

# PMTCT: Risk-based Neonatal Prophylaxis

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# Talk Outline

- **Introduction**
- When is VT risk increased?
- Boosted infant PEP reduces IP risk?
- Which ARV combination?
- Managing increased risk in breastfeeding.....
- Conclusion

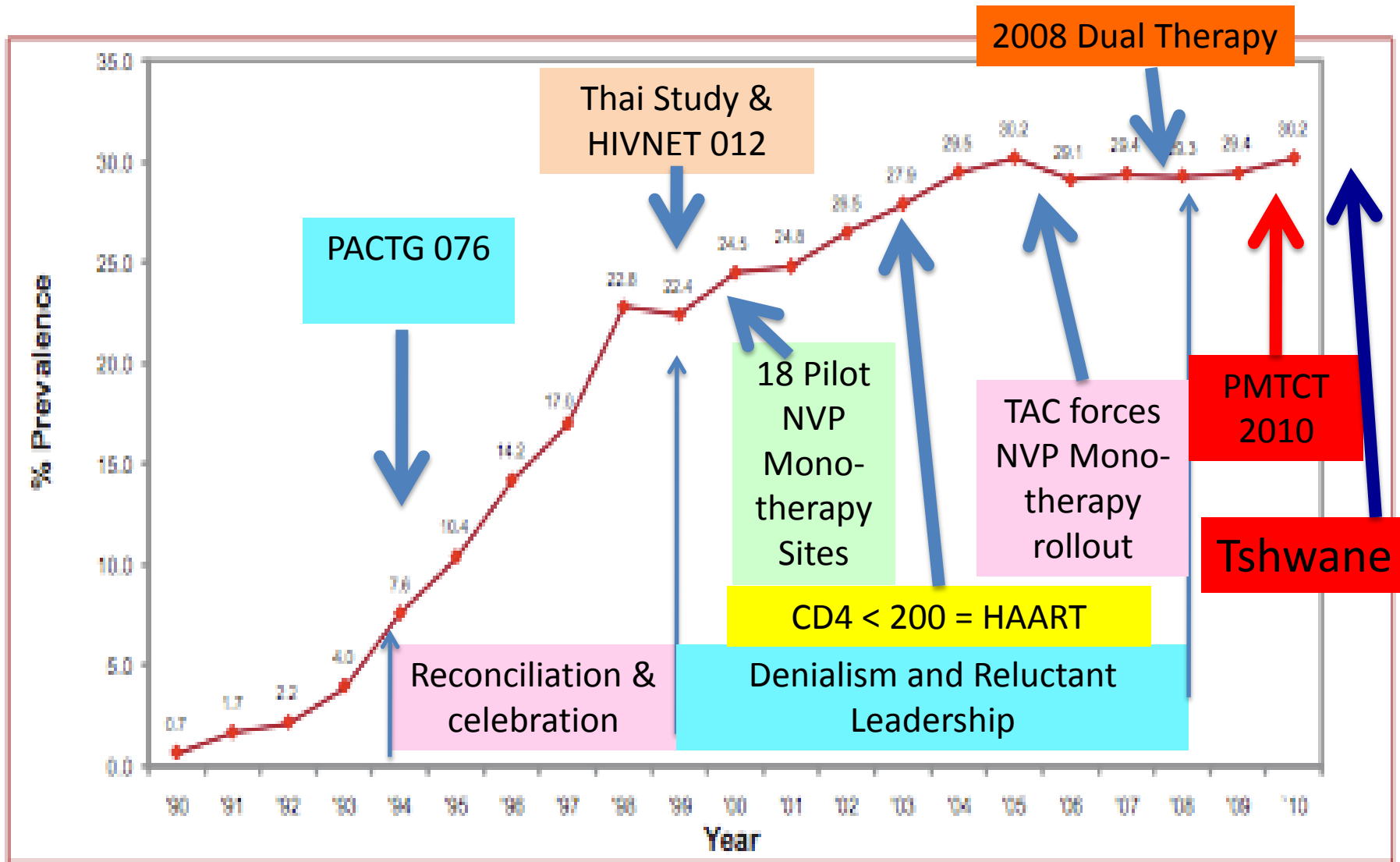


Figure 4: HIV prevalence epidemic curve among antenatal women, South Africa, 1990 -2010

# PMTCT Evolution In RSA

The National Antenatal Sentinel HIV and Syphilis Prevalence Survey, South Africa 2010

# 2011 NATIONAL SAPMTCT SURVEY RESULTS

RELEASED BY MINISTER AARON MOTSOALEDI

19 July 2012

Option A

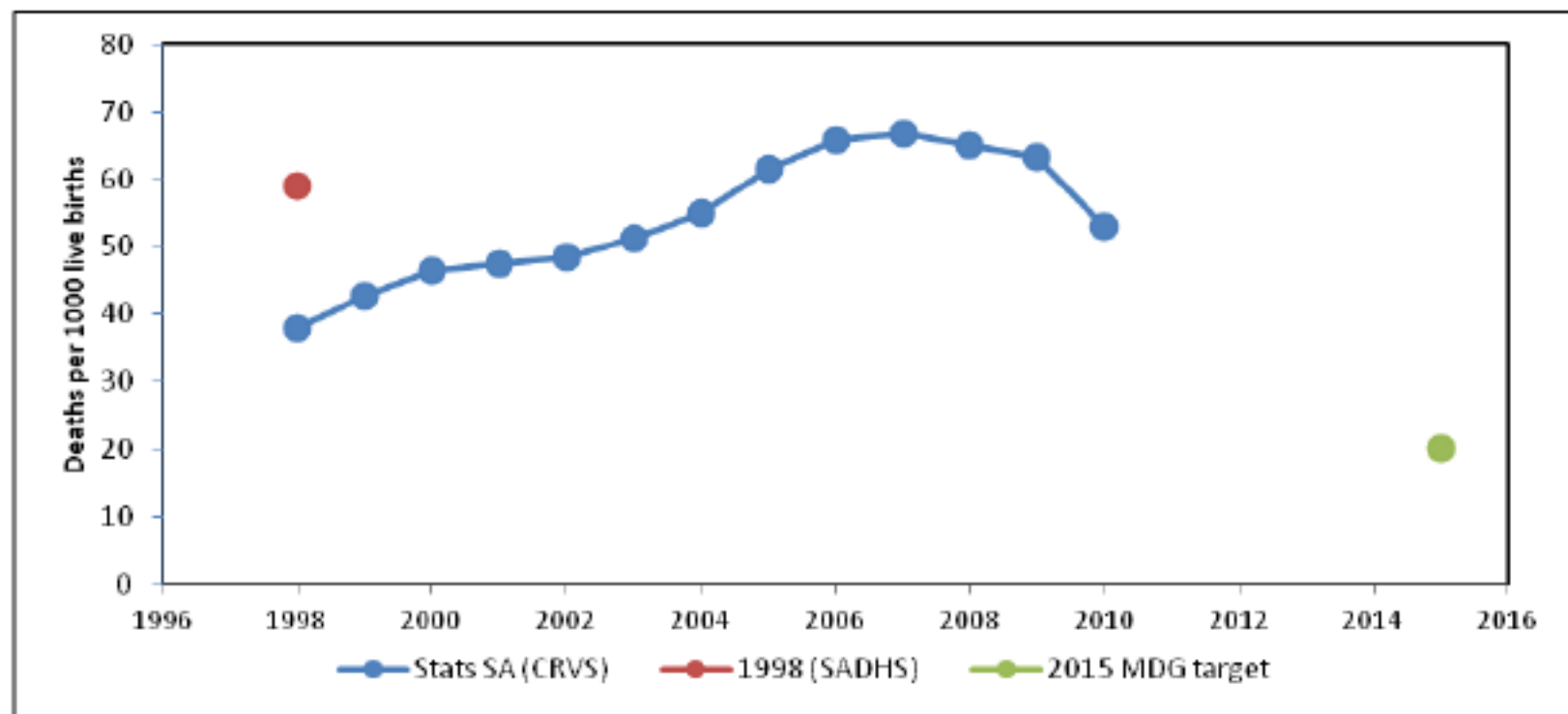
## Perinatal Infant HIV-Exposure and MTCT: Weighted Results by Province and National % (95% CI)

