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Integrating Antiretroviral Therapy into MNCH: Antenatal and Postnatal Care in the Option B+ Era

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Objectives

- Review epidemiology of HIV among women of reproductive age and children
- Describe current World Health Organization recommendations for management of HIV during pregnancy and breastfeeding (PMTCT Option B+)
- Discuss challenges and opportunities in the implementation of Option B+

Global summary of the AIDS epidemic | 2014

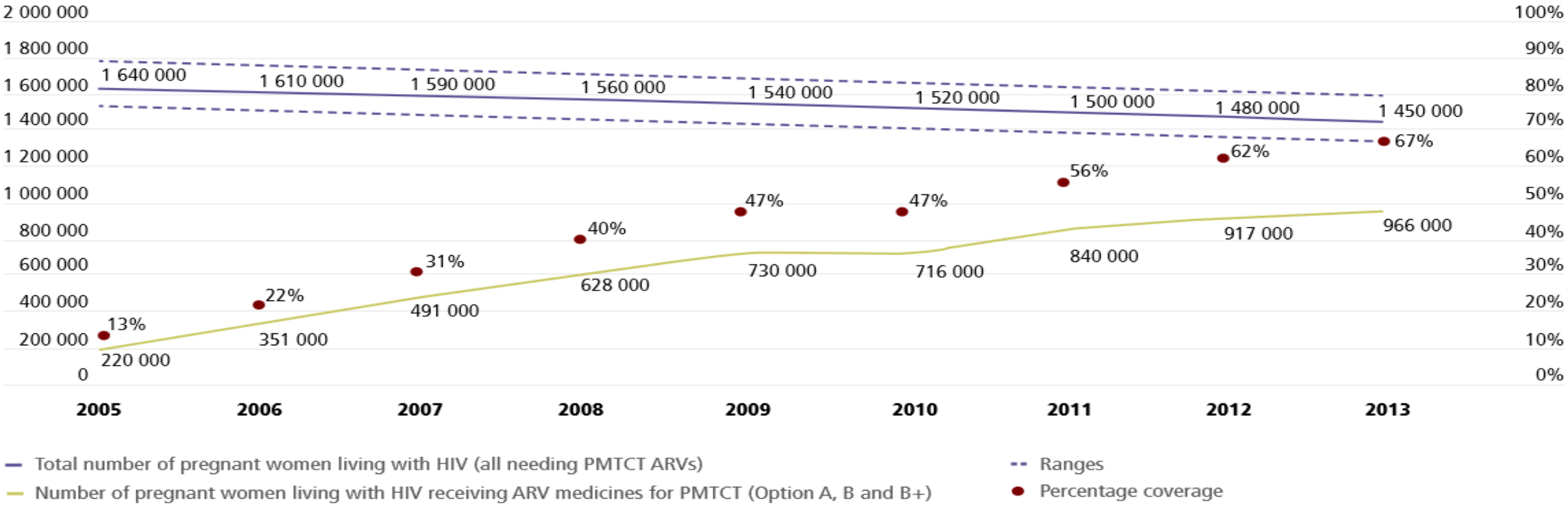
Number of people living with HIV in 2014	**Total**	36.9 million [34.3 million – 41.4 million]
	Adults	34.3 million [31.8 million – 38.5 million]
	Women	17.4 million [16.1 million – 20.0 million]
	Children (<15 years)	2.6 million [2.4 million – 2.8 million]
People newly infected with HIV in 2014	**Total**	2.0 million [1.9 million – 2.2 million]
	Adults	1.8 million [1.7 million – 2.0 million]
	Children (<15 years)	220 000 [190 000 – 260 000]
AIDS deaths in 2014	**Total**	1.2 million [980 000 – 1.6 million]
	Adults	1.0 million [890 000 – 1.3 million]
	Children (<15 years)	150 000 [140 000 – 170 000]

HIV and Maternal Mortality

- Pregnant women living with HIV are at two to 10 times greater risk of death than uninfected pregnant women

