



MRC  
Clinical  
Trials Unit



# Uptake of integrase inhibitors and virological response in children living with HIV in Europe & Thailand from 2010 to 2020

Karen Scott<sup>1</sup>, Siobhan Crichton<sup>1</sup>, Ali Judd<sup>1</sup>, Clara Carreras<sup>2</sup>, Sara Guillen<sup>3-4</sup>, Laura Marques<sup>5</sup>, Lars Naver<sup>6-7</sup>, Annemarie van Rossum<sup>8</sup>, Vana Spoulou<sup>9</sup>, Intira Jeannie Collins<sup>1</sup>, on behalf of the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC)

<sup>1</sup>MRC Clinical Trials Unit at University College London, London, UK; <sup>2</sup>Dept of Paediatrics, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; <sup>3</sup>CIBER en Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain; <sup>4</sup>Dept of Paediatrics, Hospital Universitario de Getafe, Madrid, Spain; <sup>5</sup>Dept of Pediatrics, Centro Materno Infantil do Norte, Centro Hospitalar e Universitário do Porto, Porto, Portugal; <sup>6</sup> & <sup>7</sup>Dept of Pediatrics, Karolinska University Hospital and Dept of Clinical Science, Intervention and Technology (CLINTEC), Division of Paediatrics, Karolinska Institutet, Stockholm, Sweden; <sup>8</sup>Department of Pediatrics, Erasmus MC University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands; <sup>9</sup>"Agia Sofia" Children's Hospital, 1st Dept of Paediatrics, Athens, Greece

## INTRODUCTION

- A number of integrase inhibitors (INSTIs) have been approved for paediatric HIV use from 2013.
- Dolutegravir (DTG), raltegravir (RAL) and bictegravir (BIC) are recommended as the **preferred or alternative anchor drug** for first and subsequent line antiretroviral therapy (ART) for children and adolescents living with HIV (CLWHIV) in USA, European and WHO guidelines<sup>1-3</sup>.
- We describe the trends in uptake of INSTIs, and virological response, in CLWHIV in routine HIV care in Europe and Thailand.

## METHODS

**Data source:** individual level data on participants followed in EPPICC cohorts and included in the 2020-21 data merger

**Inclusion criteria for this analysis:** CLWHIV aged <18 years at HIV diagnosis and followed-up in 18 cohorts in EPPICC between 2010 & 2020.

**Statistical methods:**

- Characteristics of CLWHIV in follow up on 01/01/2010 and 01/01/2020 were summarised.
- Trends in ART use from 2010-2020 were explored,

overall and by region, and ART status (naïve, ART interrupted for >30 days, class of regimen for those on ART) of CLWHIV in follow-up on 1st Jan each year.

- Characteristics at start of INSTI were described by INSTI drug (DTG, RAL, BIC and elvitegravir (EVG))
- Percentage (95% CI) virally suppressed (VS) (viral load <50c/mL) at 12 & 24 months was estimated among those remaining on INSTI, by ART history/viral load status at INSTI start

## RESULTS

- Of 11,055 children ever in EPPICC, 7,835 were aged <18 years and in follow-up from 1<sup>st</sup> Jan 2010 and included in the analysis.
- The median age of those in follow up increased from 10.2 to 12.3 years since 2010 (Table 1).
- The geographical distribution of those in follow-up changed over time, e.g. the proportion in Western Europe declined from 61% in 2010 to 30% in 2020, while the proportion in Eastern/Central Europe and Russia increased (Table 1).

