



**UNIVERSITA' DEGLI STUDI DI
MODENA E REGGIO EMILIA**
Clinica delle Malattie Infettive e Tropicali

Il ritardo di diagnosi nell'infezione da HIV: come intervenire

Cristina Mussini

Immunodeficiency at the start of cART

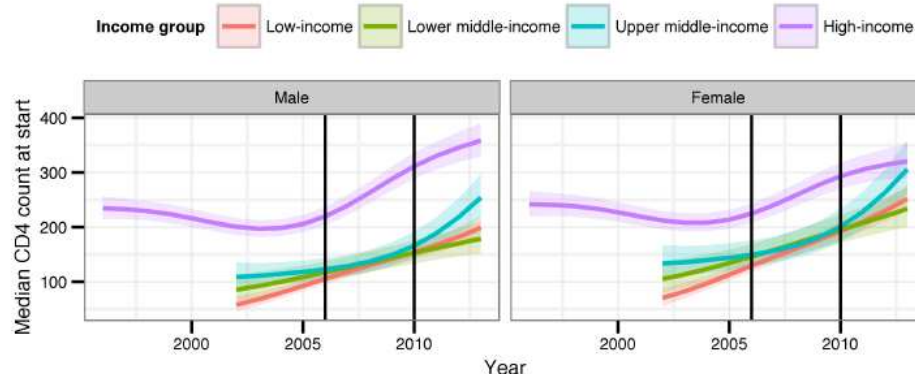


Figure 2. Modeled median CD4 by gender and country income group.
Vertical lines indicate the changes in WHO guidelines on when to start ART.

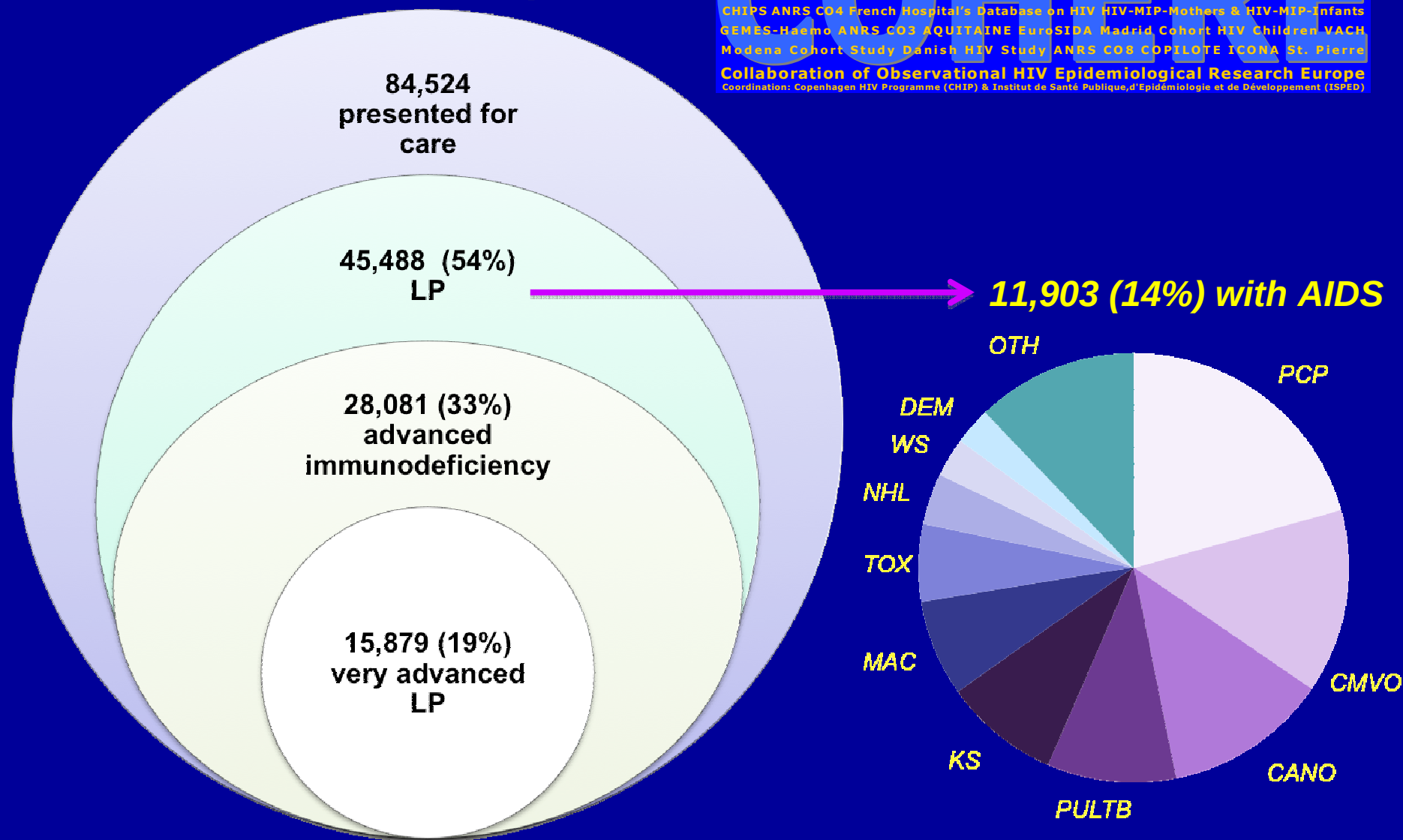
Panayidou et al. Abs 1094

	Low-income		Lower middle-income		Upper middle-income		High-income	
No. of patients	194,005		232,158		128,639		191,844	
No. of countries	14		6		6		15	
Median year of starting ART	2009		2008		2009		2005	
Median age	36		35.3		34.7		38.9	
% Women	64%		62%		64%		24%	
Median CD4 count (cells/ μ L)	Male	Female	Male	Female	Male	Female	Male	Female
2002	63	78	88	112	104	124	201	209
2004	82	102	101	128	114	136	199	206
2006	105	130	117	148	124	148	220	224
2008	129	161	135	171	139	167	262	258
2010	155	194	154	196	168	201	308	296
2011	169	211	164	209	189	226	327	311
2012	184	231	173	222	216	258	343	322
2013	200	252	183	235	248	297	357	333
Overall 2002 - 2013	136		146		150		249	
Change 2002 - 2013	+137	+174	+95	+123	+144	+172	+156	+124

Table 1. Characteristics of study population by country income group (World Bank classification).

LP across Europe :

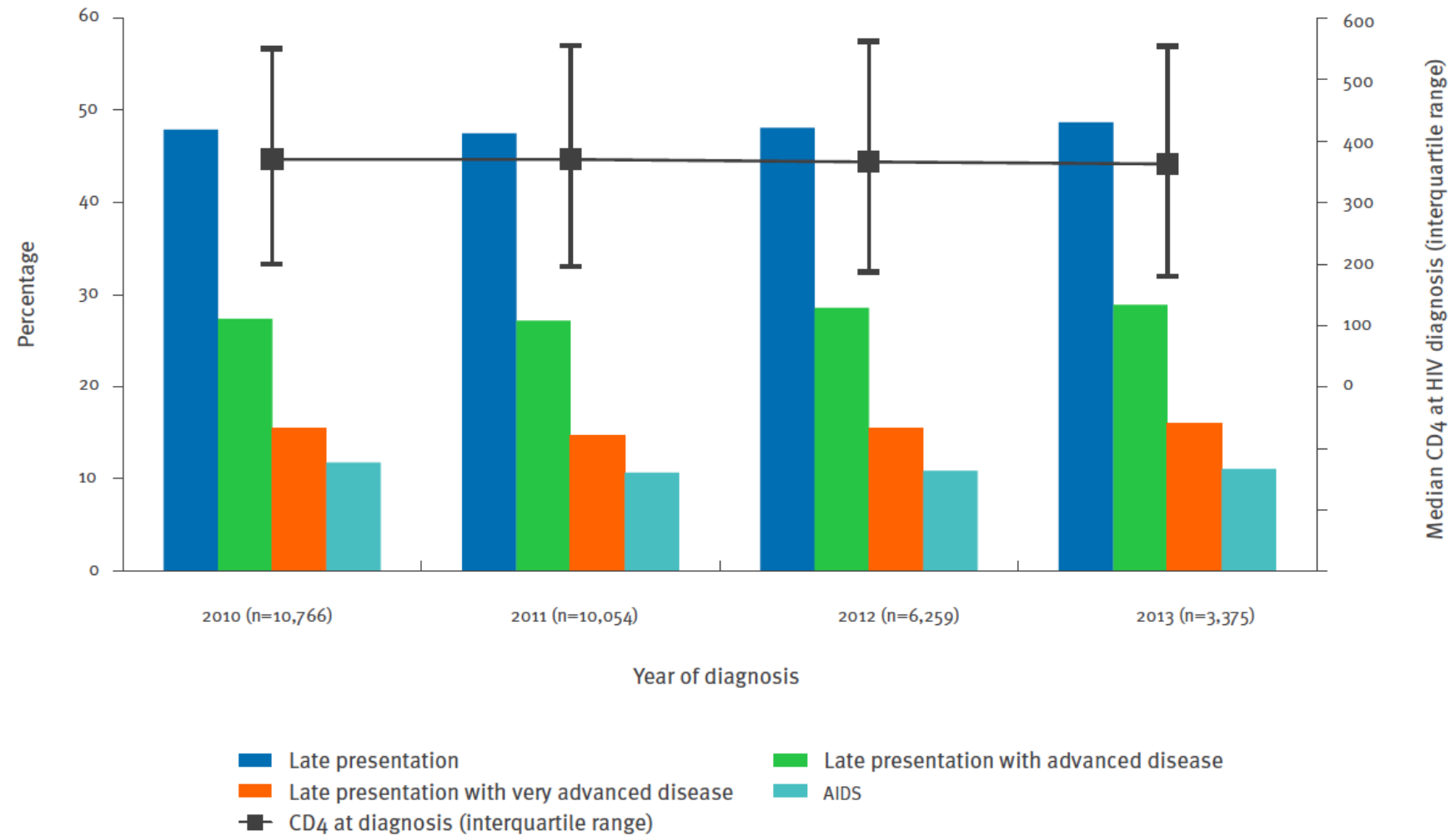
IMIT AMACS ECS-Mothers & ECS-Infants NSMPC-Mothers & NHPS-Infants PISCIS
 KOMPNET CASCADE ANRS CO2 SEROCO Frankfurt-HIV Cohort Study San Raffaele
 ANRS CO1/CO10 EPF UK CHIC Athena ITLR-Mothers & ITLR-Infants Swiss HIV Cohort Study
 ICC ANRS CO6 PRIMO Co-RIS MOCHIV-Mothers & MoCHIV-Infants The Italian MASTER Cohort
 CHIPS ANRS CO4 French Hospital's Database on HIV HIV-MIP-Mothers & HIV-MIP-Infants
 GEMES-Haemo ANRS CO3 AQUITAINE EuroSIDA Madrid Cohort HIV Children VACH
 Modena Cohort Study Danish HIV Study ANRS CO8 COPILOTE ICONA St. Pierre
Collaboration of Observational HIV Epidemiological Research Europe
 Coordination: Copenhagen HIV Programme (CHIP) & Institut de Santé Publique, d'Epidémiologie et de Développement (ISPED)