PROVINCE	2010		2011	
	Infant HIV-Exposed	MTCT % (95%CI)	Infant HIV-Exposed	MTCT % (95%CI)
Eastern Cape	30.0 (26.3-33.7)	4.7 (2.4-7.0)*	32.0 (29.6-35.5)	3.82 (2.1-5.54)
Free State	31.1 (28.9-33.3)	5.9 (3.8-8.0)	30.9 (28.6-33.3)	3.80 (2.29-5.3)
Gauteng	30.2 (27.7-32.8)	2.5 (1.5-3.6)	33.1 (29.8-36.4)	2.13 (0.91-3.36)
KwaZulu Natal	43.9 (39.7-48.0)	2.9 (1.7-4.0)	44.4 (39.8-48.9)	2.10 (0.94-3.26)
Limpopo	22.6 (20.4-24.8)	3.6 (1.4-5.8)	23.0 (19.9-26.2)	3.06 (1.21-4.91)
Mpumalanga	36.2 (33.6-38.9)	5.7 (4.1-7.3)	35.6 (33.3-37.8)	3.32 (2.17-4.48)
Northern Cape	15.6 (13.0-18.3)	1.4 (0.1-3.4)*	15.1 (12.7-17.5)	6.06 (2.48-9.63)*
Northwest	30.9 (28.6-33.1)	4.4 (2.9-5.9)	30.8 (28.5-33.1)	2.57 (1.13-4.00)
Western Cape	20.8 (16.8-24.9)	3.9 (1.9-5.8)	17.8 (14.8-20.8)	1.98 (0.65-3.31)
<b>National</b>	<b>31.4% (30.1-32.6%)</b>	<b>3.5 (2.9-4.1)</b>	<b>32.2% (30.7-33.6%)</b>	<b>2.67 (2.13-3.21)</b>

\*Note unstable estimates due to smaller sample size realisation precision is low

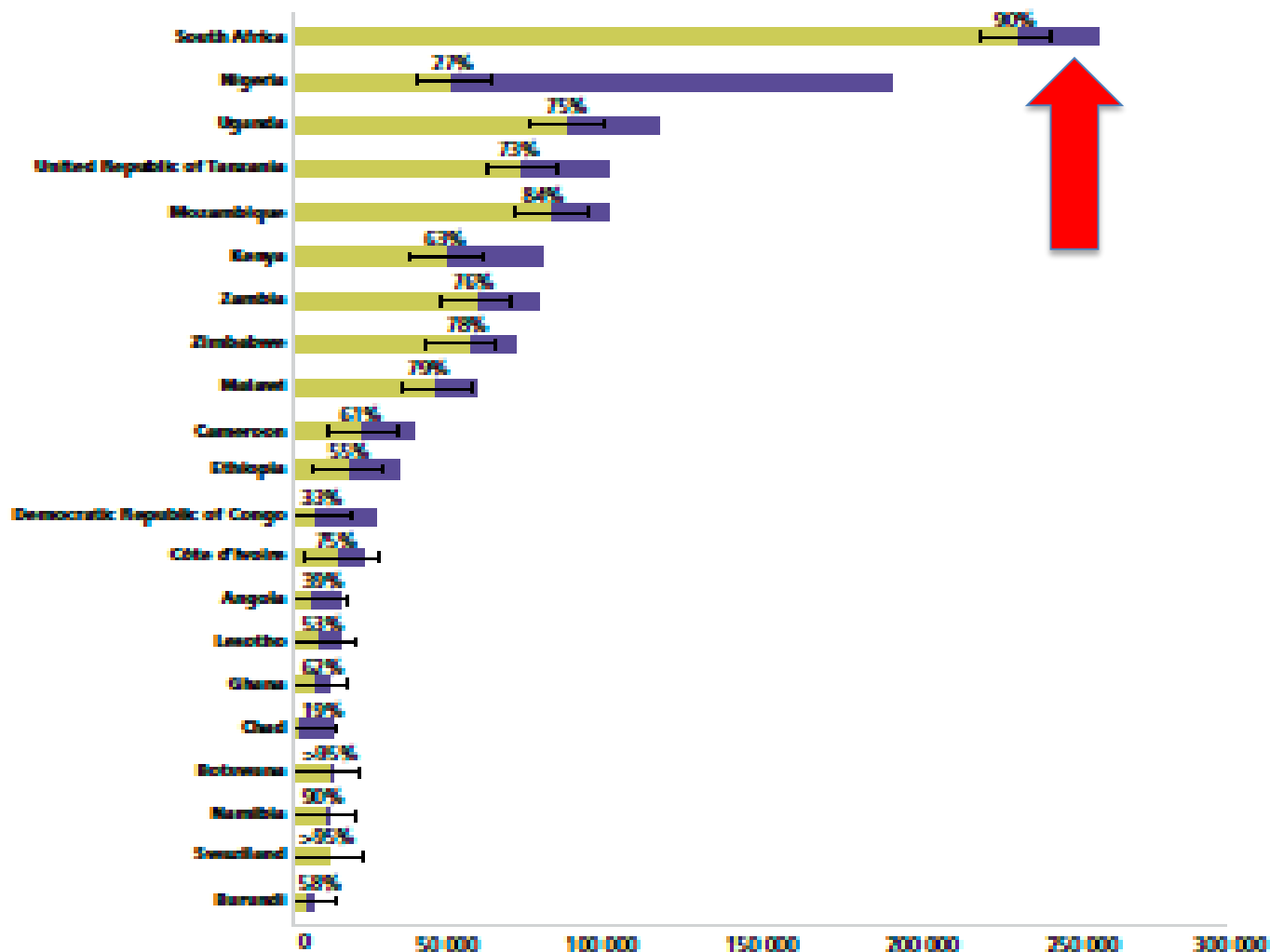
## Millennium Development Goals, Country Report 2013 / Statistics South Africa

