



I nuovi naives: la coorte ICONA

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AGGIORNAMENTI INFETTIVOLOGICI: HIV, EPATITI &...

la sottoscritta **Antonella d'Arminio Monforte**
in qualità di relatore

ai sensi dell'art. 76 sul Conflitto di Interessi, comma 4 dell'Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

dichiara

che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

Gilead

Merck Sharpe and Dohm

Pfizer

ViiV

AGGIORNAMENTI INFETTIVOLOGICI: HIV, EPATITI &...

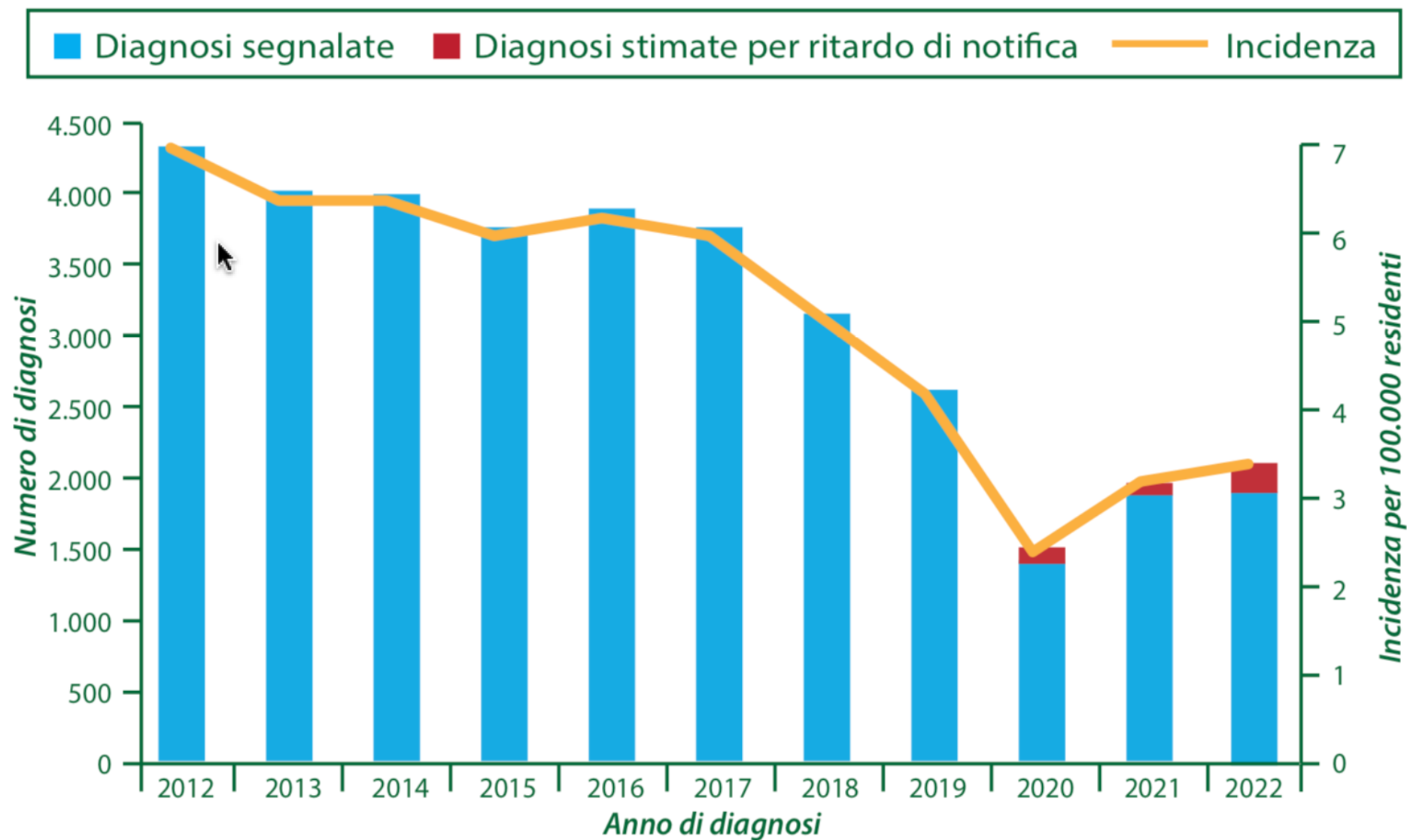
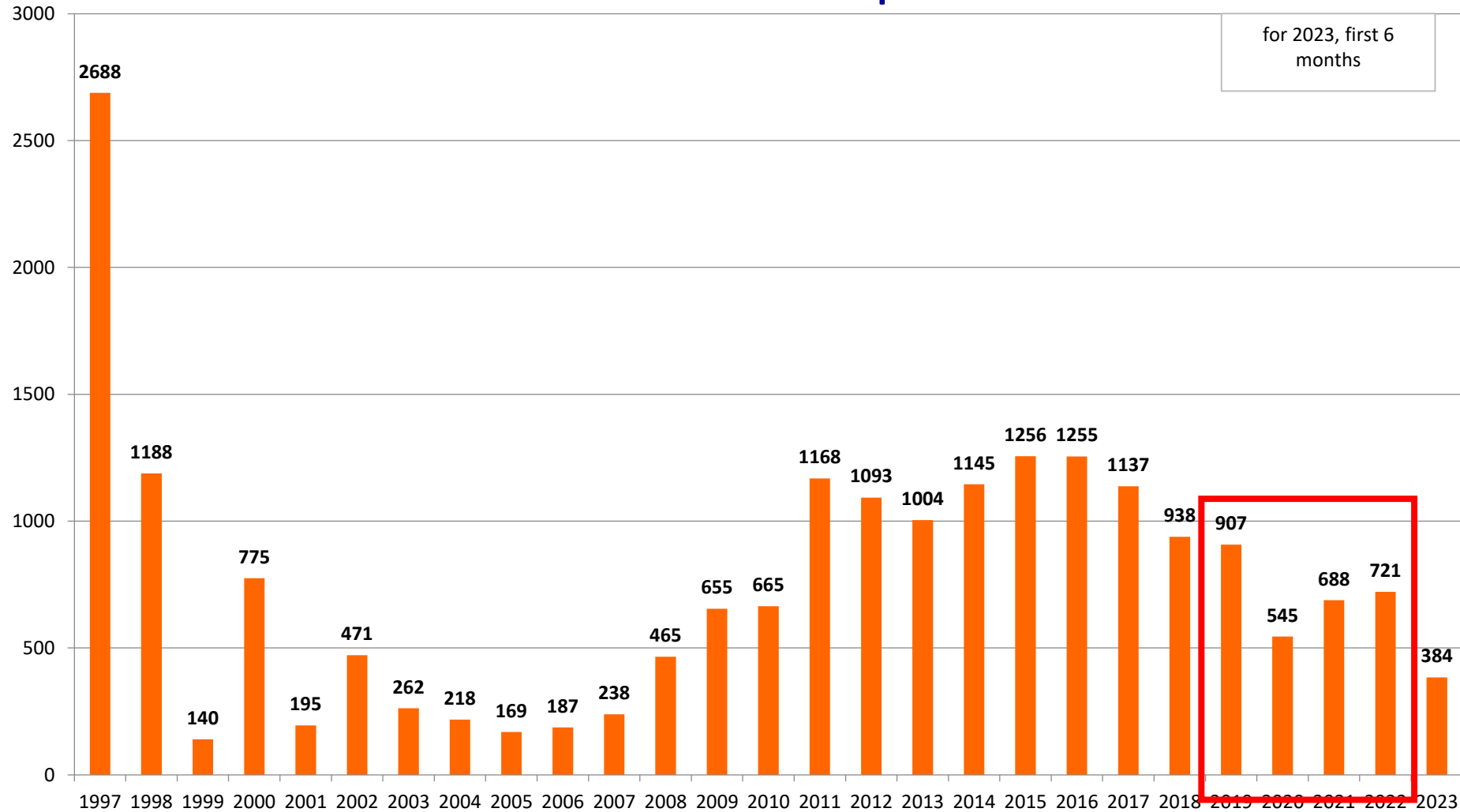
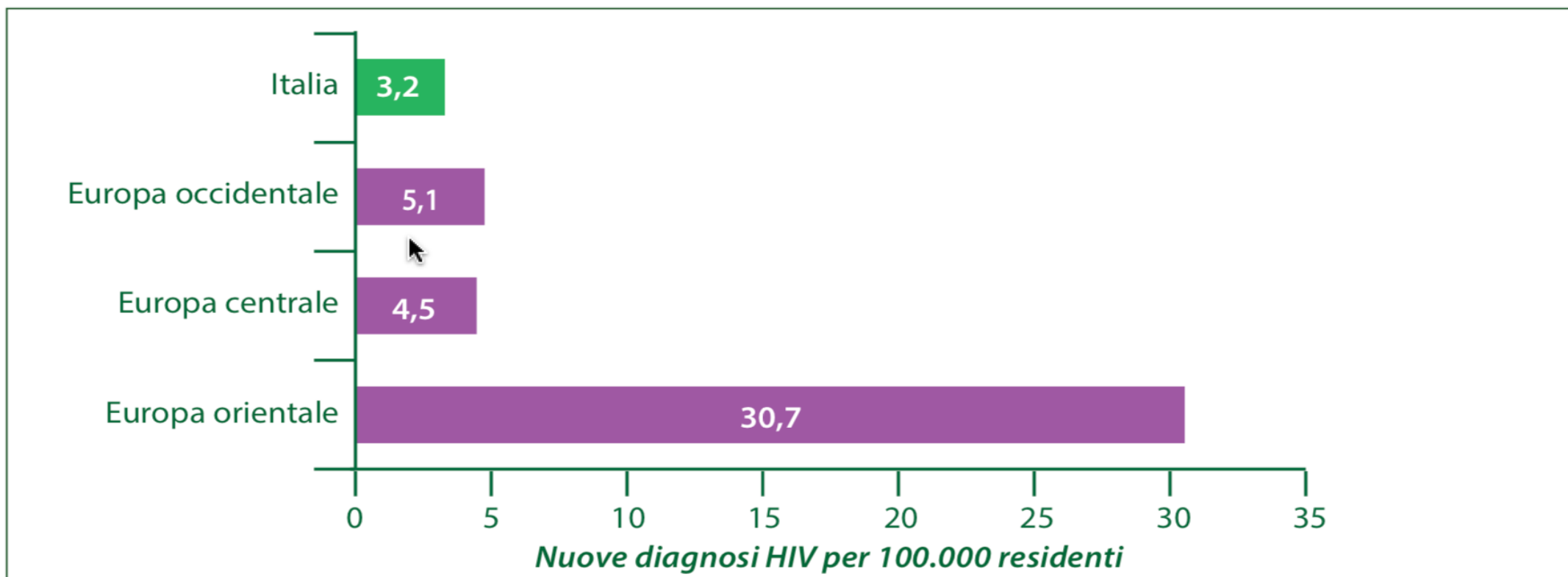


