HIV/AIDS: attualità epidemiologiche e prospettive terapeutiche nella popolazione migrante in Italia

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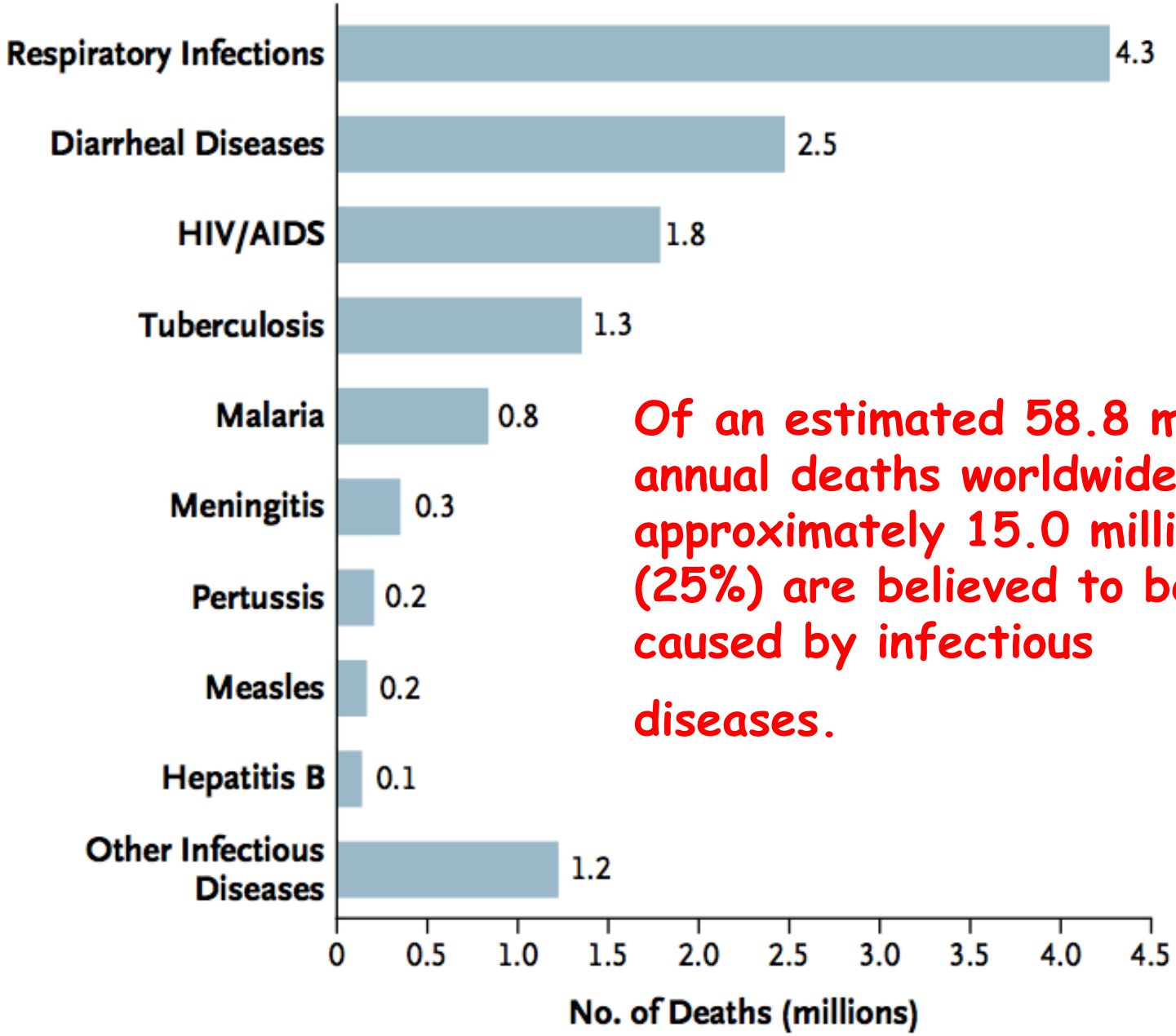
18 novembre 2016

Ferrara

December 1969, Surgeon General W. H. Stewart, contemplating the benefits realized from antibiotics and vaccines, declared victory against the threat of infectious diseases and suggested that USA turn its attention and resources to the more important threat of chronic diseases.

William H. Stewart, [U.S.] Surgeon General and Chief Delegate of the Delegation of the USA, addressing the Assembly during a plenary meeting

Leading Causes of Global Deaths from Infectious Diseases

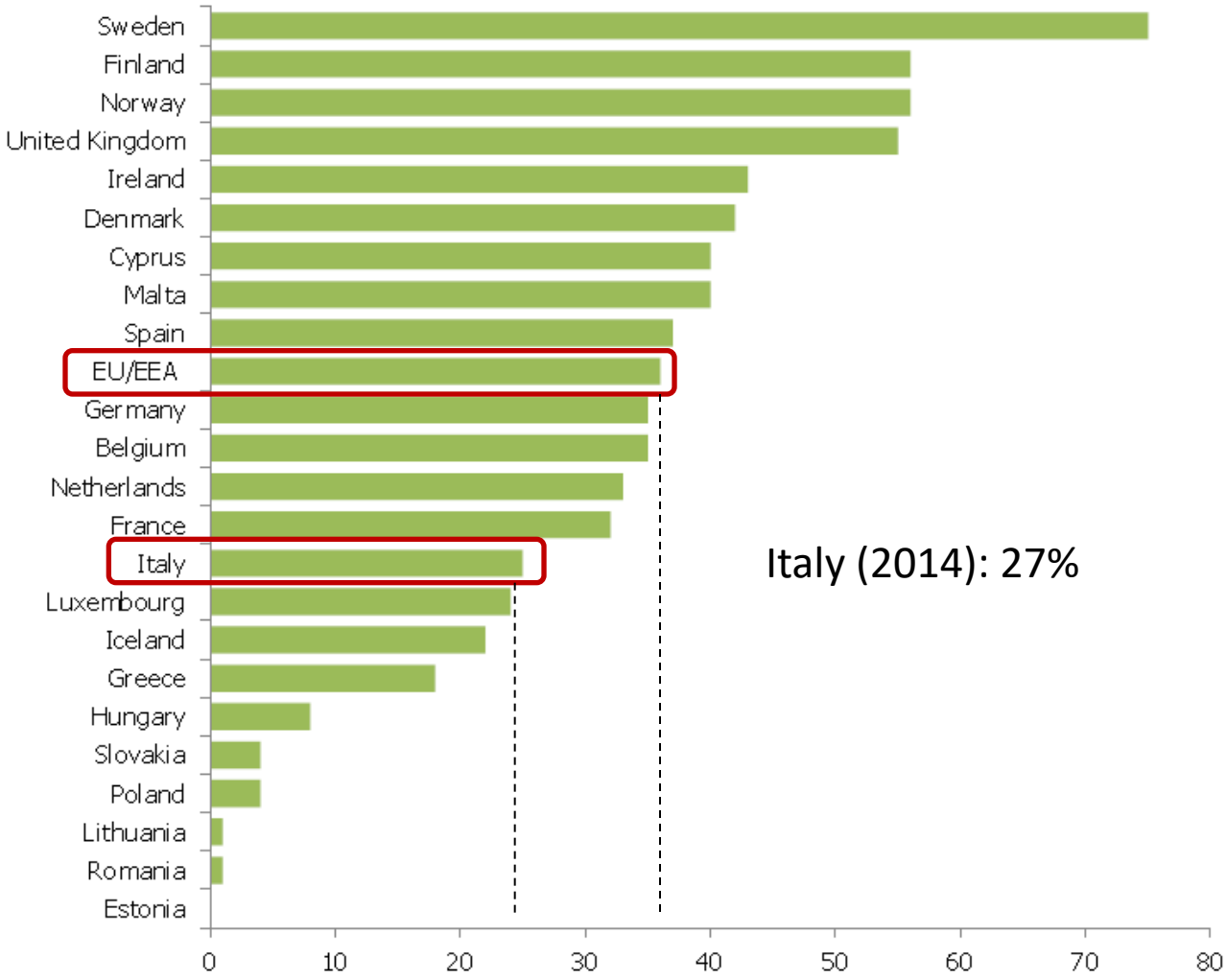


Of an estimated 58.8 million annual deaths worldwide, approximately 15.0 million (25%) are believed to be caused by infectious diseases.

