Virologic Outcomes of HIV-Infected Children Undergoing a Single-Class Drug Substitution from LPV/r- to EFV-Based cART: A retrospective cohort study.

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For the IeDEA-SA collaboration

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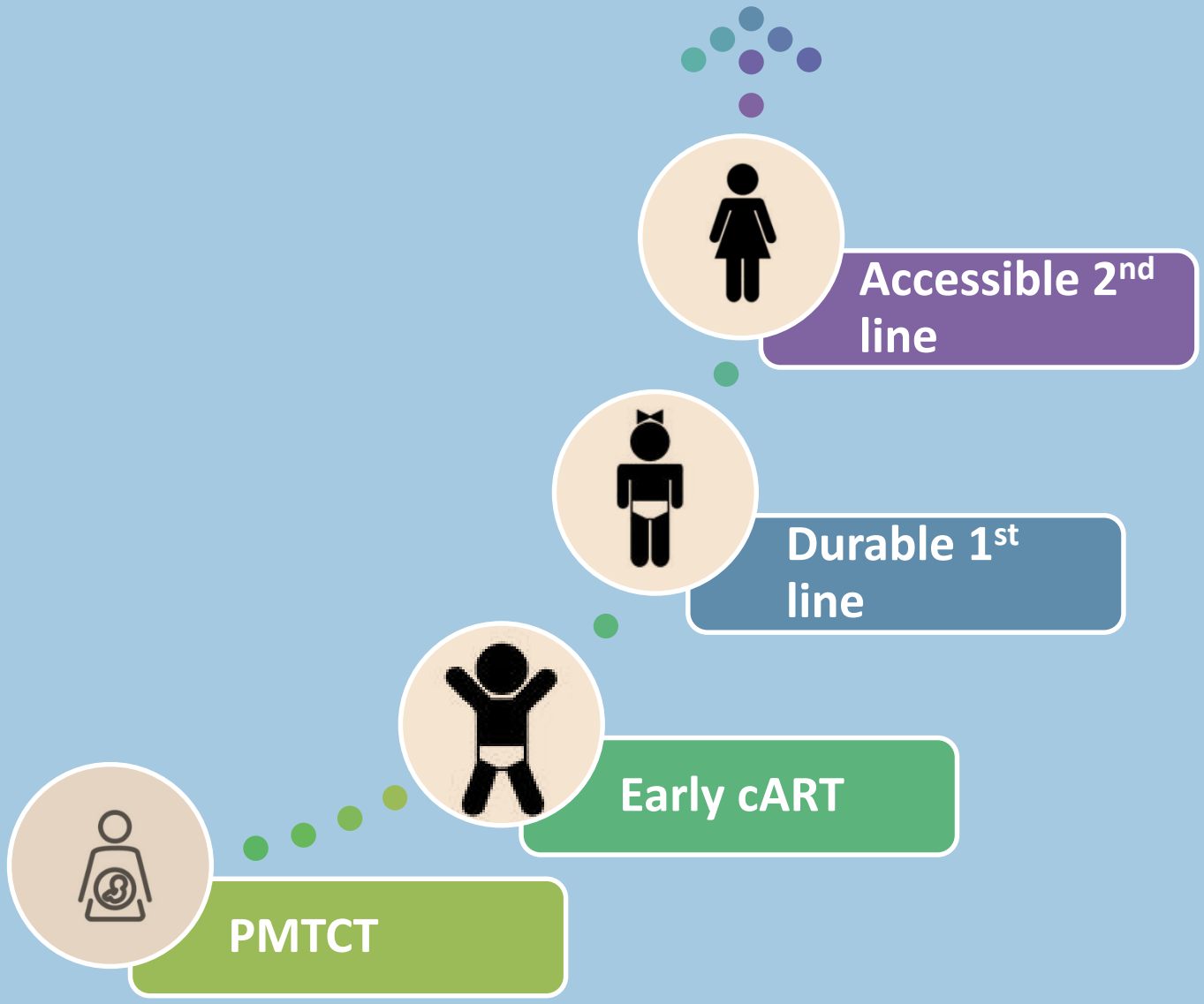
Background



