

# Analysis of the pre-ART cascade among HIV-infected children aged 0-19 years in the leDEA global network, 2004-2014

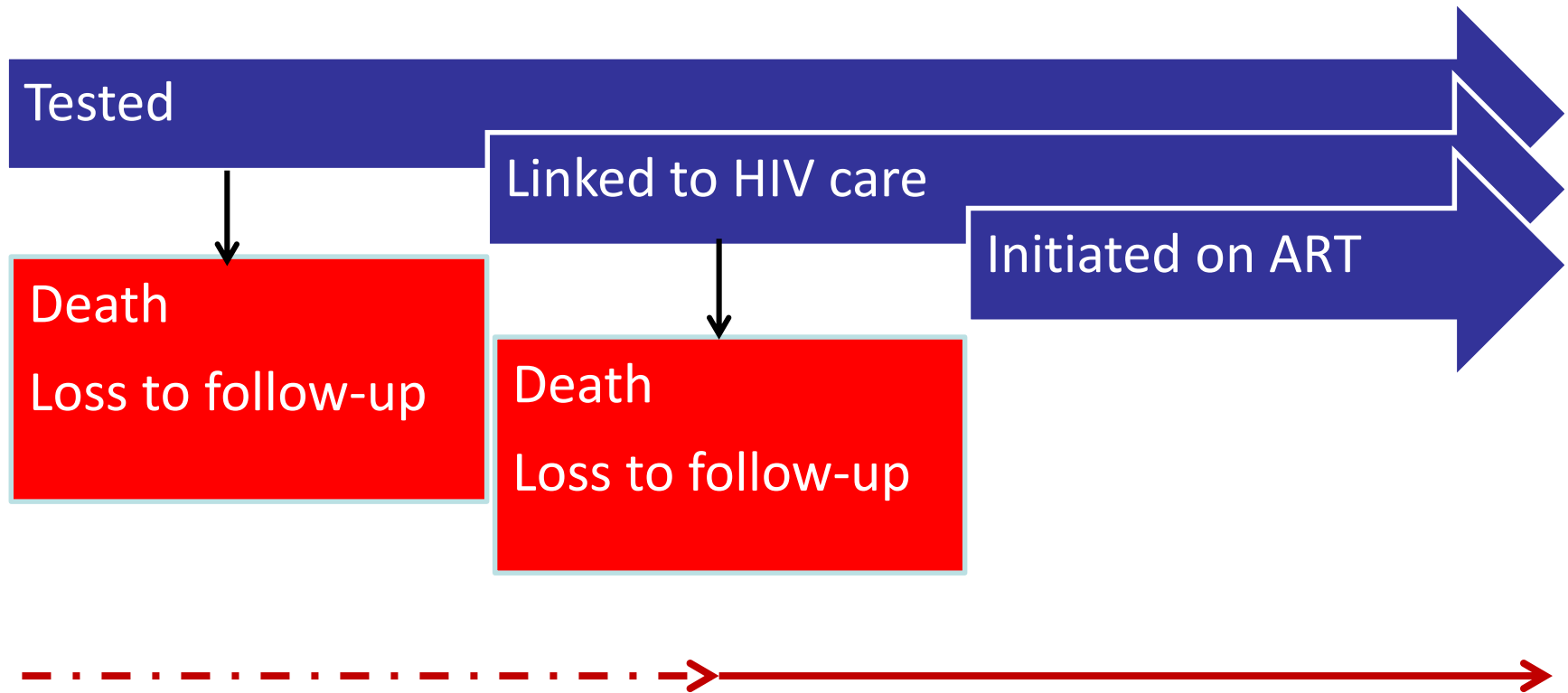
Sophie Desmonde<sup>1</sup>, Frank Tanser<sup>2</sup>, Rachel Vreeman<sup>3</sup>, Elom Takassi<sup>4</sup>,  
Andrew Edmonds<sup>5</sup>, Pagakrong Lumbiganon<sup>6</sup>, Jorge Pinto<sup>7</sup>, Karen Malateste<sup>1</sup>,  
Azar Kariminia<sup>8</sup>, Marcel Yotebieng<sup>5</sup>, Fatoumata Dicko<sup>9</sup>, Kara Wools-Kaloustian<sup>3</sup>,  
Mary-Ann Davies<sup>10</sup>, Valériane Leroy<sup>11</sup> for the International Epidemiologic  
Databases to Evaluate AIDS (leDEA) Pediatric Working Group