*Figure 31: Trends in under-five mortality rates in South Africa since 1998 and the 2015 MDG target*



*Source: Demographic and Health Survey 1998, Department of Health; Mortality and Causes of Death, Mid-year Population Estimates, Statistics South Africa*

**Fig. 3.4. Number and percentage of pregnant women living with HIV receiving ARV medicines for PMTCT of HIV in the 21 Global Plan priority countries in the WHO African Region, 2013**



■ Total number of pregnant women living with HIV (all needing PMTCT ARVs)  
 ■ Number of pregnant women living with HIV receiving ARV medicines for PMTCT (options A, B and B+)

Source: Global AIDS Response Progress Reporting (WHO/UNAIDS/UNAIDS).

# Transmission Rate: W Cape

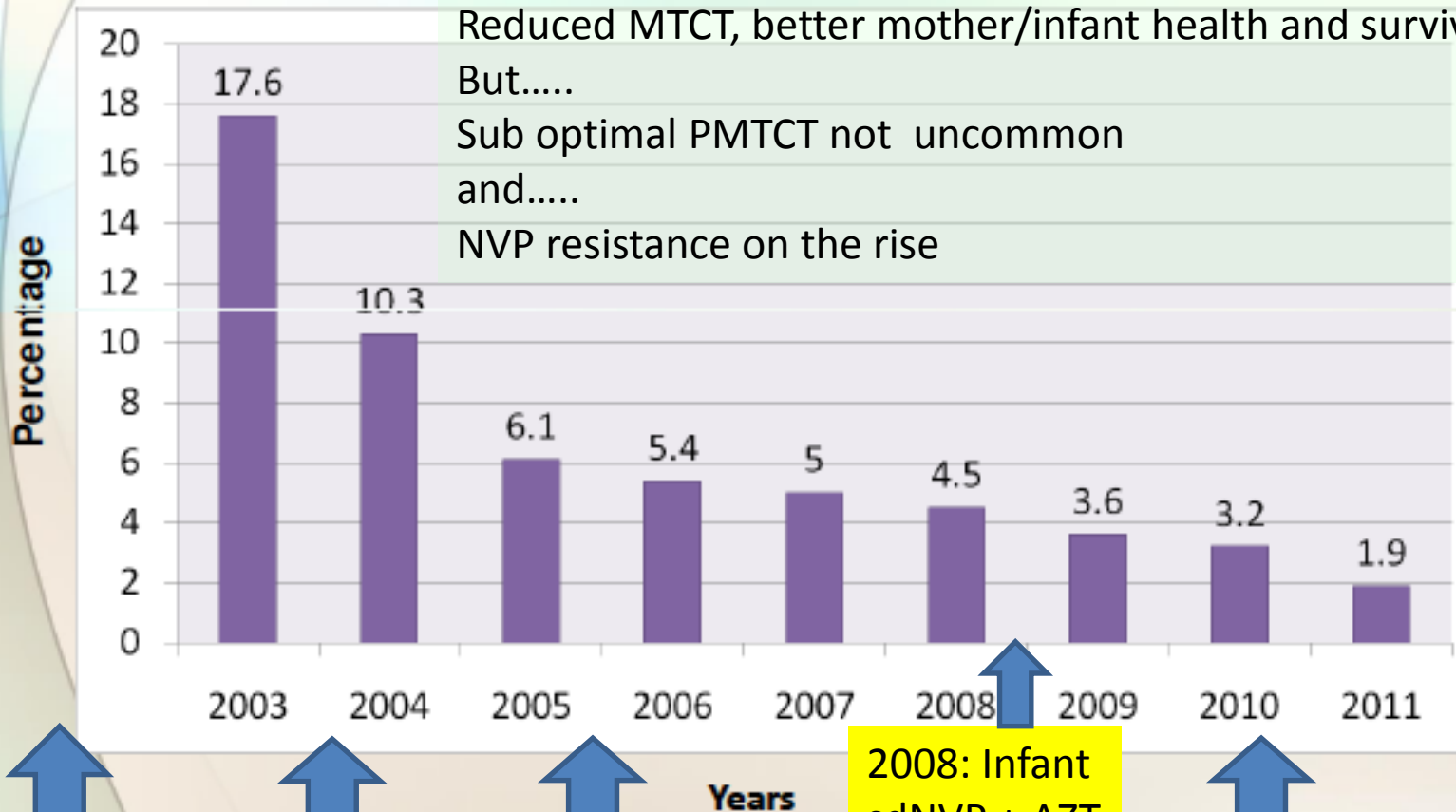
Better program, coverage and uptake

Reduced MTCT, better mother/infant health and survival

But.....

Sub optimal PMTCT not uncommon  
and.....

NVP resistance on the rise



2000: NVP  
Monotherapy

From 34wk to 28 wk AZT  
+Targeted ART (CD4<200).  
Infant sdNVP.

2008: Infant  
sdNVP + AZT

2010: Targeted ART if  
CD4<350 or 14 wk AZT.  
Infant extended NVP.

2013: Lifelong  
ART for all.  
Infant eNVP.