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Background

LPV-r

- Better virologic suppression than NVP-based cART
- Tablet size
- Palatability
- Twice-daily dosing
- Storage requirements
- Drug-drug interactions
- Long term side-effects

EFV

- Effective
- Relatively cheap
- Easy to administer
- Daily dosing
- Reasonable long term side-effect profile
- Use in <36mo old not recommended
- High-level class resistance

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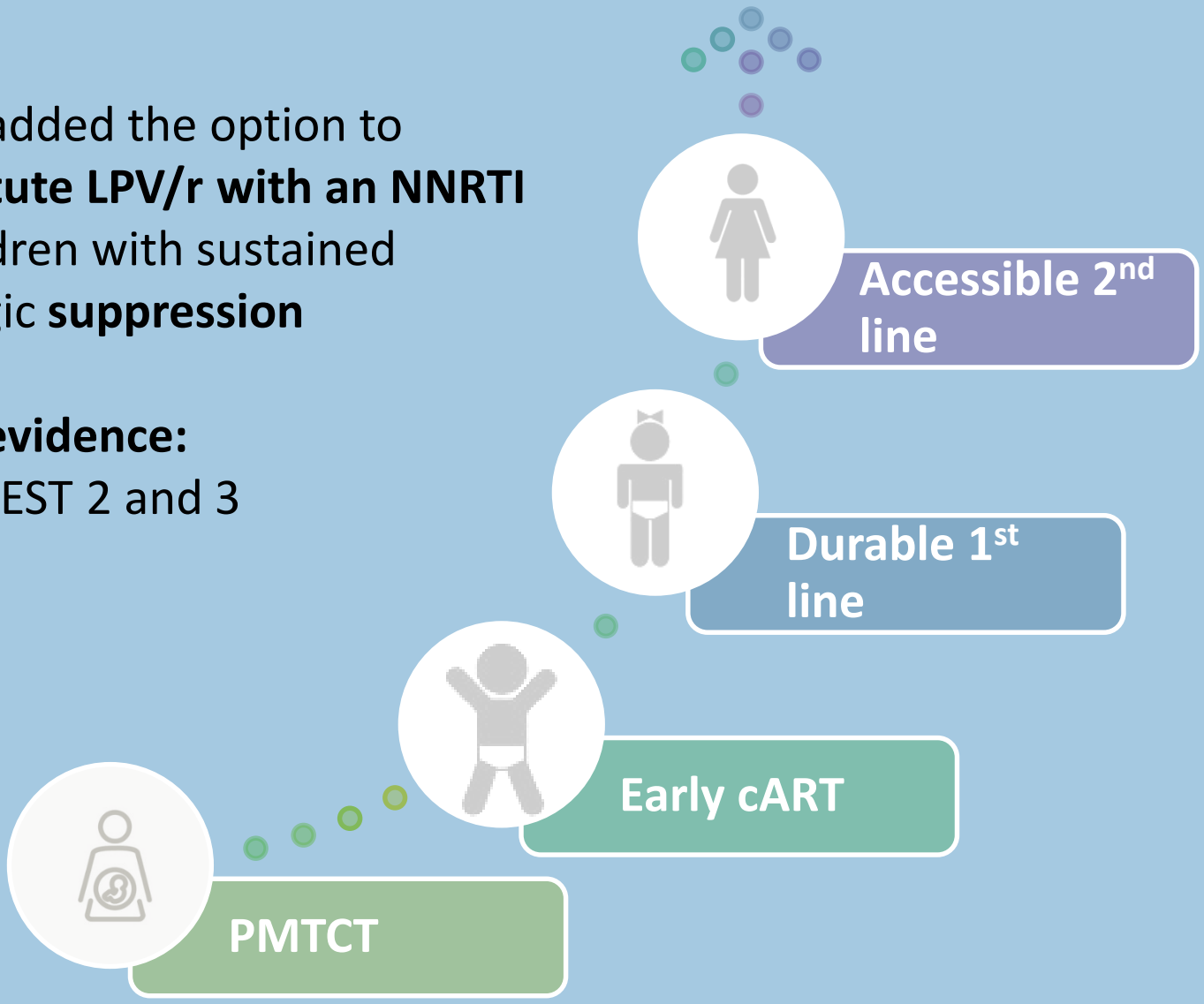
Background

