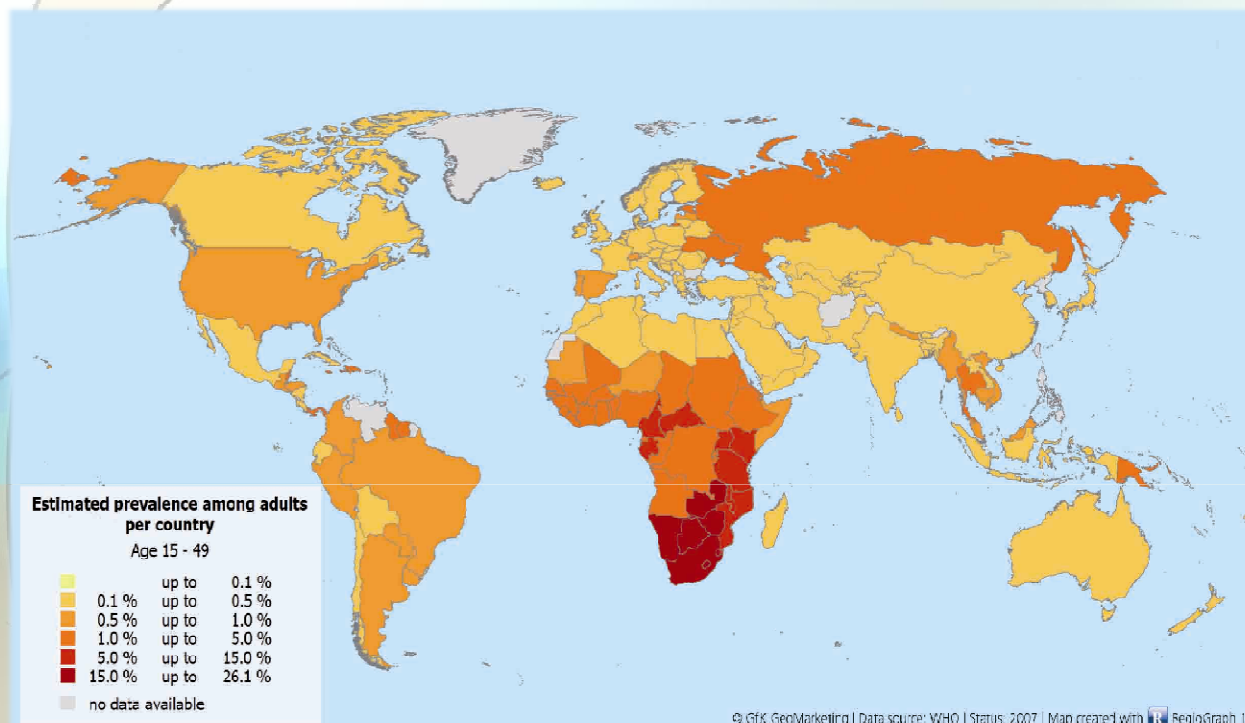


# **Infant feeding in the ARV era**

**Gerhard Theron  
Department of Obstetrics and  
Gynaecology  
Faculty of Health Sciences and  
Tygerberg Hospital**



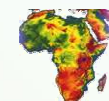
# Global HIV infections: 2007



33 million in world

2011 - 34.2 million

8 million on HAART



22 million in SSA

2011 - 23.5 million



2011

5.7 million in SA

1.7 million on HAART

**12 countries account for  
75% of world's HIV-positive pregnant women**

**South Africa has less than 1% of world's population  
but 17% of HIV infections**

THE NEW AGE  
01-02-2012

# HIV-Aids 'doubles SA death rate'

THE mortality rate in South Africa has more than doubled since 1985 and birth rates have decreased, the SA Institute for Race Relations (SAIRR) said yesterday.

"In 1985, there were 1 060 000 births and 259 000 deaths in South Africa," according to the SAIRR's latest SA Survey.

"In 2011 there were about the same number of births as in 1985, yet more than double the number of deaths (599 000)."

**Deaths due to AIDS  
2009 ~ 310,000**

# SOUTH AFRICA SURVEY 2010/2011



Demographics • The Economy • Employment & Incomes  
Business & Labour • Education • Health & Welfare  
Living Conditions & Communications • Crime & Security  
Politics & Government



South African Institute  
of Race Relations



Unit for Risk Analysis

**Projected impact of HIV/AIDS on the size of the  
South African population<sup>a</sup>, 2000-40**

<i>Year</i>	<i>Without AIDS</i>	<i>With AIDS</i>	<i>Difference</i>
	<i>Millions</i>		
2000	46.2	45.6	0.6
2005	50.6	48.6	2.0
2010	55.0	50.6	4.4
2015	59.4	51.9	7.5
2020	63.7	52.8	10.9
2025	67.6	53.4	14.2
2030	71.3	53.7	17.6
2035	74.6	53.7	20.9
2040	77.5	53.4	24.1

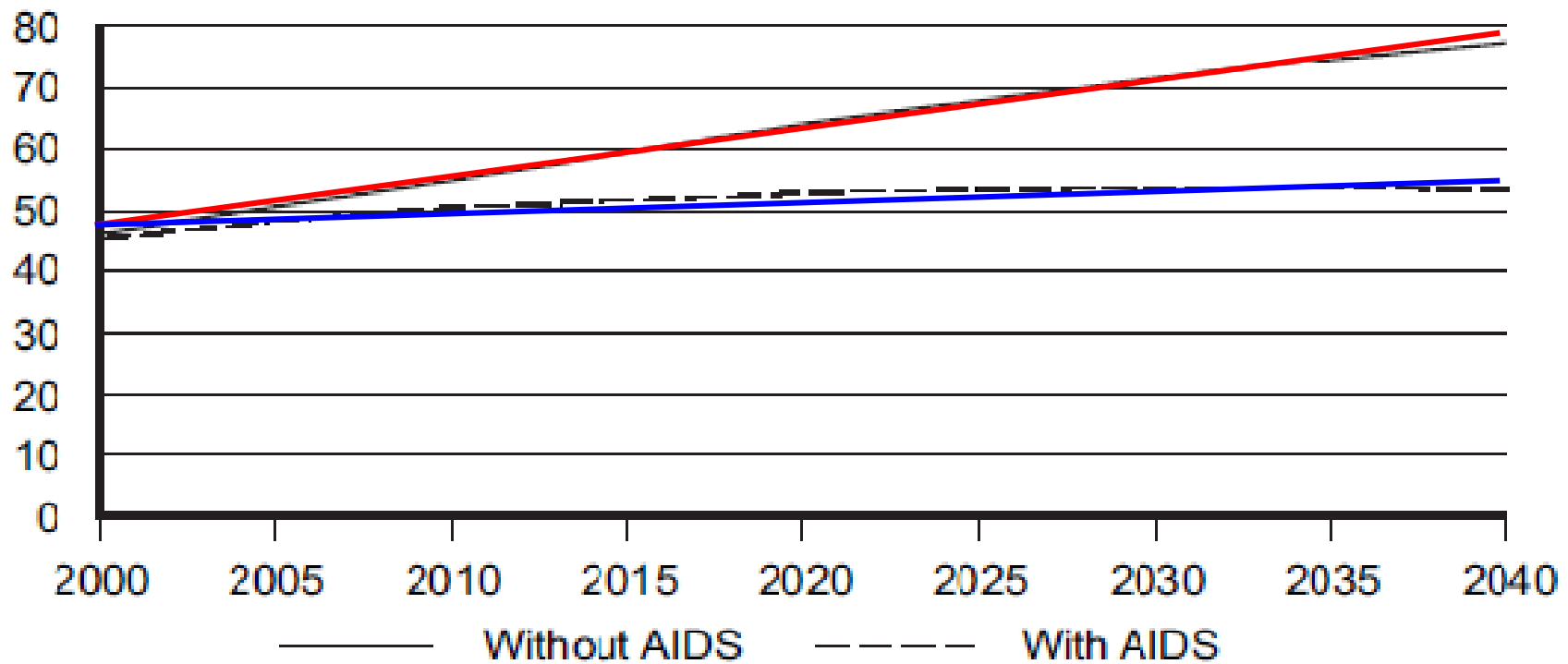
*Source: IFR, Key demographic trends for South Africa to 2040, Vol. 15 No. 2, June 2010, Figure 2, Page 2; Projections of the South African Population, 1985-2040, March 2011, Table A1, p25*

a Numbers are in millions.

