

# *The journey towards making elimination of mother to child HIV transmission (eMTCT) a reality; contribution of clinical research*



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**SUB-SAHARAN AFRICA**  
CFAR BIENNIAL MEETING  
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# Presentation outline

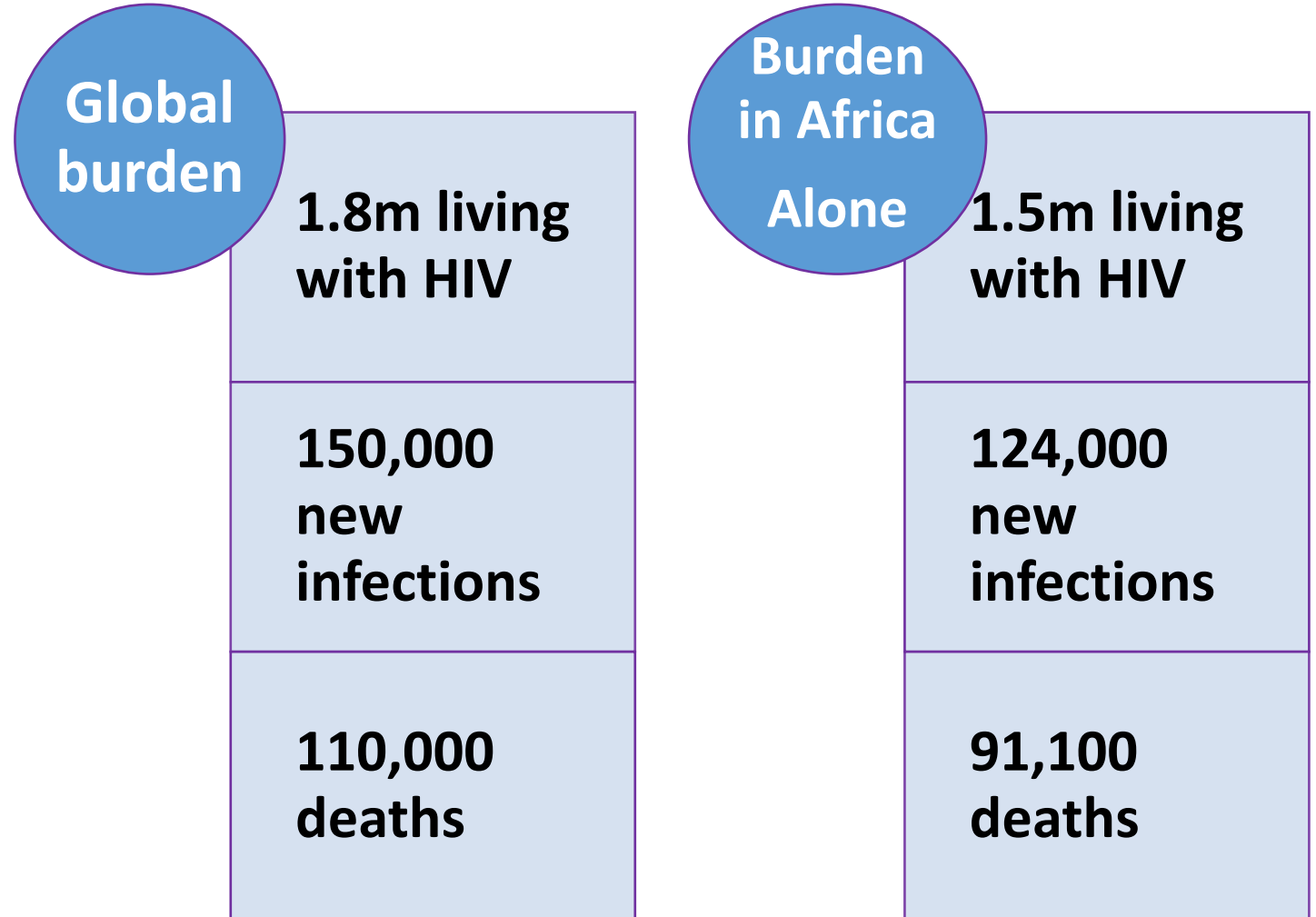
- Introduction: Burden of Mother to Child HIV transmission (MTCT)
- eMTCT-a snapshot of progress in high priority countries
- The Journey to eMTCT-what has clinical research contributed?
- Towards eMTCT: Landmark PMTCT clinical trials done at MUJHU Research collaboration, Kampala, Uganda
- Making eMTCT a reality- addressing the gaps through research
- Conclusions

# Burden of Mother To Child HIV Transmission

Between 2009 and 2015, about 4.5 million women of childbearing age in 21 African countries were newly infected with HIV

90% of all HIV infections in children are through MTCT

2015 estimates of HIV burden in children < 15 years



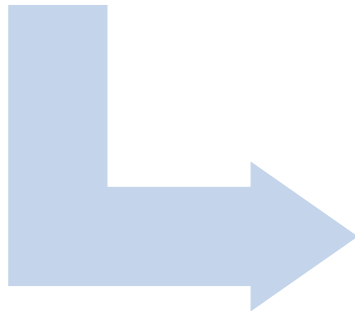
Source: UNAIDS Global AIDS Update 2016

# Journey to eMTCT

Early 1990's

No ARV interventions

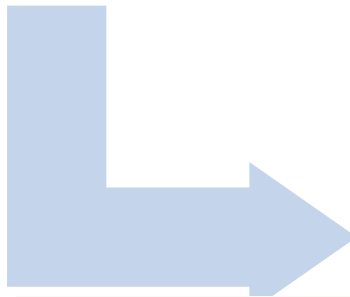
- MTCT Rates: 15-30% developed countries and Up to 45% in developing countries (Breastfeeding populations)
- Breastfeeding transmission: 5-20%



Mid 1990's  
PMTCT advent

ARV prophylaxis interventions

- Reduced MTCT rates: up to > 50% ↓ in developing countries
- MTCT rates as low as 2% in developed countries



2011 Global plan to eliminate new paediatric HIV infections

PMTCT scale up,  
More effective ART regimens

- eMTCT target: achieve <5% MTCT rates

## Global Plan towards elimination of new HIV infections in children and keeping mothers alive

(launched 2011)

### Goals by end of 2015:

- ❑ >90% reduction in new infections in children (<5% MTCT in BF settings and <2% in non BF settings)
- ❑ >50% reduction in HIV-associated maternal deaths
- ❑ Focus on 22 high priority countries

COUNTDOWN TO ZERO

Believe it.  
.....  
Do it.



GLOBAL PLAN TOWARDS THE ELIMINATION OF NEW HIV INFECTIONS  
AMONG CHILDREN BY 2015 AND KEEPING THEIR MOTHERS ALIVE

2011-2015

# eMTCT- a snap shot of progress thus far



eMTCT- status update 2015 (21 Global plan priority countries)



