

CONVEGNO NAZIONALE

*Let's stop HIV*  
Nuove prospettive  
e popolazioni speciali

*Chairs: C. Mussini, L. Sighinolfi*



Hotel Savoia *Rimini* 2-3 aprile 2019

# Focus sulla popolazione migrante: **il trattamento**

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Clinica delle Malattie Infettive



# Outline

- ART access for migrants
- ART adherence and/or retention in care
- ART outcome in the migrant population
  - Choice of the ART regimen (PDR, convenience, women childbearing age,)
- Prep for migrants?

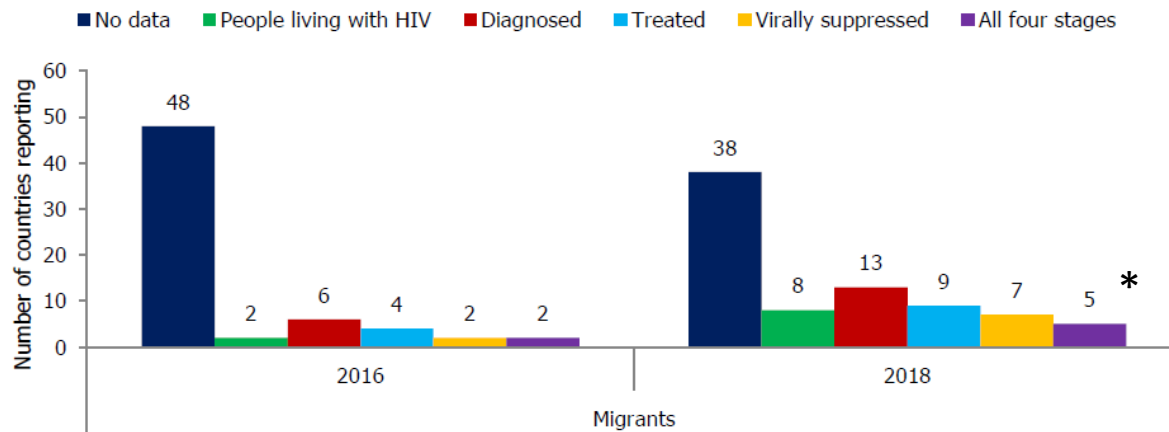


# HIV treatment cascade in migrants and mobile populations

*“Mobility”* is associated with:

- higher likelihood to enter into the healthcare system late and initiate ART late
- increased risk of ART non-adherence,
- lost to follow-up,
- deterioration in CD4 count,
- HIV-related death,
- development of drug resistance and general non continuity of HIV care.

## Number of countries reporting data for different stages of the HIV continuum of care for migrants, Europe and Central Asia in 2016 and 2018

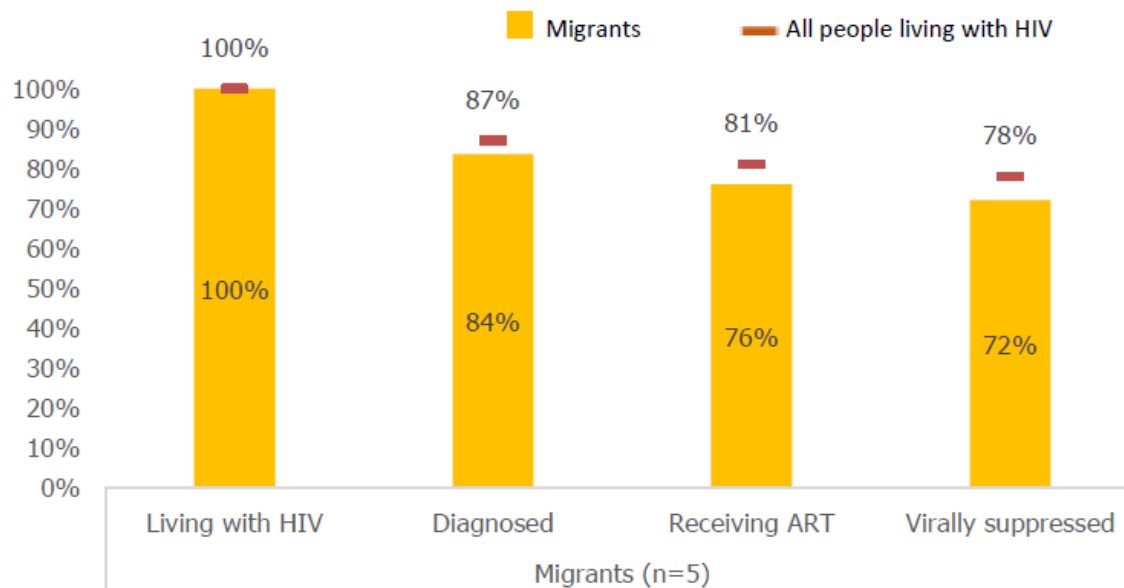


### \*Countries:

✓ Czech Republic (Central region)

✓ Austria, France, Luxembourg and the UK (West sub-region)

## Comparison of the continuum of HIV care for migrants against the national continuum of all people living with HIV, Europe and Central Asia, reported in 2018



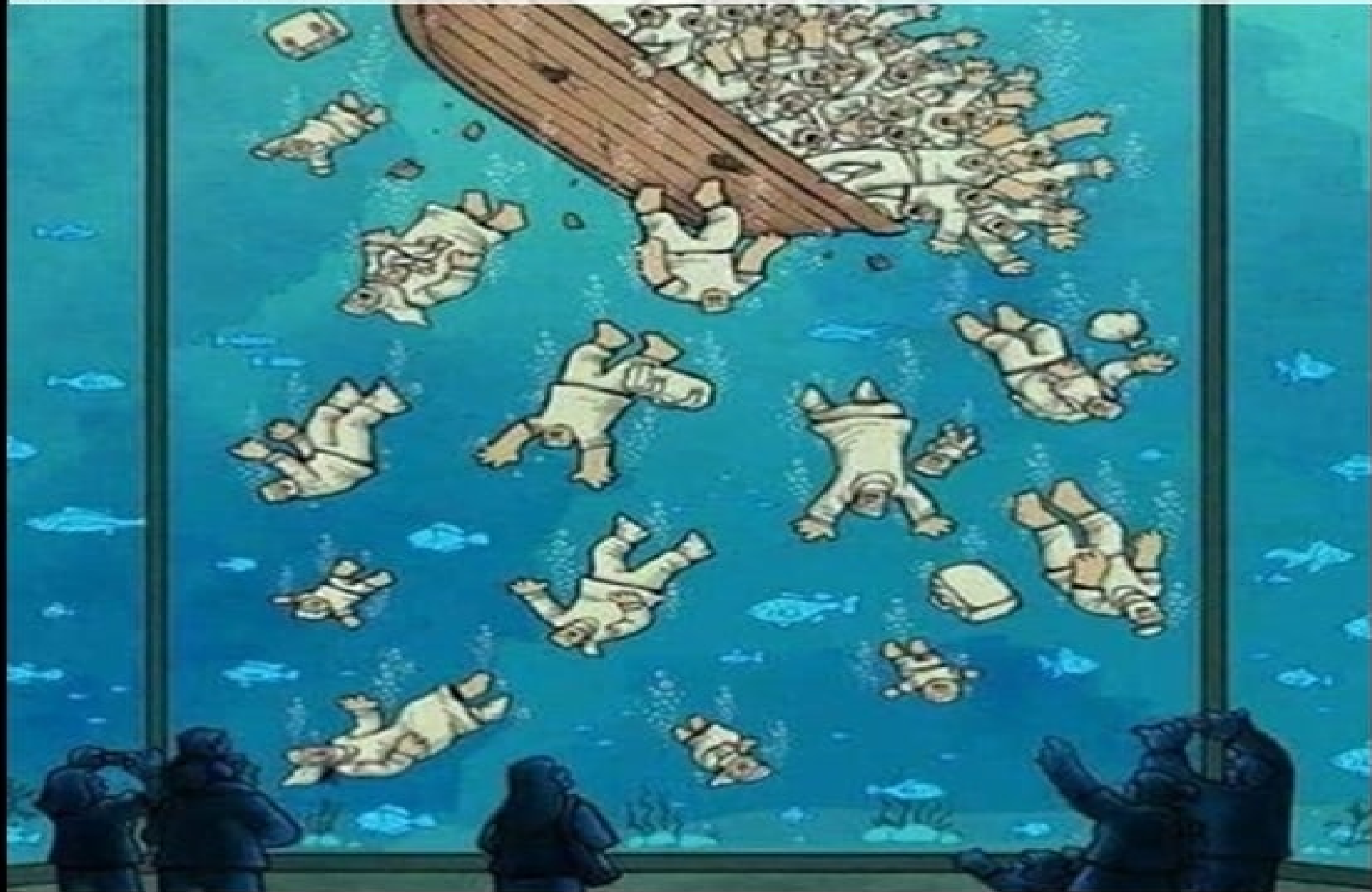
# HIV treatment cascade in migrants and mobile populations

