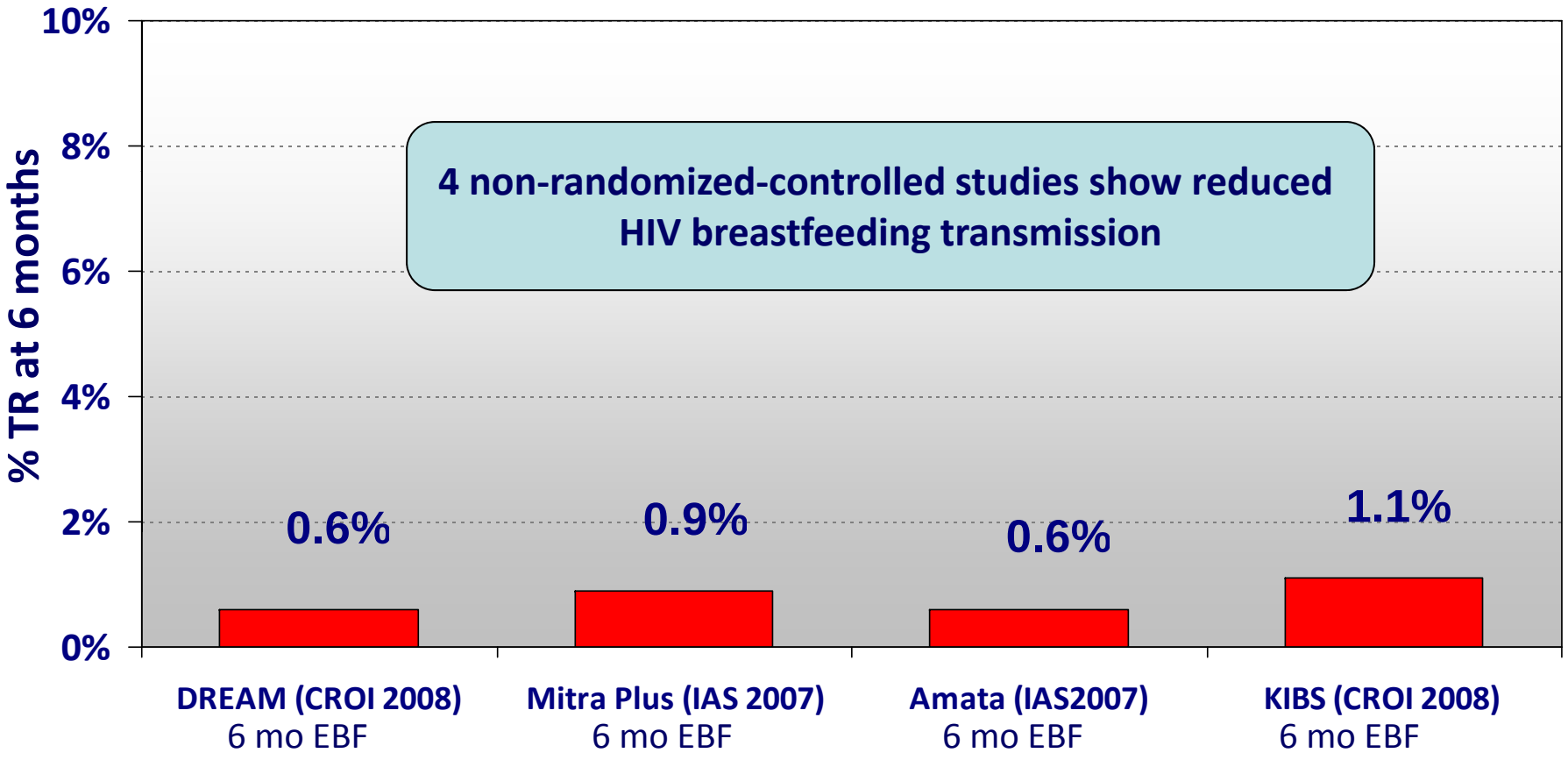
- **What is the evidence base in support of the main revisions?**
  - Efficacy and safety of ARVs to prevent HIV transmission through BF
  - The risks associated with not BF
  - The optimal duration of BF by HIV-infected mothers
  - Maternal health considerations

- **Why WHO recommends that national authorities promote a single infant feeding strategy for all HIV-infected mothers and their infants?**
  - Programmatic experiences of implementing previous recommendations
    - Counselling and outcomes
  - Financial considerations

- **What are the 'opportunities' and 'challenges' of adopting and implementing the revised recommendations?**
  - Programmatic requirements of implementing revised recommendations
    - Communication and commitment
    - Integrated approaches and scaling up
  - Rights considerations
  - MDGs 4 and 5

Maternal ARV prophylaxis studies antepartum and postpartum (Dual or triple ARVs/ART)

Between age 4-6 weeks and 6-7 months HIV transmission rates



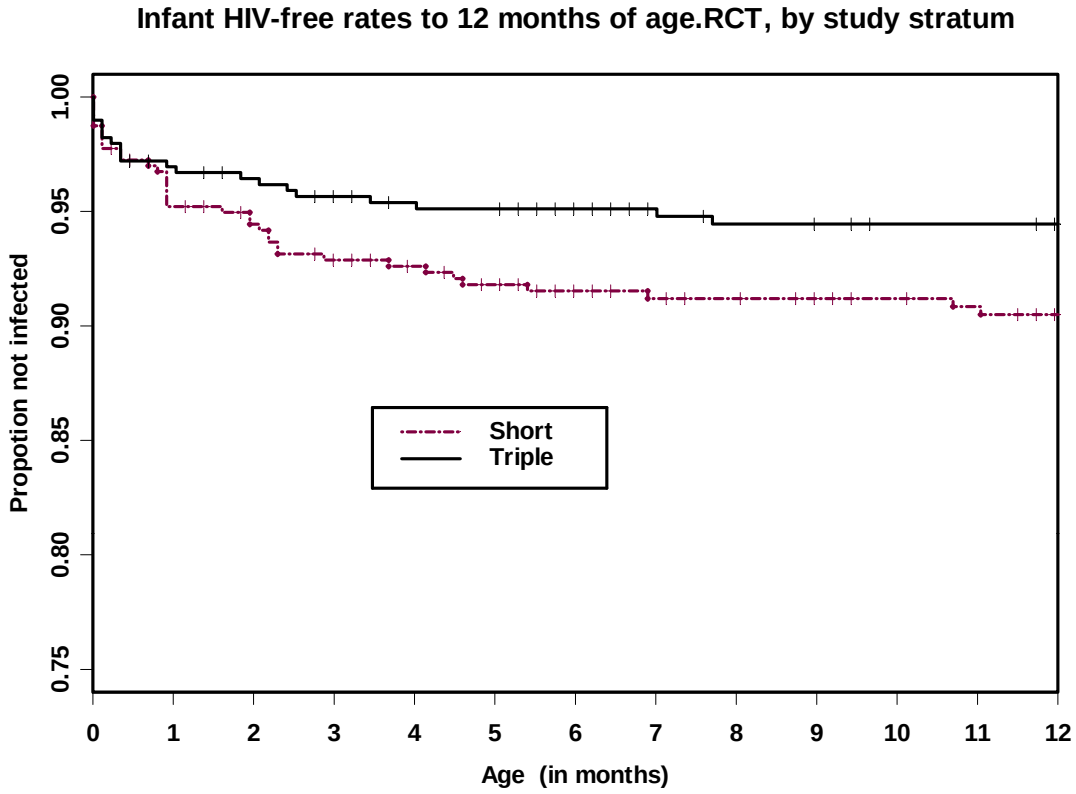
Courtesy: Lynne Mofenson

Kesho Bora: All infants: HIV infections

RCT in Kenya, Burk. Faso and SA

2 arms - AZT + 3TC + LPV/r until

- Delivery only (Short) then nil **Or**
- End of BF ~6mths (Triple)



Log rank test p = 0.039
(stratified on centre and intention to BF)

	Triple		Short		
	Events (cum) / at risk	**Rate (95% CI)**	**Events (cum) / at risk**	**Rate (95% CI)**	**Reduc -tion**
Birth	7/395	**1.8** (0.8, 3.7)	9/401	**2.2** (1.2, 4.3)	**18%**
6 weeks	13/376	**3.3** (1.9, 5.6)	19/373	**4.8** (3.1, 7.4)	**31%**
6 months	19/337	**4.9** (3.1, 7.5)	33/329	**8.5** (6.1, 11.8)	**42%**
12 months	21/275	**5.5** (3.6, 8.4)	36/249	**9.5** (6.9, 13.0)	**42%**

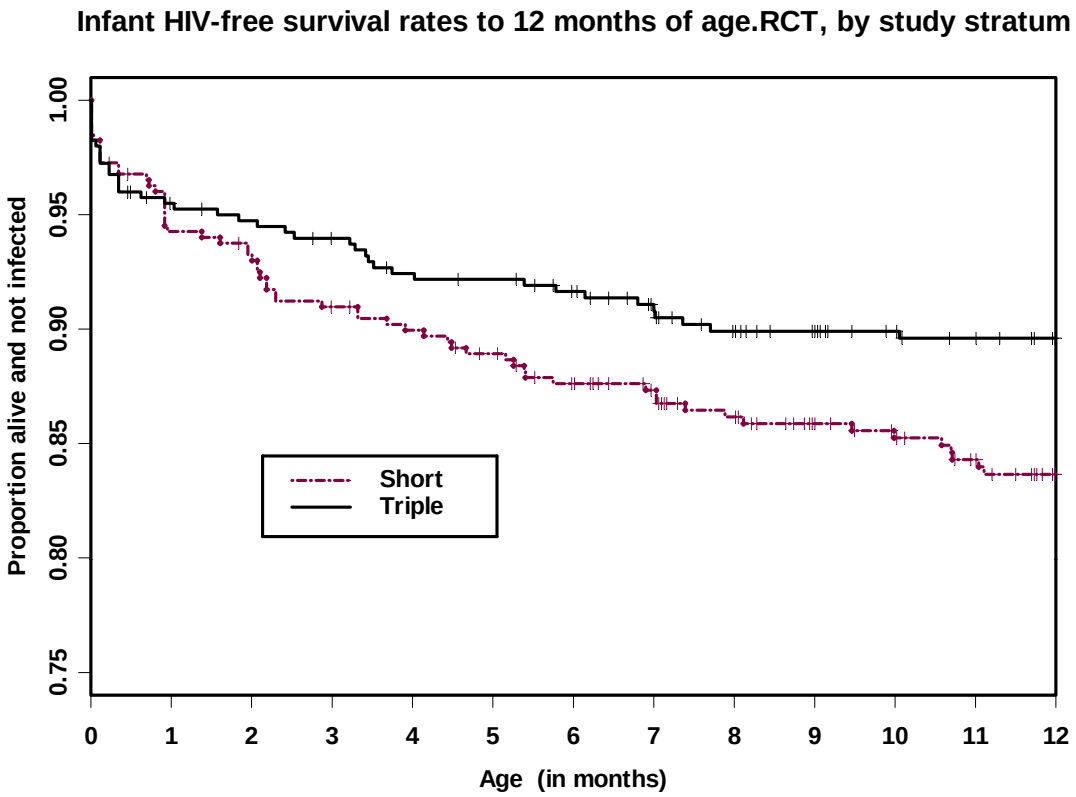
Kesho Bora: All infants: HIV-free survival

RCT in Kenya, Burk. Faso and SA

2 arms - AZT + 3TC + LPV/r until

- Delivery only (Short) then nil **Or**
- End of BF ~6mths (Triple)

Log rank test p = 0.022
(stratified on centre and intention to BF)



	Triple		Short		
	Events (cum) / at risk	Rate (95% CI)	Events (cum) / at risk	Rate (95% CI)	Reduc -tion
Birth	11/400	**2.7** (1.5, 4.9)	11/403	**2.7** (1.5, 4.9)	**0 %**
6 weeks	19/377	**4.8** (3.1, 7.4)	24/376	**6.0** (4.1, 8.8)	**20 %**
6 months	33/347	**8.3** (6.0, 11.5)	50/334	**12.6** (9.7, 16.3)	**34 %**
12 months	40/278	**10.4** (7.7, 13.9)	62/252	**16.3** (12.9, 20.5)	**36 %**

Mma bana study

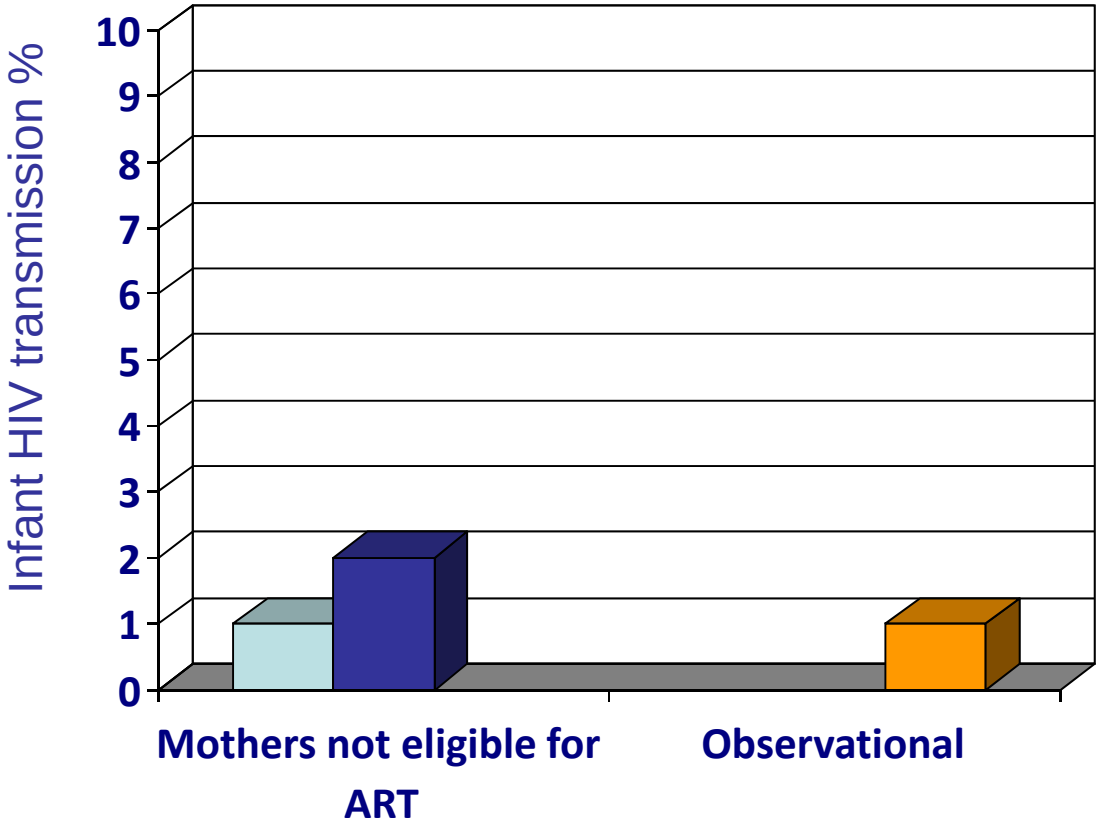
<u>2 randomised arms and one observational</u>

