HIV PMTCT
PAST EXPERIENCE AND MOVE TO THE NEW GUIDELINES

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Outline of the presentation

- Burden
- 2000 WHO recommendations
- 2006 WHO recommendations
- 2010 WHO recommendations
- 2012 WHO recommendations
- Where are we in Tanzania

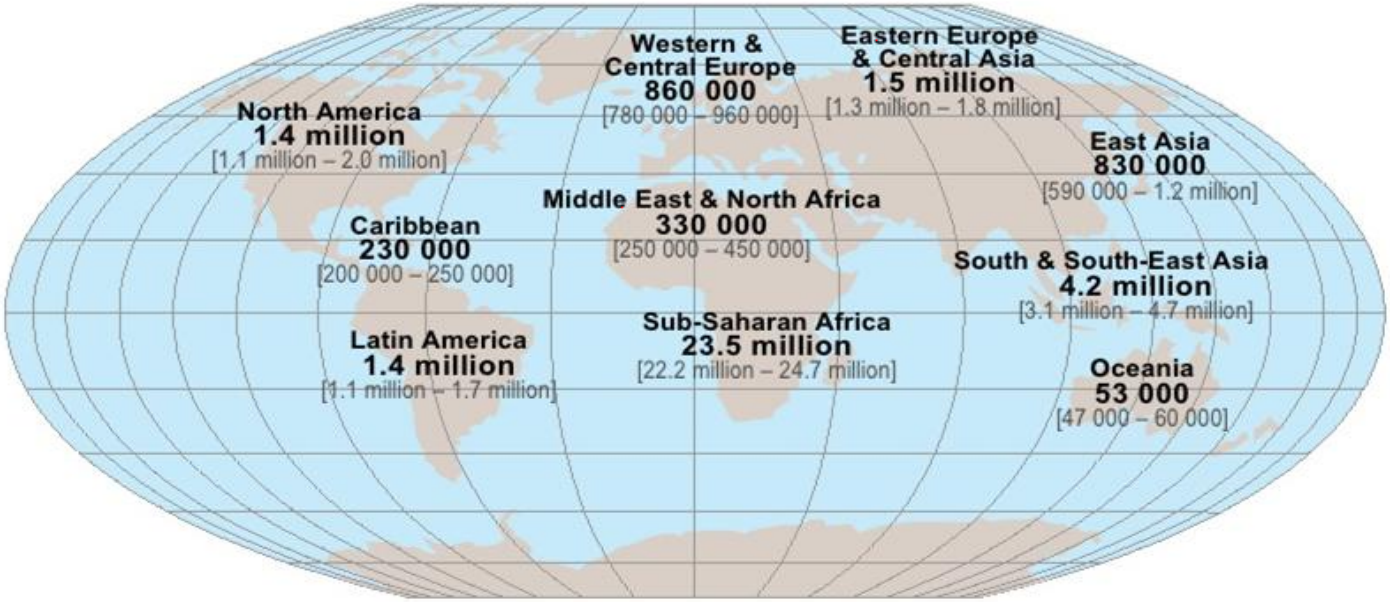
Burden of HIV *(UNAIDS Epidemic Report, 2012)*

- Public health problem, SSA

- By the end of 2011;

	Global	SSA
PLWHIV	34.0M	23.5M *(69%)*
Newly infected	2.5M	1.8M *(71%)*
AIDS deaths	1.7M	1.2M *(70%)*

Adults and children estimated to be living with HIV | 2011



Total: 34.2 million [31.8 million – 35.9 million]

World Health Organization

UNAIDS

PREVENTION OF MOTHER TO CHILD HIV TRANSMISSION

Four prong Stategy

Timing of MTCT with Breastfeeding and No ARV

Early Antenatal (<36 wks)

Early Postpartum (0-6 months)

Late Postpartum (6-24 months)

Antenatal (36 wks to labor)

5-10%

10-20%

10-20%

Slide adapted from Nathan Shaffer, CDC

MTCT in SSA

- Complex and prolonged regimens are not affordable or feasible
  - Elective Caesarian section is seldom available or safe
- Affordable, safe and acceptable alternatives to BF are not there (weight the benefits of infectious disease vs HIV transmission risk)
  - Early attendance of ANC is not common