Migrants' slow progression through the HIV treatment cascade can be attributed to:

- feelings of confusion, helplessness;
- inability to effectively communicate in the native language;
- poor knowledge about administrative or logistical requirements of the healthcare system;
- possibility of deportation or expulsion based on the legal status of the undocumented migrant;
- fear of disclosure and social isolation from the exile or compatriot group.

Travel or transition to the host country commonly makes it difficult for migrants to remain enrolled in ART programs and to maintain adherence to treatment.

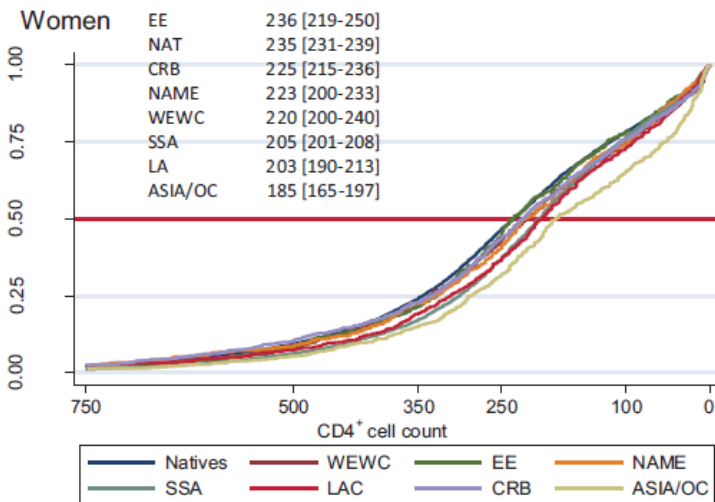
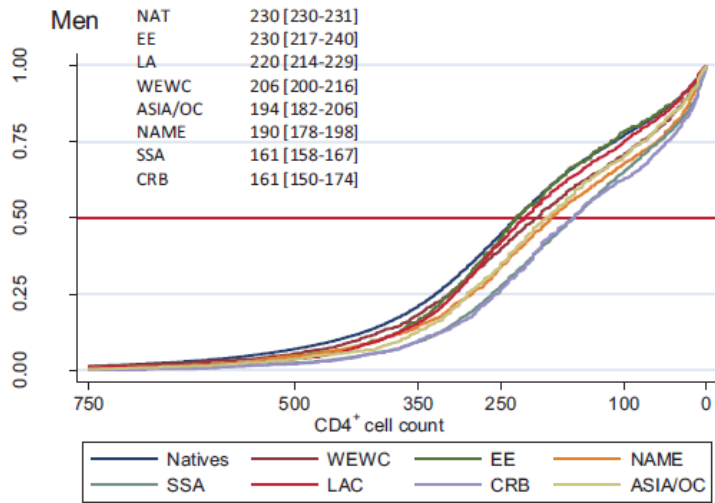
"Ricorda, non sei straniero, sei solo povero. Se fossi ricco non saresti straniero in nessun luogo."



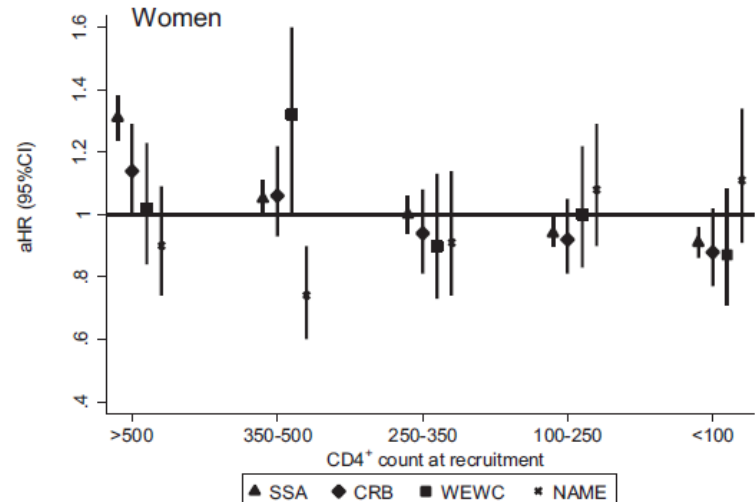
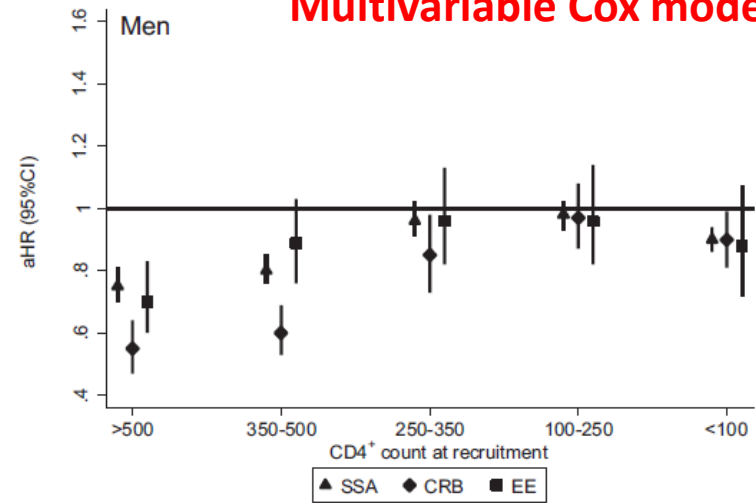
**ART access**