1. Inserm U1219, Bordeaux University, Bordeaux, France
2. Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Somkhele, South Africa
3. Indiana University School of Medicine, Indianapolis, USA
4. CHU Sylvanus OLYMPIO, Lomé, Togo
5. Department of Epidemiology, The Ohio State University, USA.
6. Khon Kaen University, Khon Kaen, Thailand
7. School of Medicine, Belo Horizonte, Brasil.
8. The Kirby Institute, UNSW Australia, Sydney
9. Hopital Gabriel Touré, Bamako, Mali
10. University of Cape Town, South Africa
11. Inserm U1027, Université Toulouse 3, Toulouse, France

# Background

- In low/middle-income countries, attrition across the continuum of care of HIV-infected children between HIV diagnosis and antiretroviral therapy (ART) initiation is not well known.
- A better understanding is needed to achieve the 90-90-90 target.
- We performed a global analysis of the pre-ART retention cascade in children within the IeDEA network from 2004 to 2014.

# Pre-ART retention cascade



# Methods (1)

- We pooled individual data from the pediatric cohorts participating in 6 regions of the IeDEA network: Asia-Pacific, sub-Saharan Africa, and Latin America.
- We included all confirmed HIV-1 infected children, aged 0-19 years, ART-naïve at inclusion into HIV care programs, between 2004 and 2014.
- Baseline : date of inclusion in the HIV program, or confirmed HIV diagnosis if this occurred later.

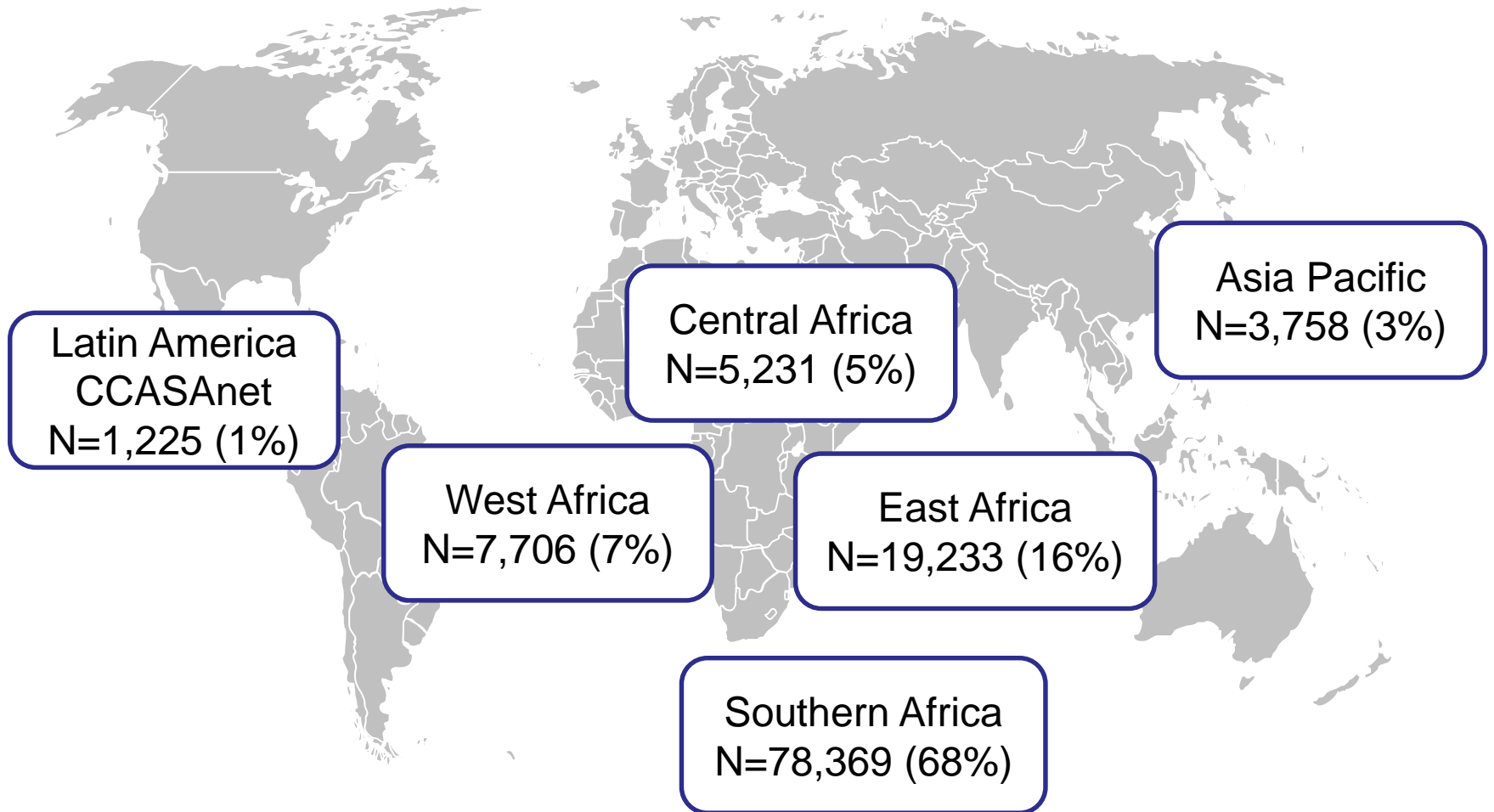
# Methods (2)

