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BREAKING BARRIERS • BUILDING BRIDGES

Addressing the second 90: How can treatment scale-up across the European region be accelerated?

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Addressing the second 90: How can treatment scale-up across the European region be accelerated?

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Disclosure

Relations that could be relevant for the meeting	Company
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I do **not** receive personal funding from any of the companies	

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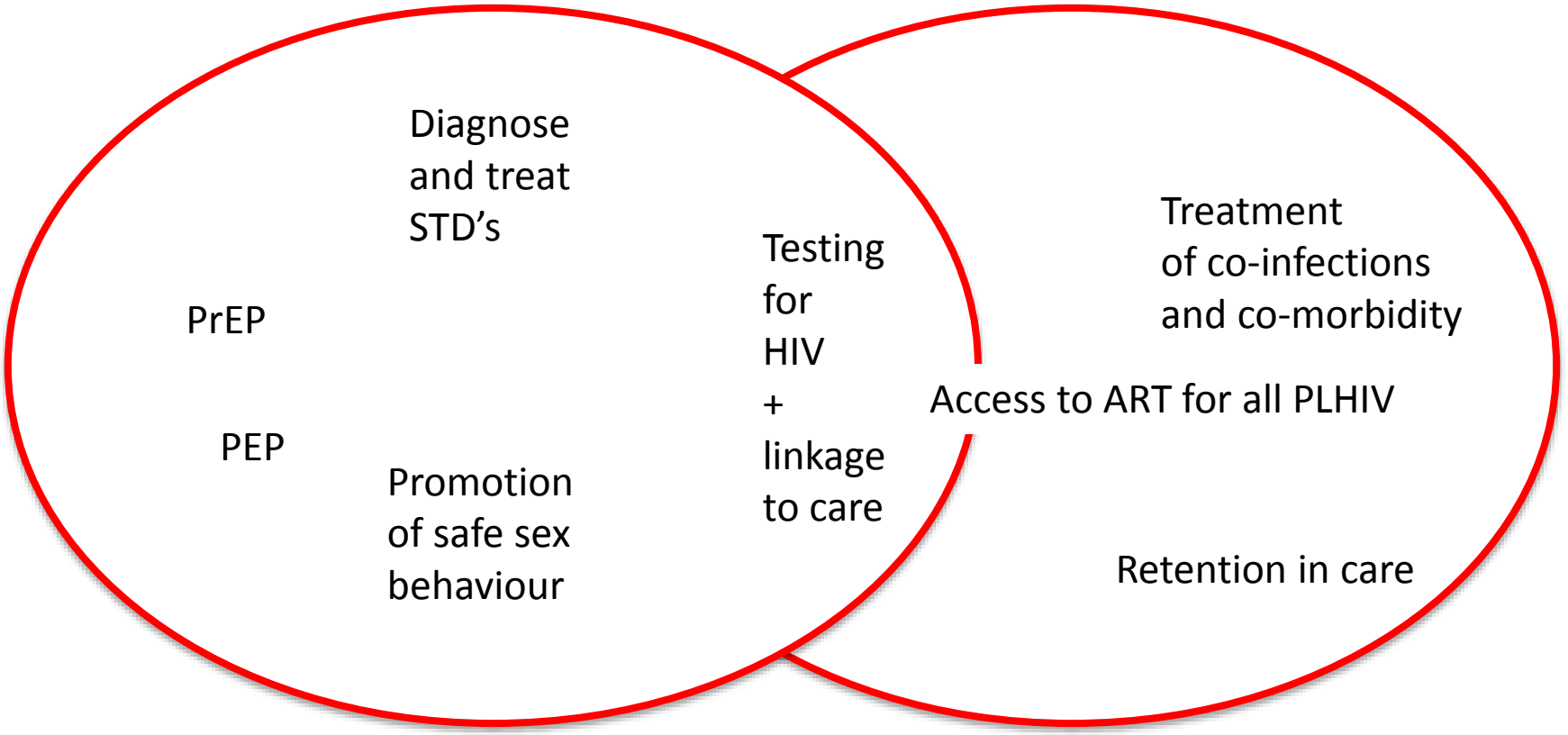
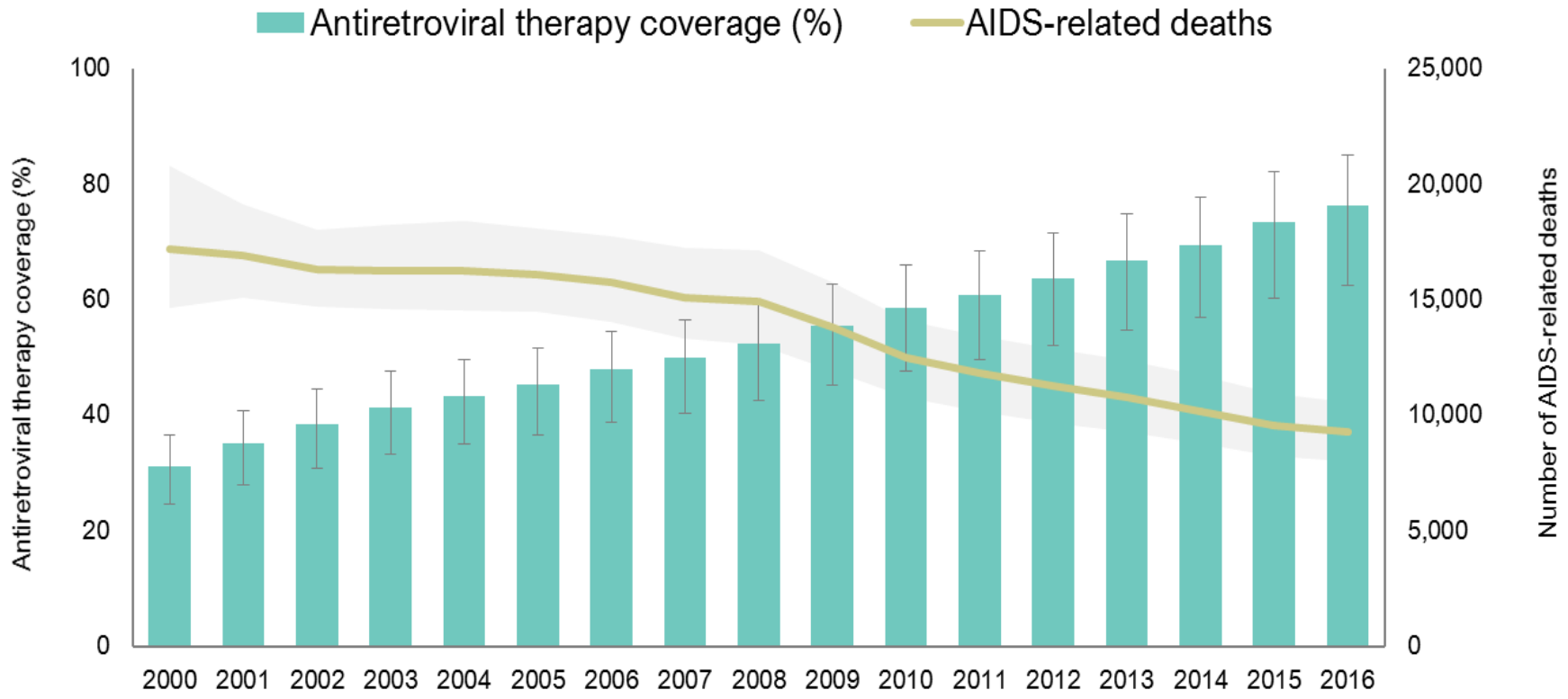
HIV control