I am a migrant.
I face these issues.

The gap report. UNAIDS 2014.

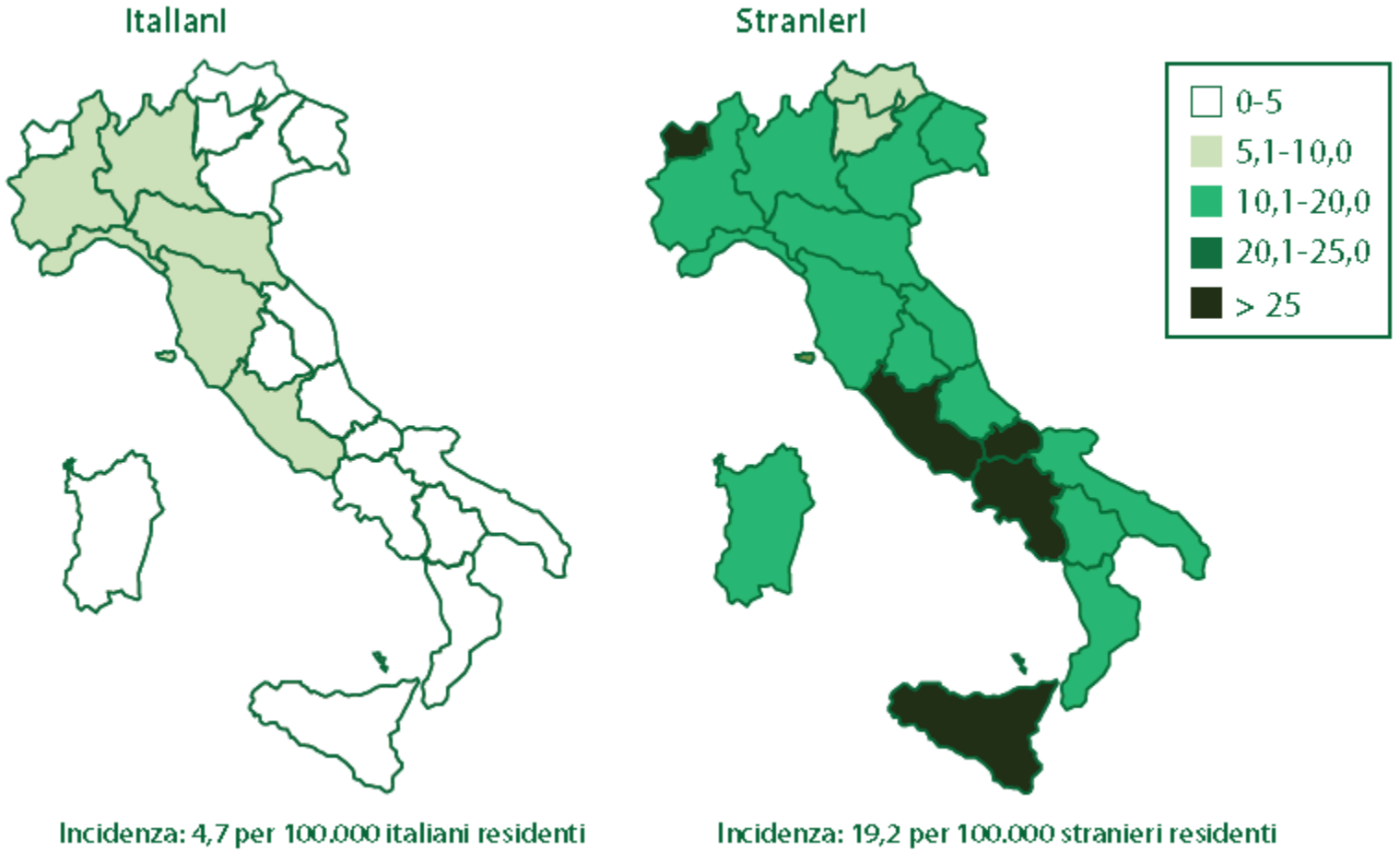
Proportion of migrants among new reported HIV cases, EU/EEA



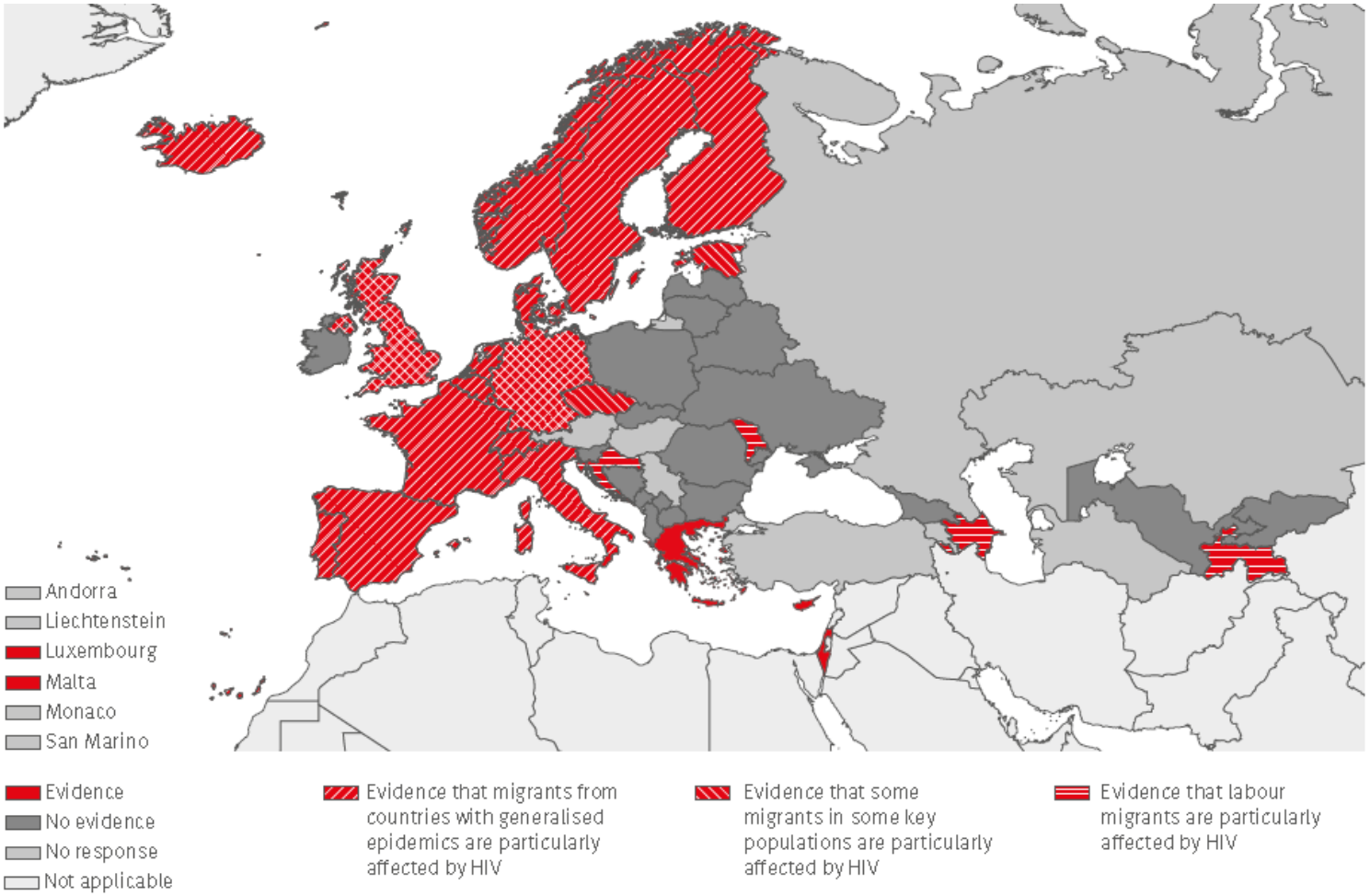
Italy (2014): 27%

Source: European Centre for Disease Prevention and Control (2013) [10]

Incidenza delle nuove diagnosi di infezione da HIV per nazionalità e regione di residenza (2014)