2013:
WHO added the option to **substitute LPV/r with an NNRTI** in children with sustained virologic **suppression**

Main evidence:
NEVEREST 2 and 3



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Objectives

To **compare outcomes** of children commencing cART with **LPV/r** and **substituting LPV/r with efavirenz** once virologically suppressed and ≥36 months old (***substitution group***)

with those **remaining on LPV/r** (***stay group***)

in a **routine clinical setting**

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Method

Retrospective cohort

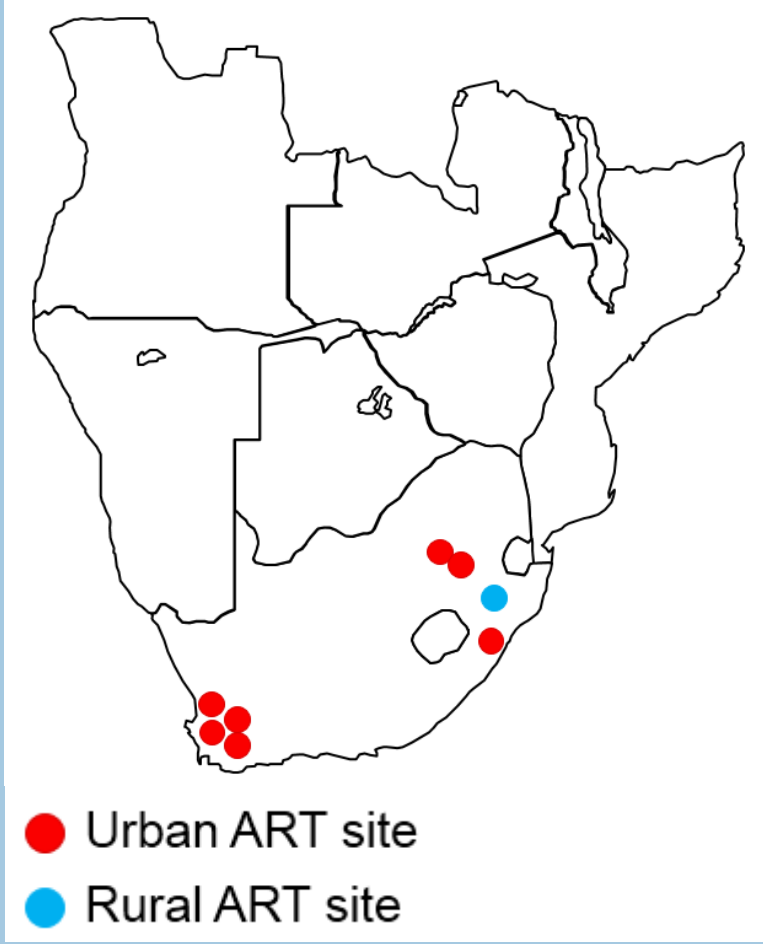
Starting cART between 2003-2010

8 South African sites

SA NDOH guidelines

- PI recommended 1st line <36mo irrespective of PMTCT

Clinician discretion to substitute LPV/r with EFV



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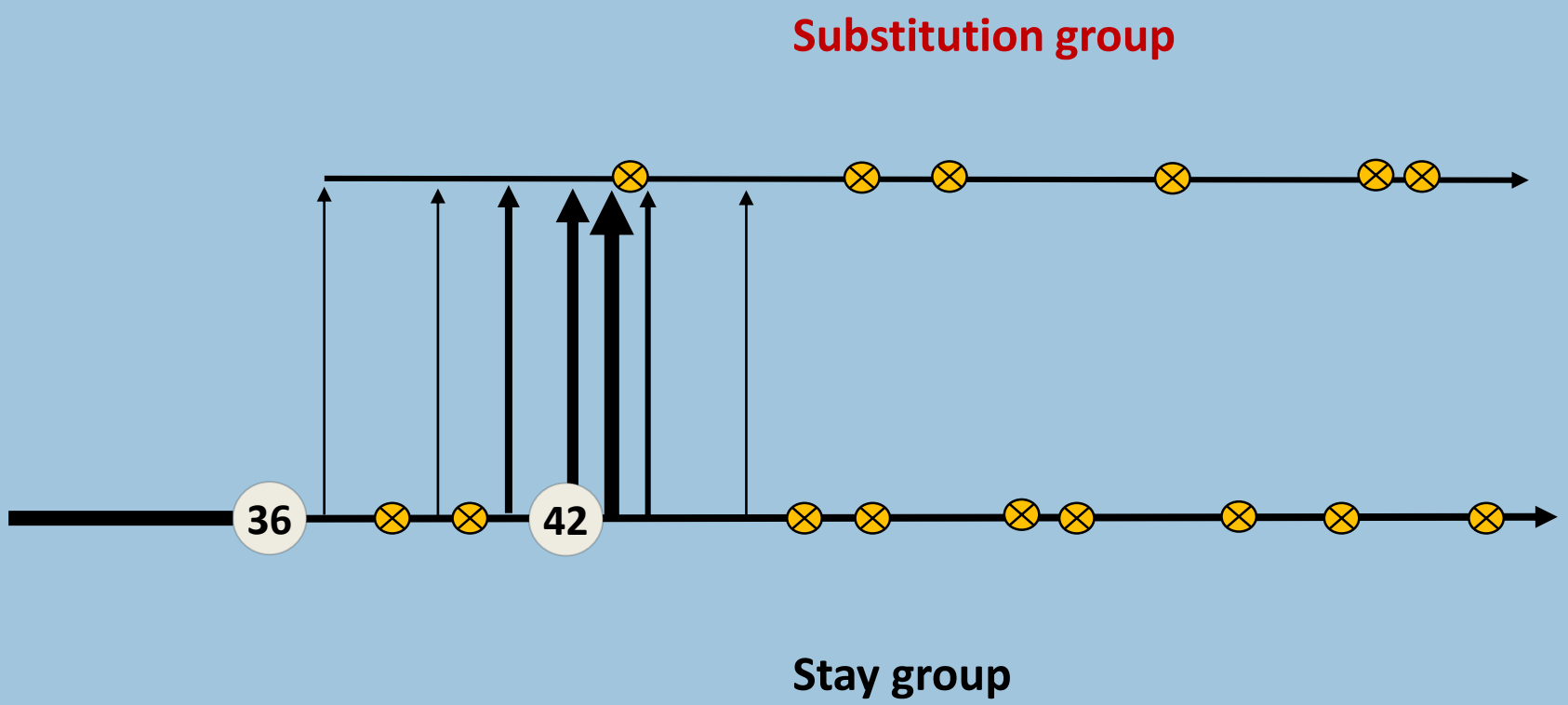
Method



⊗ First VL>400

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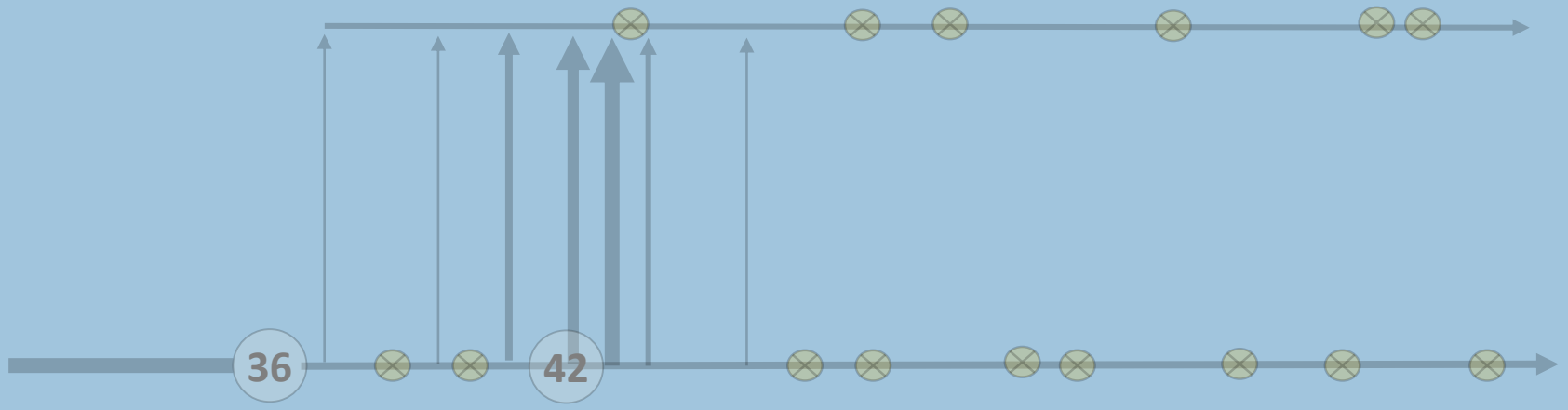
Method