Source: UNAIDS 2015 Progress report on Global plan



# eMTCT: Component of Fast track global agenda



## Fast-Track Targets

by 2020

**90-90-90**

HIV treatment

**500 000**

New HIV infections or fewer

**ZERO**

Discrimination

by 2030

**95-95-95**

HIV treatment

**200 000**

New HIV infections or fewer

**ZERO**

Discrimination

Accelerating delivery of high impact HIV prevention and treatment services

Focus on 30 countries with highest HIV burden

## eMTCT fast track target:



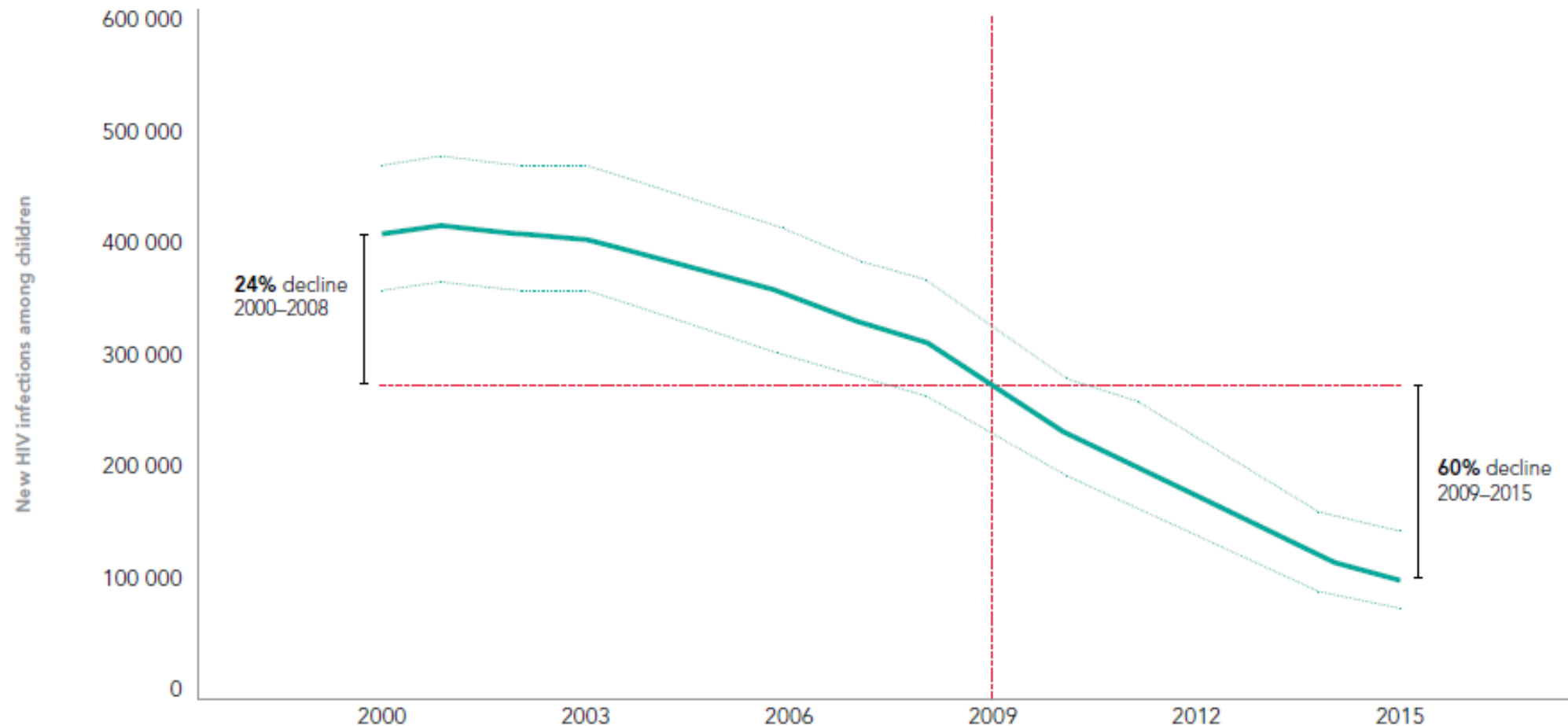
New HIV infections among children eliminated and their mother's health and well-being is sustained

## Result areas:

- Immediate ART accessible to all pregnant women living with HIV (Option B+)
- Intergration of HIV, sexual and reproductive health, including family planning, TB and MCH services
- HIV prevention services for male partners promoted, including testing and treatment

# eMTCT- a snap shot of progress thus far

Number of new infections among children in 21 Global plan priority countries 2000-2015