- While maternal deaths have decreased overall in past decade, countries with high HIV burdens have had slower declines compared to countries less affected by HIV pandemic
  - South Africa—an upper middle-income country with an antenatal HIV prevalence of 29.5%—experienced a decrease of only 0.4% in its maternal mortality ratio (MMR) between 1990 and 2013, despite a global MMR decrease of 45% in the same timeframe

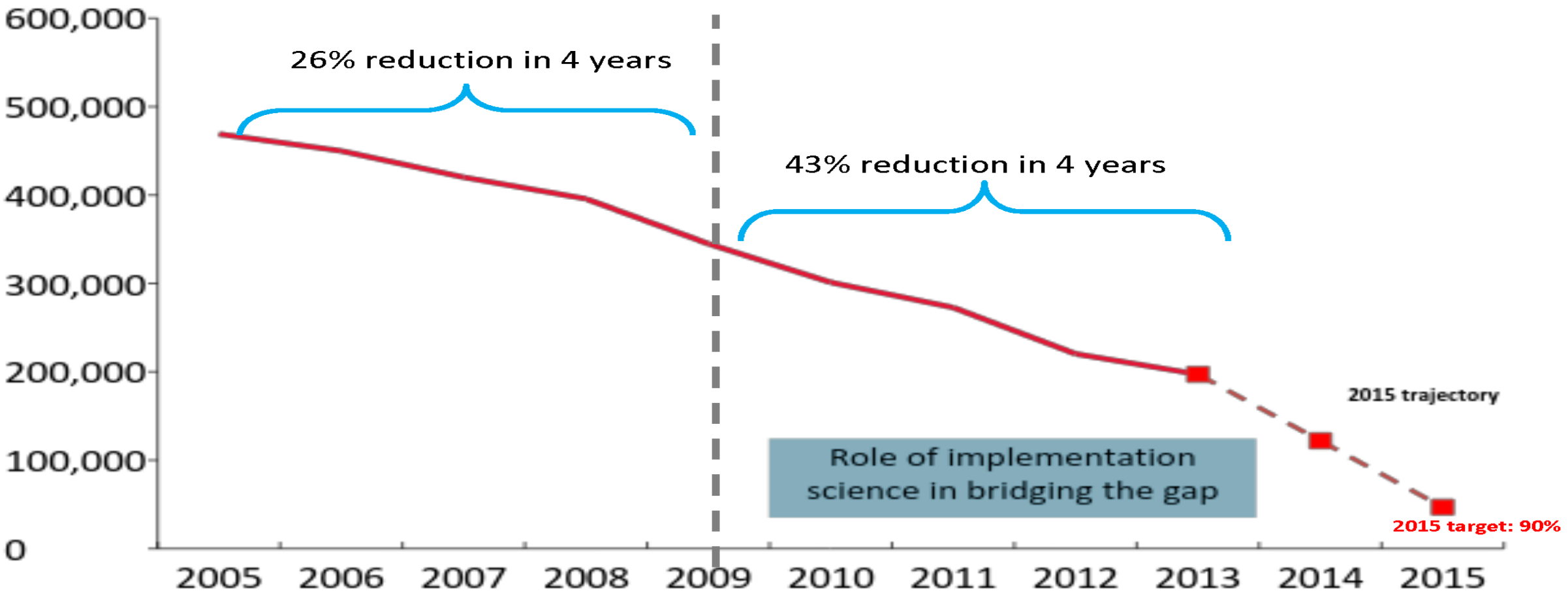
Fig. 3.2. Number of pregnant women living with HIV in low- and middle-income countries and the number and percentage of those women receiving ARV drugs for PMTCT of HIV, 2005–2013



Single-dose nevirapine is included in the data for 2005 to 2009.

Sources: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS) and validation process for the number of pregnant women living with HIV receiving ARV drugs for PMTCT, and UNAIDS 2013 estimates for the number of pregnant women living with HIV.