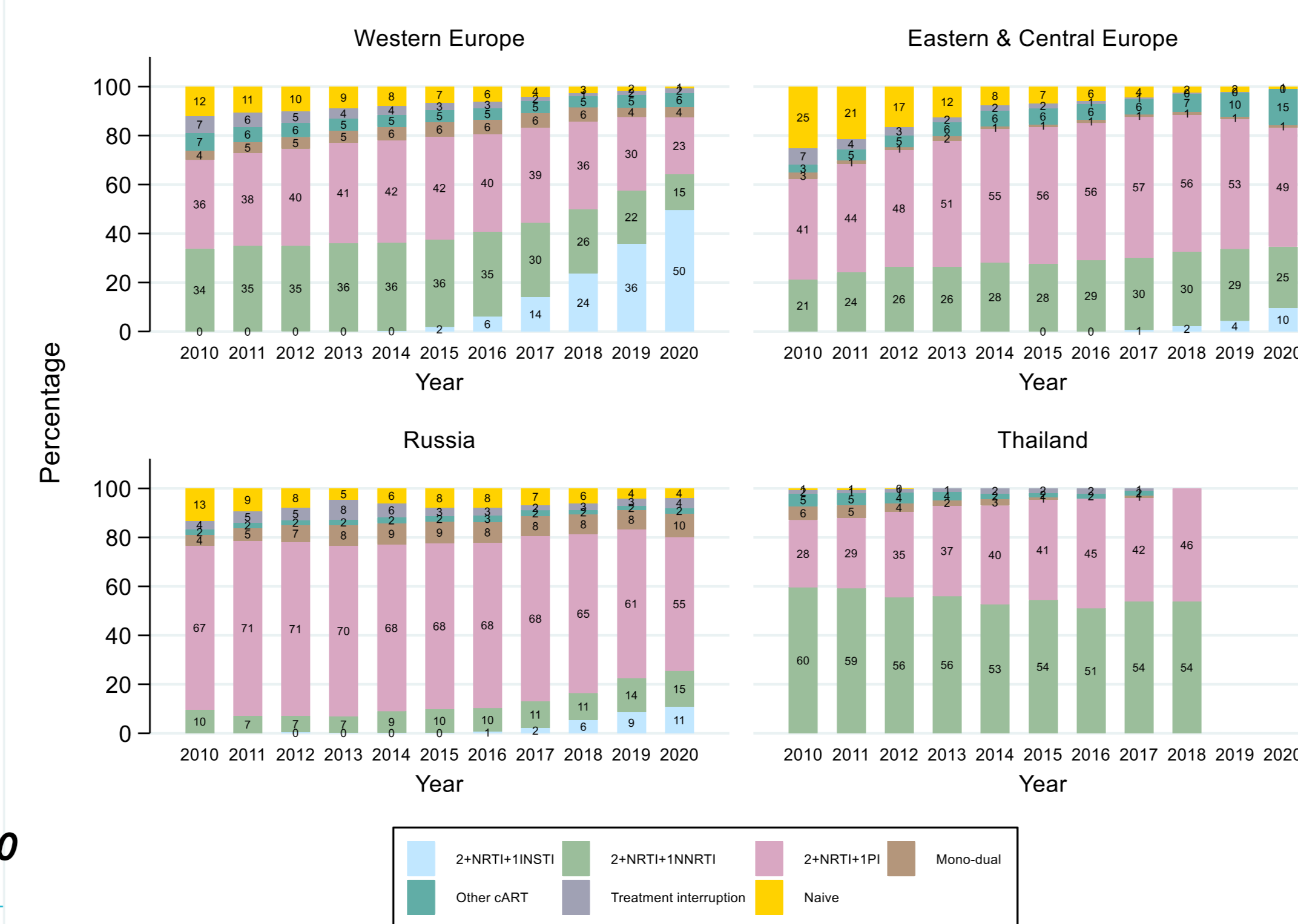


Table 1: Characteristics of children in follow-up in 2010 & 2020

Characteristic	2010 n=4769	2020 n=2524
N (%) or median [IQR]		
Sex, female	2496 (52)	1381 (55)
Age, years	10.2 [6.1,13.8]	12.3 [8.3,15.2]
Previous AIDS diagnosis	1281 (27)	750 (30)
Region:		
Western Europe	2919 (61)	751 (30)
Eastern/Central Europe	1168 (24)	989 (39)
Russia	120 (3)	784 (31)
Thailand	562 (12)	--
Perinatally acquired HIV	4584 (99)	2310 (97)
Age at HIV diagnosis, years	1.6 [0.5,3.2]	1.4 [0.4,2.8]
ART naïve	620 (13)	50 (2)
Years since ART start	6 [3,10]	8 [4,14]
CD4 count at ART start, cells/mm <sup>3</sup>	533 [265,998]	875 [431,1747]

## INSTI use in children in 2010-2020

- The proportion of CLWHIV on INSTIs increased from 1% in 2010 to 22% in 2020, but this varied by region.
- Uptake of INSTIs was highest in Western Europe, accounting for half of children in follow-up in that region by 2020 compared to ≤11% uptake in other regions (Figure 1).

Figure 1: ART status and anchor drug class in children in EPPICC 2010-2020, by region

## Characteristics at start of INSTI and viral suppression

- Of the 1,674 CLWHIV ever received an INSTI: 1,085 were ever on DTG, 532 on RAL, 176 on EVG and 18 on BIC (Table 2). All BIC use and most EVG use was in Western Europe.
- Median age at INSTI start was 13 years [IQR, 10-15], with variability across drugs. RAL had largest proportion aged <6 years (23%, 123/532) compared to ≤2% on DTG and EVG.
- The proportion ART-experienced and virally suppressed (VL<50c/mL) at INSTI start varied from 26% of those on RAL to 50% on DTG and 63% on EVG (Table 2).
- Overall, among those on INSTI at 12 and 24 months, >80% were VS on DTG and EVG compared to 69-71% on RAL (Figure 2).
- Children who were ART-experienced and viraemic at INSTI start generally had lower levels of viral suppression (at 50-66%) than those who were ART naïve or ART-experienced and virally suppressed at INSTI start.