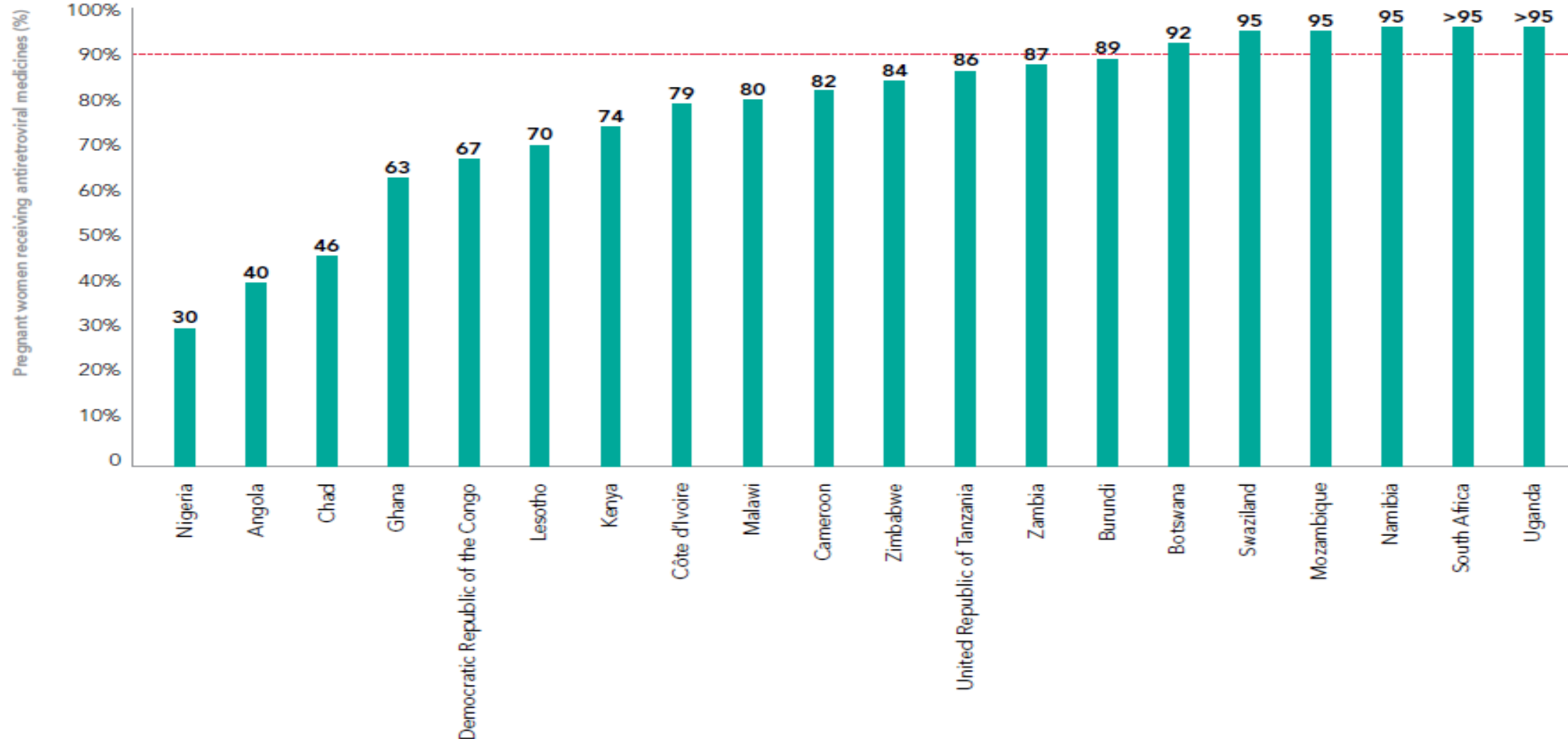


Source: UNAIDS 2016 Progress report on Global plan



# eMTCT- a snap shot on progress thus far

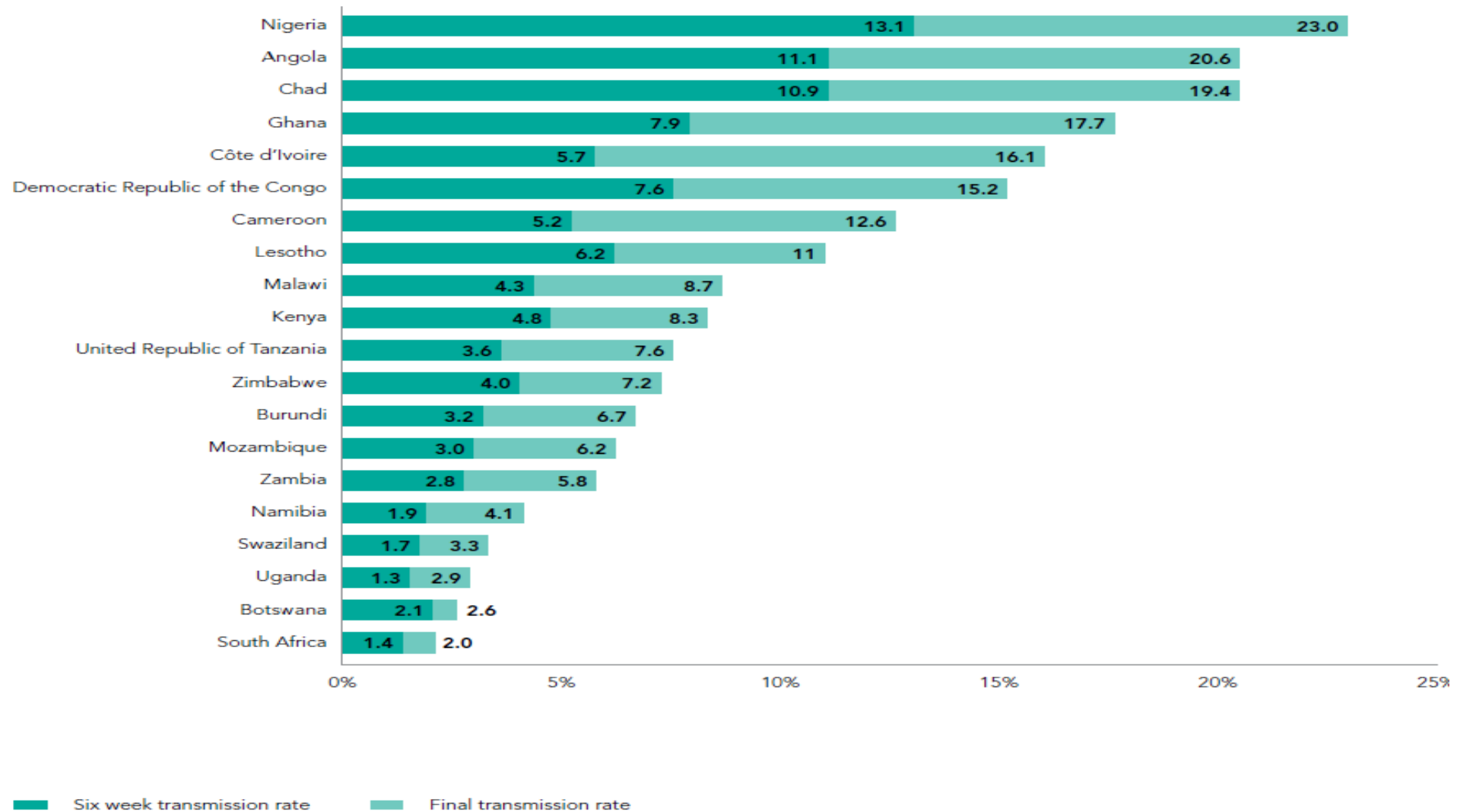
Percentage of HIV infected pregnant women who received ARV medicines for PMTCT by country in 2015



Source: UNAIDS 2016 estimates

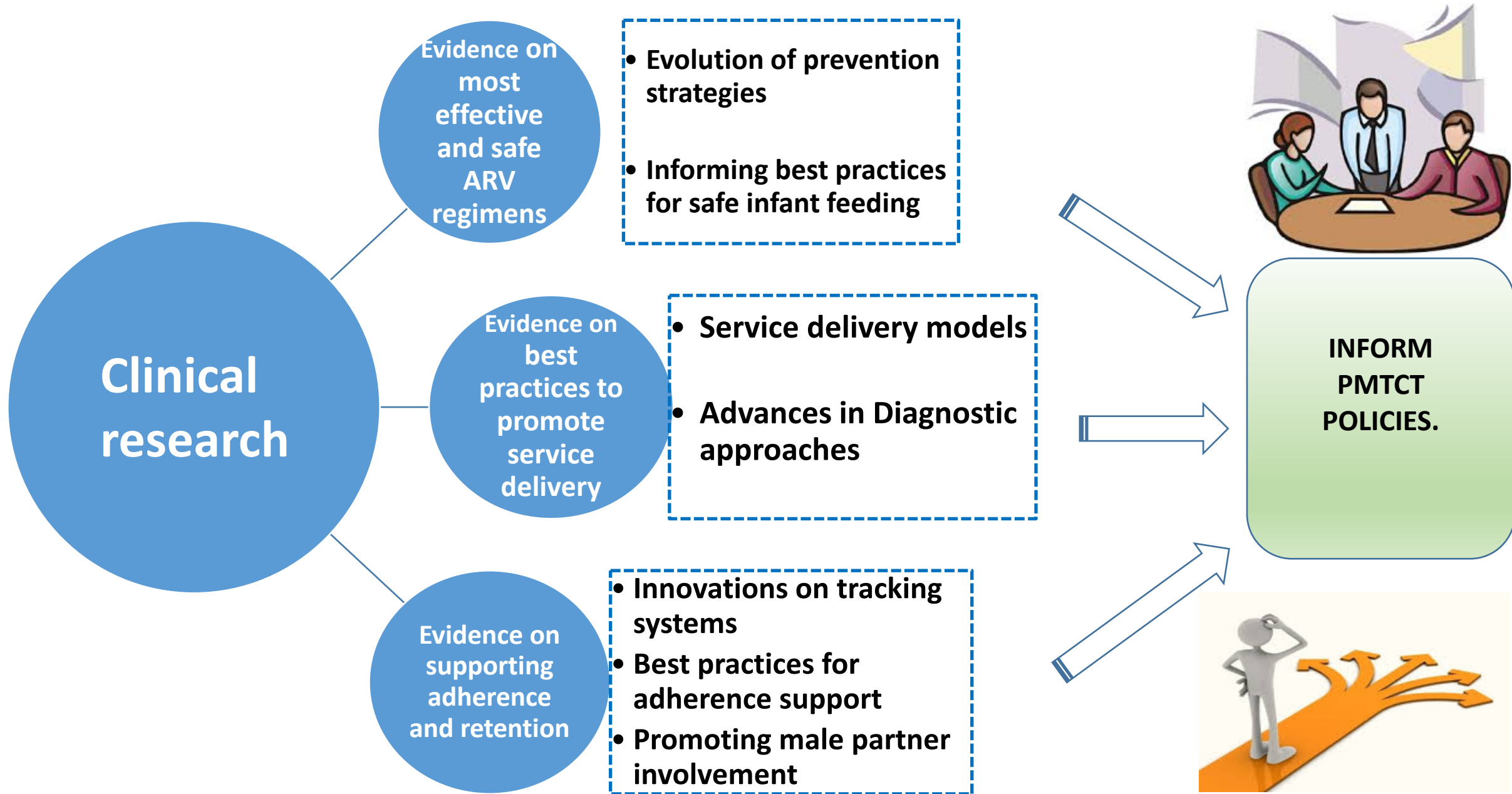
# eMTCT- a snap shot on progress thus far

Six week and final mother to child transmission rate by country 2015

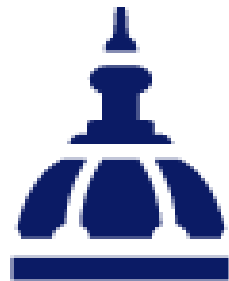


Source: UNAIDS 2016 estimates

# The Journey to eMTCT-what has clinical research contributed?



# Towards eMTCT- PMTCT clinical trials conducted MUJHU Research collaboration CRS, Uganda



# Landmark PMTCT studies done at MUJHU CRS, Uganda

Which ARV regimens are best?