- We described the proportions by region
  - Children initiating ART
  - Death and loss to follow-up (LTFU) at last visit >6 months before database closure for this analysis
- We computed the cumulative incidence functions (CIF) for ART initiation among children and analysed determinants for ART initiation accounting for death and LTFU as a competing risk until 24 months

# Methods (3)

- ART eligibility criteria were defined as follows:
  - Clinical eligibility: clinical stage IV or AIDS (not available in East and Southern Africa)
  - Severe immunodeficiency for age: CD4  $\leq$ 25% if age <5 years or CD4  $\leq$ 350 cells/ $\mu$ l if age  $\geq$ 5 years.
  - Additional age criteria according to different WHO guidelines periods
    - if age <1 year between [01/04/2008-30/06/2010]
    - if age <2 years between [01/07/2010-31/05/2013]
    - if age <5 years after 01/06/2013

# Results : 115,549 children enrolled



# Baseline description

	Asia- Pacific N=3,785	Latin America N=1,225	Central Africa N=5,231	East Africa N=19,233	Southern Africa N=78,369	West Africa N=7,706
Female (%)	48	53	58	57	58	49
Median age (years) (IQR)	4 (2;7)	<b>8 (2;16)</b>	<b>8 (3;14)</b>	6 (2;11)	6 (2;13)	<b>3 (1;7)</b>
<b>Age (%)</b>						
<1 year	17.0	18.6	10.6	12.7	15.6	30.4
[1-2[ years	11.9	7.5	7.2	7.7	11.4	13.4
[2-5[ years	30.1	14.1	17.2	24.3	16.3	21.2
[5-10[ years	<b>30.8</b>	18.0	<b>25.3</b>	<b>26.1</b>	<b>21.7</b>	<b>23.3</b>
[10-15[ years	9.5	14.9	18.0	14.8	14.6	11.1
[15-19] years	0.7	<b>26.9</b>	21.7	14.5	20.4	0.6
Median CD4 cell count (IQR)	366 (70;862)	443 (183;810)	438 (234;670)	510 (246;869)	391 (194;708)	514 (200;960)
Median CD4 percentage (IQR)	<b>13</b> (4;22)	17 (8;27)	16 (11;23)	<b>19</b> (11;27)	17 (10;24)	15 (8;24)
<b>Eligibility at inclusion according to WHO guidelines (%)</b>						
Yes	<b>64.6</b>	53.4	<b>31.5</b>	46.1	32.1	64.4
No	25.7	31.8	47.1	44.0	45.9	28.9
Missing	9.7	14.9	21.4	9.9	<b>22.0</b>	<b>6,7</b>