Note: For more information on HIV and AIDS, see the Health and Welfare chapter in this Survey.

Projected impact of HIV/AIDS on the size of the South African population, 2000-40

Million



# **Global PMTCT need**

**90% ~ 20 countries**

**High prevalence countries**

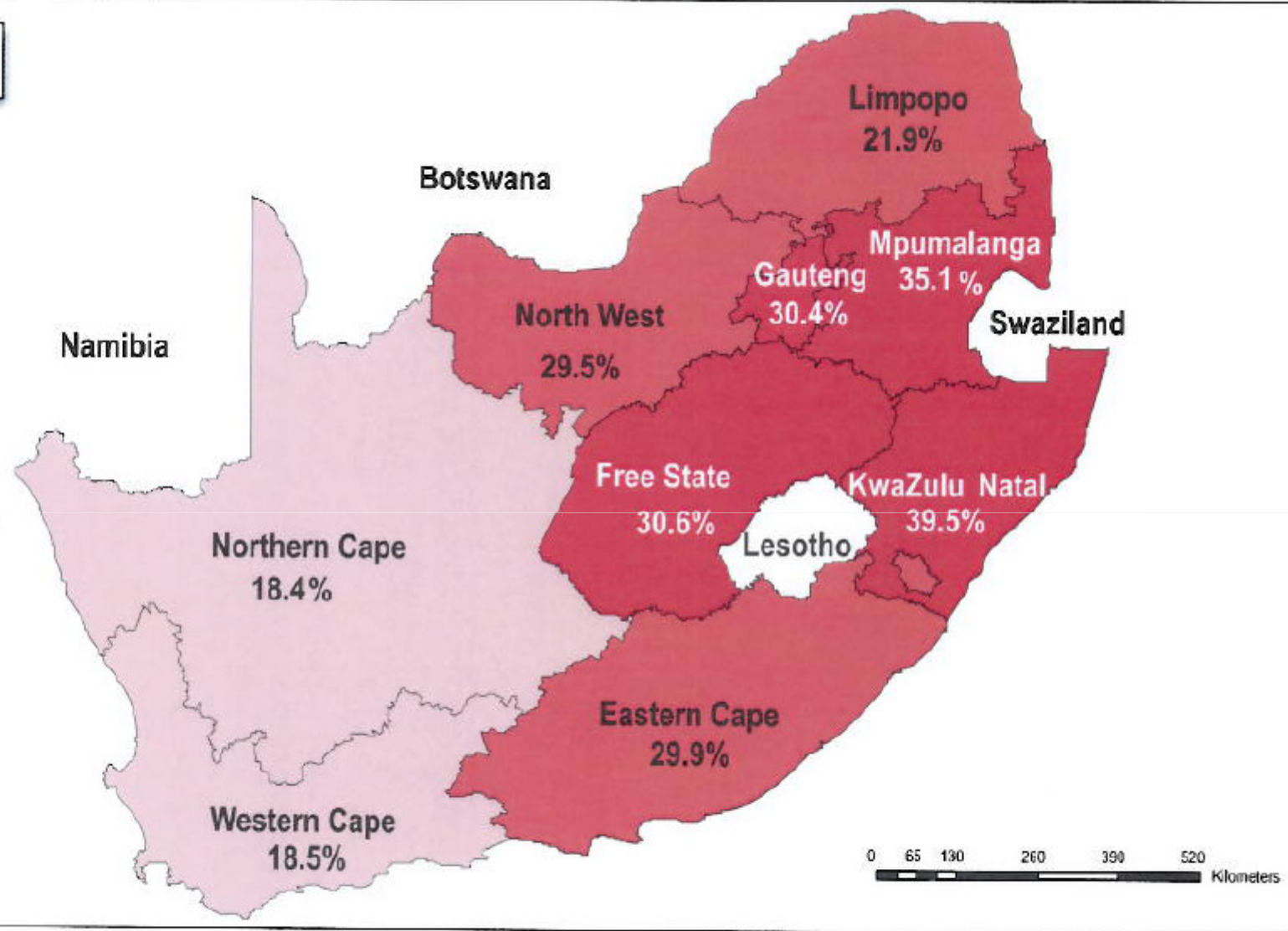
- **Sub-Saharan Africa + India**
- **Rapid scale up**
  - ❖ **effective interventions**
- **National programmes**

## HIV+ pregnant women ARV coverage

<b>Countries</b>	<b>2004 (%)</b>	<b>2007 (%)</b>	<b>2008 (%)</b>
<b>Low to middle income</b>	<b>10</b>	<b>35</b>	<b>45</b>
<b>Eastern + Southern Africa</b>	<b>9</b>	<b>46</b>	<b>58</b>