Evidence reported by European and Central Asian countries that migrants are particularly affected by HIV



Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2012 progress report

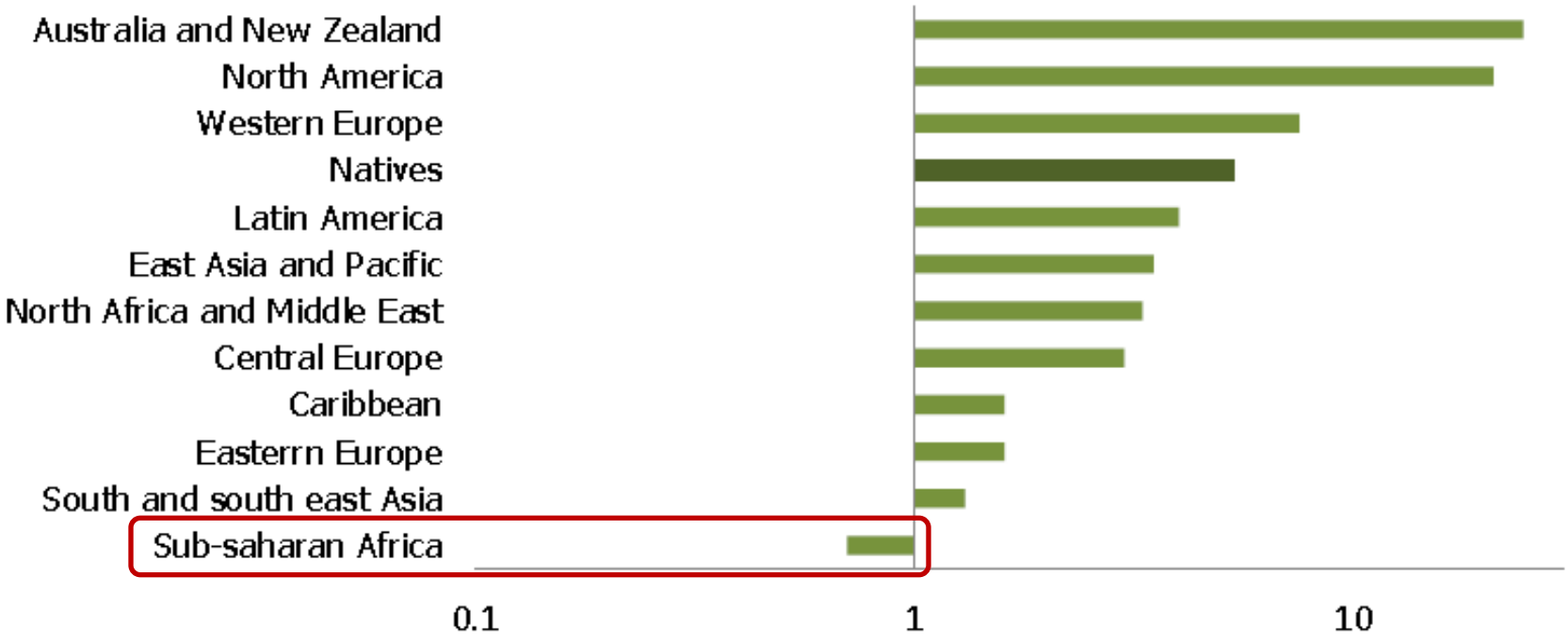
www.ecdc.europa.eu

Acquisition of HIV after arrival in the EU/EEA

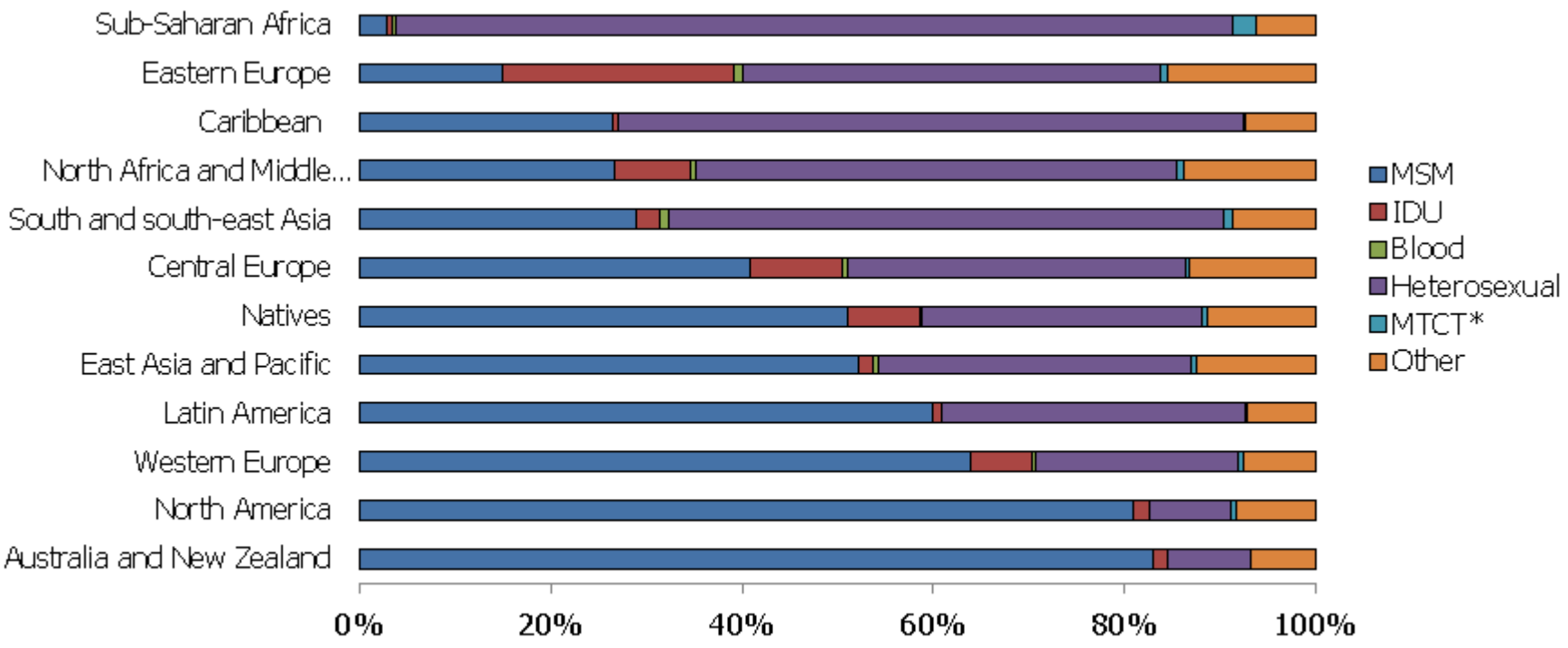
- ✓ **Data from Europe (ECDC Survey 2013)**
  - Norway (2011): **14%**
  - UK (2010): **46%** of migrants heterosexually acquired HIV infections in UK;
  - France (2011): at least **25%** among Sub-Saharan people

- ✓ A **recent metanalysis** (Fakoya et al. BMC Public Health, 2015) showed that HIV infections acquired after migration ranged from **2.0%** among sub-Saharan Africans in Switzerland to **62%** among black Caribbean MSM in the UK

Male-to-female ratio in newly diagnosed HIV cases, by region of origin, 2007–2011



Reported HIV cases by transmission category and geographical origin, EU/EEA, 2007– 2011 (n=125 225)