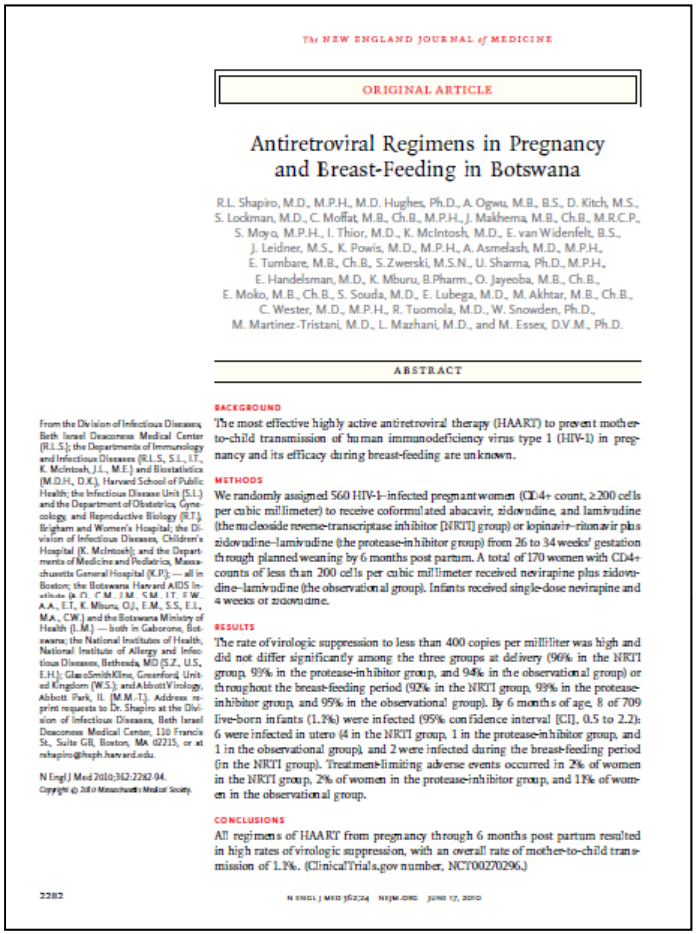
Mothers not eligible for ART received either:

lopinavir/ritonavir and combivir } for 6m

<u>or</u> abacavir/AZT/3TC } while BF

Mothers eligible for ART – outcomes observed





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antiretroviral Regimens in Pregnancy and Breast-Feeding in Botswana

R.L. Shapiro, M.D., M.P.H., M.D. Hughes, Ph.D., A. Ogwu, M.B., B.S., D. Kitch, M.S., S. Lockman, M.D., C. Moffat, M.B., Ch.B., M.P.H., J. Makhema, M.B., Ch.B., M.R.C.P., S. Moyo, M.P.H., I. Thior, M.D., K. McIntosh, M.D., E. van Widenfelt, B.S., J. Leidner, M.S., K. Powis, M.D., M.P.H., A. Asmelash, M.D., M.P.H., E. Tumbare, M.B., Ch.B., S. Zwerski, M.S.N., U. Sharma, Ph.D., M.P.H., E. Handelsman, M.D., K. Mburu, B.Pharm., O. Jayeoba, M.B., Ch.B., E. Moko, M.B., Ch.B., S. Souda, M.D., E. Lubega, M.D., M. Akhtar, M.B., Ch.B., C. Wester, M.D., M.P.H., R. Tuomola, M.D., W. Snowden, Ph.D., M. Martinez-Tristani, M.D., L. Mazhani, M.D., and M. Essex, D.V.M., Ph.D.

ABSTRACT

BACKGROUND

The most effective highly active antiretroviral therapy (HAART) to prevent mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) in pregnancy and its efficacy during breast-feeding are unknown.

METHODS

We randomly assigned 560 HIV-1–infected pregnant women (CD4+ count, ≥200 cells per cubic millimeter) to receive coformulated abacavir, zidovudine, and lamivudine (the nucleoside reverse-transcriptase inhibitor [NRTI] group) or lopinavir–ritonavir plus zidovudine–lamivudine (the protease-inhibitor group) from 26 to 34 weeks' gestation through planned weaning by 6 months post partum. A total of 170 women with CD4+ counts of less than 200 cells per cubic millimeter received nevirapine plus zidovudine–lamivudine (the observational group). Infants received single-dose nevirapine and 4 weeks of zidovudine.

RESULTS

The rate of virologic suppression to less than 400 copies per milliliter was high and did not differ significantly among the three groups at delivery (96% in the NRTI group, 93% in the protease-inhibitor group, and 94% in the observational group) or throughout the breast-feeding period (92% in the NRTI group, 93% in the protease-inhibitor group, and 95% in the observational group). By 6 months of age, 8 of 709 live-born infants (1.1%) were infected (95% confidence interval [CI], 0.5 to 2.2): 6 were infected in utero (4 in the NRTI group, 1 in the protease-inhibitor group, and 1 in the observational group), and 2 were infected during the breast-feeding period (in the NRTI group). Treatment-limiting adverse events occurred in 2% of women in the NRTI group, 2% of women in the protease-inhibitor group, and 1% of women in the observational group.

CONCLUSIONS

All regimens of HAART from pregnancy through 6 months post partum resulted in high rates of virologic suppression, with an overall rate of mother-to-child transmission of 1.1%. (ClinicalTrials.gov number, NCT00270296.)

From the Division of Infectious Diseases, Beth Israel Deaconess Medical Center (R.L.S.); the Departments of Immunology and Infectious Diseases (R.L.S., S.L., I.T., K. McIntosh, J.L., M.E.) and Biostatistics (M.D.H., D.K.), Harvard School of Public Health; the Infectious Disease Unit (S.L.) and the Department of Obstetrics, Gynecology, and Reproductive Biology (R.T.), Brigham and Women's Hospital; the Division of Infectious Diseases, Children's Hospital (K. McIntosh); and the Departments of Medicine and Pediatrics, Massachusetts General Hospital (K.P.) — all in Boston; the Botswana Harvard AIDS Institute (A.O., C.M., J.M., S.M., I.T., S.W., A.A., E.T., K. Mburu, O.J., E.M., S.S., E.L., M.A., C.W.) and the Botswana Ministry of Health (L.M.) — both in Gaborone, Botswana; the National Institutes of Health, National Institute of Allergy and Infectious Diseases, Bethesda, MD (S.Z., U.S., E.H.); GlaxoSmithKline, Greenford, United Kingdom (W.S.); and Abbott Virology, Abbott Park, IL (M.M.-T.). Address reprint requests to Dr. Shapiro at the Division of Infectious Diseases, Beth Israel Deaconess Medical Center, 110 Francis St., Suite GB, Boston, MA 02215, or at rshapiro@rhsph.harvard.edu.

N Engl J Med 2010;362:2282-94.

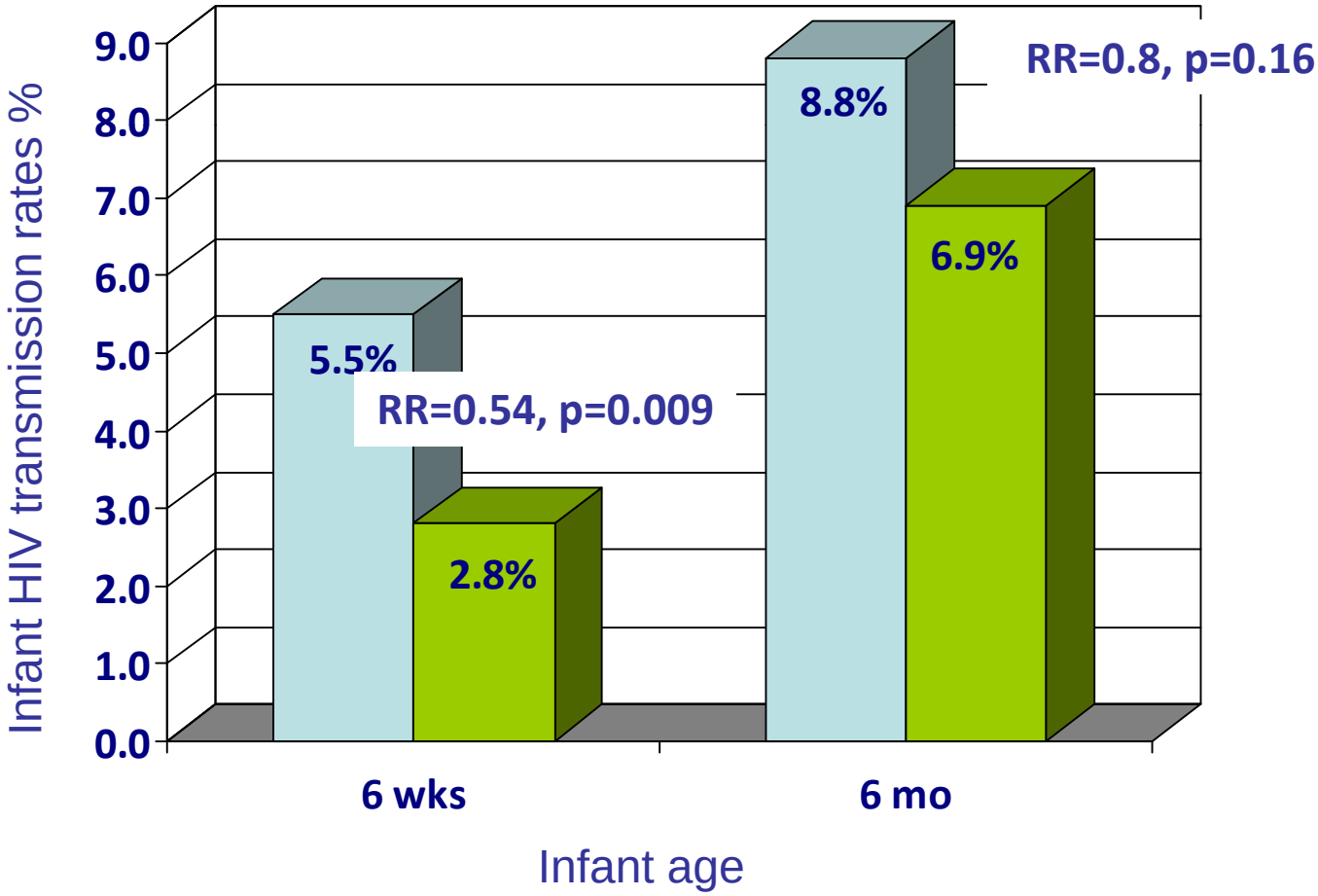
Viral suppression >92% all groups

- LPV/r + combivir
- Abacavir/AZT/3TC
- Observational

Six Week Extended Nevirapine Lancet 2008

Breastfeeding infants received either sdNVP only (n=986) or daily NVP for 6 weeks (n=901)

Modified ITT analysis (excluded infants HIV infected on D1 sample)

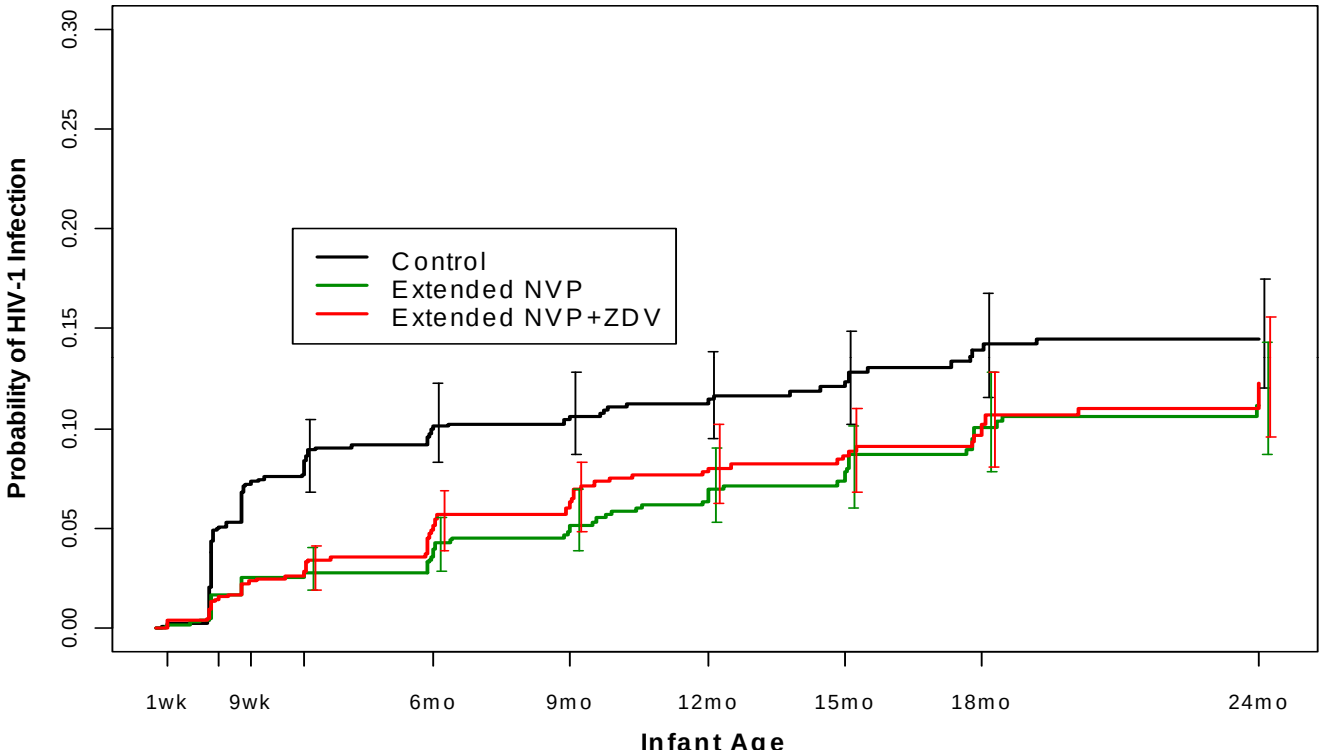


AEs	
sdNVP	393
Inf NVP	346
	p=0.54

Probability of HIV-1 Infection in Infants Uninfected at Birth by Treatment Arm: PEPI-Malawi

3 arms:

- **Control**
- **NVP to infants for 14 wks**
- **NVP and AZT to infants for 14wks**



Age	1 wk	6 wks	9 wks	14 wks	6 mos	9 mos	12 mos	15 mos	18 mos	24 mos
Estimates (%)										
Control	0.3	5.1	7.4	8.4	10.1	10.6	11.5	12.4	13.9	14.5
Extended NVP	0.1	1.7	2.6	2.8	4.0	5.2	7.0	7.8	10.1	11.2
Extended NVP+ZDV	0.2	1.6	2.4	2.8	5.2	6.4	8.1	8.7	10.2	12.3

MASHI study

Factorial design testing whether AZT to infants reduces HIV transmission through breastfeeding

ORIGINAL CONTRIBUTION

Breastfeeding Plus Infant Zidovudine Prophylaxis for 6 Months vs Formula Feeding Plus Infant Zidovudine for 1 Month to Reduce Mother-to-Child HIV Transmission in Botswana

A Randomized Trial: The Mashi Study

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Context Postnatal transmission of human immunodeficiency virus-1 (HIV) via breastfeeding reverses gains achieved by perinatal antiretroviral interventions.