**2010**

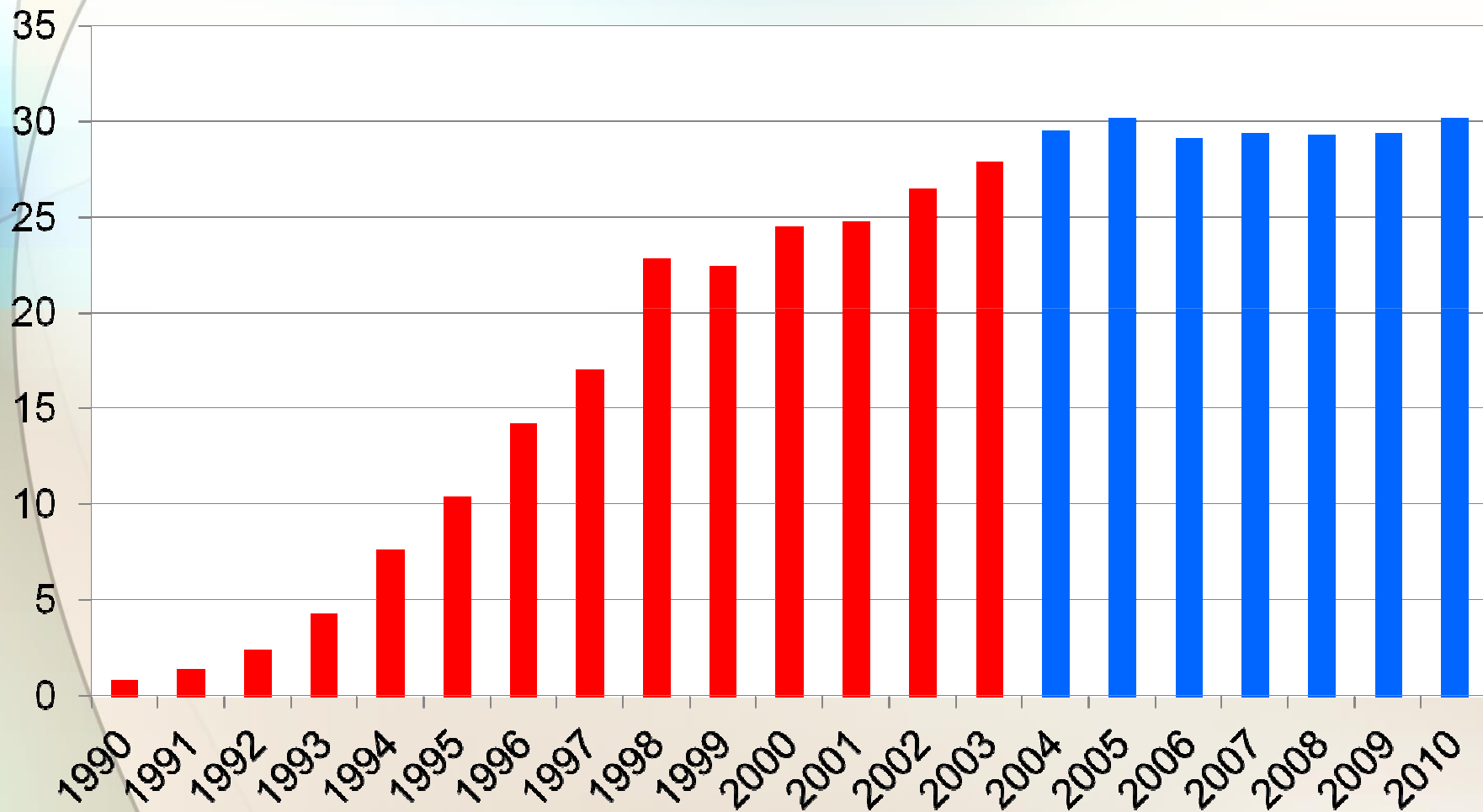


**Figure 5:** HIV prevalence distribution by province, South Africa, 2010

# Prevalence by age group

Age group	2005	2006	2007	2008	2009	2010
<20	15.9	13.7	13.1	14.0	13.7	14.0
20 - 24	30.6	28.0	28.0	26.9	26.6	26.7
25 - 29	39.5	38.7	37.5	37.9	37.1	37.3
30 - 34	36.4	37.0	39.4	40.4	41.5	42.6
35 - 39	28.0	29.3	33.0	32.4	35.4	38.4
40 - 44	19.8	21.3	22.2	23.3	25.6	30.9
45+		15.5	20.6	17.6	23.9	28.2

# Antenatal HIV Prevalence South Africa (%)



# Our Challenge

- **An effective PMTCT programme will reduce the number of perinatal acquired HIV infections**
  - ➔ **This is a goal within reach of the SA Public Health Sector**
- **Key Priority Area 1: SANAC HIV/AIDS & STI National Strategic Plan for 2007 - 2011**
  - ➔ **Scale up coverage + improve quality of PMTCT to reduce MTCT to <5%**

# The Health Specific MDGs

- 4. Reduce child mortality**
  - **Reduce children under 5 mortality by 2/3**
- 5. Improve maternal health**
  - **Reduce maternal mortality by 3/4**
  - **Universal access to reproductive health**
- 6. Combat HIV/AIDS, malaria and other diseases (TB)**

# A Comparison of Primary Obstetric Causes of Death between 1999-2007

Primary Obstetric Cause	1999-2001		2002-2004		2005-2007	
	N	%	N	%	N	%
<b>Direct</b>	<b>1462</b>	<b>59.8</b>	<b>1767</b>	<b>53.6</b>	<b>1819</b>	<b>45.9</b>
Hypertension	507	20.7	628	19.1	622	15.7
Postpartum haemorrhage	240	9.8	313	9.5	383	9.7
Antepartum haemorrhage	100	4.1	129	3.9	108	2.7
Ectopic pregnancy	27	1.1	47	1.4	55	1.4
Abortion	120	4.9	114	3.5	136	3.4
Pregnancy Related Sepsis	210	8.6	274	8.3	223	5.6
Anaesthetic related	76	3.1	91	2.8	107	2.7
Embolism	48	2	64	1.9	57	1.4
Acute collapse	134	5.5	107	3.2	128	3.2
<b>Indirect</b>	<b>939</b>	<b>38.4</b>	<b>1430</b>	<b>43.4</b>	<b>1966</b>	<b>49.7</b>
Non pregnancy related Infections	768	31.4	1246	37.8	1729	43.7
AIDS	416	17	662	20.1	915	23.1
Pre-existing Maternal Disease	171	7	184	5.6	237	6.0
<b>Unknown</b>	<b>44</b>	<b>1.8</b>	<b>99</b>	<b>3</b>	<b>174</b>	<b>4.4</b>
<b>Total</b>	<b>2445</b>	<b>100</b>	<b>3296</b>	<b>100</b>	<b>3959</b>	<b>100</b>
Coincidental	45		110		118	

# National PMTCT - 2010

## Antenatally

- **1<sup>st</sup> visit - PIT & C + HIV rapid testing**
  - HIV+ posttest counseling
  - CD4 count
- **2<sup>nd</sup> visit ONE week later**
  - infant feeding options
- **CD4 count**
  - > 350/ $\mu$ l + stage 1 or 2**
- **AZT 300mg 2/day 14 wks  $\Rightarrow$  labour**
  - $\leq$  350 / $\mu$ l  $\pm$ 30% or stage 3 & 4**
- **HAART (ART clinics)**

# National PMTCT - 2010

**Intrapartum** - knowledge of status

**sdNVP 200mg + AZT 300mg 3hrly**

**Neonataly**

**>2kg NVP 0.6 ml at birth + daily ⇨ 6 wks**

- **Formula / exclusive breast feeding**
- **BF continue NVP ⇨ 1 wk after weaning  
for dual therapy group**
- **Follow-up: 6wks co-trimoxazole**
- **PCR at 6 weeks**



## **PMTCT ~ Questions**

- **HAART vs dual therapy CD4 >350?**
- **Neonatal PEP ~ mothers no ARVs?**
- **NVP resistance?**
- **Protease inhibitors and preterm labour?**
- **BF and ARV prophylaxis?**
- **Present transmission rates?**

## Option B+

**WHO Programmatic update – April 2012**

- **HAART regardless CD4 count for life**
- **Single pill fixed dose – TDF/3TC/EFV**
- **USD 180/yr**