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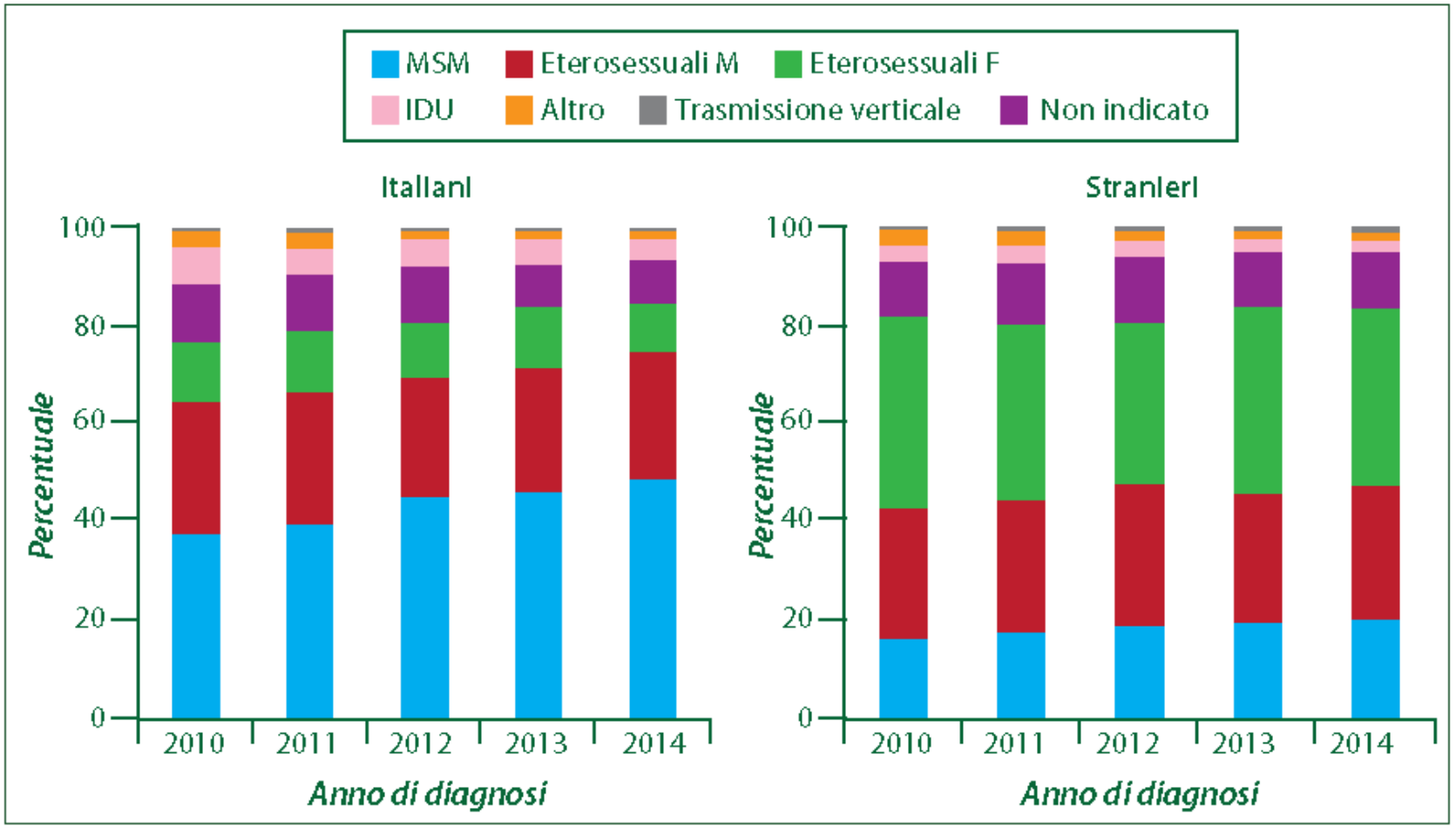
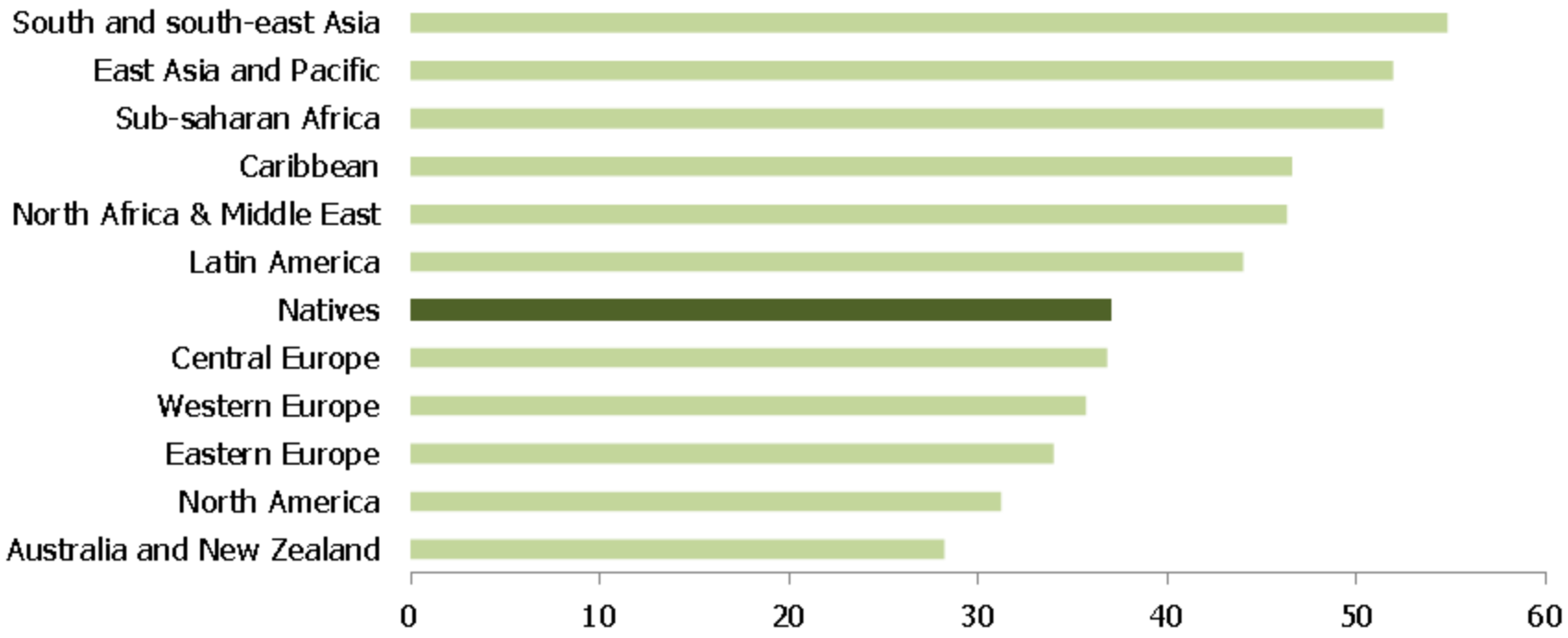
Distribuzione delle nuove diagnosi di infezione da HIV, per modalità di trasmissione, anno di diagnosi e nazionalità (2010-2014)



ISS-CoA_Dec2015

Late diagnosis of HIV in migrants



Percentage of late HIV diagnosis, by geographic origin, EU/EEA, 2007–2011

(CD4 cell count <350 cells/mm3 or AIDS)

www.ecdc.europa.eu

Clinical and epidemiological features of HIV/AIDS infection among migrants at first access to healthcare services as compared to Italian patients in Italy: a retrospective multicentre study, 2000–2010

G. Sulis · I. El Hamad · M. Fabiani · S. Rusconi · F. Maggiolo · G. Guaraldi · G. Bozzi · C. Bernardini · M. Lichtner · C. Stentarelli · L. Carenzi · D. Francisci · A. Saracino · F. Castelli · The HIV/Migrants Study Group

Logistic regression analysis of variables associated with late presentation

Variable	Number[a]	Adjusted odds ratio (95% CI)	*P*-value
Mode of transmission			
Heterosexual	2487	1	
MSM[b]	1255	0.51 (0.44-0.60)	< 0.001
Injecting drug users	1061	0.89 (0.76-1.05)	0.160
Other/undetermined	216	0.98 (0.74-1.32)	0.915
Age			
< 30 years	1150	1	
30-39 years	2073	1.72 (1.48-2.00)	< 0.001
40-49 years	1232	2.76 (2.31-3.29)	< 0.001
≥ 50 years	564	3.89 (3.09-4.91)	< 0.001
Sex			
Females	1397	1	
Males	3622	1.19 (1.03-1.38)	0.020
Country of origin			
Italy	3695	1	
Other	1324	1.77 (1.53-2.05)	< 0.001