LP : CD4 < 350/AIDS; advanced immunodeficiency : CD4 < 200/AIDS;
 very advanced LP : CD4 < 50/AIDS

IAC Washington 2012

Changes over time in stages of late presentation and CD4 count at HIV diagnosis, COHERE study, 2010–2013 (N=30,454)



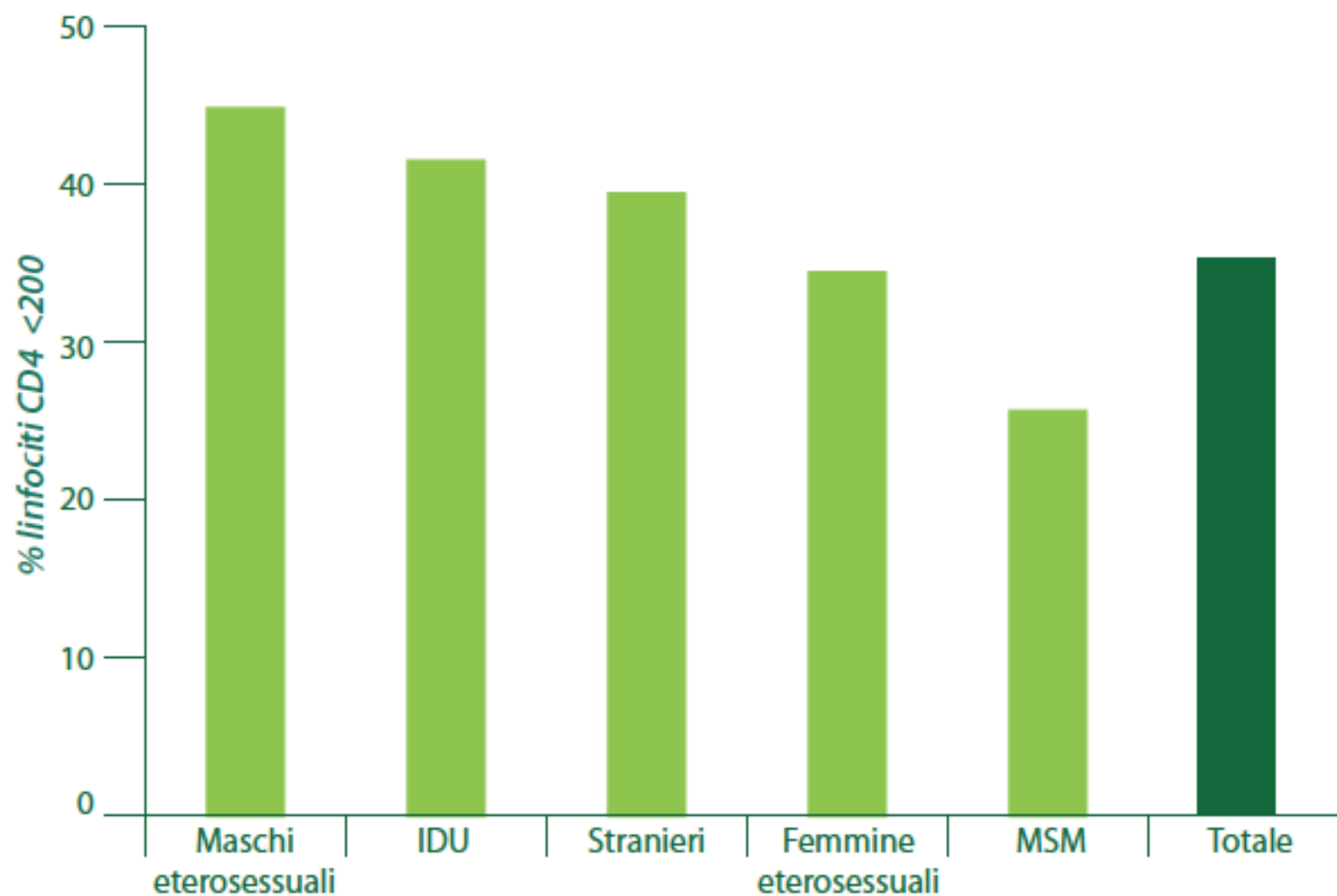
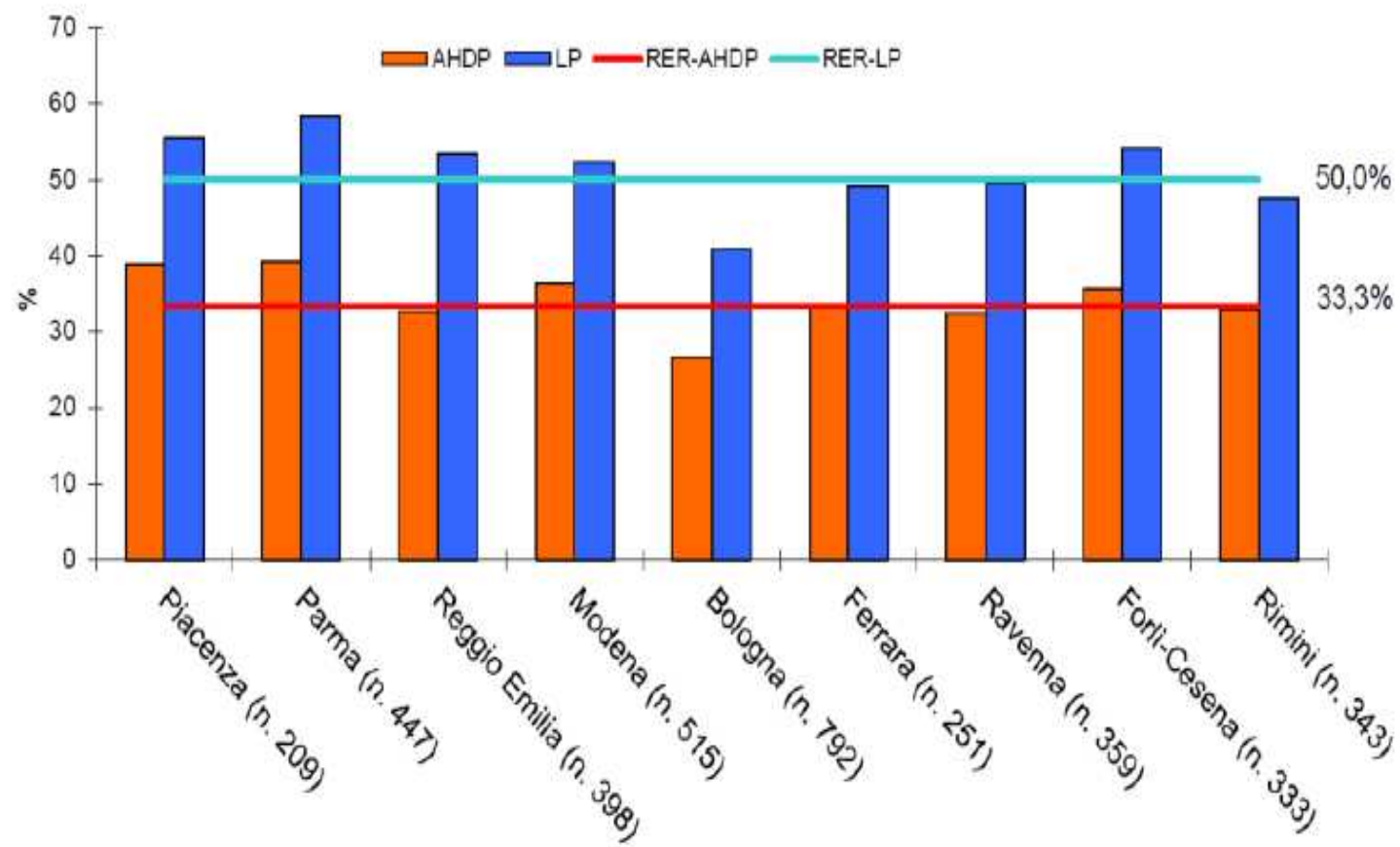


Figura 6 - Caratteristiche delle persone con una nuova diagnosi di infezione da HIV e CD4 <200 cell/μL (Anno 2011)