p < 0.001 for all variables



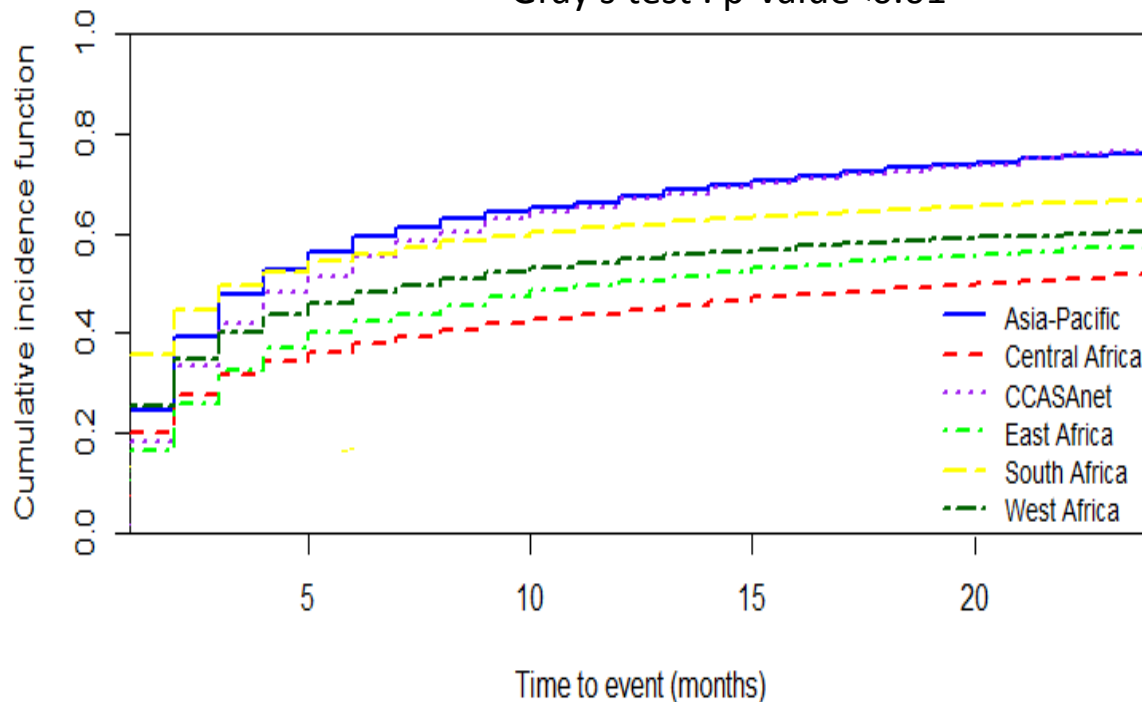
# 24-month outcomes (%)

Region	Asia-Pacific N=3,785	Latin America N=1,225	Central Africa N=5,231	East Africa N=19,233	Southern Africa N=78,369	West Africa N=7,706	Total N=115,549
ART initiation	85.7	<b>91.7</b>	64.5	65.6	67.8	<b>63.3</b>	<b>67.8</b>
Death	2.2	0.7	1.5	3.4	1.7	2.8	2.0
Transfer out	6.2	0.3	1.9	1.1	5.8	1.2	4.5
Loss to Follow-up	2.4	7.0	25.8	23.5	<b>20.3</b>	25.9	<b>20.8</b>
Alive not on ART	3.5	0.3	6.3	6.4	4.4	6.8	4.9

For those eligible, the overall median delay between inclusion into care and ART initiation was 1 month (inter-quartile range [IQR]: 0-6 months)