# METRO WEST Jan-June 2013

	2010	2011	2012	2013 Jan-June
Caesarean Section Rate	24.2%	25.3%	27.8%	28%
Births Before Arrival	3.6%	3.5%	3.2%	2.9%
No Antenatal care "UNBOOKED"	5.8%	5.9%	5.1%	5.5%

- Thanks to Metro West PPIP Team
- Dr C Nelson, Dr L Dietrich, Dr D Nage and Dr L Jacobs



# MMH Register of Positive PCRs: 2009 – 2013

- 24 unbooked/ no or minimal prelabour ARVs
- 1 Substance abuse (unbooked)
- 2 Substance abuse (one with congenital syphilis; both unbooked)
- 1 Congenital CMV (despite AZT)
- 2 Rebound viraemia (twins NNRTI resistance)  
– ART many years but alcoholic defaulter
- 1 Maternal TB (pre initiation of ART at 12wks before delivery)



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# Low Risk

- Adequate maternal ART
- Good adherence, no resistance
- Good viral control early in pregnancy
- Good viral control by labour and delivery
- No obstetric complications or co-morbidities
- FF or maternal VL control in breastfeeding
- Infant mono-ARV PEP 4-6 weeks only

# Timing of HIV Transmission (pre ARVs and non-Breastfeeding)

1334 Rouzioux et al. Am J Epidemiol 1995; 142:1330-7.

- Transmission risk is small prior to 28 weeks gestation, rises towards term and peaks during labour and delivery
- Maternal IP Rx + infant PEP reduce IP risk but not IU risk
- Infant PEP reduces IP proportion and some early PP risk
- Boosted infant PEP targets brief period of intense IP risk

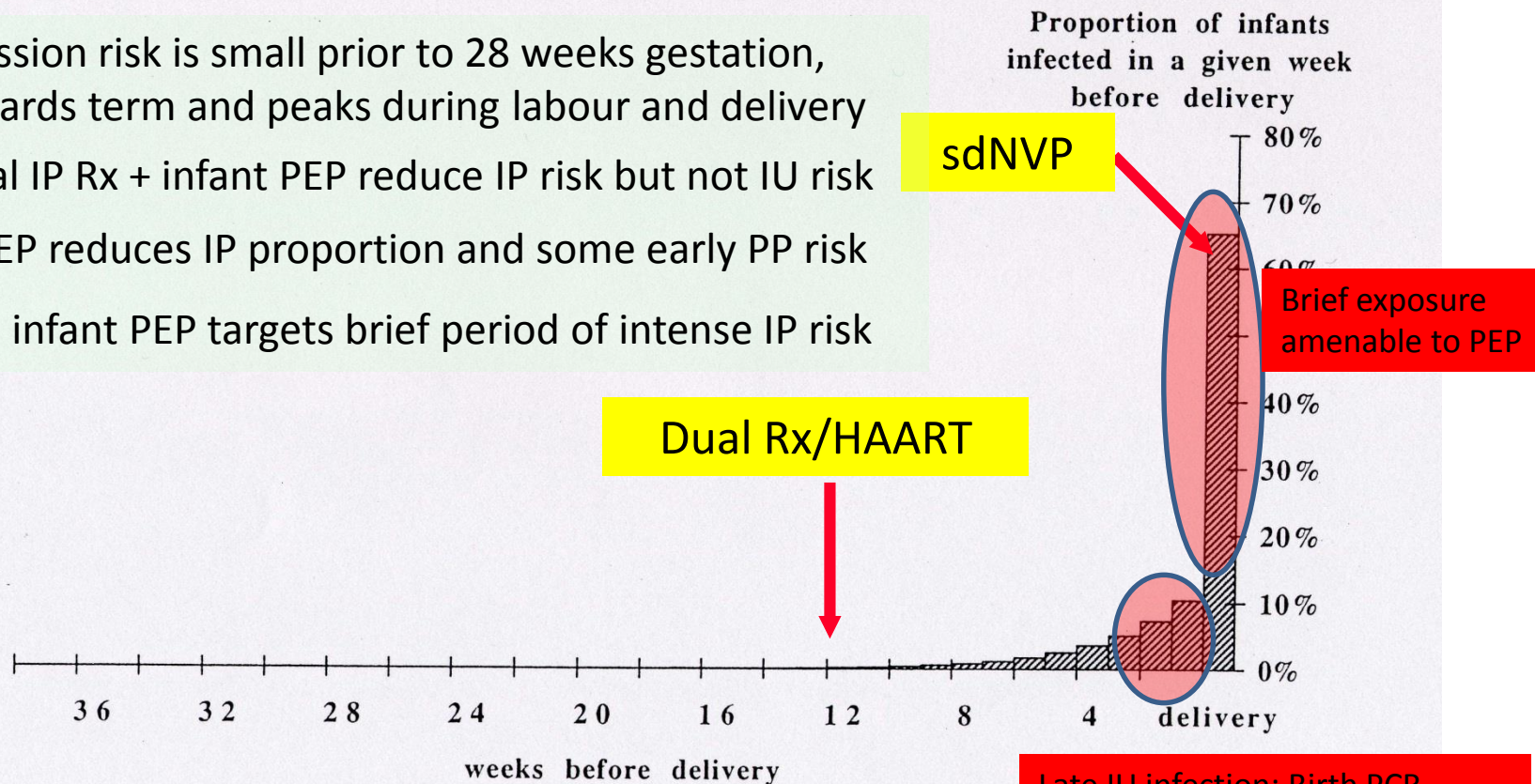
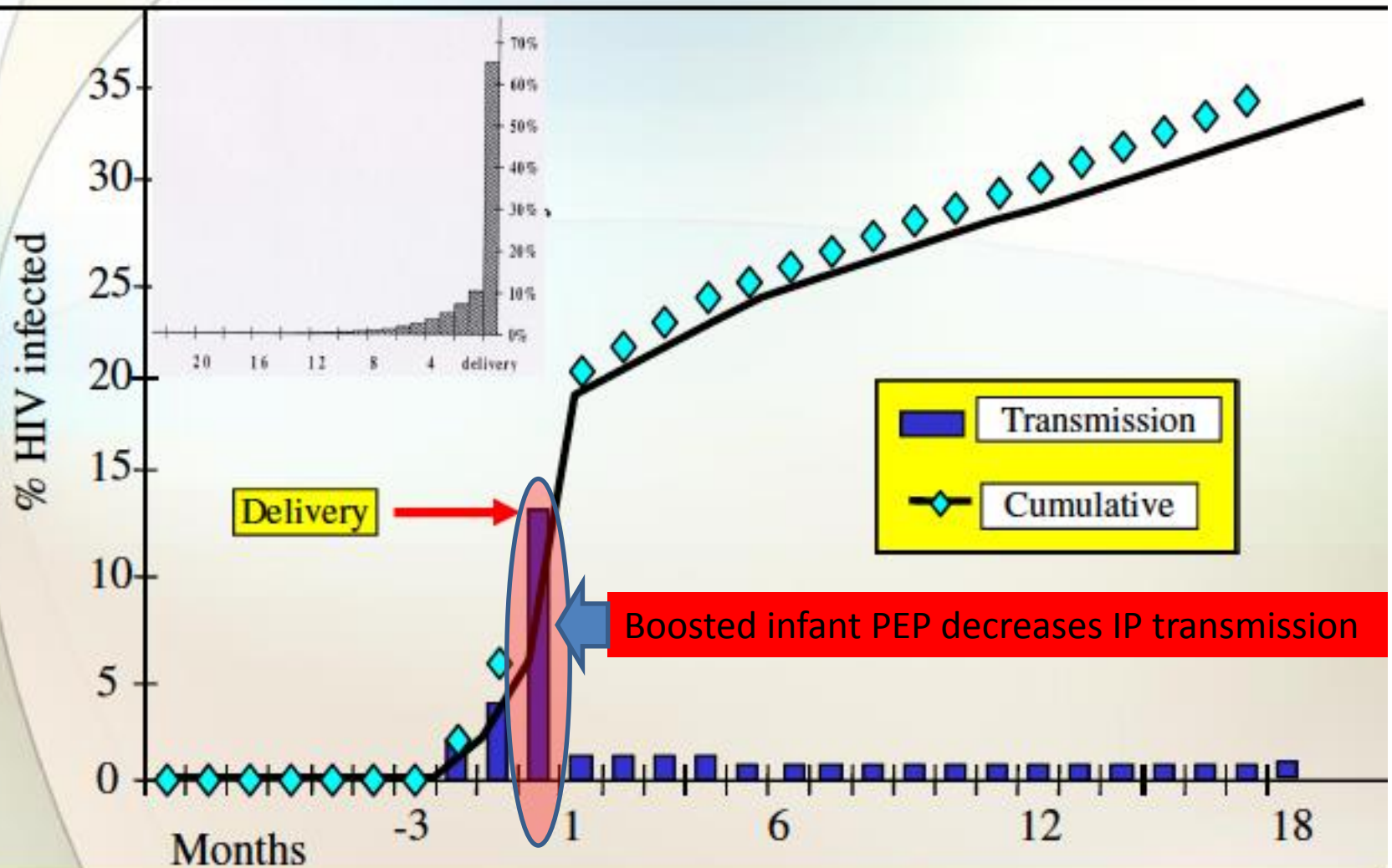