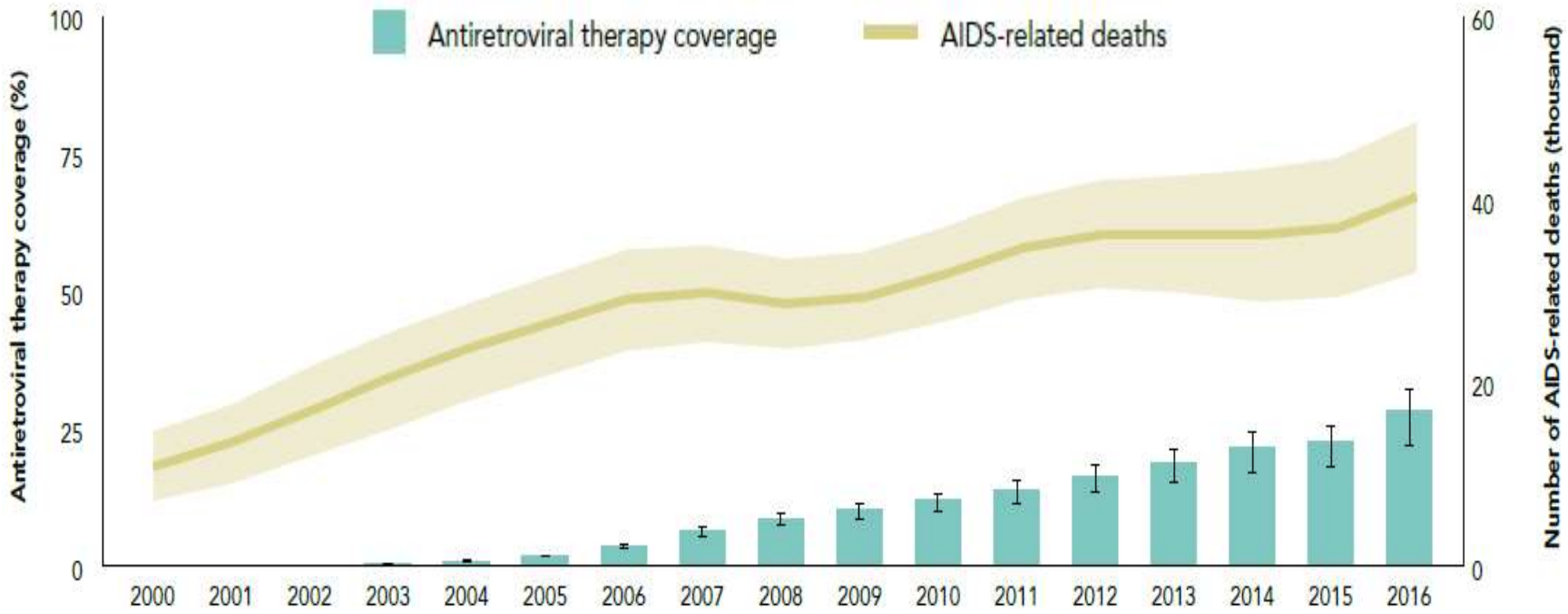
Limit transmission Improve health for PLHIV

ART coverage and AIDS related deaths, Western and Central Europe, 2000-2016



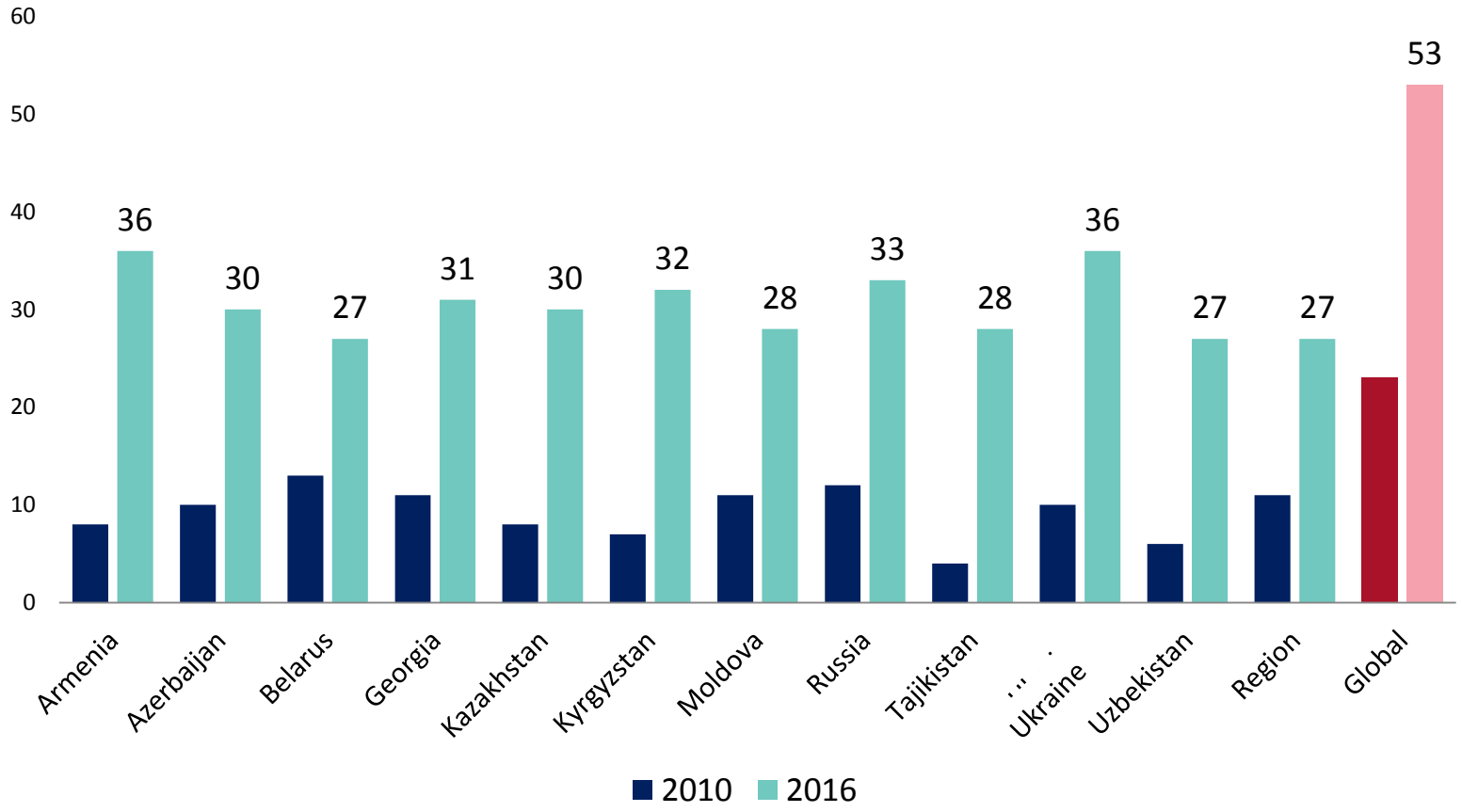
Source: UNAIDS. Global AIDS Update 2017.