Preventing MTCT in resource-poor settings

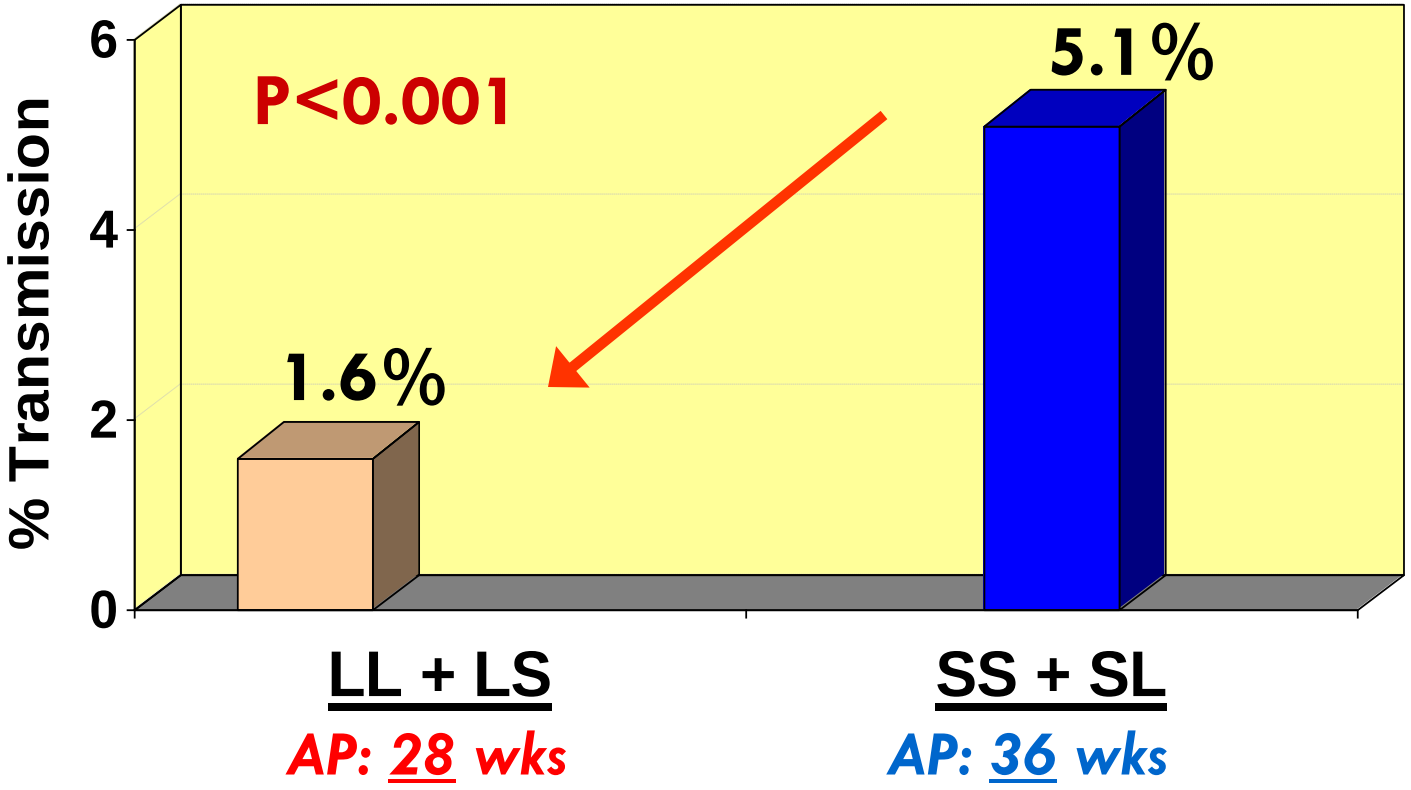
- Research has focused on short regimens of peri-partum ARV drugs
  - Use AZT, sdNVP, AZT + 3TC etc (both in BF and non-BF populations)

- Prophylactic ARV drug with single drug have shown to prevent ~ half (41-47%) of infections occurring during peripartum period

(The PETRA study team, Lancet 2002; Jackson B *et al*, Lancet 2003; Leroy V *et al*, AIDS 2002; Eshlemann S *et al*, JAIDS 2002, Leroy V 2006, Mashi study 2007)

For Maximal Efficacy of Any Regimen, Need to Start Early in Pregnancy to Prevent *In Utero* Transmission

Lallemant M et al. N Engl J Med 2000;343:982-91



Even if intervention is 100% effective for IP/PP transmission, still have "residual infection" of 1.6% starting at 28 weeks

Alternative Antiretrovirals: Single-Dose Nevirapine vs Ultra-Short AZT - HIVNET 012