## **HIVNET 012 (1997)**

- ❑ Sd NVP to mother at onset of labour and to baby within 72 hours Vs AZT regimen through labour and to baby for 7 days
- ❑ 50% reduction in HIV transmission with sdNVP (breastfeeding setting)

## **Petra (1996-2000)**

- ❑ RCT done in S.Africa, Uganda (MUJHU), and Tanzania. About 1800 participants enrolled
- ❑ Compared prepartum+intrapartum+postpartum regimen vs intrapartum+ postpartum vs intrapartum regimen
- ❑ 6 week transmission rate was lowest with the prepartum+intrapartum+postpartum regimen (5.7%)

# Landmark PMTCT studies done at MUJHU CRS, Uganda

## HPTN 046: Extended Infant NVP prophylaxis, 2008-2010

1527 infants enrolled and randomized

Extended NVP arm

N=762

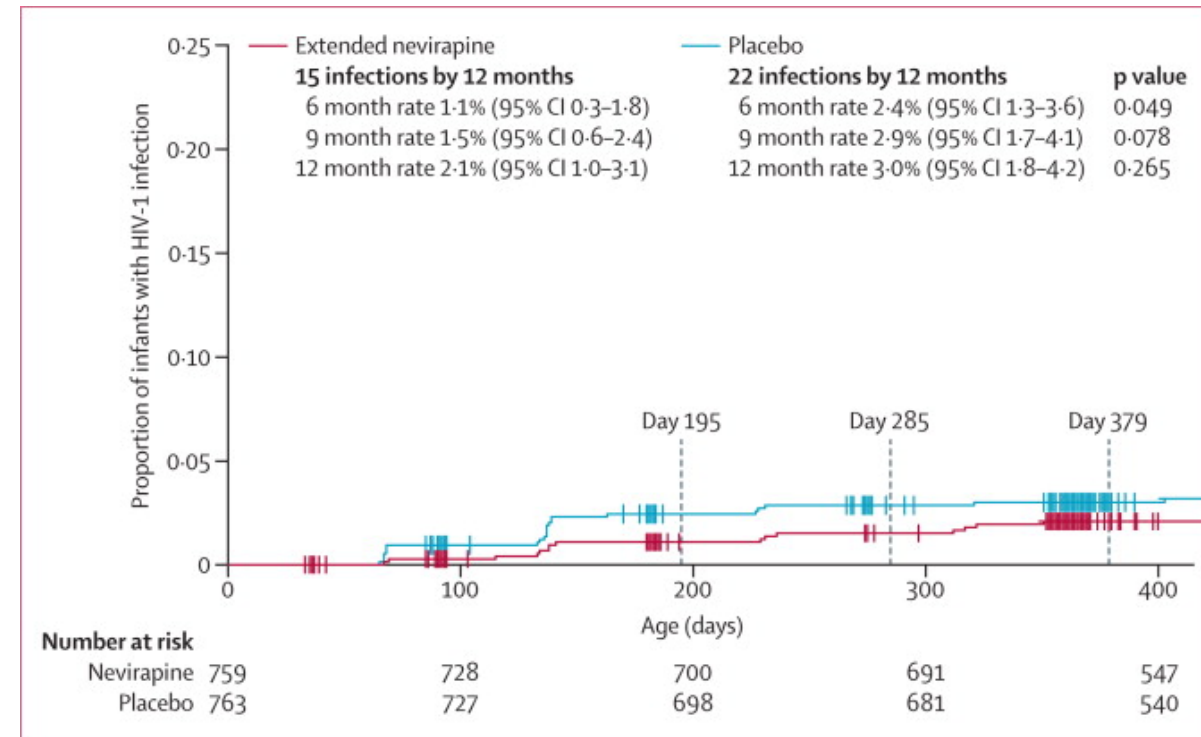
NVP through 6 months of age

Placebo arm N=765

NVP for 6 weeks then placebo through 6 months

Study done in *Uganda (MUJHU CRS), Tanzania, South Africa, Zimbabwe*

*Kaplan-Meier analysis of cumulative rates of HIV-1 infection, by study group*





# Recent PMTCT study: Which ARV regimens are best?



## Main Goals

- ❑ Maximize prevention of mother-to-child HIV transmission (PMTCT) and optimize maternal/child health and survival.
- ❑ Assess the relative safety and efficacy of triple ARVs compared to other proven regimens among healthy HIV women with higher CD4 counts.

## NIH IMPAACT Clinical Research Sites

### Study Sites in:

- India (1)
- Malawi (2)
- South Africa (5)
- Tanzania (1)
- Uganda (**MUJHU CRS**)
- Zambia (1)
- Zimbabwe (3)