# Timing of combined antiretroviral treatment initiation in male and female migrants living with HIV in Western Europe

151,674 individuals, 1997-2013



## Multivariable Cox models



Cumulative probability of cART initiation

(COHERE) in EuroCoord AIDS 2017, 31:835-846



# Migrant status associated with a reduced probability of ART initiation in ICONA

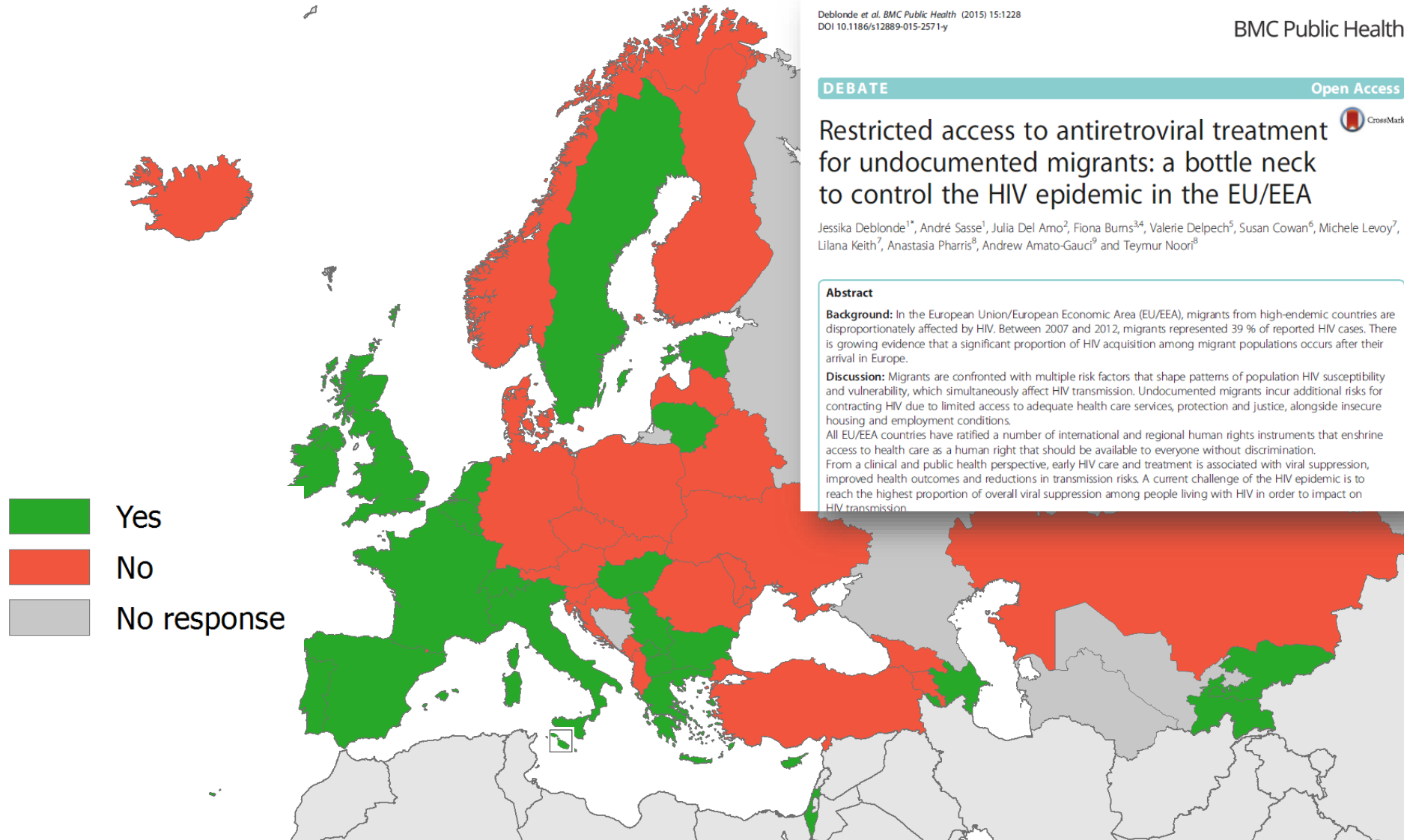
## Logistic regression analysis of factors associated with ART initiation

4126 patients (71.5%) on ART at the time of analysis, including 842 migrants (71.7%) and 3284 (71.4%) Italian-born patients.

Characteristic	OR	95% CI		p	AOR	95% CI		p
		Upper	Lower			Upper	Lower	
Male gender vs. female	0.87	0.75	1.00	0.057	1.11	0.91	1.36	0.307
Age (per 10-year increase)	1.27	1.20	1.35	<0.001	1.01	1.01	1.02	0.001
Migrants vs. natives	1.01	0.87	1.17	0.912	0.80	0.67	0.95	0.012
Years from first HIV test to enrolment	0.97	0.96	0.99	<0.001	0.98	0.97	1.00	0.071
Education					1.00			
Elementary school	1.00				1.00			
Junior high school	0.86	0.64	1.16	0.333	1.06	0.75	1.49	0.750
High school	0.71	0.53	0.94	0.017	0.97	0.70	1.36	0.872
University	0.54	0.40	0.74	<0.001	0.85	0.59	1.23	0.396
Missing data	0.60	0.45	0.79	<0.001	0.89	0.64	1.23	0.470
Occupation					1.00			
Full-time worker	1.00				1.00			
Unemployed	1.00	0.83	1.20	0.978	0.90	0.72	1.12	0.341
Self-employed	0.80	0.68	0.96	0.015	0.77	0.63	0.93	0.007
Temporary employed	0.88	0.63	1.24	0.467	0.85	0.57	1.25	0.402
Housewife	1.28	0.87	1.89	0.214	0.92	0.59	1.46	0.732
Retired	1.72	1.14	2.60	0.009	0.85	0.52	1.37	0.503
Student	0.49	0.37	0.66	<0.001	0.76	0.54	1.05	0.096
Other/missing	0.71	0.61	0.82	<0.001	0.72	0.59	0.87	0.001
Mode of HIV transmission					1.00			
Heterosexual contacts	1.00				1.00			
Homosexual contacts	0.57	0.50	0.65	<0.001	0.77	0.65	0.91	0.002
Intravenous drug use	0.69	0.55	0.86	0.001	0.67	0.51	0.88	0.004
Other/unknown	0.74	0.59	0.93	0.010	0.78	0.60	1.01	0.058

# Availability of ART for undocumented migrants

## 2018



Deblonde et al. *BMC Public Health* (2015) 15:1228  
DOI 10.1186/s12889-015-2571-y

BMC Public Health

DEBATE

Open Access



## Restricted access to antiretroviral treatment for undocumented migrants: a bottle neck to control the HIV epidemic in the EU/EEA

Jessika Deblonde<sup>1\*</sup>, André Sasse<sup>1</sup>, Julia Del Amo<sup>2</sup>, Fiona Burns<sup>3,4</sup>, Valerie Delpéch<sup>5</sup>, Susan Cowan<sup>6</sup>, Michele Levoy<sup>7</sup>, Lilana Keith<sup>7</sup>, Anastasia Pharris<sup>8</sup>, Andrew Amato-Gauci<sup>9</sup> and Teymur Noori<sup>8</sup>

### Abstract

**Background:** In the European Union/European Economic Area (EU/EEA), migrants from high-endemic countries are disproportionately affected by HIV. Between 2007 and 2012, migrants represented 39% of reported HIV cases. There is growing evidence that a significant proportion of HIV acquisition among migrant populations occurs after their arrival in Europe.

**Discussion:** Migrants are confronted with multiple risk factors that shape patterns of population HIV susceptibility and vulnerability, which simultaneously affect HIV transmission. Undocumented migrants incur additional risks for contracting HIV due to limited access to adequate health care services, protection and justice, alongside insecure housing and employment conditions.

All EU/EEA countries have ratified a number of international and regional human rights instruments that enshrine access to health care as a human right that should be available to everyone without discrimination. From a clinical and public health perspective, early HIV care and treatment is associated with viral suppression, improved health outcomes and reductions in transmission risks. A current challenge of the HIV epidemic is to reach the highest proportion of overall viral suppression among people living with HIV in order to impact on HIV transmission.

# Access to Highly Active Antiretroviral Therapy in HIV-Infected Immigrants: A Retrospective Multicenter Italian Study

AIDS PATIENT CARE and STDs  
Volume 19, Number 9, 2005

A. SARACINO,<sup>1,2</sup> I. EL-HAMAD,<sup>1,3</sup> R. PRATO,<sup>4</sup> D.C. CIBELLI,<sup>2</sup> A. TARTAGLIA,<sup>2</sup>  
E. PALUMBO,<sup>2</sup> M.C. PEZZOLI,<sup>3</sup> G. ANGARANO,<sup>2</sup> G. SCOTTO,<sup>1,2</sup>  
and the SIMIT STUDY GROUP\*

## ANALYSIS OF FACTORS INFLUENCING THE PROBABILITY OF BEING TREATED WITH HAART

<i>Univariate analysis</i>	<i>OR</i>	<i>(95% CI)</i>	<i>p value</i>
Male gender	1.37	(0.74–2.54)	0.2
Country of origin			
Africa	0.55	(0.27–1.13)	0.08
Asia	0.98	(0.20–6.37)	0.9
Eastern Europe	1.74	(0.38–10.94)	0.4
Central-South America	1.83	(0.80–4.36)	0.1
Risk factor			
Heterosexual	0.68	(0.32–1.39)	0.2
Homosexual	3.57	(0.82–21.89)	0.06
Legal status (legal vs undocumented)	2.09	(1.07–4.08)	0.01
Registration in the National Health System	2.22	(1.10–4.47)	0.01
Years in Italy ( $\leq 10$ yrs vs. $> 10$ yrs)	0.62	(0.22–1.64)	0.3
Profession (employed vs. unemployed)	2.05	(0.92–4.51)	0.05
Use of intercultural mediator	2.11	(0.69–7.16)	0.1

**ART outcome**

# Immunological and virological response to antiretroviral treatment in migrant and native men and women in Western Europe; is benefit equal for all?