Table 2: Characteristics at start of INSTI

	INSTI			
	DTG (n=1085)	EVG (n=176)	RAL (n=532)	BIC (n=18)
	n (%) or median [IQR]			
Sex, female	577 (53)	87 (49)	292 (55)	12 (67)
Age, years	14 [11-15]	14 [11-16]	11 [6-15]	16 [15-17]
Age group:				
<2 years	2 (0)	0 (0)	26 (5)	0 (0)
2 to <6 years	22 (2)	1 (1)	97 (18)	0 (0)
6 to <12 years	259 (24)	48 (27)	161 (30)	0 (0)
12 to <18 years	802 (74)	127 (72)	248 (47)	18 (100)
Ethnicity:				
Black	453 (43)	51 (33)	110 (21)	12 (71)
White	187 (18)	47 (30)	274 (53)	1 (6)
Other	63 (6)	5 (3)	29 (6)	0 (0)
Missing	340 (33)	53 (34)	100 (19)	4 (24)
Region:				
Western Europe	844 (78)	172 (98)	341 (64)	18 (100)
Eastern & Central Europe	192 (18)	4 (2)	25 (5)	0 (0)
Russia	49 (5)	0 (0)	163 (31)	0 (0)
Thailand	0 (0)	0 (0)	3 (1)	0 (0)
Perinatal HIV acquisition	961 (97)	158 (97)	469 (96)	14 (93)
Calendar year	2018 [2016-19]	2017 [2016-18]	2016 [2012-18]	2020 [2019-20]
Tx status:				
Naïve	93 (9)	6 (3)	43 (8)	2 (11)
Tx exp. & VL<50	540 (50)	110 (63)	139 (26)	7 (39)
Tx exp. & viraemic (≥50)	244 (22)	31 (18)	207 (39)	4 (22)
Tx exp. & missing VL	208 (19)	29 (16)	143 (27)	5 (28)
Years since ART start	9 [4-12]	10 [6-13]	6 [2-12]	9 [6-16]
CD4 count (mm <sup>3</sup> )	710 [480-970]	765 [545-1000]	661 [358-1069]	670 [477-781]

Note: Tx = Treatment; exp = experienced. A patient can be included more than once as the complete ART history is considered.

