МИНИСТЕРСТВО
ЗДРАВООХРАНЕНИЯ
РОССИЙСКОЙ ФЕДЕРАЦИИ

Тест на ВИЧ
Экспедиция

IV Всероссийский форум для специалистов по профилактике и лечению ВИЧ/СПИДа

Москва, 26-27 ноября 2018

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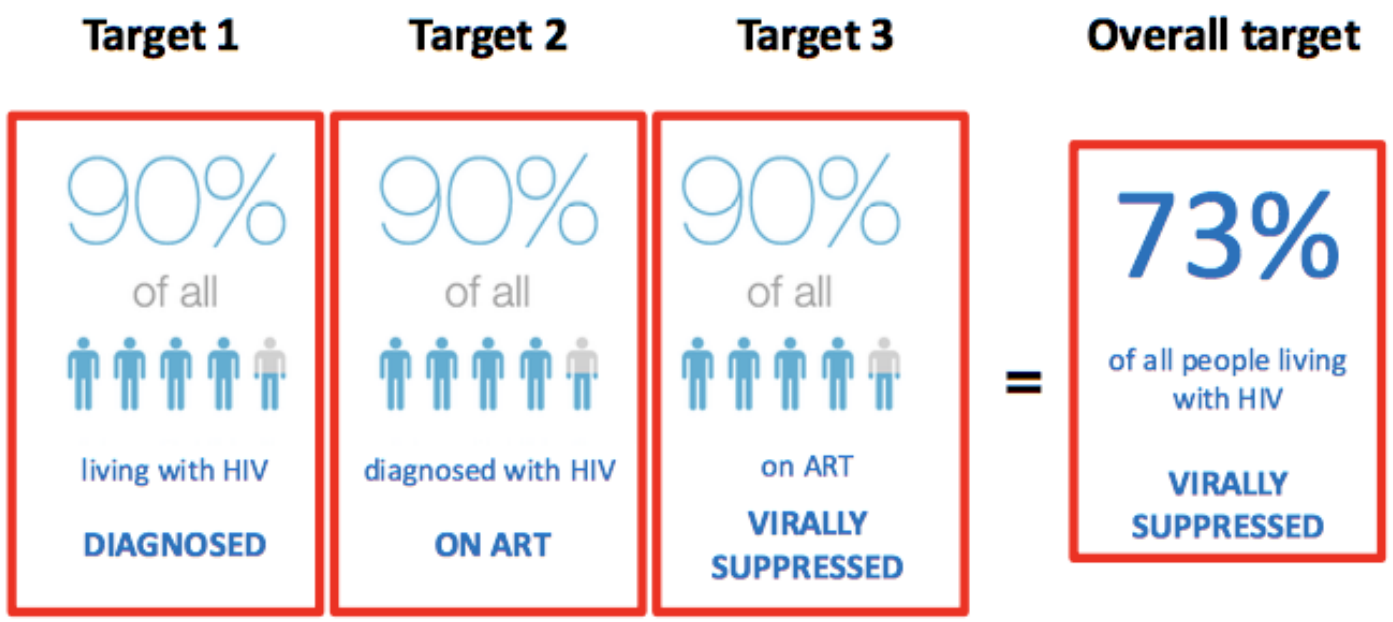
European approaches to antiretroviral therapy

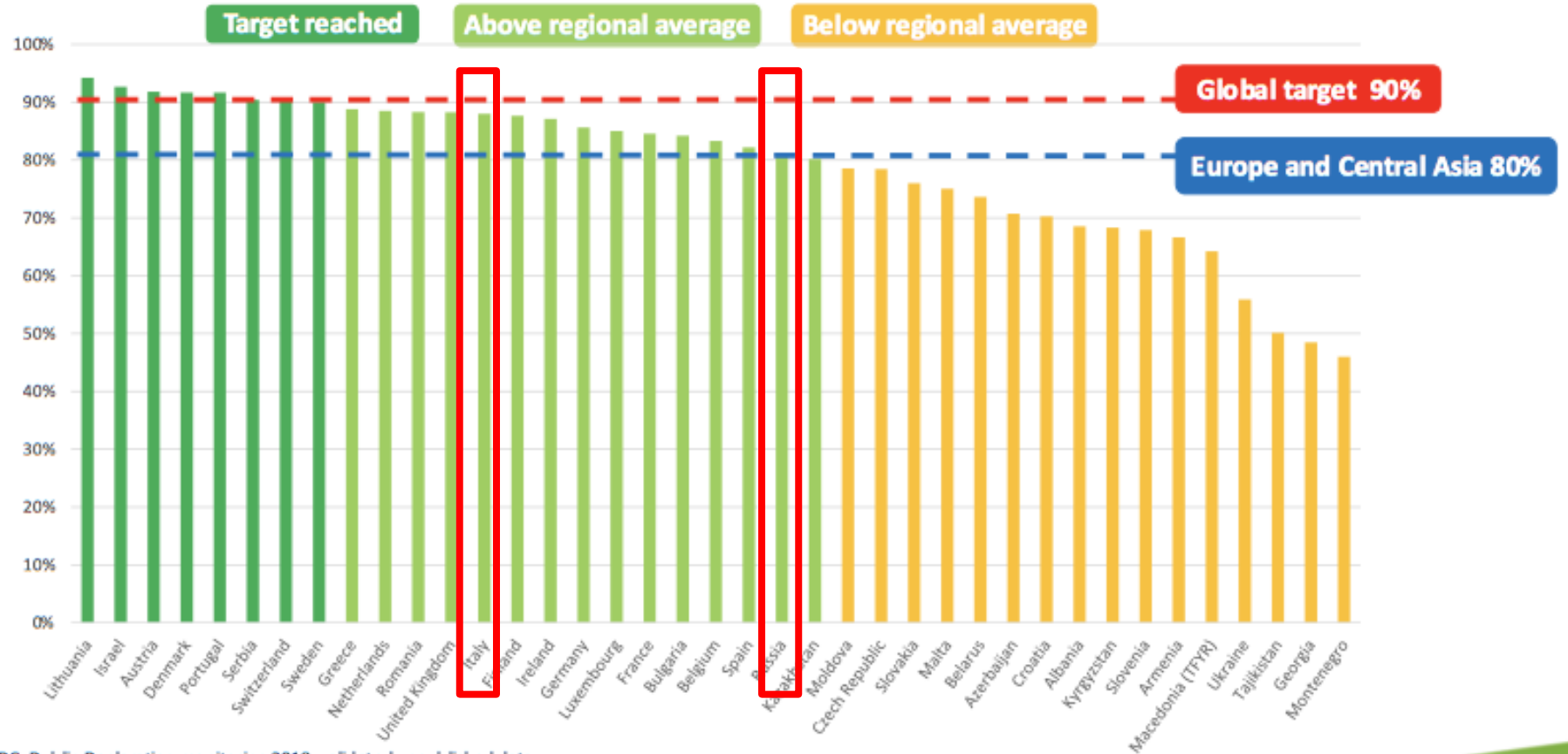
Cristina Mussini

Fast Track Targets by 2020



Progress toward achieving the 1st 90

90% of all PLHIV who know their status (n=39)