FIGURE 2. Estimated distribution of the dates of transmission.

# Timing of HIV Transmission – pre ARV era



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

# Increased Risk & Timing

- CD4 <350c/mL = > 80% of MTCT (IU +IP)
- Inadequate maternal ART (IU +IP)
- VL >1000cps/mL (IU +IP) or lower if no ART
- Primary HIV in pregnancy (IU)
- Rebound viraemia (IU)
- Comorbidity (syphilis, tuberculosis) (IU)
- PTL + PROM, chorioamnionitis (IP)
- ARV resistance

# Risk assessment considerations

- “Non-low risk” vs “high risk”
  - BHIVA: maternal VL > 50cps/mL
  - NIH: minimal prelabour ART, IP ART only, no ART
- Timing of risk (IU, IP, PP?)
  - IP risk may be low if > 4 wks ART suppresses VL by labour
  - VL at time of delivery important
- Resistance (NNRTI, ? others)

# “Risk” Precedents in SA Guidelines

- National:
  - 2008 sdNVP + 4 weeks AZT if mother < 4 wks ARVs
  - 2010 National: No concession to risk
  - 2013 STG/PEDL: Birth PCR if BWt <2500g or symptomatic; extend NVP for BF prophylaxis if high risk.
- WCP:
  - 2010 Preterm guideline – risk based early PCR
  - 2013 Risk-based birth PCR (resistance/no prelabour ARVs) and boosted infant PEP (AZT + NVP) clinician discretion.
  - 2014 Birth PCR and AZT/NVP for increased risk
- WHO
  - 2013 – no concession



# MMH Protocol (Oct 2013)

- **Maternal factors:**

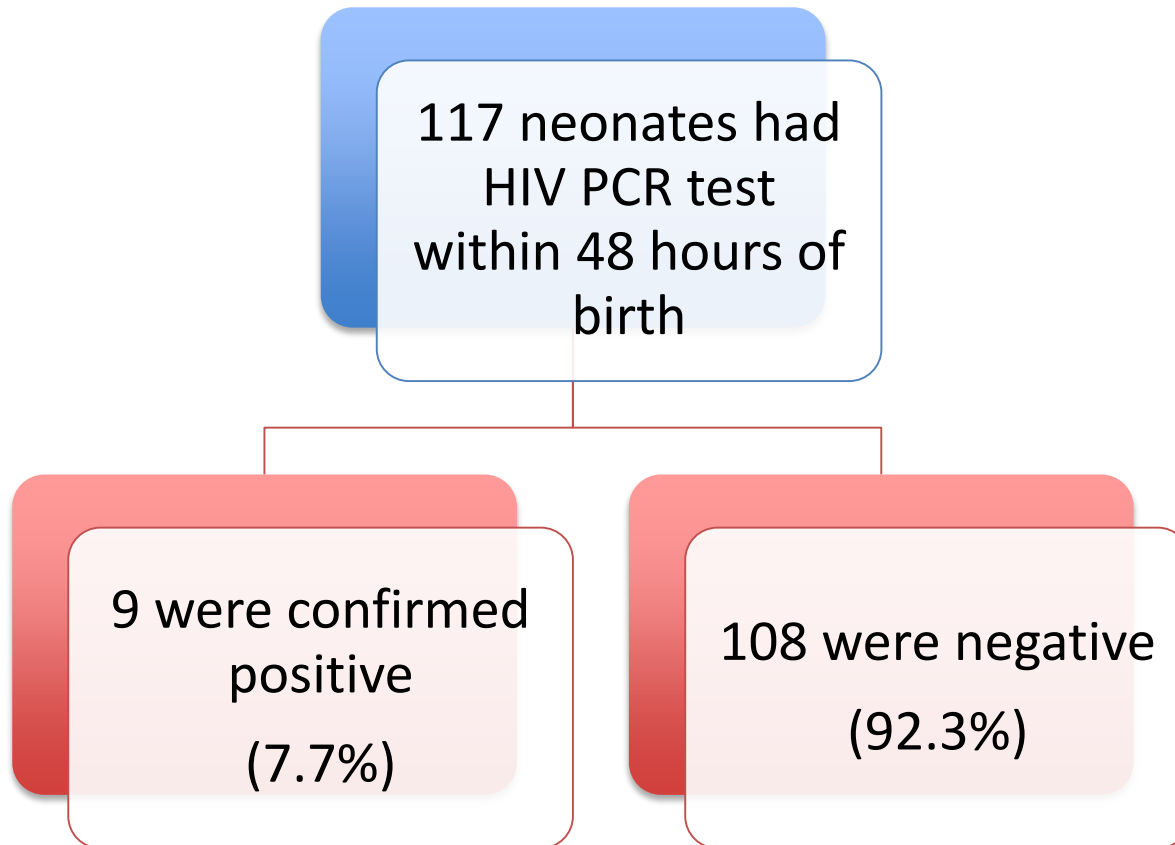
- Maternal antiretroviral therapy < 8 weeks
- Maternal viral load > 1000 copies/ml
- Maternal viral rebound
- Maternal comorbidity
- Maternal substance abuse
- Incident/recent infection (initial HIV test negative , subsequent tests positive)
- Adolescent pregnancy (possible perinatally acquired HIV infection, more likely to have problems with follow up)
- Likely NNRTI resistance