ART coverage and AIDS related deaths, Eastern Europe and Central Asia 2000-2016



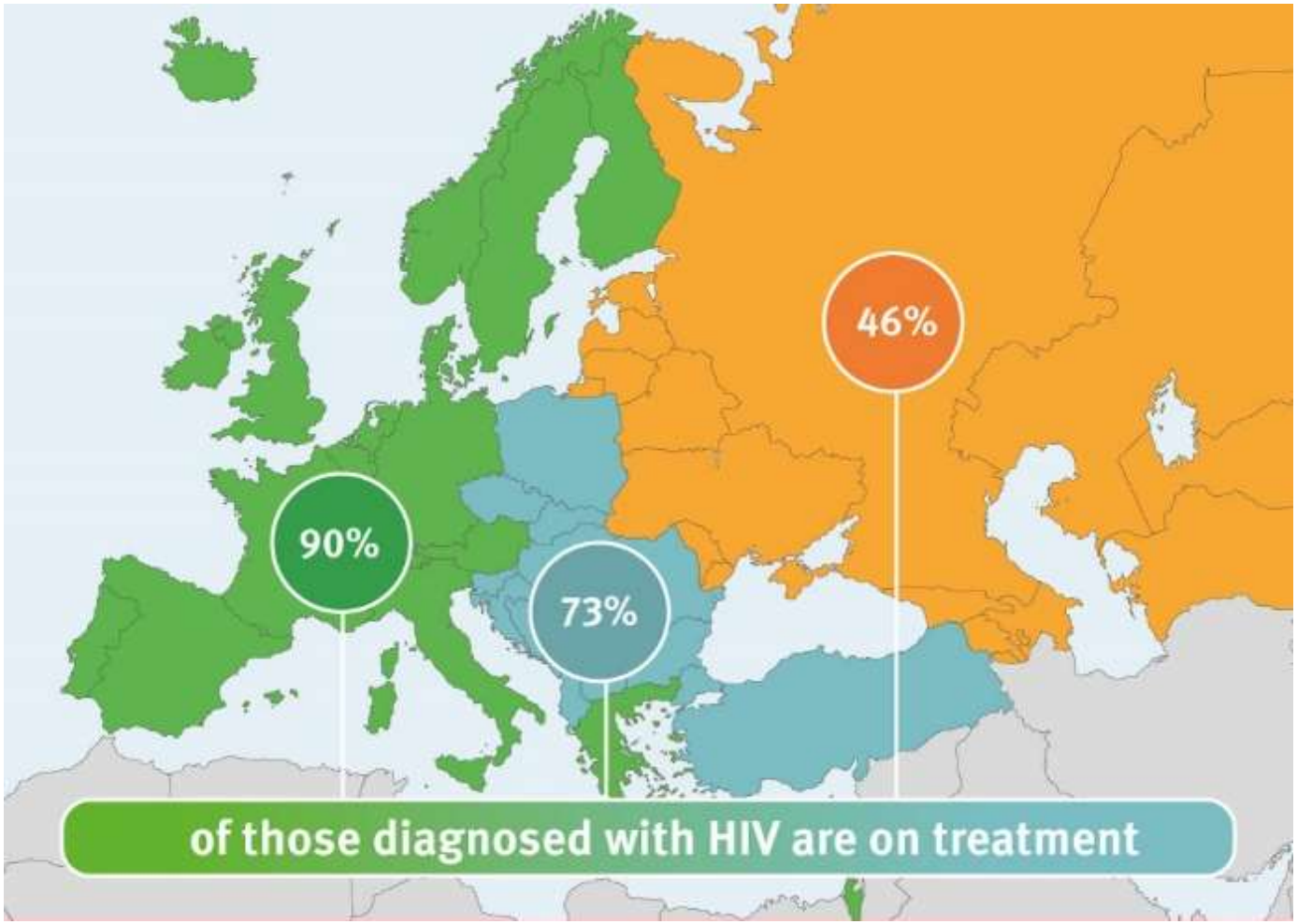
Source: UNAIDS. Global AIDS Update 2017.

HIV treatment coverage by country Eastern Europe and Central Asia, 2016



Source: UNAIDS. Global AIDS Update 2017.

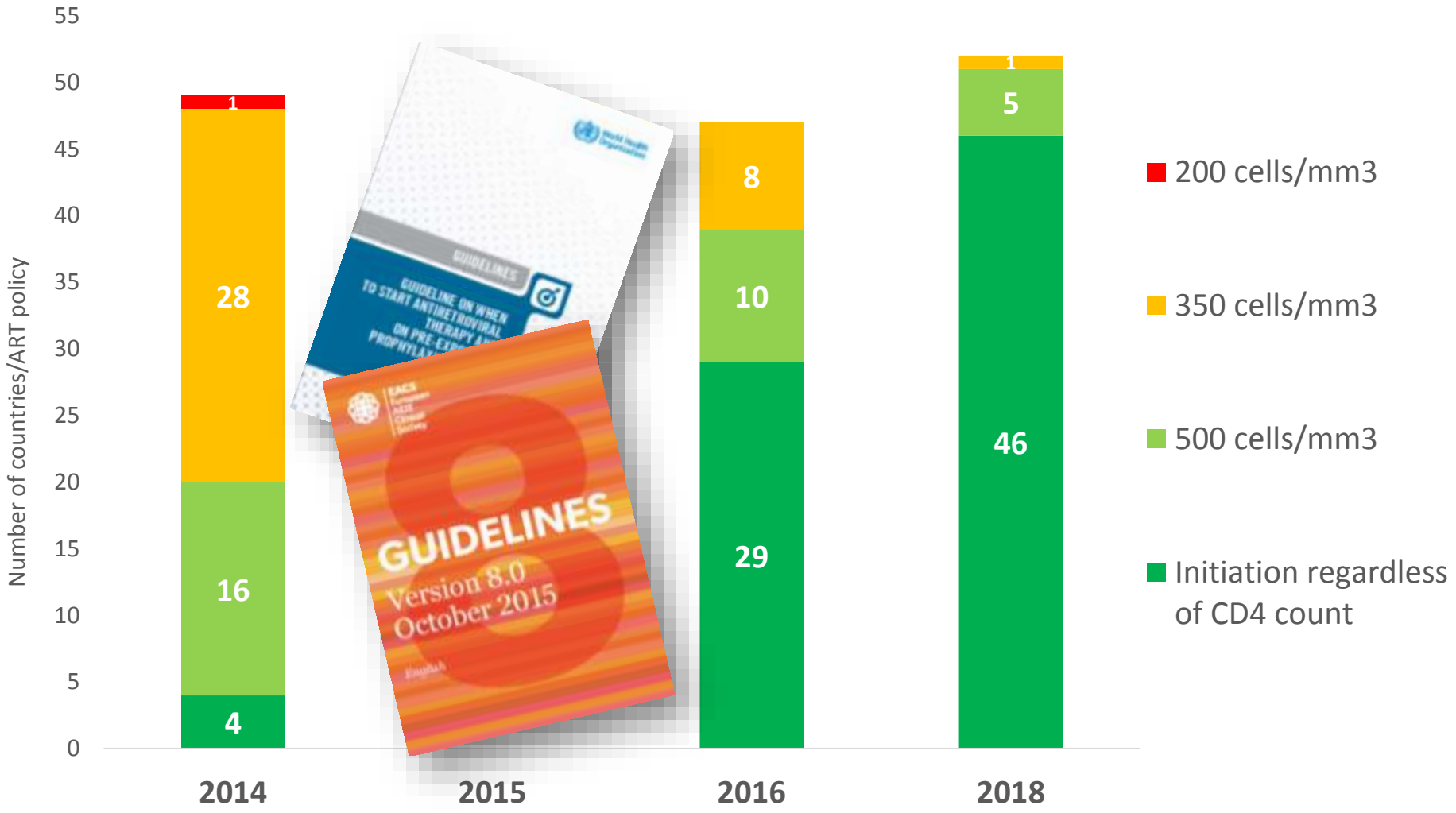
Progress toward achieving the second 90:
90% of those diagnosed on ART