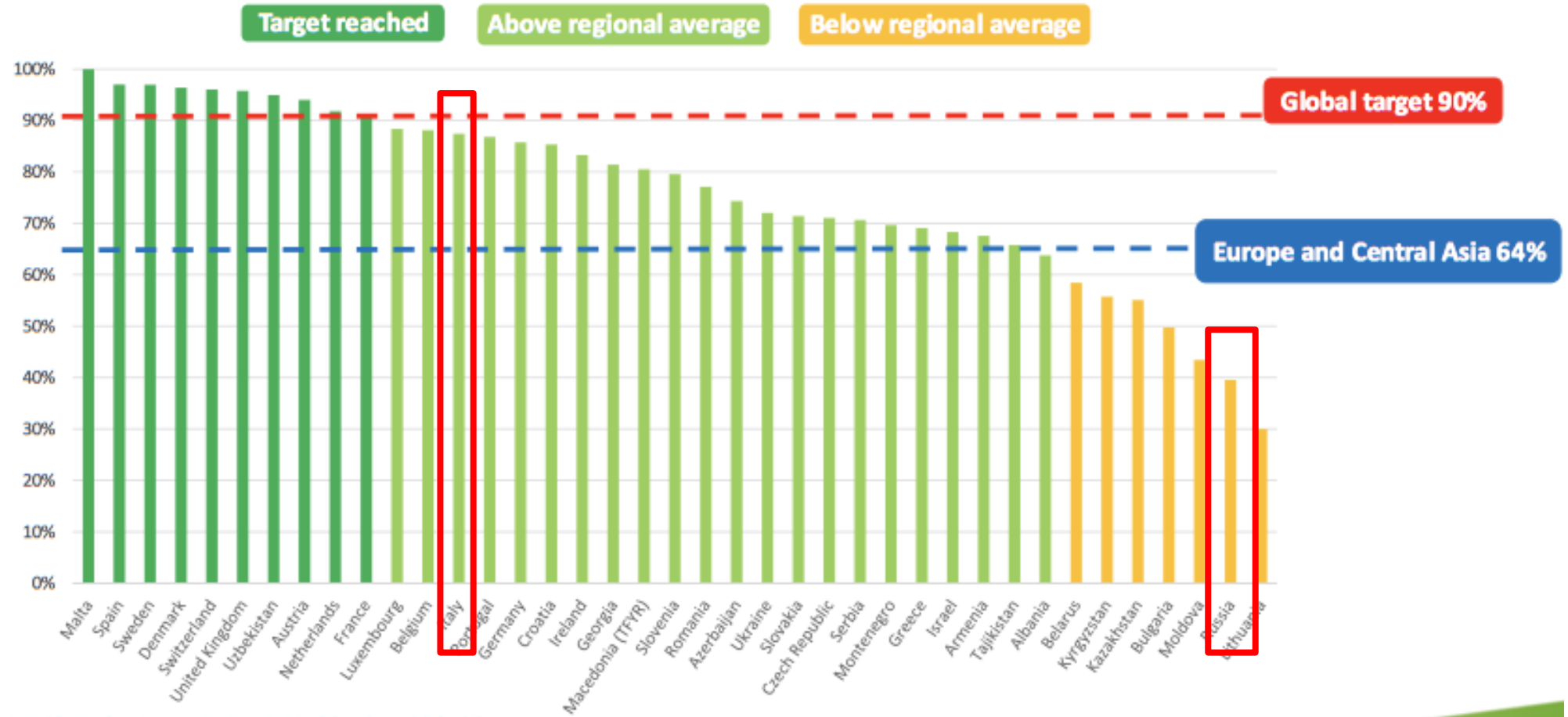


Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.
Latest available data reported, ranging from 2014-2017.

@ECDC_HIVAIDS

Progress toward achieving the 2nd 90

90% of those diagnosed on ART (n=39)



Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.
Latest available data reported, ranging from 2014-2017.

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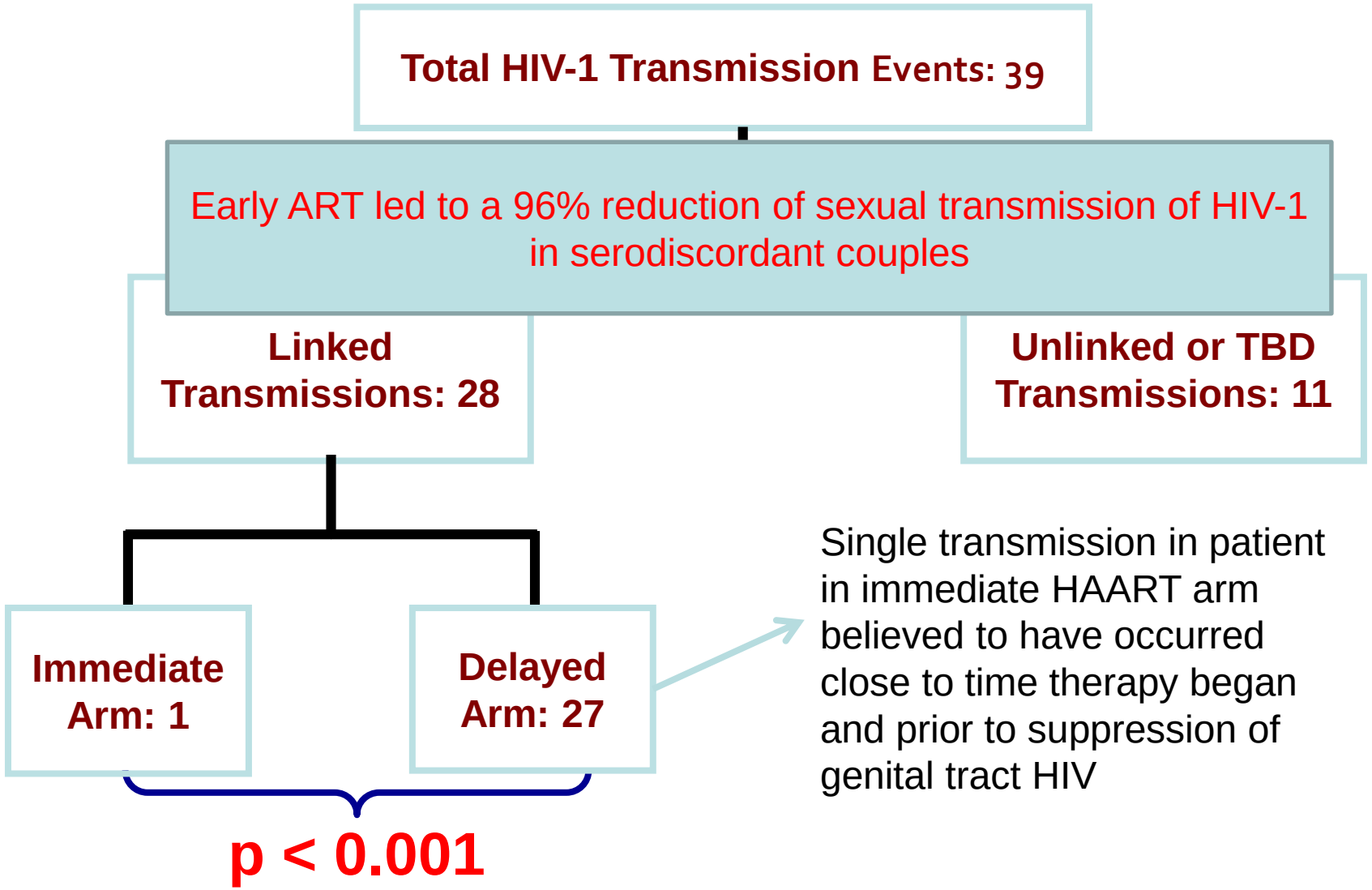
Evolution of DHHS recommendations to initiating treatment early to improve outcomes

FACTOR	RECOMMENDATION FOR TREATMENT						
AIDS	Treat	Treat	Treat	Treat	Treat	Treat	Treat
CD4	<500	Recommended at <200 Offer at <350 Individualize decision at >350			Recommended <350 Risks/Benefits >350	Recommended <500 Favor/optional >500	Recommended for any CD4 cell counts
Viral load	>20,000		>55,000	>100,000	No specific viral load		No specific viral load
Other factors					Pregnant women HBV co-infected HIVAN		ART is also recommended for HIV-positive individuals for the prevention of HIV transmission