- **Infant factors:**

- Symptomatic
- PT delivery regardless of cause and/or LBW infants
- Abandoned infants (if Alere Determine test or HIV ELISA test positive)

# MMH Results: Early HIV PCR Tests



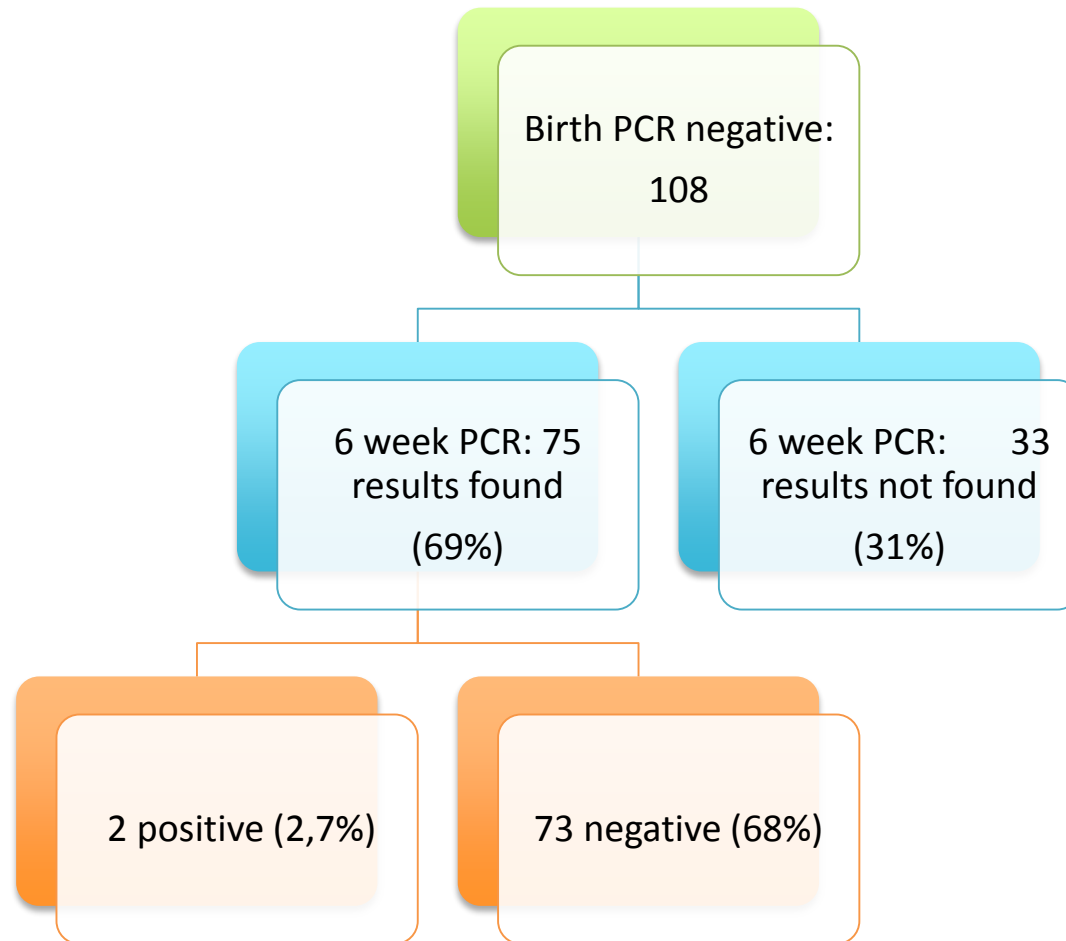
**In utero HIV transmission rate = 7.7%**



# Intra-partum Risk

- Very early PCR test cannot detect transmission during labour and delivery
- PCR negative at <48 hrs/positive after 7 days means IP transmission likely
- Relatively brief IP exposure lends itself to PEP
- Boosted infant PEP further reduces IP MTCT

# MMH Results: 6-week HIV PCR tests in infants with negative early HIV PCR test and AZT/NVP PEP



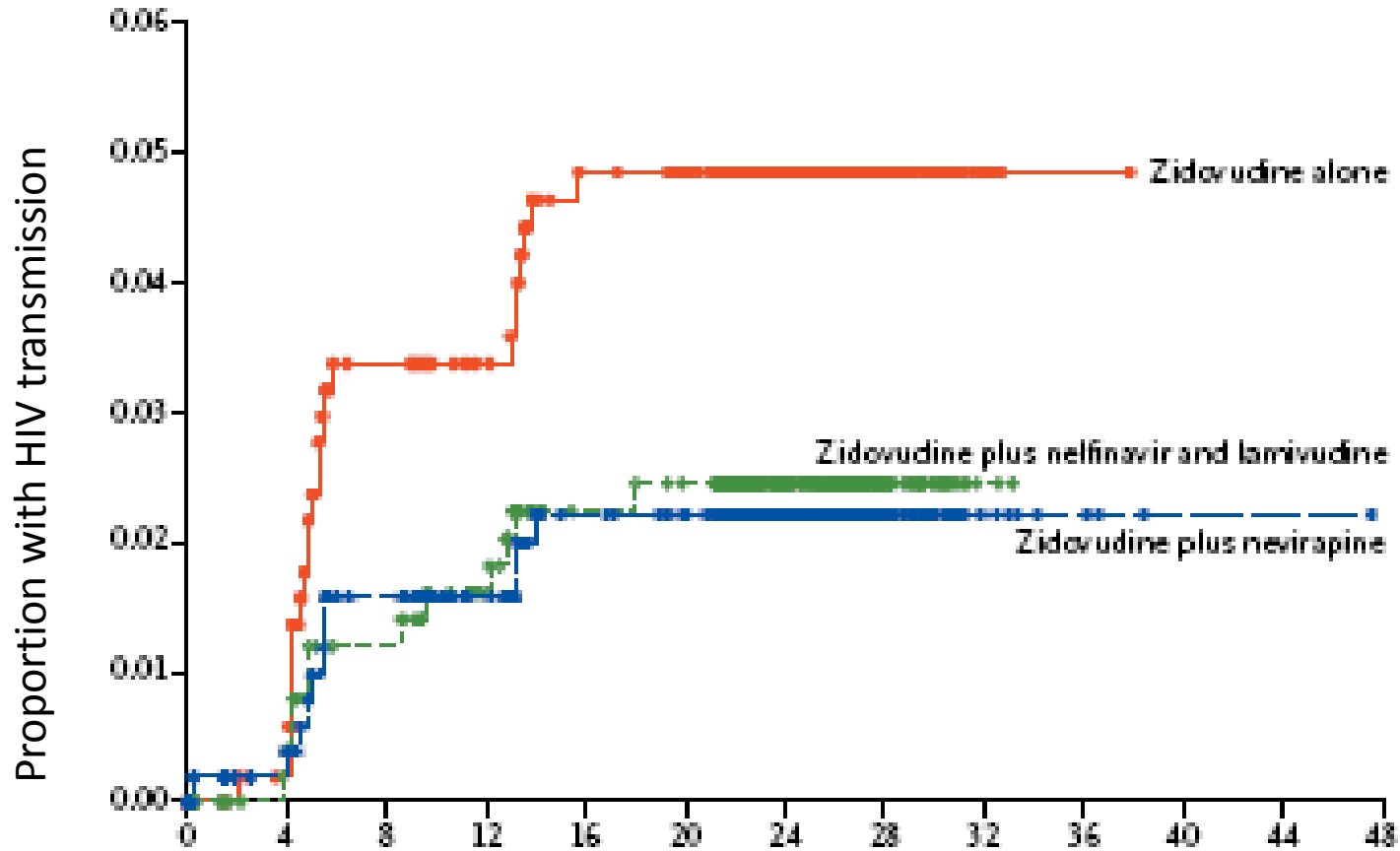
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# Evidence for infant multi-ARV PEP