**Motivation – E Schouten, Lancet, July 2011**

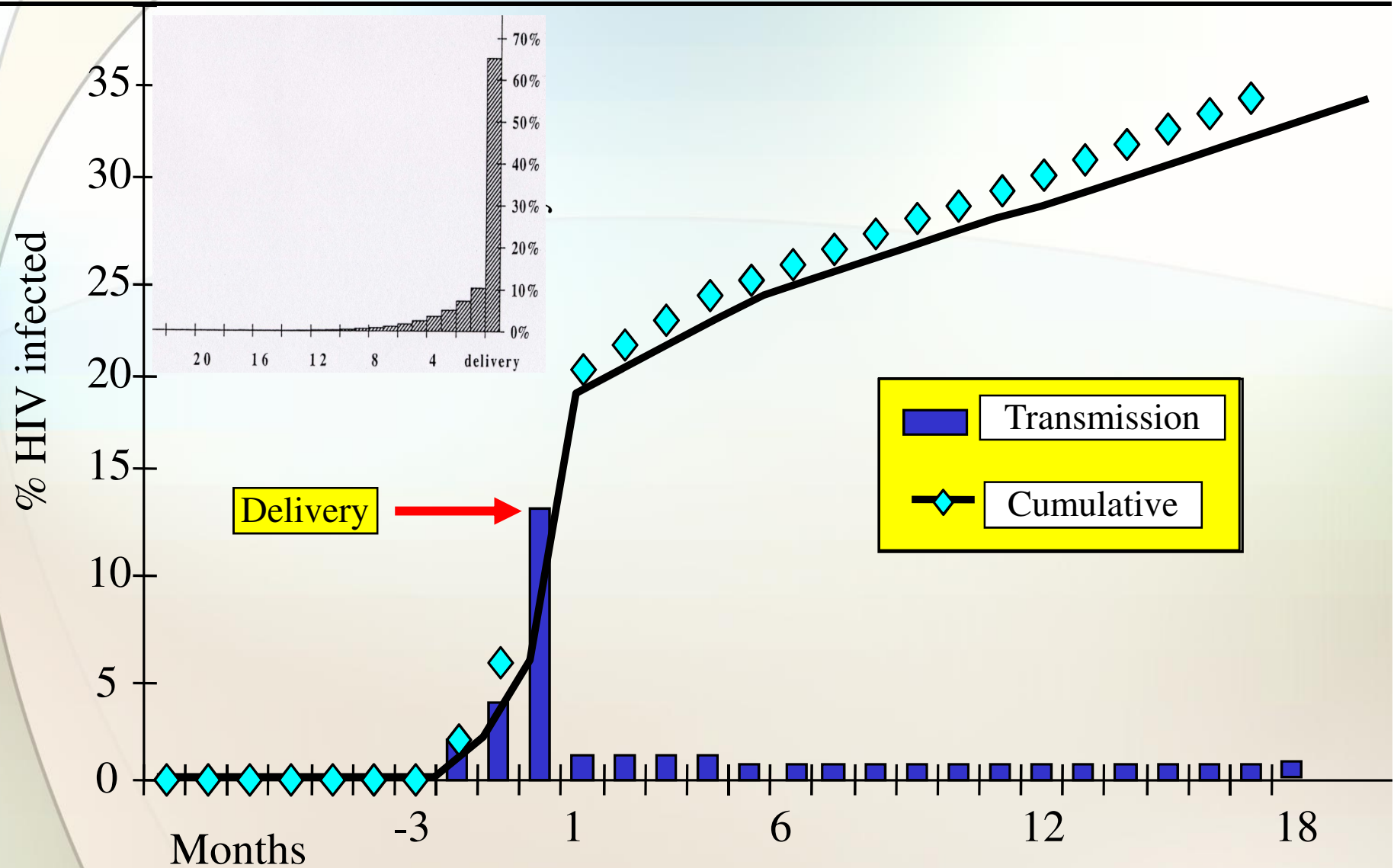
- **# CD4 count often not possible**
- **Death rate HIV+ CD4 >350 ~ <24 mths**
- **6 fold↑ ~ Zimbabwe vs HIV neg**  
{AIDS 2010 JW Hargrove}
- **2 - 3 yrs ~ research results not ethical**

## Concerns - Option B +

### EFV exposure – 1<sup>st</sup> trimester

- **Ford et al AIDS 2011**
    - ❖ **EVF vs non-EFV based regimens**
    - ❖ **RR 0.85 (95% CI 0.61 – 1.20)**
  - **Knapp et al Pediatr Infect Dis J 2012**
    - ❖ **Prospective studies (P1025)**
    - ❖ **47 1<sup>st</sup> trim expos 6 (12.8%) cong abn**
- ### TNF-containing HAART
- **Siberry et al AIDS 2012**
    - ❖ **↓ length of age + head circum at 1yr**

# Timing of HIV Transmission – pre ARV era



**4% Transmission of HIV for every 6 months of breast-feeding**

# ARV's + PMTCT

**Transmission remains significantly higher**

- **↑ viral load**
- **Vaginal delivery vs C/S prior to onset of labour**
- **Preterm delivery**

## Protease inhibitors + preterm labour

- Tuomala et al\* ~ 7 PACTG studies
- N = 2173

HAART	Without PI n = 396 (%)	With PI n = 137 (%)	P-value
LBW <2500g	41 (11)	27 (20)	0.009
<32 weeks	10 (3)	6 (4)	0.17
CD4 <200	28%	43%	

- HAART + PI ~ more advanced disease?
- European Collaborative Group # NS

\*NEJM 2002

# CID 2005

# HAART + preterm labour

## More recent studies (BJOG Oct 2010)

- 1.4 – 3.4 increased risk
- Dual therapy vs HAART  
(HAART containing PIs ↑ risk)
- Lack of control of cofounders ~  
comparisons difficult
- Possible mechanism
  - ❖ Reversal TH1 + TH2 cytokine switch
  - ❖ TH2 cytokines IL10 + IL4 maintain  
fetal allograft

# Infants exposed to maternal sdNVP

## Lockman et al\*

- **Maternal sd NVP exposed infants**
  - **1° end point ~ at 24 weeks**
  - **Virologic failure or death**

<b>Trial 1 ~ n 241</b>	<b>End point (%)</b>	<b>HR (95% CI)</b>
<b>PI# + Truvada</b>	<b>10 (8)</b>	<b>3.6 (1.7 – 7.5)</b> <b>p 0.001</b>
<b>NVP + Truvada</b>	<b>32 (26)</b>	

**\*NEJM Oct 2010**

**#ritonavir-boosted lopinavir**

**24 months post NVP exp (n 65) HR 1.3 (0.3 – 6.1)**



# NVP naïve infants

## Lockman et al\*

- **Not exposed to maternal sd NVP**
  - **1° end point ~ at 24 weeks**
  - **Virologic failure or death**

<b>Trial 2 ~ n 452</b>	<b>End point (%)</b>	<b>HR (95% CI)</b>
<b>PI# + Truvada</b>	<b>12.3</b>	<b>3.6 (1.7 – 7.5)</b> <b>p 0.001</b>
<b>NVP + Truvada</b>	<b>28.6</b>	

**\*NIAID Web Bulletin Nov 2010**

**#ritonavir-boosted lopinavir**

# Policy on infant + young child feeding

- 2010 WHO Guidelines
  - ~ promotes breast feeding
- August 2011 – adopted by SA