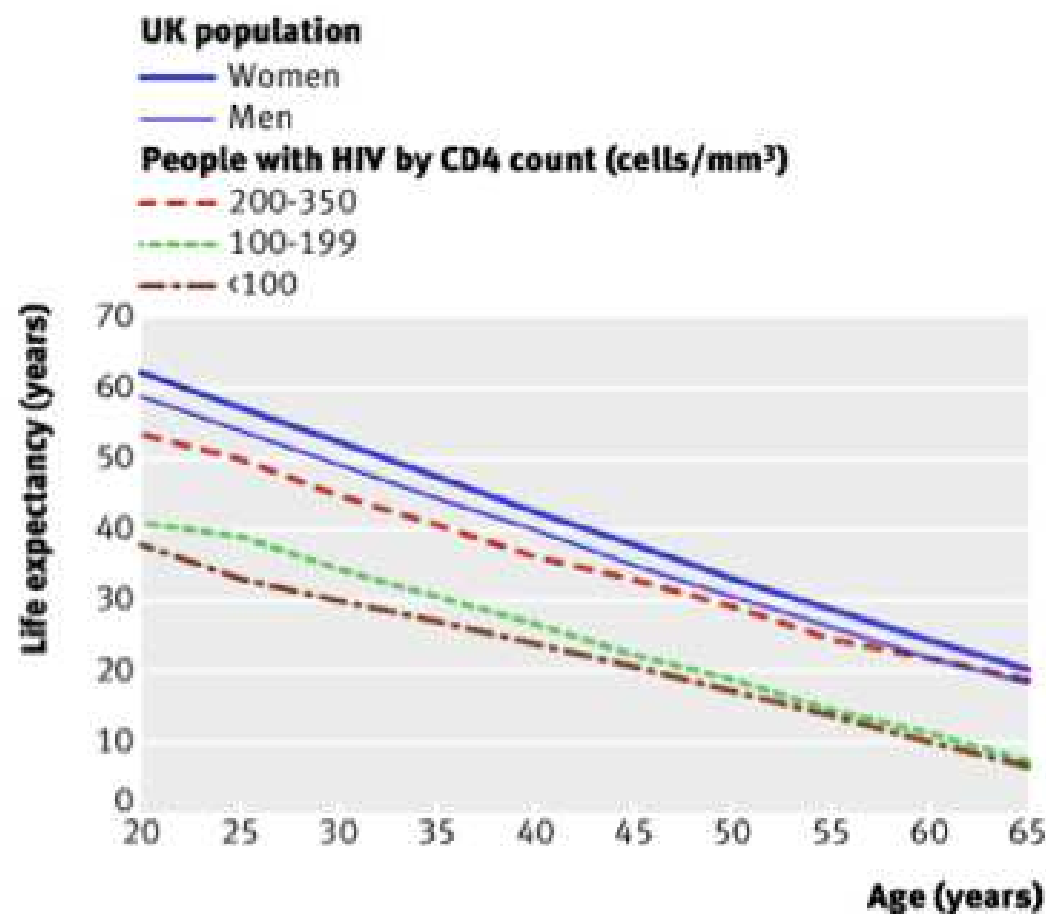


Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study

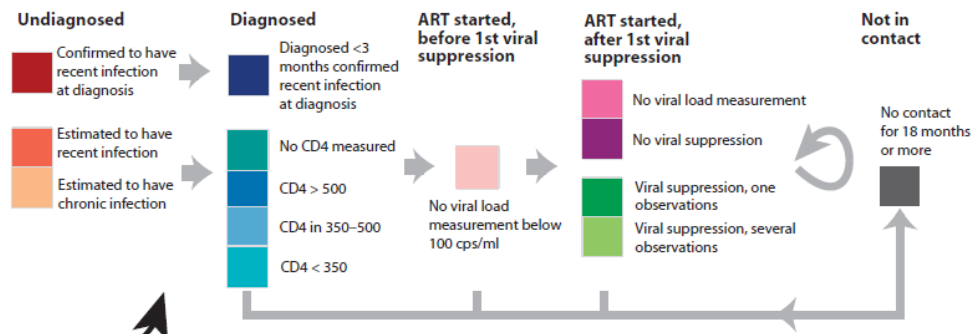
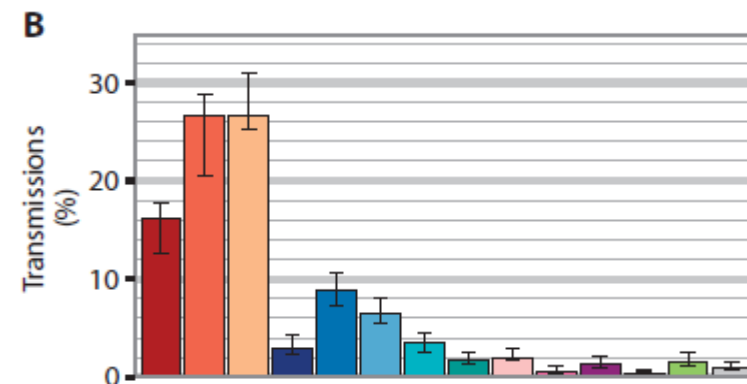
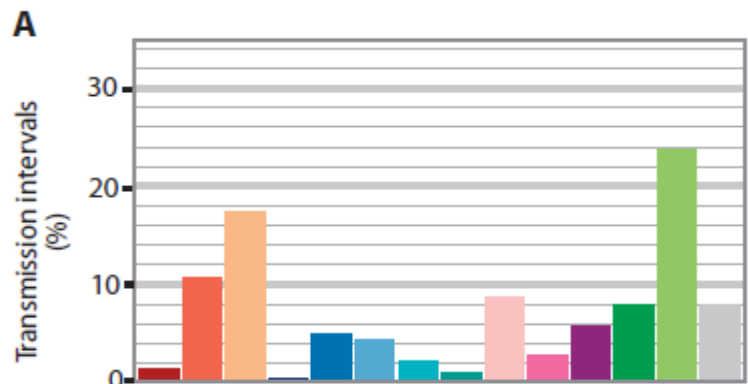
 OPEN ACCESS

Life expectancy from age 20-65 of people who started antiretroviral therapy in 2000-8 by CD4 cell count group at start of antiretroviral therapy compared with that of UK population (2000-6 women and men)

BMJ 2011;343:d6016 doi:
10.1136/bmj.d6016



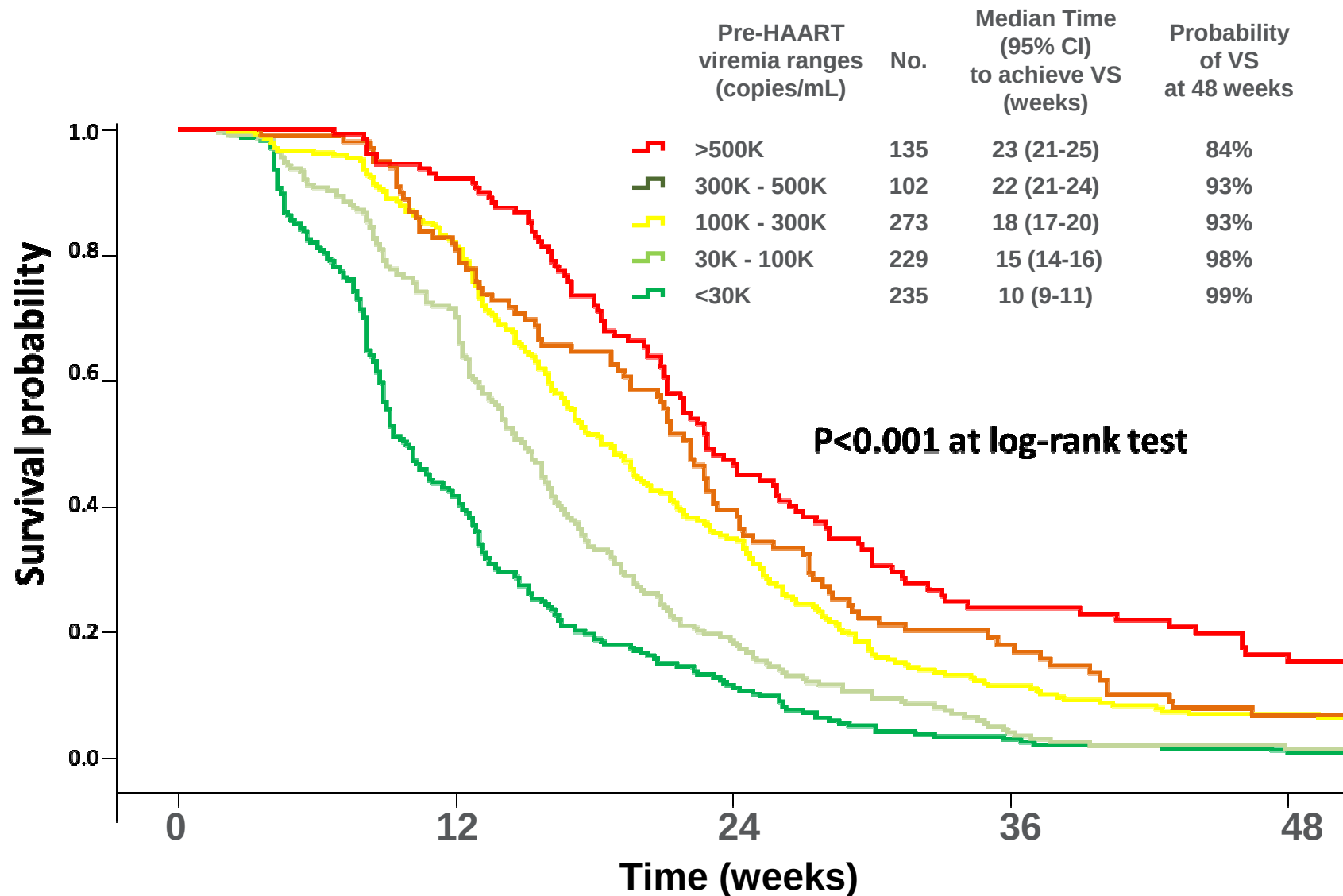
Proportion of transmissions by stage in the infection and care continuum versus proportion of these stages among infected men The Netherlands



- 71% of transmission events originated from undiagnosed men
- 22% from diagnosed but not yet treated men
- 6% from men who initiated ART
- 1% from men with no contact to care for at least 18 months.
- An estimated 43% of the recipient MSM were infected by men undergoing their first year of infection.

**Come si caratterizzano da un punto di
vista viro-immunologico?**

The time to achieve virological undetectability and the rate of success at 48 week are pre-HAART viremia dependent



Perno et al., EACS 2011
Santoro et al. Antivir Ther 2013

Normalisation of CD4 counts in patients with HIV-1 infection and maximum virological suppression who are taking combination antiretroviral therapy: an observational cohort study



A Mocroft, A N Phillips, J Gatell, B Ledergerber, M Fisher, N Clumeck, M Losso, A Lazzarin, G Fatkenheuer, J D Lundgren for the EuroSIDA study group*

CD4 count at initiation of cART (cells per μ L)	Time since starting cART (years)	N* (%)	Rate of CD4 count increases per year (cells per μ L) [†] mean (95% CI)	Current CD4 (cells per μ L) mean (95% CI)
≤200	<1	711 (5.1)	76 (53 to 99)	204 (195 to 213)
	1–3	2124 (15.4)	69 (63 to 76)	322 (315 to 327)
	3–5	2109 (15.3)	50 (36 to 69)	431 (422 to 440)
	>5	2164 (15.7)	32 (18 to 46)	497 (488 to 507)
201–350	<1	539 (3.9)	129 (91 to 166)	374 (363 to 385)
	1–3	1158 (8.4)	50 (25 to 74)	519 (507 to 530)
	3–5	1088 (7.9)	47 (24 to 69)	618 (604 to 631)
	>5	1184 (8.6)	23 (2 to 44)	676 (661 to 692)
>350	<1	343 (2.5)	90 (37 to 144)	580 (558 to 602)
	1–3	851 (6.2)	50 (18 to 82)	684 (666 to 701)
	3–5	791 (5.7)	17 (–17 to 51)	781 (760 to 801)
	>5	747 (5.4)	21 (–12 to 54)	794 (770 to 818)

*Number of viral load pairs included in analysis. †Adjusted for age, cART regimen started, nucleoside pair started, time taken for initial virological suppression, and change in CD4 since starting cART.