Reduction in New Pediatric Infections 2005-2013



Source: UNAIDS 2013 Estimates

Evolution of WHO Prevention of Mother-to-Child Transmission (PMTCT) ARV Guidelines Over Time

	2001	2004	2006	2010	2013
PMTCT	4 weeks AZT; AZT+ 3TC; or SD NVP	AZT from 28 wks + sdNVP	AZT from 28 wks + sdNVP + AZT/ 3TC 7d	**Option A** AZT/sdNVP + infant NVP if BF **Option B** ART preg/BF	**Option B** ART preg/BF **Option B+** Life-long ART
Treatment	No rec	ART if CD4 <200	ART if CD4 <200	ART if CD4 ≤350	ART if CD4 ≤500

Modified slide from Elaine Abrams

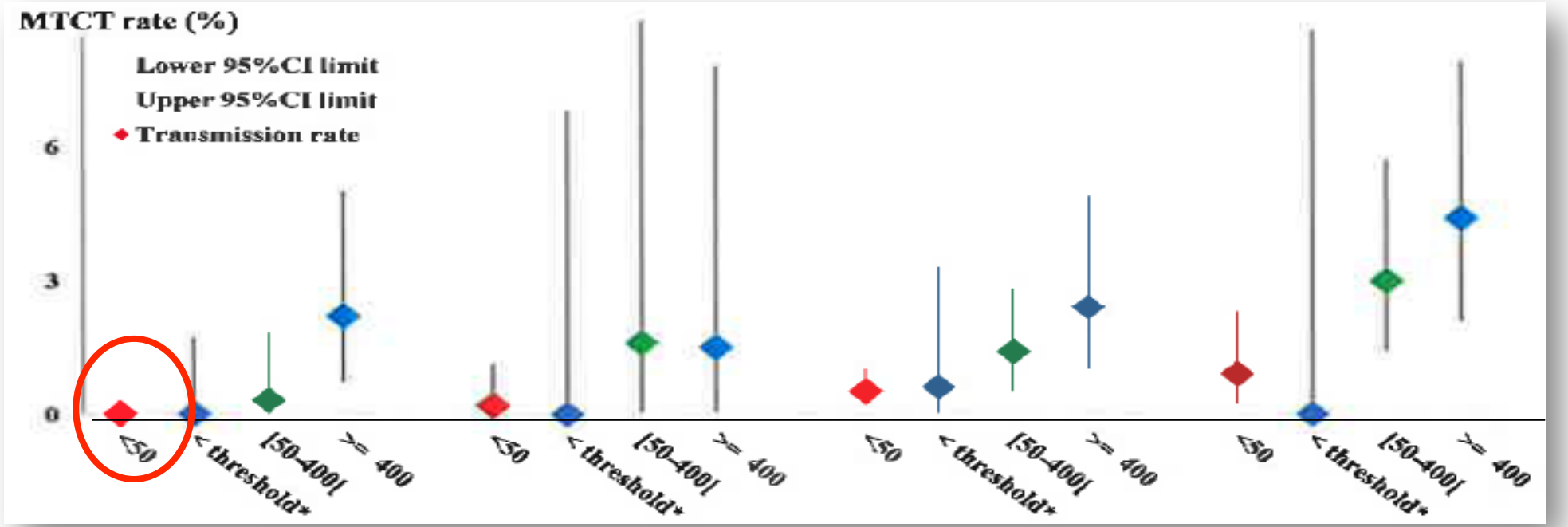
BEFORE 2013: Three options for PMTCT			
	Women with CD4 count above 350 cells/mm³	**Women with CD4 count below 350 cells/mm³**	**HIV-exposed infant receives**
Option A	During pregnancy: AZT starting as early as 14 weeks of pregnancy At delivery: single-dose NVP and first dose of AZT/3TC After delivery: daily AZT/3TC through 7 days postpartum	Triple ARVs started as soon as diagnosed and continued for life	Daily prophylaxis (NVP) from birth until 1 week after all breastfeeding has finished; or, if not breastfeeding or if mother is on treatment, through age 4–6 weeks
Option B	Triple ARVs starting as early as 14 weeks of pregnancy continued through childbirth (if not breastfeeding) or until 1 week after all breastfeeding has finished		Daily prophylaxis (NVP or AZT) from birth through age 4–6 weeks regardless of infant feeding method
Option B+	Triple ARVs started as soon as diagnosed and continued for life		

New Support for Option B+: Lowest MTCT with Preconception ART If Stay Suppressed

Madelbrot L et al. CROI 2015. Seattle, WA. Abs. 867

- French Perinatal Cohort: Overall MTCT 0.7% and was 0% (95% CI 0-0.1%) in 2,651 women starting ART before conception and RNA <50 at delivery.