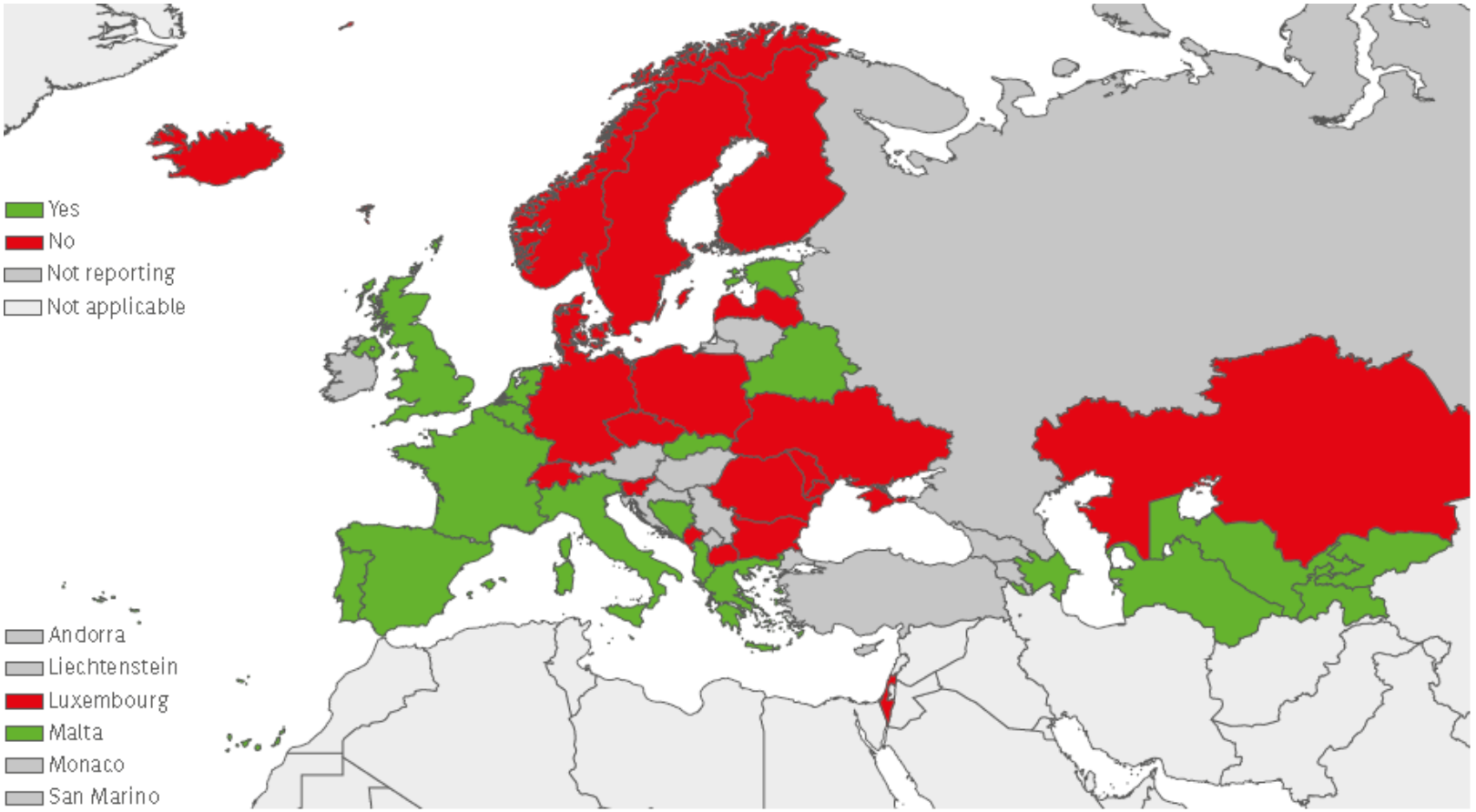
[a] This model is based on a total of 5019 cases (85.9%) for which all information were available.

Infection 2014

Barriere per Screening e counselling

- Informazioni scarse e poco chiare circa i diritti dei migranti all'assistenza sanitaria nel paese di destinazione
- Difficoltà linguistica che impedisce una comunicazione esauriente in ambito sanitario
- Differenze culturali e comportamentali
- Bassa percezione del rischio di infezione da HIV nei migranti
- Stigma e discriminazione in alcune comunità di migranti
- Povertà ed il basso statuts sociale

Countries reporting whether antiretroviral therapy is available for undocumented migrants



Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2012 progress report

www.ecdc.europa.eu

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

Analysis of factors influencing the probability to be on HAART

	OR	(95% CI)	P- value
• Male sex	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
omosexual	3.57	(0.82 – 21.89)	0.06
• Legal status	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 (≤10 yrs vs > 10 yrs)	0.62	(0.22 – 1.64)	0.3
• Employement	2.05	(0.92 – 4.51)	0.05
• Use of intercultural mediator	2.11	(0.69 – 7.16)	0.1

Saracino et al, AIDS Patient Care 2005

Possibili determinanti di disparità nella risposta alla ART per gli immigrati HIV-positivi rispetto ai nativi

- **Caratteristiche virali** (sottotipo HIV-1, tropismo corecettoriale. tasso di TDR)

- **Fattori genetici dell'ospite** (es. HLA B5701)

- Epidemiologia di **co-infezioni o comorbidità (es. TB, HIVAN)**

- Dieta e stile di vita

- **Fattori culturali** (stigma, diversa percezione di malattia)

- Barriere all'**accesso alle cure**

- Differenti profili di **tollerabiilità ed effetti collaterali**

ART-CC, CID 2013; McFall for WIHS, JAIDS 2013; Pérez Molina JA et al., HIV Clin Trials. 2012; Jarrin I et al, CID 2012

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

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

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

✓ **5773 HIV-positive, ART-naïve patients enrolled from 2004 to 2014**

	Migrants **1175 (20.4%)**	**Natives** **4598 (79.6%)**	**p**
Male gender, n(%)	670 (57.0%)	3914 (85.1%)	<0.001
Age, yrs, median (IQR)	34 (28-40)	39 (32-47)	<0.001
Nationality, n(%)			
Sub-Saharan Africa (SSA)	416 (35.5%)	-	
Latin America (LA)	342 (29.1%)	-	
Western Country (WE)	319 (27.1%)	-	
North Africa and Middle East (NAME)	47 (4.0%)	-	
Asia (ASIA)	51 (4.3%)	-	
Years of residency in Italy, median (IQR)	5 (1-10)	-	
Months from first HIV test and first visit, median (IQR)	1.2 (0.4-8.4)	2.2 (0.5-16.1)	<0.001
Mode of HIV transmission, n(%)			
Heterosexual contacts	702 (59.7%)	1634 (35.5%)	<0.001
Homosexual contacts	310 (26.4%)	2194 (47.7%)	
IVDU	47 (4.0%)	436 (9.5%)	
Other/unknown	116 (9.9%)	334 (7.3%)	

Baseline characteristics

	Migrants 1175 (20.4%)	Natives 4598 (79.6%)	p
HIV Subtype, n (%)			
B subtype	203 (17.2%)	1344 (29.2%)	<0.001
Non-B subtype	215 (18.3%)	316 (6.9%)	
Unknown	757 (64.5%)	2938 (63.9%)	
Pregnancy status at enrolment, n (%)	51 (4.3%)	17 (0.4%)	<0.001
CDC C stage at enrolment, n (%)	138 (11.7%)	362 (7.9%)	<0.001
First HIV RNA, log cp/mL, median(IQR)	4.5 (IQR 3.7-5.2)	4.6 (IQR 3.9-5.2)	0.008
First CD4 count, cell/mmc, median (IQR)	317 (IQR 137-509)	396 (223-577)	<0.001
First CD4 cell/mmc, n(%)			
<200	323 (27.5%)	876 (19.1%)	0.003
200-350	225 (19.1%)	732 (15.9%)	
>350	440 (37.5%)	2197 (47.7%)	
missing	187 (15.9%)	793 (17.3%)	
HCV co-infection, n (%)			
Positive	70 (6.0%)	446 (9.7%)	<0.001
Negative	792 (67.4%)	2882 (62.7%)	
Unknown	313 (26.6%)	1270 (27.6%)	
HBV co-infection, n (%)			
Positive	58 (4.9%)	144 (3.1%)	0.008
Negative	782 (66.6%)	3060 (66.6%)	
Unknown	335 (28.5%)	1394 (30.3%)	
CMV co-infection, n (%)			
Negative	43 (3.7%)	246 (5.3%)	<0.001
Positive	492 (41.9%)	1579 (34.3%)	
Unknown	640 (54.4%)	2773 (60.4%)	
Sexually Transmitted Diseases (STDs)*, n (%)	97 (8.2%)	425 (9.2%)	0.292

A total of 4126 patients (71.5%) had initiated ART at the time of analysis:

- 842 migrants (71.7%)
- 3284 natives (71.4%)

At multivariable analysis:

• **migrant status resulted associated with a reduced frequency of ART initiation compared to natives**

• the main confounder of the association between migration and use of ART was the CD4 cell count at enrolment (p at interaction test <0.001)

Table 2. Logistic regression analysis of factors associated with ART initiation.

