Outcomes of second-line antiretroviral therapy (ART) in HIV-infected children:
a Collaborative Initiative for
Paediatric HIV Education & Research (CIPHER)
Global Cohort Collaboration analysis

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Background

- 1.8 million are children living with HIV globally

  - 180,000 new infections in 2017

- ART recommended for all children and adolescents

  - 52% of children living with HIV receiving ART

- Few studies evaluating outcomes associated with second-line ART, particularly in resource-limited settings

Objective

To describe characteristics at initiation of second-line ART and subsequent immunological and clinical outcomes among children living with HIV globally

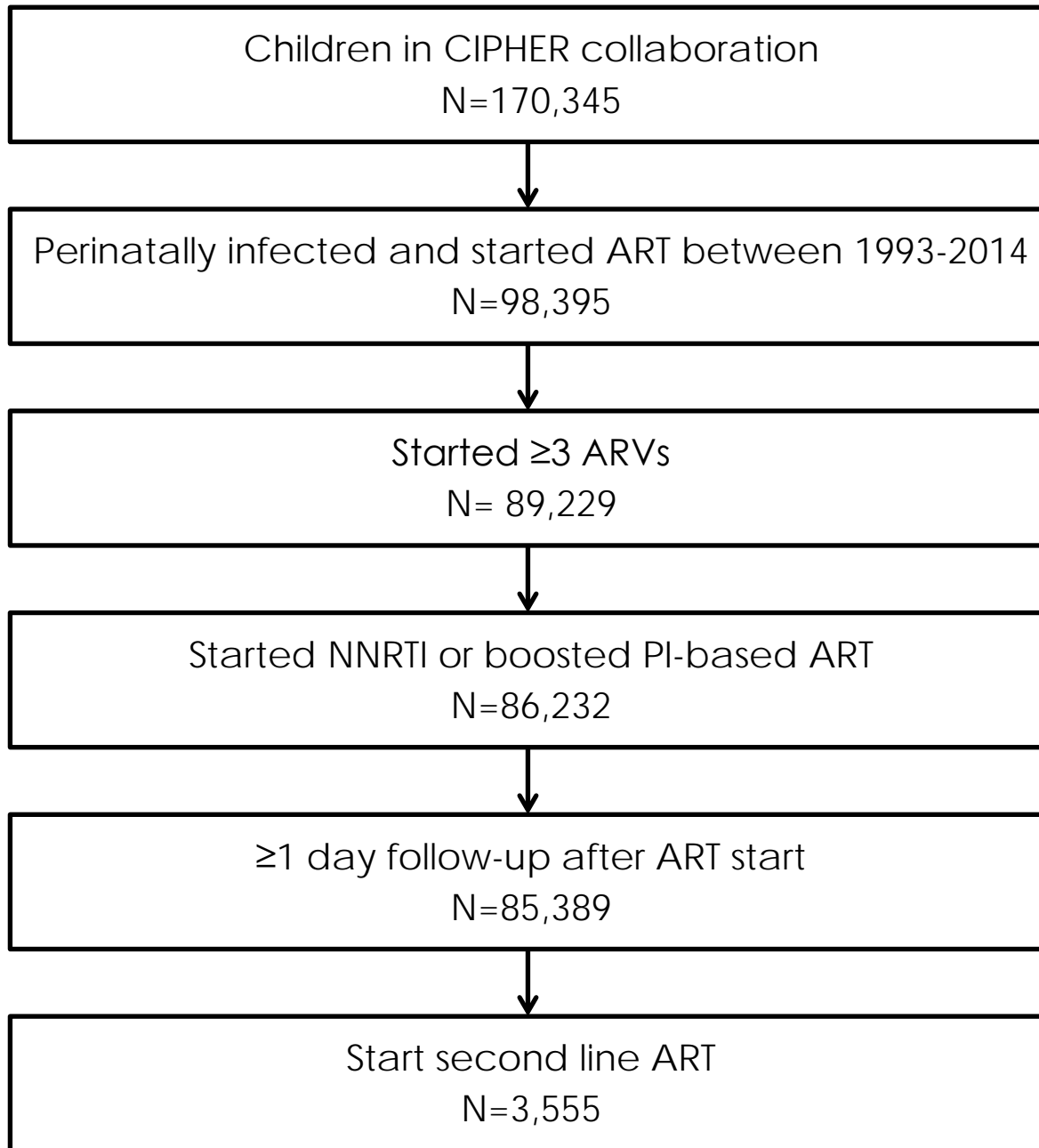# Study Population

- Individual level data through 2015 from 11 cohort networks

  - North America

  - Latin America (Caribbean, Central & South America)