### Sample size

3543 Mother-infant pairs



# Recent PMTCT study: Which ARV regimens are best?

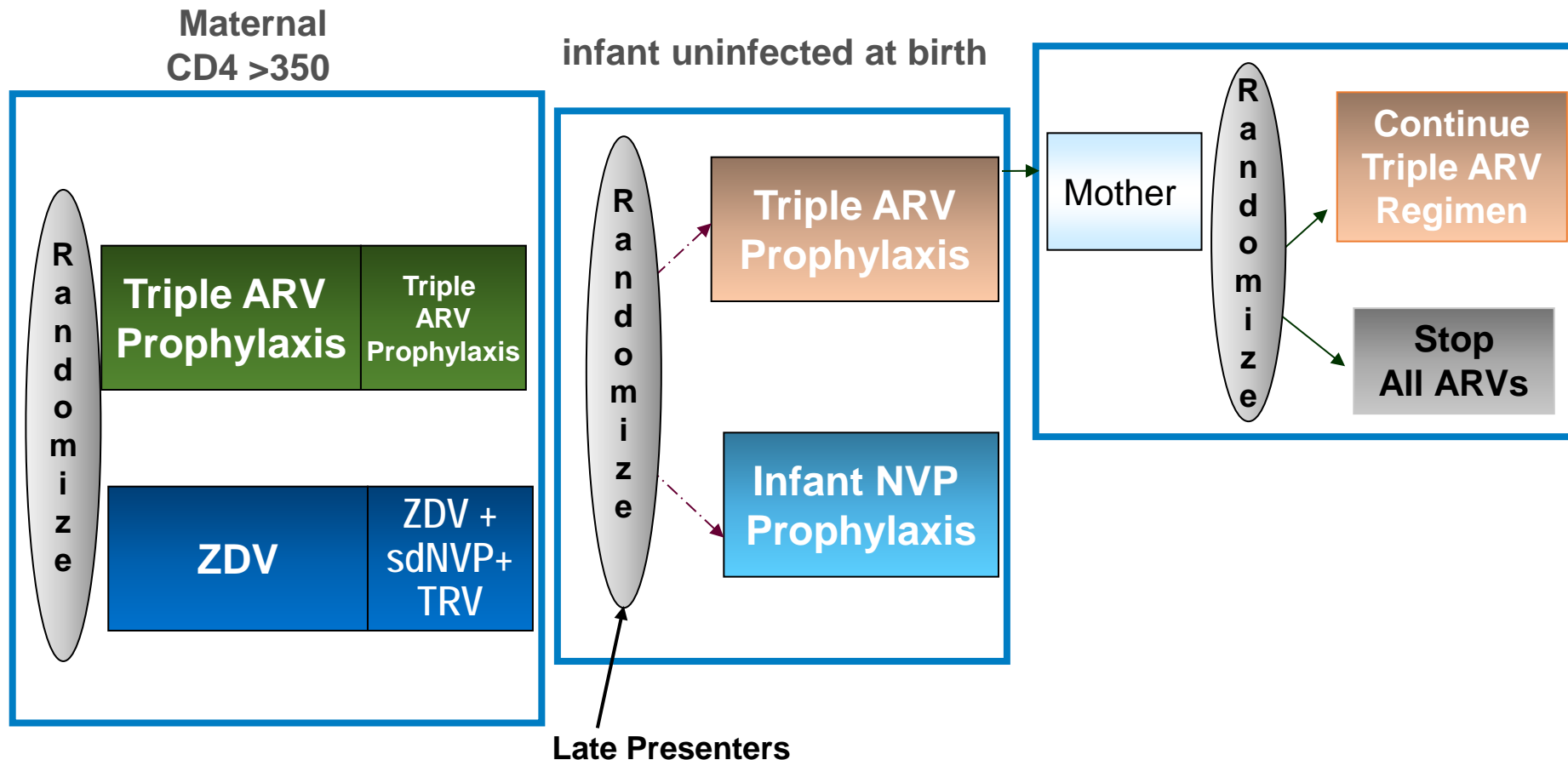
## PROMISE study Randomizations

**Antepartum**  
(14 wks-term)

**Labor/  
Delivery**

**Postpartum**  
(for duration of BF)

**Maternal Health**  
(after BF cessation)



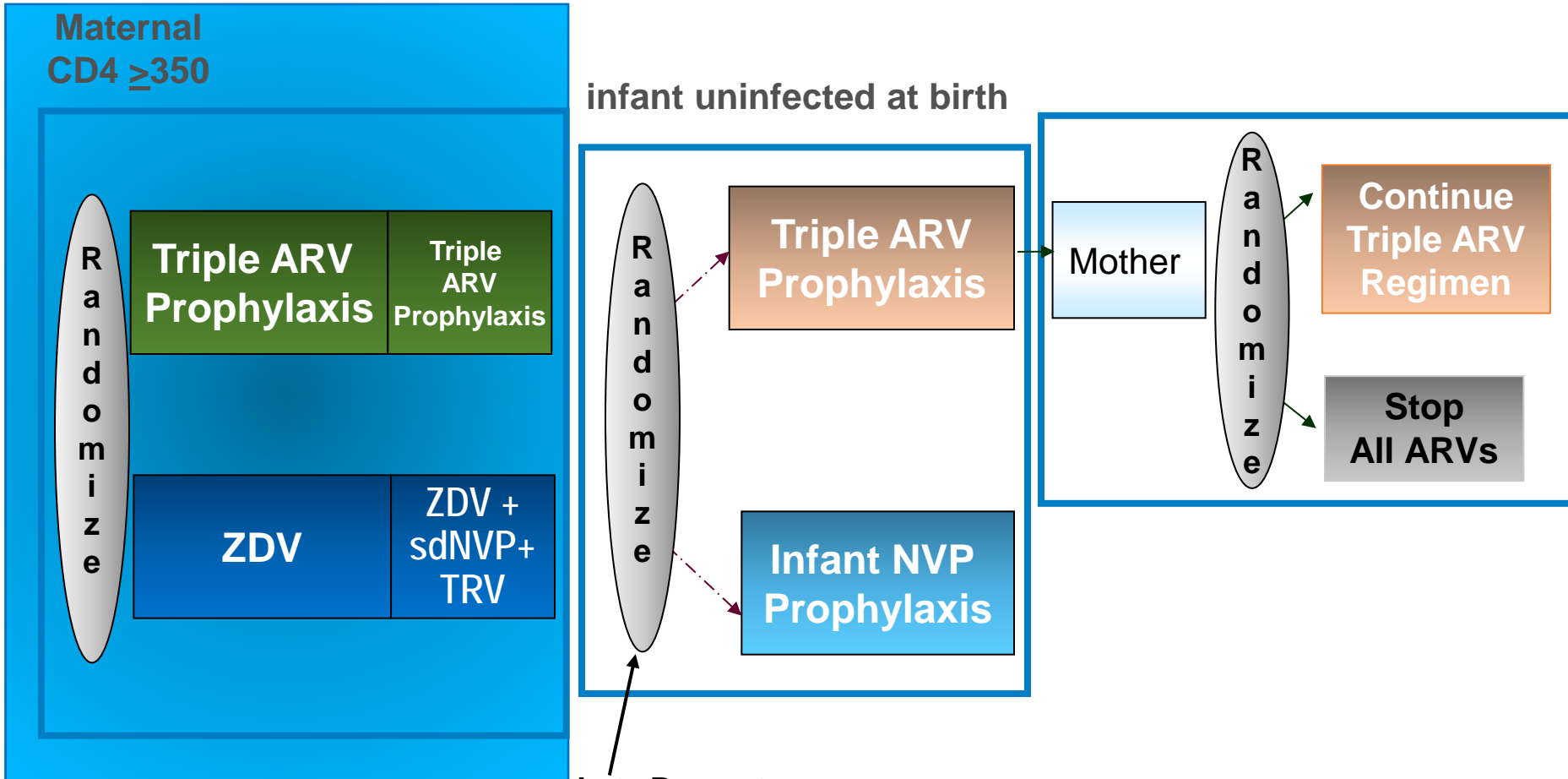
# Recent PMTCT study: Which ARV regimens are best?

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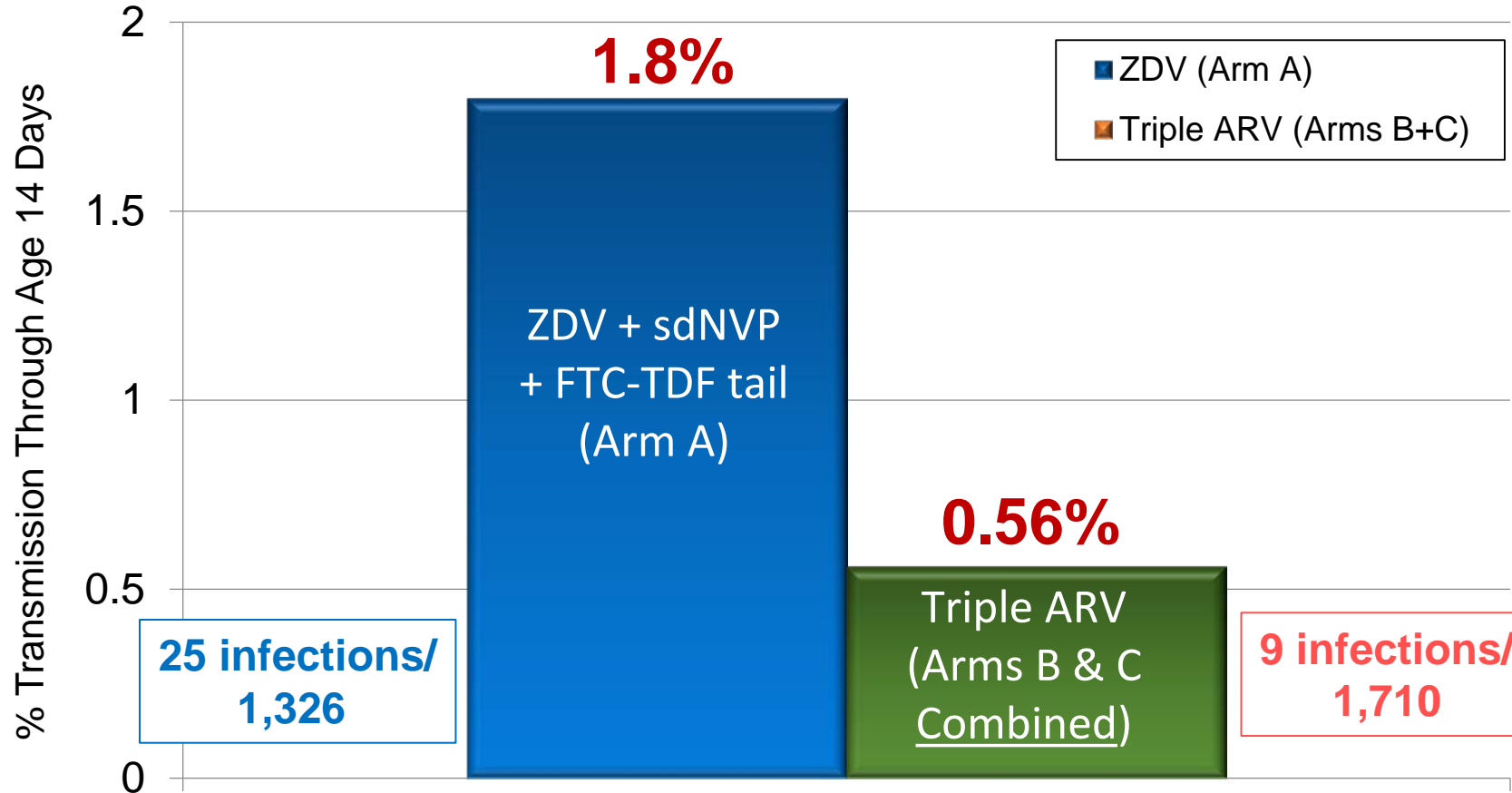