Objective To compare the efficacy and safety of 2 infant feeding strategies for the prevention of postnatal mother-to-child HIV transmission.

Design, Setting, and Patients A 2 × 2 factorial randomized clinical trial with peripartum (single-dose nevirapine vs placebo) and postpartum infant feeding (formula vs breastfeeding with infant zidovudine prophylaxis) interventions. In Botswana between March 27, 2001, and October 29, 2003, 1200 HIV-positive pregnant women were randomized from 4 district hospitals. Infants were evaluated at birth, monthly until age 7 months, at age 9 months, then every third month through age 18 months.

Intervention All of the mothers received zidovudine 300 mg orally twice daily from 34 weeks' gestation and during labor. Mothers and infants were randomized to receive single-dose nevirapine or placebo. Infants were randomized to 6 months of breastfeeding plus prophylactic infant zidovudine (breastfed plus zidovudine), or formula feeding plus 1 month of infant zidovudine (formula fed).

Main Outcome Measures Primary efficacy (HIV infection by age 7 months and HIV-free survival by age 18 months) and safety (occurrence of infant adverse events by 7 months of age) end points were evaluated in 1179 infants.

Results The 7-month HIV infection rates were 5.6% (32 infants in the formula-fed group) vs 9.0% (51 infants in the breastfed plus zidovudine group) ($P = .04$; 95% confidence interval for difference, -6.4% to -0.4%). Cumulative mortality or HIV infection rates at 18 months were 80 infants (13.9%, formula fed) vs 86 infants (15.1% breastfed plus zidovudine) ($P = .60$; 95% confidence interval for difference, -5.3% to 2.9%). Cumulative infant mortality at 7 months was significantly higher for the formula-fed group than for the breastfed plus zidovudine group (9.3% vs 4.9%; $P = .003$), but this difference diminished beyond month 7 such that the time-to-mortality distributions through age 18 months were not significantly different ($P = .21$).

Conclusions Breastfeeding with zidovudine prophylaxis was not as effective as formula feeding in preventing postnatal HIV transmission, but was associated with a lower mortality rate at 7 months. Both strategies had comparable HIV-free survival at 18 months. These results demonstrate the risk of formula feeding to infants in sub-Saharan Africa, and the need for studies of alternative strategies.

Trial Registration clinicaltrials.gov identifier: NCT00197587

JAMA. 2006;296:794-805 www.jama.com

ACCORDING TO SOME ESTIMATES, approximately 25% to 48% of infants born to human immunodeficiency virus (HIV)-infected breastfeeding women in certain populations may become infected with HIV-1.[1,2] A relatively high proportion of mother-to-child transmission in breastfeeding populations may occur through breastfeeding, perhaps more than 40%.[3,4] Perinatal antiretroviral prophylaxis can greatly reduce the risk of mother-

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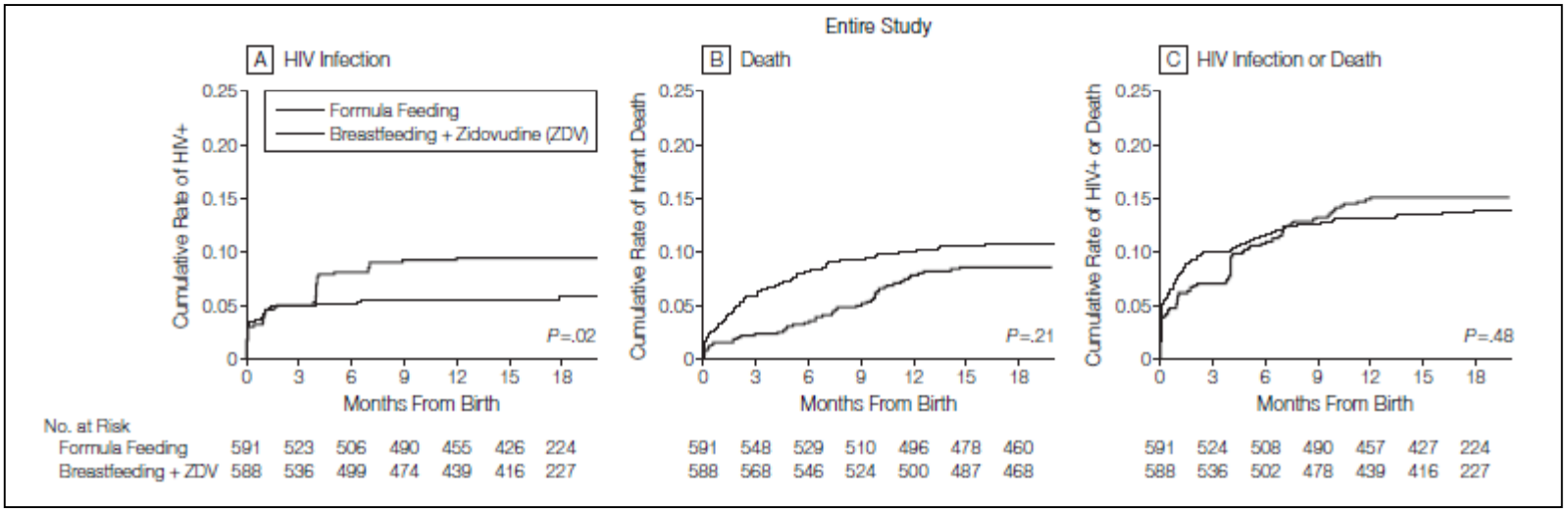
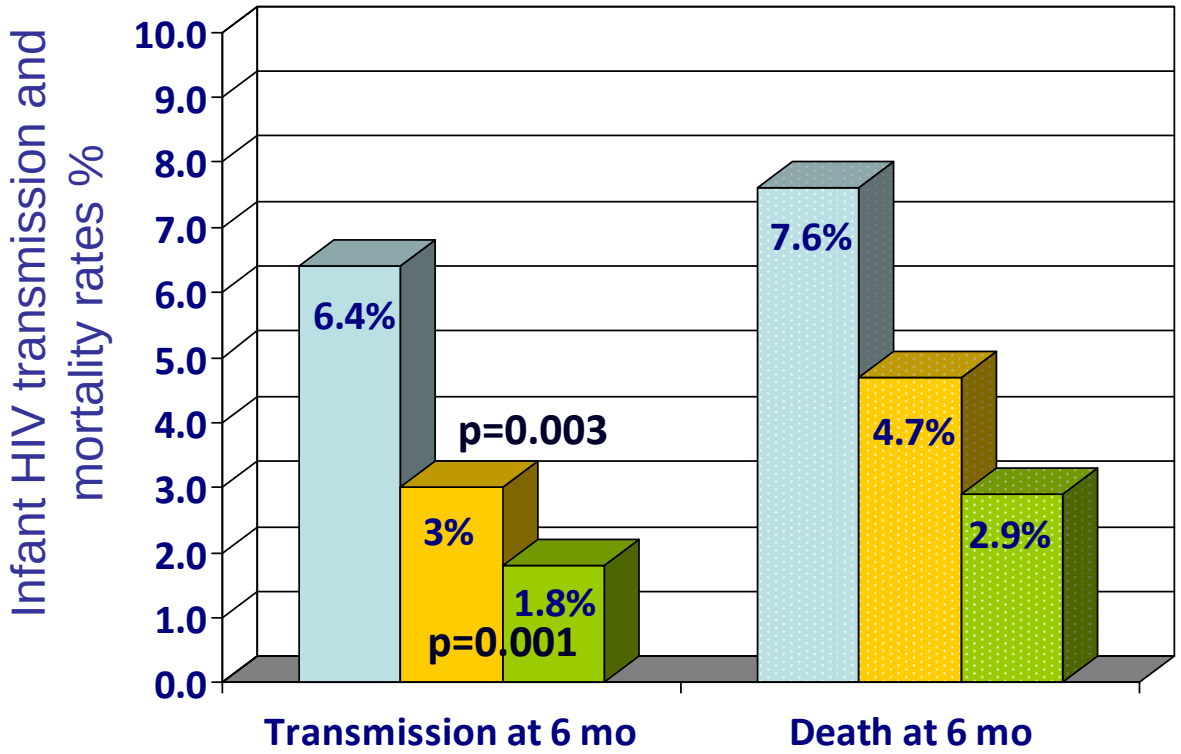


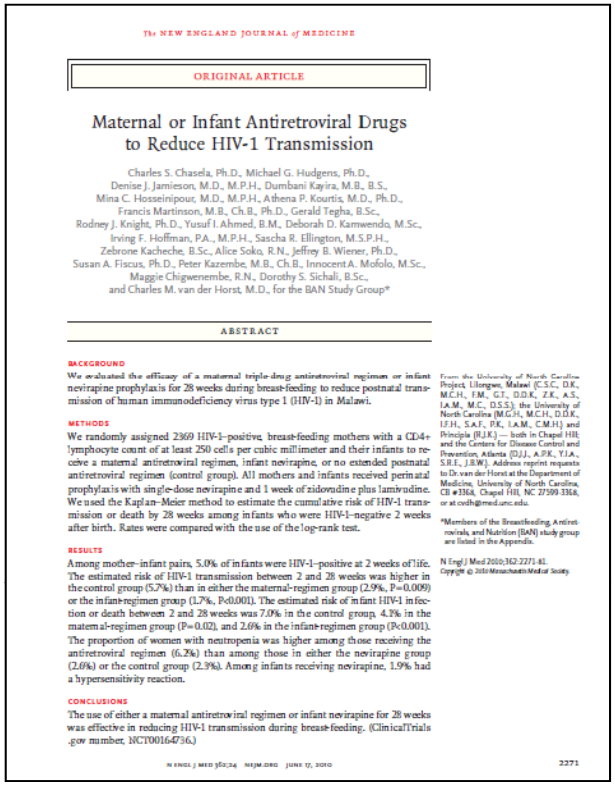
Breastfeeding, Antiretroviral and Nutrition (BAN) study

3 Arms: Control

Mothers receive lopinavir/ritonavir for 28 wks throughout BF period

Breastfeeding infants received daily NVP for 6 mths





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Maternal or Infant Antiretroviral Drugs to Reduce HIV-1 Transmission

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ABSTRACT

BACKGROUND

We evaluated the efficacy of a maternal triple-drug antiretroviral regimen or infant nevirapine prophylaxis for 28 weeks during breast-feeding to reduce postnatal transmission of human immunodeficiency virus type 1 (HIV-1) in Malawi.

METHODS

We randomly assigned 2369 HIV-1–positive, breast-feeding mothers with a CD4+ lymphocyte count of at least 250 cells per cubic millimeter and their infants to receive a maternal antiretroviral regimen, infant nevirapine, or no extended postnatal antiretroviral regimen (control group). All mothers and infants received perinatal prophylaxis with single-dose nevirapine and 1 week of zidovudine plus lamivudine. We used the Kaplan–Meier method to estimate the cumulative risk of HIV-1 transmission or death by 28 weeks among infants who were HIV-1–negative 2 weeks after birth. Rates were compared with the use of the log-rank test.

RESULTS

Among mother–infant pairs, 5.0% of infants were HIV-1–positive at 2 weeks of life. The estimated risk of HIV-1 transmission between 2 and 28 weeks was higher in the control group (5.7%) than in either the maternal-regimen group (2.9%, P=0.009) or the infant-regimen group (1.7%, P<0.001). The estimated risk of infant HIV-1 infection or death between 2 and 28 weeks was 7.0% in the control group, 4.1% in the maternal-regimen group (P=0.02), and 2.6% in the infant-regimen group (P<0.001). The proportion of women with neutropenia was higher among those receiving the antiretroviral regimen (6.3%) than among those in either the nevirapine group (2.6%) or the control group (2.9%). Among infants receiving nevirapine, 1.9% had a hypersensitivity reaction.

CONCLUSIONS

The use of either a maternal antiretroviral regimen or infant nevirapine for 28 weeks was effective in reducing HIV-1 transmission during breast-feeding. (ClinicalTrials.gov number, NCT00164736.)

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*Members of the Breastfeeding, Antiretrovirals, and Nutrition (BAN) study group are listed in the Appendix.

N Engl J Med 2010;362:2271-81.

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N ENGL J MED 362;24 NEJM.ORG JUNE 17, 2010

2271

- Strong evidence that
  - ARV interventions to infants or mothers significantly reduce HIV transmission through breastfeeding
    - No evidence of diminished protection over time
  - No evidence of significant drug-related adverse events
    - No increased adverse events with prolonged ARV intervention.
    - NVP adverse events occur within first few weeks and do not accumulate with longer exposure
    - Dose of NVP given to infants as prophylaxis is less than that routinely given as ART for infected infants

Risks associated with not breastfeeding

- Non breastfeeding from birth
- Early cessation of BF

- While the risks of not breastfeeding by HIV uninfected mothers in resource-limited settings were recognised in 2000, there was hope that HIV-infected mothers
  - with additional counselling and support, and,
  - the added motivation of preventing all HIV transmission

  ... would somehow be different

Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: A pooled analysis – WHO, Lancet 2000

Protection provided by breastmilk

	< 2 mths	2-3 mths	4-5 mths	6-8 mths	9-11 mths
Odd ratio	**5.8**	**4.1**	**2.6**	1.8	1.4

	< 6 mths	6-11mths
Diarrhoea	**6.1**	2.4
ARI	**1.9**	2.5

Breastfeeding recognised as the single most important intervention to prevent child deaths

Lancet 2003; **362**: 65–71

Child survival II

How many child deaths can we prevent this year?

*Gareth Jones, Richard W Steketee, Robert E Black, Zulfiqar A Bhutta, Saul S Morris, and the Bellagio Chi Group**

This is the second of five papers in the child survival series. The first focused on continuing l mortality (over 10 million each year) from preventable causes: diarrhoea, pneumonia, measles, mala underlying cause of undernutrition, and a small group of causes leading to neonatal deaths. We re interventions feasible for delivery at high coverage in low-income settings, and classify these as evidence of effect), level 2 (limited evidence), or level 3 (inadequate evidence). Our results show level-1 intervention is available for preventing or treating each main cause of death among chil 5 years, apart from birth asphyxia, for which a level-2 intervention is available. There is also li several other interventions. However, global coverage for most interventions is below 50%. If level 1 were universally available, 63% of child deaths could be prevented. These findings show that the int to achieve the millennium development goal of reducing child mortality by two-thirds by 2015 are they are not being delivered to the mothers and children who need them.

