Road to elimination of mother-to-child transmission in South Africa

Act, Connect and End the Epidemic

20 - 23 June

2023

11th SA AIDS CONFERENCE

Durban ICC

www.saaids.co.za

Road to the Elimination of Mother-To-Child HIV Transmission in South Africa

Terusha Chetty
MBChB, MMed, FCPHM, PhD

21 June 2023

The South African Medical Research Council

recognizes the catastrophic and persisting consequences of colonialism and apartheid, including land dispossession and the intentional imposition of educational and health inequities.

Acknowledging the SAMRC's historical role and silence during apartheid,

we commit our capacities and resources to the continued promotion of justice and dignity in health research in South Africa.

OVERVIEW

Definition of eMTCT

Current landscape in South Africa

Evolution of the PMTCT programme in SA

4-prong approach towards eMTCT

Challenges in progress

Current and future interventions

DEFINITION OF eMTCT: An HIV infection case rate of ≤50/100 000 live births is needed to validate a country's elimination of vertical transmission as a public health problem and **a transmission rate of < 5% in breastfed infants for at least a year** [1]

FULL VALIDATION [1]

- 95% antenatal care coverage (at least one visit)
- 95% HIV testing coverage among pregnant women
- 95% antiretroviral therapy coverage among pregnant women living with HIV

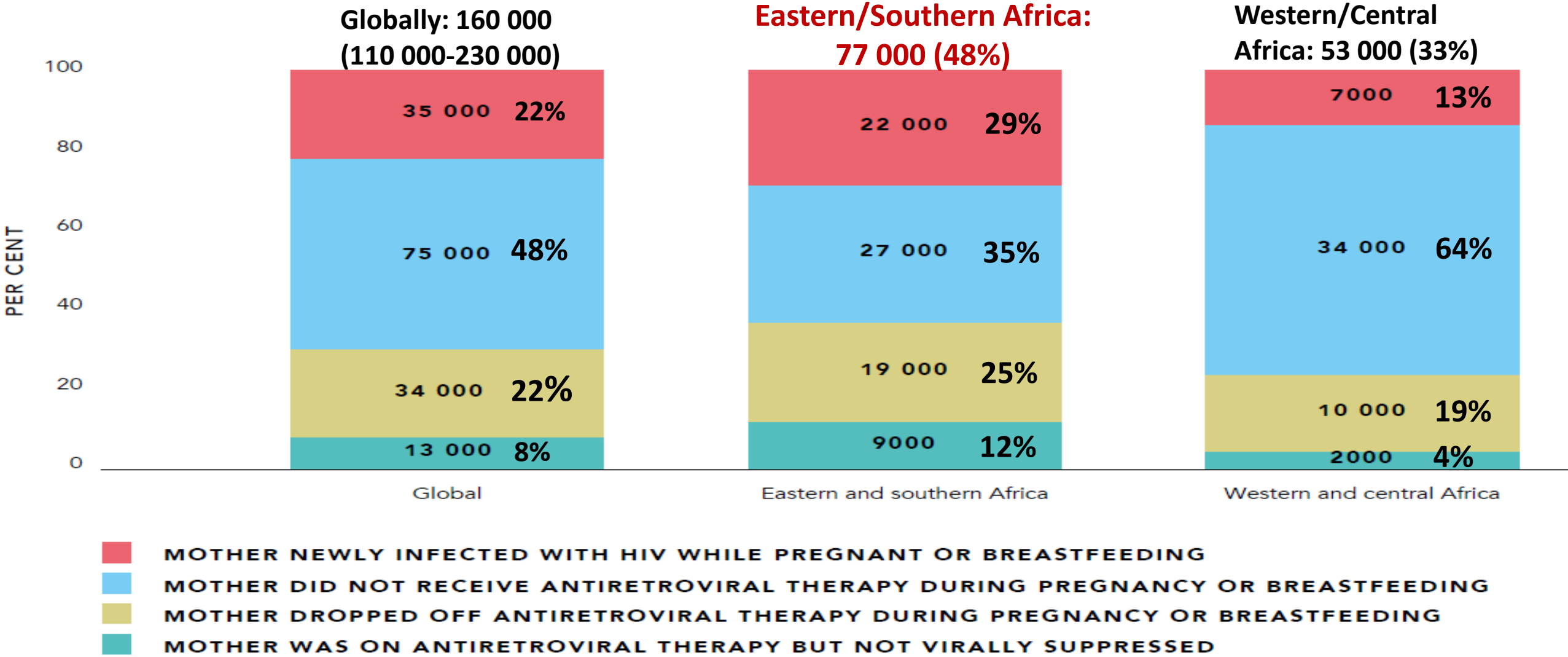
2017: intrauterine MTCT rate 0.9% [2]