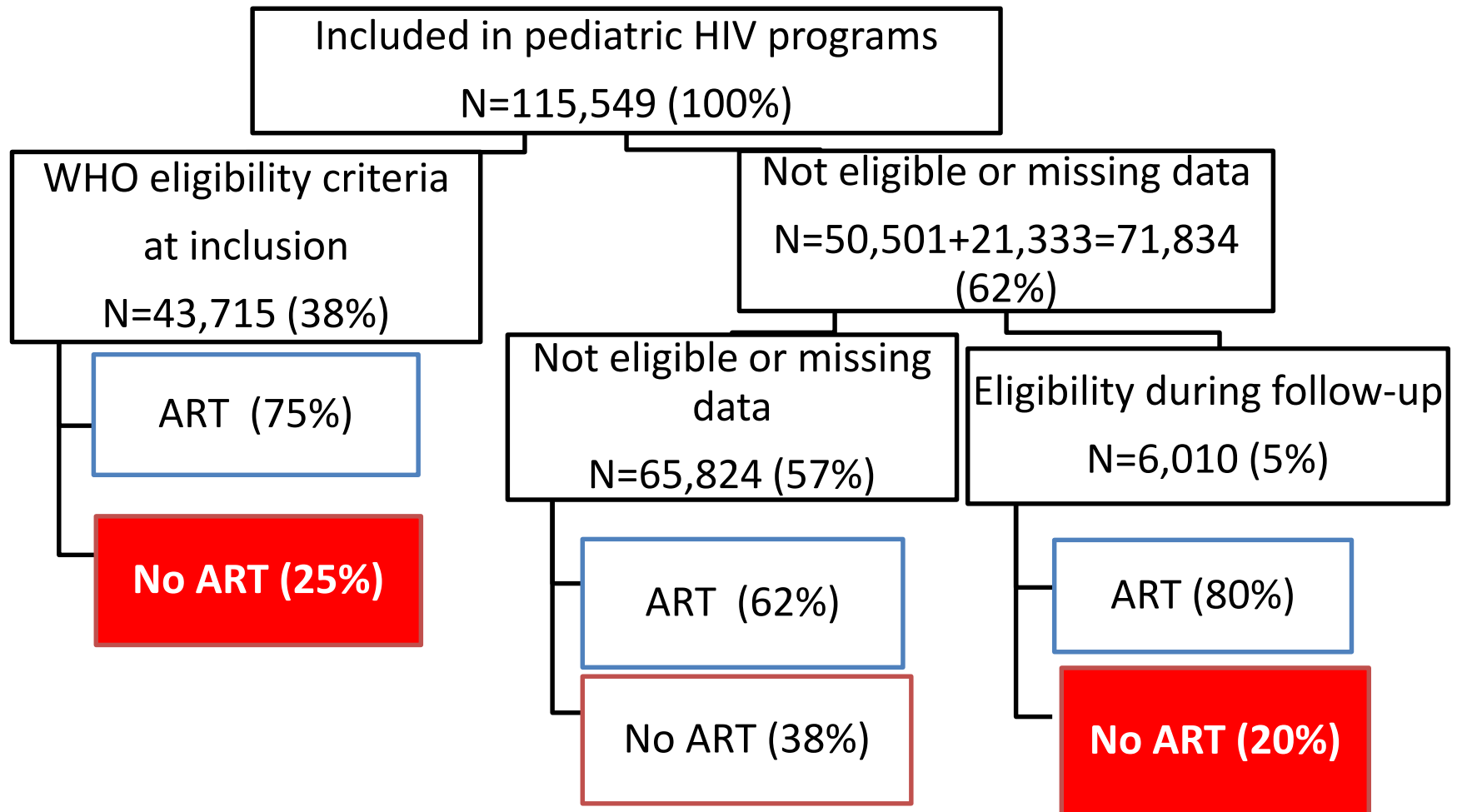
# 24-month cumulative incidence functions of ART initiation by region (%)