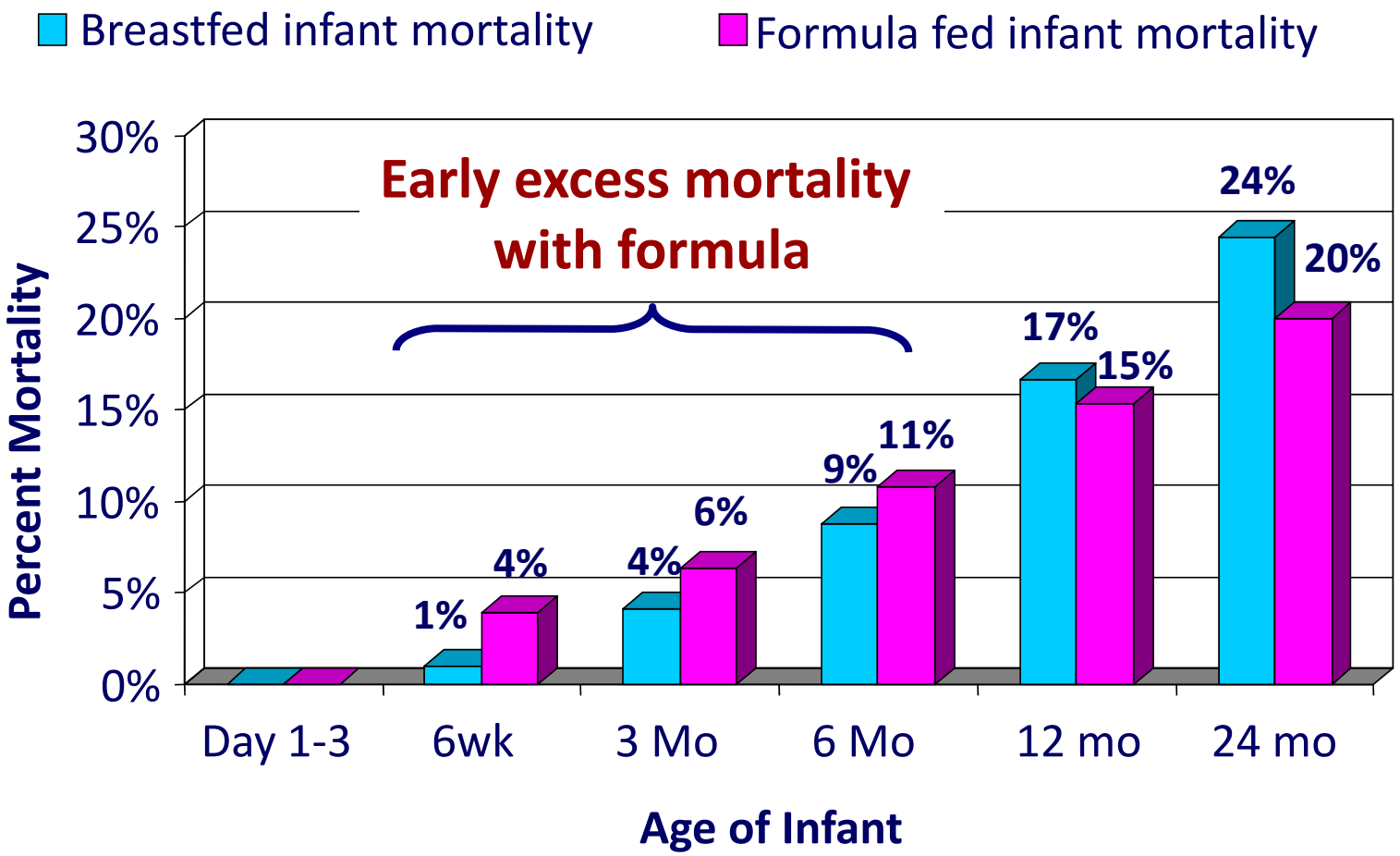
	Estimated under-5 deaths prevented	
	Number of deaths (×10³)	Proportion of all deaths
Preventive interventions		
Breastfeeding	1301	13%
Insecticide-treated materials	691	7%
Complementary feeding	587	6%
Zinc	459 (351)*	5% (4%)*
Clean delivery	411	4%
Hib vaccine	403	4%
Water, sanitation, hygiene	326	3%
Antenatal steroids	264	3%
Newborn temperature management	227 (0)*	2% (0%)*
Vitamin A	225 (176)*	2% (2%)*
Tetanus toxoid	161	2%
Nevirapine and replacement feeding	150	2%
Antibiotics for premature rupture of membranes	133 (0)*	1% (0%)*
Measles vaccine	103	1%
Antimalarial intermittent preventive treatment in pregnancy	22	<1%
Treatment interventions		
Oral rehydration therapy	1477	15%
Antibiotics for sepsis	583	6%
Antibiotics for pneumonia	577	6%
Antimalarials	467	5%
Zinc	394	4%
Newborn resuscitation	359 (0)*	4% (0%)*
Antibiotics for dysentery	310	3%
Vitamin A	8	<1%

*Numbers represent effect if both levels 1 (sufficient) and 2 (limited) evidence are included, value number in brackets shows effect if only level-1 evidence is accepted. Interventions for which only one value is cited are all classified as level 1.

Table 2: **Under-5 deaths that could be prevented in the 42 countries with 90% of worldwide child deaths in 2000 through achievement of universal coverage with individual interventions**

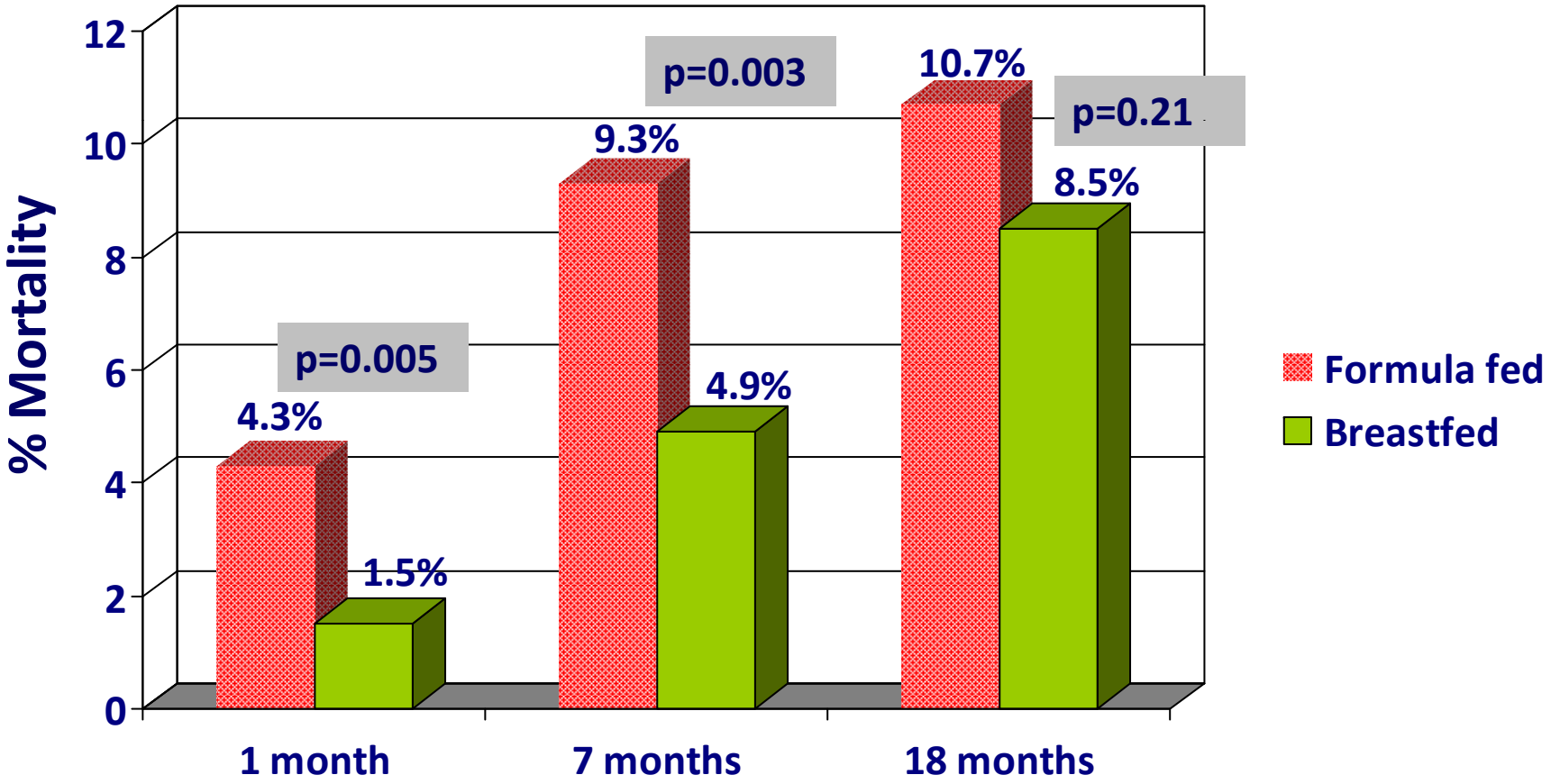
Early Mortality in Formula-Fed Infants in Nairobi FF vs. BF trial

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



Early Mortality (Through Age 7 Months) is Higher in Formula-Fed than Breastfed + AZT Infants

Thior I et al. JAMA 2006;296:794-805



Predominant causes infant death: Diarrhoeal diseases and pneumonia

Survival in the first 6 months of life – VTS S. Africa

Coovadia H. Lancet 2007

- 94 deaths amongst 1034 infants started on EBF
- 73 of these children were HIV-infected
- Overall HIV-free survival was 75.41% at 6 months (i.e. 223 deaths or infections amongst 1037 infants)

- 8 deaths amongst 101 infants on RF from birth
- Deaths occurred in first 3 months of life

Cumulative mortality according to initial infant feeding type

Feeding type	N	1m	2m	3m	4m	5m	6m
EBF	1037	1.92%	3.69%	6.12%	8.02%	9.07%	10.1%
RF	101	4.22%	9.90%	15.12%	-	-	-

Hospitalization and Mortality Among Primarily Non-breastfed Children During a Large Outbreak of Diarrhea and Malnutrition in Botswana, 2006

Tracy L. Creek, MD, Andrea Kim, PhD,* Lydia Lu, MPH,* Anna Bowen, MD, MPH,* Japhter Masunge, MD,† Wences Arvelo, MD, MSc,* Molly Smit, MBChB, DPH, DHA,‡ Ondrej Mach, MD, MPH,* Keitumetse Legwaila,‡ Catherine Motswere,‡ Laurel Zaks, MPH, RD,*†† Thomas Finkbeiner, MD,* Laura Povinelli, PhD, MSPH,§ Maruping Maruping,‡ Gibson Ngwaru,‡ Goitebetswe Tebele,‡ Cheryl Bopp, MS,* Nancy Puhr, BS,* Stephanie P. Johnston, MS,* Alexandre J. Dasilva, PhD,* Caryn Bern, MD, MPH,* R. S. Beard, BS,* and Margarett K. Davis, MD, MPH*‡*

J Acquir.Immune.Defic.Syndr. 2010;53(1):14-9

Jan-Mar 2006

- x3 increase diarrhoea cases and x25 increase in deaths
- 35% of all infants are born to HIV-infected mothers and do not BF
- Of infants admitted to 2nd largest hospital in Botswana
  - 97% less than 2 yrs
  - 88% were not BF
  - 87% households used piped water
  - Severe acute malnutrition developed in 25% patients and 22% died
  - Only one BF infant died
  - Mothers commonly reported inconsistent supply of FF
  - Cryptosporidium and enteropathogenic E.coli were common

Breastfeeding, Mother-to-Child HIV Transmission, and Mortality Among Infants Born to HIV-Infected Women on Highly Active Antiretroviral Therapy in Rural Uganda

Jaco Homsy, MD, MPH, David Moore, MD, MPH,† Alex Barasa, MBChB,‡ Willi Were, MBChB,‡ Celina Likicho, RN, RM,‡ Bernard Waiswa, MBChB, MPH,‡ Robert Downing,‡ Samuel Malamba, PhD,* Jordan Tappero, MD, MPH,‡ and Jonathan Mermin, MD, MPH§*

J Acquir.Immune.Defic.Syndr. 2010;53(1):28-35

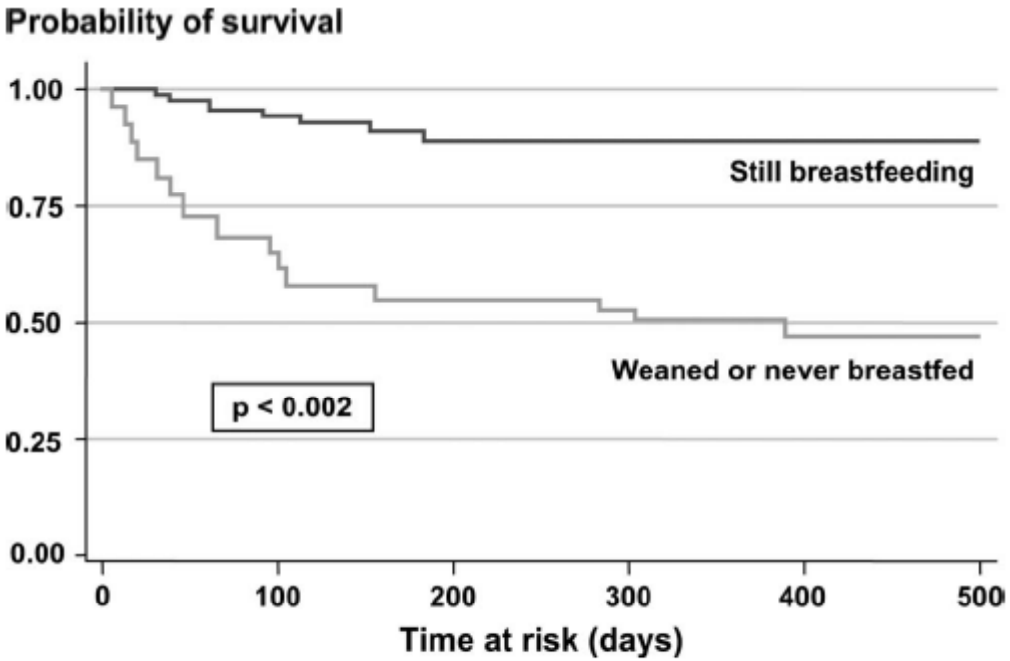


FIGURE 1. Kaplan–Meier estimates of infant survival in relation to breastfeeding status at the time of death.

Decreased survival among infants who stopped BF early or who were never BF.

AHR = 6.19; (95% CI 1.41–27.0, P = 0.015)

97% infants were tested at 6 wks – none infected.