**Time to virological response from combination cART initiation according to geographical origin, in men and women**

32 817 individuals

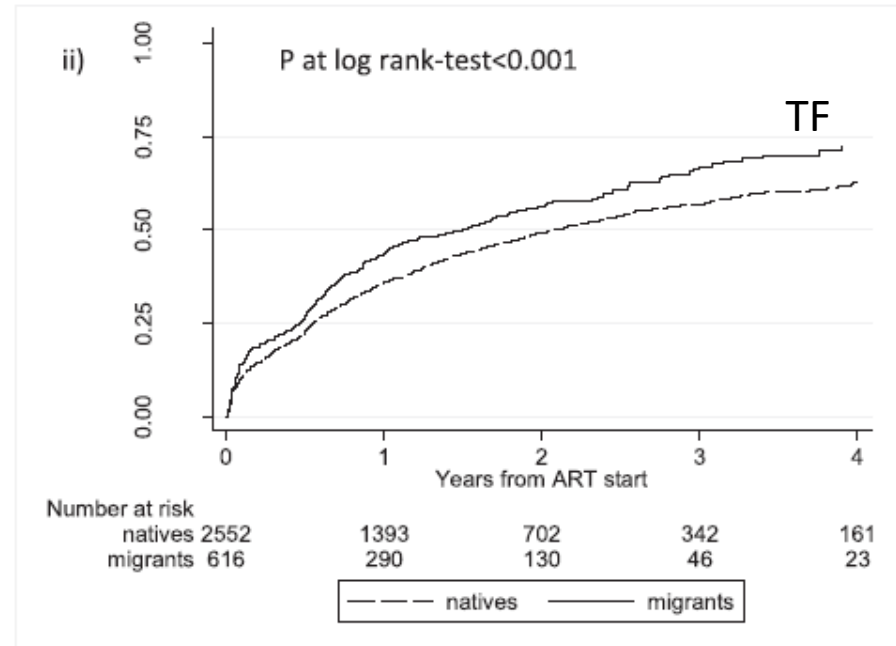
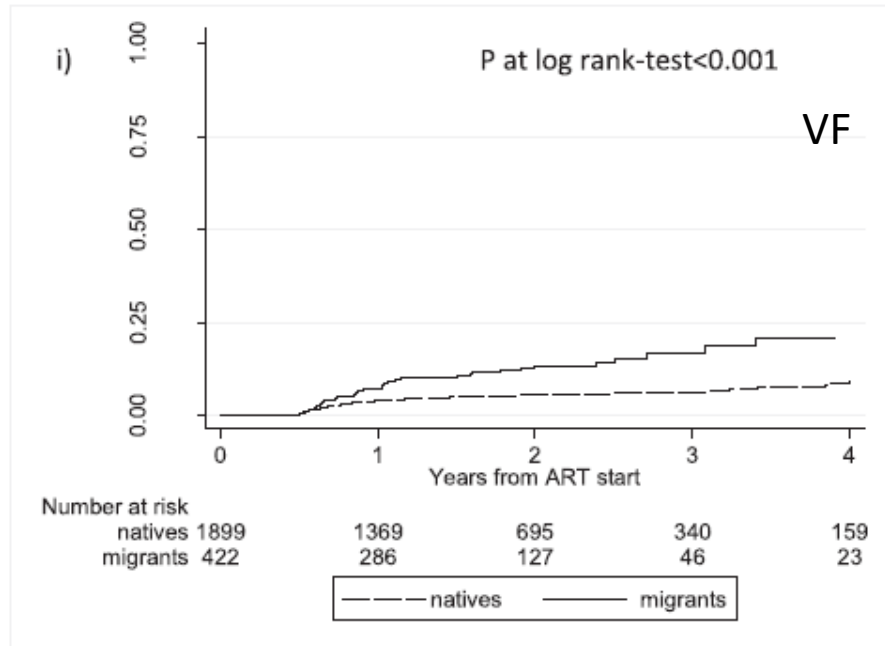
	Men				Women			
	Univariable analysis		Multivariable analysis*		Univariable analysis		Multivariable analysis*	
	sHR (95% CI)	P-value	sHR (95% CI)	P-value	sHR (95% CI)	P-value	sHR (95% CI)	P-value
NAT	1.00		1.00		1.00		1.00	
WEWC	0.98 (0.90; 1.06)	0.60	0.98 (0.87; 1.10)	0.71	0.90 (0.73; 1.11)	0.32	0.90 (0.74; 1.09)	0.29
EE	1.05 (0.96; 1.15)	0.31	1.06 (0.96; 1.17)	0.24	1.17 (1.00; 1.37)	0.055	1.17 (0.98; 1.39)	0.09
NAME	0.85 (0.76; 0.95)	0.005	0.91 (0.86; 0.97)	0.004	1.00 (0.86; 1.17)	0.98	1.00 (0.90; 1.11)	0.94
SSA	0.80 (0.76; 0.84)	<0.001	0.88 (0.82; 0.95)	0.001	1.05 (0.98; 1.12)	0.18	1.04 (0.96; 1.12)	0.30
LA	1.00 (0.90; 1.11)	0.98	0.95 (0.87; 1.03)	0.23	1.08 (0.95; 1.24)	0.23	1.08 (0.94; 1.25)	0.27
CRB	0.90 (0.61; 1.32)	0.58	0.95 (0.73; 1.24)	0.71	0.79 (0.65; 0.96)	0.02	0.77 (0.67; 0.89)	<0.001
ASIA/OCE	1.09 (0.94; 1.27)	0.24	1.07 (0.93; 1.23)	0.33	1.17 (0.95; 1.44)	0.14	1.14 (0.90; 1.45)	0.27
Overall P-value		<0.001		<0.001		<0.001		<0.001

**Lower VR in North and Sub-Saharan African men and in Caribbean women**

# Increased risk of virologic failure to the first antiretroviral regimen in HIV-infected migrants compared to natives: data from the ICONA cohort

A. Saracino<sup>1</sup>, P. Lorenzini<sup>2</sup>, S. Lo Caputo<sup>3</sup>, E. Girardi<sup>4</sup>, F. Castelli<sup>5</sup>, P. Bonfanti<sup>6</sup>, S. Rusconi<sup>7</sup>, P. Caramello<sup>8</sup>, N. Abrescia<sup>9</sup>, C. Mussini<sup>10</sup>, L. Monno<sup>1</sup> and A. d'Arminio Monforte<sup>11</sup>, for the ICONA Foundation Study Group

*Clin Microbiol Infect* 2016; 22: 288.e1–288.e8



✓ Virological failure (VF)	migrants	<b>6.4 per 100 PYFU</b>	<b>(95% CI 4.8–8.5)</b>	
	natives	2.7 per 100 PYFU	(95% CI 2.2–3.3)	p < 0.001
✓ Treatment discontinuation (TD)	migrants	<b>38.4 per 100 PYFU</b>	<b>(95% CI 34.4–42.8)</b>	
	natives	30.8 per 100 PYFU	(95% CI 29.2–32.6)	p < 0.001
✓ Treatment failure (TF)	migrants	<b>44.9 per 100 PYFU</b>	<b>(95% CI 40.4–49.9)</b>	
	natives	33.2 per 100 PYFU	(95% CI 31.5–35.1)	p < 0.001

# Does region of origin influence the timing and outcome of first-line antiretroviral therapy in France?

C Gatey,<sup>1</sup> A Brun,<sup>2</sup> G Hamet,<sup>2</sup> S Diamantis,<sup>3</sup> P Sellier,<sup>4</sup> O Bouchaud,<sup>5,6</sup> V Garrait,<sup>7</sup> W Rozenbaum,<sup>1,2</sup> JM Molina<sup>1,8</sup> and S Abgral <sup>9,10,11</sup> for the COREVIH Ile de France Est Research Group\*

HIV Medicine (2019), 20, 175–181

## Objectives

The aim of the study was to assess whether the timing of combination antiretroviral therapy (cART) initiation, the choice of cART and virological response differ in migrants versus European natives in the north and east of Paris area, after dissemination of French recommendations for universal treatment.