HIV Infection

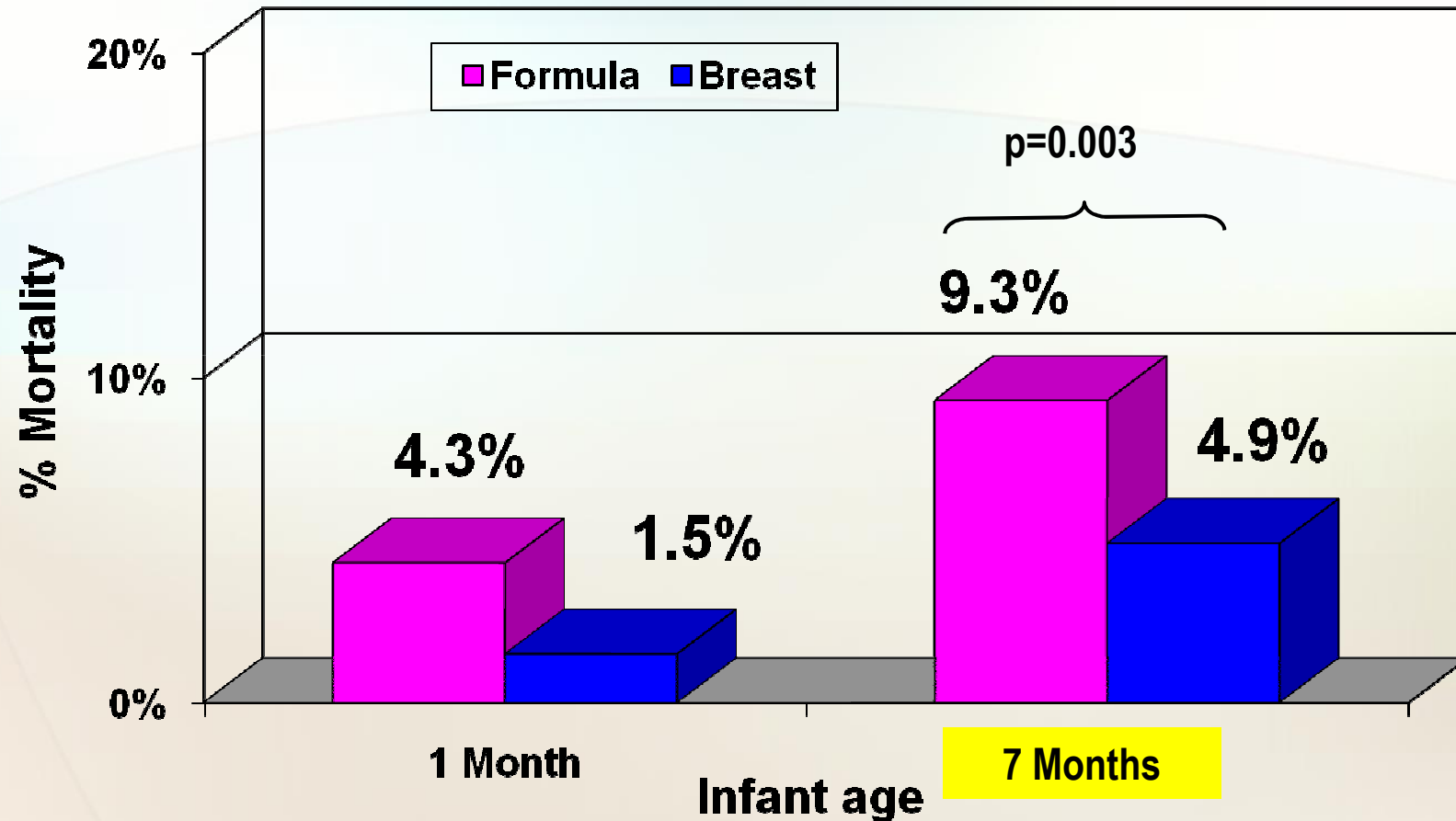


Mortality



Balancing Act

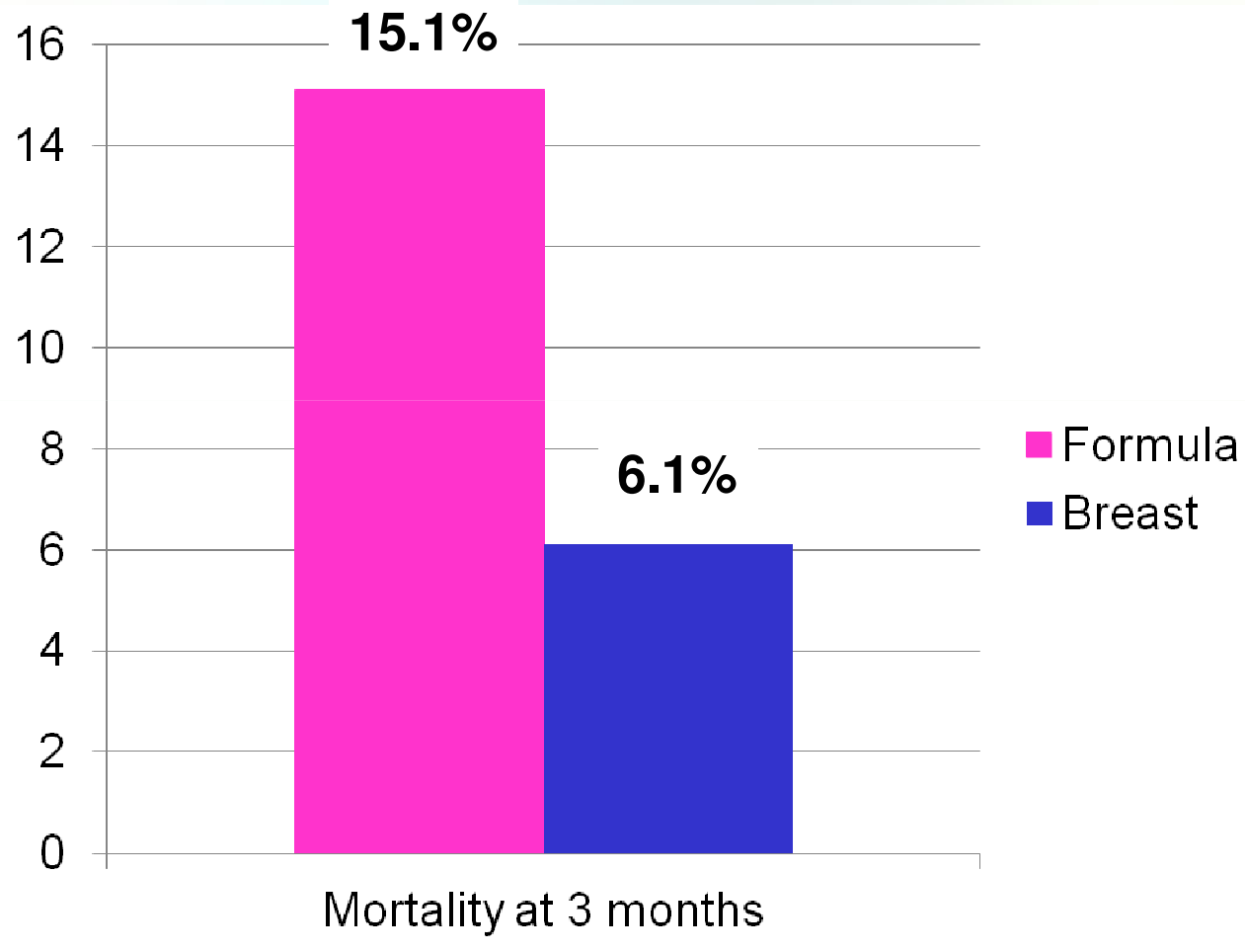
# Mortality through Age 7 Months is Higher in Formula Fed than Breast Fed Infants



Main causes infant death: diarrheal disease + pneumonia  
Death of HIV+ by 18 months  $p=0.6$  Mashi study JAMA 2006