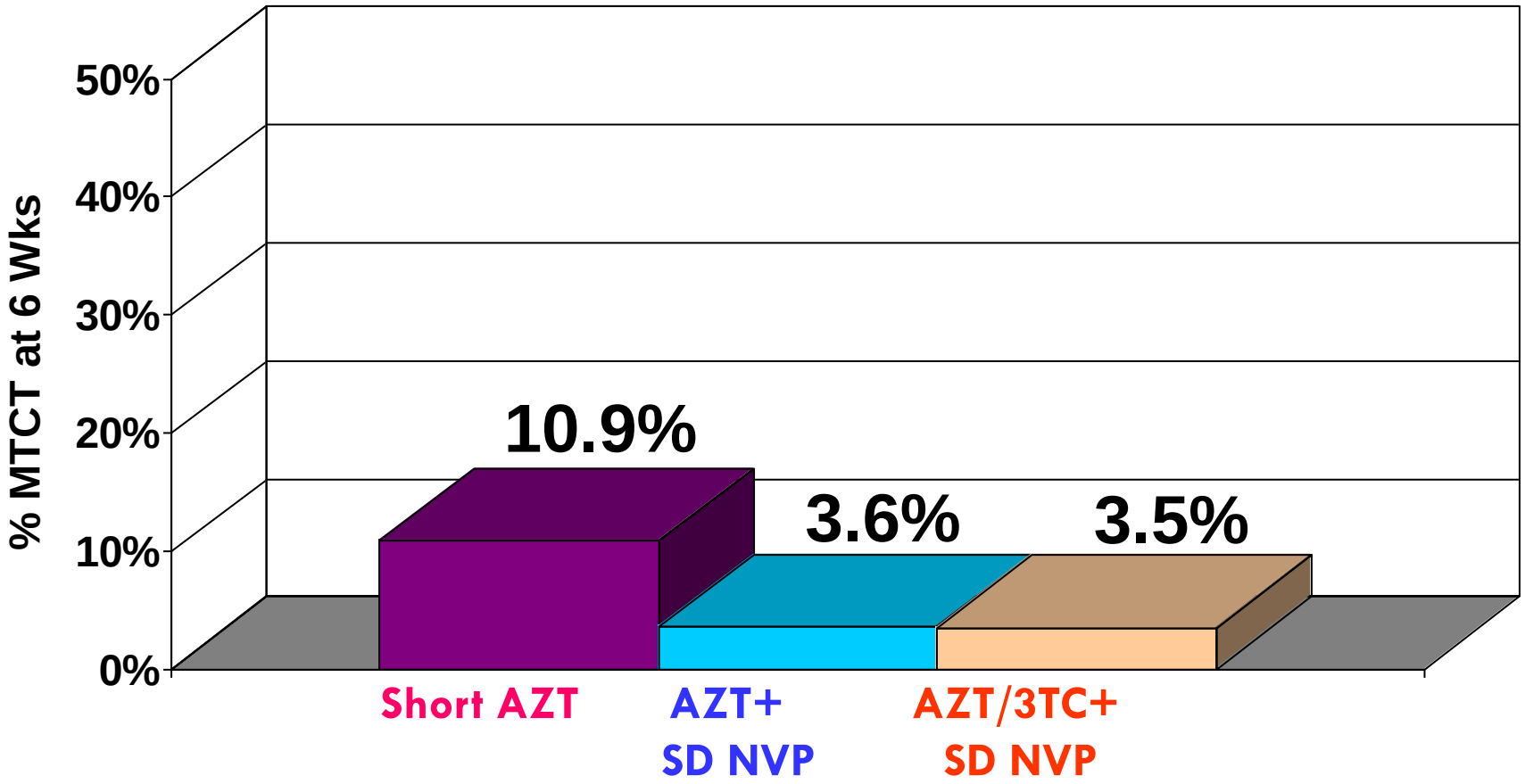
Guay L et al. Lancet 1999;354:795-802

Breastfed Infants

		% Transmission 14-16 Wks	% Transmission 18 Mos
Nevirapine	INTRA: 200 mg x1; POST: 2 mg/kg x1	13.1%	15.7%
versus			
Ultra-Short AZT	INTRA: 300 mg q 3 hr; POST: 4 mg/kg bid x1 wk	22.1%	25.8%
		Efficacy	
		47%	*41%*

MTCT Risk in Women Not Meeting WHO Criteria* for ART Who Receive Short-Course ARV Prophylaxis