Delivery RNA and MTCT According to Time ART Initiation



Started before conception	Started 1st trimester	Started 2nd trimester	Started 3rd trimester
MTCT 0.2%	MTCT 0.4%	MTCT 0.9%	MTCT 2.2%

*threshold if assay LLD >50 c/mL

All Countries with Highest HIV Burden Have Now Adopted Either Option B or B+

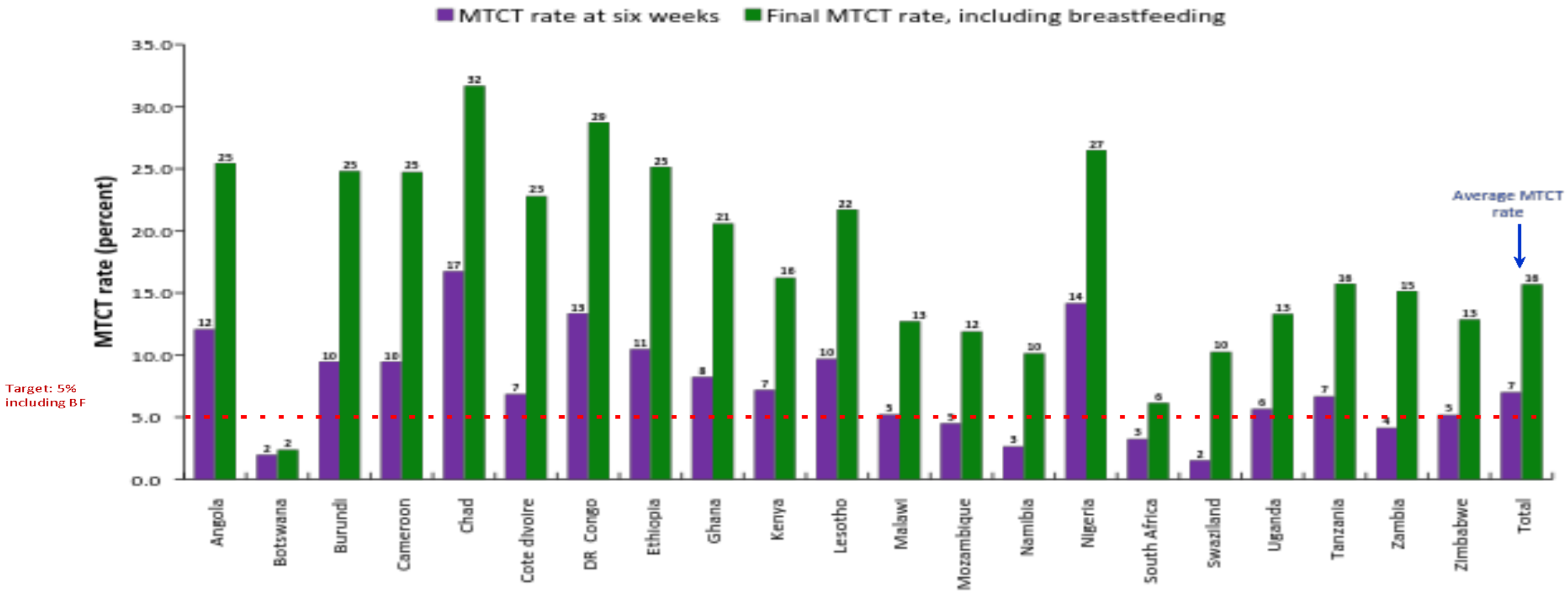
MOH PMTCT GUIDELINE POLICY

MAP KEY

- OPTION B
- OPTION B+: 1) PLANNING, PILOTS AND EARLY IMPLEMENTATION
- OPTION B+: 2) SCALE-UP
- OPTION B+: 3) NATIONAL
- NOT A PRIORITY COUNTRY