Table 3: Adjusted rate of CD4 count increases (per year) with viral load of less than 50 copies per mL, and relation between CD4 count at starting cART (cells per μ L) and time since starting cART

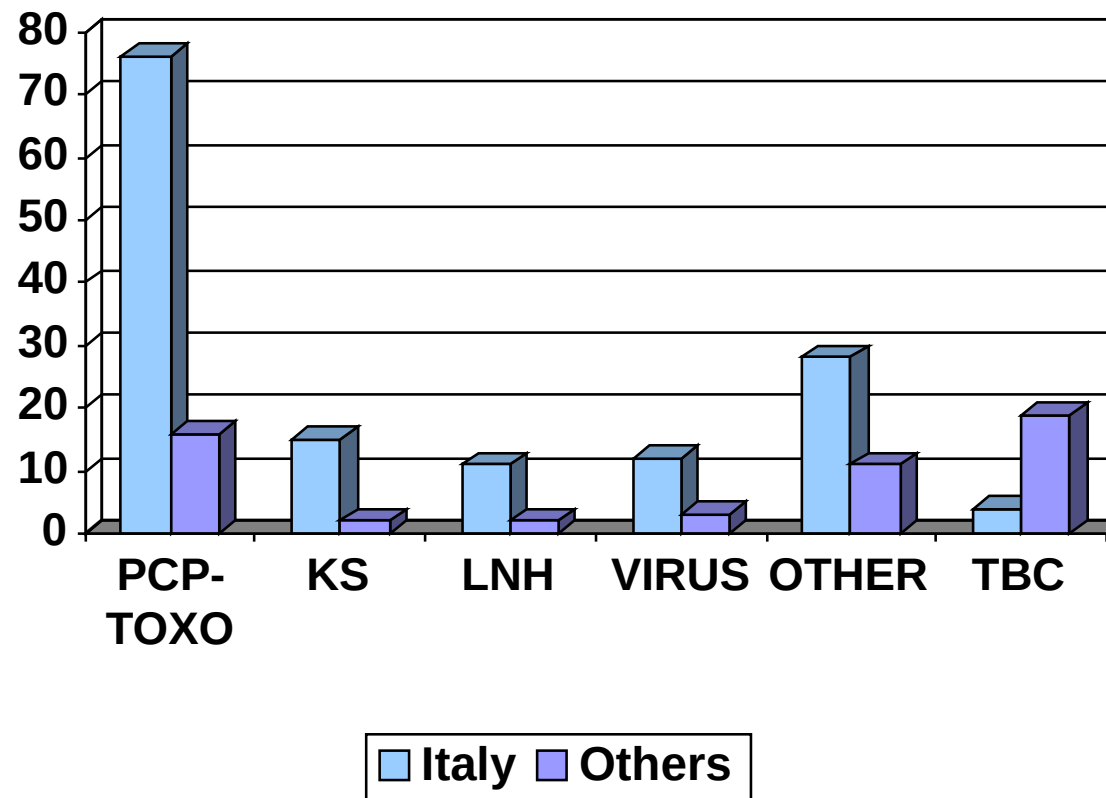
Normalization of CD4/CD8 Ratio and Non-AIDS Events in ICONA Cohort

- Analysis of 3236 pts with virologic suppression on ART and CD4/CD8 ratio ≤ 0.8
 - 458 pts reached CD4/CD8 ≥ 1
 - Median time to normalization: 10.1 yrs
 - Younger pts, those starting ART in recent yrs, and those with higher CD4+ counts more likely to normalize
- Current CD4/CD8 ratio predicted incidence of clinical progression (serious non-AIDS¹²–related events or all-cause death)
 - Remained predictive after adjusting for current CD4+ cell count

Time	Probability of CD4/CD8 Normalization (95% CI)
1 yr	4.4 (3.7-5.2)
2 yrs	11.5 (10.2-13.0)
5 yrs	29.4 (26.7-32.4)

Current CD4/CD8 Ratio	Incidence of Clinical Progression (95% CI)
< 0.30	4.8 (3.9-5.9)
0.30-0.45	2.4 (1.9-3.1)
> 0.45	2.0 (1.7-2.3)

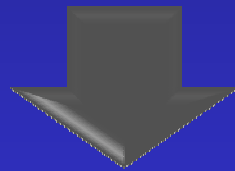
OPPORTUNISTIC INFECTIONS AMONG ITALIANS AND FOREIGNERS



Personal communication

Perchè I pazienti arrivano alla diagnosi tardivamente?

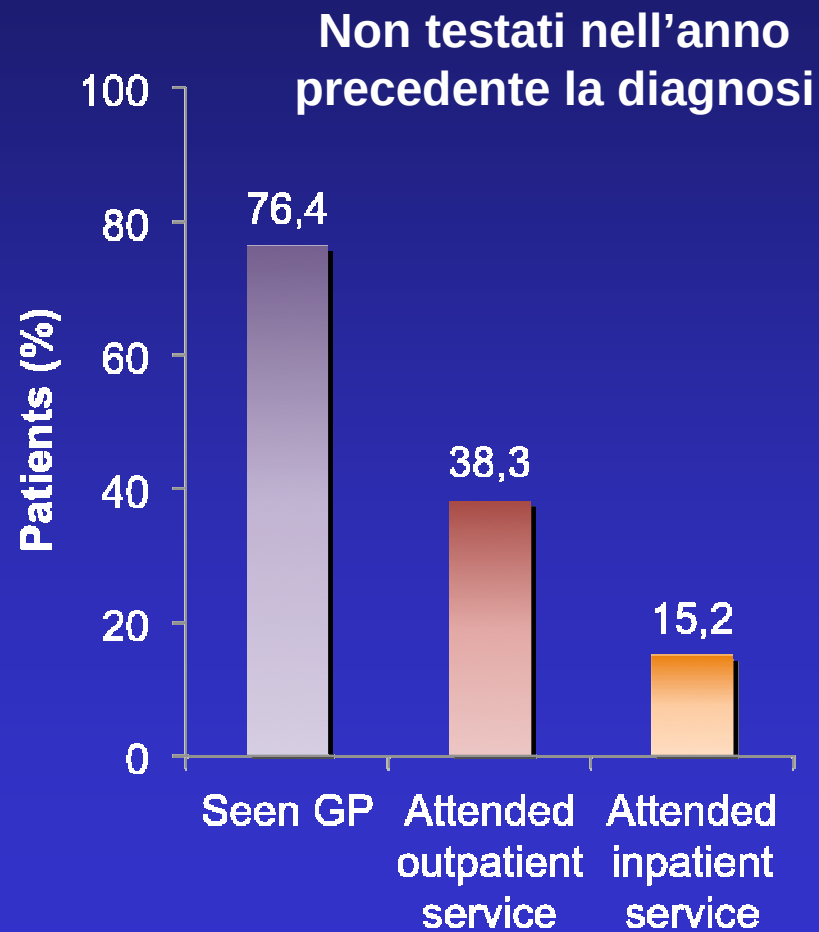
- Barriere nei confronti del test a livello del paziente
- Barriere nei confronti del test a livello del medico