Difference was independent of maternal health or if receiving ART

OPEN ACCESS Freely available online

PLoS one

Survival of Infants Born to HIV-Positive Mothers, by Feeding Modality, in Rakai, Uganda

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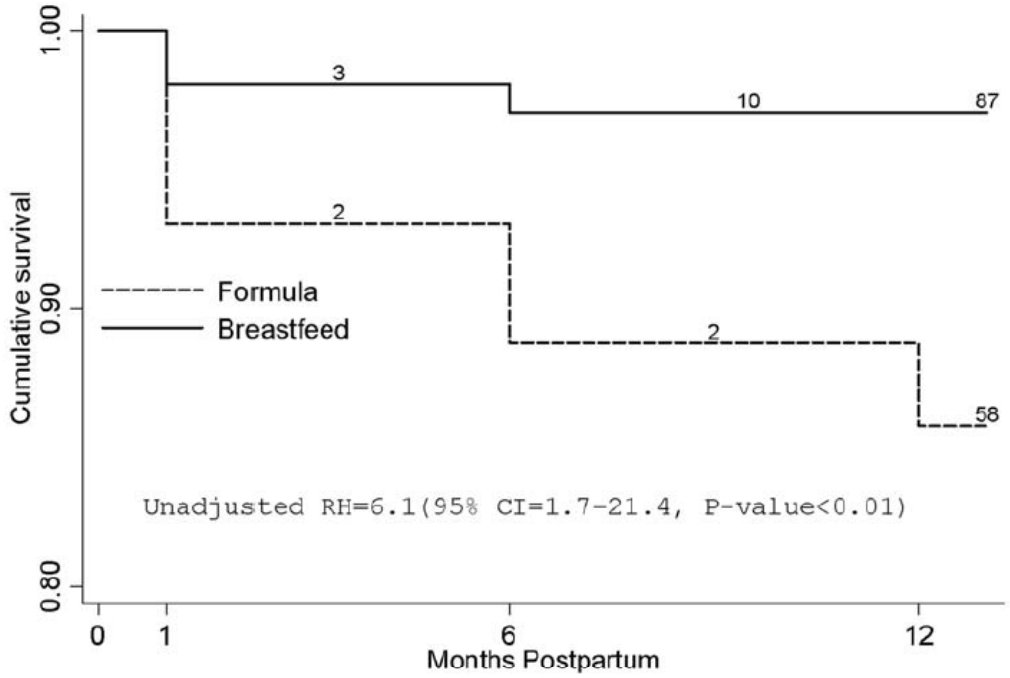
December 2008 | Volume 3 | Issue 12 | e3877



Number of infant deaths/Risk set				
Breast-fed	0/107	2/103	1/98	0/87
Formula-fed	0/75	5/75	5/68	3/61

Figure 2. Kaplan-Meier cumulative probabilities of survival from death by feeding group. Actual visits grouped by the three scheduled visits at one, six and twelve months after birth.

Mortality in FF vs. BF infants (excl. infants weaned before 12m)
HR 6.3 (95%CI = 1.4-28.0, p=0.02)

In the absence of ARVs interventions, HIV free survival of uninfected infants who were BF or FF @12 m was equivalent.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

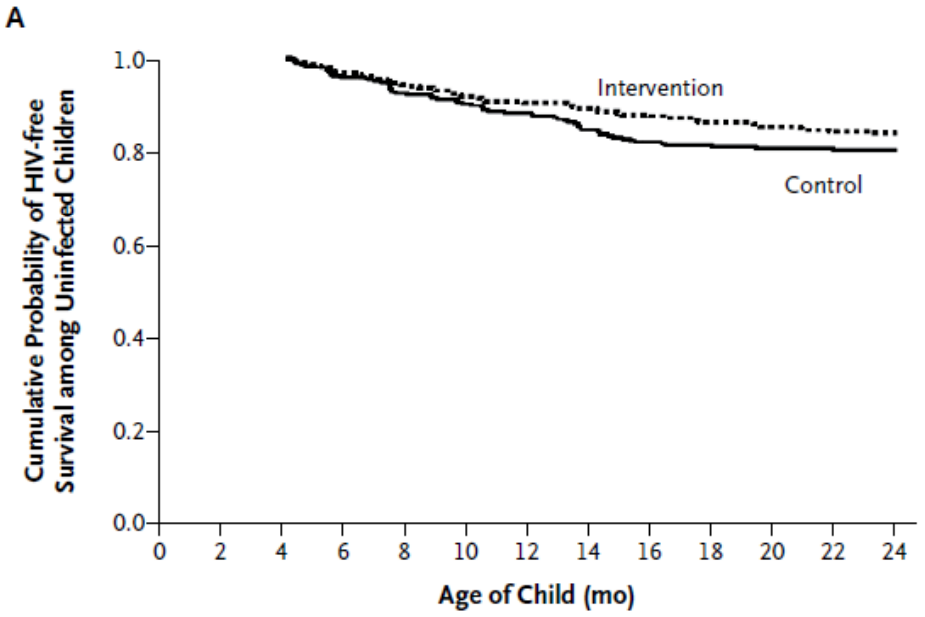
Effects of Early, Abrupt Weaning for HIV-free Survival of Children in Zambia

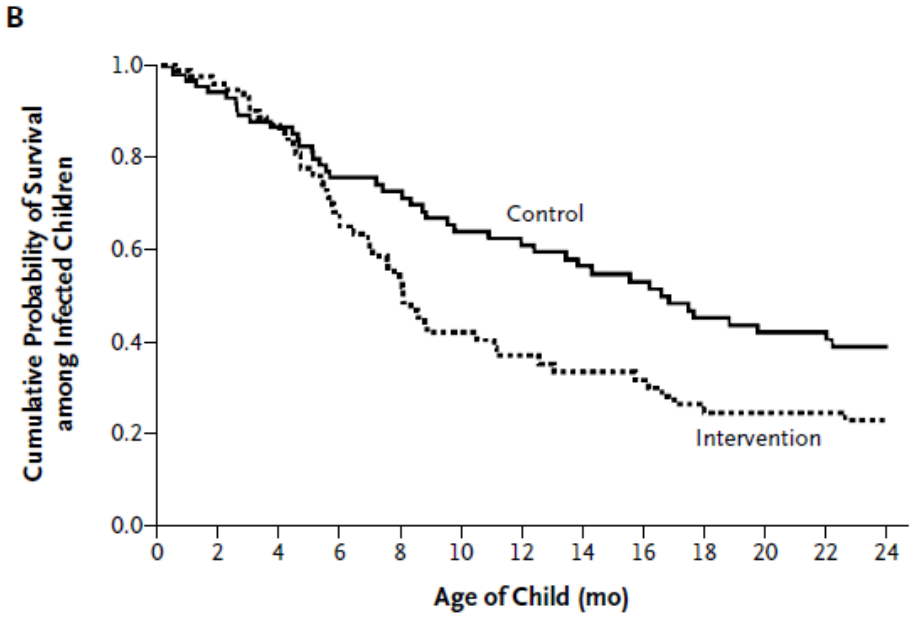
Louise Kuhn, Ph.D., Grace M. Aldrovandi, M.D., Moses Sinkala, M.D., M.P.H., Chipepo Kankasa, M.D., Katherine Semrau, M.P.H., Mwiya Mwiya, M.B., Ch.B., Prisca Kasonde, M.D., Nancy Scott, M.P.H., Cheswa Vwalika, M.B., Ch.B., Jan Walter, Ph.D., Marc Bulterys, M.D., Ph.D., Wei-Yann Tsai, Ph.D., and Donald M. Thea, M.D., for the Zambia Exclusive Breastfeeding Study

N.Engl.J Med.
2008;359(2):130-41.

A. In the absence of ARV interventions, HIV free survival of uninfected infants who were BF for 16m equal to HIV FS of infant who stopped BF @ 4m. Additional mortality in early cessation group = additional transmissions in continued BF group

B. Infants already HIV-infected by 4 m, early cessation of BF resulted in significantly worse HIV free survival compared to those who continued to BF. For infants that are HIV-infected, continued BF prolongs survival.





Growth faltering due to breastfeeding cessation in uninfected children born to HIV-infected mothers in Zambia[1–3]

Stephen Arpadi, Ashraf Fawzy, Grace M Aldrovandi, Chipepo Kankasa, Moses Sinkala, Mwiya Mwiya, Donald M Thea, and Louise Kuhn

ABSTRACT

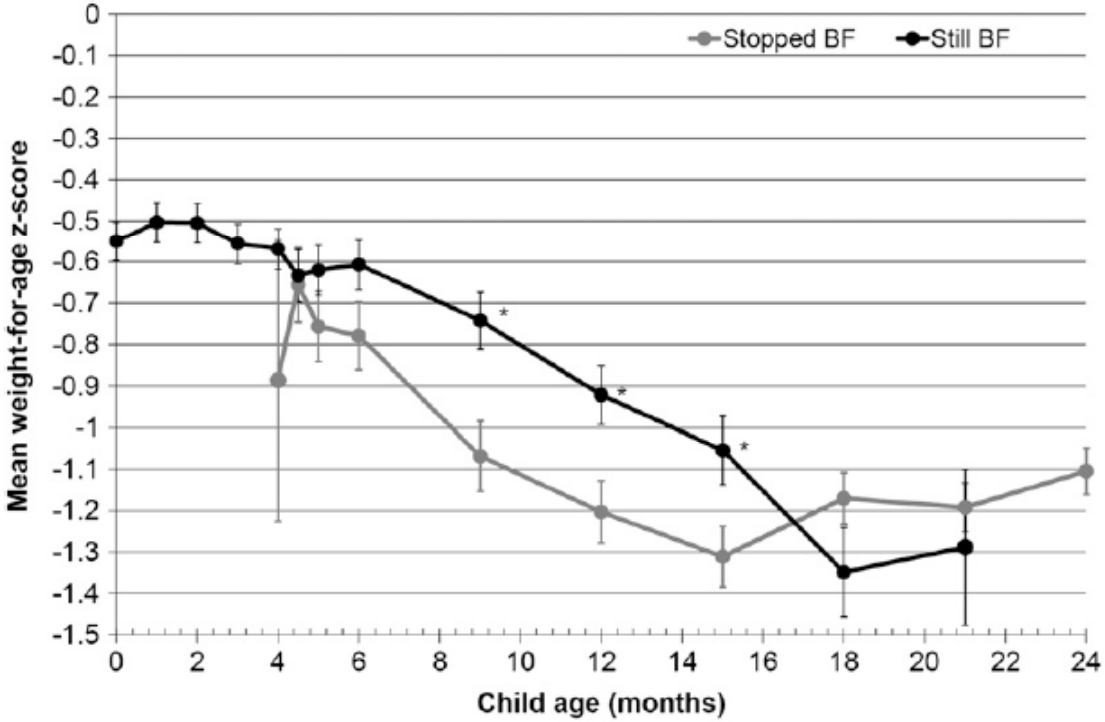
Background: The effect of breastfeeding on growth in HIV-exposed infants is not well described.

Objective: The objective was to evaluate the effect of early breast-feeding cessation on growth.

tended to be vague. Typically, decisions about when to stop breastfeeding are left to the mother and rest on the family's ability to provide milk, animal-source, and other complementary foods and on many social, cultural, and family influences (10).

In addition to minimizing postnatal transmission of HIV,

Am J Clin Nutr 2009;90:344–53



Month	0	1	2	3	4	4.5	5	6	9	12	15	18	21	24
Still BF (N)	564	554	550	558	533	330	353	359	298	266	200	114	40	9
Stopped BF (N)	-	-	-	-	14	167	192	213	224	240	254	347	403	442

Significant weight loss between 4 and 16 months in infants who stop BF early at 4 months and given replacement feeds

GASTROENTERITIS AND EARLY WEANING

Frequency of Gastroenteritis and Gastroenteritis-Associated Mortality with Early Weaning in HIV-1–Uninfected Children Born to HIV-Infected Women in Malawi

George Kafulafula, MBBS, MMed, Donald R. Hoover, MPH, PhD,† Taha E. Taha, MD, PhD,‡ Michael Thigpen, MD,§ Qing Li, MSc,‡ Mary Glenn Fowler, MD, MPH,¶ Newton I. Kumwenda, PhD,‡ Kondwani Nkanaunena, MSc,‖ Linda Mipando, RN, MN,‖ and Lynne M. Mofenson, MD§*

J Acquir.Immune.Defic.Syndr. 2010;53(1):6-13

Non-BF after 6 mo associated with increased:

- **hospitalisations**
- **GE-related mortality**
- **all-cause mortality**

Outcome		PEPI (early BF cessation)	NVAZ (prolonged BF)	p
GE Hospitalisation	0-6m	0.06-0.9%	0-0.32%	
	7-9m	2.9%	0.1%	<0.001
	10-12m	1.6%	0.2%	<0.001
GE mortality	0-6m	5/1000	3/1000	
	0-9m	19/1000	7/1000	
	0-12m	24/1000	12/1000	0.0002
All mortality	0-6m	35/1000	40/1000	
	0-9m	62/1000	54/1000	
	0-12m	79/1000	66/1000	0.03

- **What is the evidence base in support of the main revisions of the 2000 and 2007 recommendations?**
  - Efficacy and safety of ARVs to prevent HIV transmission through BF
  - The risks associated with not BF
  - The optimal duration of BF by HIV-infected mothers
  - Maternal health considerations
- **Why WHO recommends that national authorities promote a single infant feeding strategy for all HIV-infected mothers and their infants?**
  - Programmatic experiences of implementing previous recommendations
    - Counselling and outcomes
  - Financial considerations

Replacement feeding in PMTCT sites

- **Sample of milk collected from bottles (n=94) being offered to infants brought by mothers to PMTCT clinic follow-up visits**
  - 63% heavily contaminated with E.coli
  - 28% diluted (based on protein concentration)