  - Europe

  - Asia

  - Southern Africa (South Africa & Botswana)

  - Rest of sub-Saharan Africa (SSA)

- Children aged <10 years at cohort enrollment

  - proxy for perinatal HIV infection

- Age <18 years at initiation of 'standard' combination first-line ART

- ≥1 day of follow-up after switch to second-line ART

Study Definitions

- 'Standard' combination ART: ≥ three drugs, with ≥ 2 nucleoside reverse transcriptase inhibitors (NRTIs) plus either a non-NRTI (NNRTI) or a ritonavir-boosted protease inhibitor (PI)

- Switch to second-line was defined as:

  i. change of ≥1 NRTI plus either change in drug class (NNRTI to PI or vice versa) or PI change; or

  ii. change from single to dual PI; or

  iii. addition of a new drug class

- AIDS was defined as progression to a WHO Stage 3/4 or CDC Stage C clinical diagnosis

Children in CIPHER collaboration
N=170,345

↓

Perinatally infected and started ART between 1993-2014
N=98,395

↓

Started ≥3 ARVs
N= 89,229

↓

Started NNRTI or boosted PI-based ART
N=86,232

↓

≥1 day follow-up after ART start
N=85,389

↓

Start second line ART
N=3,555

IAS

CIPHER
PAEDIATRIC HIV MATTERS

North America
72 (2.0%)
PHACS, IMPAACT

Europe
464 (13.1%)
EPPICC

Total
N = 3,555

Asia
442 (12.4%)
EPPICC, IeDEA-Asia
Pacific

Latin America
123 (3.5%)
CCASAnet

Southern Africa
1255 (35.3%)
BIPAI, IeDEA-Southern
Africa

Rest of
Sub-Saharan Africa
1199 (33.7%)
BIPAI, IeDEA-Central Africa,
IeDEA-East Africa, IeDEA-
Southern Africa, IeDEA-West
Africa, Optimal Models

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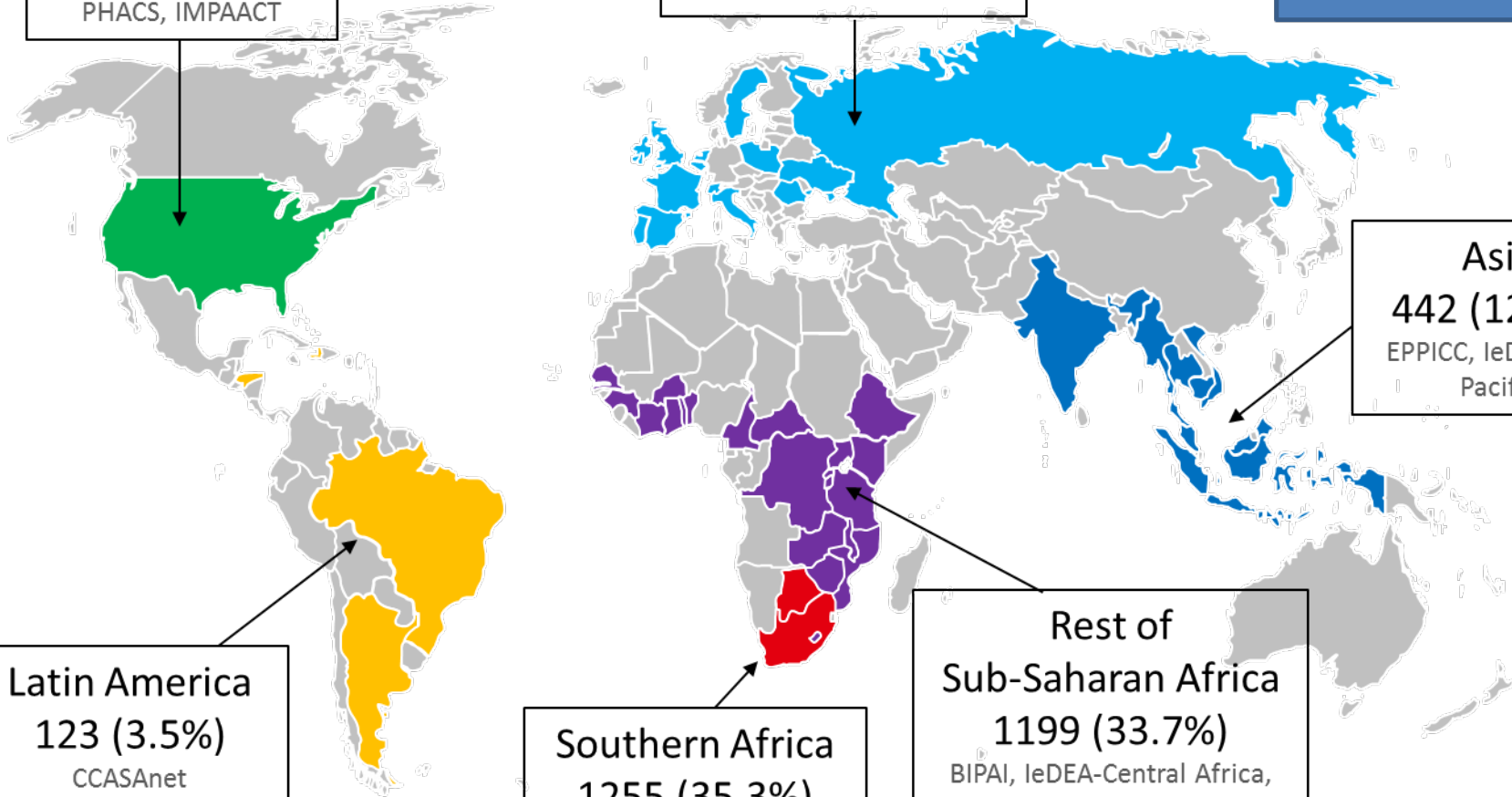
Characteristics at start of second-line ART, N(%)	Total (n=3,555)
Female sex	1564 (44.0)
Age (years)	
Median (IQR)	8.4 (5.3, 11.4)
≤5	800 (22.5)
6-9	1484 (41.7)
≥10	1271 (35.8)
Time on first-line ART (years), Median (IQR)	2.8 (1.6, 4.7)
Monitoring Strategy[1]	
Clinical only	126 (3.5)
Routine CD4	575 (16.2)
Routine CD4 + targeted VL	402 (11.3)
Routine CD4 + routine VL	2452 (69.0)