Figura 1 - Nuove diagnosi di infezione da HIV e incidenze corrette per ritardo di notifica (2012-2022)

Number of patients enrolled by calendar year 20557 Icona patients



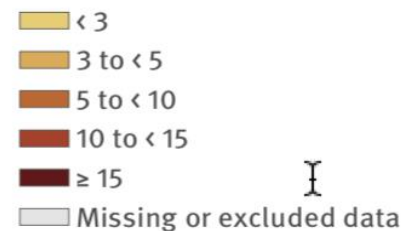
Incidenza HIV 2022



Incidenza HIV: numero di nuove diagnosi HIV per 100.000 residenti in Italia e nelle principali aree geografiche europee.

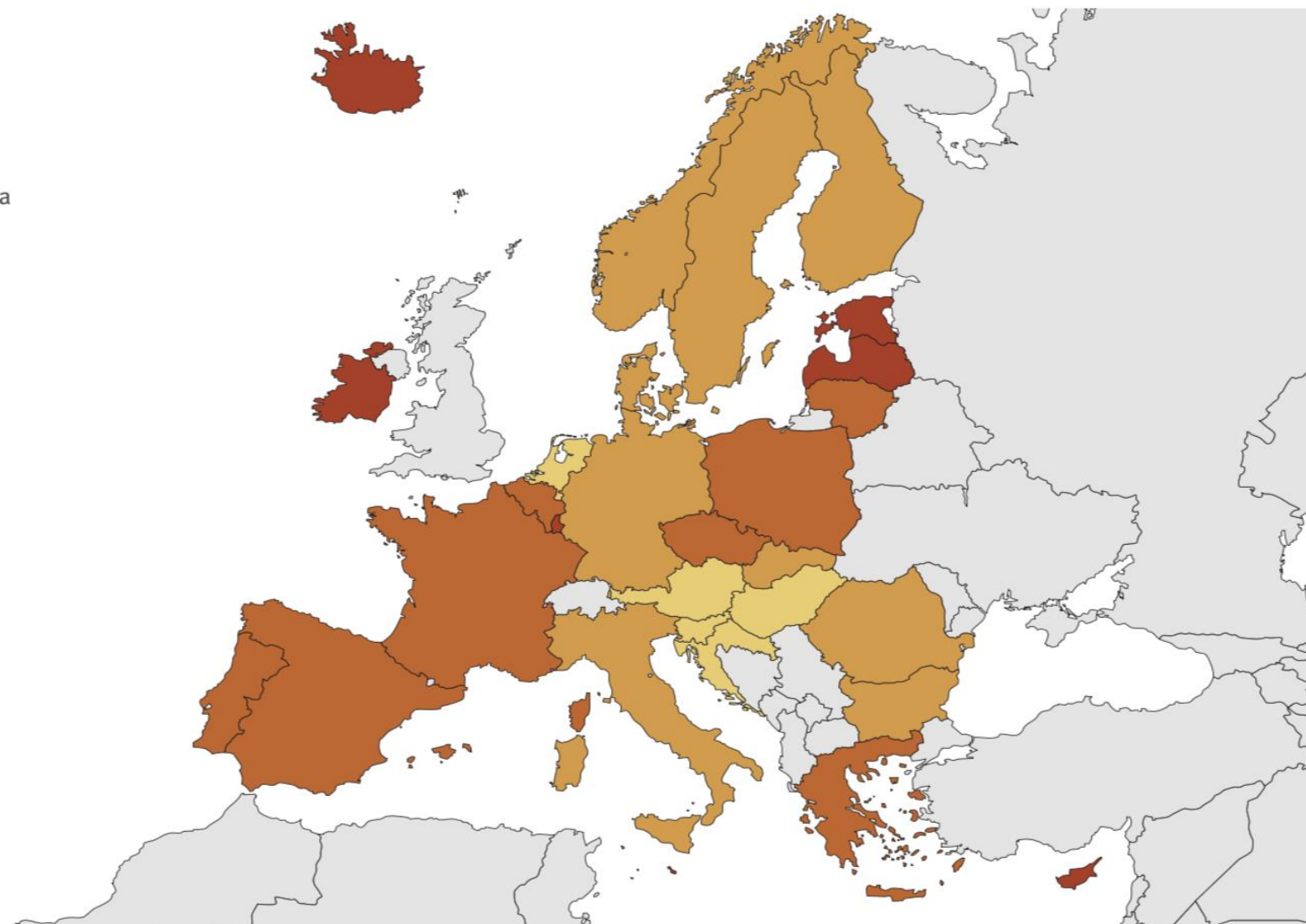
Fonti: Sistema di Sorveglianza HIV nazionale, ECDC/WHO. HIV/AIDS Surveillance in Europe 2023-2022 data (1)