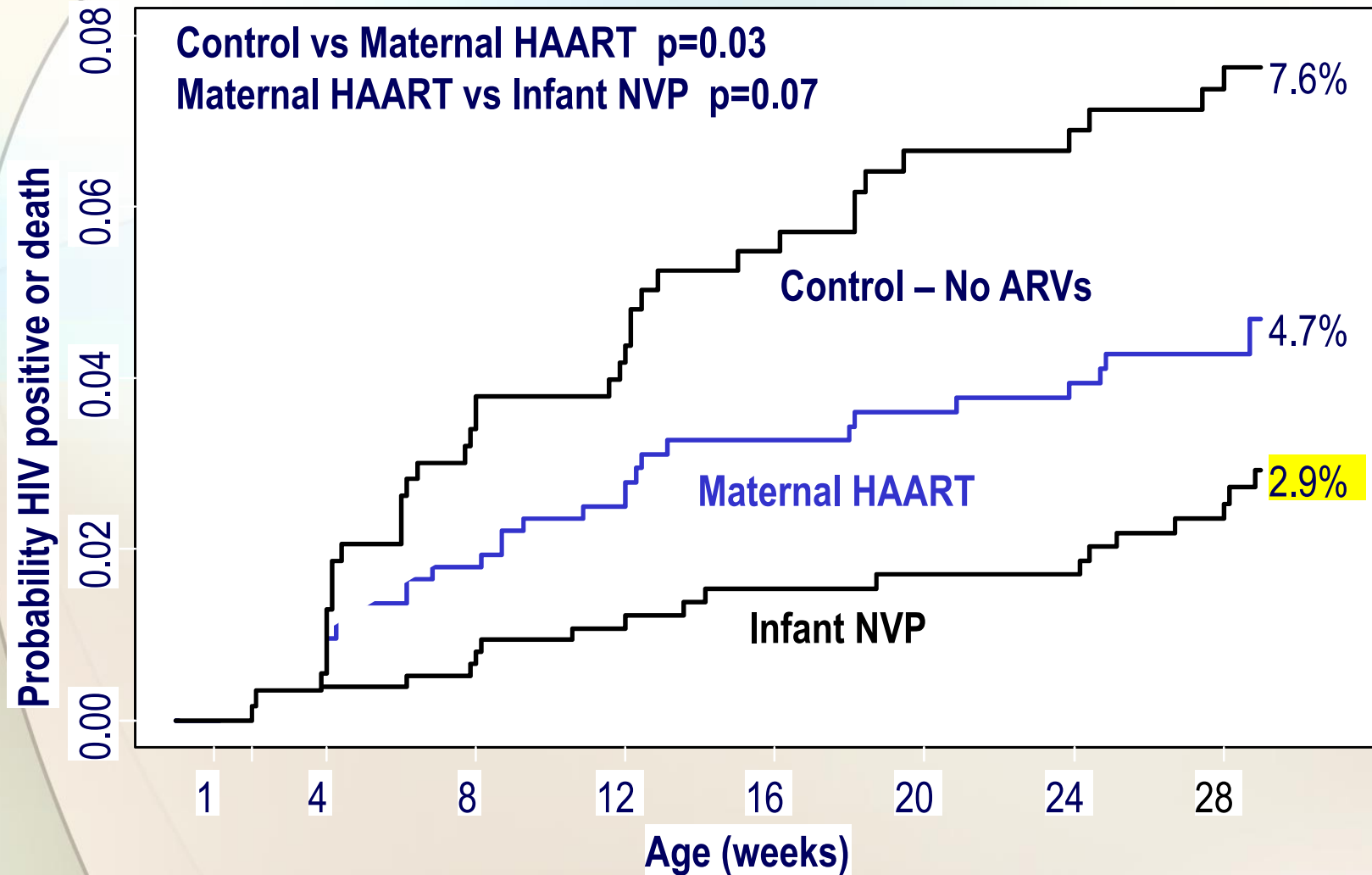
# KwaZulu Natal Clinics

7 rural, 1 semi urban, 1 urban ~ Lancet 2007



**p=0.051 HR 2.1 (1.0 – 4.3)**

# BAN\* Study: Probability of HIV+ or Death by 28 week visit in infants uninfected at birth



\*NEJM 2010

# Cost analysis

## WHO analysis ~ southern Africa

- Cost per 10,000 HIV + mothers
- CD4  $\leq$ 350 HAART
- CD4  $>$ 350 Dual therapy

<b>Breastfeeding</b>	<b>US\$ 522,542</b>
<b>Formula milk for 6 mths</b>	<b>US\$ 2,063,100</b>

# **Prevention of postnatal transmission HPTN 046**

## **Safety and efficacy**

**Once day NVP extended ⇒ 6 months**

- SA, Tanzania, Uganda + Zimbabwe**
- HIV neg 6 wks ⇒ HIV + at 6 months**
- 1527 infants randomised**
- Lancet Dec 2011**

# HPTN 046 - results

6 months	Extended NVP	Placebo	Rel RR	P value
All patients*	8/700 1.1%	18/699 2.4%	54% ↓	0.049
On HAART ~ CD4	1/210 0.5%	0/203 --	--	--
No HAART ~ CD4*	7/490 1.3%	18/492 3.4%	62% ↑	0.027
≥CD4 no HAART#	3/418 0.7%	13/434 2.8%	75% ↓	0.014
<CD4 no HAART	4/71 4.8%	5/54 8.1%	41% ↓	0.44