[1]Cohort-level variable derived from the frequency and availability of CD4 and VL measures across all ART-treated children

Characteristics at start of second-line ART, N (%)	Total (n=3,555)
AIDS diagnosis	
Prior to start of first line	1450 (40.8)
Between first and second line	333 (9.4)
CD4 count (cells/mm^3)	
N (%)	2786 (78.4)
<200	731 (26.2)
>500	1261 (45.3)
HIV Viral load (copies/ml)	
N (%)	2185 (61.5)
>1000	1783 (81.6)
Weight z-score[1]	
N (%)	2953 (83.1)
Median, IQR	-1.5 (-2.5, -0.5)

[1]UK-1990 reference population used to calculate z-scores

2nd line regimens after NNRTI-based 1st line
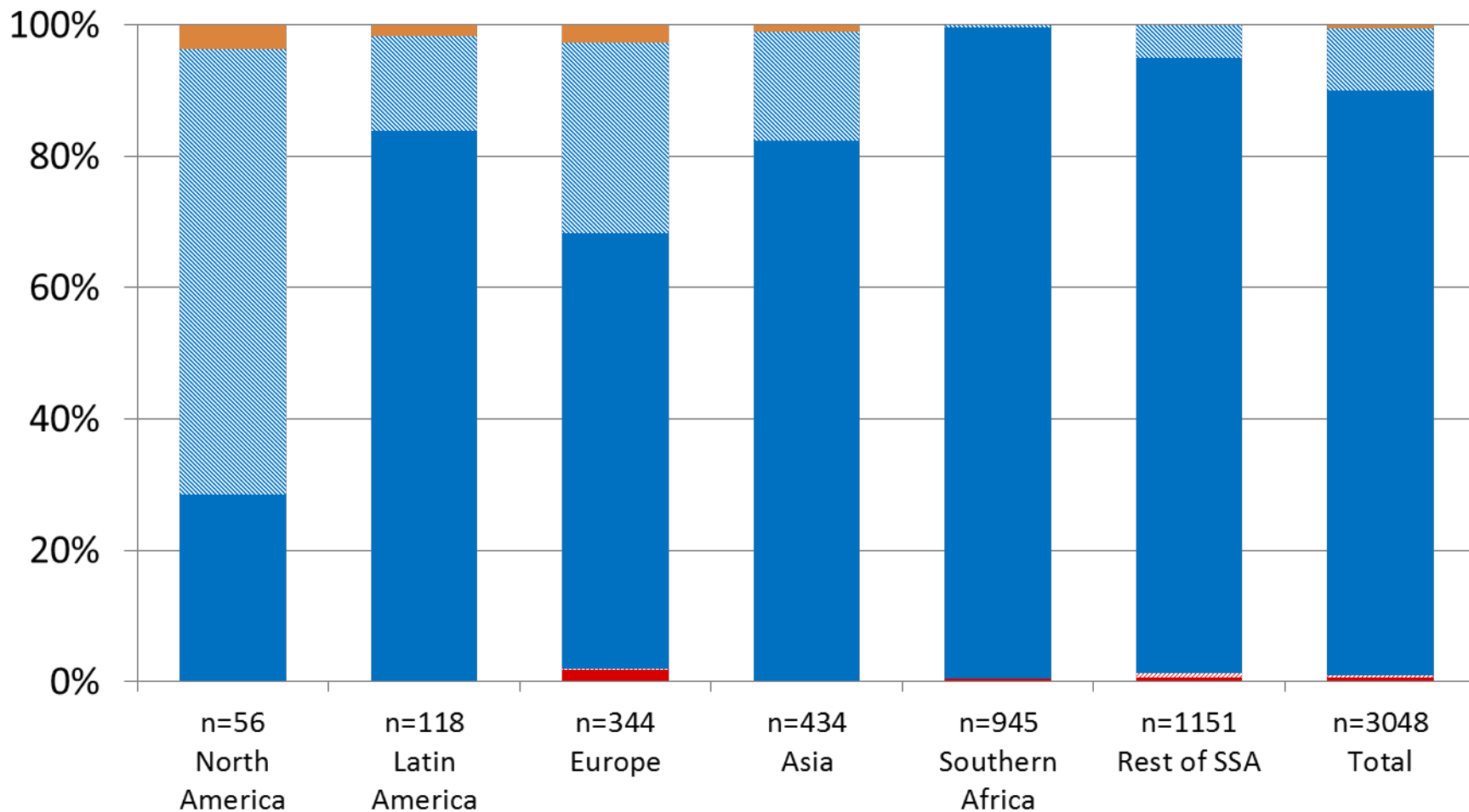
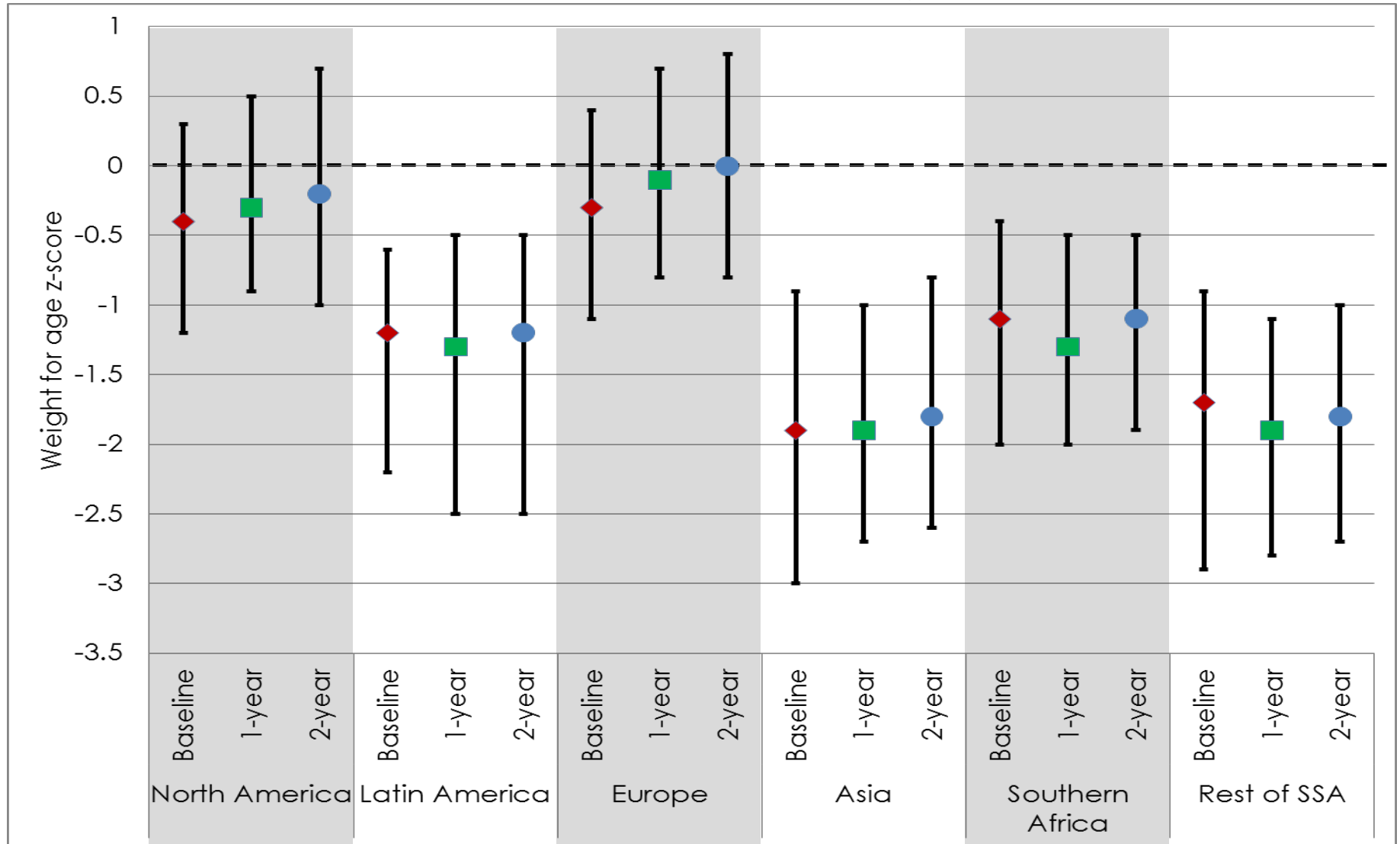# 2ⁿᵈ line regimens after PI-based 1ˢᵗ line
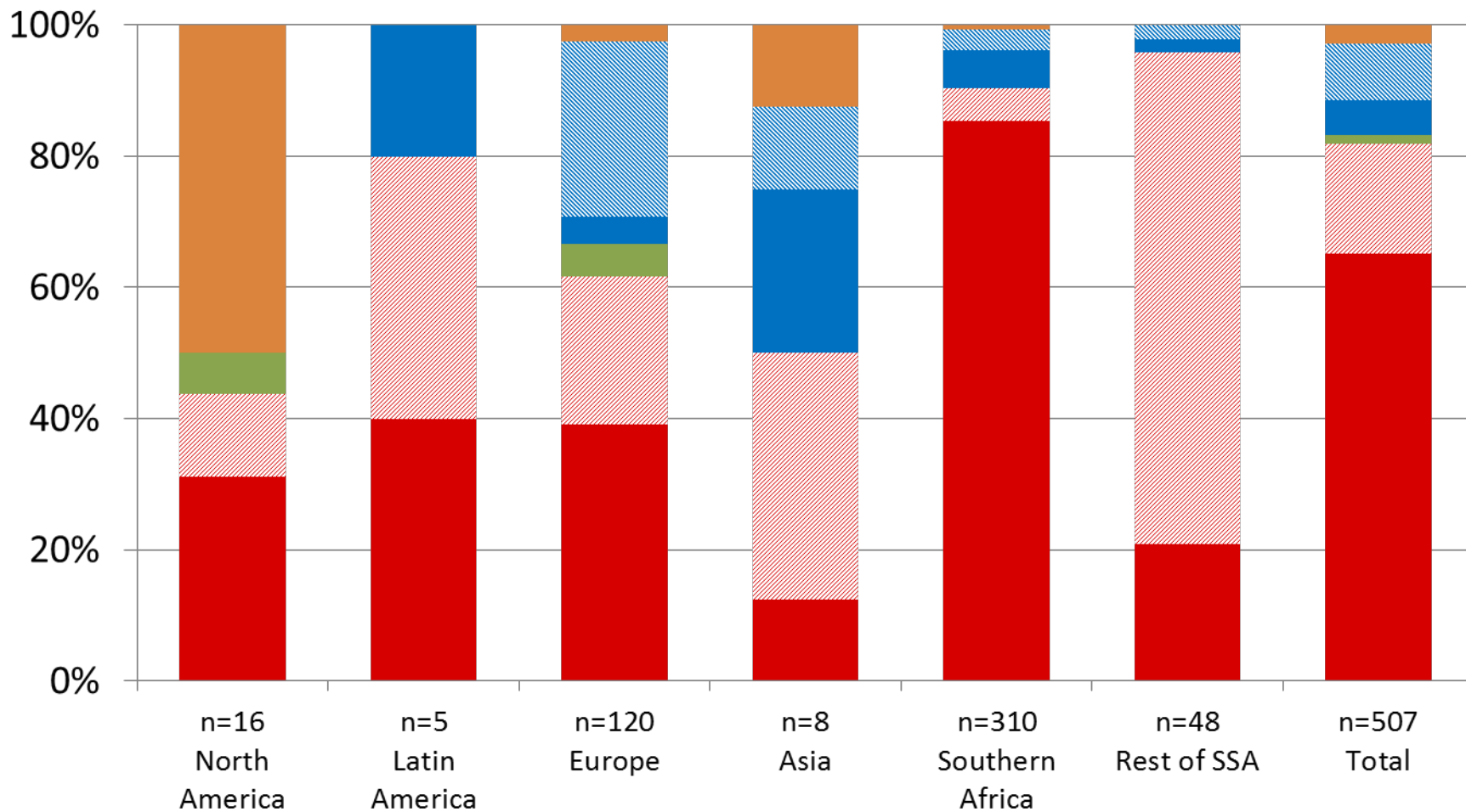