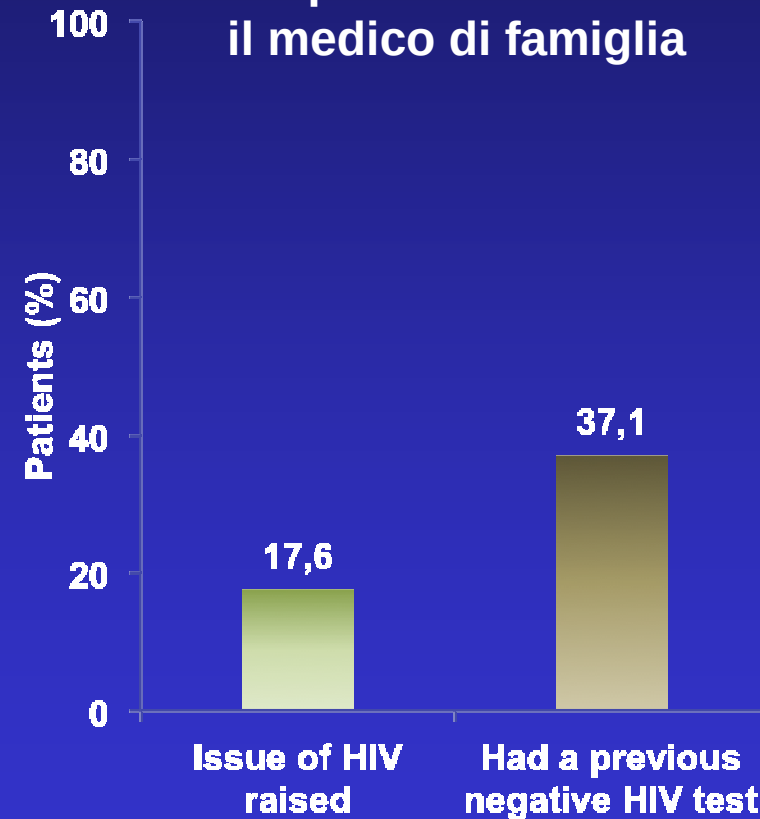
Perdita di opportunità

Occasioni perse per i medici

Survey population: 263 Africans in London diagnosed as HIV-positive



Del 76.4% dei pazienti che avevano visto il medico di famiglia

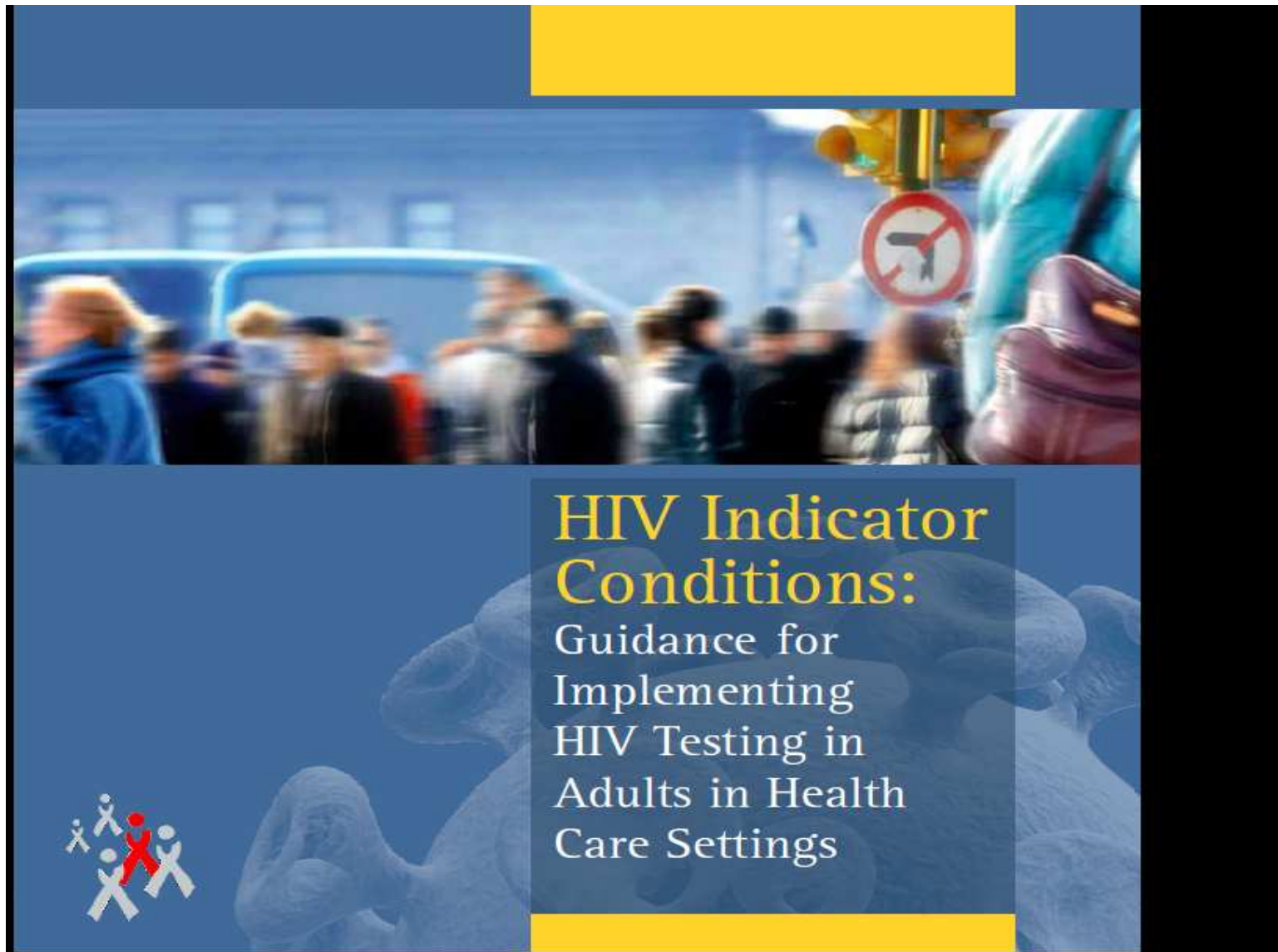


ANRS – Opportunités study

HIV test proposal at the first contact with a healthcare setting with a HIV related symptom *

HIV related symptom*	N	HIV test proposal
Recurrent bacterial infections	87	2 (2%)
Generalized lymphadenopathy	46	5 (11%)
Varicella zoster	35	5 (14%)
Unexplained weight loss $\geq 10\%$	45	7 (16%)
Diarrhea ≥ 1 month	36	6 (17%)
Fever ≥ 1 month	22	5 (23%)
Sexually transmitted diseases	101	54 (53%)

HIV in Europe www.hiveurope.eu



October 26, 2012.

Condizioni Indice (IC)

Malattie Sessualmente Trasmesse (MST)

Epatitis B e C

Linfoma

Displasia anale o della cervice uterina

Piastrinopenia o neutropenia per >4 settimane

Herpes zoster <65 anni

Dermatite seborroica o esantema

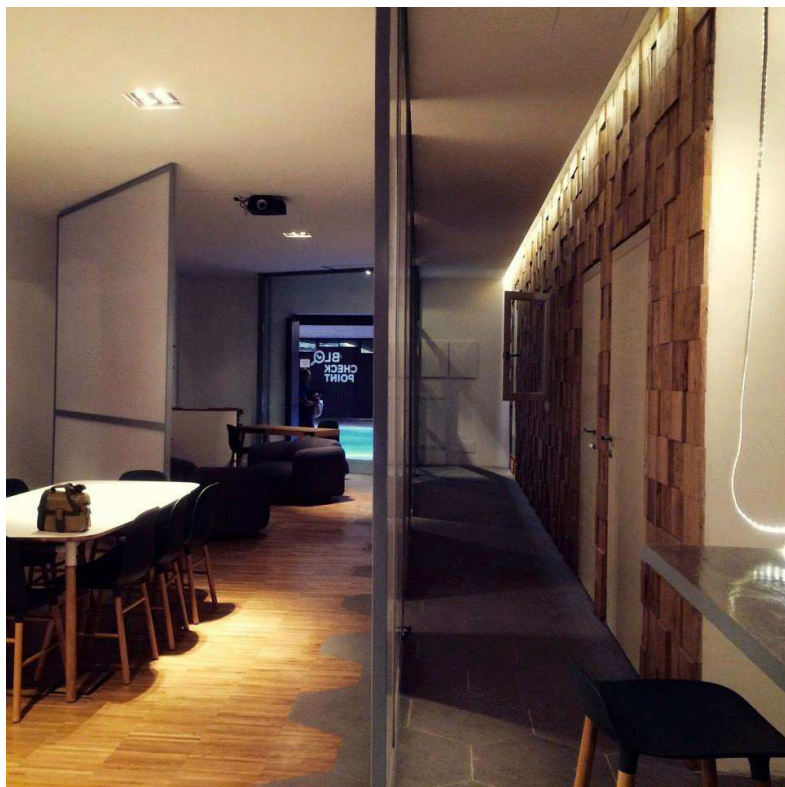
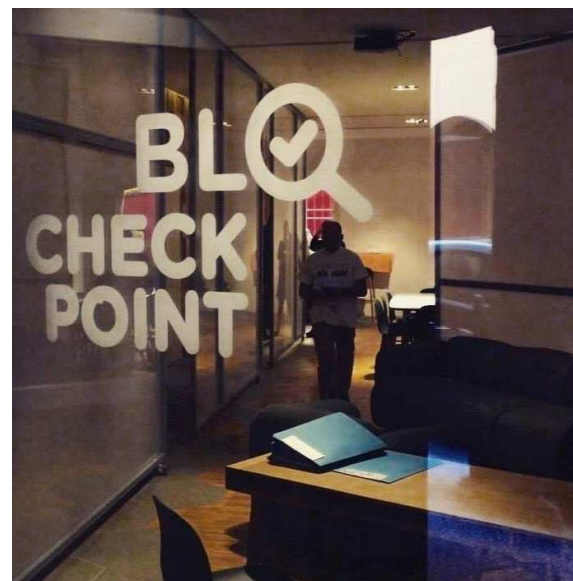
Sindrome simil-mononucleosica

BISOGNA FACILITARE L'ACCESSO AL TEST

Uscire dall'ospedale ed effettuare il test rapido



**Una possibile
soluzione: andare fuori
dagli
ospedali ed effettuare
i test rapidi**



Proteggi l'amore

Aids e non solo

*TEST DAYS: Aids, cosa fai per **test**esso*

*e per gli altri? **Fai il test!***

Test
gratuito per
l'infezione HIV
counselling e informazioni
per le malattie trasmesse sessualmente
c/o l'INFORMAGIOVANI in piazza Grande, 17

I quattro sabati in cui si terrà l'iniziativa sono:

18 maggio ore 17.00 - 19.00
14 settembre ore 17.00 - 19.00
30 novembre ore 17.00 - 19.00
15 febbraio 2014 ore 17.00 - 19.00

È una iniziativa dell'Azienda Usl di Modena,
Azienda Ospedaliero - Universitaria di Modena e Reggio Emilia
e Comune di Modena, assieme alle Associazioni di volontariato