Map 1b: HIV diagnoses per 100 000 population, 2022, EU/EEA

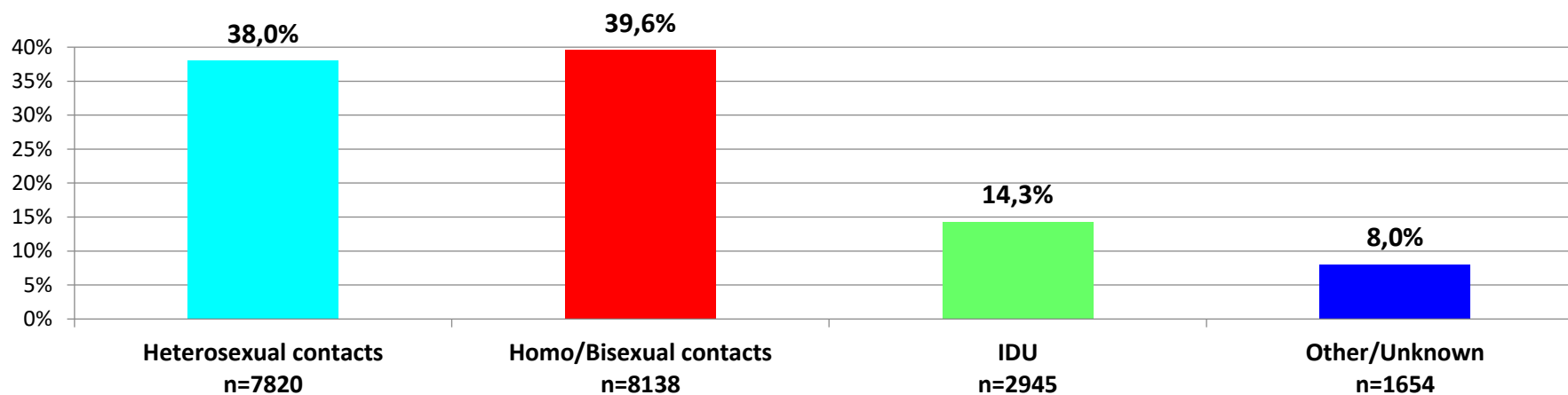


Non-visible countries

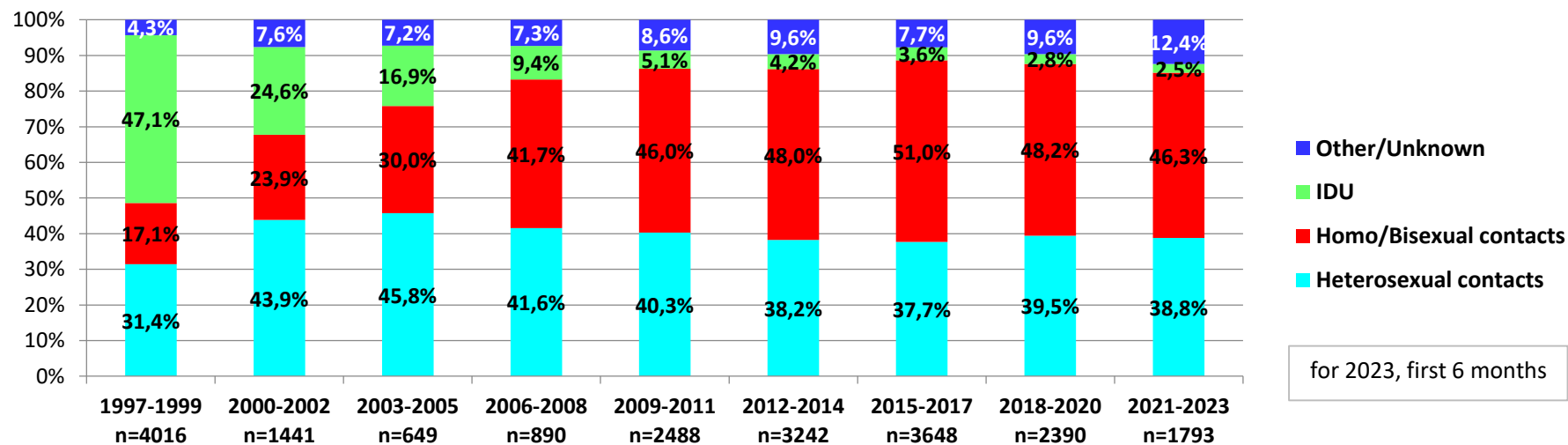
- Liechtenstein
- Luxembourg
- Malta



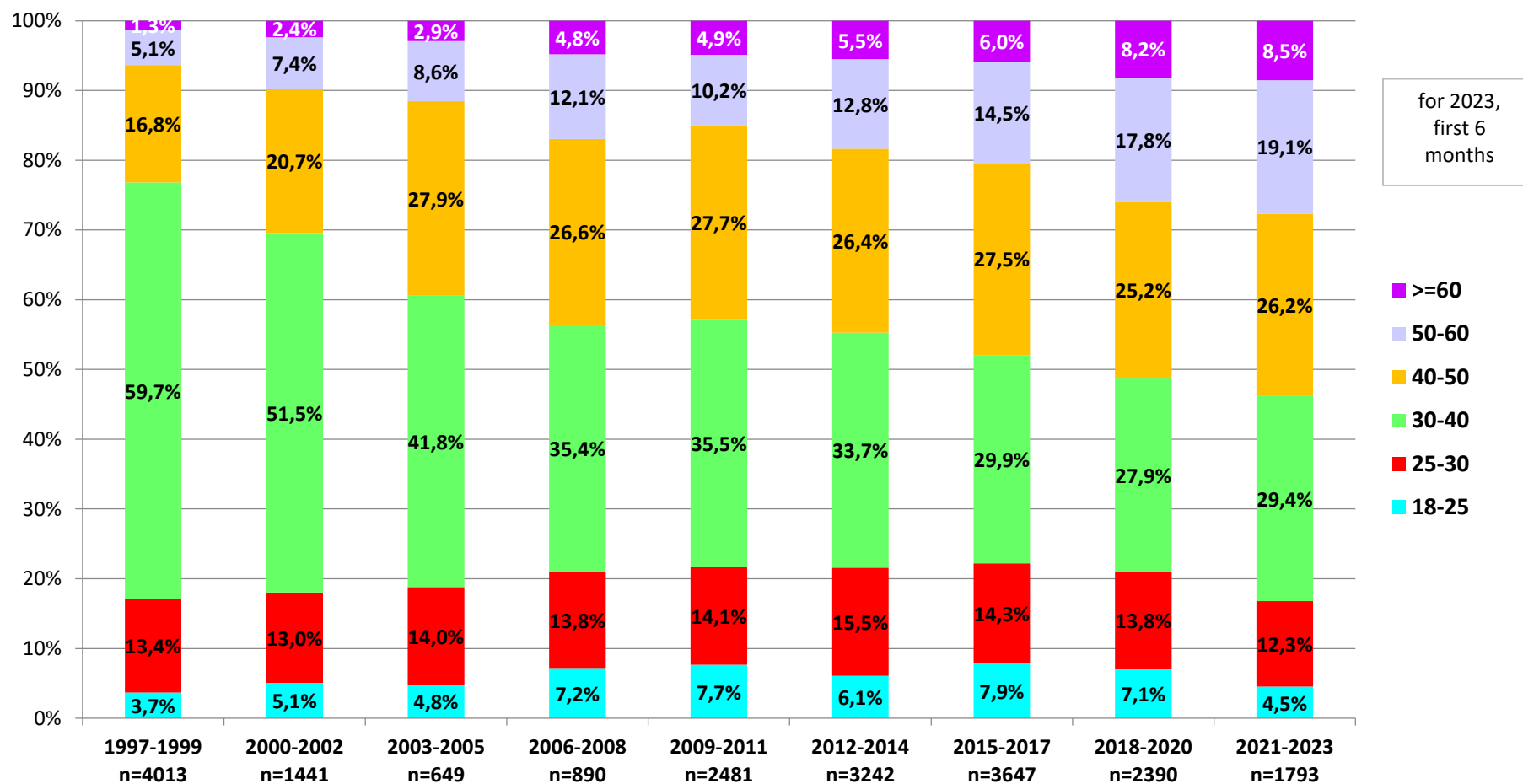
Mode of HIV transmission in 20557 Icona patients