Cote d'Ivoire Trials Data, F. Dabis 6/05

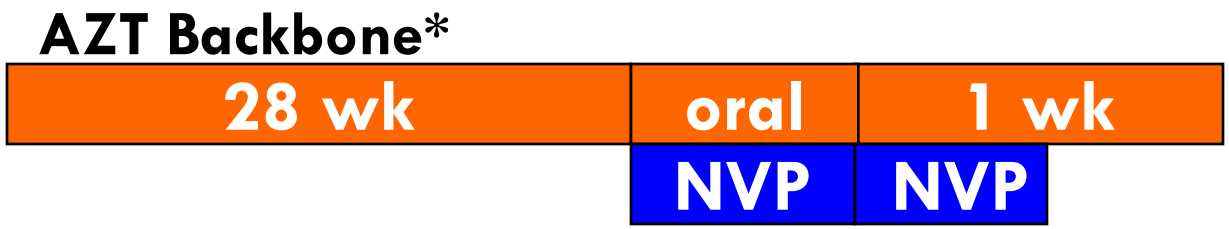


*** Does not Meet WHO criteria if: WHO Stage 3 and CD4 ≥350 *or* Stage 1-2 and CD4 ≥200**

Slide obtained from Lynne Mofenson, NIH

Longer Maternal AZT Therapy = Lower Transmission: Comparing Thai AZT + SD Mother/Infant NVP Trials

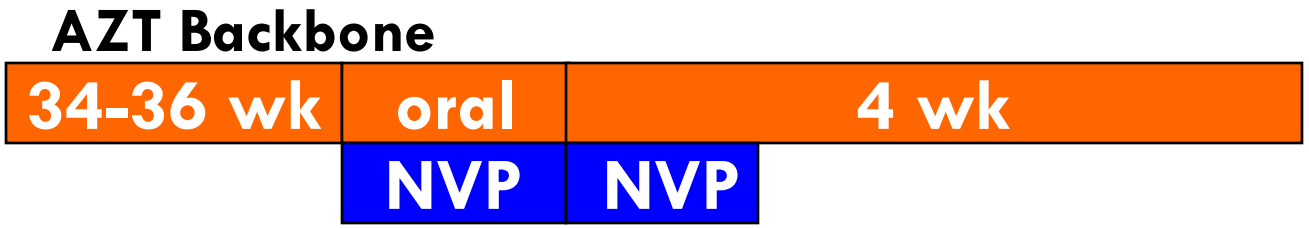
Lallemant M et al. NEJM 2004;351:217-28



*If mom <4 wk AZT, infant gets 4 wks AZT

Transmission 2.0% (95% CI 1.2-3.4%) [N=693]

Chalermchokcharoenkit et al. 11th Retrovirus Conf, Feb 2004 (abs 96)



Transmission 4.6% (95% CI 2.5-8.5%) [N=220]

Thailand Studies (Formula-Fed Infants)