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena
Policlinico



UNIVERSITÀ DEGLI STUDI
DI MODENA E REGGIO EMILIA



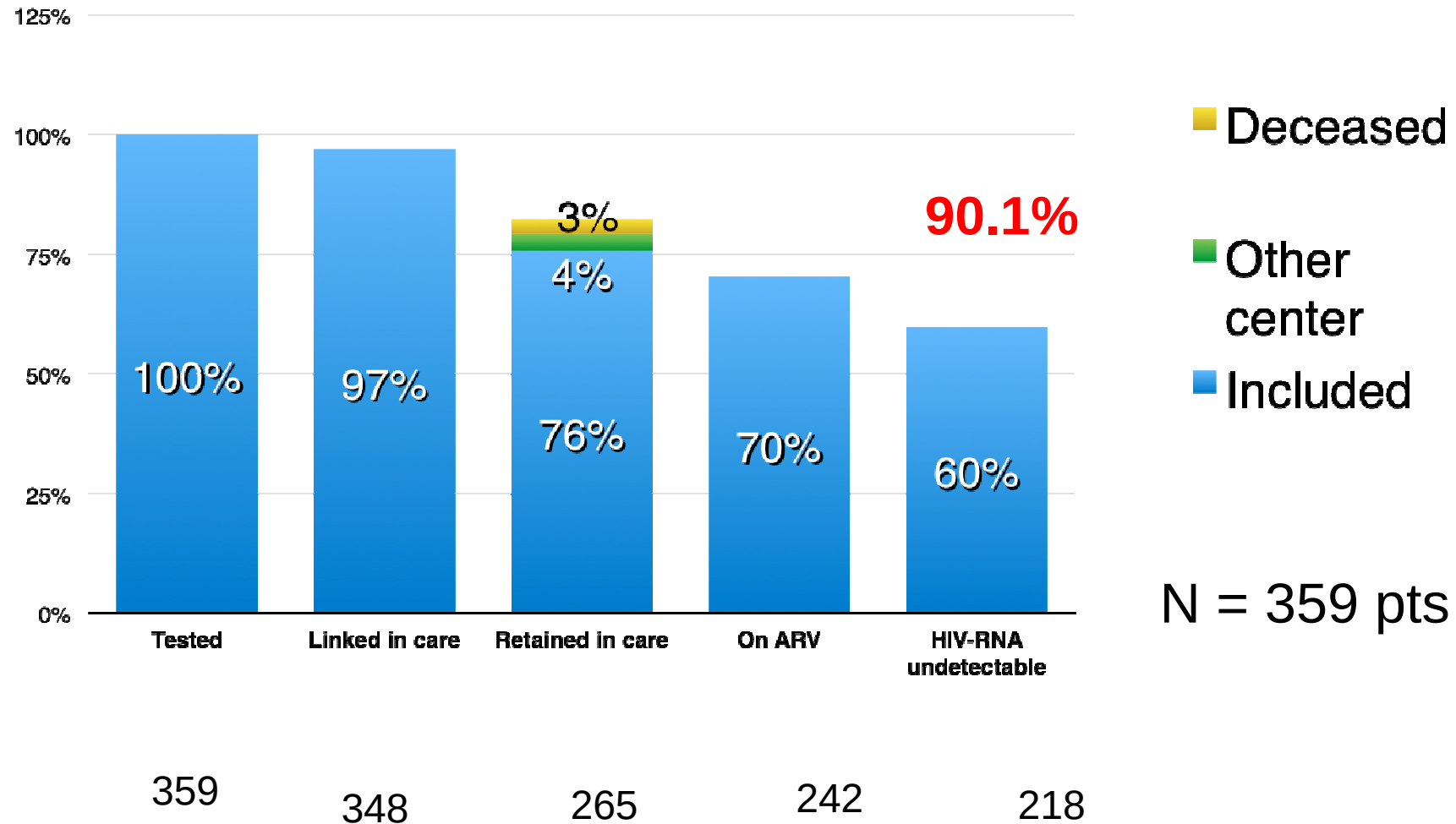
Comune di Modena



WWW.ARCIGAYMODENA.ORG

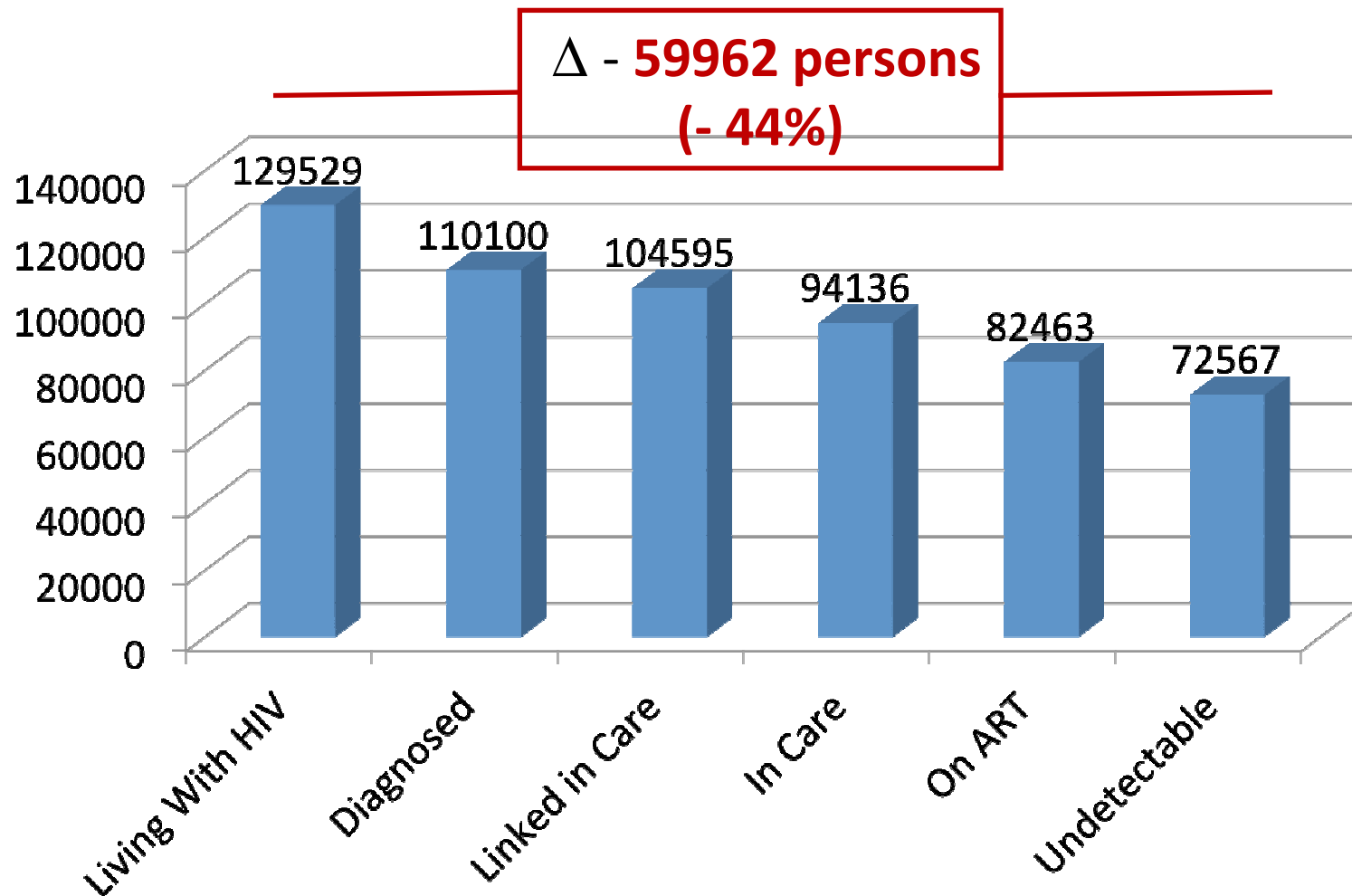
**BISOGNA MIGLIORARE LA
CONTINUITA' DI CURA**

Cascade



The continuum of HIV care in Italy, 2012

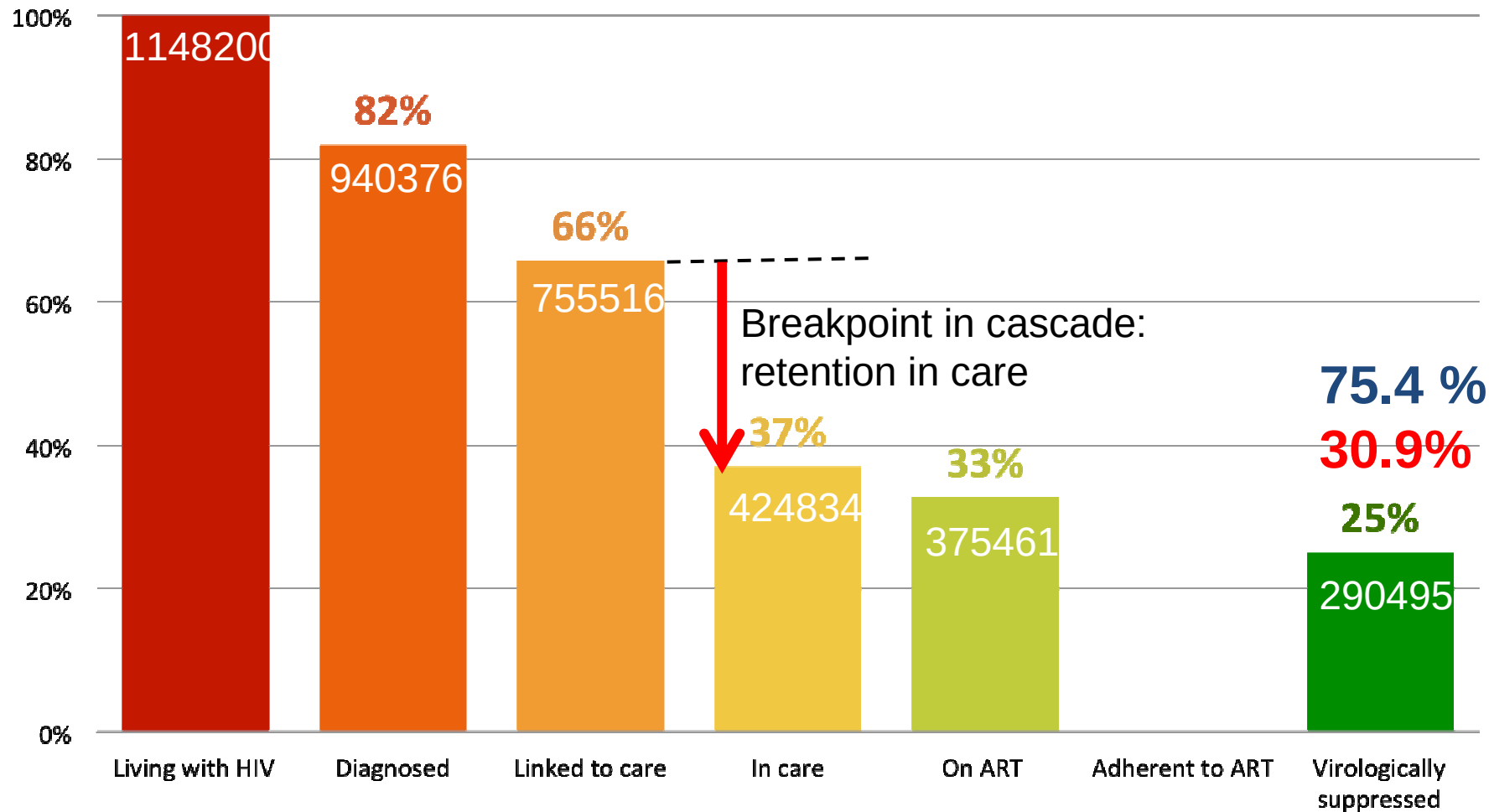
A tentative description



HIV treatment cascades in European and high-income countries

	France	Netherlands	USA	UK	Australia	British Columbia	Denmark	Georgia
% diagnosed	81	–	82	–	75	71	85	52
% linked to care	>74	73	66	79	–	67	81	44
% on ART	>60	59	33	67	35	51	62	26
% Undetect. VL	52	53	25	58	32	35	59	20