Mode of HIV transmission according to calendar period of enrolment

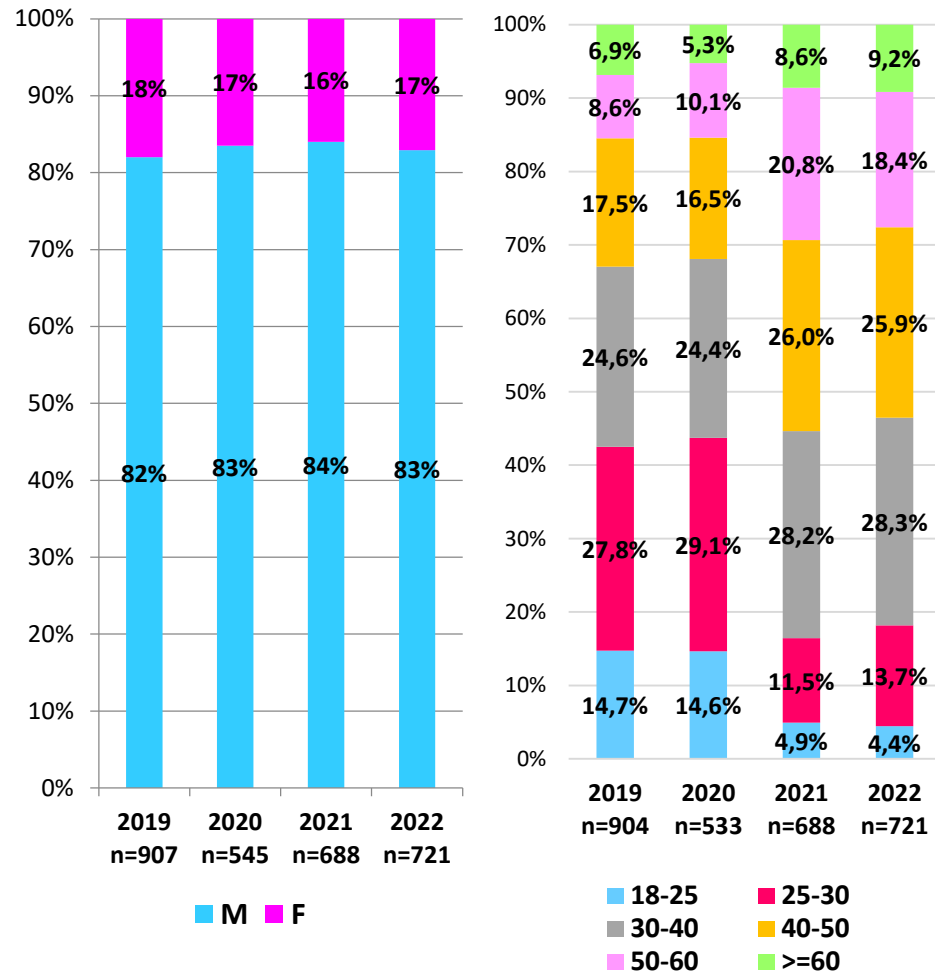


Age strata at enrolment according to calendar period

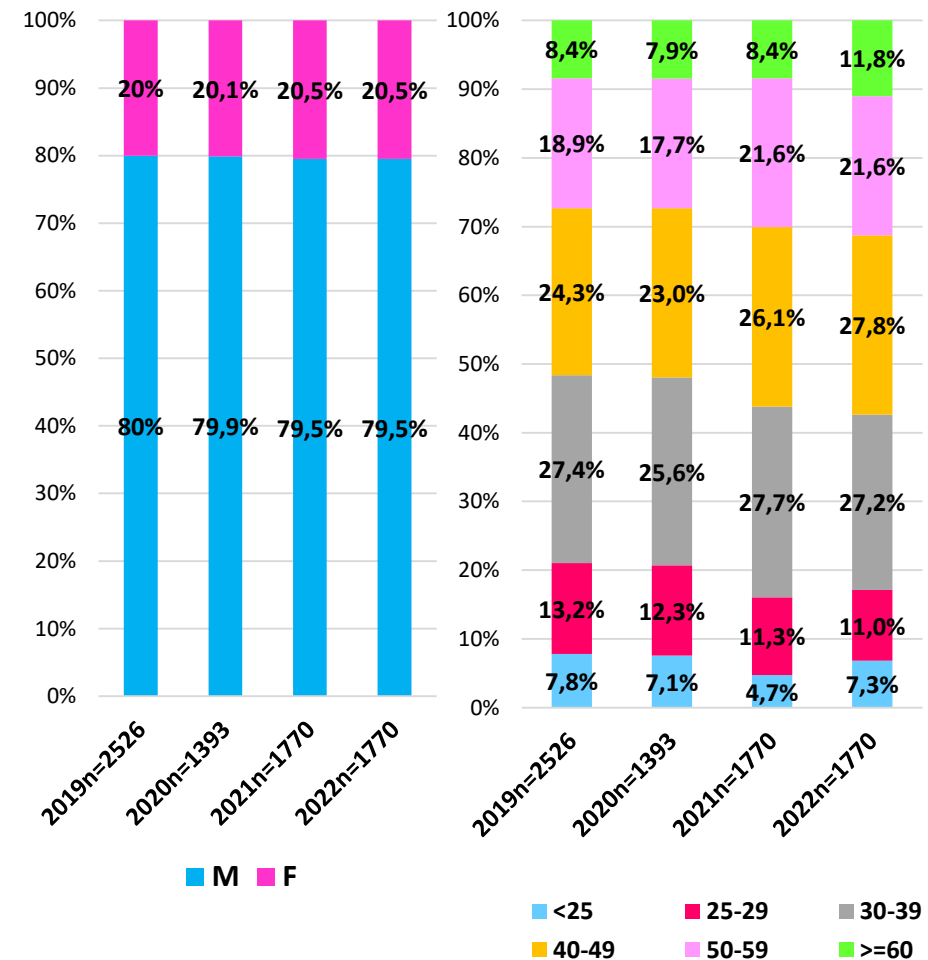


Gender and age strata according to calendar year of enrolment (2019 to 2022): ICONA cohort and ISS_CoA Registry

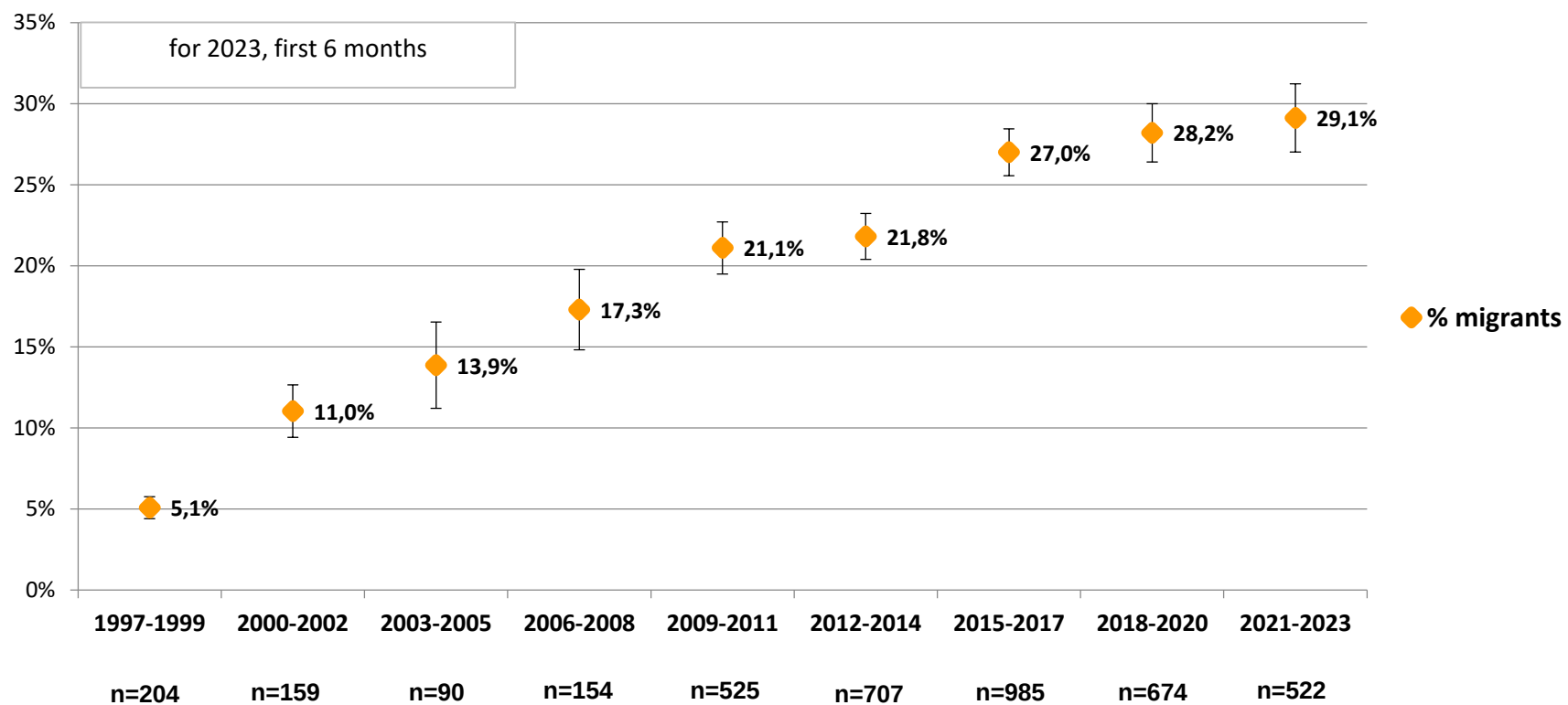
ICONA (n=2861)