**ENROLLED 3,529 WOMEN**

MG Fowler et al CROI 2015

# Recent PMTCT study: Which ARV regimens are best.....?

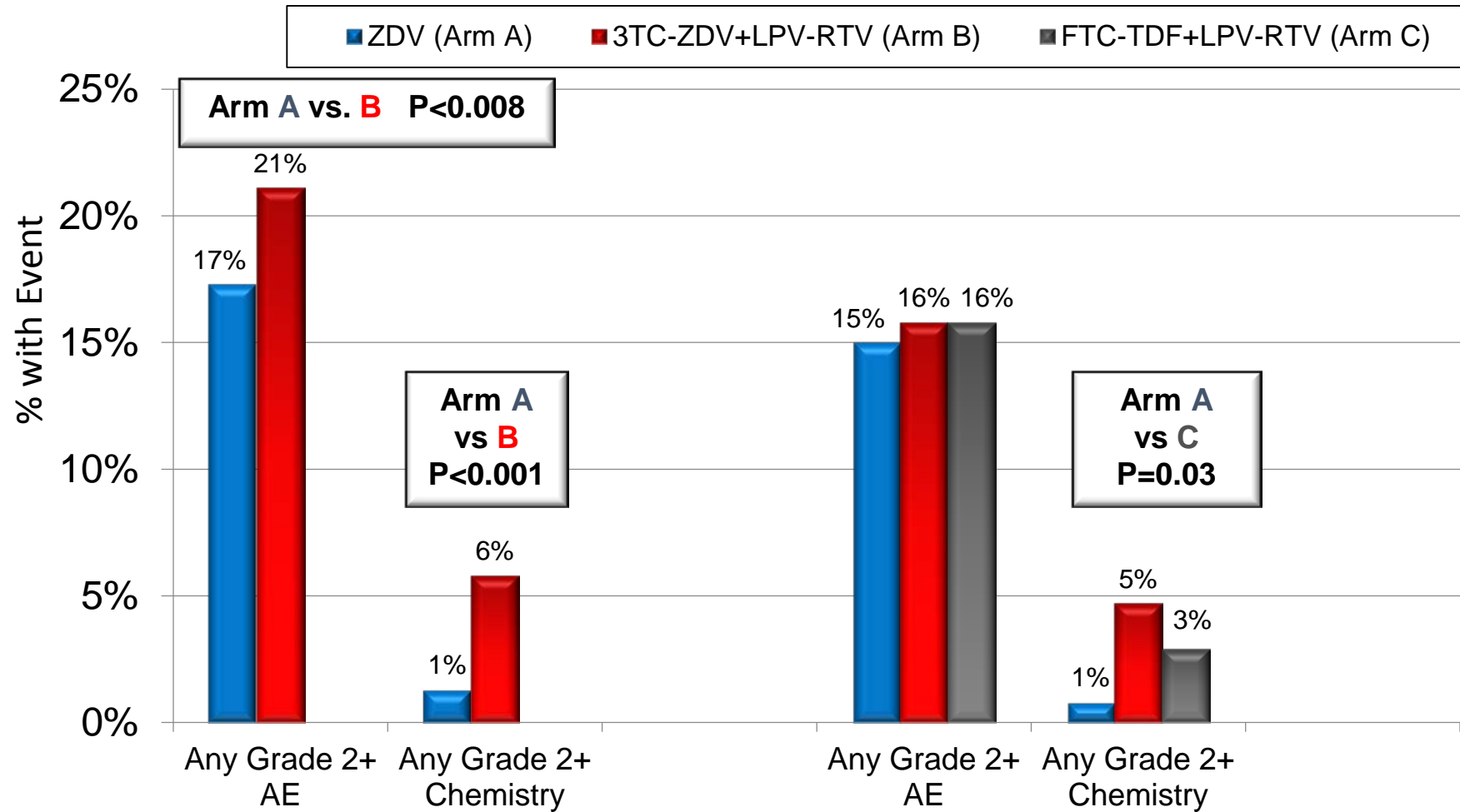
PROMISE Antepartum component results: MTCT Through Age 14 days significantly lower in triple ARV Arms



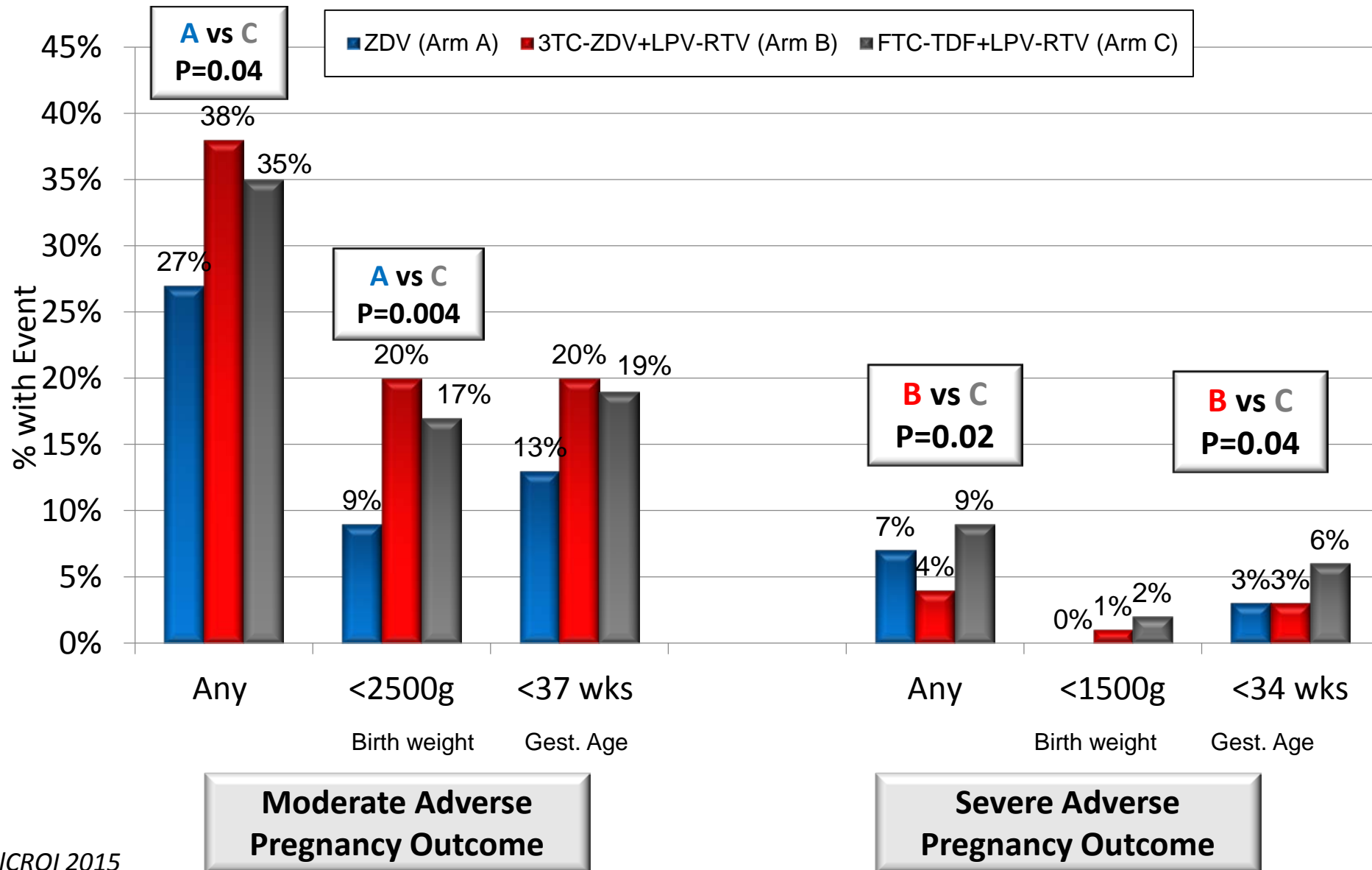
**Difference in MTCT Risk (Repeated Confidence Interval): -1.28% (95% CI -2.11%, -0.44%)**