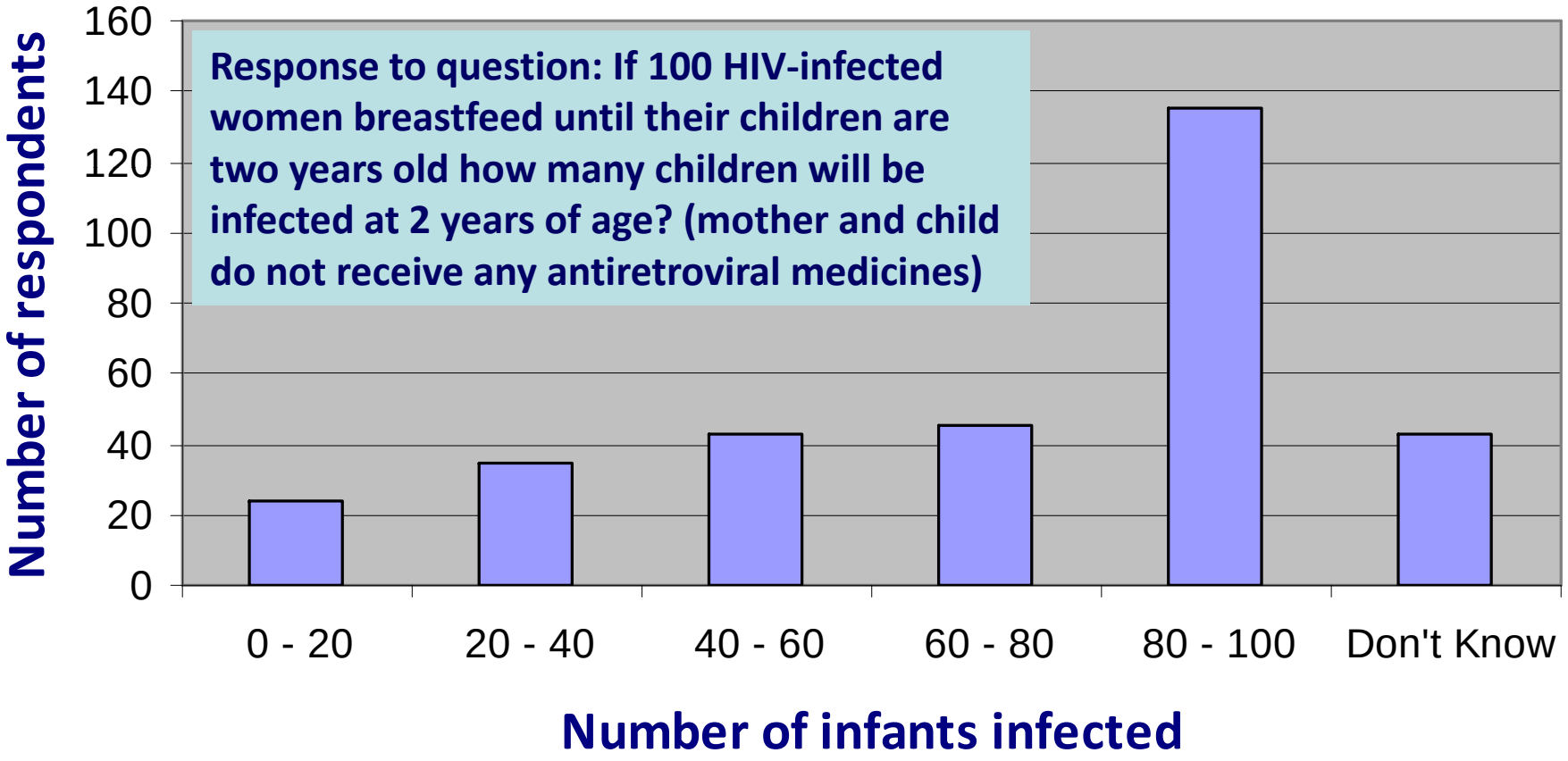
In spite of

- All mothers having completed 12 years of education
- 72% having fridges
- All received good counselling on IFP

- **15-20% mothers reported free FF being used for something other than index child**
  - Sold
  - Exchanged
- **50-75% reported running out**
  - Mainly because of clinic supply

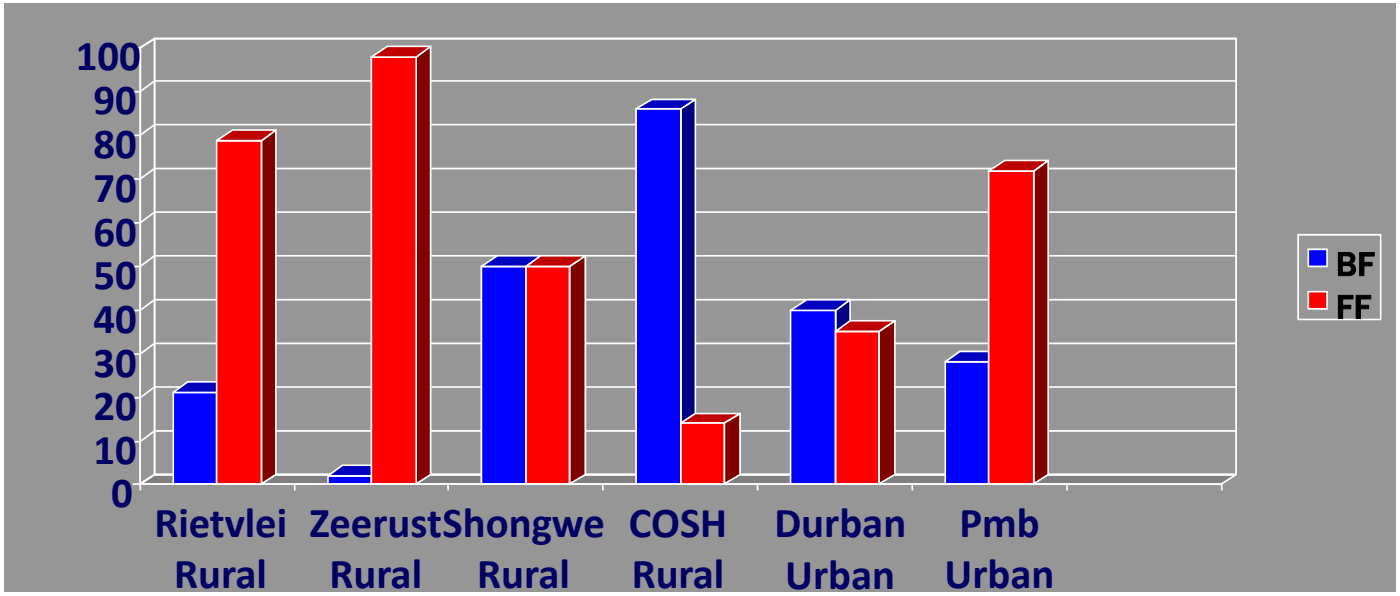
Bergstrom. Acta Paeds 2007

Knowledge of nurses and counsellors about risk of BF transmission



Chopra and Rollins, Arch. Dis. Child. 2008

Feeding at some PMTCT sites



The quality of infant feeding counselling translated into HIV free survival of infants

Woldenbeset. IAS 2009

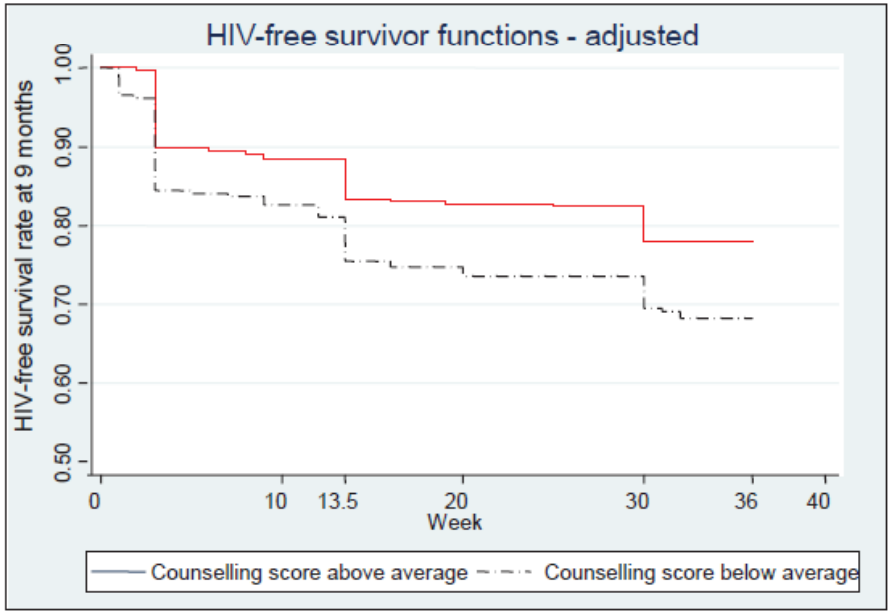


Figure 1: Kaplan Meier survival curve of the HIV free survival rate by counselling group

Balancing cost and outcomes

- While financial costs need to be considered, these must be placed against the health impact of each scenario in terms of infant HIV free survival

Cost of scenarios - 10,000 HIV mothers (US$)

Assume eligibility criteria for ART <350

Health system provides commodities for			6 months	12 months
Scenario A	<350	ART + FF	1,212,542	2,425,085
	>350	BF+NVP for 12m		
Scenario B	<350	ART + FF	1,212,542	3,275,642
	>350	BF+NVP 6m, then FF		
Scenario C	<350	ART+FF	2,063,100	4,126,200
	>350	FF		
Scenario D	<350	ART+BF for 12m	522,542	1,045,985
	>350	BF+NVP for 12m		
Scenario E	<350	ART+BF 6m then FF	522,542	2,585,642
	>350	BF+NVP 6m then FF		
Scenario F	No CD4 and no ART	All BF+NVP for 12m	307,404	614,808
Scenario G	No CD4 and no ART	All FF	1,725,000	3,450,000

Balancing cost and outcomes

- While financial costs need to be considered, these must be placed against the health impact of each scenario in terms of infant HIV free survival
- If equivalent health impacts, then what is the best investment and how could savings be reinvested?
  - Improved quality of adherence counselling
  - Better drug regimens
  - More extensive ART services

… in settings where national authorities decide to promote and support BF and ARVs to improve HIV FS in exposed infants …

Which breastfeeding practices and for how long?

Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

When HIV-infected mothers decide to stop breastfeeding (at any time) they should do so gradually within one month

---

- 12 months represents the duration for most HIV-infected mothers that capitalizes on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In the presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection vs. risk

Quality of evidence

- The **quality of evidence** describes the extent to which one can be confident that an estimate of effect or association is correct,
- For the purposes of the GRADE process, evidence is categorized as *high, moderate , low* or *very low*.
- Low, or very low '***quality of evidence***' does not necessarily imply that the studies were conducted poorly but that the data were not perhaps optimal for developing this recommendation.
- Quality of evidence downgraded if:
  - Not a RCT
  - Not designed for outcome of interest (indirectness)
  - Small sample sizes (e.g. feeding of HIV infected infants)
  - Publication bias – few authors on a given subject (e.g. expressed HTBM)
  - Inconsistency between studies
- Evidence from other sources e.g. non-HIV populations can offer strong support

'12 months' or more?

- In the presence of ARV interventions, being able to breastfeed to 12 months avoids many of the complexities associated with stopping breastfeeding and providing a safe and adequate diet without breast-milk to infants 6-12 months of age.
- No evidence of harm to the mother if she continues breastfeeding.

- WHO not confident to recommend, *without any qualification*, for all HIV-infected mothers to breastfeed indefinitely, or beyond 12 months to 24 months, unless there were no other options

Preparation of mothers to stop BF

- ✓ Counsellors gave limited practical advice to guide mothers to successfully stop BF early and rapidly

  "*I usually tell them, if it is cold, rainy or sunny, the day you have chosen to stop BF, it is THE day when you stop BF once and for all.*" (PMTCT counsellor, 23 years)

  "*We just tell them that when the baby is crying you have to try by all means to give formula or just anything to him/her.*"
  (PMTCT counsellor, 22 years)

Ad hoc feeding plans

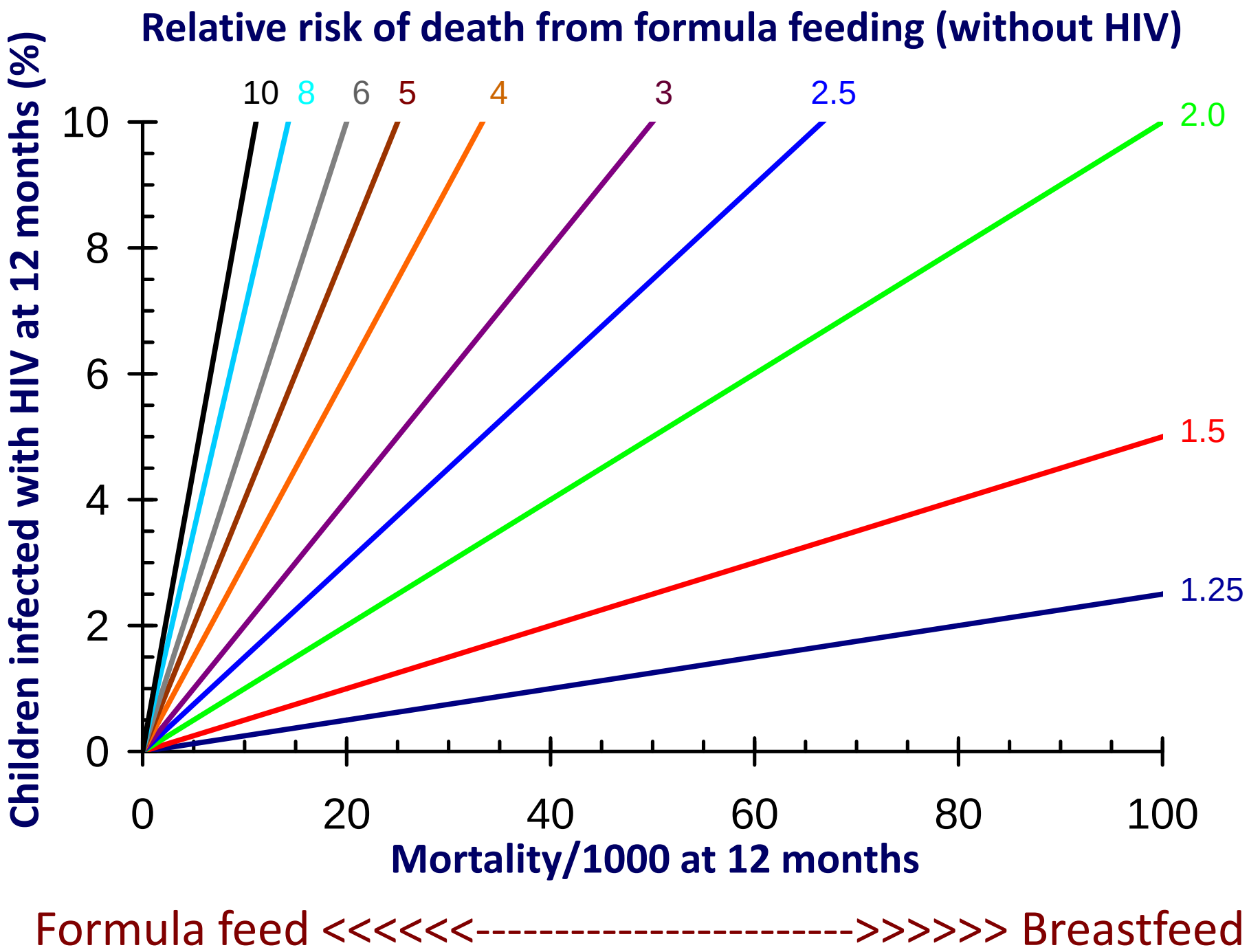
"*I will stop BF tomorrow afternoon. But, I do not know what to feed the twins. I am not sure how to go about it. I will take a chance and ask my sister to give 'something'. I have not disclosed to her, but I had told her that I was only going to BF for 6 months and then I would get free milk from the clinic. My sister has a job, and I do not think that she will refuse me money as there is no milk at the clinic.*

I will not ask the father of the babies. We are not on good terms since I disclosed my HIV-status to him. When I ask him for money he gets upset."