= **240 per 100 000 live births** [3]

(does not include intra and postpartum transmissions)

1. World Health Organization. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis. 2014.
2. Goga et al. S Afr Med J. 2018;108(3a)
3. Moyo et al. S Afr Med J. 2022;112(3)

DESPITE GREAT PROGRESS SINCE THE EARLY DAYS, THE HIV RESPONSE IS STILL FAILING CHILDREN

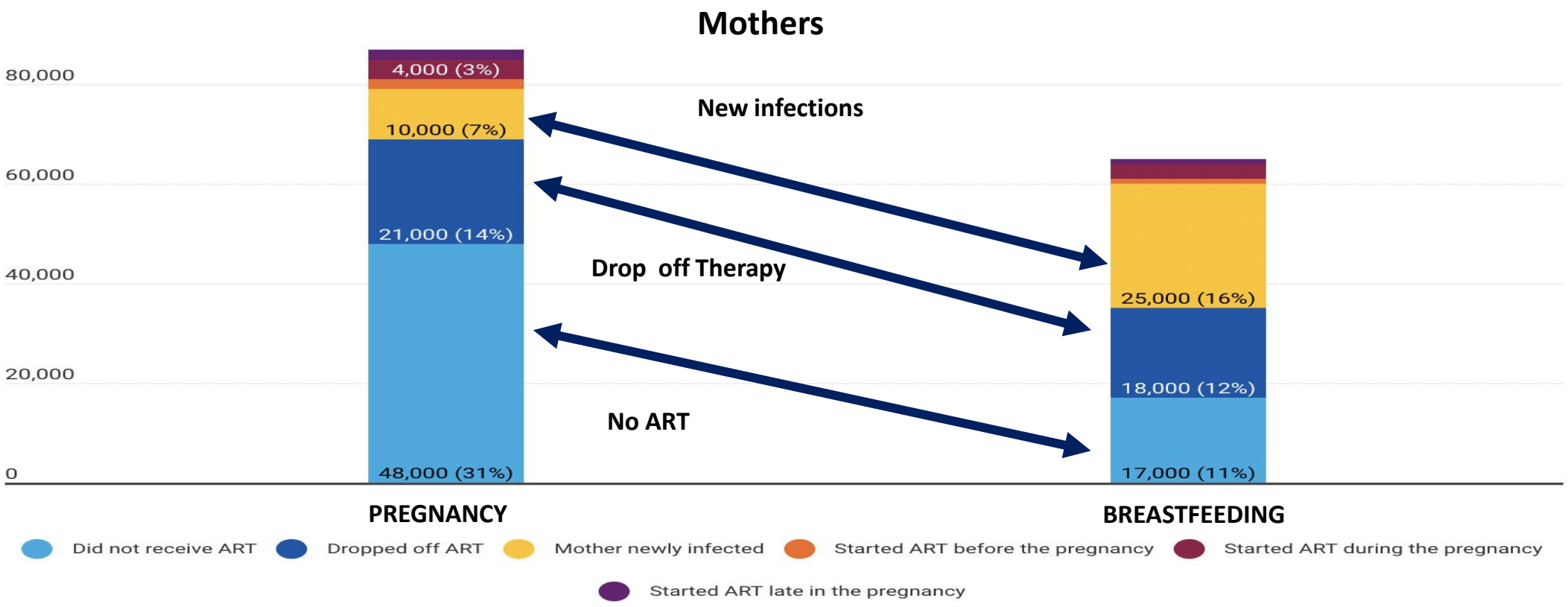


Source: UNAIDS Global AIDS Update 2022: https://www.unaids.org/sites/default/files/media_asset/2022-global-aids-update_en.pdf

REASONS FOR VERTICAL HIV TRANSMISSION

The majority of paediatric HIV infections are due to new mothers not receiving ART, dropping off ART, or becoming infected during breastfeeding