# Recent PMTCT study: Which ARV regimens are best....?

## PROMISE Study: Antepartum Component results: Adverse events



# Recent PMTCT study: Which ARV regimens are best....?



# Research informing policy: Evolving WHO PMTCT guidelines



2001



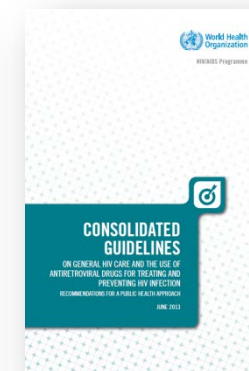
2004



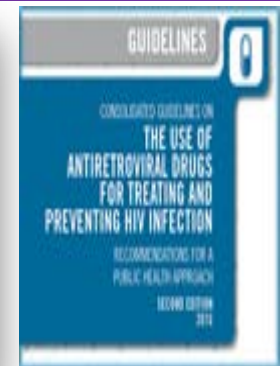
2006



2010



2013



2015

<b>PMTCT</b>	4 weeks AZT; AZT+ 3TC, or SD NVP	AZT from 28 wks + SD NVP	AZT from 28 wks + sdNVP +AZT/3TC 7days	Option A (mat AZT + infant NVP to end BF) Option B (mat triple ARVs to end of BF)	Option B or B+ Moving to ART for all pregnant / BF women	<b>TREAT All</b>
<b>KEY STUDIES</b>	HIVNET 012 PETRA	HIVNET 012 THAI STUDY	DITRAME SWEN	HPTN 046 BAN KESHO BORA	SMART HPTN 052 PROMISE	<b>START TEMPRANO</b>
<b>ART</b>	None	CD4 <200	CD4 <200	CD4 ≤350	CD4 ≤500	Test and Treat All

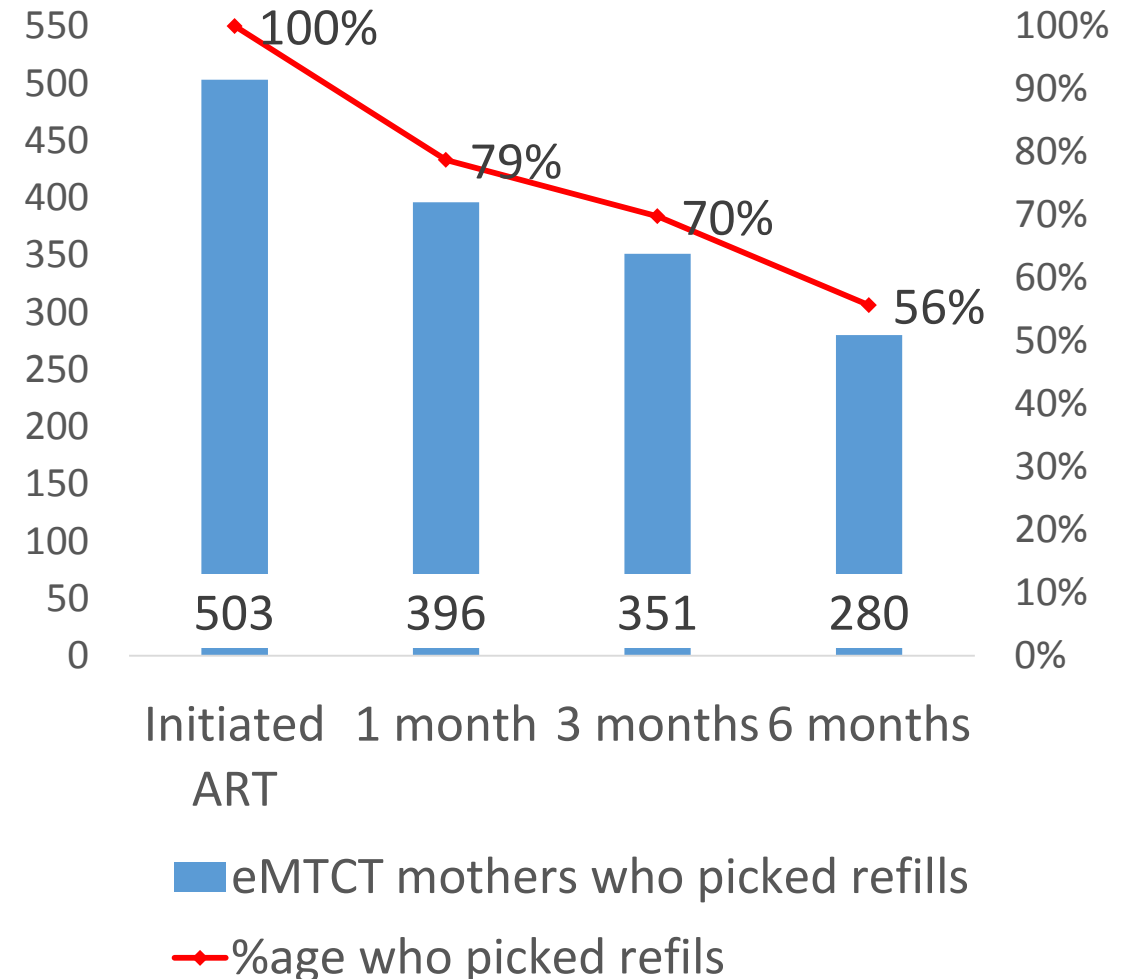
Research has informed move to use of *more effective ARV drugs, extending coverage throughout MTCT risk period, and ART for the mother's health as well as safe infant feeding options*

# Making eMTCT a reality-what are the challenges?

## Main challenges

- Unmet family planning needs
- Low PMTCT coverage
- Adherence challenges with life long ART (Option B+)
- Poor retention in care
- Stigma
- Male involvement and community support
- Intergration of Maternal and child health services

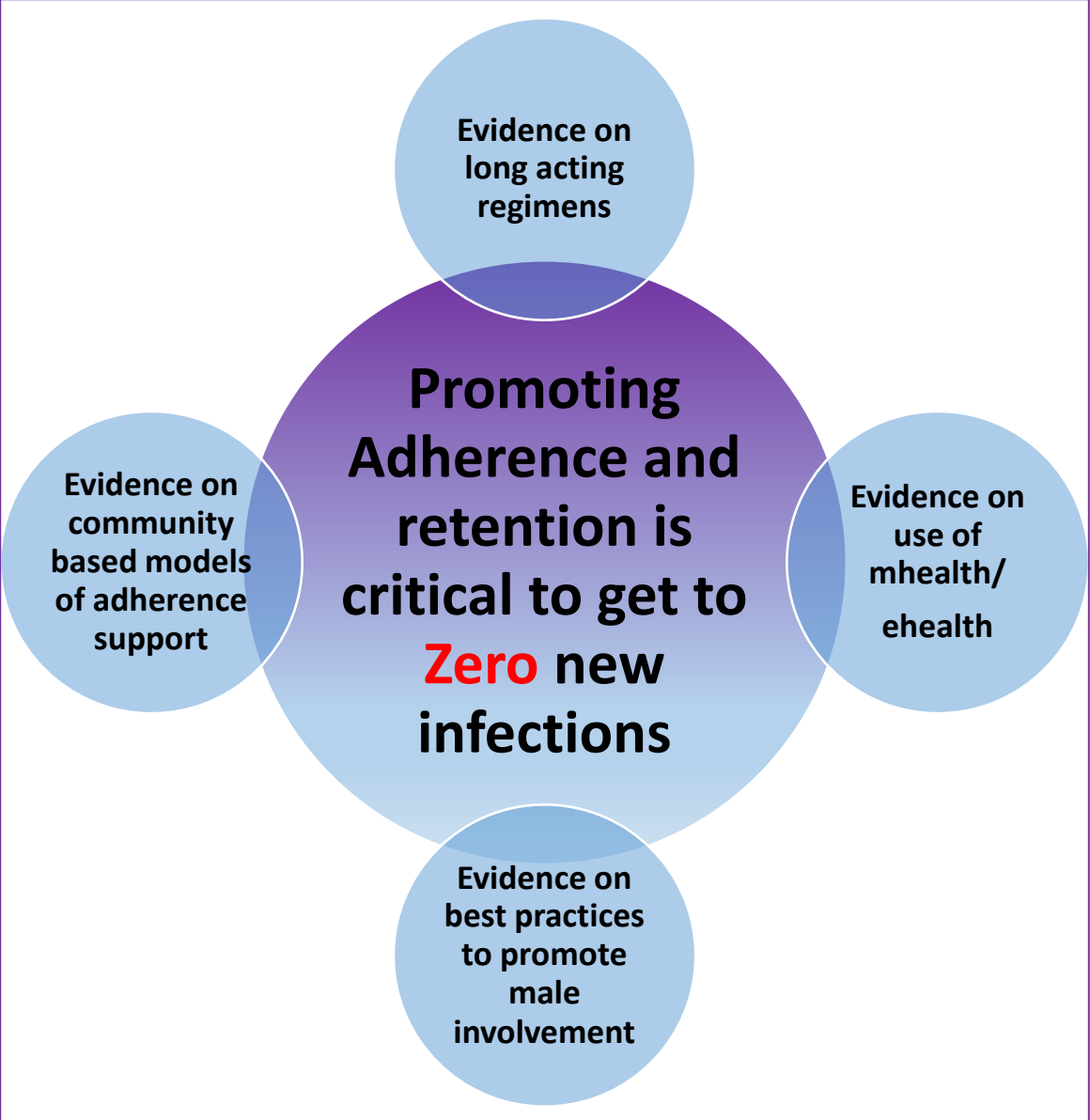
**Retention of mothers in eMTCT-Uganda data 2015**