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

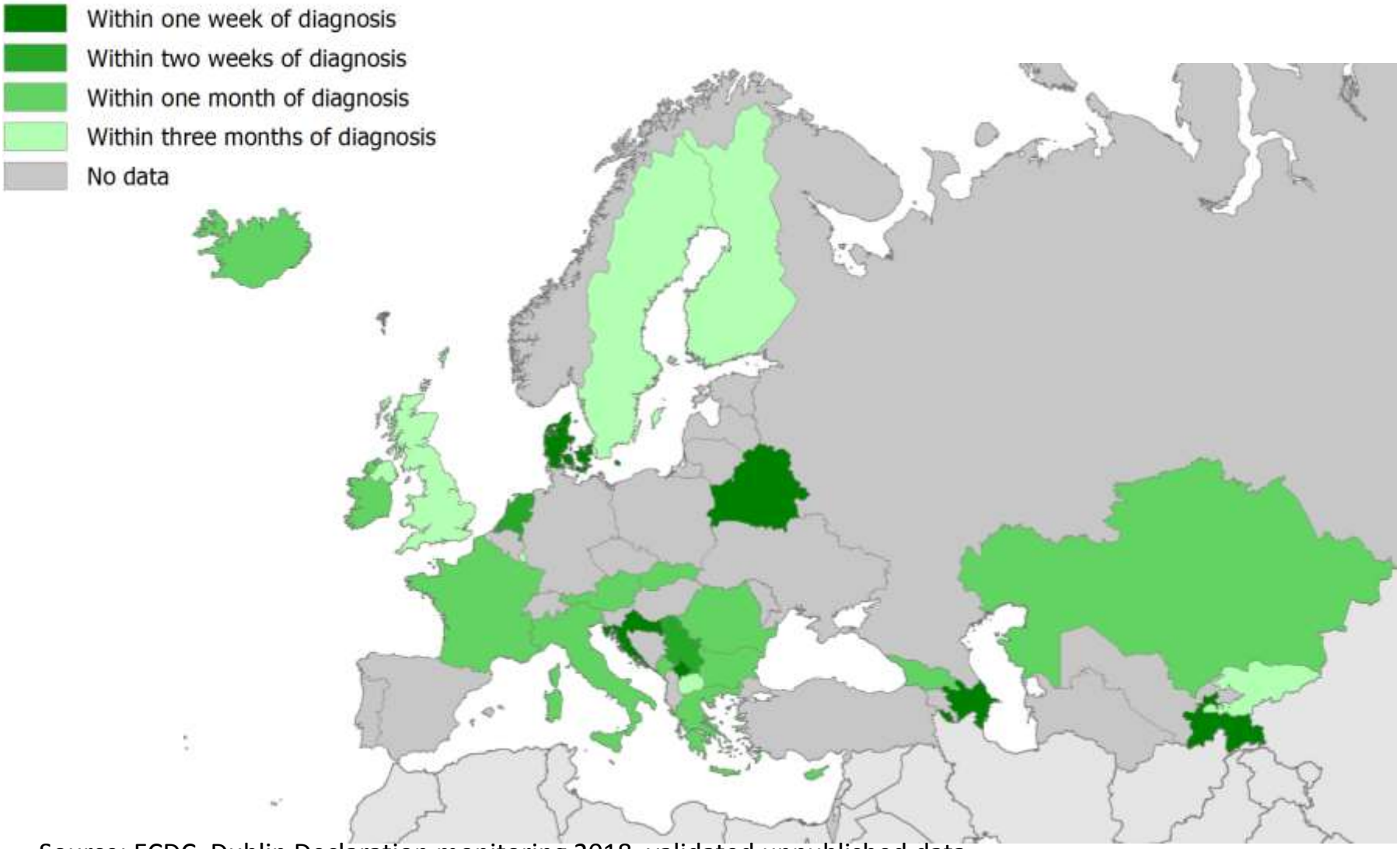
Policies on ART initiation in European countries

2014 (n=49), 2016 (n=47), 2018 (n=52)



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

What is the average length of time between a confirmed HIV diagnosis and the start of treatment?



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

PARTNER Study

(Partners of people on ART: a New Evaluation of the Risks)

Design: an observational multi-centre study of HIV serodifferent couples (MSM and HT) in which the positive partner is on ART in 75 European clinical sites:

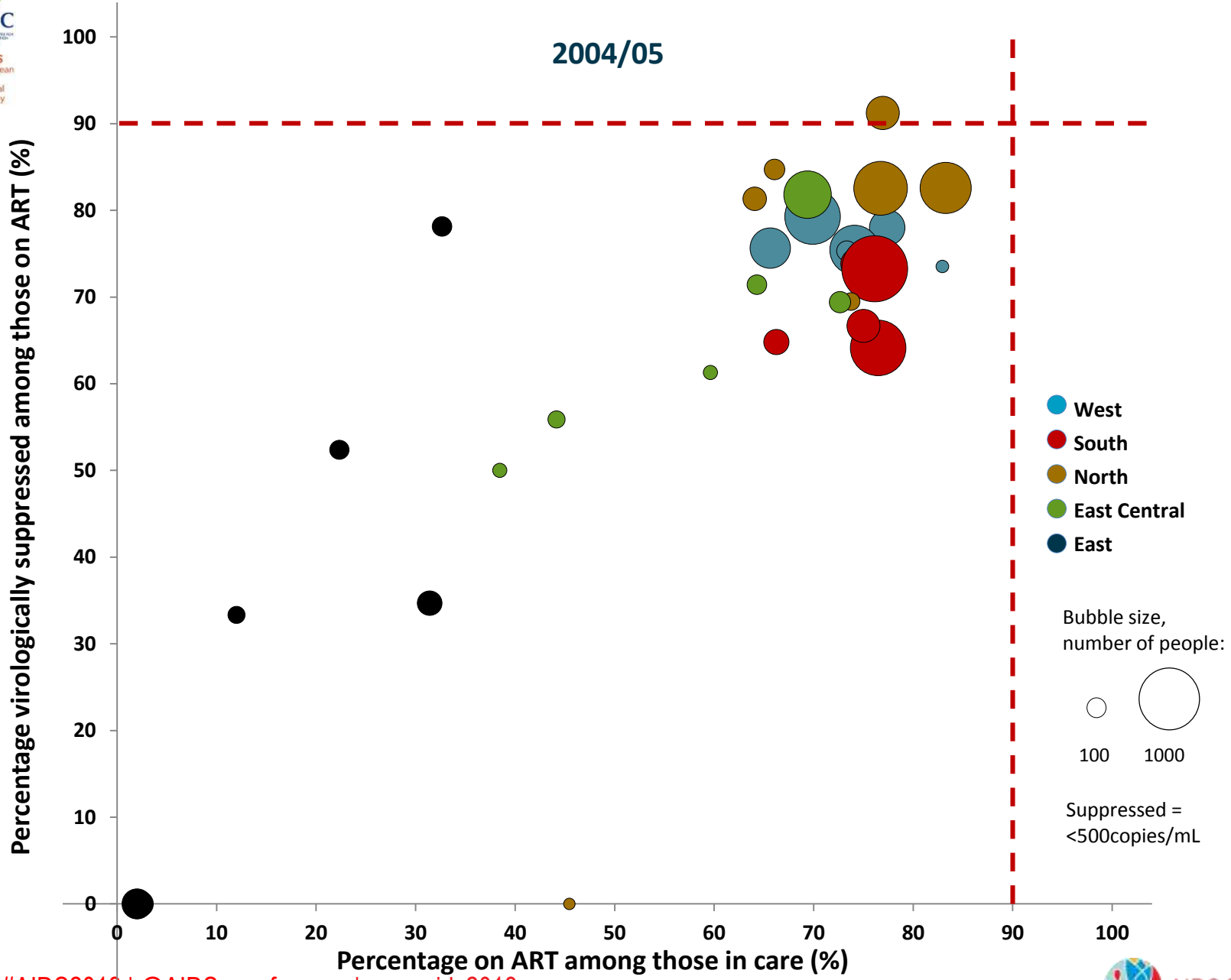
- **Phase 1:** 2011-2014 (HT+MSM)
- **Phase 2:** 2014-2018 (MSM only)