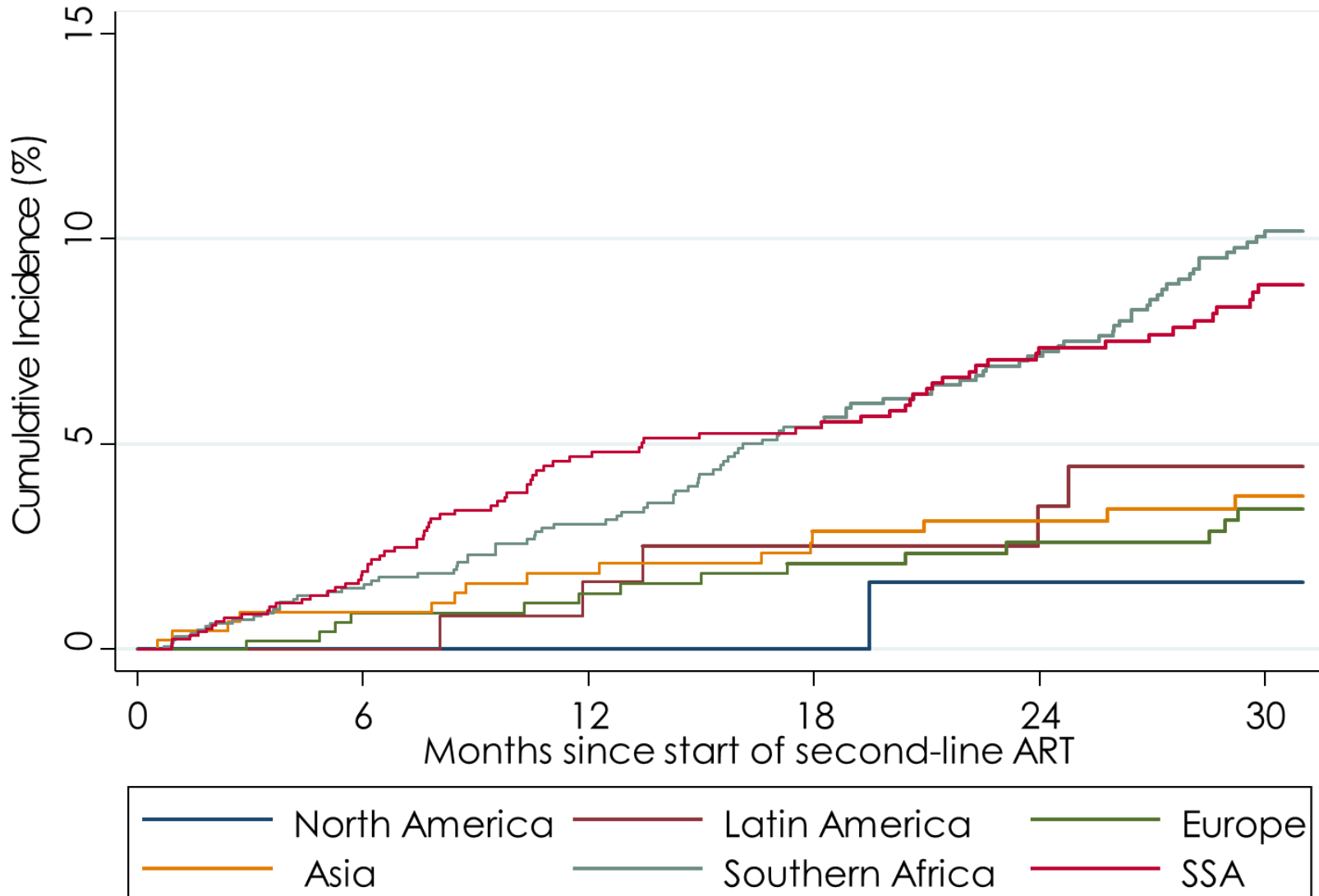# Median (IQR) CD4 counts over 2-year follow-up by region
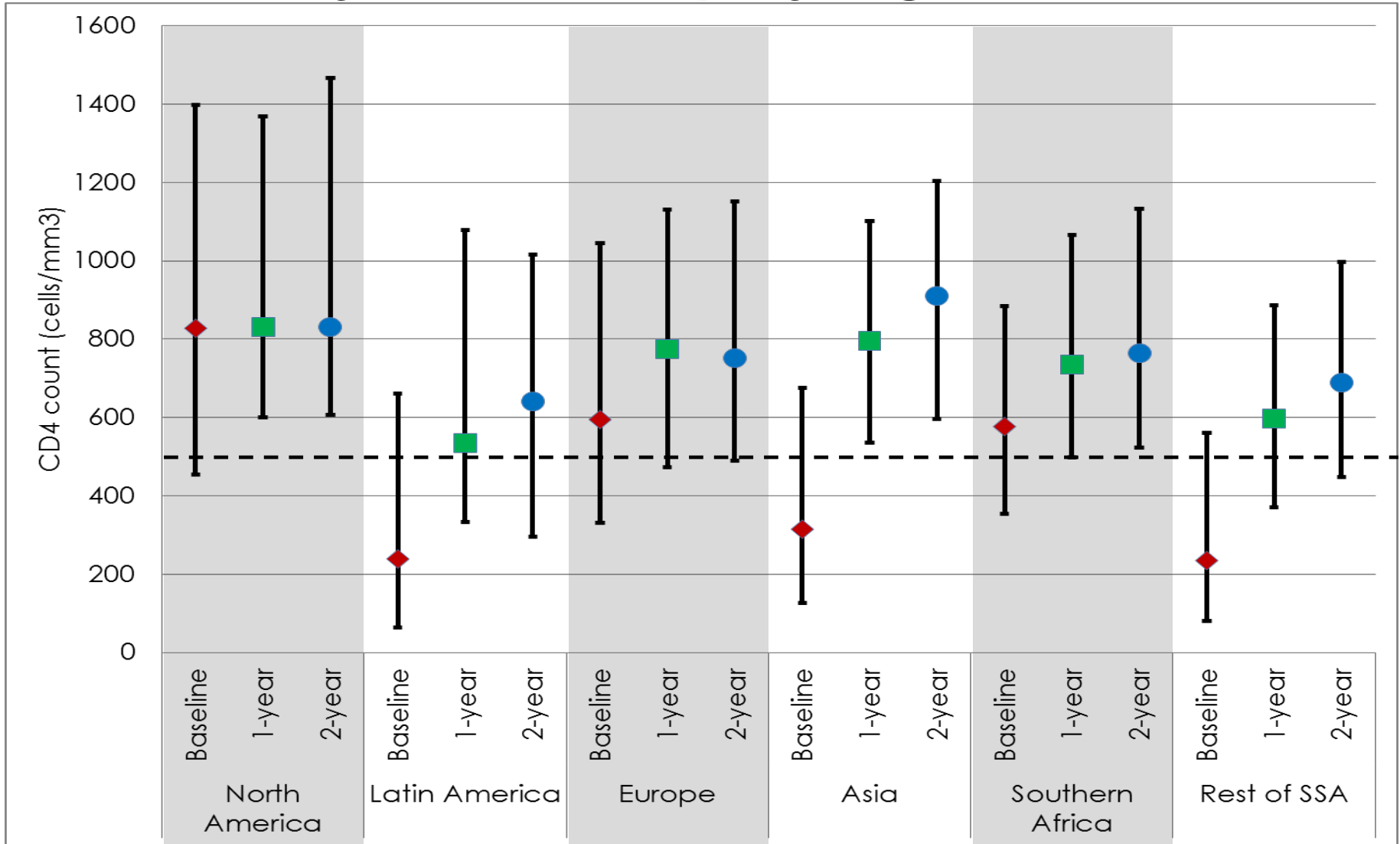
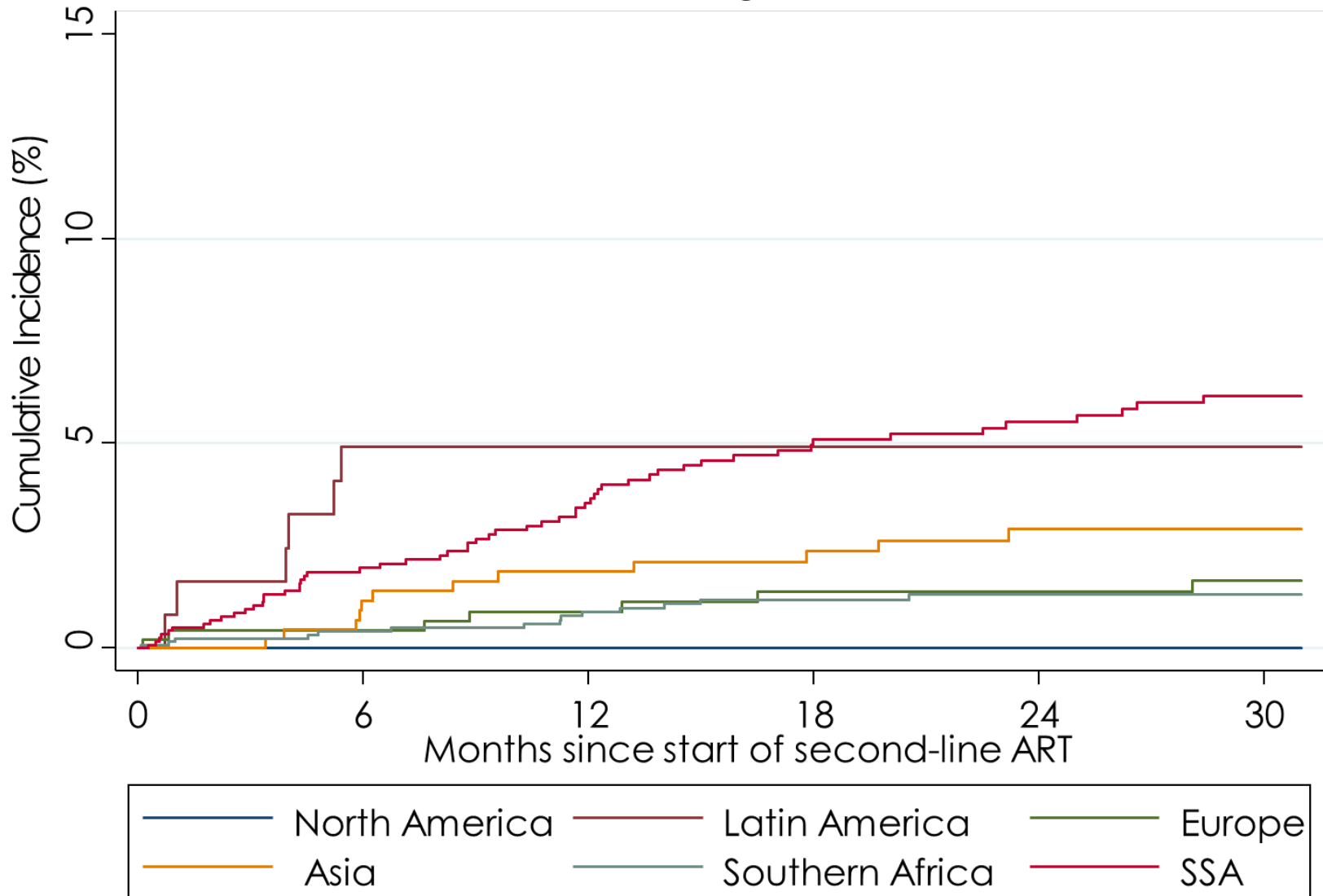# Median (IQR) weight for age z-scores over 2-year follow-up by region

Cumulative incidence of loss to follow-up (LTFU)

Cumulative incidence of mortality

Summary/Conclusions

- Children with perinatally acquired HIV have responded well to second-line ART with increases in CD4 and low to moderate rates of early LTFU and mortality

- Current generation on second-line ART largely switched before adolescence after less than 3 years on first-line ART

  - Emphasizes importance of providing adherence support for those on first-line ART and those who have already switched to second-line ART

  - Raises concerns about future drug options should the need for third- and fourth-line regimens arise through adolescence and adult life

Second-Line Project Team

Co-chairs: Kunjal Patel and Rachel Vreeman

UCL Data Center: Colette Smith, Ruth Goodall, Intira Jeannie Collins

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- **BIPAI (Baylor):** Mary Paul
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- **IeDEA-Southern Africa:** Mary-Ann Davies
- **IeDEA-West-Africa:** Valériane Leroy
- **PHACS/IMPAACT:** Russell Van Dyke
- **Optimal Models:** Harriet Nuwaqaba-Biribonwoha and Elaine Abrams

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- CIPHER Global Cohort Collaboration Oversight Group
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  - UCL-MRC (Ali Judd)
  - HSPH-PHACS DOC (George Seage)
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