	OR	95% CI		p	AOR	95% CI		p
Male gender vs female	0.87	0.75	1.00	0.057	1.11	0.91	1.36	0.307
Age (per 10 years 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								
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								
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								
Heterosexual contacts	1.00				1.00			
Homosexual contacts	0.57	0.50	0.65	<0.001	0.77	0.65	0.91	0.002
IVDU	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
HIV RNA, log cp/mL at enrolment								
<4	1.00				1.00			
4-4.999	1.49	1.28	1.73	<0.001	1.42	1.20	1.67	<0.001
>=5	4.44	3.67	5.37	<0.001	2.61	2.11	3.23	<0.001
Missing data	1.13	0.96	1.34	0.130	0.85	0.64	1.13	0.260
CD4 cell/mmc at enrolment								
<200	1.00				1.00			
200-350	0.48	0.35	0.65	<0.001	0.68	0.49	0.94	0.020
>350	0.09	0.07	0.11	<0.001	0.13	0.10	0.17	<0.001
Missing data	0.12	0.09	0.15	<0.001	0.24	0.17	0.35	<0.001
Smoking habit								
no	1.00				1.00			
yes	0.81	0.71	0.93	0.002	0.93	0.80	1.08	0.359
Unknown	0.86	0.74	1.00	0.047	0.98	0.83	1.18	0.864
Pregnancy status at enrolment	4.18	1.80	9.67	0.001	6.21	2.58	14.93	<0.001
CDC C stage at enrolment	5.07	3.65	7.04	<0.001	2.36	1.64	3.39	<0.001
HBV-Ag								
negative	1.00				1.00			
positive	1.48	1.05	2.08	0.024	1.39	0.95	2.02	0.009
Unknown	1.07	0.94	1.21	0.305	1.36	1.17	1.57	<0.001

Type of ART

	Migrants 1175 (20.4%)	Natives 4598 (79.6%)	p
Type of first regimen, n(%)			
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%)	
No ART start	333 (28.3%)	1314 (28.6%)	

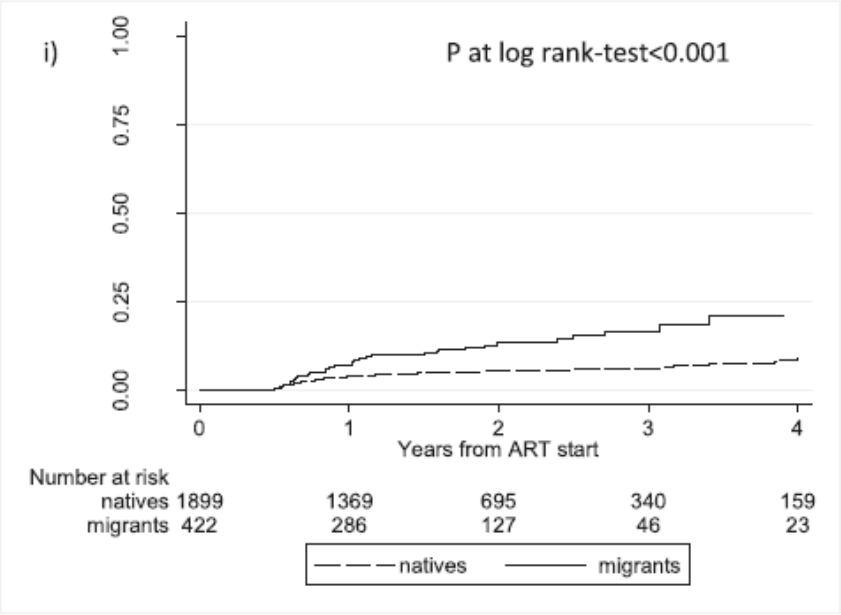
ART outcome

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

- The multivariable models confirmed that migrants had a significantly higher rate of both VF (incidence rate ratio (IRR) 1.90, 95% CI 1.25–2.91, p 0.003) and TF (IRR 1.16, 95% CI 1.01–1.33, p 0.031), while no difference was observed for the TD rate.

✓ **5773 HIV-positive, ART-naïve patients enrolled from 2004 to 2014**

Virological failure



Treatment failure

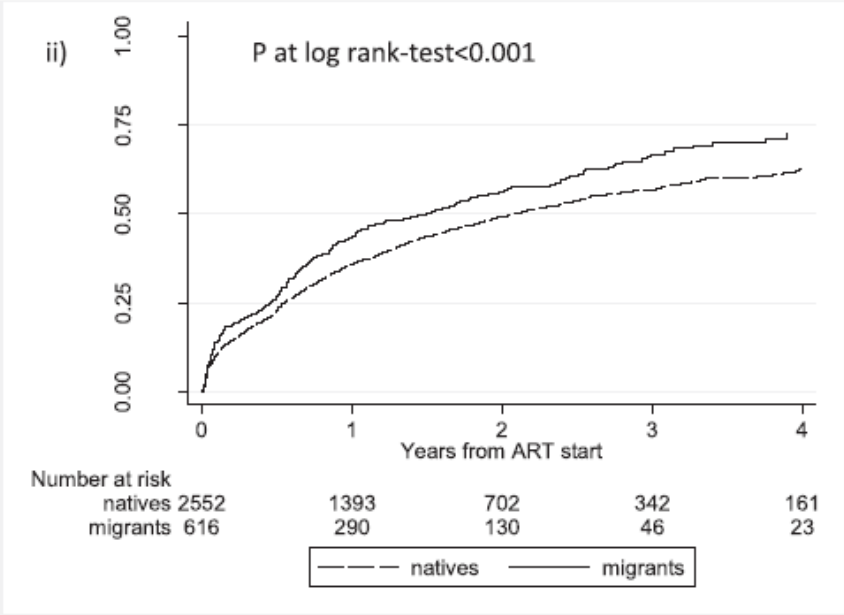


FIG. 1. Kaplan-Meier curves representing cumulative probability of (i) virologic failure (HIV RNA >200 copies/mL) and (ii) treatment failure of first antiretroviral regimen.

Determinants of failure

Table 3. Multivariable Poisson regression models of factors significantly associated with virological failure (VF) and treatment failure (TF).

	VF				TF			
	ARR	95% CI		p	ARR	95% CI		p
Male gender vs female	0.87	0.54	1.40	0.574	0.80	0.70	0.91	0.001
Migrants vs natives	1.90	1.25	2.91	0.003	1.16	1.01	1.33	0.031
Occupation								
Full-time worker	1.00				1.00			
Unemployed	2.09	1.31	3.32	0.002	1.15	0.99	1.34	0.074
CD4 cell/mmc at enrolment								
<200	1.00				1.00			
200-350	0.57	0.37	0.90	0.016	0.83	0.72	0.95	0.008
>350	0.57	0.35	0.93	0.024	0.93	0.81	1.07	0.317
Missing data	0.86	0.35	2.12	0.739	0.93	0.72	1.21	0.597
CDC C stage at enrolment	2.36	1.64	3.39	<0.001	1.14	0.98	1.33	0.084
Tuberculosis before enrolment	-	-	-	-	1.51	1.05	2.15	0.025
Pregnancy status at enrolment	-	-	-	-	2.25	1.57	3.21	0.000
Type of first regimen								
nrti+nnrti	1.00				1.00			
nrti+pib	1.79	1.19	2.69	0.005	1.55	1.39	1.74	0.000
nrti+ii	1.13	0.27	4.74	0.869	0.96	0.63	1.46	0.840
nrti-sparing	2.13	0.82	5.53	0.121	1.44	1.07	1.92	0.015
other	4.05	1.91	8.59	0.000	3.56	2.92	4.35	0.000

Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study

The TenoRes Study Group*

Lancet Infect Dis 2016; 16: 565–75

1926 patients from 36 countries with TF between 1998 and 2015

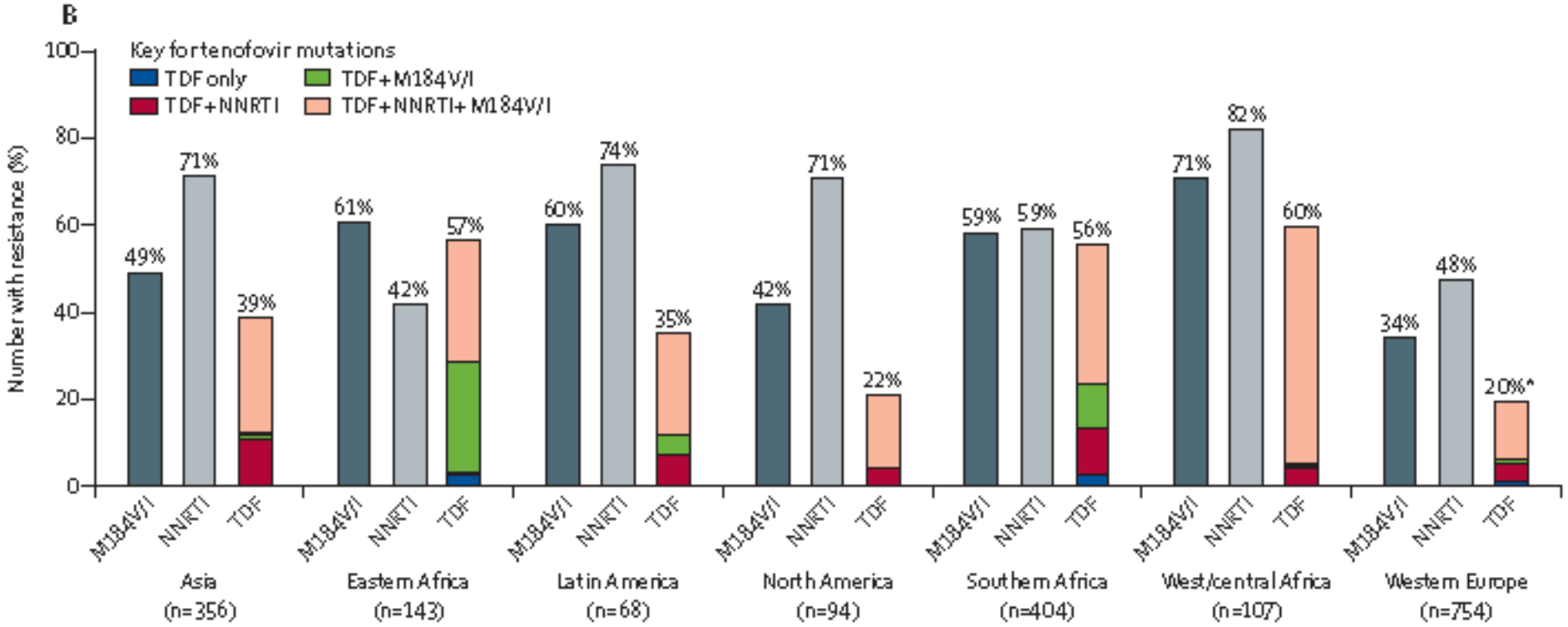
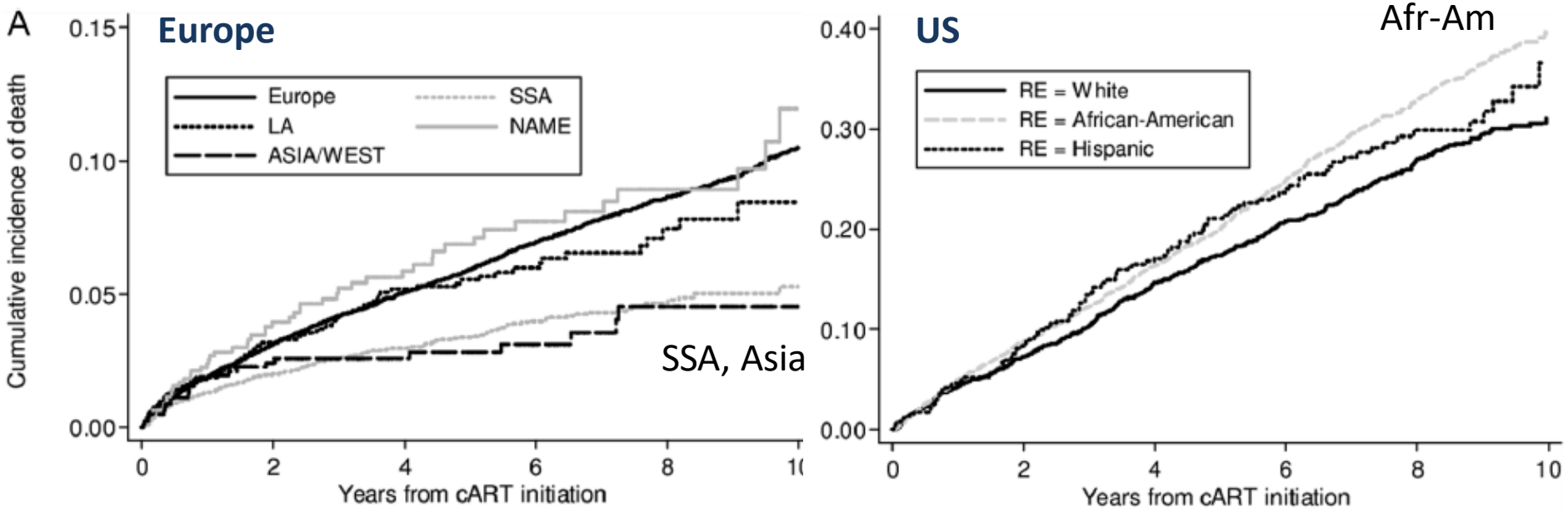


Fig (B) prevalence of drug resistance by mutation and by region

*24% (n=462) of participants had tenofovir resistance when genotypes from VL>1000 copies HIV-1 RNA per mL were considered.

Influence of Geographical Origin and Ethnicity on Mortality in Patients on ART in Canada, Europe, and US



Conclusions. The lower mortality observed in migrants suggests "healthy migrant" effects, whereas the higher mortality in First Nations people and African Americans in North America suggests social inequality gaps.

ART-CC, CID 2013

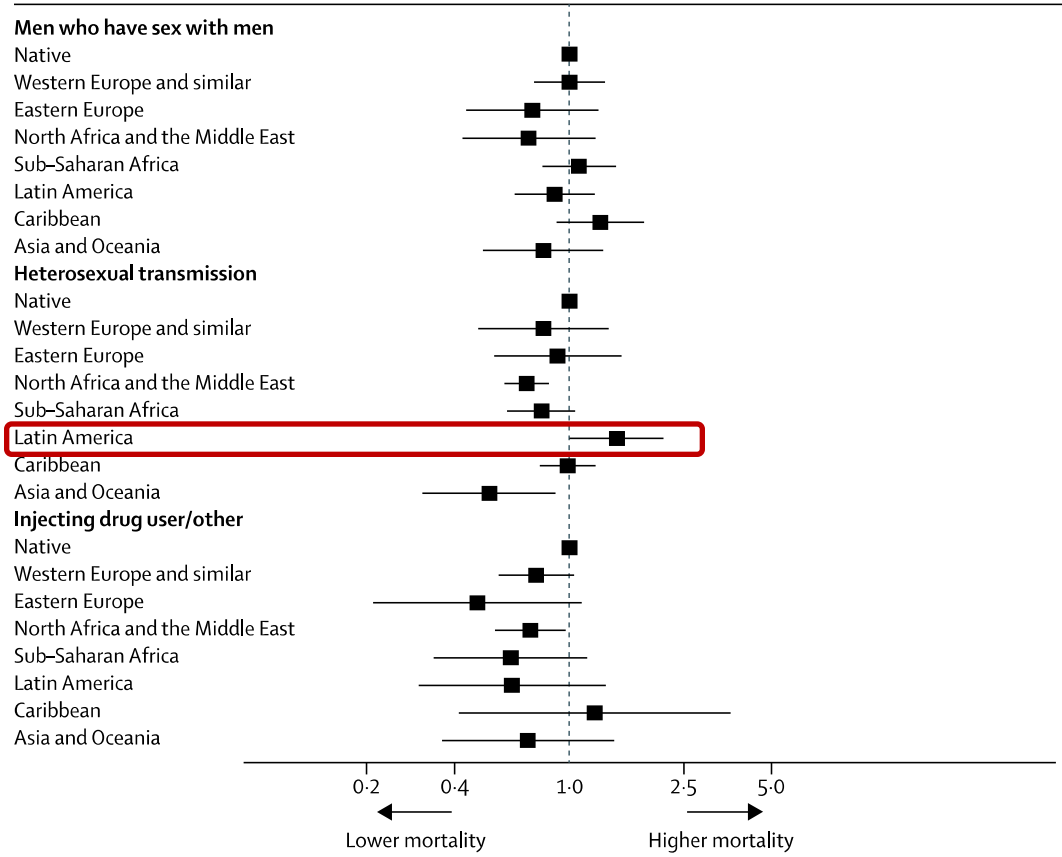
Mortality in migrants living with HIV in western Europe (1997–2013): a collaborative cohort study