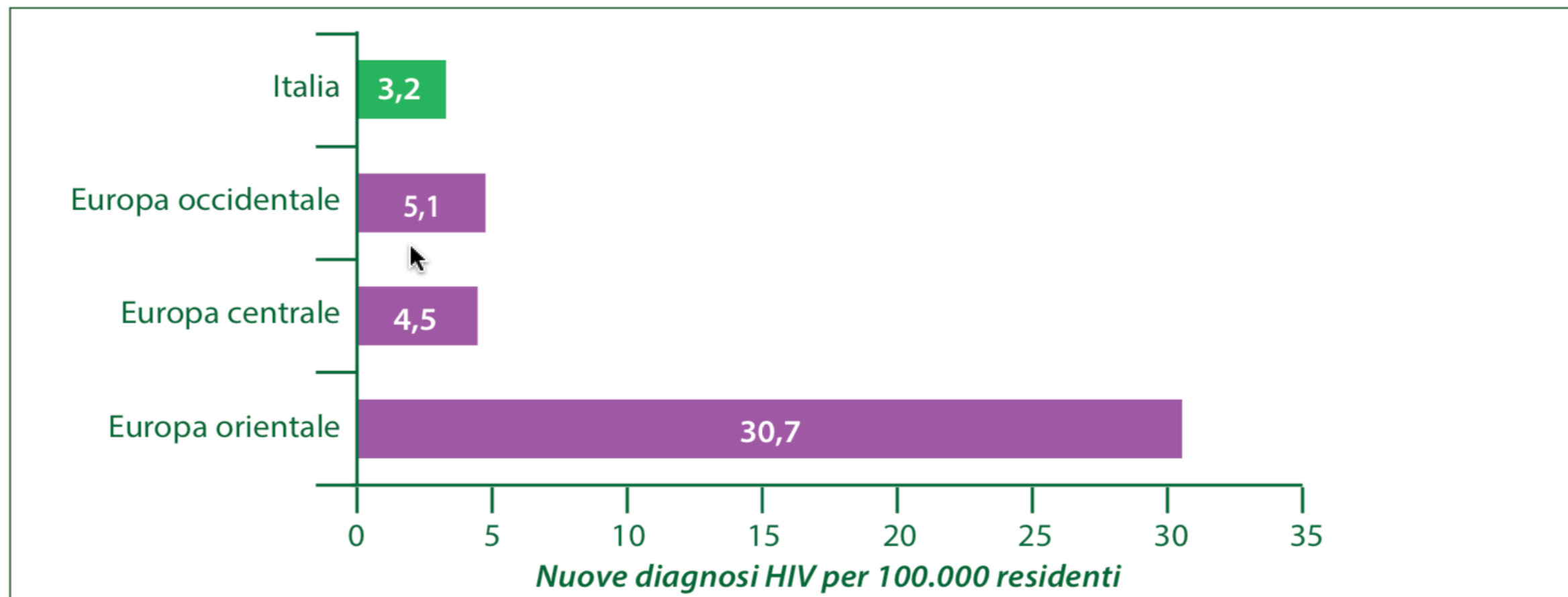
ISS-CoA (n=7459)



Prevalence of migrants by calendar period of enrolment in 20557 Icona patients



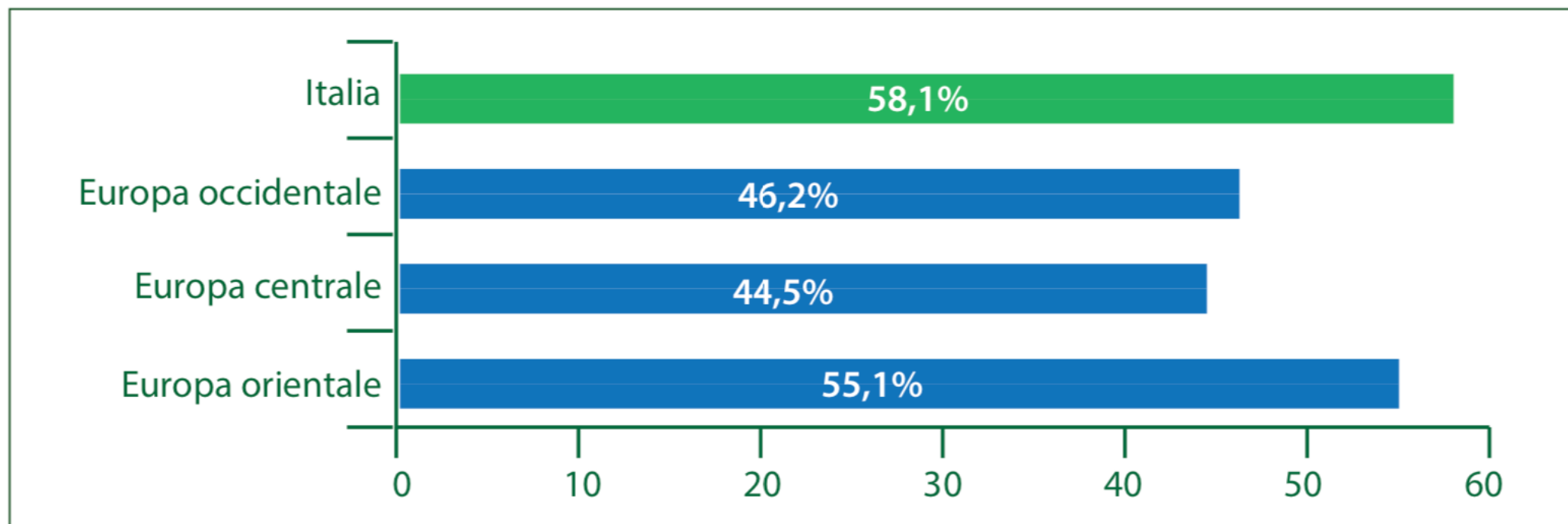
Incidenza HIV 2022



Incidenza HIV: numero di nuove diagnosi HIV per 100.000 residenti in Italia e nelle principali aree geografiche europee.

Fonti: Sistema di Sorveglianza HIV nazionale, ECDC/WHO. HIV/AIDS Surveillance in Europe 2023-2022 data (1)

Late presenters 2022*

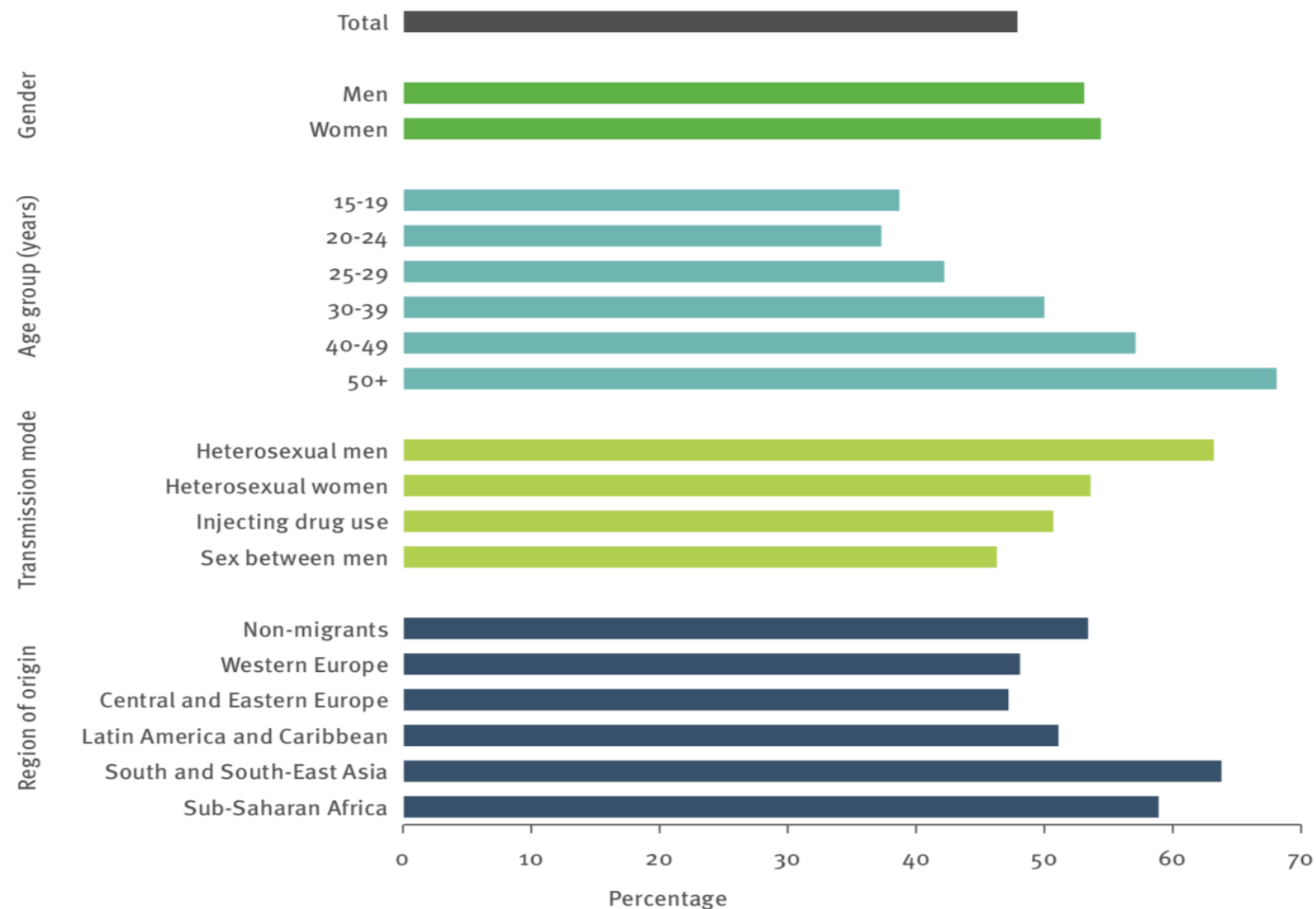


(*) *Late presenters*: nuove diagnosi di infezione da HIV con numero di linfociti CD4 <350 cell/ μ l.