## Methods

Antiretroviral therapy-naïve HIV-1-infected adults with at least two follow-up visits at one of 15 participating centres between 1 January 2014 and 31 March 2015 were included in the study. Factors associated with cART initiation before 31 March 2015, with protease inhibitor (PI)-containing cART among individuals initiating cART, and with 1-year virological success after cART initiation were assessed using multivariable logistic regression models. Sex, age, region of origin [Western Europe, sub-Saharan Africa (SSA) or other], HIV transmission group, baseline AIDS status, CD4 cell count and plasma viral load (VL), and hepatitis B and/or C virus infection were considered in the analyses.

## Results

Among 912 individuals, only 584 (64%) started cART during the study period. After adjustment, migrants from SSA were half as likely to initiate cART and to have a subsequent virological response compared with individuals from Western Europe [adjusted odds ratio (aOR) 0.54; 95% confidence interval (CI) 0.36–0.82; and aOR 0.52; 95% CI 0.28–0.98, respectively]. PI-containing cART was more frequently prescribed in migrants from SSA, in people with lower CD4 cell counts and in people with higher VL.

## Conclusions

Even in the context of universal cART recommendations and of free access to care, migrants from SSA still have delayed access to cART and a lower virological response. Efforts are still necessary to provide immediate cART to all people living with HIV.

**ART adherence and/or  
retention in care**



# Linkage to Care Is Important and Necessary When Identifying Infections in Migrants

1. Collaboration between primary care, public health, and specialist care in order to ensure continuity of care tailored to all the needs of the person involved.
2. Single point-of-referral to a migrant-friendly clinical service with culturally competent staff that deal with migrants and infectious diseases (as well as other health needs). This clinic could be facilitated by being staffed by specialists with a broad range of skill-sets who can manage all infections alongside interpreters and other support services to support treatment adherence and completion.
3. Robust data collection to facilitate sharing of best practice with respect to linkage to care and treatment completion for migrants with infectious diseases.

Evidence-based guidance emphasising methods of implementation supported by appropriate resources and migrant communities' views

# Effect of Legal Status on the Early Treatment Outcomes of Migrants Beginning Combined Antiretroviral Therapy at an Outpatient Clinic in Milan, Italy

*Anna L. Ridolfo, MD, Letizia Oreni, BS, Paolo Vassalini, MD, Chiara Resnati, MD, Giorgio Bozzi, MD, Laura Milazzo, MD, Spinello Antinori, MD, Stefano Rusconi, MD, and Massimo Galli, MD*

**TABLE 2. Adjusted Logistic Regression Model Assessing the Effect of Undocumented Status on the Probability of Being LTFU 12 Months After Starting cART**

Variable	Adjusted OR (95% CI)	P			
Age, each year more	0.99 (0.96 to 1.02)	0.552			
Gender					
Women	1				
Men	0.97 (0.41 to 2.26)	0.936			
Transgender women	1.03 (0.22 to 4.87)	0.975			
Region of origin					
Italy	1				
Latin America	0.74 (0.21 to 2.56)	0.631			
Sub-Saharan Africa	1.62 (0.50 to 5.26)	0.427			
Other regions	0.44 (0.07 to 2.77)	0.380			
Type of health card used					
SSN	1				
STP	8.05 (2.51 to 25.84)	<0.001			
HIV risk factor					
Heterosexuals	1				
IVDUs	5.98 (2.30 to 15.54)	<0.001			
MSM	0.96 (0.35 to 2.64)	0.930			
Other/unknown	3.41 (1.11 to 10.51)	0.033			
			AIDS diagnosis		
			No	1	
			Yes	0.82 (0.35 to 1.90)	0.640
			CD4 cell counts, cells/ $\mu$ L		
			<350	1	
			>350	1.65 (0.77 to 3.55)	0.201
			HIV-RNA copies/mL, each log <sub>10</sub> more	0.95 (0.67 to 1.34)	0.777
			HBV-Ag and/or HCV-Ab status		
			Negative	1	
			Positive	0.45 (0.17 to 1.22)	0.118
			Initial cART regimen		
			NNRTI-based	1	
			PI-based	1.32 (0.64 to 2.72)	0.447

# Risk factors for non adherence in immigrant PLWHIV

Univariable and multivariable logistic regression analyses were conducted among 301 participants who had used cART  $\geq 6$  months prior to inclusion.

Independent risk factors for self-reported non-adherence were:

- (I) not having attended formal **education** or only primary school (OR = 3.25; 95% CI: 1.28–8.26, versus University),
- (II) experiencing low levels of **social support** (OR = 2.56; 95% CI: 1.37–4.82), and
- (III) reporting low treatment adherence **self-efficacy** (OR = 2.99; 95% CI: 1.59–5.64).
- (IV) internalized **HIV-related stigma** was marginally associated ( $P < 0.10$ ) with non-adherence (OR = 1.82; 95% CI: 0.97–3.43).

# HIV testing history and access to treatment among migrants living with HIV in Europe

Ibidun Fakoya<sup>1</sup>, Débora Álvarez-Del Arco<sup>2</sup>, Susana Monge<sup>3</sup>, Andrew J Copas<sup>1</sup>, Anne-Francoise Gennotte<sup>4</sup>, Alain Volny-Anne<sup>5</sup>, Claudia Wengenroth<sup>6</sup>, Giota Touloumi<sup>7</sup>, Maria Prins<sup>8,9</sup>, Henrique Barros<sup>10</sup>, Katharine EA Darling<sup>11</sup>, Tullio Prestileo<sup>12</sup>, Julia Del Amo<sup>2,\*</sup> and Fiona M Burns<sup>1,13,\*§</sup>, on behalf of the aMASE Study Team<sup>‡</sup>

## HIV treatment characteristics of aMASE clinic survey respondents, by gender (men separated by sexual orientation)

	Women	Heterosexual men	Gay/bisexual men
Most recent CD4 cell count $\geq 350$ cells mm <sup>3</sup> (n = 2011)	494 (76.8)	282 (65.4)	814 (86.9)
Undetectable viral load (<50 copies/mL) (n = 1540) <sup>a</sup>	409 (77.2)	290 (75.9)	489 (77.9)
Currently not on HIV treatment (n = 2090) <sup>b</sup>	105 (16.0)	40 (9.0)	312 (31.6)
Reason not on HIV treatment (n = 457)			
Doctor's advice or newly diagnosed	90 (85.7)	33 (82.5)	276 (88.5)
High cost or otherwise inaccessible	3 (2.9)	0 (0.0)	15 (4.8)
Fear of side effects or other difficulties taking medication	9 (8.6)	5 (12.5)	25 (8.0)
Other reason	7 (6.7)	3 (7.5)	16 (5.1)
Access to primary care (n = 2076)	552 (85.1)	369 (83.5)	833 (84.6)
Government-funded HIV treatment and care (n = 972) <sup>b,c</sup>	244 (78.2)	162 (78.6)	319 (70.3)
Experienced difficulties with health service in CCOR (n = 2093)	211 (32.3)	132 (29.9)	272 (27.7)
No GP/Health card/insurance (n = 628)	33 (15.3)	18 (13.1)	58 (20.9)
Unclear of rights to access medical care (n = 629)	43 (19.9)	35 (25.5)	70 (25.3)
Long waiting times for an appointment/in the clinic (n = 628)	72 (33.3)	29 (21.2)	111 (40.1)
Does not trust the GP confidentiality (n = 628)	48 (22.2)	31 (22.6)	37 (13.4)
Difficulty communicating with staff because of language differences (n = 628)	55 (25.5)	38 (27.7)	38 (13.7)
Difficulty negotiating healthcare system (e.g. finding GP, payment, travel) (n = 629)	22 (10.2)	13 (9.5)	31 (11.2)
Missed clinical appointments because of <u>travel expenses</u> (n = 2071)	77 (11.9)	66 (15.1)	68 (6.9)
Delayed/forwent medication because of <u>prescription costs</u> (n = 2078) <sup>d</sup>	54 (8.3)	39 (8.8)	48 (4.9)