Global Update on the Health Sector Response to HIV. WHO 2014

Vertical Transmission Rates at 6 Weeks and Weaning in Selected African Countries



Source: UNAIDS 2013 estimates

Reasons for Residual MTCT

- Woman not offered HIV testing (test kit stock-outs) or she declines
- Late presentation to ANC in pregnancy limits opportunity to bring viral load down before childbirth
- Lack of early and sustained control of viral load (Tubiana et al. Clin Infect Dis 2010;50:585)
  - Access to the most effective regimens (resistance testing)
  - Reluctance to initiate ART due to stigma (lack of disclosure to partner/family a predictor of poor adherence)
  - Avoiding treatment interruption in pregnancy and breastfeeding (frequency of visits for new ART patients a burden on pregnant and postpartum women)
- Maternal genital tract infection-associated with HIV-RNA discordance between plasma and genital tract

Reasons for Residual MTCT (cont)

- Acute HIV infection in pregnancy and breastfeeding (Birkhead et al. Obstet Gynecol 2010;115:1247; Patterson et al. AIDS 2007;21:2303)
  - Associated with increased MTCT
  - Pregnancy a period of increased risk for HIV acquisition (Gray. Lancet 2005;366:1182; Bernasconi. J Clin Virol 2010;48:180; Moodley. AIDS 2009;23:1255)
- Poor retention and adherence to ART especially during breastfeeding, lack of infant prophylaxis

Option B+: Various Models

- ART is initiated by ANC nurse in the same ANC exam room
  - Mom and baby followed in MNCH until 6 week EID visit, then transferred to HIV clinic
  - Mom and baby followed in MNCH until weaning, then transfer to HIV clinic
- HIV testing is conducted by the ANC nurse; women who test HIV+ are referred to HIV clinic (which could be in a different facility)

ARVs in an exam room in Malawi

Option B+: Models and Record Keeping Implications

- Increasingly, women come into ANC as “known positives” and may already be on ART
  - Should she continue to get her ART at HIV clinic? Or should her HIV be managed in MNCH during pregnancy/postpartum? What if HIV and ANC clinic days are different? What if HIV clinic is in a different facility altogether?

- What are the record keeping implications of women bouncing between MNCH and HIV clinic? One of the goals of Option B+ was to reduce treatment interruptions in women with high fertility, but transfer from one service to another represents an opportunity to fall out of care

Option B+: Results to Date

- Long-term Follow-Up (LTFU): Malawi: 577/2930 (20%) missed scheduled clinic visit by 3+ weeks: 47% did not return after initial initiation
  - LTFU associated with age <25, ART initiation in pregnancy, or started ART soon after introduction B+ (retention rates improved as program matured)
  - Patient tracing (219): 57% had stopped ART or never started (Trop Med Int Health 2014;19:1360)

Adherence and Retention in Pregnancy and Postpartum

- Systematic review/meta-analysis: 51 studies (27% US, 32% Africa): pooled estimate **75.7% adherence in pregnancy, 53% postpartum** (Nachega et al. AIDS 2012:26:2039)
- South Africa: 7510 ART naïve women initiating ART: 896 pregnancies: compared with non-pregnant women, increased risk of non-adherence in postpartum period (RR 1.46) but not in pregnancy (JAIDS 2015;68:477)
- Systematic review: barriers to adherence/retention in pregnancy/PP- poor understanding, difficulty managing practical demands ART, lack of disclosure/partner involvement, stigma (PLoS One 2014;9:e111421)

Conclusions

- PMTCT programs have dramatically reduced the number of new pediatric infections
- Option B+ represents an opportunity to virtually eliminate pediatric HIV whilst keeping HIV+ mothers alive and healthy
- Despite an overwhelming scientific and policymaker consensus in favor of Option B+, many implementation challenges remain