Primary Aim

- To follow serodifferent partnerships that have penetrative sex without using condoms where the HIV-positive partner is on ART with a plasma HIV-1 RNA load <200 copies/mL to study risk of HIV transmission through anal **sex** in the absence of condom use

Rodger et al, #AIDS2018 (late breaker)

Country-specific estimates of people on ART and virologically suppressed



EuroSIDA: Laut et al, Eurosurveillance 2018

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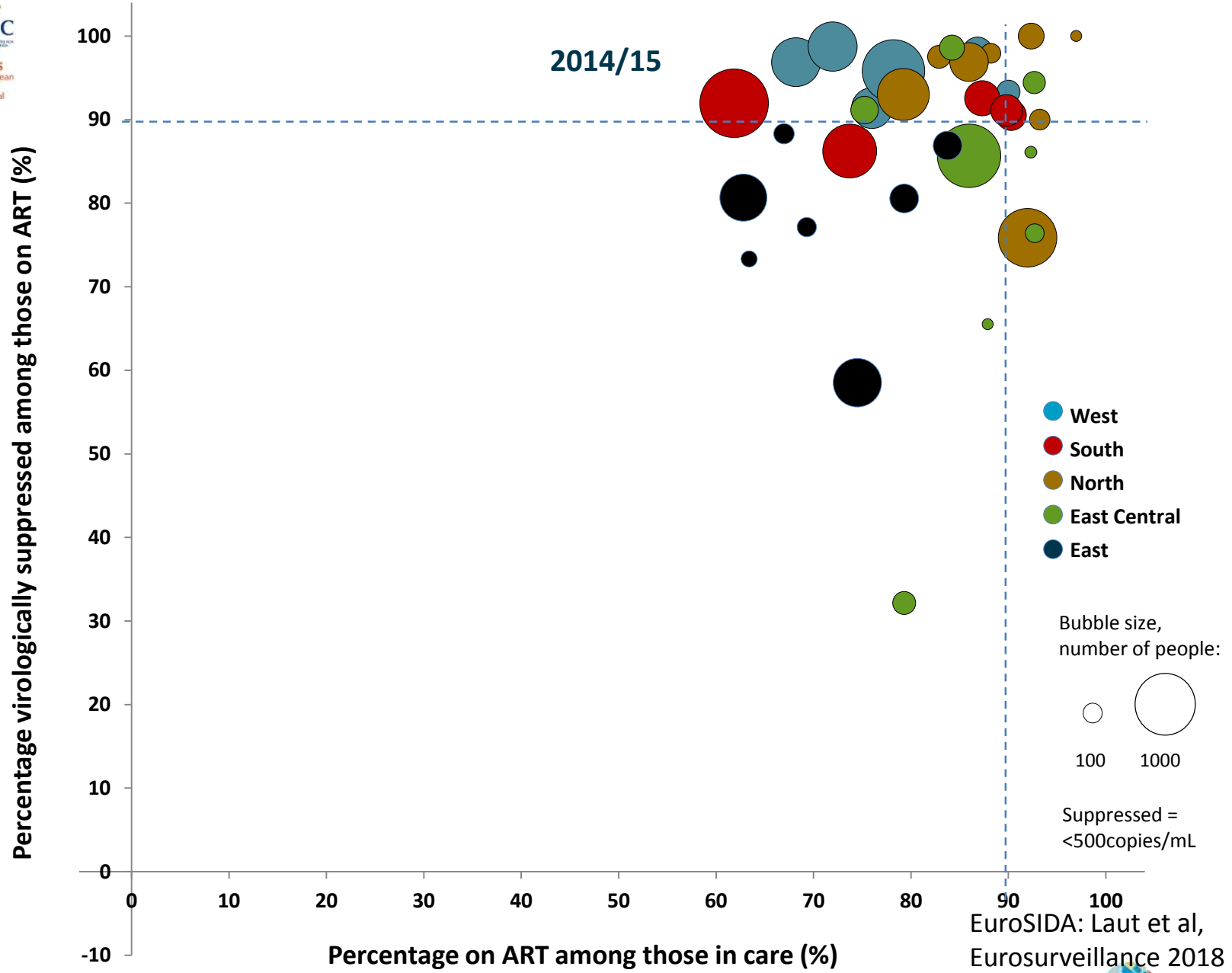


EuroSIDA: Laut et al, Eurosurveillance 2018

RESPOND right side CoC project

AIM: Development of an online tool to assess % on ART and % virally suppressed (right side of CoC) on clinic/cohort level

Phase 1

- Compare existing data in EuroSIDA with surveillance data from sites in **Poland, Belarus, Georgia and Serbia**
- Explore sampling techniques of entire clinic population required to provide an accurate CoC

Phase 2

- Standardised tool enabling clinics to establish CoC.
- Clinics in other countries in region to validate prospectively the tool's performance