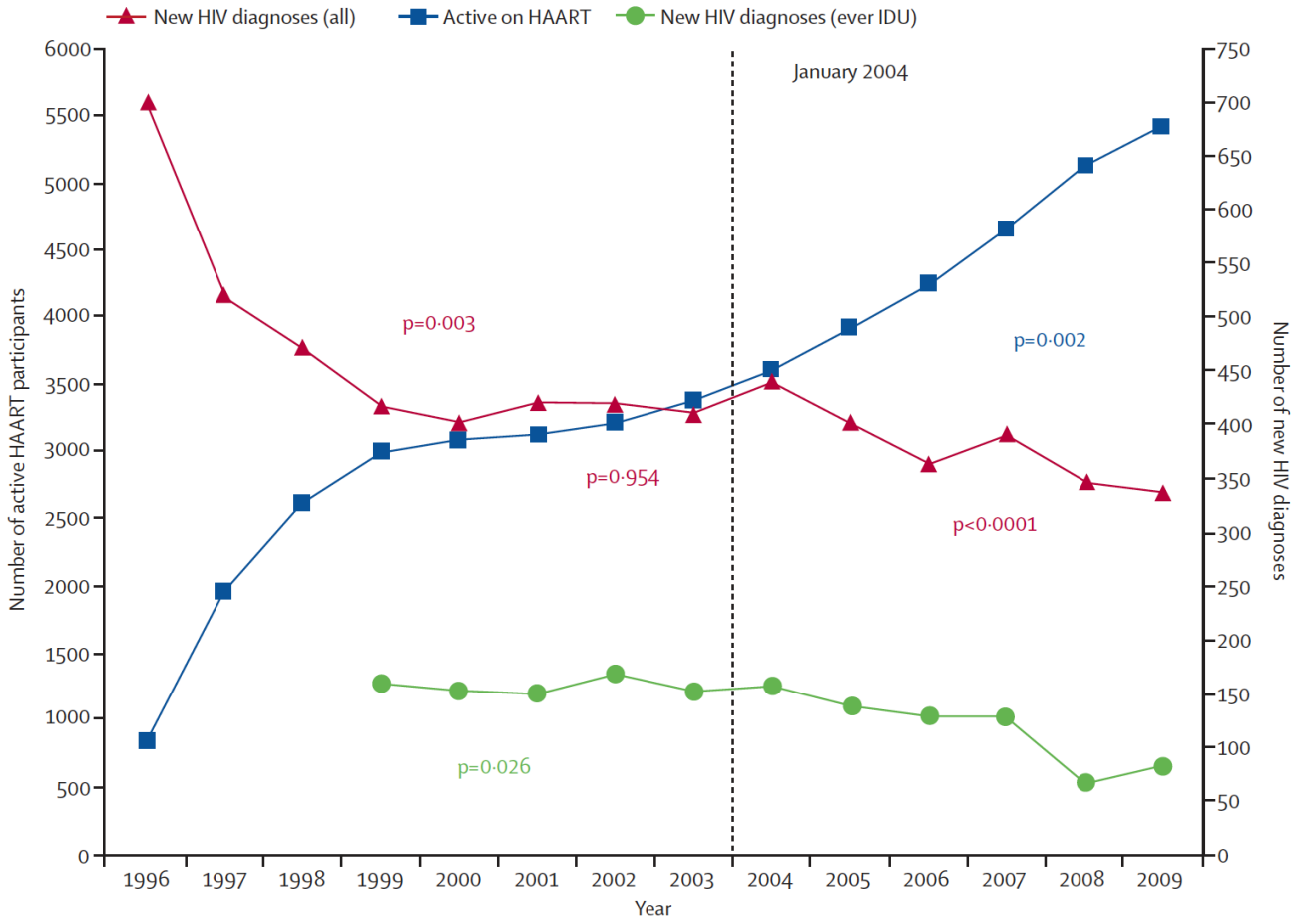
ART, antiretroviral therapy; HBV, hepatitis B; HIVAN, HIV-associated nephropathy

DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. January 28, 2016, & other years as noted: http://www.aidsinfo.nih.gov/Guideline (accessed September 2016)

HPTN 052: HIV-1 Transmission



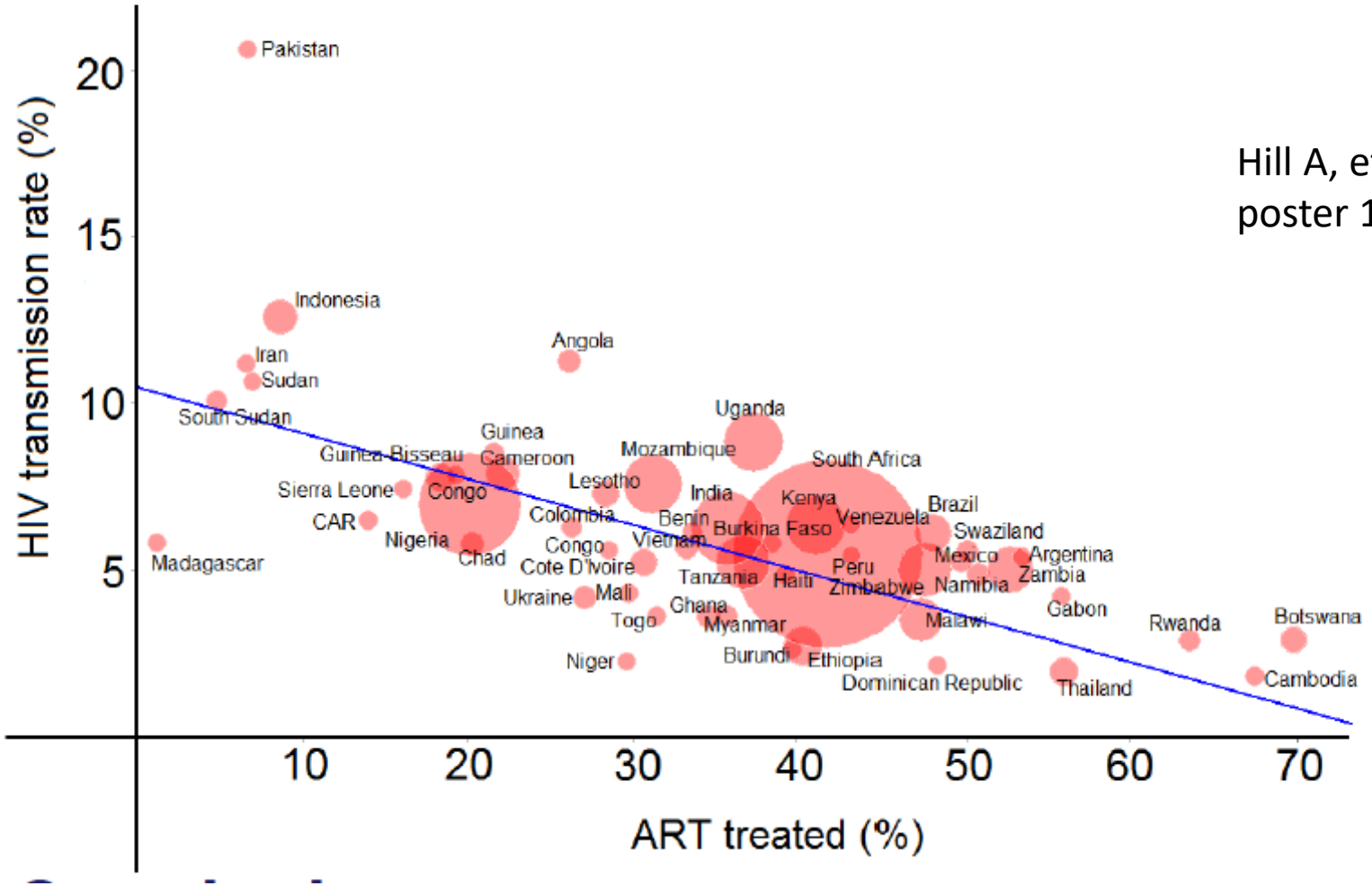
Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996–2009



Montaner JSG, et al. Lancet, 2010

Effects of ARV scale up on HIV transmission in 53 low and middle income countries

Figure 2: HIV transmission rate (new infections in 2013 / total HIV-infected people) versus ART coverage in 53 countries, weighted by epidemic size.