Fonti: Sistema di Sorveglianza HIV nazionale, ECDC/WHO. HIV/AIDS Surveillance in Europe 2023-2022 data (1)

AGGIORNAMENTI INFETTIVOLOGICI: HIV, EPATITI &...

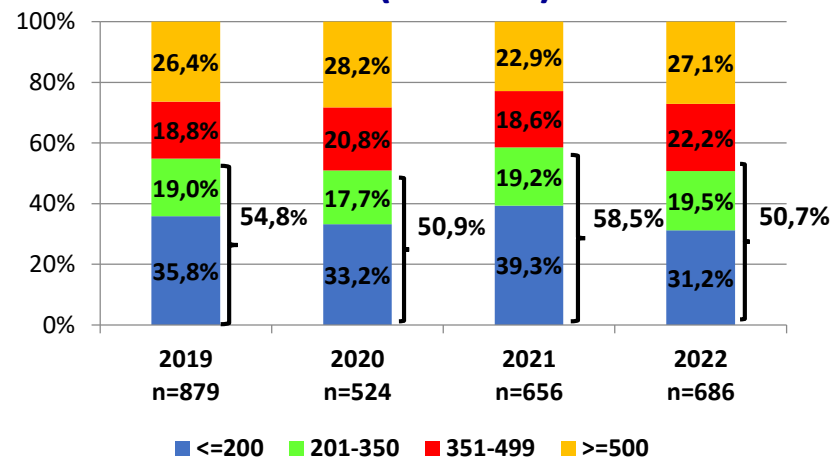
Figure 1.8: Percentage of people diagnosed late (CD4 cell count < 350 per mm³) by demographic, EU/EEA, 2022 (n = 6 451)



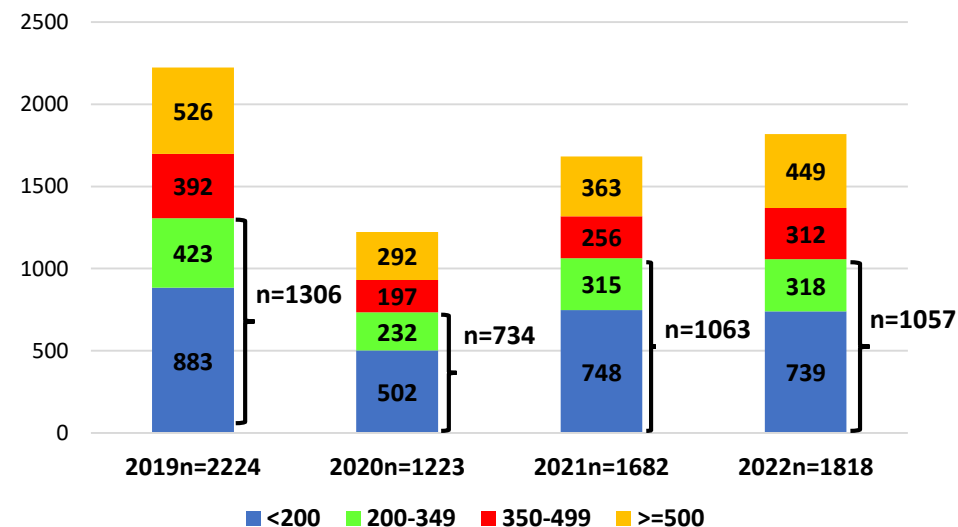
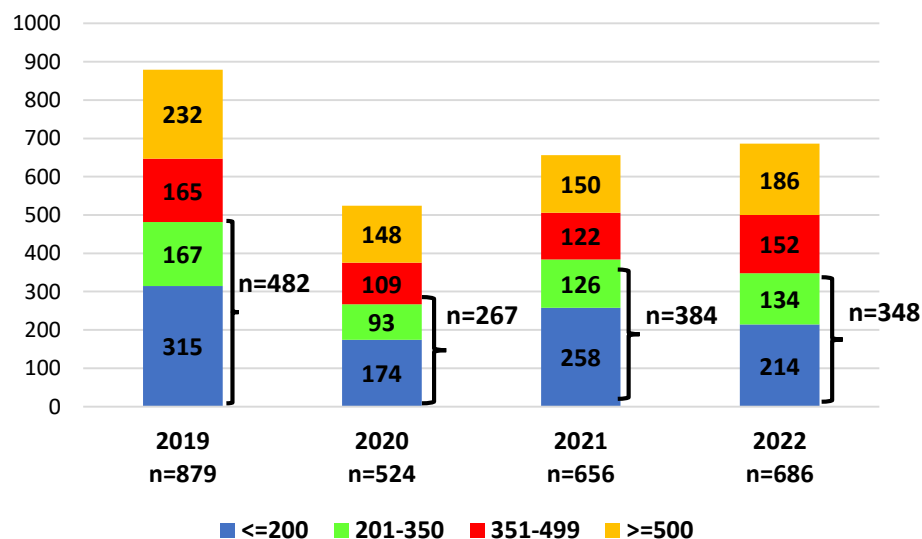
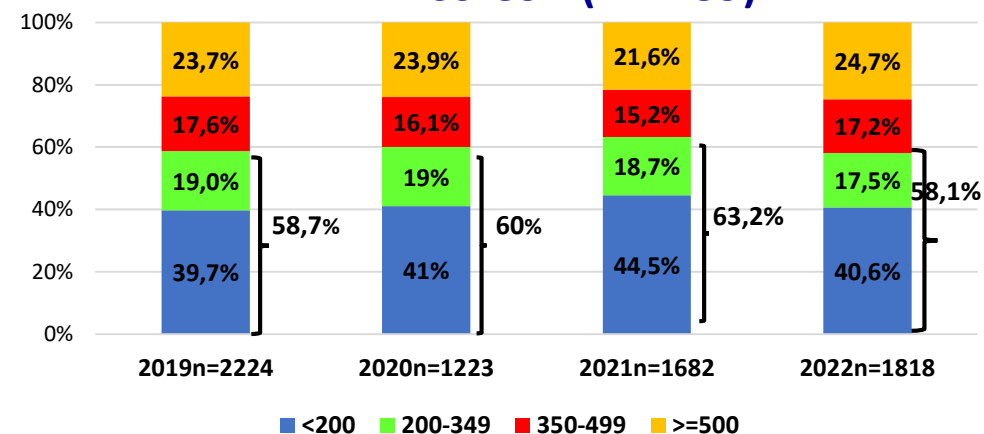
CD4 count strata according to calendar year of enrolment (2019 to 2022):

ICONA cohort and ISS_CoA Registry

ICONA (n=2861)