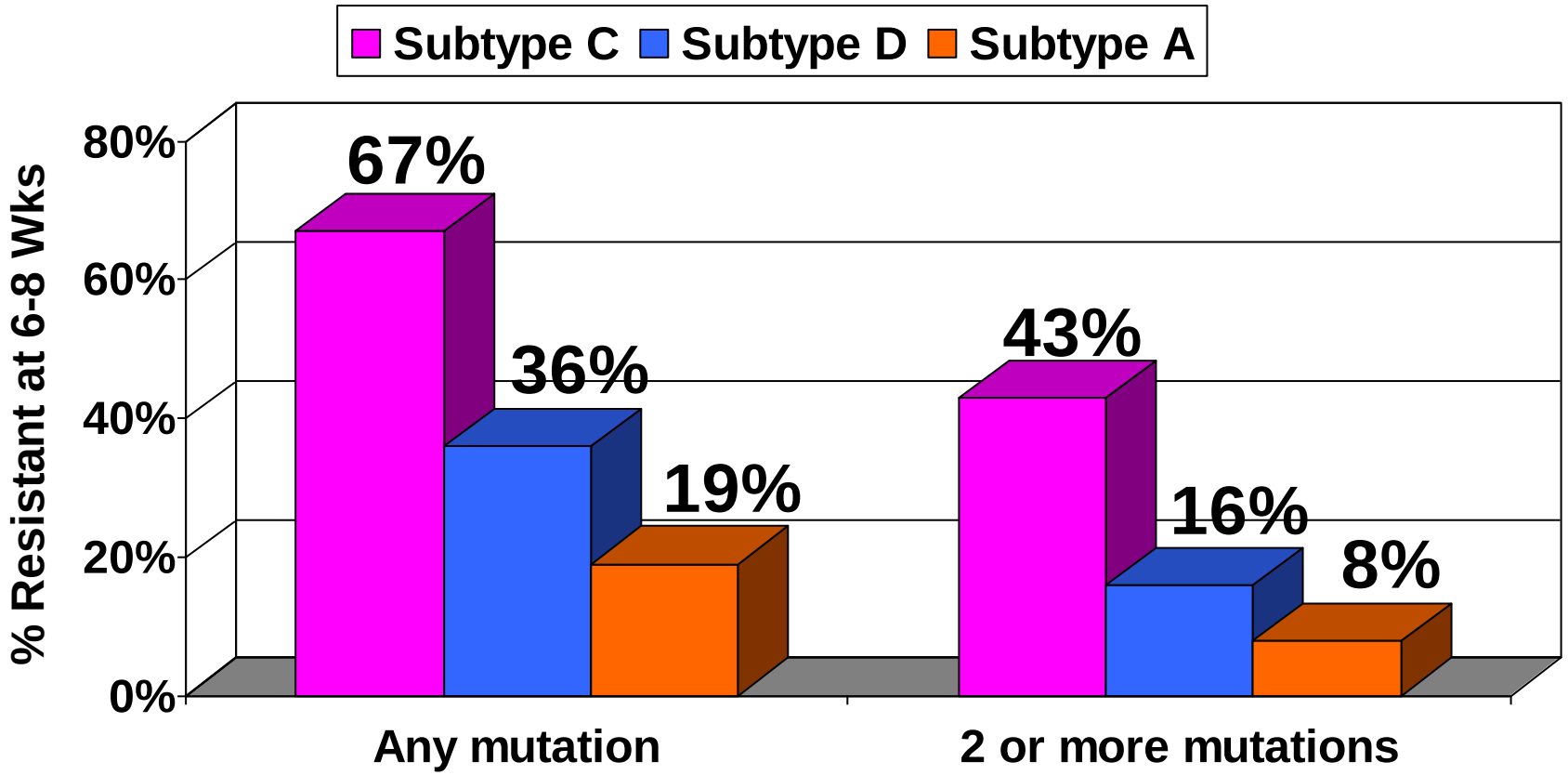
Slide adapted from Lynne Mofenson NIH

2004 revised guideline

- Countries should offer the following as minimum of package
  - ANC counseling and testing for HIV
  - sdNVP for mother and infant for PMTCT
  - CTX prophylaxis to the exposed infants until when tested

NVP Resistance After SD NVP is More Common In Malawi Women with Subtype C Infection than Ugandan Women Subtype A or D Infection

Eshleman S et al. 12th Retrovirus Conf, Boston 2005 (Abs 799)



Risk factors for resistance: Viral subtype, Delivery RNA

Lower Rates of NNRTI Resistance Observed with AZT/3TC "Tail" in Mothers/Infected Babies

McIntyre J. 3rd IAS Conf, Rio de Janiero, Brazil, 2005 (TuFo0204)
Gray G. 3rd IAS Conf, Rio de Janiero, Brazil, 2005 (TuPe5.4P01)

	Standard Population Genotyping			
	Mother Resistance at 2 or 6 Weeks PP		Infant Resistance at 2 or 6 Weeks PP	
	N	% Resistant	N	% Resistant
SD NVP	41/68	60%	5/9	56%
SD NVP + 4 d AZT/3TC	8/67	12%	1/8	13%
SD NVP + 7 d AZT/3TC	7/68	10%	1/7	14%

WHO 2006 PMTCT Recommendations

- Move from sdNVP for mother & child to more efficacious ARVregimen combinations (MERC)
- Prophylasix starts earlier at 28 wks
- Provides lifelong ART to pregnant women for their own health with CD4 cell count of ≤200 cells mm^3 (1st time focus on the mother)

2006 WHO PMTCT Guidelines

Pregnant Woman Who Doesn't Require Therapy for Own Health

	Pregnancy	Labor	Postpartum	Comments
Recommended	AZT (>28 wks)	•SD NVP + AZT/3TC	•Mother: AZT/3TC x 7d •Infant: SD NVP + AZT x7d	•Effective, reduces *in utero* •Reduces resistance •Most complex
Alternative	AZT (>28 wks)	•SD NVP	•Infant: SD NVP + AZT x7d	•Effective, reduces *in utero* •Risk resistance
Minimum	-	•SD NVP + AZT/3TC	•Mother: AZT/3TC x7d •Infant: SD NVP	•Effective but less than recommended •Reduces resistance •More complex •Not reduce *in utero*
Minimum	-	•SD NVP	•Infant: SD NVP	•Effective but less than recommended •Risk resistance •Not reduce *in utero*

WHO, 2006

PMTCT Prophylaxis Summary

General "tiered" approach:

- HAART for eligible women
- Combination prophylaxis (eg. AZT + SD NVP)
- SD NVP only where other interventions not feasible. This should be the exception not the rule.
- *NVP resistance is continuing concern*

Tanzania (revised 2009)

- Adapted WHO 2006 guidelines

- March 2008 – "dual therapy"