Hill A, et al.
poster 1118

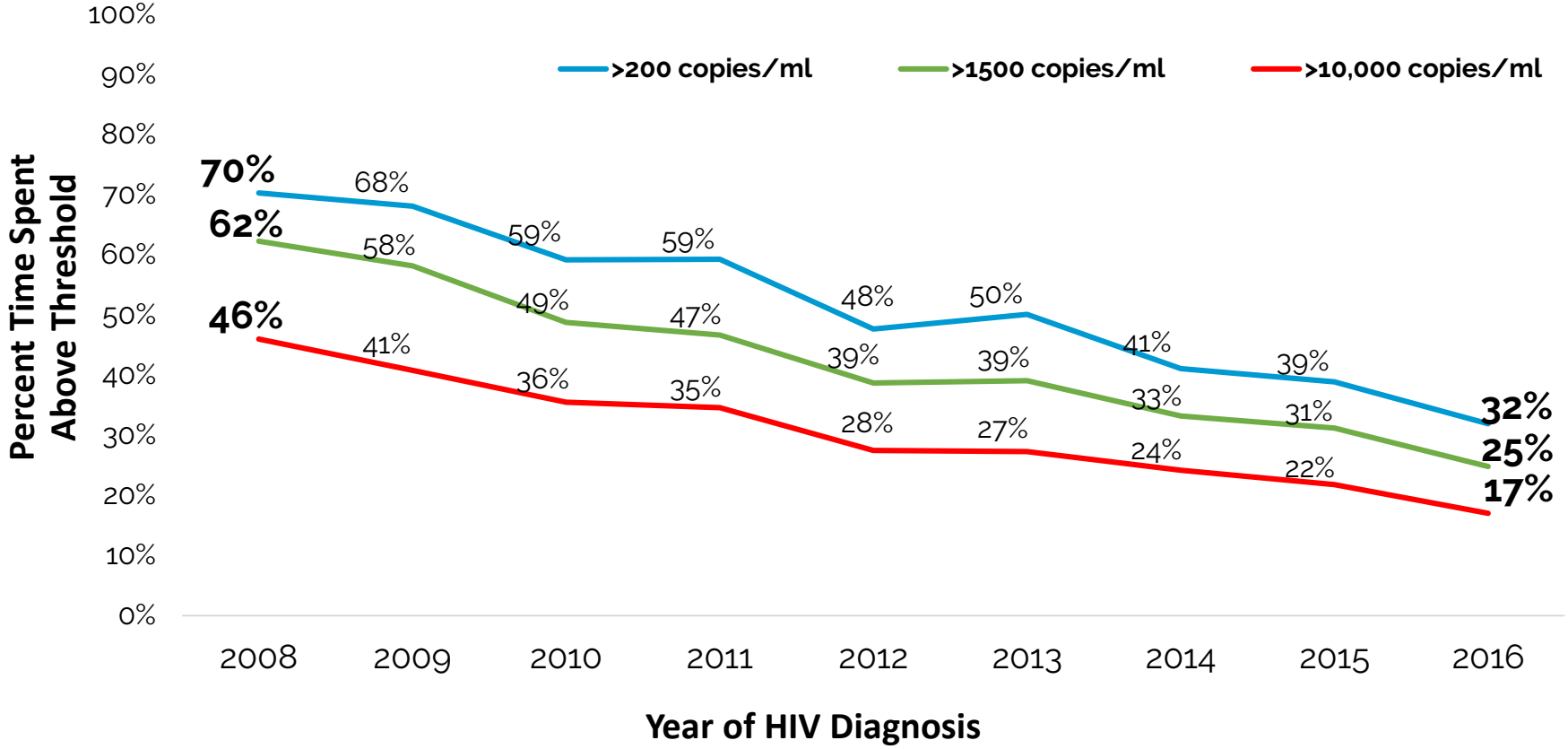
ART initiation policies in European countries

2014 (n=49), 2016 (n=47)

Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.

Rapid Initiation of Treatment (San Francisco, CA USA)

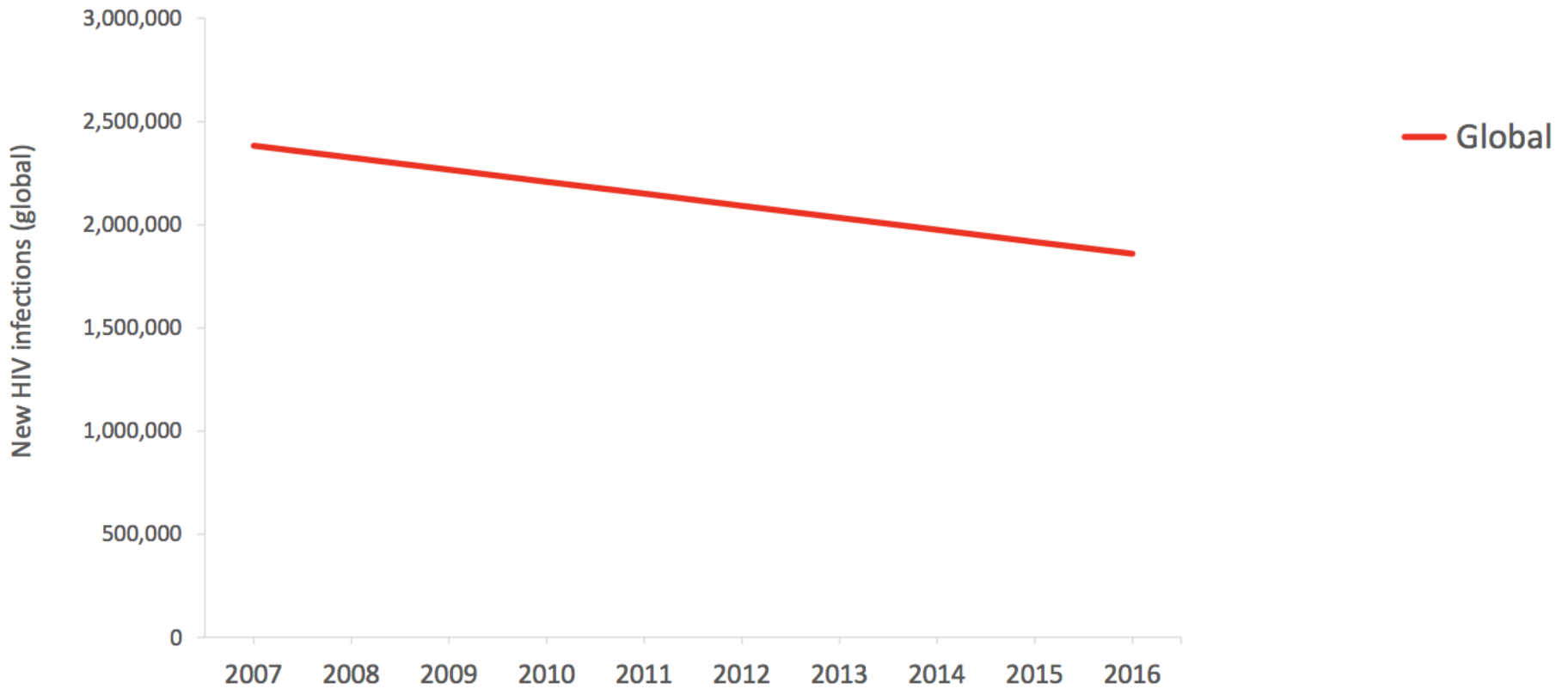
Trends in Percent Time Spent Viremic among Persons Newly Diagnosed with HIV



Time spent above each viremic level decreased significantly among newly diagnosed persons from 2008 to 2016 and likely contributed to the decreased HIV incidence observed

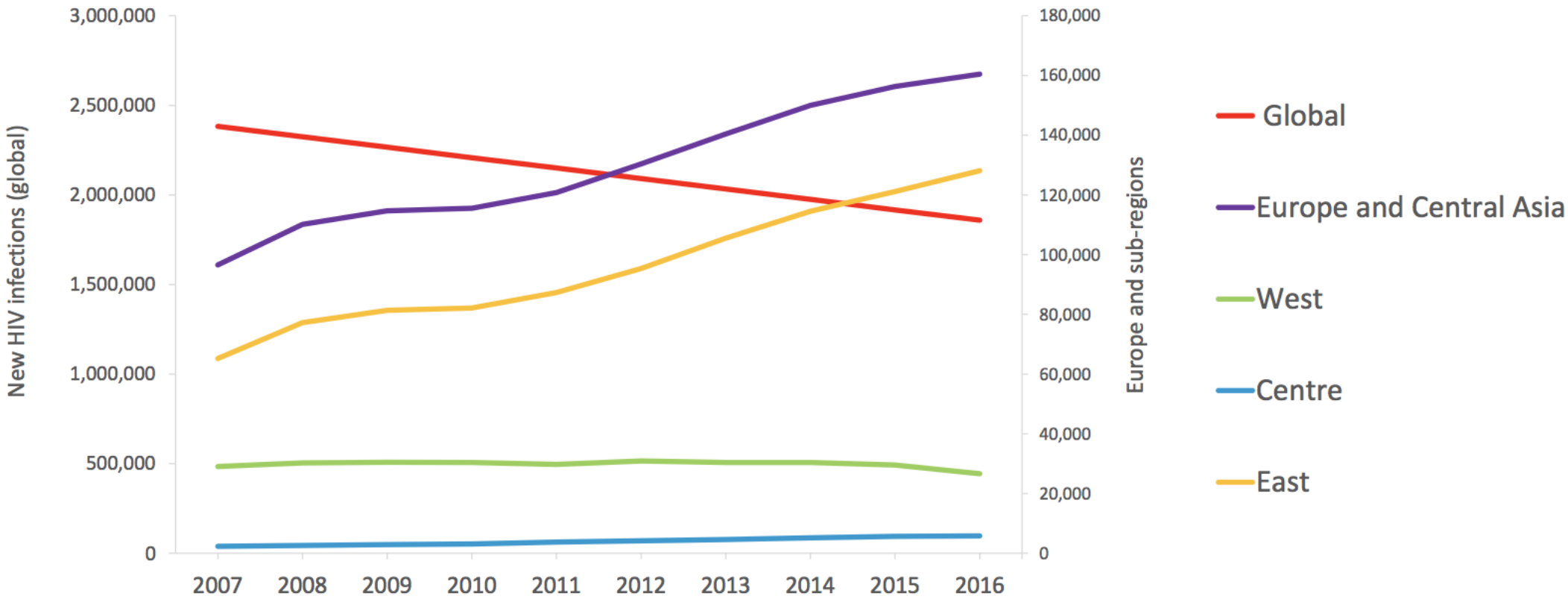
Hughes A. et al. AIDS 2018. Amsterdam, NL. Poster TUAC0104