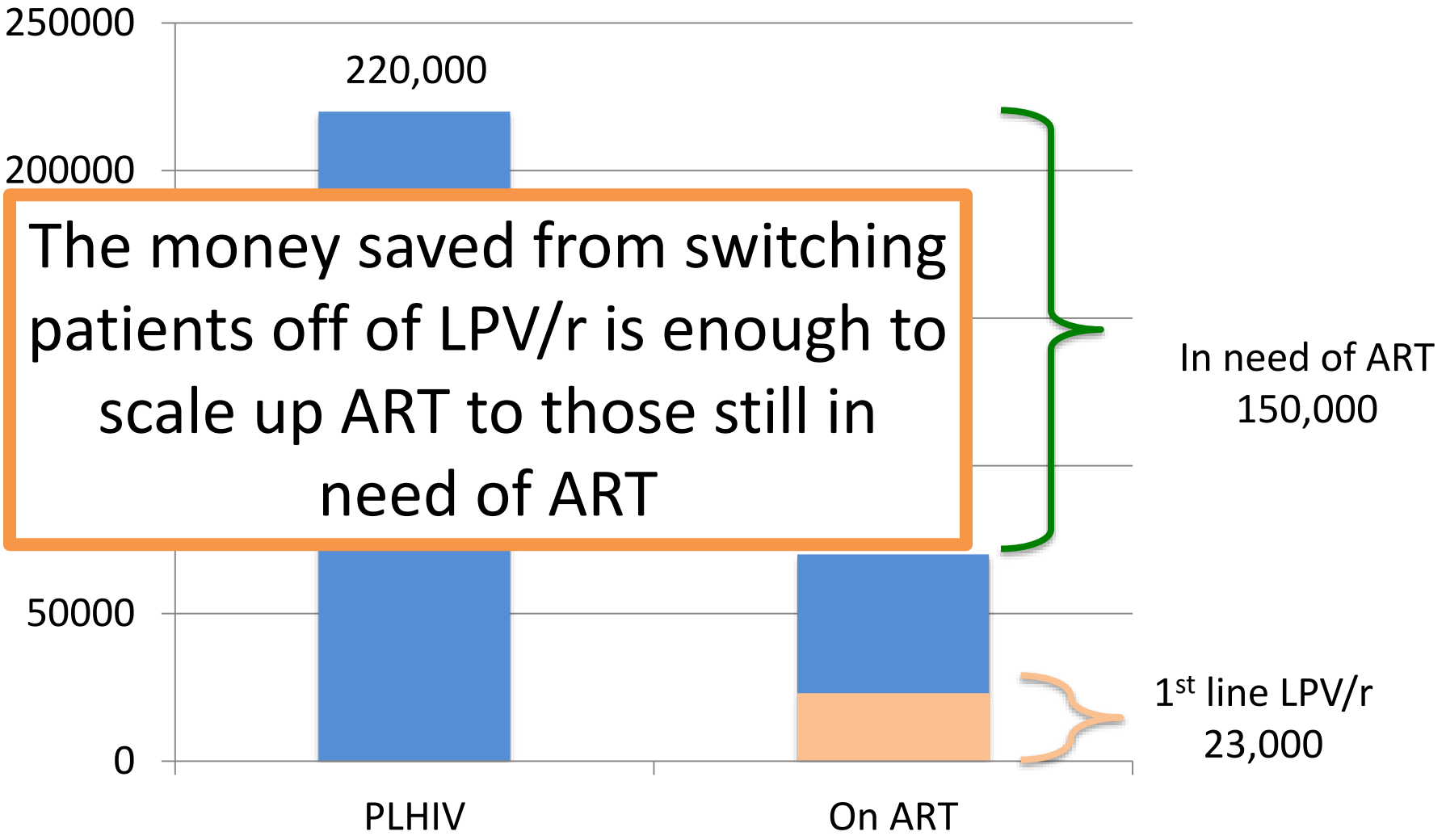
Optimization

"making the best or most effective use of a resource"

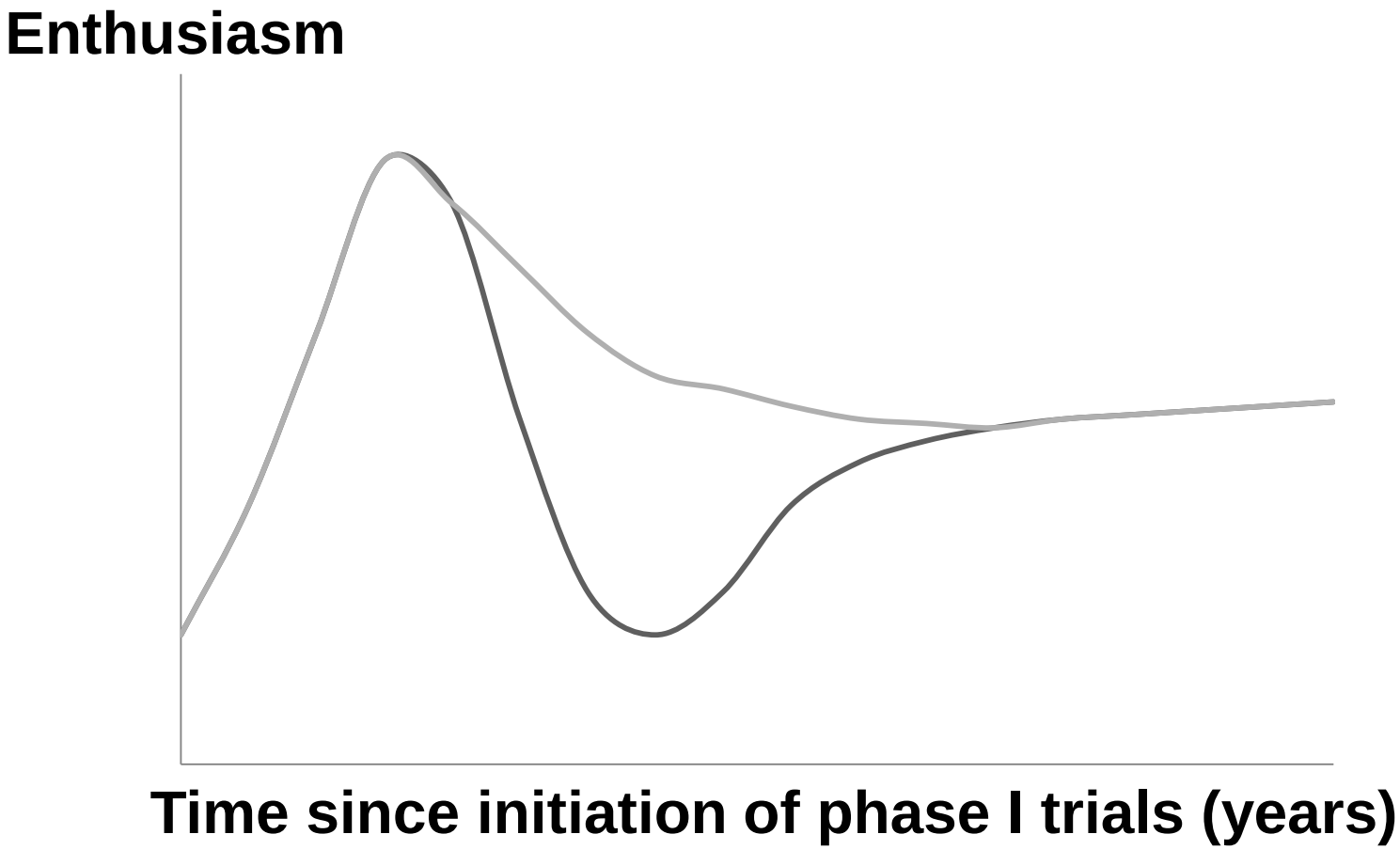
Major Areas for ARV Optimization in HIV Therapy

Major Areas for ARV Optimization	efficacy and safety	simplification	harmonization	cost
Co-formulations	↔	↑	↑ or ↔	↓
New drug class	↑	↑ or ↔	↑	↓ or ↑
Dose adjustment	↑ or ↔	↑	↑ or ↔	↓ or ↑
Drug manufacturing process	↔	↔	↔	↓
New formulations	↑ or ↔	↑	↑	↓
New strategies	↑ or ↔	↑	↔	↓

Where Should Optimization Focus ?