Number of new HIV infections among children by source of infection, 2020



https://data.unicef.org/topic/hivaids/emtct/

PERINATAL AND POSTNATAL VERTICAL HIV TRANSMISSION (VHT): SOUTH AFRICA

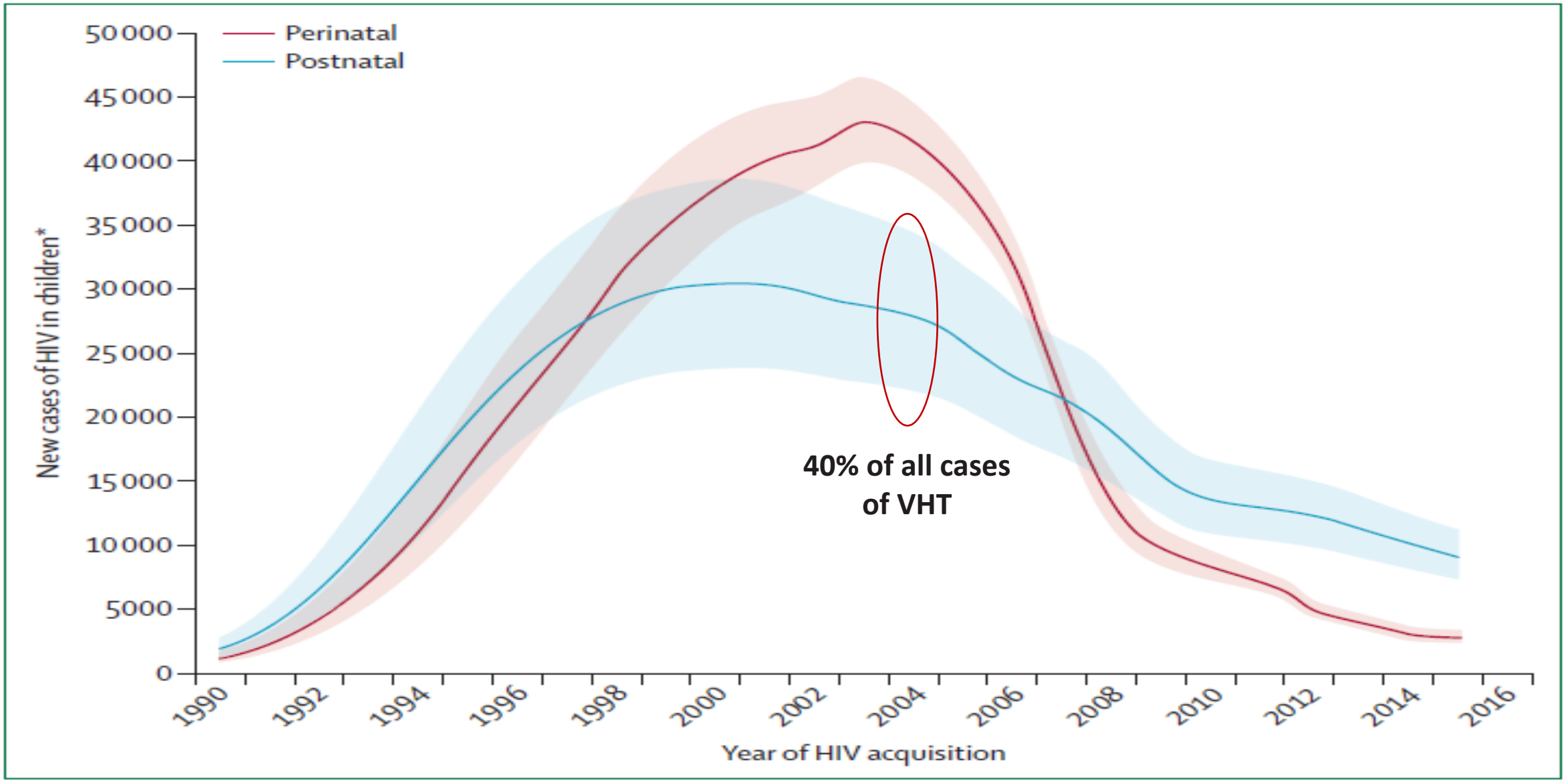
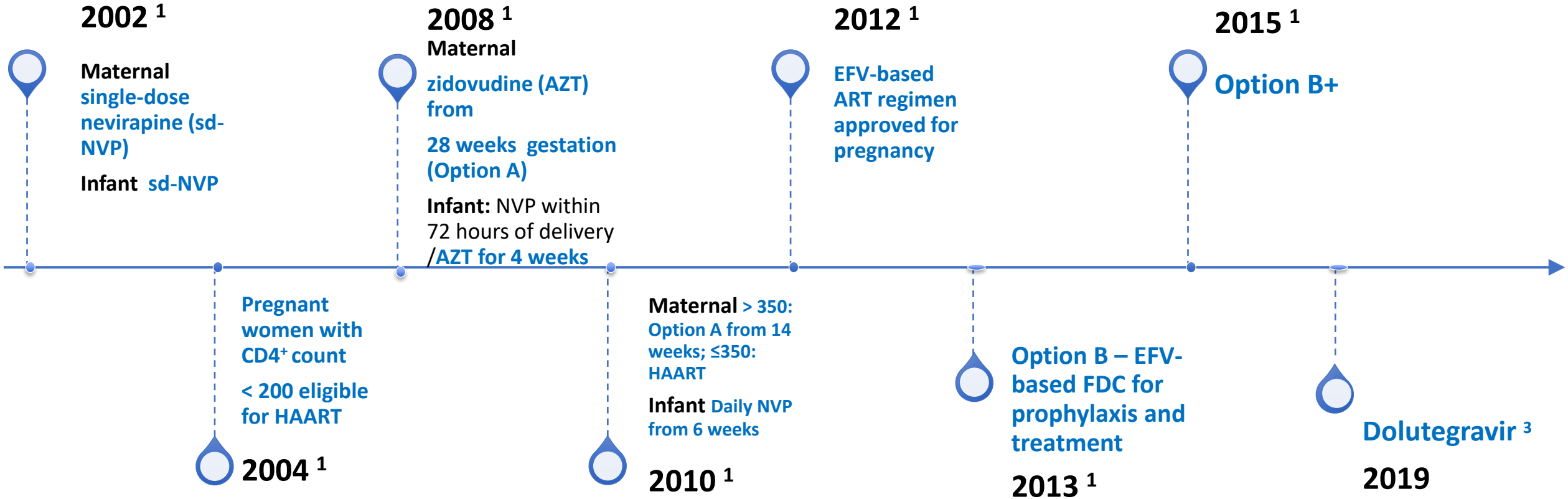