# Which ART regimen?

Consider:

- Regimen convenience (STR?): consider pregnancy planning in women
- Genotype if available; level of PDR in country of origin

# First ART Regimen in ICONA cohort

Characteristic	Migrants	Natives	p
Type of first regimen, <i>n</i> (%)			
2 NRTIs + NNRTI	278 (23.7%)	1233 (26.8%)	<0.001
2 NRTIs + PI boosted	502 (42.8%)	1661 (36.2%)	
2 NRTIs + II	12 (1.0%)	94 (2.0%)	
NRTI sparing	20 (1.7%)	97 (2.1%)	
Other	30 (2.5%)	199 (4.3%)	

# Which STR in migrant women of childbearing age?



EACS European AIDS Clinical Society

## ART in pregnancy

Same as non-pregnant

If on RAL (400 mg bid), RPV or DRV/r: could be continued

No data on RAL 1200 mg qd: not recommended

Women on EVG/c need to be informed that more monitoring of HIV-VL and drug levels may be necessary during pregnancy

Women on DTG need to be switched to a different third agent, at least for the first trimester (evidence of increased risk of neural tube defect in newborns exposed to DTG from one observational cohort)

Among PI/r, prefer ATV/r

RTV is the recommended booster for women on treatment with boosted PI during pregnancy

DRV/c is not recommended during pregnancy due to significant lower exposures of DRV and COBI in the second and third trimester of pregnancy

EFV is a suitable alternative for pregnant persons needing to start treatment. It can be continued if already started before pregnancy

NVP not to be initiated, but continuation is possible if started before pregnancy