## Viral suppression at 12 and 24 months after INSTI start

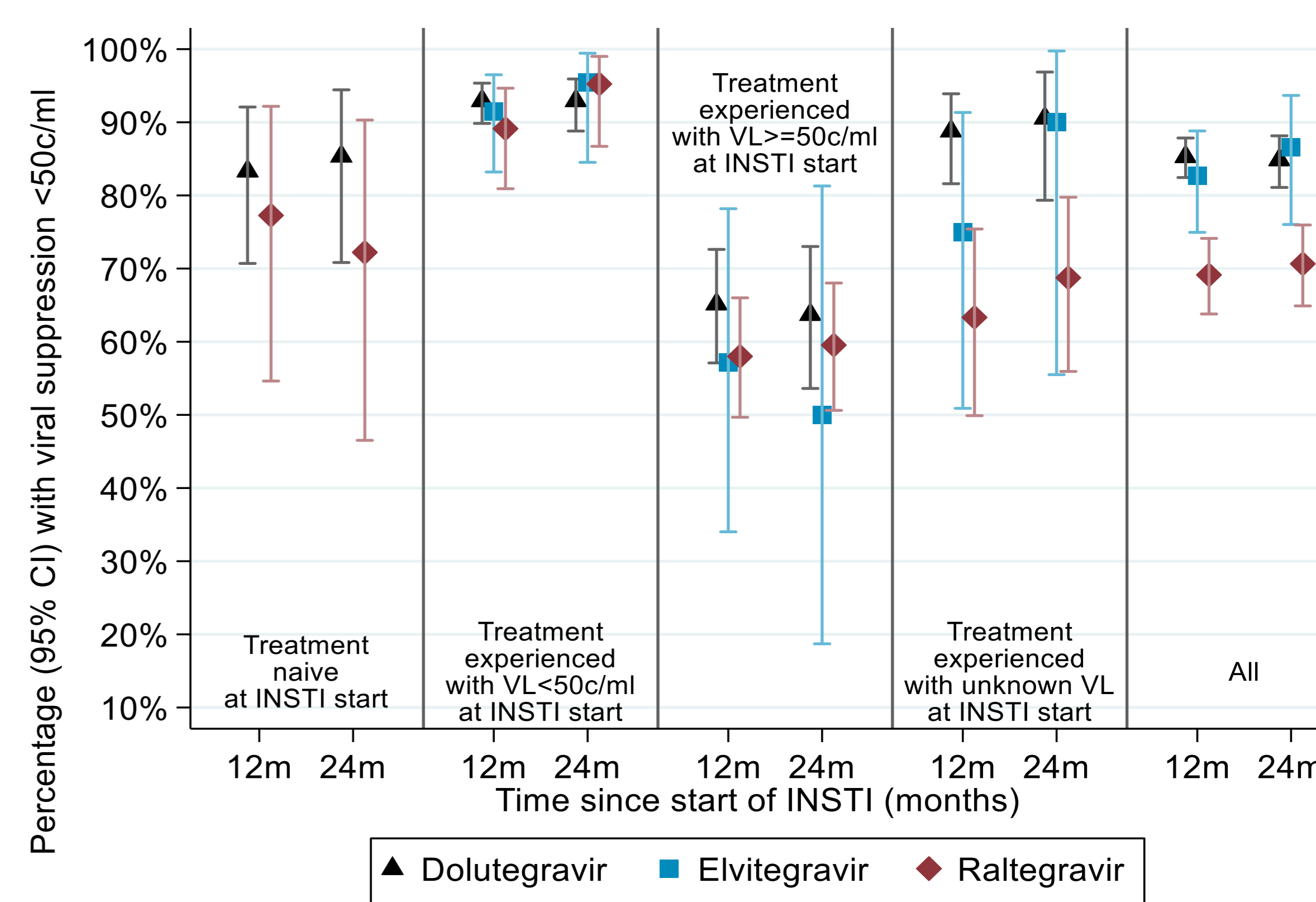


Figure 2: Viral suppression at 12 and 24 months after INSTI start, by drug and viral load status at drug start (outcomes shown where ≥10 CLWHIV with a viral load available)

## CONCLUSION

- Overall, one-in-four CLWHIV in our EPPICC cohort were on INSTI-based regimens in 2020. Half of CLWHIV in western Europe were on INSTIs by 2020 but there was much less usage in Eastern/Central Europe and Russia. Differences by region may reflect limited access and differences in national guidelines with some countries adopting newer ART drugs later
- Overall, over 80% were virally suppressed at 12-24 months on DTG and EVG, and ~70% on RAL, though there were key differences in characteristics of children on each of these drugs. Viral suppression was markedly lower (<70%) among children who were ART-experienced and viraemic at INSTI start.
- It is important to continue to monitor the uptake of new drugs in children to ensure equity in access to optimal treatments and to assess long term effectiveness in real-world settings.

## ACKNOWLEDGEMENTS

Hospital St Pierre Cohort, Brussels, Belgium (T Goetghebuer); Greece Cohort, Greece (V Spoulou); Italian Register for HIV infection in children, Italy (E Chiappini, L Galli); ATHENA Cohort, Netherlands (H. Scherpbier, C.Smit); Paediatric Cohort, Poland (M Marczyńska); "Victor Babes" Hospital Cohort, Romania (L Ene); Centro Hospitalar do Porto, Portugal (L Marques); The Republican Hospital of Infectious Diseases, St Petersburg, Russia (E Voronin, L Okhonskaia, V Rozenberg); The City HIV Centre, St Petersburg, Russia (A Samarina); Irkutsk AIDS Centre (Y Plotnikova); CoRISPE-cat, Catalonia, Spain (A Noguera Julian); CoRISPEs, rest of Spain cohort, Spain (A Navarro); Karolinska University Hospital, Stockholm, Sweden (L Naver); Swiss Mother and Child HIV Cohort Study, Switzerland (C Kahler); Thailand Program for HIV Prevention and Treatment (PHPT) Study Group, Thailand (G Jourdain, N Ngo-Giang-Huong); Integrated Screening Outcome Surveillance Service, UK and Ireland (C Thorne); Collaborative HIV Paediatric Study, UK and Ireland (A Judd); Paediatric HIV Cohort Studv. Odessa. Ukraine (A Volokha, R Malvuta).

## References:

- DHHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. 2023 Apr;
- EACS. European AIDS Clinical Society Guidelines Version 11.0. 2021 Oct;
- WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. 2021