Estimated new HIV infections are decreasing globally



Source: UNAIDS 2018, ECDC/WHO, HIV Surveillance in Europe 2017, 2016 data

Estimated new HIV infections are decreasing globally but increasing in the European region



Source: UNAIDS 2018, ECDC/WHO, HIV Surveillance in Europe 2017, 2016 data

RAPIT trial

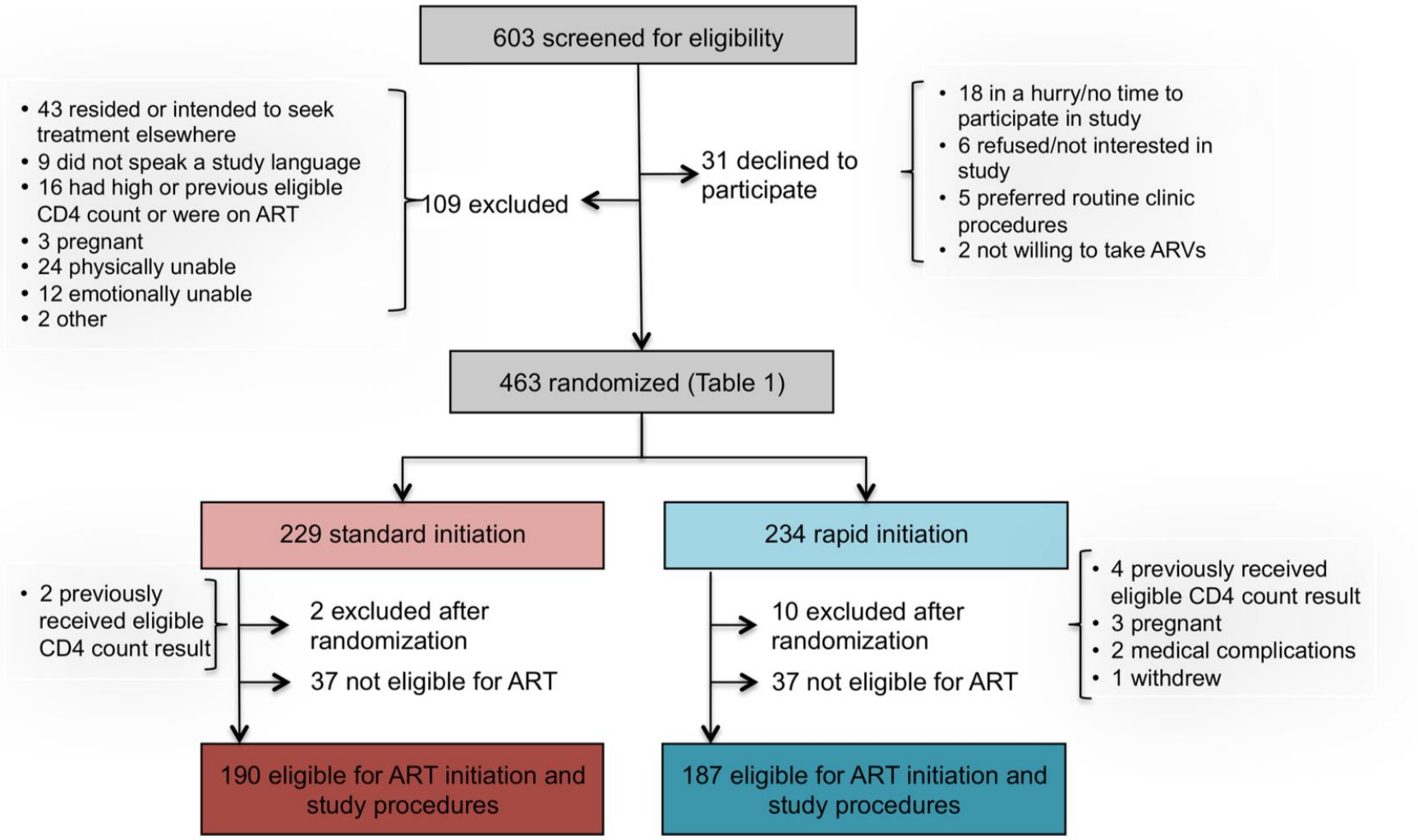


Fig 2. Study enrollment and randomization.

PLOS Medicine | DOI:10.1371/journal.pmed.1002015 May 10, 2016

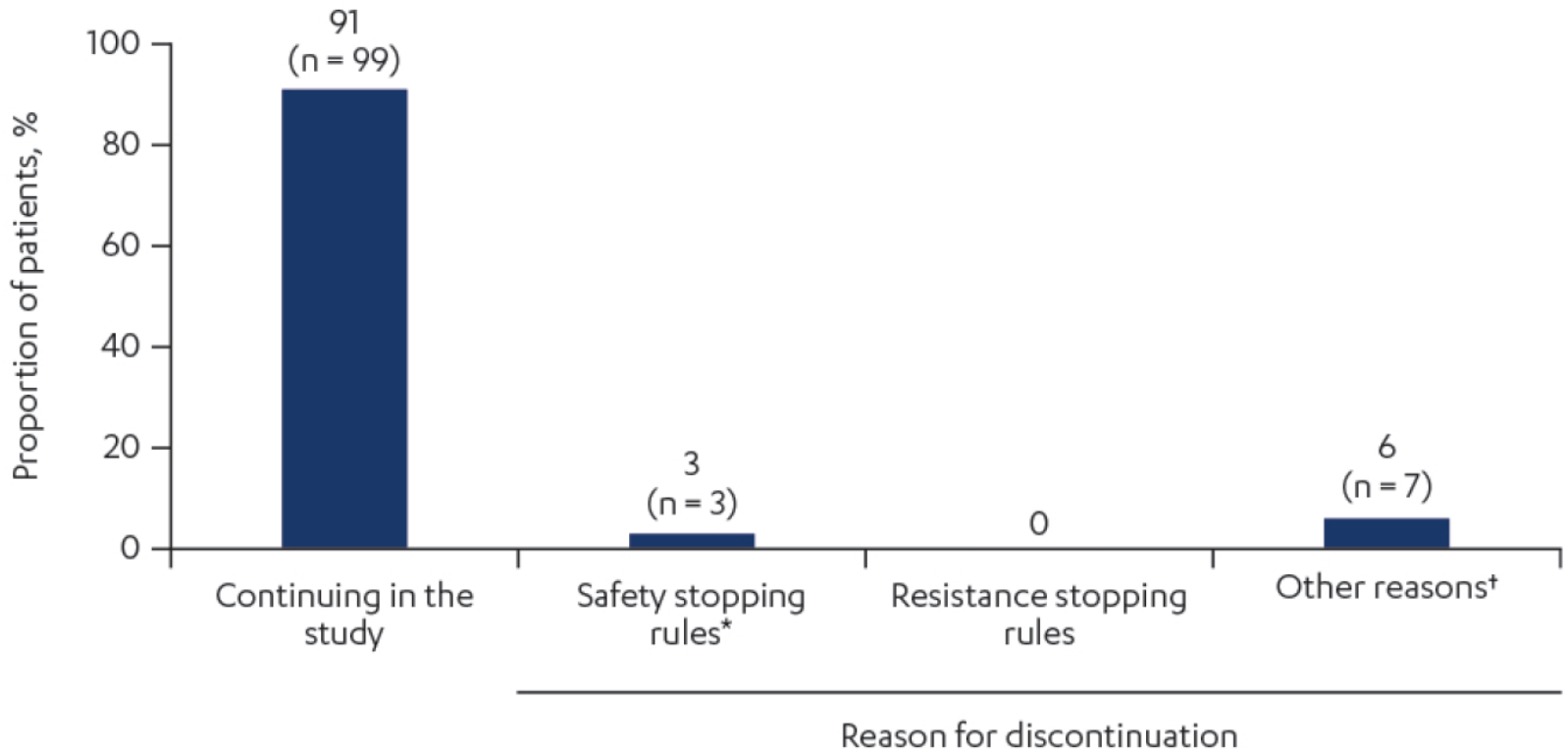
Table 2. ART initiation, 10-mo retention in care, and 10-mo viral suppression.