Cascade of HIV care – United States

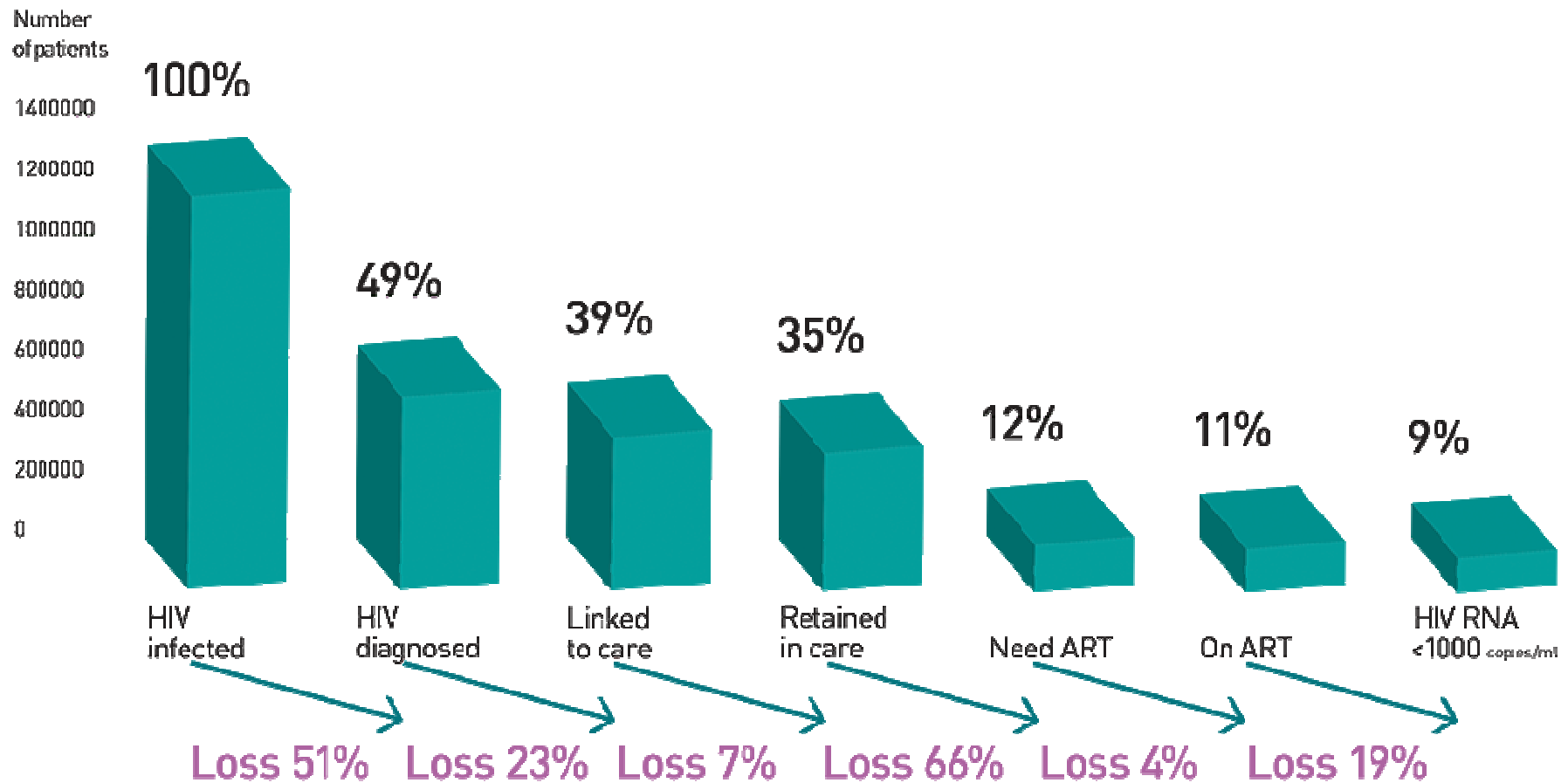


Reference: Hall et al. *JAMA internal medicine* 2013; 173(14) 1337-1344.

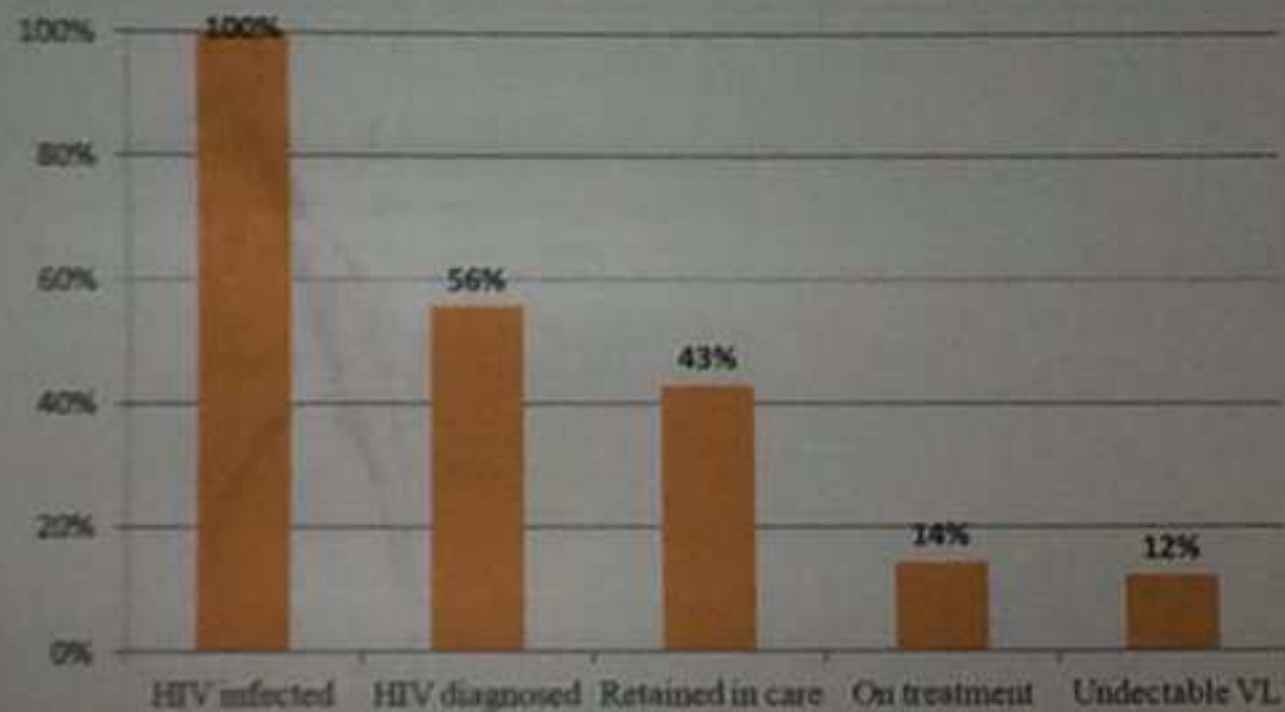
Centres for Disease Control Fact sheet, December 2013