(Mother, 23 years)

Probability of HIV infection or death by maternal status, ART/ARV intervention and infant feeding practice *among infants who are HIV uninfected at birth*

Infant Feeding scenario #	Mothers fulfil eligibility criteria and on ART			Mothers do not fulfil criteria for ART. Infant NVP prophx. or maternal triple ARV prophx.			Probability of infant HIV infection or death if maternal ART criteria	
	Feeding practice			**Feeding practice**			**CD4 <200**	**CD4 <350**
	0-6m	6-12m	12-18m	0-6m	6-12m	12-18m		
1	RF	RF	RF	EBF	CBF	CBF	0.103	0.100
2	RF	RF	RF	EBF	CBF	RF	0.101	0.097
3	RF	RF	RF	EBF	RF	RF	0.107	0.101
4	RF	RF	RF	RF	RF	RF	0.141	0.141
5	EBF	CBF	CBF	EBF	CBF	CBF	0.095	0.099
6	EBF	CBF	RF	EBF	CBF	RF	0.091	0.094
7	EBF	RF	RF	EBF	RF	RF	0.097	0.099
8	EBF	CBF	RF	RF	RF	RF	0.128	0.137
Where CD4 count is unknown								
9	RF	RF	RF	RF	RF	RF	0.141	0.141
10	EBF	CBF	CBF	EBF	CBF	CBF	0.174	0.174



Formula feed <<<<<<----------->>>>>> Breastfeed

Convergence of recommendations and benefits

- Major opportunity to improve maternal and child HIV-free survival
- 'Cost' of implementing all three guidelines outweighs the 'cost' of not introducing the revisions
  - Cost of infections averted vs. lifetime gains
- Effective PMTCT enables care and treatment to be delivered to children who still become infected
- Simplified messages provides the best opportunity in 20 years to promote the best infant feeding practices for both HIV-infected and uninfected mothers and their infants without compromising safety

Guidance to countries

- Review position/policies
  - Review the evidence
  - Assess type of epidemic
  - Assess contribution of infectious diseases and malnutrition to infant mortality and potential impact of safer BF on HIV-free survival
  - Assess quality and coverage of PMTCT/ART services
  - Consider financial and human resource costs of options
  - Formulate national infant feeding and HIV strategy

Guidance to countries

- Review position/policies
  - Review the evidence
  - Assess type of epidemic
  - Assess contribution of infectious diseases and malnutrition to infant mortality and potential impact of safer BF on HIV-free survival
  - Assess quality and coverage of PMTCT/ART services
  - Consider financial and human resource costs of options
  - Formulate national infant feeding and HIV strategy
- Plan implementation
  - Advocacy to health care workers, health professionals and communities to gain confidence for support in implementation
  - Training, commodities,
  - Local prototypes and plan for scale-up
  - Identify what national materials need to be revised
  - Funding applications e.g. Global fund

Programmatic/Protocol questions

- What is the rationale for extending ARV prophylaxis to 12 m when the research data only provides evidence up to 6 months?
- How would mothers respond to recommendations other than default formula feeds?
- Are there consequences of breastfeeding for maternal health?
- How would a breastfeeding/ARV approach relate to the national policy on IYCF?
- How would a decision to support BF and ARVs translate into approaches in clinics and hospitals – initial messages / support provided?
- What support is needed beyond clinics to improve infant feeding practices?
- How should 'success' of HIV/PMTCT interventions be defined?

What is the rationale for extending ARV prophylaxis to 12 m when the research data only provides evidence up to 6 months?

- Linear relationship between exposure to ARV interventions (0-6m) and protection
  - Once interventions stopped, the risk of transmission reverted to higher rate
  - No indication of reduced protection over time
- No increase with AEs with longer ARV exposure
  - NVP SEs occur early
  - Kesho Bora and observational studies report very low AEs
- NVP – dose used as prophylaxis to infants is lower than the dose used as ART to infants already infected
- Potential gains significantly outweigh any likely adverse outcome
- Quality of drugs (efficacy and AE profiles) and cost will improve over time

How would mothers respond to recommendations other than default formula feeds?

- The effectiveness of ARVs to reduce HIV transmission transforms the landscape in which decision can/should be made;
- In conjunction with the known benefits of breastfeeding to reduce mortality from other causes, an approach that strongly recommends a single option as the standard of care can be justified:
  - Information about options should be made available but services would principally support one approach.

- Consider: "What does the 'reasonable patient' want to hear?"
  - If there is a medical consensus in favour of a particular option, the reasonable patient would prefer a recommendation.

A continuum of options

Confidence in intervention

- Balance of risks between options not clear (equipoise)
- Effective interventions supported by high quality evidence and cost-benefit
- Danger to others if intervention not adhered to

'Counselling' approach

- Non-directive counseling (e.g., genetic testing; medical research)
- Disclosure of all options combined with professional recommendation (e.g., most major medical treatment)
- Disclosure of single option as standard, with notification of right to refuse (e.g., HIV testing)
- Disclosure of single option as standard; right to refuse may be recognized, but patients are not notified of this right (e.g., TB treatment)
- Nonconsensual interventions (e.g., psychotropic medications to stabilize dangerous patients)

Mma bana study

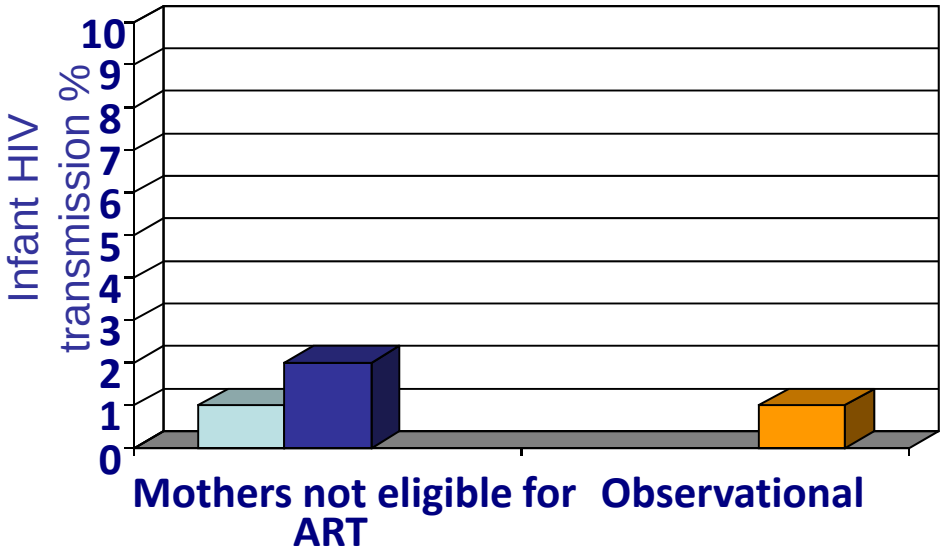
2 randomised arms and one observational

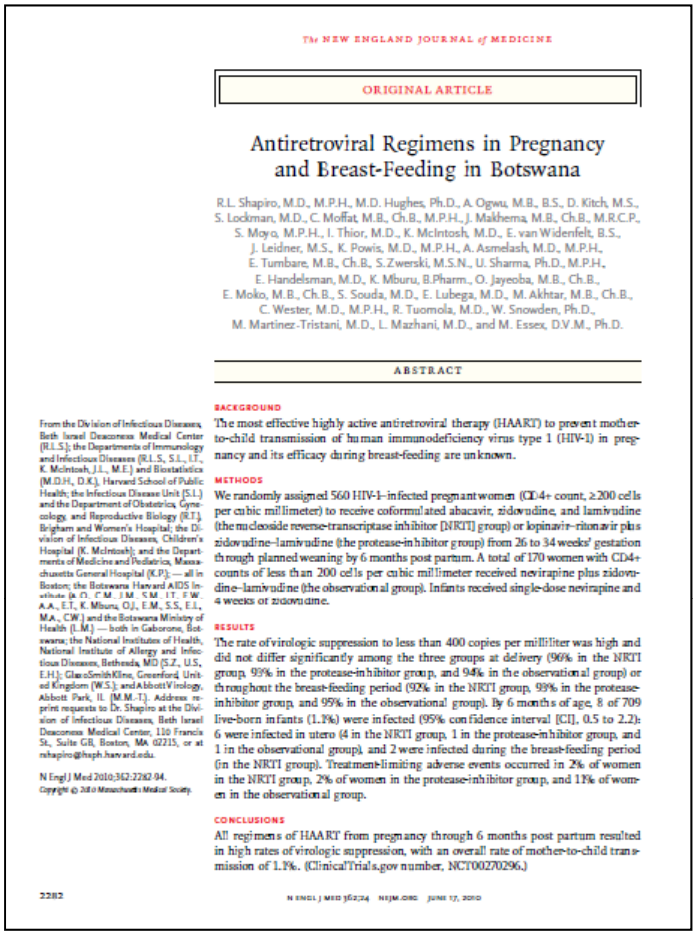
Mothers not eligible for ART received either:

lopinavir/ritonavir and combivir } for 6m

or abacavir/AZT/3TC } while BF

Mothers eligible for ART – outcomes observed





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antiretroviral Regimens in Pregnancy and Breast-Feeding in Botswana

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ABSTRACT

BACKGROUND

The most effective highly active antiretroviral therapy (HAART) to prevent mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) in pregnancy and its efficacy during breast-feeding are unknown.

METHODS

We randomly assigned 560 HIV-1–infected pregnant women (CD4+ count, ≥200 cells per cubic millimeter) to receive coformulated abacavir, zidovudine, and lamivudine (the nucleoside reverse-transcriptase inhibitor [NRTI] group) or lopinavir–ritonavir plus zidovudine–lamivudine (the protease-inhibitor group) from 26 to 34 weeks' gestation through planned weaning by 6 months post partum. A total of 170 women with CD4+ counts of less than 200 cells per cubic millimeter received nevirapine plus zidovudine–lamivudine (the observational group). Infants received single-dose nevirapine and 4 weeks of zidovudine.

RESULTS

The rate of virologic suppression to less than 400 copies per milliliter was high and did not differ significantly among the three groups at delivery (96% in the NRTI group, 95% in the protease-inhibitor group, and 94% in the observational group) or throughout the breast-feeding period (92% in the NRTI group, 93% in the protease-inhibitor group, and 95% in the observational group). By 6 months of age, 8 of 709 live-born infants (1.1%) were infected (95% confidence interval [CI], 0.5 to 2.2): 6 were infected in utero (4 in the NRTI group, 1 in the protease-inhibitor group, and 1 in the observational group), and 2 were infected during the breast-feeding period (in the NRTI group). Treatment-limiting adverse events occurred in 2% of women in the NRTI group, 2% of women in the protease-inhibitor group, and 1% of women in the observational group.

CONCLUSIONS

All regimens of HAART from pregnancy through 6 months post partum resulted in high rates of virologic suppression, with an overall rate of mother-to-child transmission of 1.1%. (ClinicalTrials.gov number, NCT00270296.)

From the Division of Infectious Diseases, Beth Israel Deaconess Medical Center (R.L.S.); the Departments of Immunology and Infectious Diseases (R.L.S., S.L., I.T., K. McIntosh, J.L., M.E.) and Biostatistics (M.D.H., D.K.), Harvard School of Public Health; the Infectious Disease Unit (S.L.) and the Department of Obstetrics, Gynecology, and Reproductive Biology (R.T.), Brigham and Women's Hospital; the Division of Infectious Diseases, Children's Hospital (K. McIntosh); and the Departments of Medicine and Pediatrics, Massachusetts General Hospital (K.P.); — all in Boston; the Botswana Harvard AIDS Institute (A.O., C.M., J.M., S.M., I.T., S.W., A.A., E.T., K. Mburu, O.J., E.M., S.S., E.L., M.A., C.W.) and the Botswana Ministry of Health (L.M.) — both in Gaborone, Botswana; the National Institutes of Health, National Institute of Allergy and Infectious Diseases, Bethesda, MD (S.Z., U.S., E.H.); GlaxoSmithKline, Greenford, United Kingdom (W.S.); and Abbott Virology, Abbott Park, IL (M.M.-T.). Address reprint requests to Dr. Shapiro at the Division of Infectious Diseases, Beth Israel Deaconess Medical Center, 110 Francis St., Suite GB, Boston, MA 02215, or at rshapiro@rhsph.harvard.edu.

N Engl J Med 2010;362:2282-94.

1248 pregnant women referred to study sites. After counselling about study interventions, 110 (8.8%) declined enrolment as preferred to give formula feeds.