Outcome	Standard arm(%) *n* = 190	Rapid arm(%) *n* = 187	Crude risk difference (95% CI)	Crude relative risk (95% CI)
Initiated ≤ 90 d and suppressed by 10 mo (primary outcome)	96 (51%)	119 (64%)	13% (3%–23%)	1.26 (1.05–1.50)
Of those not initiated ≤ 90 d and suppressed by 10 mo	*94 (49%)*	*68 (36%)*		
Not initiated	*54 (28%)*	*5 (3%)*		
Initiated but not suppressed	*40 (21%)*	*63 (34%)*		
Of those initiated but not suppressed:				
Retained, unsuppressed viral load test reported	*11 (6%)*	*17 (9%)*		
Retained, no viral load test reported	*14 (7%)*	*16 (9%)*		
Transferred to another clinic	*1 (1%)*	*6 (3%)*		
Died	*3 (2%)*	*0 (0%)*		
Lost to follow-up	*11 (6%)*	*24 (13%)*		
Initiated ≤ 90 d	136 (72%)	182 (97%)	25% (19%–33%)	1.36 (1.24–1.49)
Initiated ≤ 90 d and retained at 10 mo (secondary outcome)	121 (64%)	151 (81%)	17% (5%–23%)	1.27 (1.12–1.44)
Of those not initiated ≤ 90 d and retained at 10 mo:	*69 (36%)*	*36 (19%)*		
Initiated but not retained	*15 (8%)*	*31 (17%)*		
Not initiated	*54 (28%)*	*5 (3%)*		

doi:10.1371/journal.pmed.1002015.t002

DIAMOND Results

- At the time of the Week 24 interim analysis, 99 (91%) patients remained on D/C/F/TAF and 10 (9%) patients had discontinued (**Figure 3**)
  - Three (3%) patients discontinued due to protocol-defined safety stopping rules
  - No patients discontinued due to resistance stopping rules
  - Seven (6%) patients discontinued for other reasons

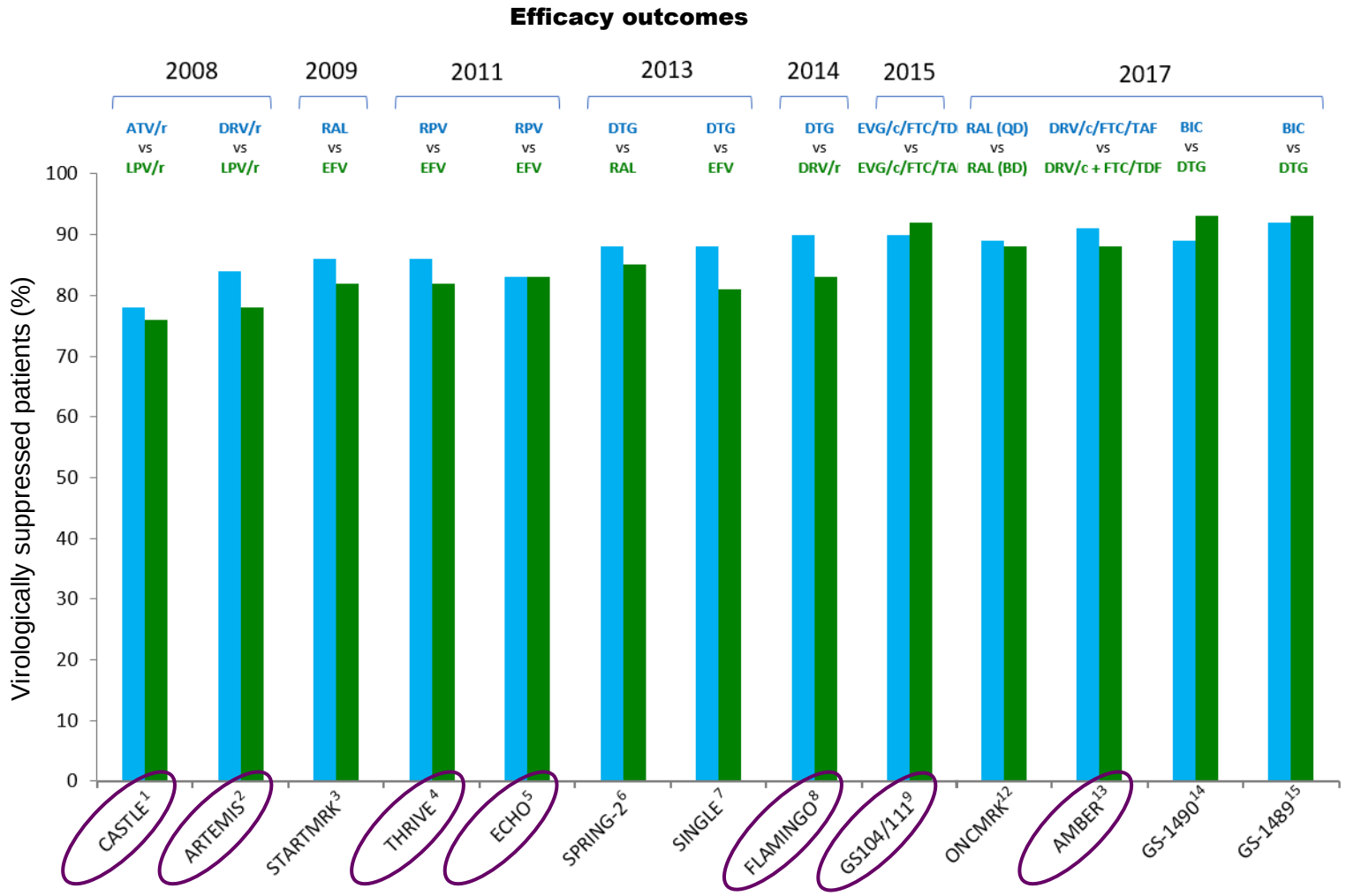


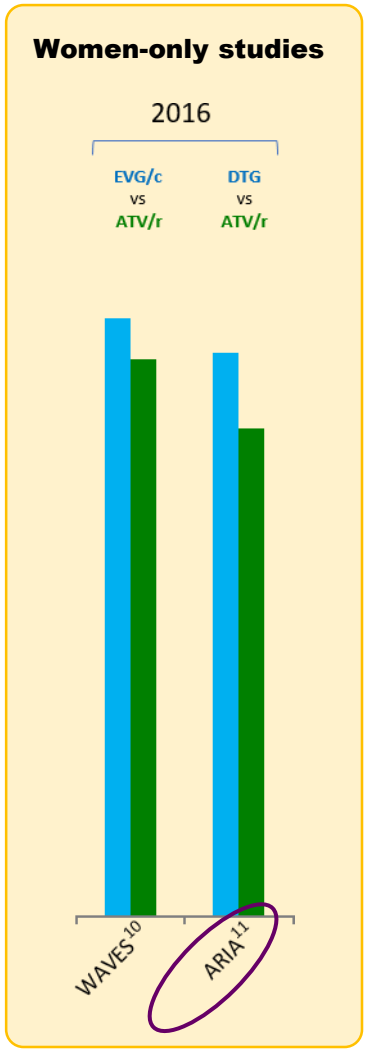
*Five patients met safety stopping rules criteria, all with confirmed elevations in AST or ALT ≥2.5 times the ULN at the screening/baseline visit. Three of these patients discontinued according to the protocol and 2 remained in the study based on clinical assessment by the investigator and agreement of the sponsor. Transaminases appeared to normalize after screening/baseline in all 5 patients, suggesting that treatment may have been beneficial for these patients.