- HPTN 040. Nielson-Saines. NEJM 2012. No prelabour ARVs.
  - 6wk AZT vs 6wk AZT + 3 doses NVP
  - AZT-alone: 24 IP infections (4.8%)
  - AZT + NVP: 11 IP infections (2.2%; P=0.046)
- NVAZ. Taha et al. Lancet 2003.
  - sdNVP vs sdNVP + 1 wk AZT: 12,1% vs 7,7% (p=0,03)
- PEPI Malawi 2008 – 1 wk AZT not enough
- Thai sdNVP add on. Lallemand et al. NEJM 2004

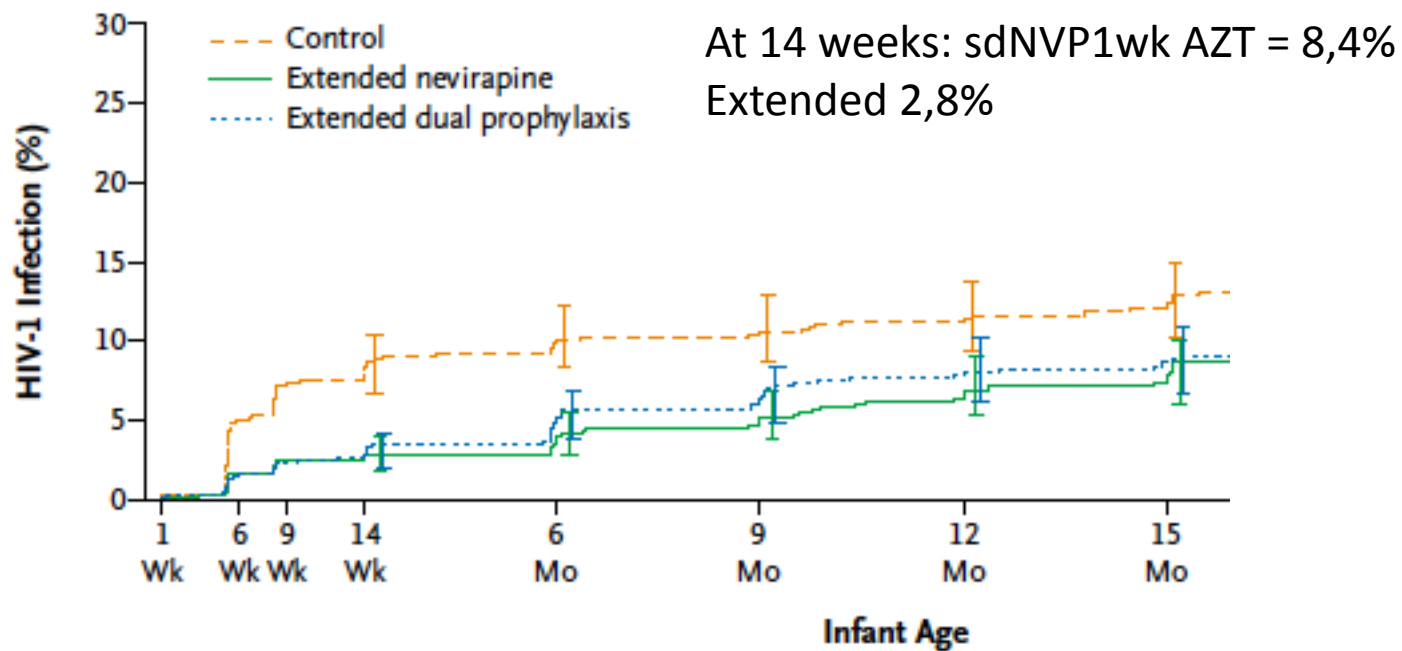
# HPTN 040



Nielsen Saines NEJM 2012;366: 2368-79

PEPI Malawi. NEJM 2008

**A**



**No. at Risk**

Control	992	870	813	756	660	548	454	386
Extended nevirapine	1005	934	879	812	710	593	490	412
Extended dual prophylaxis	986	904	854	803	695	589	488	416



# When to consider multi-ARV PEP

## *General Considerations for Choice of Infant Prophylaxis*

All HIV-exposed infants should receive postpartum antiretroviral (ARV) drugs to reduce perinatal transmission of HIV. The 6-week neonatal zidovudine chemoprophylaxis regimen is recommended for all HIV-exposed infants.<sup>1, 2</sup> [Table 9](#) shows recommended zidovudine dosing based on the status of maternal antepartum ARV regimens. Infants born to mothers who have received standard antepartum and intrapartum ARV prophylaxis and have undetectable viral loads are at very low risk of HIV transmission and should receive the 6-week zidovudine regimen alone.