Enthusiasm for a treatment as a function of time since first entering clinical testing



First trimester exposure and possible teratogenicity

- Efavirenz
  - Birth defects (efv vs no efv; n=2,026):
    - [RR] 0.78, [95% CI, 0.56–1.08]
  - NTD (n=1/2,026):
    - 0.05% [95% CI, < 0.01 to 0.28]
- Dolutegravir
- NTD:
  - 0.9% (4 of 426) on DTG vs 0.1% (14 of 11,173) if on other ARV's
  - Study is ongoing – 600 additional pregnancies on DTG (Feb 2019)

Ford *et al. AIDS.* 2014;28 Suppl 2:S123-131 + announcement from EMA May 2018.

Response to dolutegravir/efavirenz based ART in persons on rimampicin-based TB treatment: interim report from INSPIRING trial

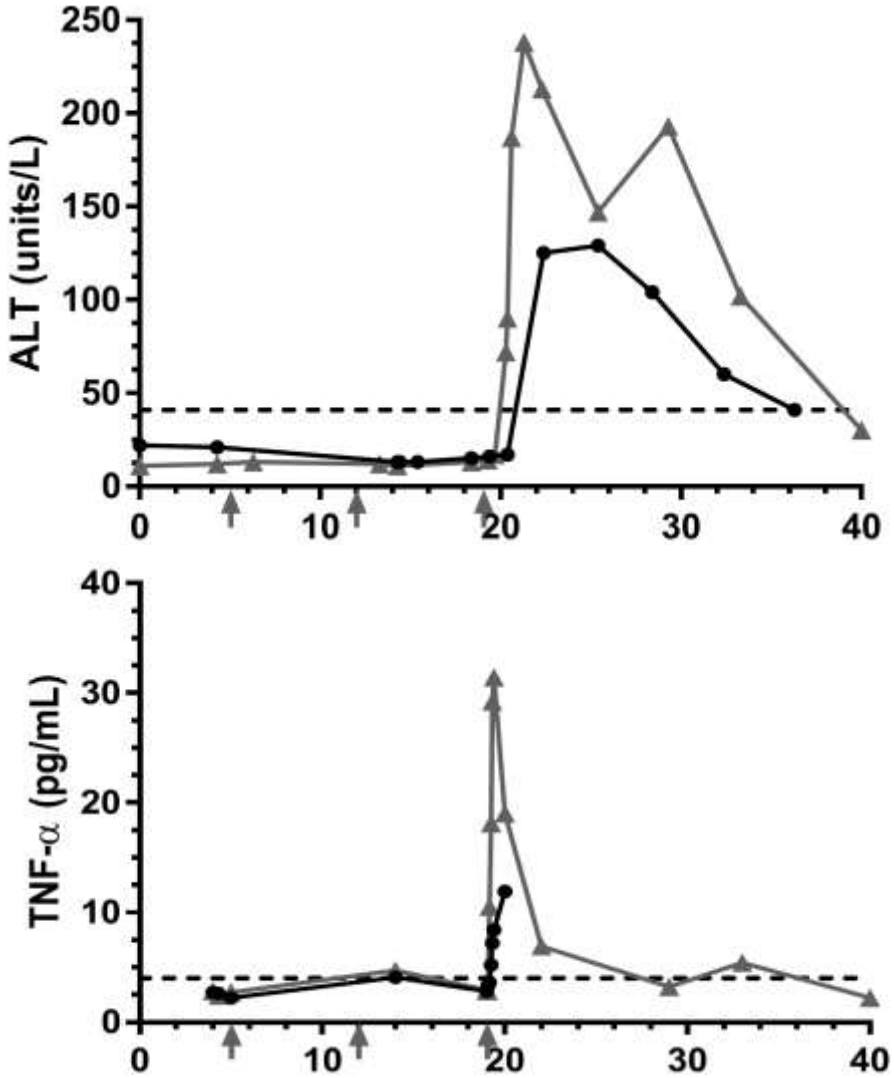
	No. *	HIV-RNA viral load / CD4 count **	HIV-RNA < 50 copies/mL @ week 24 (95% CI)
DTG 50 mg bid + 2NRTI's	69	5.10 $\log_{10}$ c/mL / 208 cells/µL	**81%** (95% CI: 72%, 90%)
EFV 600 mg qd + 2 NRTI's	44	5.24 $\log_{10}$ c/mL 202 cells/µL	**89%** (95% CI: 79%, 98%