†Other reasons were: lost to follow-up (n = 3), withdrawal of consent (n = 2), protocol violation (n = 1), and AE (n = 1 [allergic dermatitis]).

Glasgow 2018

Lower efficacy in VL >100,000 c/mL subgroup





ATV, atazanavir; BD, twice daily; BIC, bictegravir; c, cobicistat; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; LPV, lopinavir; QD, once daily; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate.

1. Molina JM, *et al. Lancet* 2008;372:646–55; 2. Ortiz R, *et al. AIDS* 2008;22:1389–97; 3. Lennox JL, *et al. Lancet* 2009;374:796–806; 4. Cohen CJ, *et al. Lancet* 2011;378:229–37;
5. Molina JM, *et al. Lancet* 2011;378:238–46; 6. Raffi F, *et al. Lancet* 2013;381:735–43; 7. Walmsley SL, *et al. N Engl J Med* 2013;369:1807–18;
8. Clotet B, *et al. Lancet* 2014;383:2222–31; 9. Sax PE, *et al. Lancet* 2015;385:2606–15; 10. Squires K, *et al. Lancet HIV* 2016;3:e410–20;
11. Orrell C, *et al. Lancet HIV* 2017;4:e536–46; 12. Cahn P, *et al. Lancet* HIV 2017;4:e486–94; 13. TBA; 14. Sax PE, *et al. Lancet* 2017;390:2073–82;
15. Gallant J, *et al. Lancet* 2017;390:2063–72.

What to Start 2018

Regimens recommended/preferred in at least one guideline

Regimen	DHHS 2018	IAS-USA 2018	EACS 2017	BHIVA 2016	SIMIT 2017	GESIDA 2018	ANRS-CNS 2017
RPV/TFV*/FTC	Alternative#	Alternative	Recommended§	Preferred§	Recommended#	Alternative*	Recommended§
DRV/r + TFV*/FTC	Alternative**	Alternative	Recommended	Preferred	Recommended**	Alternative	Recommended
DRV/c + TFV*/FTC	Alternative**	Alternative	Recommended		Recommended**	Alternative	
RAL + TFV*/FTC	Recommended	Alternative	Recommended	Preferred	Recommended	Preferred	Recommended
EVG/COBI/TDF/FTC	Recommended	Alternative	Recommended	Preferred	Recommended	Alternative	
EVG/COBI/TAF/FTC	Recommended	Alternative	Recommended	Preferred	Recommended	Preferred	Recommended
DTG + TFV*/FTC	Recommended	Recommended	Recommended	Preferred	Recommended	Preferred	Recommended
DTG + ABC/3TC	Recommended	Recommended	Recommended	Preferred	Recommended	Preferred	Recommended
BIC/TAF/FTC	Recommended	Recommended					

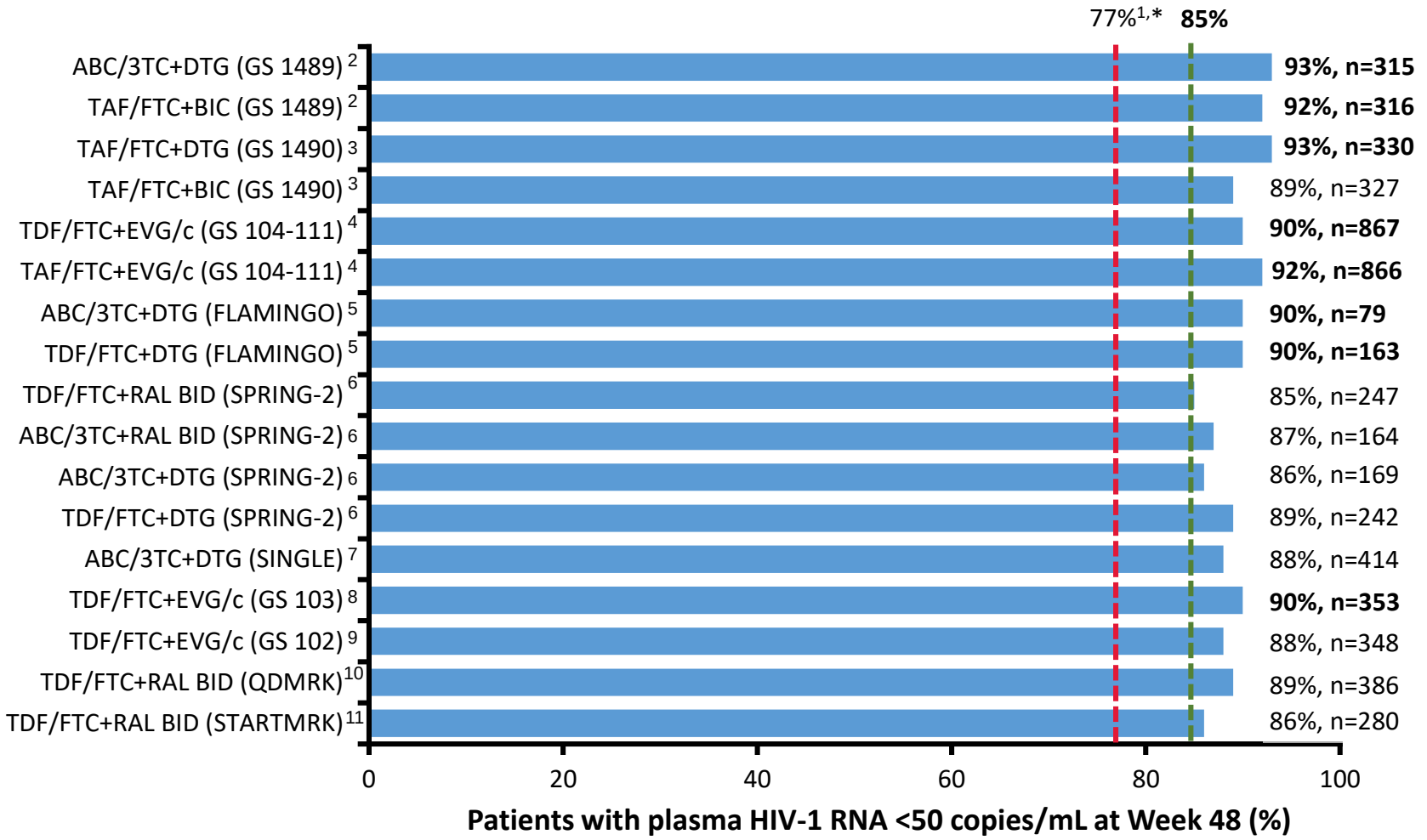
** Tenofovir (TFV) in all but two documents was recommended not differently as TDF (tenofovir disoproxil fumarate) or TAF (tenofovir alafenamide) ; in IAS-USA 2018 only TAF was recommended; in ANRS-CNS 2017, only TDF was recommended;*

§ RPV-containing regimens, recommended/preferred only if HIV-RNA <100.000 c/mL;

 # RPV-containing regimens, recommended/preferred only if HIV-RNA <100.000 c/mL and CD4 >200 cell/mm3;

*** Regimen recommended only for specific conditions*

With the introduction of the INSTIs, the 48-week efficacy of first-line treatment has risen to >85%



*Mean 48-week efficacy among 82 treatment groups from ARV studies of all core-agent classes initiated ≥2005 (N=16,795) and reported through 2012.

1. Lee FJ, et al. PLoS One 2014;9:e97482; 2. Gallant J, et al. Lancet 2017;390:2063-72; Sax PE et al. Lancet 2917;390:2073-82; 4. Sax PE, et al. Lancet 2015;385:2606-15; 5. Clotet B, et al. Lancet 2014;383:2222-31; 6. Raffi F, et al. Lancet 2013;381:735-43; 7. Walmsley SL, et al. NEJM 2013;369:1807-18; 8. DeJesus E, et al. Lancet 2012;379:2429-38; 9. Sax PE, et al. Lancet 2012;379:2439-48; 10. Eron JJ Jr, et al. Lancet Infect Dis 2011;11:907-15; 11. Lennox JL, et al. Lancet 2009;374:796-806.