<http://www.cdc.gov/nchhstp/newsroom/docs/hivfactsheets/todaysepidemic-508.pdf>

The Cascade of HIV Care in Russia, 2013

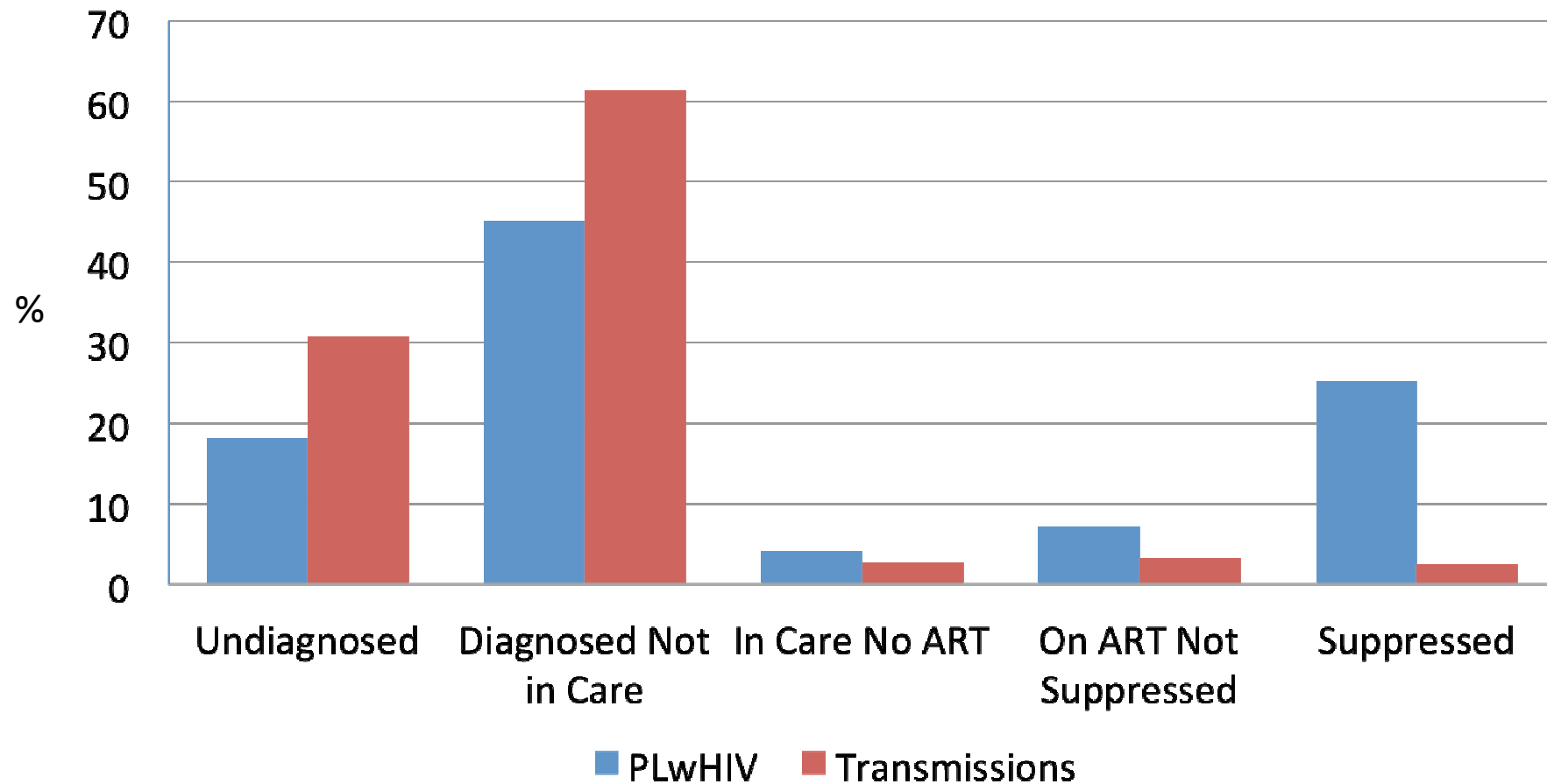


Treatment cascade of adults living with HIV in Russia, 2014



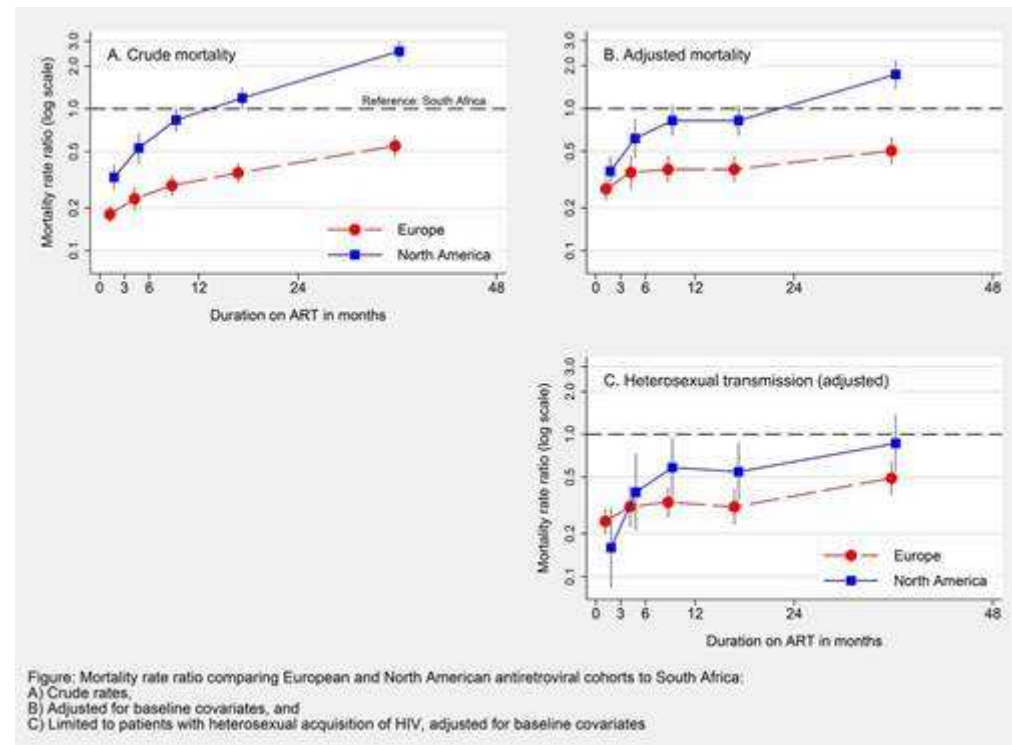
Dr. Natalya Ladnaya and Anastasia Pokrovskaya, Federal Scientific and Methodological Center for Prevention and Control of AIDS, 2014.

HIV Transmission at Each Step of the Care Continuum in the United States



Skarbinski J et al *JAMA Intern Med* 2015 - modified

Mortality after starting ART in adults in 3 Continents



Conclusions: After accounting for under-ascertainment of mortality, with increasing duration on ART, mortality in RSA declines rapidly to levels approaching or below that described in participating NA cohorts, while substantially narrowing the differential with the EUR cohorts.

Early missed visits and mortality

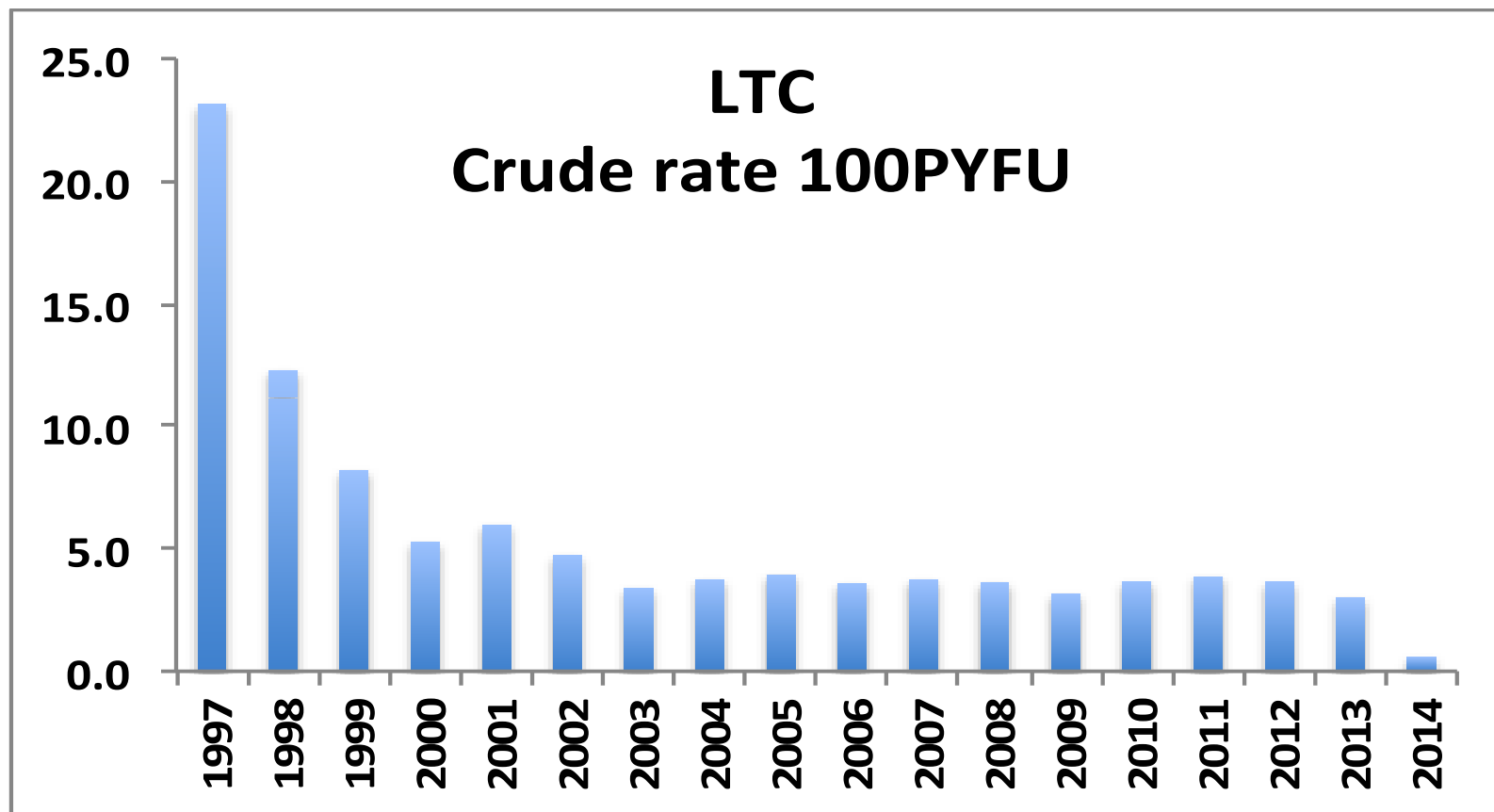
- Study of UAB 1917 Clinic patients initiating outpatient HIV care, 2000 - 2005 (N=543)

Characteristic	HR (95%CI) ^a
"No show" visit in 1 st year	2.90 (1.28- 6.56)
Age (HR per 10 years)	1.58 (1.12-2.22)
CD4 count <200 cells/ μ L	2.70 (1.00-7.30)
Log ₁₀ plasma HIV RNA	1.02 (0.75-1.39)
ART started in 1 st year	0.64 (0.25-1.62)

^a Cox proportional hazards (PH) analysis also adjusts for sex, race/ethnicity, insurance, affective mental health disorder, alcohol abuse, and substance abuse.



Risk of clinical progression among patients re-entering in care after being lost



Clinical events occurred in 100 patients (21%) within 6 months after re-entering in care: 9 (2%) died, 22 (5%) developed AIDS, 21 (5%) a serious non-AIDS event and 48 (11%) had an hospitalization. In a multivariable model adjusted for gender, risk factors, late presentation, HCV-coinfection and current CD4-cells count, patients with a gap in care had an increased risk of clinical events (RR=2.36, 95%CI: 2.06-2.71, $p<0.001$).

Caratteristiche dei pazienti persi al follow-up a Modena ad Ottobre 2012

	Mean (SD) or n (%)
Gender	
Women	84 (28.97%)
Men	206 (71.03%)
Age at last visit	41
Age at diagnosis	34
CDC C	50 (17.24%)
missing data	73 (25.17%)
Risk	
eterosessuali	94 (32.41%)
MSM	61 (21.03%)
HIV+ partner	27 (9.31%)
IDU	88 (30.34%)
Mother-to-child	1 (0.34%)
Blood transfusion	4 (1.38%)
missing data	15 (5.17%)
Stranieri	84 (28.97%)

	Mean (SD) or n (%)
On therapy	133 (45.86%)
Cumulative months of therapy at last visit, median (IQR)	43.7 (18.5 – 105.3)
HIV Viral Load undetectable at last visit	77 (57.89%)
CD4+ cell count at last visit	
≤100	16 (5.52%)
101-250/μL	23 (7.93%)
251-350/μL	34 (11.72%)
351-500/μL	51 (17.59%)
>500/μL	82 (28.28%)
missing data	84 (28.97%)

Abbiamo fatto 250 telefonate:

And we discovered that the reasons for being lost to follow-up were:

Afferiti ad altro centro	73 (25.17%)
Carceratii	2 (0.69%)
Morti	77 (26.55%)

109 (37.59%) erano irraggiungibili

31 (10.70%) sono stati raggiunti e non erano seguiti

Confronto tra l'ultima visita e quella dopo la telefonata

	At last visit	At re-engagement	p-value
Log₁₀ HIV Viral Load, median (IQR)	3.41 (1.71 – 4.41)	4.67 (3.80 – 4.94)	0.581
CD4+ cell count, median (IQR)	515.5 (399 – 643)	306 (115 – 482)	< 0.001

CD4+ cell count

≤100	0	5 (20.83%)	0.035
101-250/μL	3 (12.50%)	6 (25.00%)	0.053
251-350/μL	1 (4.17%)	2 (8.33%)	0.297
351-500/μL	8 (33.33%)	5 (20.83%)	0.671
>500/μL	12 (50.00%)	6 (25.00%)	0.158