Source: Uganda MOH eMTCT review report 2016



# Making eMTCT a reality-addressing the gaps through research



# Making eMTCT a reality-addressing the gaps through research

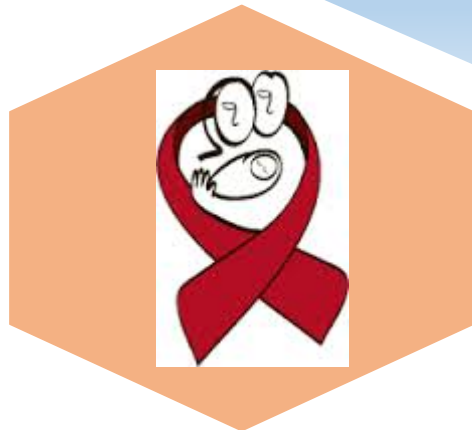


Evidence on long term safety of different ARV regimens

Infant neurodevelopment and growth, maternal and infant organ toxicities

Finding best prophylactic interventions to prevent vertical transmission

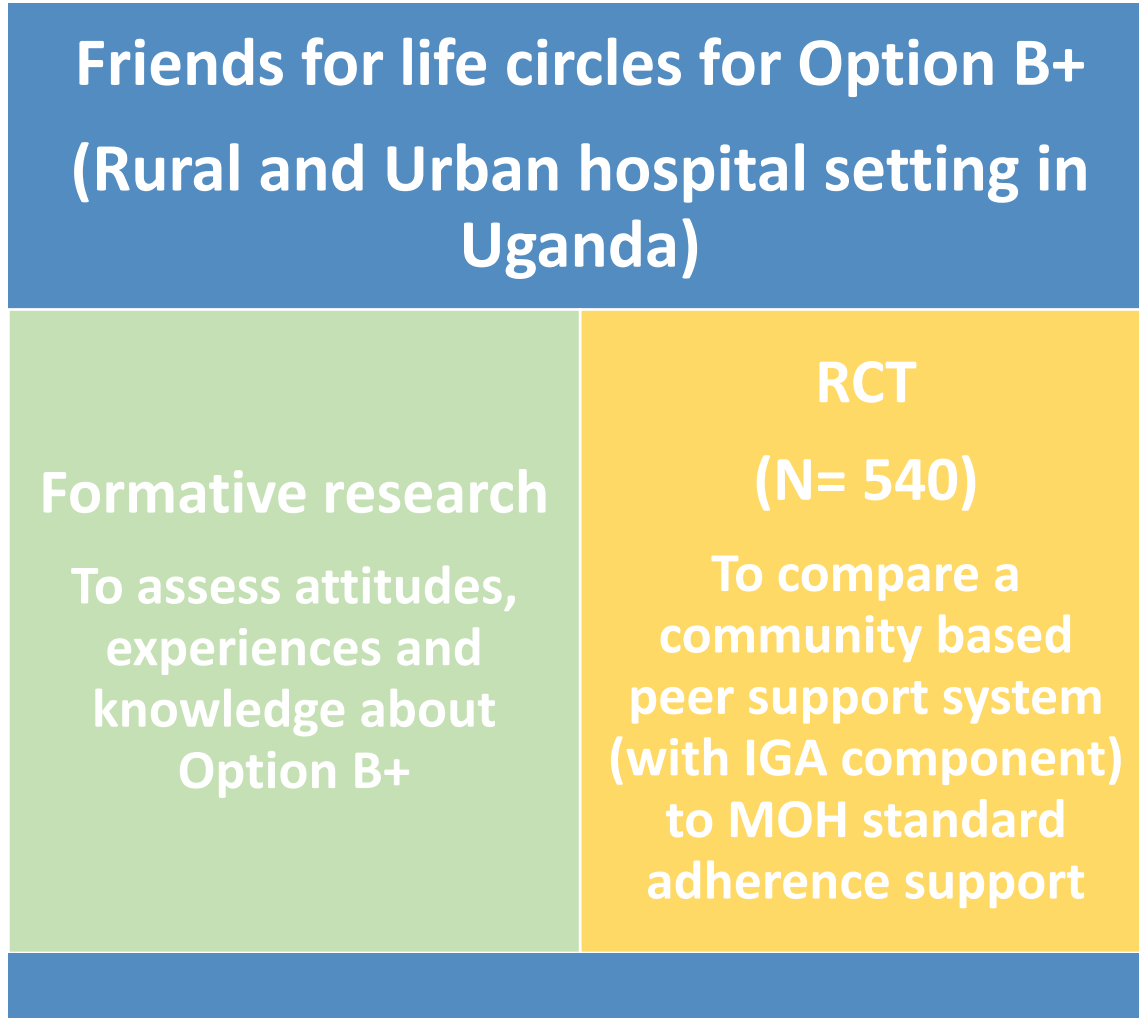
Comparing efficacy of different ARV regimens including newer drugs



Evidence on immune based interventions

HIV antibody and vaccine immunization for prevention

## Assessing strategies to support adherence and retention



### Study status

#### ❑ Formative phase:

- ❑ Conducted 7 Key Informant Interviews (health workers, community leaders, policy makers)
- ❑ Conducted 6 Focus Group Discussions (women on PMTCT Option B+ and their partners)

❑ **RCT:** 25 women enrolled as of 01 Jul

❑ Formative data analysis-ongoing

## Assessing options for Early Infant Diagnosis (EID)

### SAMBA study

- Cross sectional performance evaluation of point of care test (Simple AMplification Based Assay) for EID in RLS
- Population: HIV exposed and HIV infected infants 1 year or younger

### Study status

- Completed enrollment
- (200 HIV exposed uninfected babies and 75 HIV infected babies enrolled)
- Data analysis ongoing

# Conclusion

- ❑ Scientific evidence is critical to inform policies and programmes to advance the agenda to eliminate new paediatric HIV infections by 2020.
- ❑ A lot has been achieved, but a lot still needs to be done
- ❑ Together, we have the power to end the AIDS epidemic



# Acknowledgement

- ❑ Center For AIDS Research (CFAR)
- ❑ Site leadership - MUJHU Research Collaboration, Kampala, Uganda
- ❑ International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network
- ❑ US National Institutes of Health (NIH).



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THANK  
YOU