Figure from Van de Perre and Goga et al. The Lancet, 2021, Thembisa model

EVOLUTION OF THE PMTCT PROGRAMME IN SOUTH AFRICA

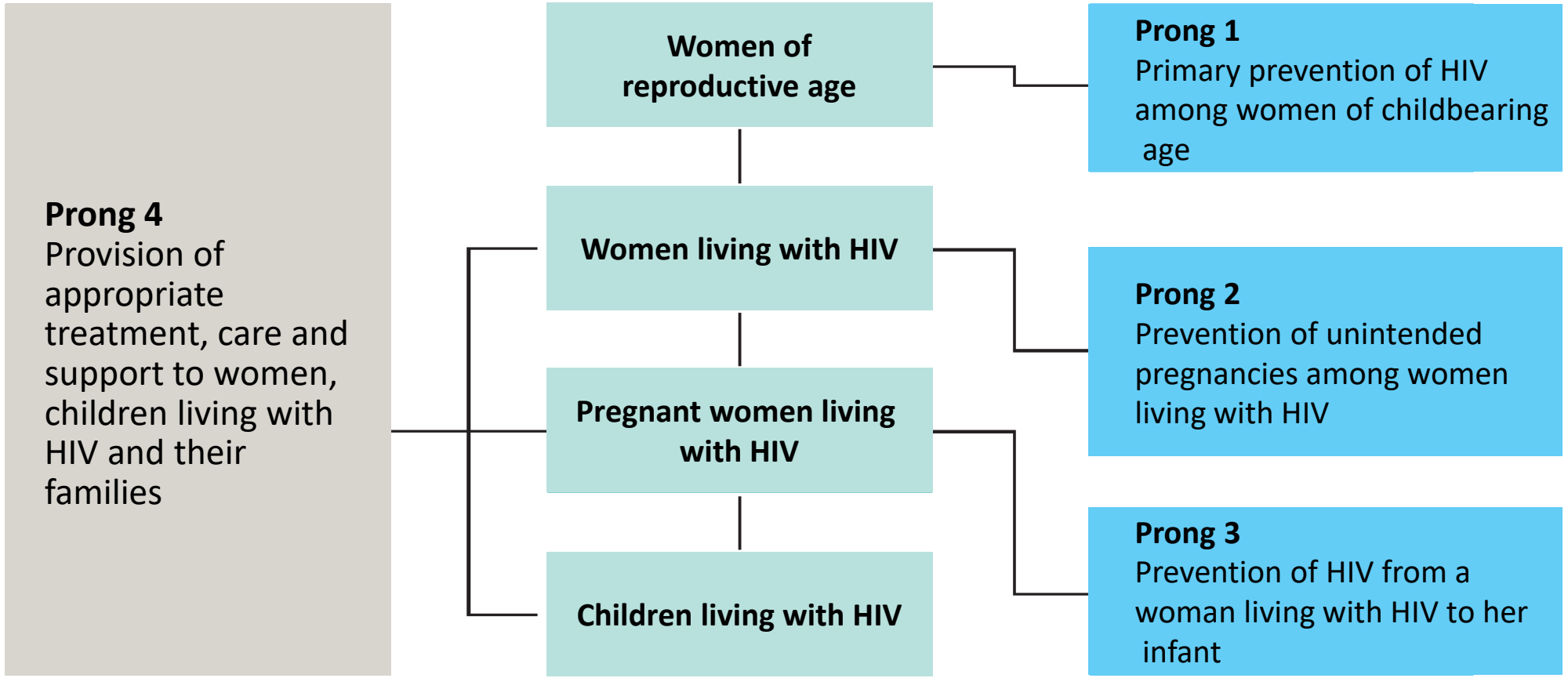


MTCT rate at 4-6 weeks 25-30% in 2001 [2]

MTCT rate ~1.4% in 2016 [2]

1. Mnyani et al. Globalization and Health. 2014.;10:36
2. Goga A et al. South African Health Review. 2017: 137-146
3. Republic of South Africa. 2019 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates. October 2019. Updated March 2020. https://www.health.gov.za/wp-content/uploads/2020/11/2019-art-guideline.pdf