Median follow –up time: **25.8mo** (15.1 – 34.2)



Median follow –up time: **24.4mo** (18.1 – 31.7)

First VL>400

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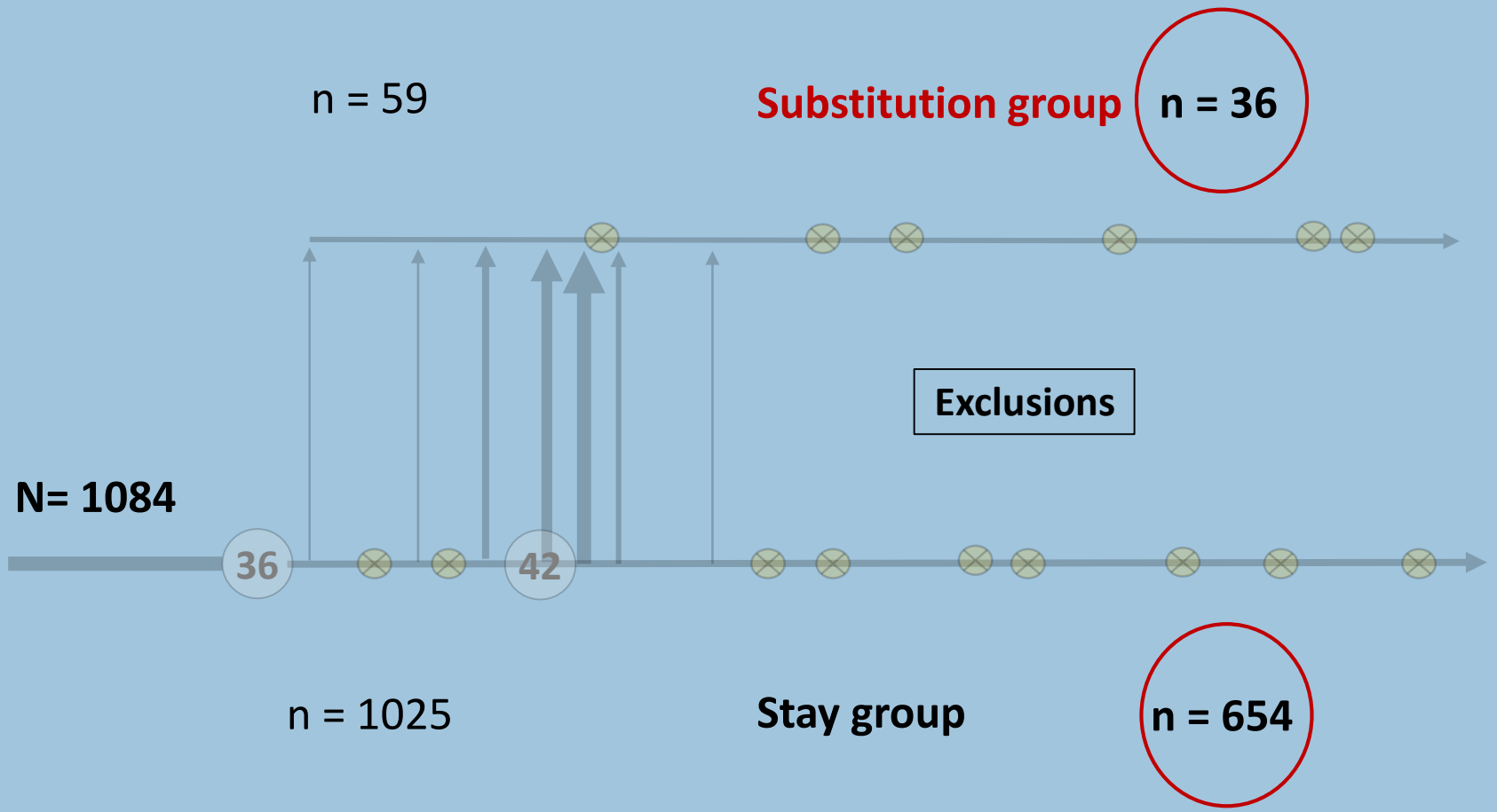
Method