Gray's test : p-value<0.01

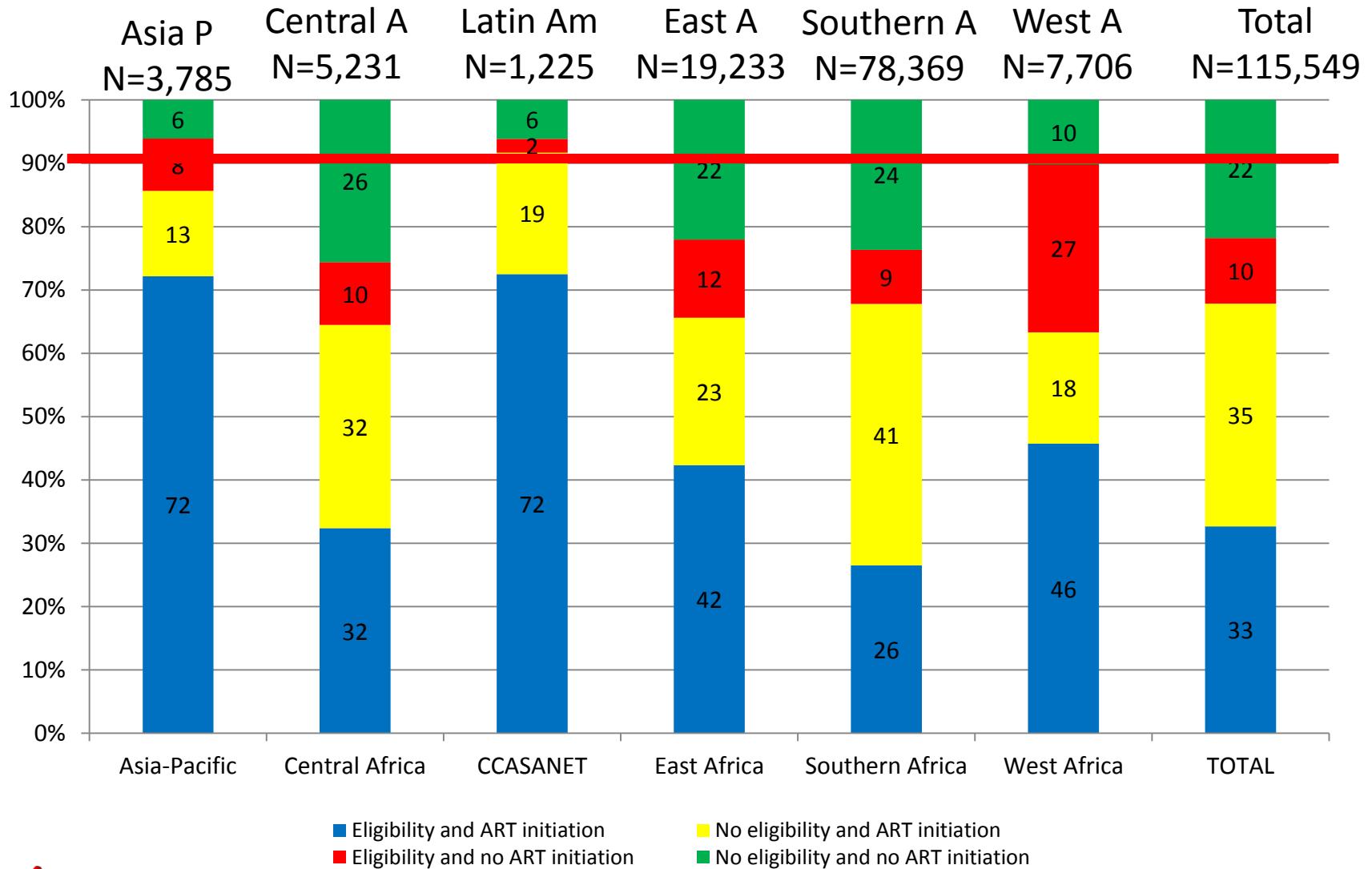


Region (%)	Month 1	Month 24
Latin America	18 (16-20)	77 (74-79)
Asia-Pacific	24 (23-26)	76 (75-78)
Southern Africa	36 (35-36)	67 (66-67)
West Africa	25 (24-26)	61 (60-62)
East Africa	16 (16-17)	58 (57-59)
Central Africa	20 (19-21)	52 (51-53)