FOUR PRONGS TO ELIMINATE MOTHER-TO-CHILD TRANSMISSION OF HIV AND IMPROVE MATERNAL HEALTH



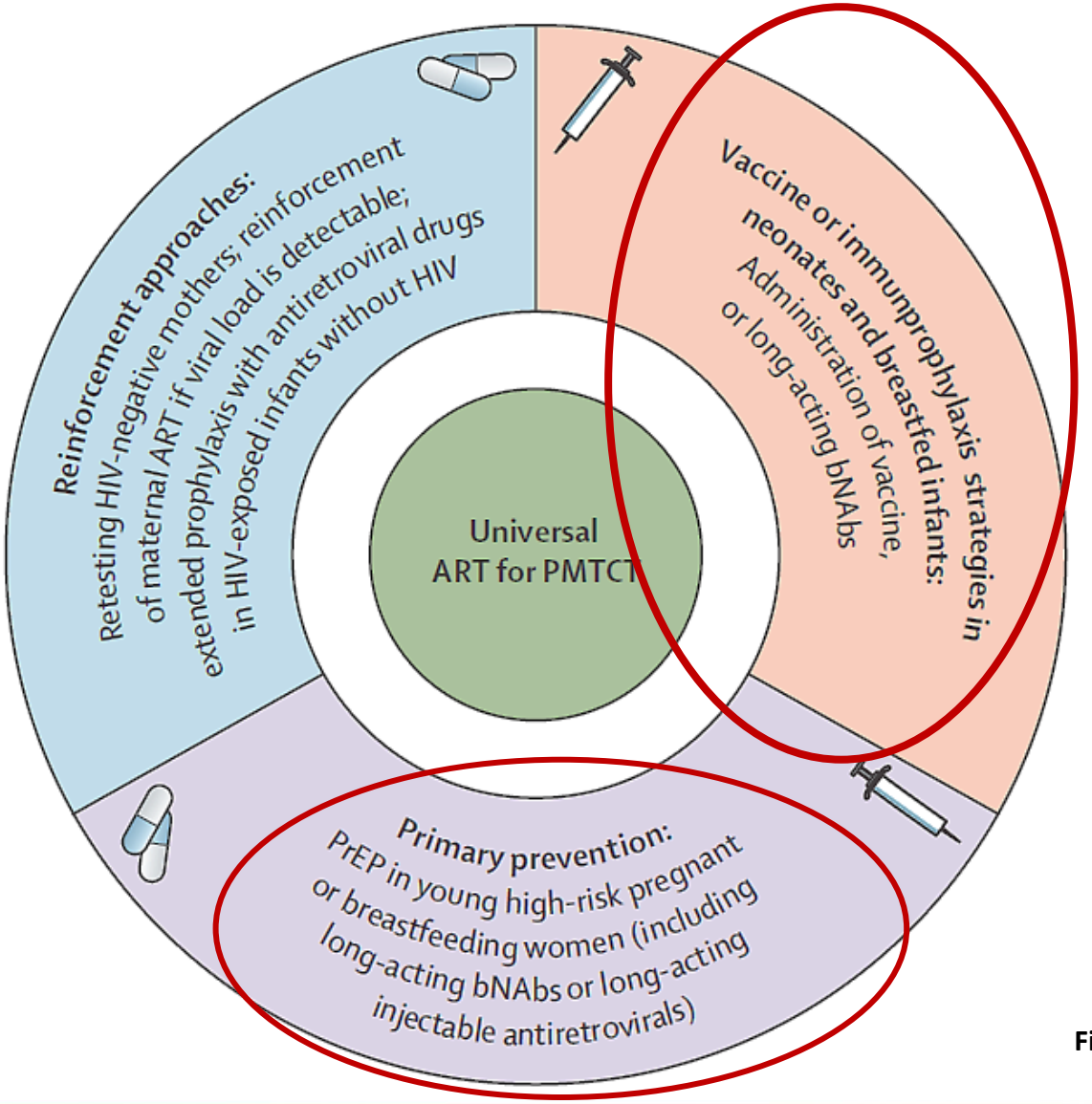
UNAIDS, 2016. Get on the Fast Track: The lifecycle approach to HIV

INTERVENTIONS TO TARGET FOR EMTCT

MISSED OPPORTUNITIES FOR EMTCT	INTERVENTION DOMAINS
Mothers infected during pregnancy/BF	HIV prevention services for women
Mothers did not receive ART during pregnancy or BF	Timely access to HIV testing
Mothers dropped off ART during pregnancy or BF	Timely ART initiation
Mothers started ART late in pregnancy	Programme retention and adherence support
Mothers started ART during pregnancy	Timely engagement in antenatal care
Mothers started ART before pregnancy	Services for infants at highest risk of HIV acquisition

Chi et al. Journal of the International AIDS Society. 2020;23:8

INTERVENTIONS TO OPTIMIZE ELIMINATION OF MTCT



- **Reinforce current approaches**
- **New strategies for primary prevention in mothers:**
  - **Oral PrEP**
  - **Long-acting PrEP**
  - **Dapivirine ring**
- **New strategies in infants:**
  - **Vaccination**
  - **Immunoprophylaxis**

Figure from Van de Perre and Goga et al. The Lancet, 2021

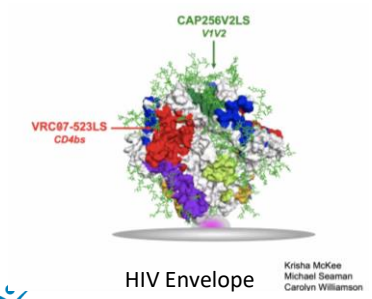
FUTURE STRATEGIES FOR INFANTS

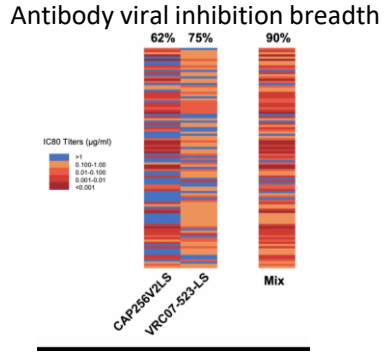
Vaccines or broadly neutralising antibodies (bNAbs):