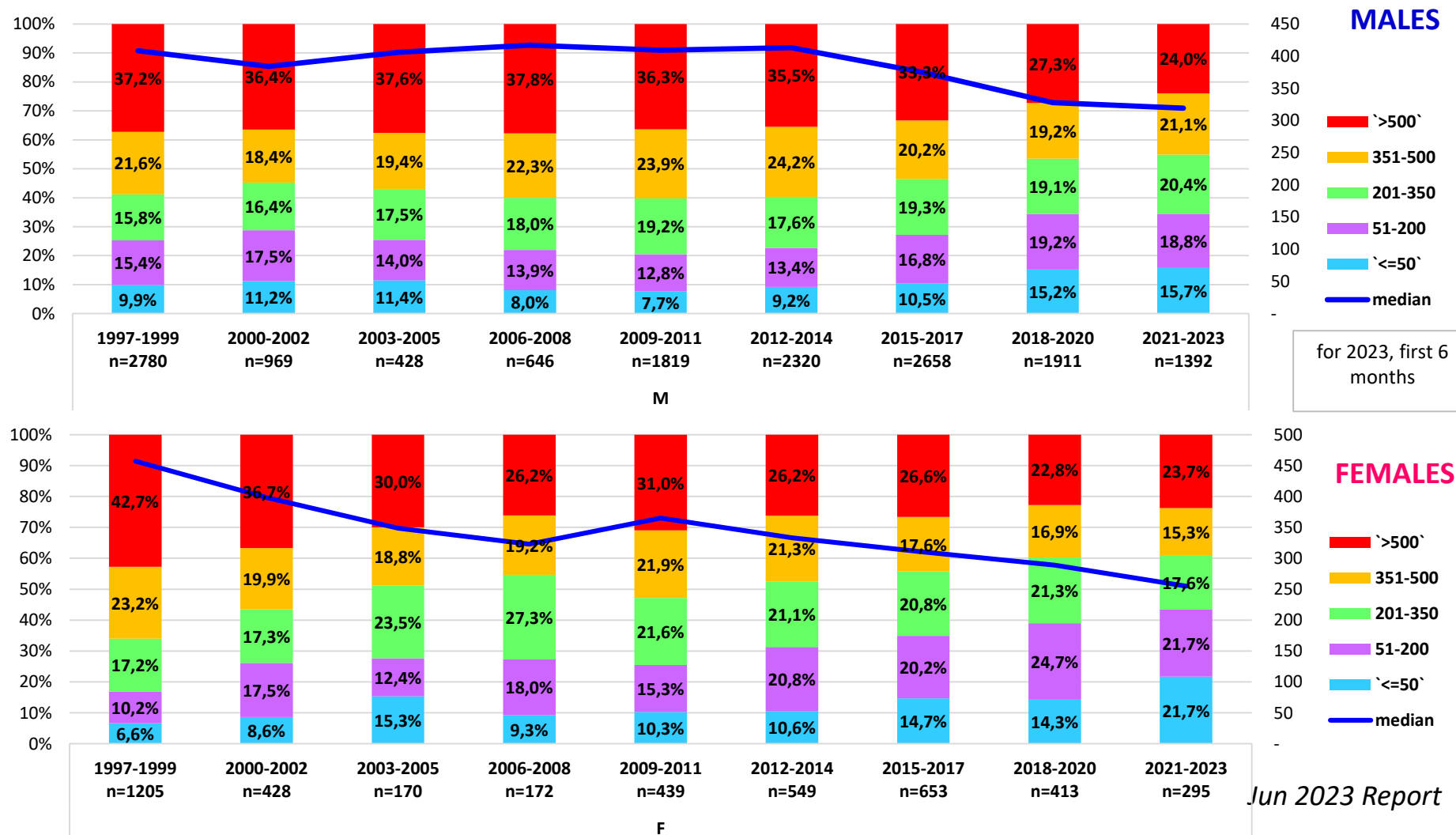


ISS-CoA (n=7459)



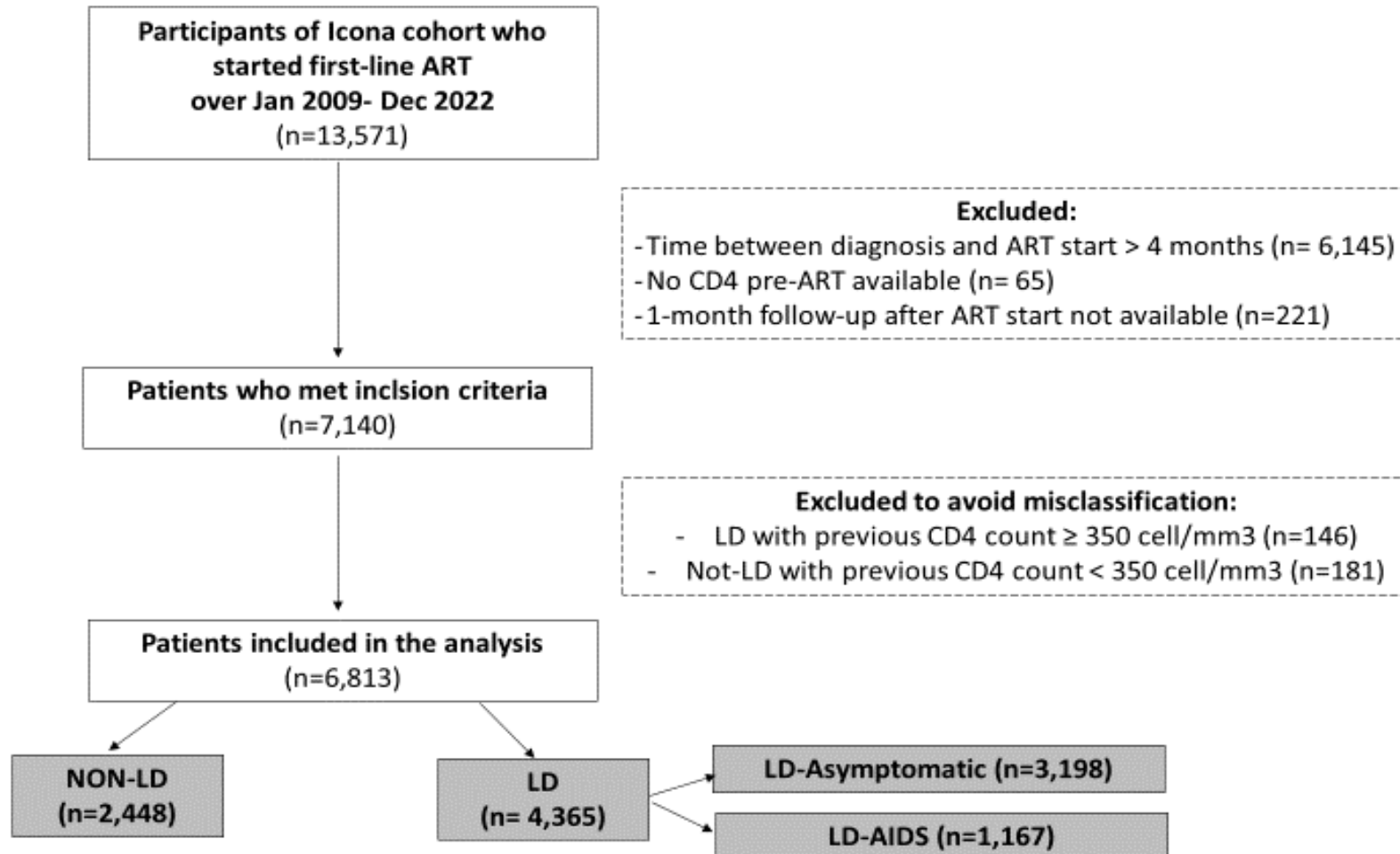


CD4 cells/mm³ strata and median values at enrolment according to calendar period and gender



PERSISTENT POOR CLINICAL OUTCOMES FOR AIDS PRESENTERS IN ITALY OVER THE LAST YEARS: DATA FROM THE ICONA COHORT 2009-2022

Annalisa Mondì et al, submitted
Patient selection and distribution flow diagram





Main characteristics of total population according to late presentation

	Total N= 6,813	Non-late Diagnosis (non-LD) N= 2,448 (35.9%)	Late Diagnosis (LD) N= 4,365 (64.1%)	p-value
Female Gender, n (%)	1,295 (19.0)	382 (15.6)	913 (20.9)	<0.001
Age, years, median (IQR)	40 (31-49)	36 (29-45)	42 (34-51)	<0.001
Mode of HIV Transmission, n (%)				<0.001
MSM	3,040 (44.6)	1,408 (57.5)	1,632 (37.4)	
Heterosexual	2,892 (42.4)	746 (30.5)	2,146 (49.1)	
IDU	322 (4.7)	118 (4.8)	204 (4.7)	
Other/Unknown	559 (8.2)	176 (7.2)	383 (8.8)	
Not Italian Nationality, n (%)	3,916 (57.5)	1,484 (60.6)	2,432 (55.7)	<0.001
CD4 cells nadir, cells/mm ³ , median (IQR)	257 (95-451)	512 (425-655)	136 (48-242)	<0.001
≤200 cells/mm ³ , n (%)	2,818 (41.4)	-	2,818 (64.6)	<0.001
HIV-RNA, log ₁₀ copies/mL, median (IQR)	4.91 (4.18-5.52)	4.51 (3.73-5.14)	5.12 (4.50-5.66)	<0.001
AIDS diagnosis, n (%)	1,167 (17.1)	-	1,167 (26.7)	<0.001
Diabetes, n (%)	160 (2.3)	33 (1.3)	127 (2.9)	<0.001
CDV disease, n (%)	56 (0.8)	11 (0.4)	45 (1.0)	0.011
Smoking, n (%)	1,942 (28.5)	788 (32.2)	1,154 (26.4)	<0.001
Education, n (%)				<0.001
University	857 (12.6)	404 (16.5)	453 (10.4)	<0.001