# Eligibility criteria and ART initiation



# ART initiation by region according to ART eligibility criteria at baseline



# Determinants of ART initiation

	Univariate analysis		Adjusted model		P
	sHR*	CI (95%)**	asHR <sup>§</sup>	CI (95%)**	
<b>Girls (ref: boys)</b>	0.85	(0.84-0.86)	<b>0.91</b>	<b>(0.89-0.92)</b>	<0.01
<b>Age at inclusion (ref: [10-15[ years)</b>					<0.01
<1 year	0.72	(0.70-0.74)	<b>0.73</b>	<b>(0.71-0.75)</b>	
[1-2[ years	0.86	(0.84-0.88)	0.83	(0.81-0.85)	
[2-5[ years	0.83	(0.81-0.85)	0.82	(0.81-0.84)	
[5-10[ years	0.89	(0.87-0.91)	0.95	(0.93-0.97)	
[15-19] years	0.62	(0.61-0.64)	<b>0.64</b>	<b>(0.62-0.65)</b>	
<b>Period of inclusion (ref: ≥ 6/2013)</b>					<0.01
< 4/2008	0.65	(0.63-0.67)	0.52	(0.50-0.54)	
[4/2008-6/2010[	0.67	(0.65-0.69)	0.57	(0.55-0.59)	
[7/2010-6/2013[	0.74	(0.71-0.77)	0.68	(0.66-0.71)	
<b>Country income (ref: upper)</b>					<0.01
Low-lower/middle	0.71	(0.70-0.72)	0.79	(0.78-0.81)	
<b>Clinical or immunological eligibility (ref: eligibility at inclusion)</b>					
During follow-up	0.50	(0.49-0.51)	<b>0.53</b>	<b>(0.51-0.54)</b>	<0.01
No	0.40	(0.39-0.41)	0.42	(0.41-0.43)	
Missing	0.64	(0.63-0.65)	0.62	(0.61-0.63)	

# Discussion

- Overall, 68% initiated ART within the 24 months after inclusion, with a substantial risk of LTFU before ART initiation, which may also represent undocumented mortality.
- Pre-ART delay underestimated from HIV diagnosis
- Inequities in ART access
  - Female children
  - Adolescents aged 15-19 years
  - Children <1 year, despite 2008 WHO guidelines
  - Children becoming eligible for ART during follow-up are less likely to start ART than those eligible at inclusion: this favour the test and treat strategy.

# Conclusion

- Female and those at the youngest and oldest ends of the paediatric age spectrum need more effective and targeted interventions to improve their ART initiation.
- Since 2015, WHO guidelines recommend universal ART in all children and adolescents, irrespective of clinical stage or CD4.
- Many obstacles remained in achieving the second 90% target of ART coverage, but there is an ethical priority to first trace and treat all children who were eligible for ART before 2015, and who are probably the sickest now.

# Acknowledgements

- All the children and caregivers followed up in the leDEA pediatric centers
- All the leDEA investigators, pediatric coordinators and data managers, and staff from the Pediatric leDEA Regions :
  - Asia-Pacific (Annette Sohn, Azar Kariminia)
  - Latin-America CCASANET (Jorge Pinto, Cathy Mc Gowan)
  - Central Africa (Marcel Yotebieng, Andrew Edmonds)
  - East Africa (Kara Wools-Kaloustian, Bev Music)
  - Southern Africa (Mary-Ann Davies, Nicky Maxwell)
  - Western Africa (François Dabis, Karen Malateste)
  - The leDEA Pediatric Working Group: Rachel Vreeman (chair)
- World Health Organization (Martina Penazzato)
- US National Institute of Allergy and Infectious Diseases (NIAID) and Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