- Vaccine study: HVTN 135 - Avy Violari – led from Soweto (PHRU)
- bNAb studies:
  - IMPAACT P1112 study - Phase 1 bNAb study
  - IMPAACT 2037 study – 3 bNAbs – protocol under development
  - 2 SAMRC-sponsored studies: **PedMAb1,** PedMAb2 and SAMBULELO

PedMAb: 2 HIV-1 bNAbs given alone or in combination in breastfeeding HIV-exposed, uninfected infants in SA

- **Phase I** clinical trial: dose finding, safety and pharmacokinetics (PedMAb1)
- **Phase II** clinical trial: safety and pharmacokinetics (PedMAb2)





PedMAb hypothesis:

Complementarity: two bNabs is better than one

- **VRC07.523LS (directed to CD4 binding site)**
- **CAP256.V2LS (to V1V2 Glycan region)**

Source: PedMAb investigators. Coordinator: Gabriella Scarlatti; Partners: Ameena Goga; Penny Moore; Philippe Van de Perre; Thorkild Tylleskär: (Antibodies provided by VRC-NIH)

TRIALS CONDUCTED OR PLANNED: PedMAb1

Single blind, three-step, proof-of-concept, Phase I study:

Safety, tolerability and PK of HIV-1 bNAbs (LS version) administered s.c. in breastfeeding HIV exposed uninfected (HEU) neonates and infants receiving standard-of-care ARV.

Step 1 : single bNAb

Group 1 : CAP256 (@<72h)	Group 2: VRC07-523 (@<72h)
Arm 1: Dose 5 Arm 2: Dose 10 Arm 3: Dose 20	Arm 4: Dose 20 Arm 5: Dose 30

Step 2 : combined bNAbs

Group 3: CAP256 + VRC07-523 (@<72h)
Arm 6: 10 + 30 Arm 7: 20 + 30

Step 3 : combined bNAbs multiple administrations

Group 3 continued: CAP256 + VRC07-523 (@8 weeks)	Group 4: (upon PK of arms 2,3 for min 4 mos and arms 6,7 for min 2 mos) CAP256 + VRC07-523
Arm 6b: 10 + 20 Arm 7b: 20 + 20	Arm 8: 10 + 30 (@<72h) and 10 + 20 (TBD @ between 3 and 6 months) Arm 9: 20 + 30 (@<72h) and 20 + 20 (TBD @ between 3 and 6 months)

Study population is 8 HEU infants per Dose arm, but target 6 with full dataset.

Doses are in mg/kg body weight.

Recruitment

Step1 In each arm recruitment will proceed according to set inclusion/exclusion criteria, and sequentially with increasing doses

Step 2 Group 3 will be initiated after completion of safety assessment of the single bNAb administration of Groups 1 and 2

Step 3 In each arm recruitment will proceed according to inclusion/exclusion criteria and will be sequential