\*Not sustained through to 9 and 12 months

#Sustained through to 9 but not to 12 months



# HPTN 046 - results

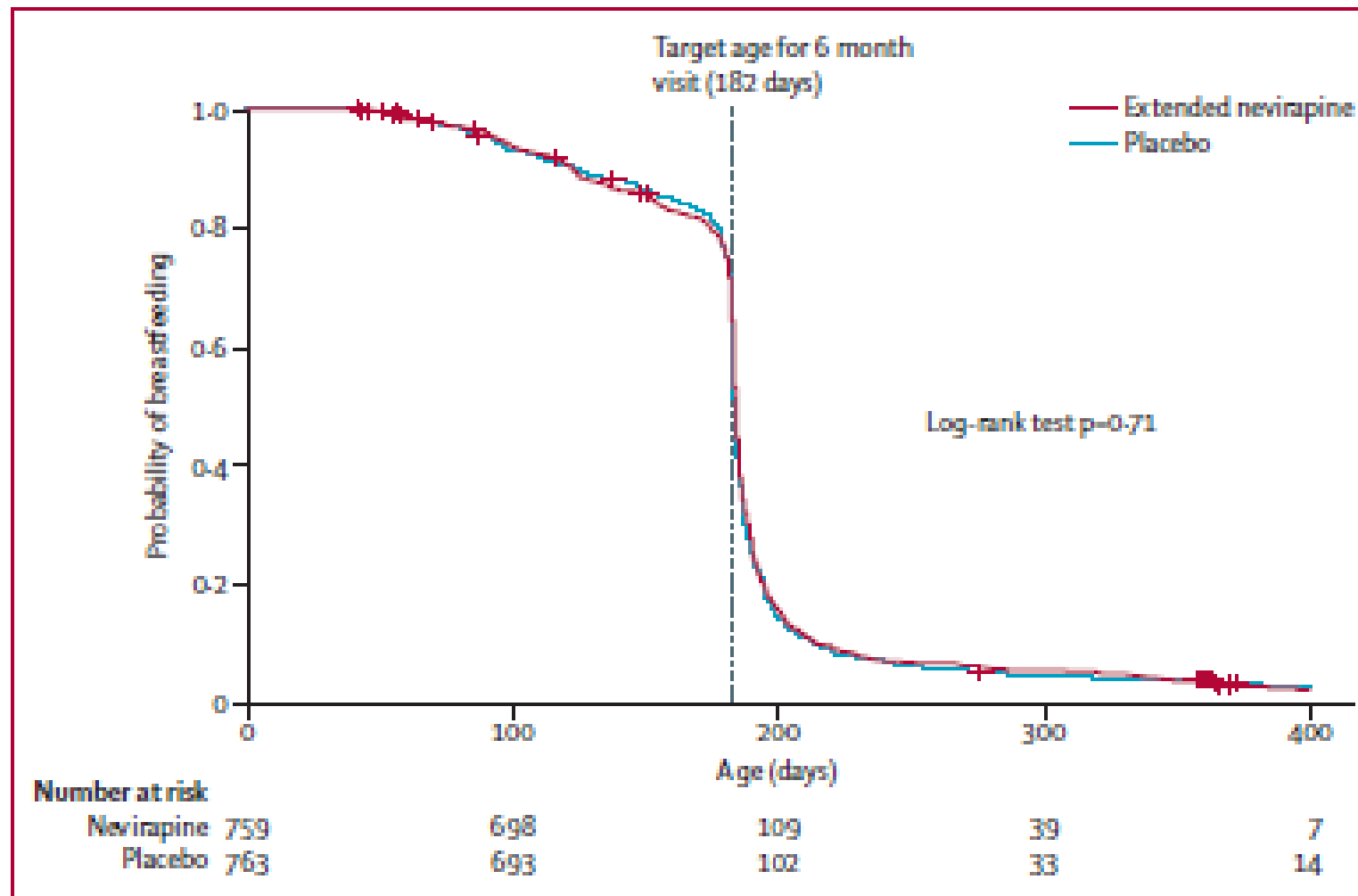


Figure 2: Kaplan-Meier analysis of breastfeeding duration, by study group

## HPTN 046 – Adverse events

<b>Adverse events</b>	<b>Overall</b>	<b>Ext NVP</b>	<b>Placebo</b>	<b>P value</b>
<b>Possibly related*</b>	<b>169 (11%)</b>	<b>87 (12%)</b>	<b>82 (11%)</b>	<b>0.66</b>
<b>Neutropenia</b>	<b>249 (19%)</b>	<b>161 (21%)</b>	<b>133 (18%)</b>	<b>0.07</b>
<b>↑ ALT</b>	<b>6 (&lt;1%)</b>	<b>3 (&lt;1%)</b>	<b>3 (&lt;1%)</b>	<b>1.00</b>
<b>Anaemia</b>	<b>354 (23%)</b>	<b>188 (25%)</b>	<b>166 (22%)</b>	<b>0.18</b>

\* **Rash**

# Suppression of lactation

## ZEB study (AIDS 2006)

- **Viral load – breast milk (median)**
  - pre-weaning 353 copies/ml
  - post-weaning 15822 copies/ml
- **Breast engorgement**
  - duct endothelium damage
  - ↑ viral load in milk

# Suppression of lactation

- **Bromocriptine (Parludel) 2.5 mg tab**
  - ❑ 2.5mg 2/day 7 days - R41.16
- **Carbocoline (Dostinex) 0.5 mg tab - R70.50**
  - ❑ 1 mg as single dose postpartum
  - ❑ 0.25 mg 2/day 2days
- **Problem**
  - ❑ expensive
  - ❑ level 2 and 3 hospitals only
- **Contra-indicated with hypertension**

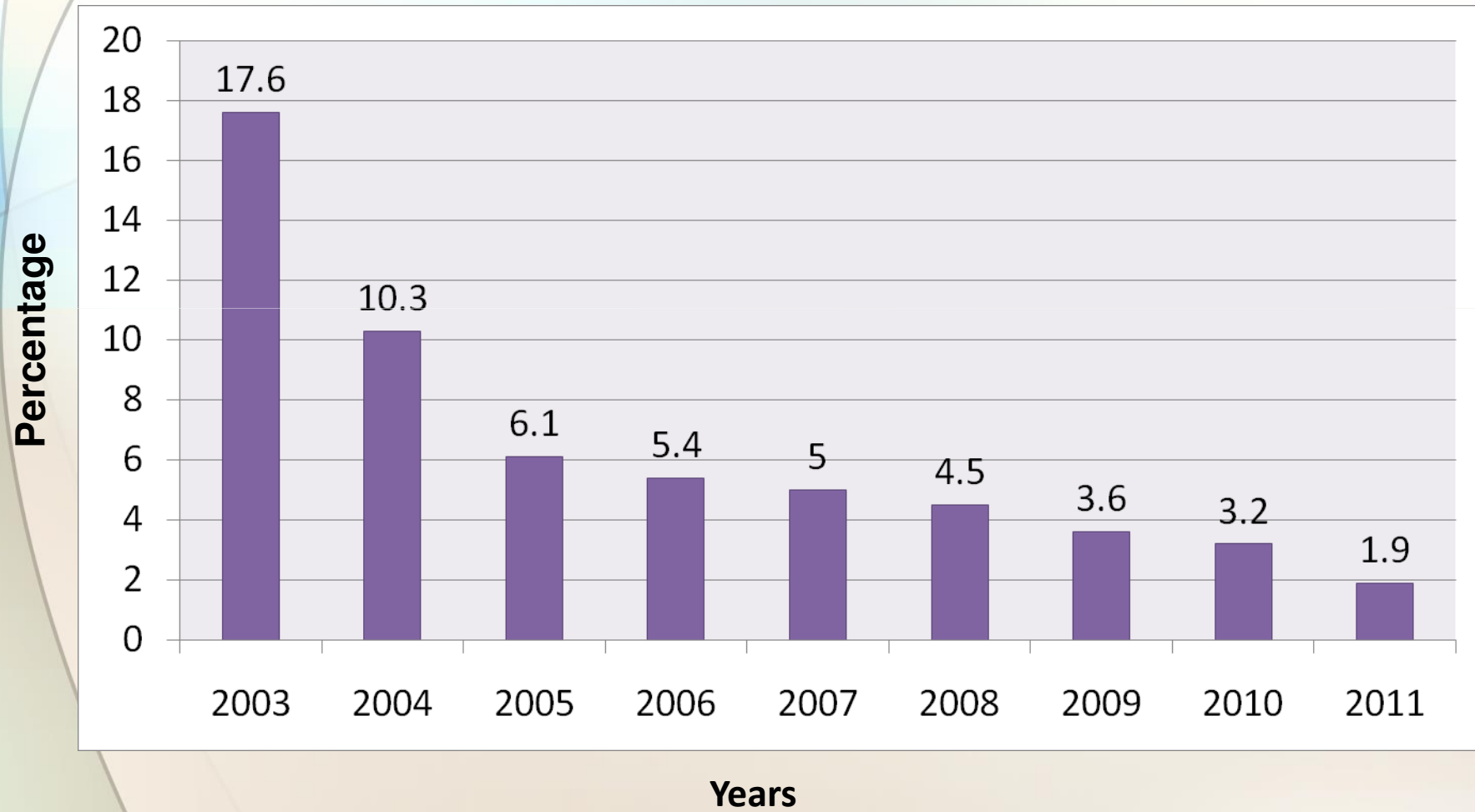
# Practical option

- **Non-pharmacologic method**
  - advice**
    - ❖ **don't resume!**
  - rapid weaning**
  - milk out until comfortable**
  - moderate compression**
- **Piridoxine** **×**