Limited experience with TAF in pregnancy: not recommended in initial regimen

No experience with BIC in pregnancy: not recommended

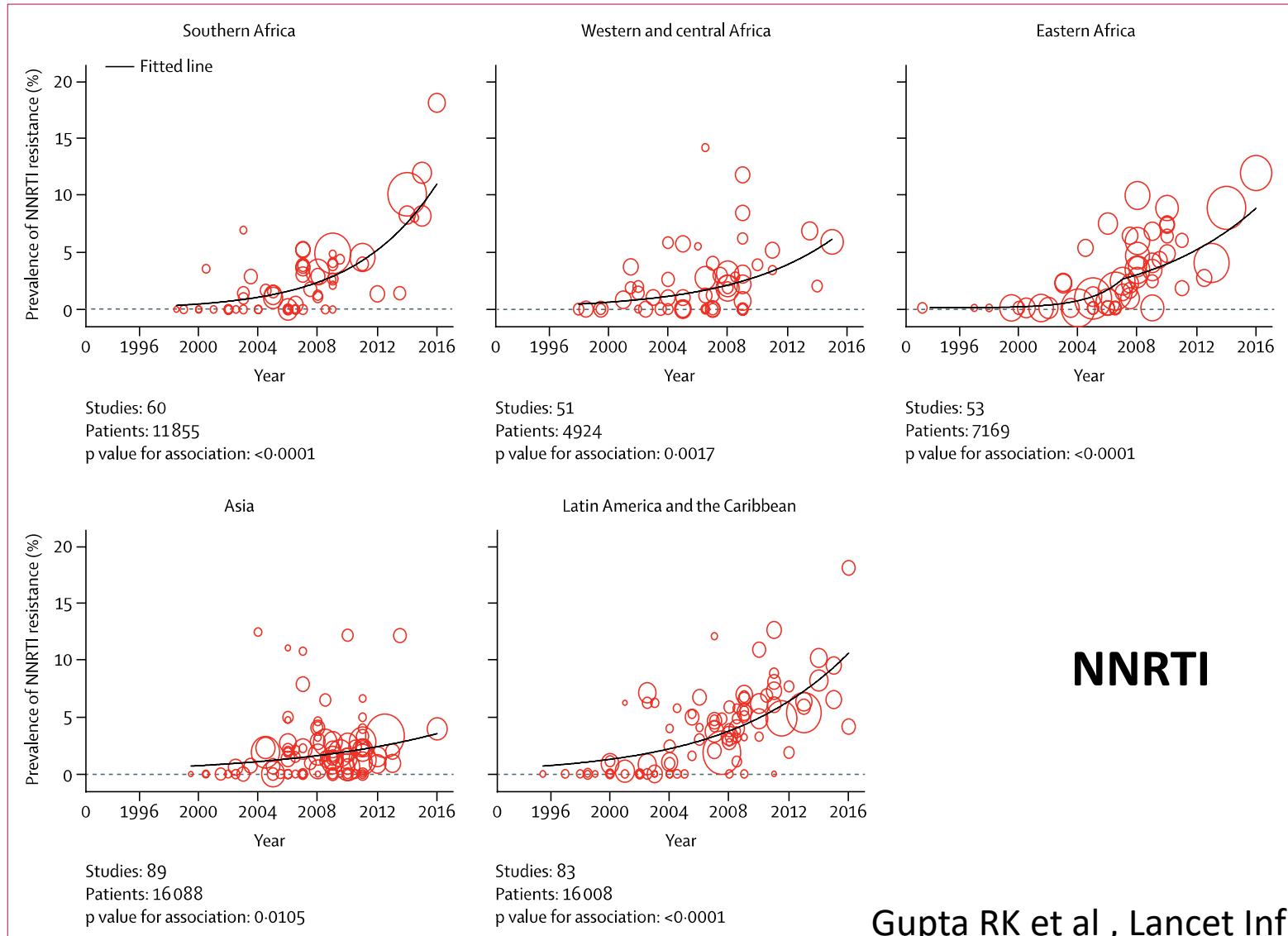
Drugs contraindicated during pregnancy

DTG (first trimester), ddi + d4T, triple NRTI combinations

Breastfeeding

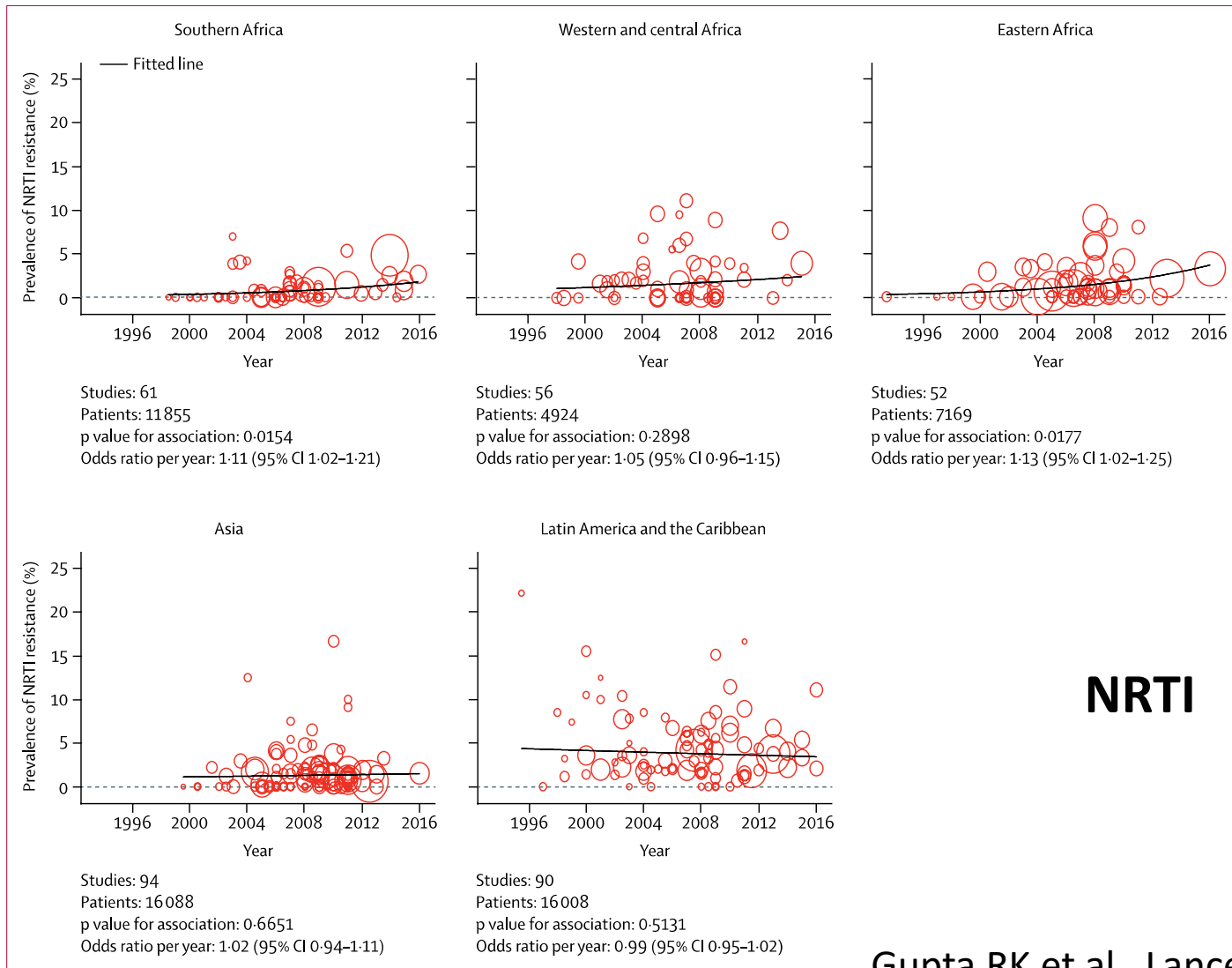
We advise against breastfeeding. In case a woman insists on breastfeeding, we recommend follow-up with increased clinical and virological monitoring of both the mother and the infant