*: randomised 3:2

**: CD4 count < 50 cells/µL excluded

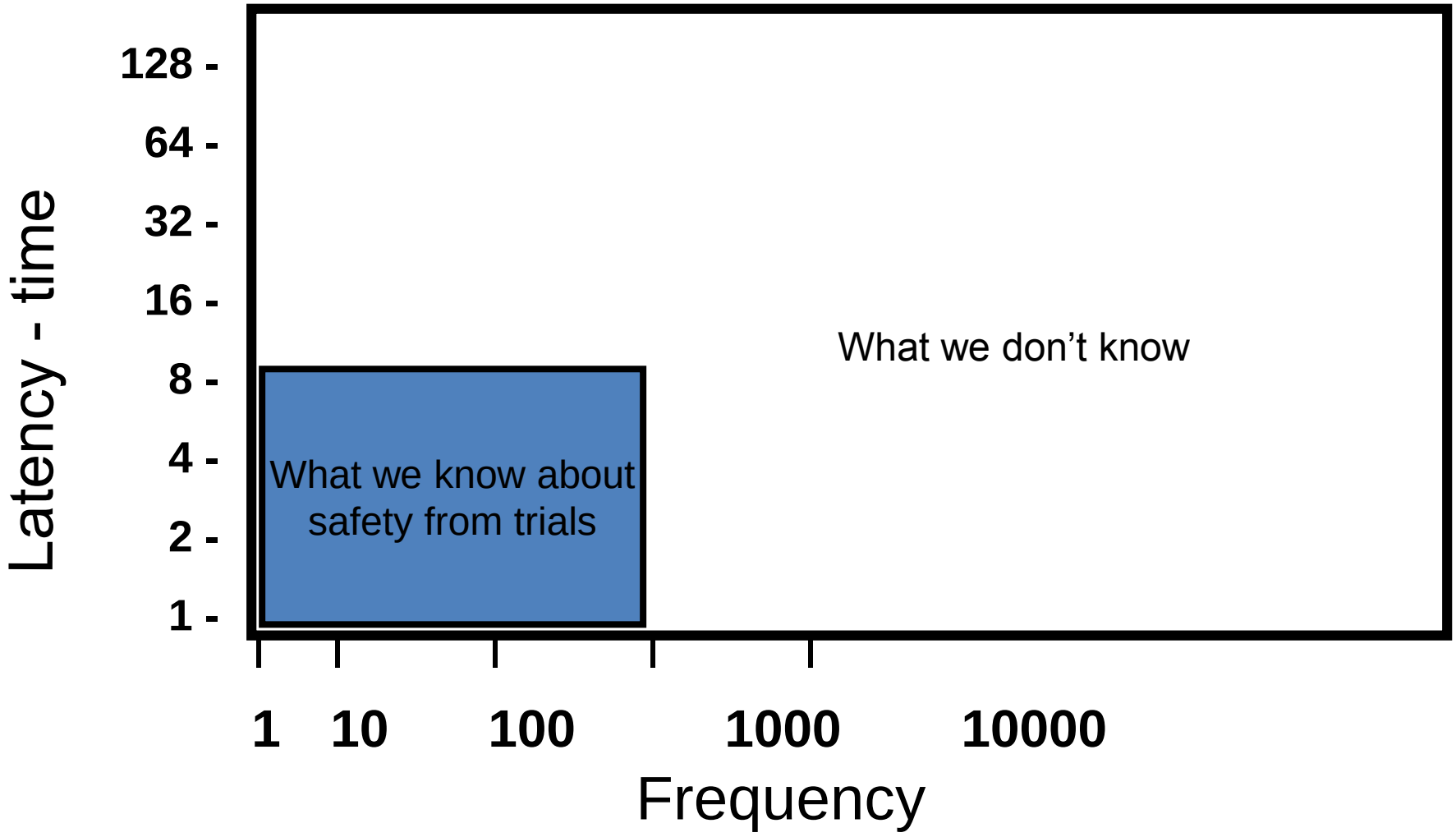
Dooley et al, CROI 2018

Dolutegravir (50 mg qd, day 0 - onwards) and Isoniazid and rifapentine (qw, day 4 – onwards) in 4 healthy persons: unexpected cytokine-storm related drug-induced liver injury in 2



Brooks et al, CID 2018

The case for ensuring longterm pharmacovigilance



Evans and Waller, MCA 2002

Summary of optimization profiles of new ARVs recommended in 2016 WHO ARV guidelines - comparative analysis

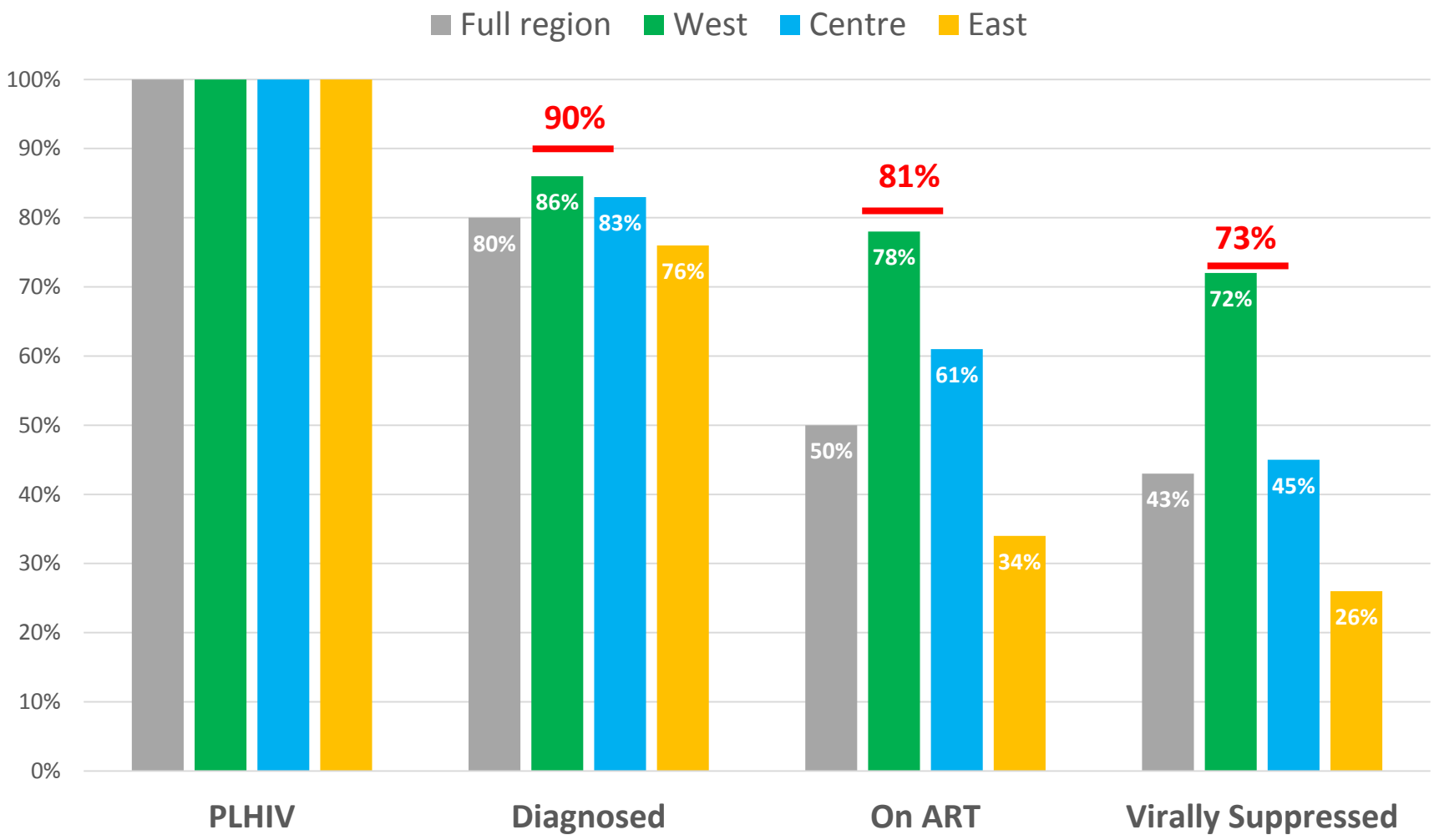
	Optimization criteria	DTG	EFV400	DRV /r	RAL
Efficacy and safety	High virologic potency	✓	✓	✓	✓
	Low toxicity	✓	✓	✓	✓
	High genetic barrier to resistance	✓	✘	✓	✘
Simplification	Available as generic FDC	✓	✓	✘	✘
	Low pill burden	✓	✓	✘	✘
Harmonization	Use in pregnant women	?	?	✓	✓
	Use in children	?	✘	✓	✓
	Use in HIV-associated TB	(✓)	?	✘	✓
	Few drug interactions	✓	✘	✘	✓
Cost	Low price	✓	✓	✘	✘

✓ yes ✘ no ? ongoing studies

Summary

- Significant progress on 2nd 90 in last few years
  - More robust scientific evidence
    - All benefit health wise from starting early – limit active TB (incl MDR)
    - Transmission is negligible if ART is fully suppressive
  - Transformed into policy – pace varies though
- Main focus areas
  - Optimise linkage & retention in care
    - Social and medical support structures if unstable lifestyle
    - Enpower sites to construct their own “right side” of CoC
  - Continue to optimize ART
    - Continuous process
    - Use highly effective and low cost / pt ART
    - Pharmacovigilance remains paramount – interpret appropriately
  - Continue to do research – health policy driven by evidence works

How close are we to reaching the 90-90-90 targets?



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

Acknowledgements

- ECDC: Teymur Noori, Anastasia Pharris, Andrew Amato, *et al*
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- CHIP: Dorthe Raben, Anne Raahauge, *et al*