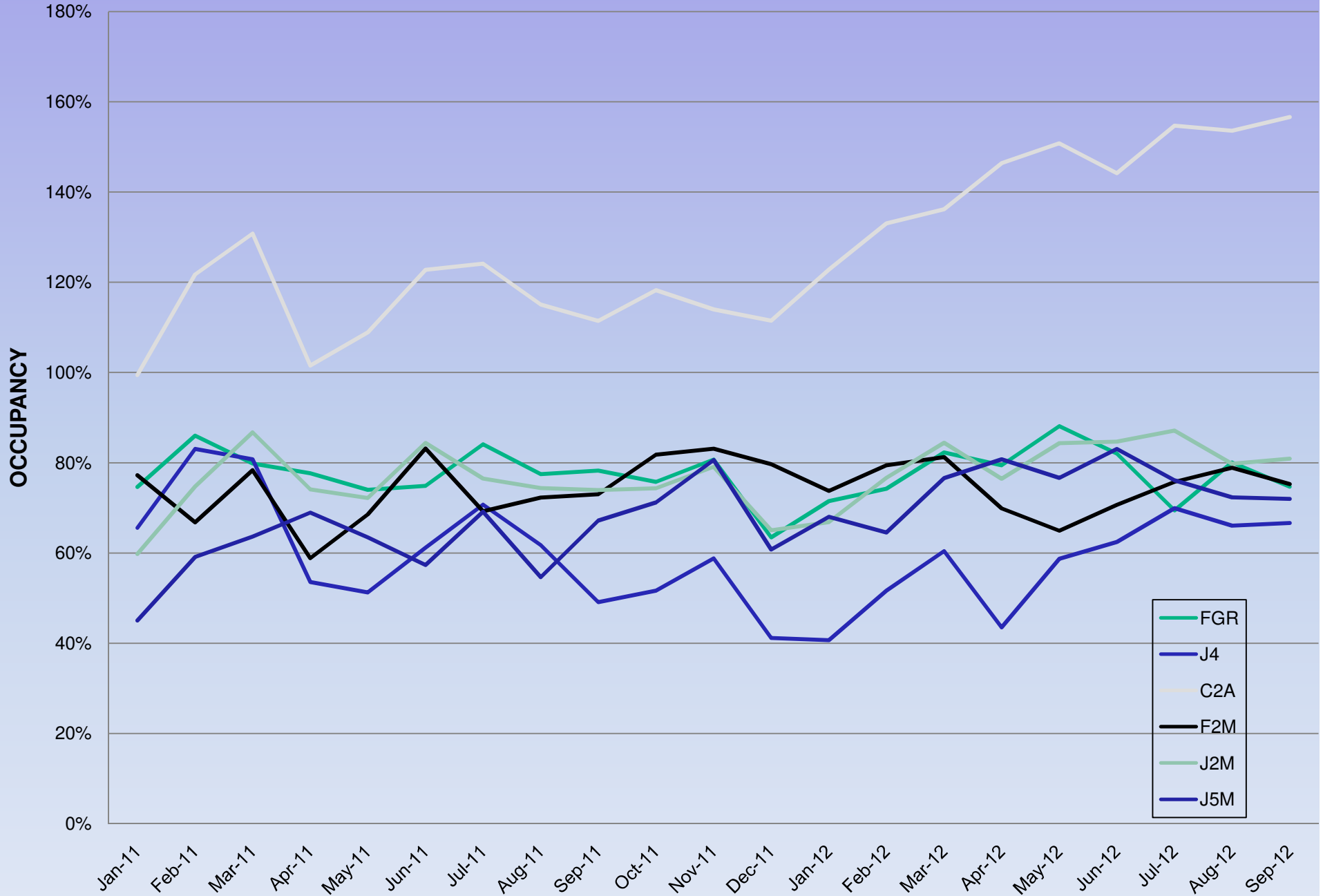
## Preterm infants - TBH

- **Large neonatal service**
- **High preterm delivery rate**
  - ❖ **Obstetric beds 107**
  - ❖ **Neonatal high care beds 140**
- **Mother's milk always used**
  - ❖ **Pasteurised if HIV+**
  - ❖ **Kangaroo care**
- **Mother's choice at discharge respected**

# Transmission Rate: W Cape



# BED OCCUPANCY RATE (BOR)





## World AIDS Day 2009:

“It is the time to act decisively,  
and to act together.”

Thank you  
Enkosi kakhulu  
Baie dankie!



# Evaluation of Effectiveness of the National PMTCT Programme Six Weeks Postpartum South Africa

**Ameena Goga, MRC/HSRU**

**Thu-Ha Dinh, US CDC/GAP**

**Debra Jackson, UWC, MRC/HSRU**



# Background - Sample Size

Province	Desired SS	Actual SS (prov%)
Eastern Cape	1400	753 (54%)
Free State	1300	1123 (86%)
Gauteng	1800	1712 (95%)
KwaZulu-Natal	1400	1205 (86%)
Limpopo	1400	982 (70%)
Mpumalanga	1600	1252 (78%)
Northern Cape	700	390 (56%)
North West	1200	1156 (96%)
Western Cape	1400	1342 (96%)
<b>SA</b>	<b>12 200</b>	<b>9915 (81%)</b>

Sample size calculated to obtain valid national and provincial level MTCT rates

# Weighted MTCT Rate at 4-8 weeks

Province	Infant HIV exposure (%)	MTCT (%) 95% CI
Eastern Cape	30.0 (26.3 - 33.7)	3.5 (1.2 - 5.8)
Free State	31.1 (28.9 - 33.3)	5.7 (3.5 - 7.9)
Gauteng	30.2 (27.7 - 32.8)	2.3 (1.3 - 3.3)
KwaZulu-Natal	43.9 (39.7 - 48.0)	2.8 (1.7 - 4.0)
Limpopo	22.6 (20.4 - 24.8)	3.4 (1.0 - 5.8)
Mpumalanga	36.2 (33.6 - 38.9)	6.2 (4.5 - 7.9)
Northern Cape	15.6 (13.0 - 18.3)	1.9 (0.1 - 4.5)
Northwest	30.9 (28.6 - 33.1)	4.6 (3.0 - 6.1)
Western Cape	20.8 (16.8 - 24.9)	3.3 (1.3 - 5.2)
<b>SA</b>	<b>31.4 (30.1 - 32.6)</b>	<b>3.5 (2.9 - 4.1)</b>

# MTCT Rate at 4-8 weeks ~ 2010 +2011

<b>Province</b>	<b>2010 (%)</b>	<b>2011 (%)</b>
<b>Eastern Cape</b>	<b>3.5</b>	<b>3.8</b>
<b>Free State</b>	<b>5.7</b>	<b>3.8</b>
<b>Gauteng</b>	<b>2.3</b>	<b>2.1</b>
<b>KwaZulu-Natal</b>	<b>2.8</b>	<b>2.1</b>
<b>Limpopo</b>	<b>3.4</b>	<b>3.1</b>
<b>Mpumalanga</b>	<b>6.2</b>	<b>3.3</b>
<b>Northern Cape</b>	<b>1.9</b>	<b>6.1</b>
<b>Northwest</b>	<b>4.6</b>	<b>2.6</b>
<b>Western Cape</b>	<b>3.3</b>	<b>2.0</b>
<b>SA</b>	<b>3.5</b>	<b>2.7</b>