# Pre-treatment drug resistance (PDR) in low income countries



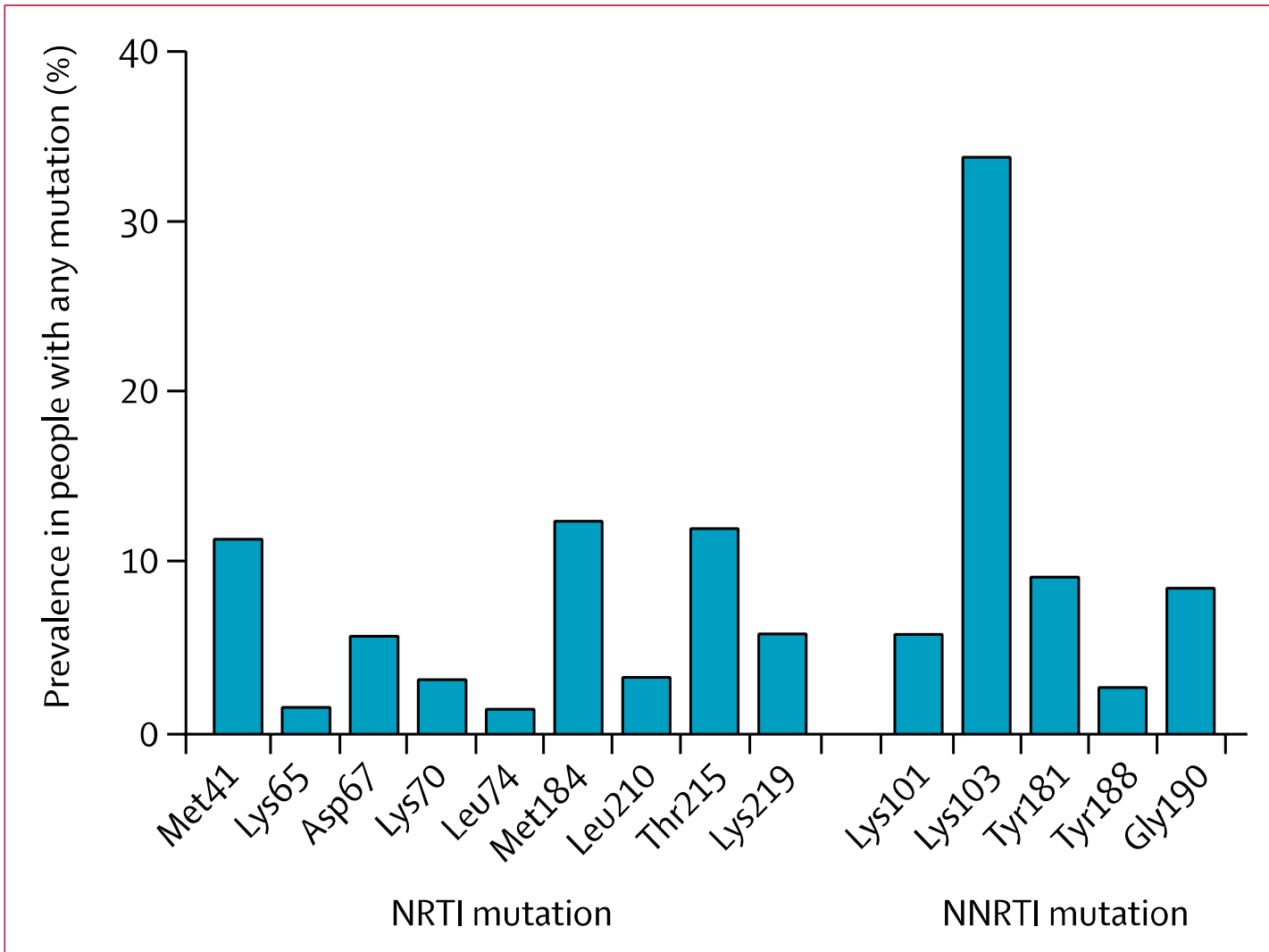


# Pre-treatment drug resistance (PDR) in low income countries



**NRTI**

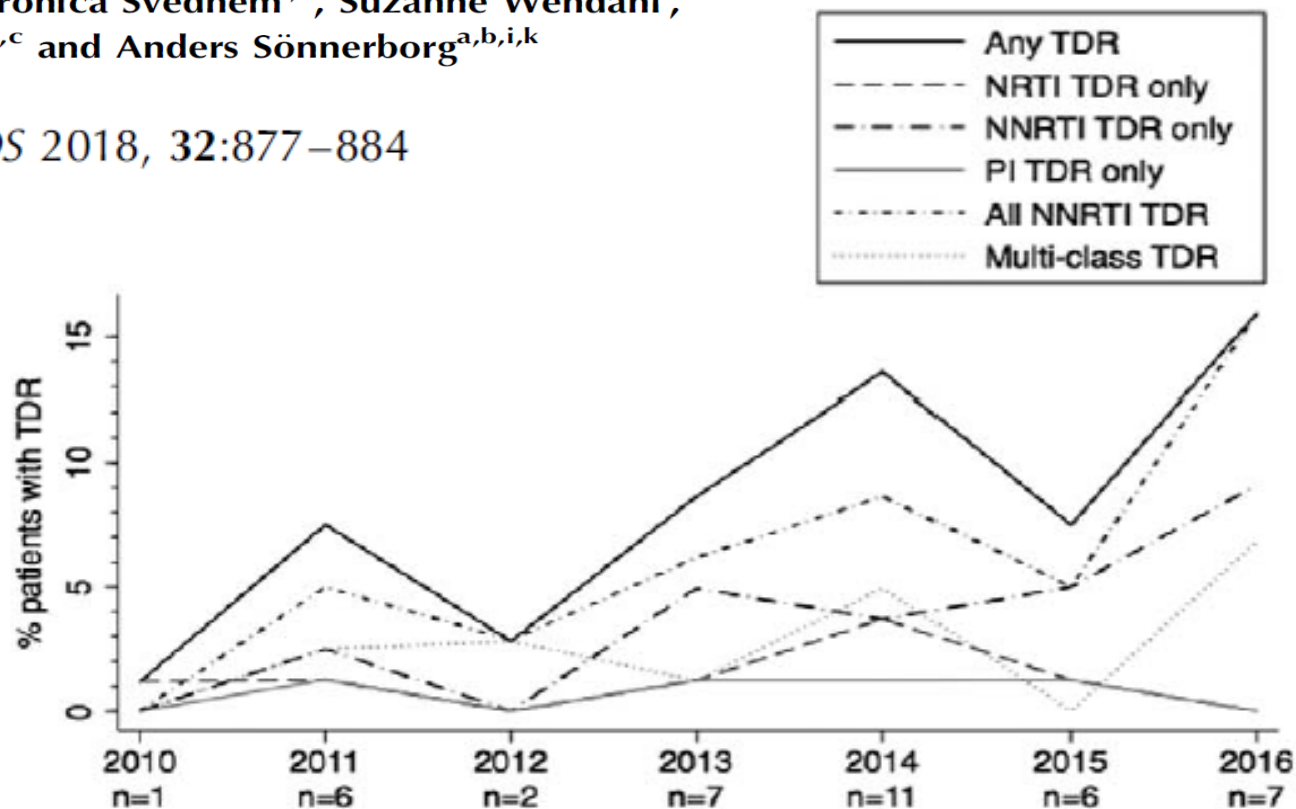
# Pre-treatment drug resistance (PDR) in low income countries



# Increase in transmitted drug resistance in migrants from sub-Saharan Africa diagnosed with HIV-1 in Sweden

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*AIDS* 2018, 32:877–884



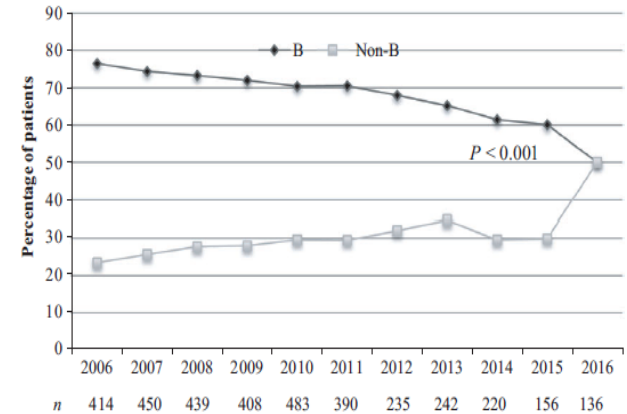
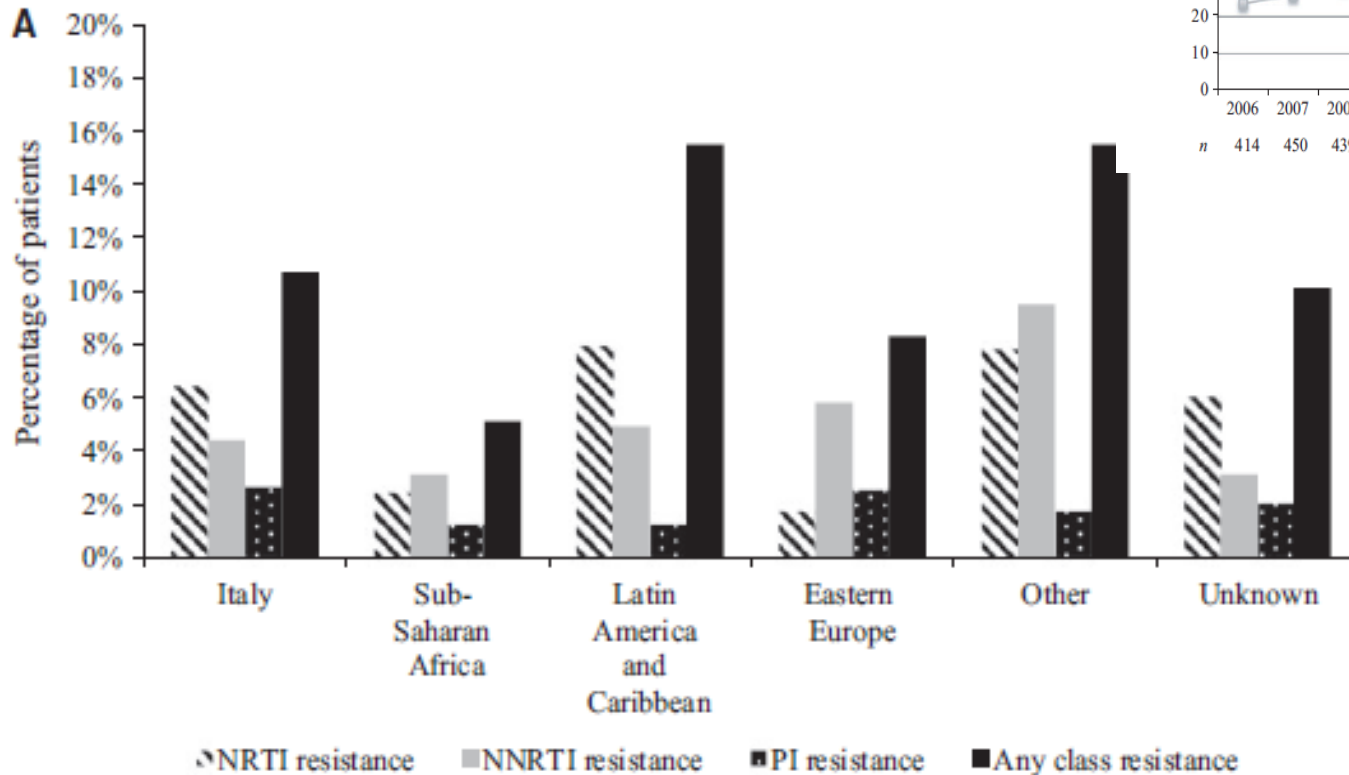
**Fig. 2.** Prevalence of transmitted drug resistance per drug class in patients infected in sub-Saharan Africa. *n* = absolute number of patients with any TDR per year. TDR, transmitted drug resistance.

# Evolution of transmitted HIV-1 drug resistance and viral subtypes circulation in Italy from 2006 to 2016

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*HIV Medicine* (2018), 19, 619–628

TDR declined from 14.5% in 2006 to 7.3% in 2016 ( $p=0.003$ ),  
 > in B than non-B subtypes



# PrEP for African migrants in Europe? A research agenda

- WHO guidelines recommend PrEP for populations with HIV incidences of 3% per year or higher
- Clinical trials and demonstration projects in Europe have focused solely on men having sex with men (MSM); so far more than 95% of people using Prep are MSM
- In Western Europe, sub-Saharan Africa migrants are the most affected group after MSM, accounting for 15.6% of new HIV diagnoses in 2014.
- In Europe, up to 31% of migrants from sub-Saharan Africa living with HIV acquired HIV in their host countries
- PrEP research should assess the eligibility of subpopulations of migrants from sub-Saharan Africa and define culturally sensitive screening questions for their inclusion

# Conclusions

- Even in the context of free access to cART and universal recommendations for cART initiation, **migrants still have delayed access to cART** and a **lower virological response** on treatment.
- As they represent a significant proportion of new HIV diagnoses, efforts are still necessary to **provide immediate cART**
- **Political and public health decisions** are necessary to **reduce the socioeconomic insecurity** experienced by most recent migrants, who are frequently undocumented and vulnerable to HIV infection.
- **Educational interventions culturally tailored** to the general migrant population would also help to reduce the fear of stigmatization and improve linkage to care in order to achieve the “4”90 UNAIDS target.