  AZT from 28 weeks and SdNVP

  ART at CD4 $\leq 200/mm^3$

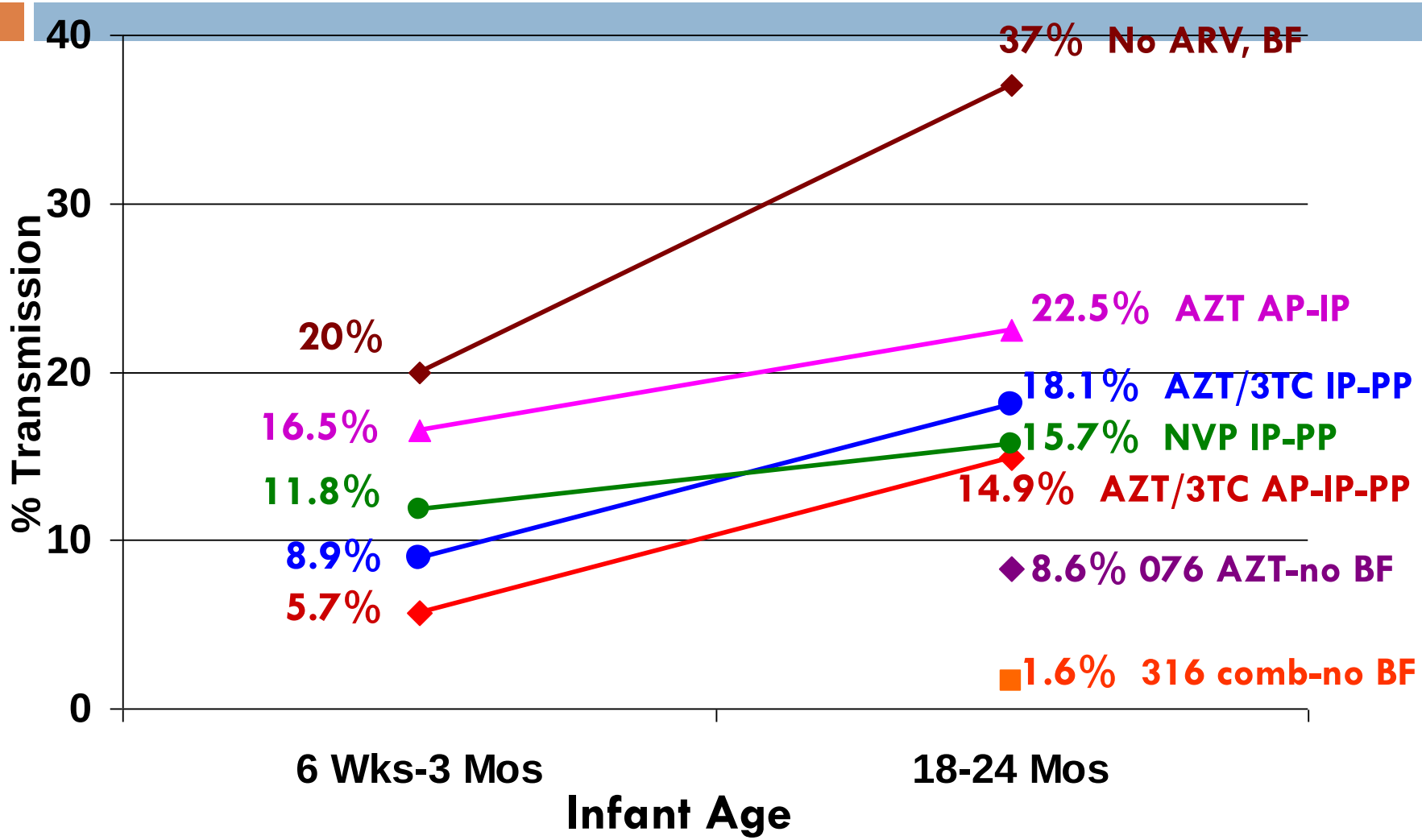
-

Combination ARV prophylaxis to PMTCT *(NACP, 2009)*

	Pregnancy	Labour	Postpartum	Comments
Recommended	AZT 300mg BD (≥ 28 weeks)	sd NVP + AZT/3TC	Mother: AZT/3TC x7d Infant: sdNVP + AZT* x 7d	7 days tail AZT/3TC to reduce NVP resistance
Present at labour		sd NVP + AZT/3TC	Mother: AZT/3TC x7d Infant: sdNVP + AZT* x 28d	
Test positive immediate post delivery			Mother: To CTC Infant: sdNVP + AZT* x 28d	

* sd-NVP and AZT+3TC can be omitted if mother receives >4 weeks of AZT antepartum