A substantial proportion of people on ART will not have viral rebound over their lifetime

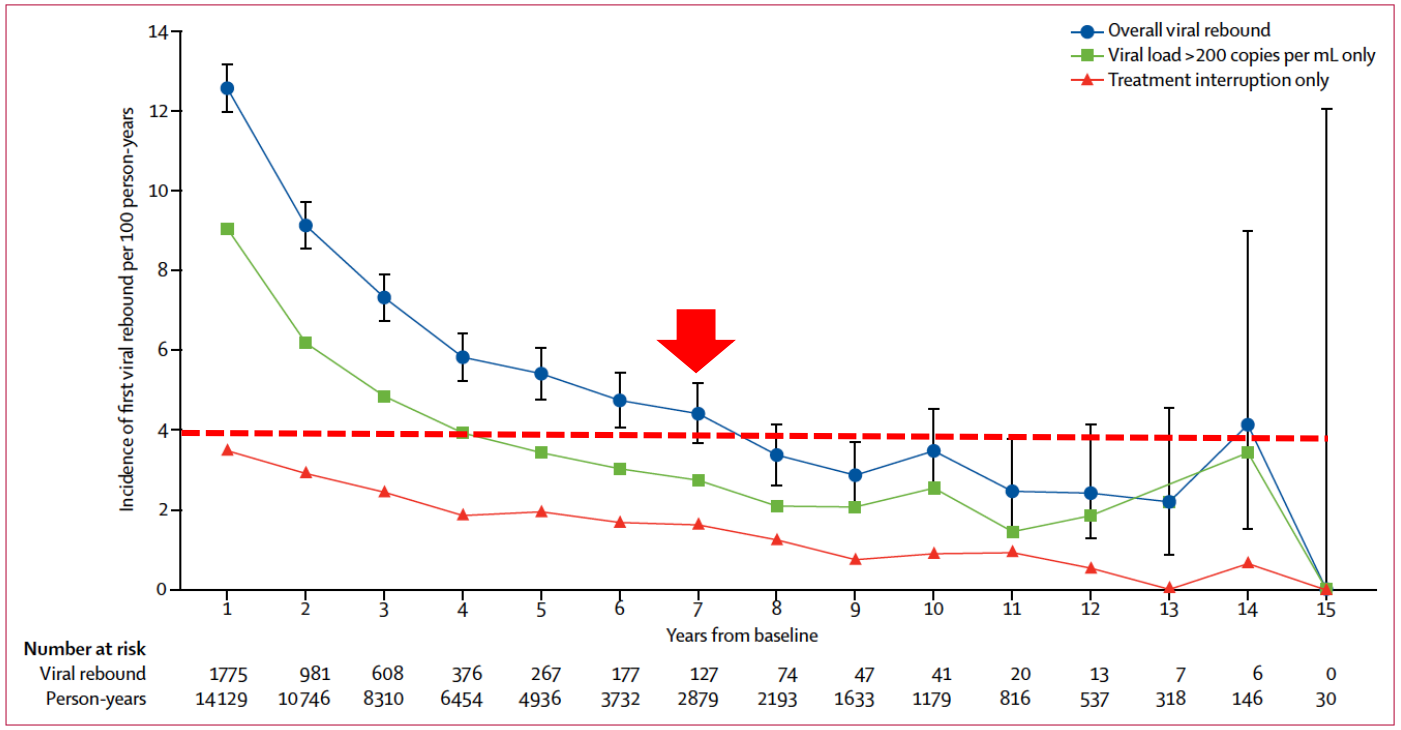


Figure: **Incidence of first viral rebound by time since study baseline (9 months after start of ART)**
Error bars show 95% CI.

Of the 16,101 people included, 4,519 had a first viral rebound over 58,038 person-years (**7·8 per 100 person-years, 95% CI 7·6–8·0**).

The rate of first viral rebound declined substantially over time until 7 years from baseline.

O'Connor J, et al. Lancet HIV 2017; 4: e295–302.

Conclusions

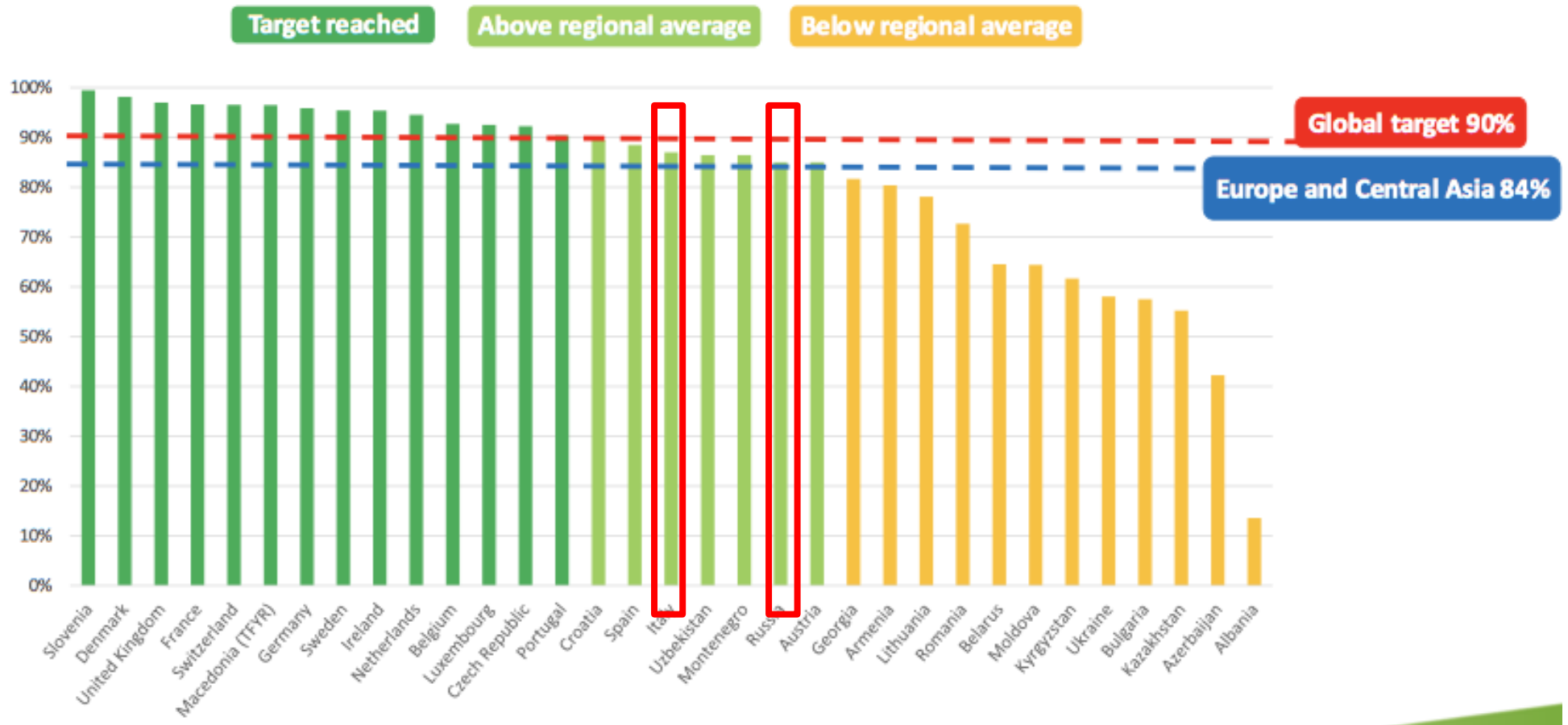
What really changed the epidemic in Europe was starting treatment in all patients independently from CD4 count.

If we want to start treatment on the same day of diagnosis in order to increase adherence we should use drug with high genetic barrier.

Actually, once patients reach viral suppression very rarely they loose it, thus it should be really a story of a great success.

Progress toward achieving the 3rd 90

90% of those on ART virally suppressed (n=33)



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