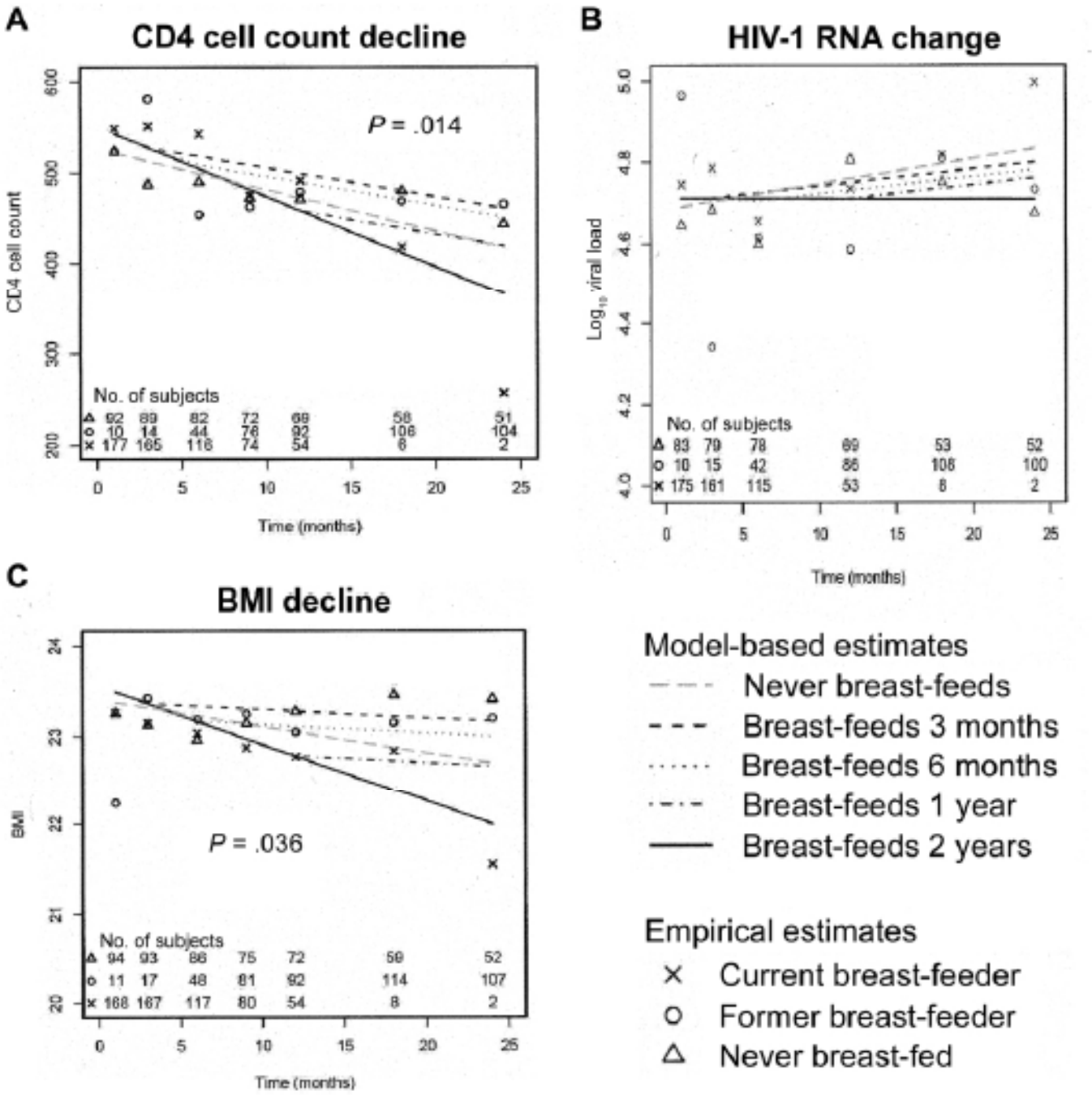
Health and survival of HIV-infected breastfeeding mother

- Data has not demonstrated any increased mortality
- Data reported has been in the context of no ARV interventions – ART or extended ARV prophylaxis
- Kesho Bora – extended triple ARVs through BF period. At 18m, in women who received ARVs
  - Reduced rate of CD4 decline
  - Reduced number of women with clinical progression
  - But, if analyses according to time from stopping ARVs e.g. 12 m after stopping, then no difference in outcomes

HIV infected breastfeeding mothers lost more weight and fat mass than HIV uninfected breastfeeding mothers

	Change between 8 and 24 weeks postpartum		
	HIV positive	HIV negative	p
	n=65	n=41	
Weight Kg (SD)	-1.4 (3.1)	0.4 (3.3)	0.004
BMI Kg/m^2(SD)	-0.54 (2.0)	0.15 (1.3)	0.005

Papathakis P. JAIDS 2006. 33(4)



Otienne et al.
JID 2007

Mortality Among HIV-1–Infected Women According to Children's Feeding Modality

An Individual Patient Data Meta-Analysis

*Breastfeeding and HIV International Transmission Study Group**

Background: Two recent analyses of HIV-1–infected mothers' mortality according to their children's feeding modality have produced conflicting results.

Key Words: HIV-1, mortality, women, breast-feeding, meta-analysis

(*J Acquir Immune Defic Syndr* 2005;39:430–438)

Two prior analyses of HIV-1–infected mothers' mortality according to their children's feeding modality had produced conflicting results.

No difference in mortality in this individual patient meta analysis of 4237 HIV-infected mothers

TABLE 1. Cumulative Probability of Death for HIV-1–Infected Mothers Through 18 Months After Delivery for the Overall Study Population and by Children's Feeding Modality

Months After Delivery	Cumulative Probability of Death (95% CI)*		
	Overall (n = 4237)	Never Breast-Fed† (n = 520)	Ever Breast-Fed (n = 3717)
3	0.6 (0.4–0.8)	0.8 (0.02–1.5)	0.5 (0.3–0.8)
6	1.3 (0.9–1.7)	0.8 (0.02–1.5)	1.4 (1.0–1.8)
9	2.0 (1.5–2.4)	1.7 (0.5–2.9)	2.0 (1.5–2.5)
12	2.9 (2.3–3.4)	2.2 (0.8–3.5)	3.0 (2.4–3.5)
15	3.9 (3.3–4.6)	2.8 (1.2–4.4)	4.2 (3.4–4.9)
18	4.8 (4.1–5.6)	3.3 (1.4–5.1)	5.0 (4.2–5.8)

*Kaplan-Meier method.
†$P = 0.16$ for comparison of the 2 children's feeding modalities.

How would a breastfeeding/ARV approach relate to the national policy on IYCF?

- Simplified messages.
  - All infants can now gain the protection and benefits of breastfeeding
  - If mothers have HIV-infection, then clinics will provide ARV interventions (ART or prophylaxis) that significantly reduce the risk of transmission
  - Mothers who are HIV-infected should breastfeed for 12 m while HIV uninfected mothers should breastfeed for 24m

How would a decision to support BF and ARVs translate into approaches in clinics and hospitals – initial messages / support provided?

Key principle 4.
Informing mothers known to be HIV-infected about infant feeding alternatives

Pregnant women and mothers known to be HIV-infected should be informed of the infant feeding strategy recommended by the national or sub-national authority to improve HIV-free survival of HIV-exposed infants and the health of HIV-infected mothers, and informed that there are alternatives that mothers might wish to adopt;

- This principle is included to affirm that individual rights should not be forfeited in the course of public health approaches.

Key principle 5.
Providing services to specifically support mothers to appropriately feed their infants

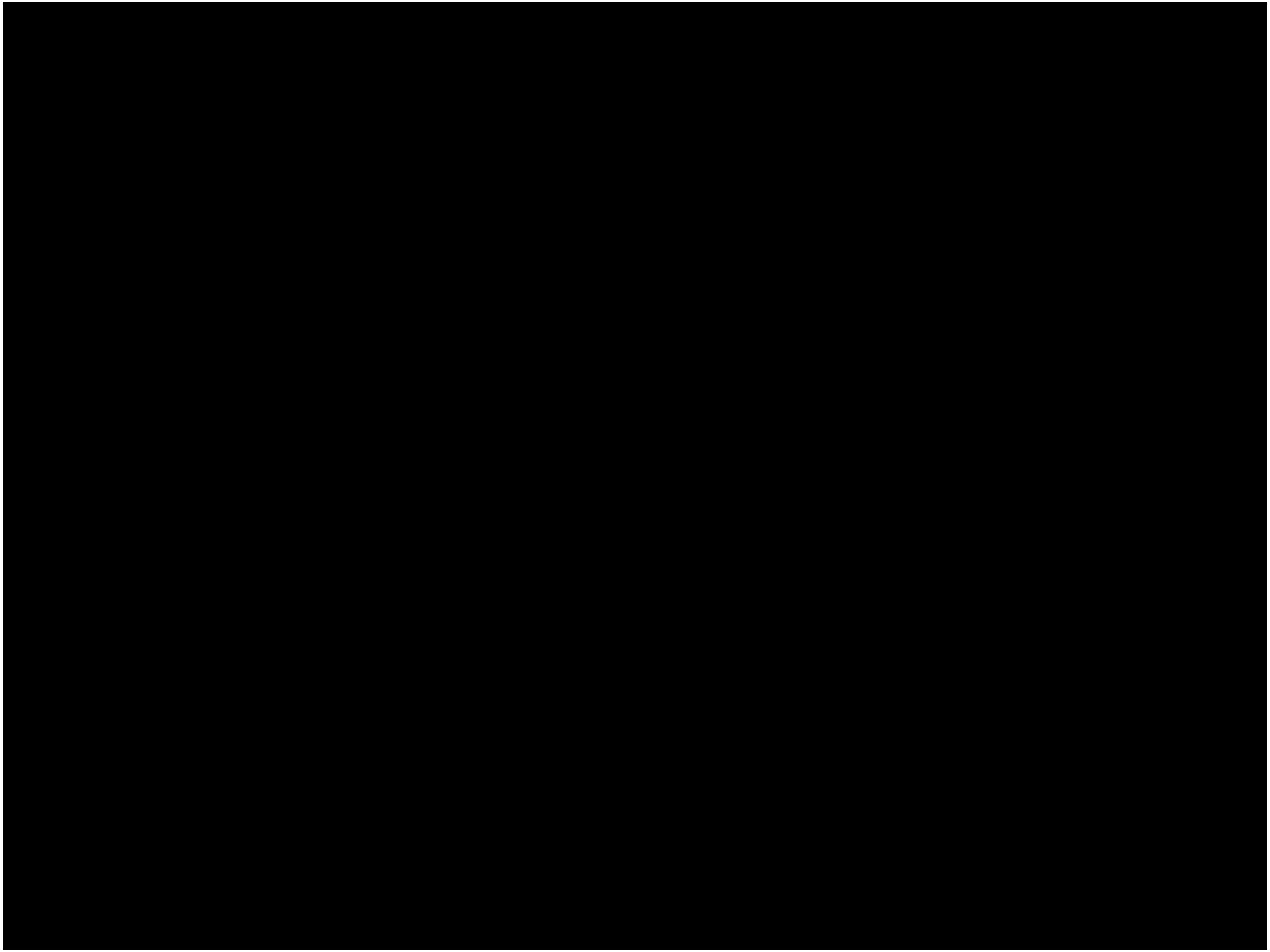
Skilled counselling and support in appropriate infant feeding practices and ARV interventions to promote HIV-free survival of infants should be available to all pregnant women and mothers;

- Recommending a single option within a national health framework does not remove the need for skilled counselling and support to be available to pregnant women and mothers.
- The nature and content of counselling and support that are required will be specified in implementation guides and training courses

Key principle 6.
Avoiding harm to infant feeding practices in the general population

Counselling and support to mothers known to be HIV-infected, and health messaging to the general population, should be carefully delivered so as not to undermine optimal breastfeeding practices among the general population;

- Included to reinforce the protection and promotion of breastfeeding in the general population especially for mothers who are known to be HIV uninfected.
- The application of the International Code of Marketing of Breast-milk Substitutes has particular importance.



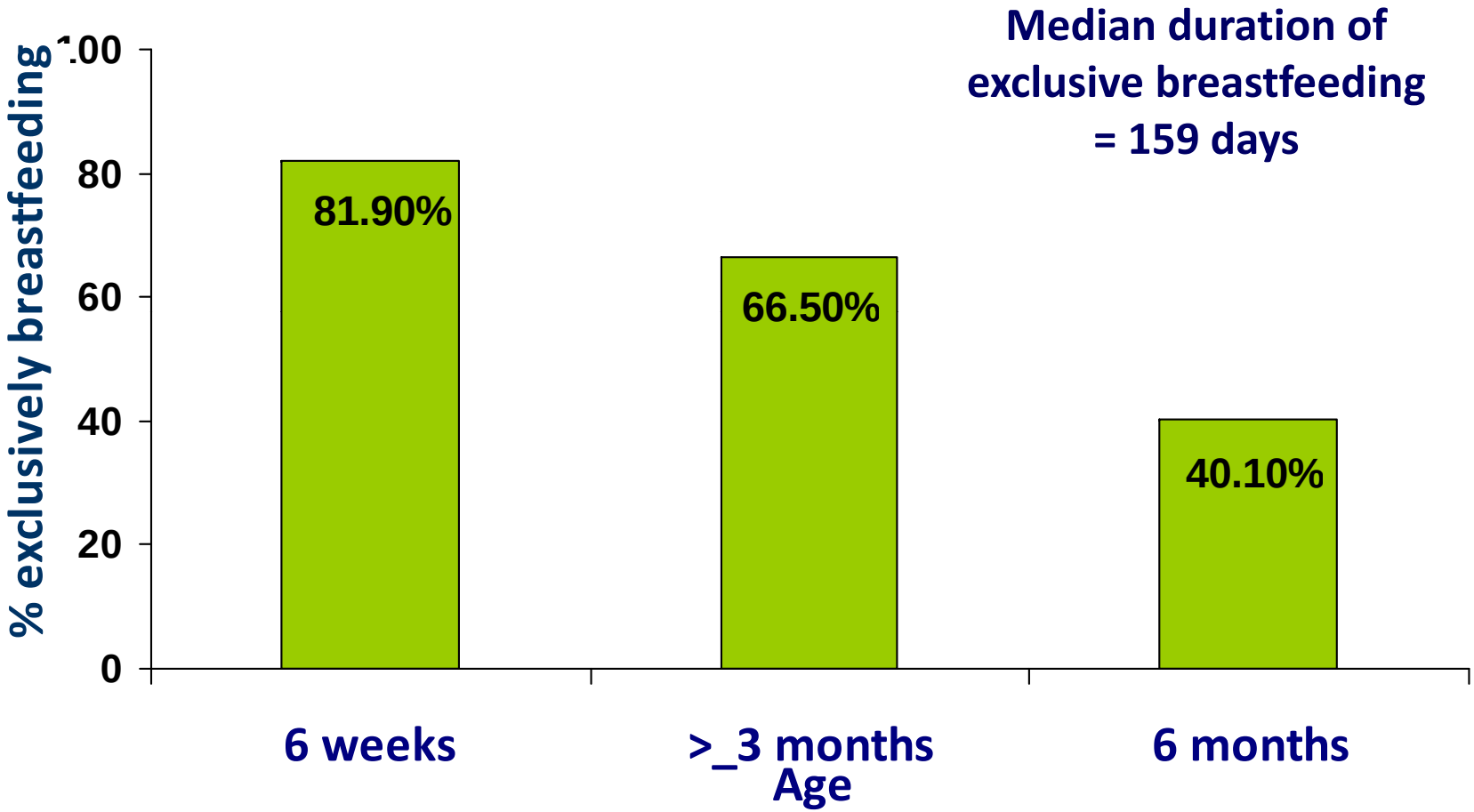
Questions raised at recent workshops

- How would mothers and communities respond to an approach that promotes breastfeeding and ARVs?
- How to give health workers confidence in an approach that promotes breastfeeding and ARVs?
- How can an approach that promotes breastfeeding be promoted when EBF rates are already low?
- How can the impact of PMTCT interventions best be estimated?
- Maternal health and breastfeeding
- Option A vs. option B

What to do when ARVs are not available

- **When antiretroviral drugs are not (immediately) available, breastfeeding may still provide infants born to HIV-infected mothers with the greatest chance of HIV-free survival**
  - Exclusive breastfeeding in the first 6 months of life and continued breastfeeding thereafter remain, even in the absence of ARVs, key infant feeding practices to increase survival among infants born to mothers known to be HIV-infected. While ARV interventions are being scaled up or in exceptional situations such as emergencies, national authorities should not be deterred from recommending HIV-infected mothers to breastfeed as the most appropriate infant feeding practice.
  - Need to avoid the misconception that mothers can only breastfeed if they have ARVs
  - Every effort should be made to accelerate access to ARVs for both maternal health and also prevention of HIV transmission to infants.

Myth: Exclusive breastfeeding for 6 months is impossible



Coovadia et al., *Lancet* 2007