Effect of Breastfeeding on PMTCT Prophylaxis

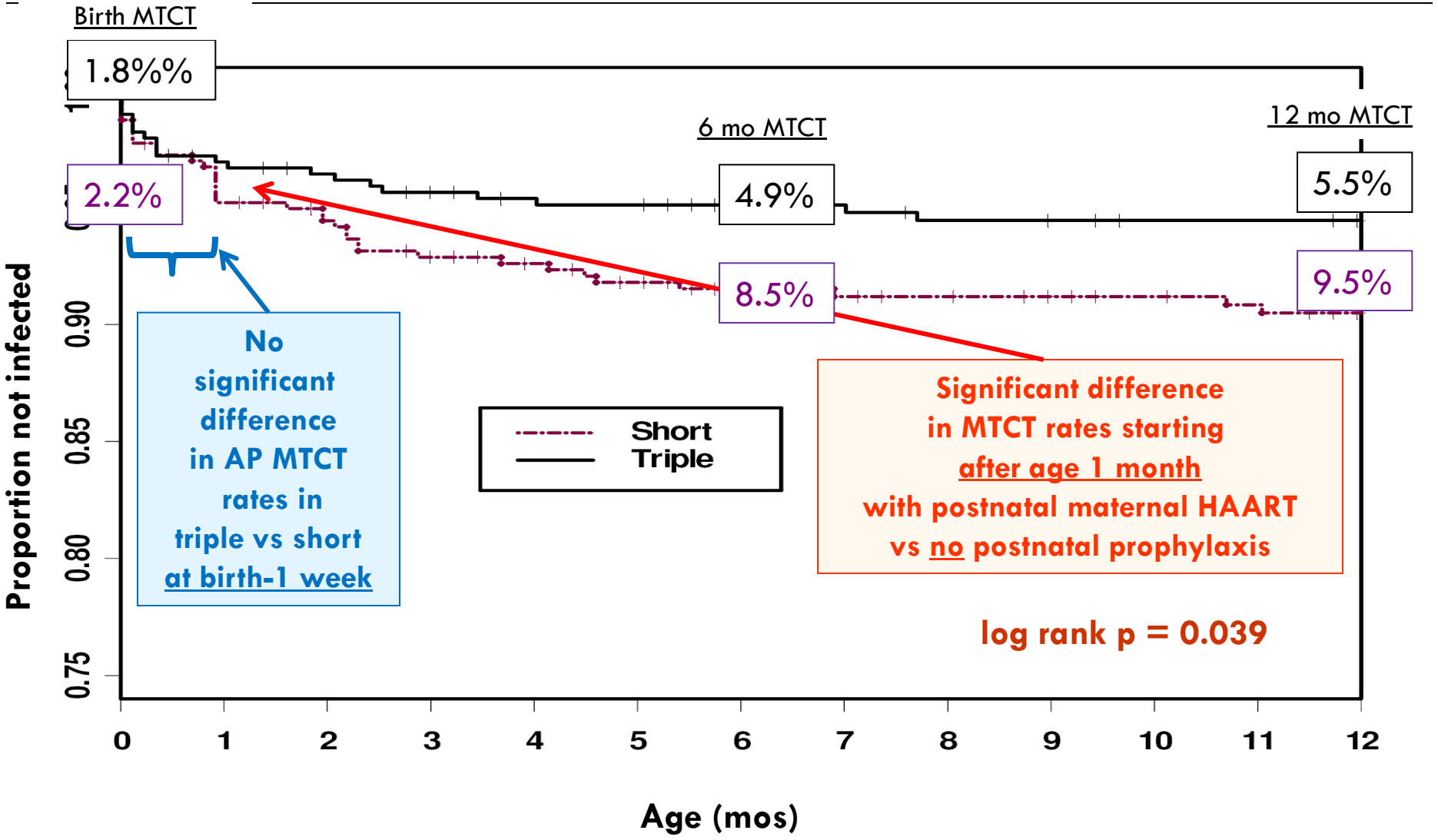


After 2006 recommendations….

- The search for preventive methods during breast feeding period
- Results of several New Clinical Trials on PMTCT were published

Kesho Bora: HIV Infection Over Time in HAART through Breastfeeding Vs Short AZT/sdNVP Arms

De Vincenzi I et al. IAS, Capetown, South Africa, July 2009 Abs LBPEC01



2010 WHO PMTCT Guidelines *(prophylaxis)*

Pregnant Woman Who Doesn't Require Therapy for Own Health

	Pregnancy	Labor	Postpartum	Comments
Option 1	AZT (at 14 wks)	•sd NVP + AZT/3TC	•Mother: AZT +3TC x 7d •Infant: NVP daily until 1 week after stopping BF	•Labor and PD maternal can be omitted if got AZT > 4 weeks in pregnancy
Option 2	Triple ARV (from 14 wks)	•Triple ARV	•Mother Triple ARV until 1 week after stopping BF •Infant: NVP x 6 weeks	