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Results

Comparison of groups at *initiation* of cART

	Stay	Substitution	p-value
Median age (months)	17.6	15.3	0.381
Median pre-cART CD4 %	13.9	13.0	0.571
Weight-for-age z-score	-2.34	-2.56	0.130
WHO stage 3 or 4	89.9 %	80.8 %	0.157
HIV VL (log_{10} copies/ml)	5.69	5.51	0.708

Comparison of groups at *36 months of age*

Median CD4 %	28.9	29.4	0.751
Weight-for-age z-score	-0.86	-0.32	0.074
HIV VL <400 copies/ml	all	all	

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Results

Comparison of groups at *42 months of age or date of substitution*

	Stay	Substitution	p-value
Median CD4 %	29.6	28.5	0.562
Weight-for-age z-score	-0.83	-0.58	0.420
≥ Viral blip	318 (**48.6**%)	10 (**27.8**%)	**0.015**

Viral blip

an isolated VL >1000 copies/ml which subsequently returned to <400 copies/ml at the next measurement (conducted within 24 months) with no change in cART regimen

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Results

Factors associated with single-drug substitution

- **Favourable clinical response to cART**
  - **adjusted OR 1.34** per 1 weight-for-age z-score increase, 95% CI 0.96 - 1.80
  - **associated with undergoing a single-drug substitution**

- **Viral blips**
  - **adjusted OR 0.34**, 95% CI 0.15 - 0.79
  - **associated with <u>not</u> undergoing a single-drug substitution**

- Immune recovery

- ~~PMTCT exposure~~

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Results

Primary outcomes after substitution

Incidence rate ratio of time to first VL >400 copies/ml:

1.03 (95% CI 0.43 to 2.08) in the substitution relative to the stay group

Cox regression model HR

Adjusted **HR=1.43** (95% CI 0.62 - 3.32, p=0.401)

adjusted for other predictors of non-suppression

- WAZ at initiation of cART
- Duration on cART
- VL blip(s) prior to 36 months

in the substitution relative to the stay group

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Results

Secondary outcomes after substitution

	Stay (n=654)	Substitution (n=36)	p-value
Died	3 (0.43)	0	
TFO	**278 (42.5)**	9 (25.0)	0.039
LTFU	35 (5.4)	4 (11.1)	0.139
Virologic failure	64 (9.8)	2 (5.6)	0.565
Changed back to LPV/r	-	**7 (19.4)**	-

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Conclusions

- In this cohort, **virologic outcomes** of children suppressed on LPV/r-based cART and subsequently changed to EFV were **no worse** than of those remaining on LPV/r.

- However, this cohort was not exposed to more than a single postpartum dose of NVP as infant prophylaxis.

- Thus, in carefully selected children who have had no or only a sdNVP as PMTCT, this may be a virologically safe regimen-sparing and side-effect limiting simplification strategy.

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Thanks to

All the children who participated as well as their caregivers

NICHD (National Institute of Child Health and Human Development)

NIAID

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University of Stellenbosch Department of Paediatrics
Tygerberg Academic Hospital

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Rahima Moosa Mother and Child Hospital

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McCord Hospital

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Hlabisa HIV Program and Africa Centre for Health and Population Studies:

- **t, Maternal and Pediatric Infectious Disease Branch**

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University of Bern,
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