*The Migrants Working Group on behalf of COHERE in EuroCoord**

Lancet HIV 2015

N=279 659 individuals

Men



	aRR (95% CI)	p values	cRR (95% CI)
Men who have sex with men			
Native	1		1
Western Europe and similar	1·00 (0·75–1·33)	p=1·00	1·07 (0·78–1·45)
Eastern Europe	0·74 (0·44–1·26)	p=0·27	0·56 (0·32–1·00)
North Africa and the Middle East	0·72 (0·43–1·23)	p=0·23	0·76 (0·43–1·33)
Sub-Saharan Africa	1·08 (0·81–1·44)	p=0·60	0·88 (0·62–1·26)
Latin America	0·89 (0·64–1·22)	p=0·46	0·75 (0·54–1·04)
Caribbean	1·28 (0·90–1·82)	p=0·17	1·08 (0·75–1·56)
Asia and Oceania	0·81 (0·50–1·31)	p=0·39	0·73 (0·46–1·17)
Heterosexual transmission			
Native	1		1
Western Europe and similar	0·81 (0·48–1·37)	p=0·43	0·88 (0·54–1·42)
Eastern Europe	0·91 (0·55–1·52)	p=0·72	0·66 (0·40–1·09)
North Africa and the Middle East	0·71 (0·60–0·85)	p<0·0001	0·79 (0·62–1·01)
Sub-Saharan Africa	0·80 (0·61–1·05)	p=0·10	0·65 (0·50–0·84)
Latin America	1·46 (1·00–2·12)	p=0·049	1·19 (0·72–1·97)
Caribbean	0·99 (0·79–1·23)	p=0·90	0·90 (0·71–1·13)
Asia and Oceania	0·53 (0·31–0·90)	p=0·02	0·47 (0·26–0·85)
Injecting drug user/other			
Native	1		1
Western Europe and similar	0·77 (0·57–1·03)	p=0·08	0·86 (0·60–1·24)
Eastern Europe	0·48 (0·21–1·10)	p=0·08	0·38 (0·18–0·78)
North Africa and the Middle East	0·73 (0·55–0·97)	p=0·03	0·83 (0·63–1·10)
Sub-Saharan Africa	0·63 (0·34–1·15)	p=0·13	0·68 (0·42–1·11)
Latin America	0·63 (0·30–1·33)	p=0·23	0·70 (0·34–1·44)
Caribbean	1·22 (0·41–3·62)	p=0·72	1·16 (0·42–3·17)
Asia and Oceania	0·72 (0·36–1·42)	p=0·34	0·76 (0·37–1·57)

High mortality was identified in heterosexual men from Latin America [RR=1·46, 95% CI 1·00–2·12, p=0·049]

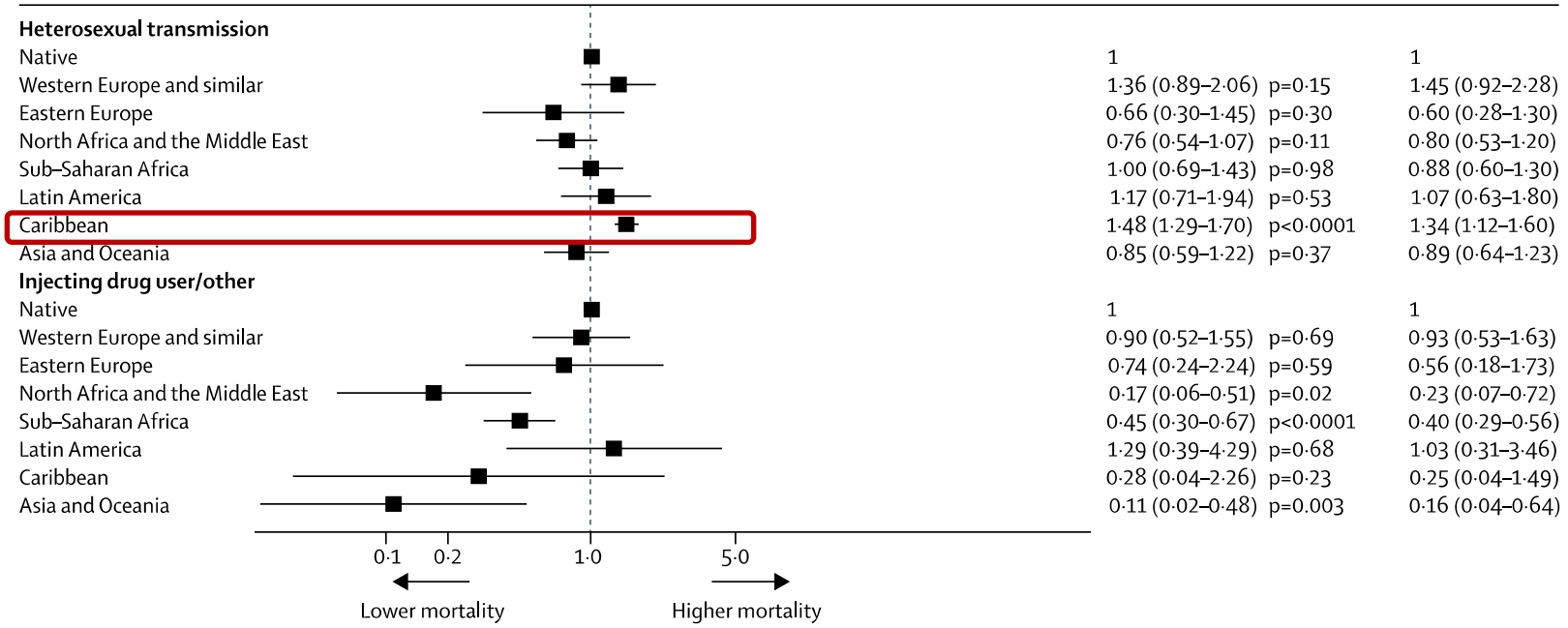
Mortality in migrants living with HIV in western Europe (1997–2013): a collaborative cohort study

*The Migrants Working Group on behalf of COHERE in EuroCoord**

Lancet HIV 2015

N=279 659 individuals

Women



High mortality was identified heterosexual women from the Caribbean [RR=1·48, 1·29–1·70, p<0·0001]

Conclusioni

- La diagnosi di infezione da HIV nella popolazione migrante è tardiva rispetto alla popolazione italiana, pertanto è fondamentale incrementare lo screening nella popolazione migrante.

- Nonostante i migranti abbiano diritto all'assistenza sanitaria, sono scarsamente inclini allo screening ed alla ART; configurando quella fascia della popolazione associata ad un maggiore tasso di fallimento terapeutico.

- La popolazione migrante non è una popolazione omogenea, vanno pertanto studiate le diseguaglianzedei popoli, è mantenute le differenze nei gruppi a rischio

- Sono da preferirsi regimi di trattamento più semplici che favoriscano la compliance