WHO, 2010

D. Pregnant woman not needing ART for her own health

TABLE 2. ARV-prophylaxis options recommended for HIV-infected pregnant women who do not need treatment for their own health

Option A: Maternal AZT	Option B: Maternal triple ARV prophylaxis
MOTHER	**MOTHER**
• Antepartum AZT (from as early as 14 weeks gestation) • sd-NVP at onset of labour* • AZT + 3TC during labour and delivery* • AZT + 3TC for 7 days postpartum* * sd-NVP and AZT+3TC can be omitted if mother receives >4 weeks of AZT antepartum	Triple ARV from 14 weeks until one week after all exposure to breast milk has ended • AZT + 3TC + LPV/r • AZT + 3TC + ABC • AZT + 3TC + EFV • TDF + XTC + EFV
INFANT	**INFANT**
Breastfeeding infant Daily NVP from birth until one week after all exposure to breast milk has ended *Non-breastfeeding infant* AZT or NVP for 6 weeks	*Breastfeeding infant* Daily NVP from birth to 6 weeks *Non-breastfeeding infant* AZT or NVP for 6 weeks

Main revisions

	2006 guidelines	2010 guidelines
Starting ART (Rx)	CD 4 count ≤ 200 cells/mm3	CD 4 count ≤ 350 cells/mm3
ARV prophylaxis (not eligible to start Rx)	ARV prophylaxis in 3rd trimester (28 weeks) Infant prophylaxis for 1 week	ARV prophylaxis should start at 14 weeks or sooner Options 1 or 2 Infant prophylaxis for 6 weeks
ARVs to prevent transimission during BF	Insufficient data to give recommendations	If woman got AZT, child given NVP till1 week after stopping BF If woman got triple ARV, continue til stop BF

PMTCT Milestones in Tanzania

2000

After a successful pilot phase PMTCT was scaled up using sdNVP at ANC, maternity

2006- 2008

Start AZT combination prophylaxis

Reliance on CD4 + clinical staging for ART

2010- 2011

Adoption of Option A

Roll out of PIMA machines at lower level for CD4

2012 to date

PMTCT updates Option B+

Summary of Changes in Recommendations: What to Start in Adults

FIRST-LINE REGIMENS (PREFERRED ARV REGIMENS)			
TARGET POPULATION	**2010 ART GUIDELINES**	**2013 ART GUIDELINES**	**STRENGTH & QUALITY OF EVIDENCE**
HIV+ ARV-NAIVE ADULTS	AZT or TDF + 3TC (or FTC) + EFV or NVP	**TDF + 3TC (or FTC) + EFV** (as fixed-dose combination)	***Strong, moderate-quality evidence***
HIV+ ARV-NAIVE PREGNANT WOMEN	AZT + 3TC + NVP or EFV		
HIV/TB CO-INFECTION	AZT or TDF + 3TC (or FTC) + EFV		
HIV/HBV CO-INFECTION	TDF + 3TC (or FTC) + EFV		

Evidence Summary: Safety of EFV and TDF in Pregnancy

EFV

No increased risk of birth defects with EFV when compared with other ARVs

- Systematic review (including Antiretroviral Pregnancy Registry), reported **outcomes for 1502 live births to women receiving EFV in the first trimester** and found **no increase in overall birth defects**
- Excludes > 3 fold increased risk in overall birth defects

TDF

- **Potential concerns include renal toxicity, adverse birth outcomes and effects on bone density**
- Systematic review assessed the toxicity of fetal exposure to TDF in pregnancy
- Limited studies showed no difference in fetal growth between exposed/unexposed
- No studies of TDF among lactating women, who normally have bone loss during breastfeeding
- **Current data reassuring**
- More extensive studies ongoing

Source: Ford N et al. AIDS, 2011. Ford N et al. AIDS, 2013. Ekouevi DK et al.J AIDS, 2011. WHO, Geneva Use of EFV during pregnancy. 2012. http://www.who.int/hiv/pub/treatment2/efavirenz/en
Nightingale SL. JAMA, 1998. British HIV Association. Guidelines for the management of HIV infection in pregnant women. HIV Medicine. 2012. De Santis M et al. Arch of Int Medicine, 2002.
Source: Antiretroviral Pregnancy Registry Steering Committee http://www.APRegistry.com Siberry GK et al. AIDS, 2012

Where are we in Tanzania

- In 2012, WHO proposed that all HIV-infected pregnant women should receive triple ART for life irrespective of CD4 count.
- Tanzania has recently switched from Option A to B+
- Increase pMTCT coverage and contribute to the goal of eliminating MTCT (EMTCT) in sub-Saharan Africa by 2015