The risk of transmission is increased when maternal viral load at delivery is high or maternal antepartum and/or intrapartum prophylaxis was not received. Most experts feel that the potential benefit of combining zidovudine infant prophylaxis with additional ARV drugs may exceed the risk of multiple drug exposure to infants born to:

- a. mothers who received antepartum and intrapartum ARV drugs but who had suboptimal viral suppression at delivery, particularly if delivery was vaginal;
- b. mothers who received only intrapartum ARV drugs;
- c. mothers who received neither antepartum nor intrapartum ARV drugs; and
- d. mothers with known ARV drug-resistant virus.

# BHIVA 2012 INFANT PEP

## 8.1 *Infant post-exposure prophylaxis*

- 8.1.1 Zidovudine monotherapy is recommended if maternal VL is <50 HIV RNA copies/mL at 36 weeks' gestation or thereafter before delivery (or mother delivered by PLCS while on zidovudine monotherapy). Grading: 1C
- 8.1.2 Infants <72 h old, born to untreated HIV-positive mothers, should immediately initiate three-drug therapy for 4 weeks. Grading: 1C
- 8.1.3 Three-drug infant therapy is recommended for all circumstances other than Section 8.1.1 where maternal VL at 36 weeks' gestation/delivery is not <50 HIV RNA copies/mL. Grading: 2C
- 8.1.4 Neonatal post-exposure prophylaxis (PEP) should be commenced very soon after birth, certainly within 4 h. Grading: 1C
- 8.1.5 Neonatal PEP should be continued for 4 weeks. Grading: 1C

# Neonatal PEP Anomaly

- Standard PEP is for 4 weeks
- Occupational: Risk = 0,3% - multi ARV PEP
- Sexual assault: Risk = ?% - multi ARV PEP
- Intrapartum exposure is relatively brief and comparable to scenarios in which PEP used
- Intrapartum (no ARVs): Risk = 15% - NVP or AZT monotherapy PEP!!!!

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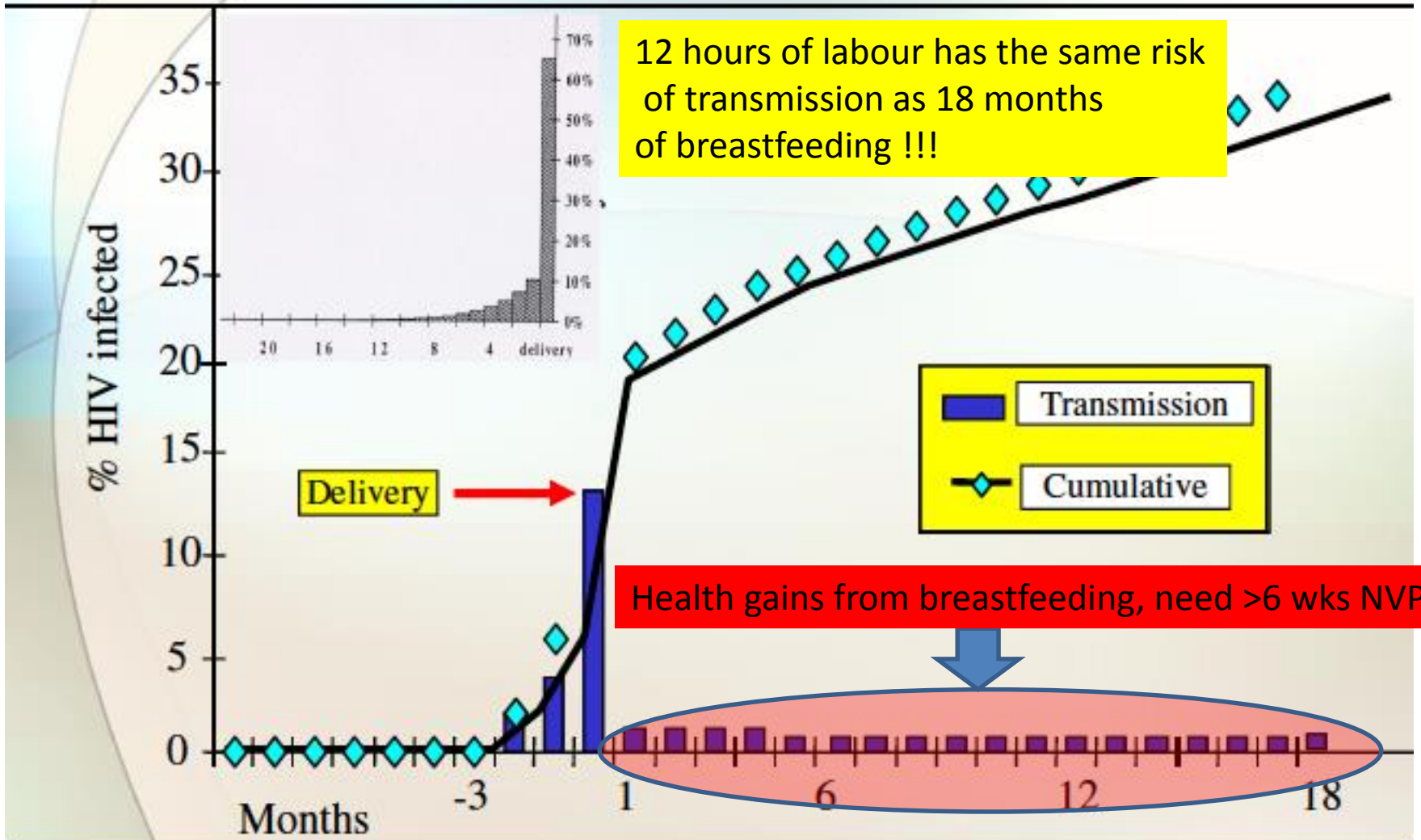
# Which ARV Combo?

- BHIVA (AZT, 3TC for 4 wks + NVP for 2 wks)
- NIH (AZT for 6 wks, NVP 3 doses in 1<sup>st</sup> week)
- SA 2008 (sdNVP+ AZT as per Lallemand 2004)
- Need to consider BF prophylaxis
- Role of genotyping if resistance likely?

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# Timing of HIV Transmission – pre ARV era



12 hours of labour has the same risk of transmission as 18 months of breastfeeding !!!

Delivery

Transmission  
Cumulative

Health gains from breastfeeding, need >6 wks NVP

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

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# Conclusion

- Significant gains from PMTCT program
- Sub optimal PMTCT still not uncommon
- Address by
  - systems strengthening
  - Improve early maternal ART uptake
- Further improve outcomes by
  - recognition of high risk newborns
  - Boosted infant PEP to reduce IP risk
  - Very early diagnosis
  - Early treatment of IU infection
- Prevention is better than cure

# HIV-EXPOSED INFANT