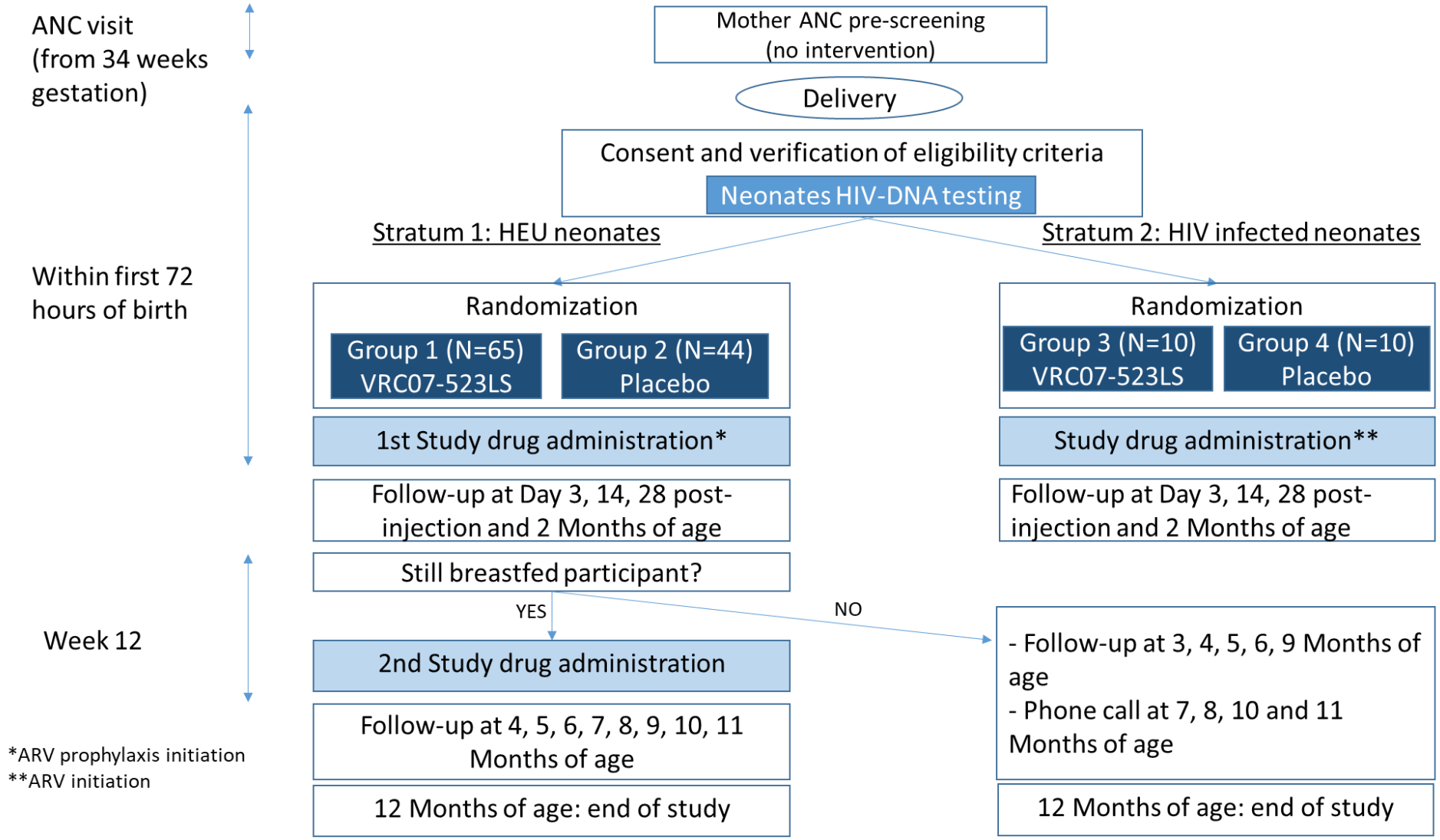
Randomization will occur sequentially, and will occur between Arms (i) 2 & 4, (ii) 3 & 5, (iii) 6 & 7 and (iv) 8 & 9.

Followed by **PedMAb 2**

Source: PedMAb investigators. Coordinator: Gabriella Scarlatti; Partners: Ameena Goga; Penny Moore; Philippe Van de Perre; Thorkild Tylleskär

SAMBULELO

Source: Phillipe van der Perre and Ameena Goga; 2023



CONCLUSION

Main issue or key question(s)?

- Intense efforts are needed to eliminate vertical HIV transmission (VHT)
- Comprehensive approach to address breastmilk transmission
- Remaining gaps relate to **delayed maternal HIV diagnosis**, **delayed referral into ART care** and **poor retention in ART care**.

ACKNOWLEDGEMENTS

Philippe Van de Perre
Nicolas Nagot
Jean-Pierre Moles
Yoann Cazaubon
Anaïs Mennecier

Gabriella Scarlatti
Priscilla Biswas
Laura Galli
Stefania Dispinseri

Ameena Goga
Trisha Ramraj
Terusha Chetty
Nobubelo Ngandu
Brodie Daniels
Reshmi Dassaye
Ishen Seocharan
Yages Singh
Tarylee Reddy
Chatsworth CRS (PedMAb)

Penny Moore
Nono Mkhize
Rahima Moosa Team (SAMBULELO)

Thorkild Tylleskär

UP Clinical Research site (SAMBULELO)
Department of Paediatrics and Child Health (SAMBULELO)

VRC, NIH
Lucio Gama

Thank you to Salim Abdool-Karim and Sharana Mahomed: CAPRISA

Penny Moore

Funders