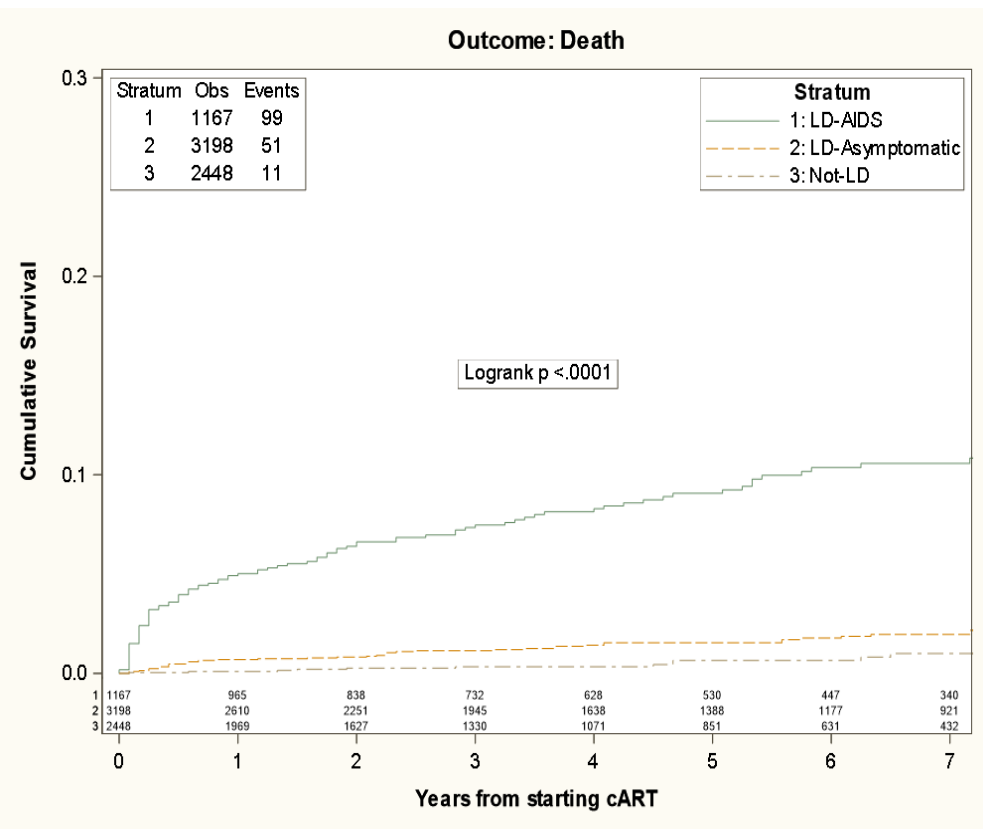
Main characteristics of late presenters according to AIDS

	LD N= 4,365 (n=100%)	LD-Asymptomatic N=3,198 (73.3%)	LD-AIDS N=1,167 (26.7%)	p
Female Gender, n (%)	913 (20.9)	660 (20.6)	253 (21.7)	<0.001
Age, years, median (IQR)	42 (34-51)	41 (33-50)	45 (37-53)	<0.001
Mode of HIV Transmission, n (%)				<0.001
MSM	1,632 (37.4)	1,256 (39.3)	376 (32.2)	
Heterosexual	2,146 (49.1)	1,526 (47.7)	620 (53.1)	
IDU	204 (4.7)	140 (4.4)	64 (5.5)	
Not Italian Nationality, n (%)	2,432 (55.7)	1,805 (56.4)	627 (53.7)	<0.001
CD4 nadir, cells/mm ³ , median (IQR)	136 (48-242)	179 (78-264)	49 (20-120)	<0.001
HIV-RNA, log ₁₀ cps/mL, median (IQR)	5.12 (4.50-5.66)	5.05 (4.45-5.57)	5.32 (4.63-5.86)	<0.001
AIDS diagnosis, n (%)	1,167 (26.7)	-	1,167 (100.0)	<0.001
Diabetes, n (%)	127 (2.9)	78 (2.4)	49 (4.2)	<0.001
CDV disease, n (%)	45 (1.0)	27 (0.8)	18 (1.5)	0.003
Smoking, n (%)	1,154 (26.4)	888 (27.8)	266 (22.8)	<0.001
Education. University n (%)	453 (10.4)	339 (10.6)	114 (9.8)	<0.001

First-line ART regimens in total population

	Total N= 6,813	Non-late Diagnosis (non-LD) N= 2,448 (35.9%)	Late Diagnosis (LD) N= 4,365 (64.1%)	p-value
Calendar year of baseline, median (IQR)	2016 (2014-2019)	2017 (2015-2019)	2016 (2013-2019)	<0.001
Type of regimen started, n of drugs, n (%)				<0.001
2-drug regimen (3TC+DTG)	130 (1.9)	89 (3.6)	41 (0.9)	
3-drug regimen	6332 (92.9)	2171 (88.7)	4161 (95.3)	
- INSTI-based	3319 (48.7)	1293 (52.8)	2026 (46.4)	
- PI-based	1931 (28.3)	409 (16.7)	1522 (34.9)	
- NNRTI-based	1032 (15.1)	460 (18.8)	572 (13.1)	
- other	50 (0.7)	9 (0.4)	41 (0.9)	
≥4-drug regimen	351 (5.2)	188 (7.7)	163 (3.7)	

Mortality



all-cause mortality[#]

LD-Asymptomatic

1

95% CI

-

p-value

LD-AIDS

4.42

3.14-6.22

<0.001

Non-LD

0.35

0.17-0.69

0.002

^x interaction test exposure group and calendar year of ART start: p=0.07

aSHR*

95% CI

p-value

AIDS-related mortality

LD-Asymptomatic

1

-

LD-AIDS

16.86

8.24-34.46

<0.001

Non-LD

-

-

-

^x interaction test exposure group and calendar year of ART start: p=0.42

not AIDS-related mortality

LD-Asymptomatic

1

-

LD-AIDS

1.74

1.08-2.78

0.022

Non-LD

0.53

0.26-1.11

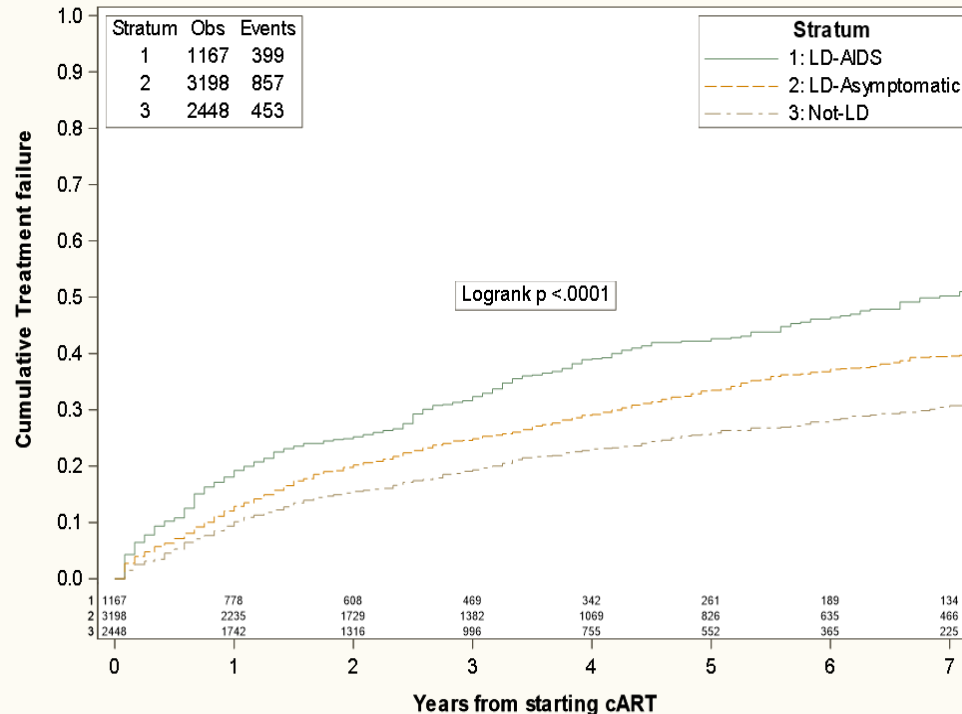
0.093

^x interaction test exposure group and calendar year of ART start: p=0.65



Treatment failure

Outcome: Confirmed VL>200 after >6 months of ART or stop of ≥1 drug due to failure/toxicity



all-LD vs Non-LD

aHR* 95% CI p-value

Non-LD

1

-

LD

1.21

1.08-1.36

0.001

^xinteraction test exposure group and calendar year of ART start: p<0.01

LD-AIDS vs non AIDS

LD-Asymptomatic

1

-

LD-AIDS

1.30

1.15-1.47

<0.001

Non-LD

0.88

0.78-1.00

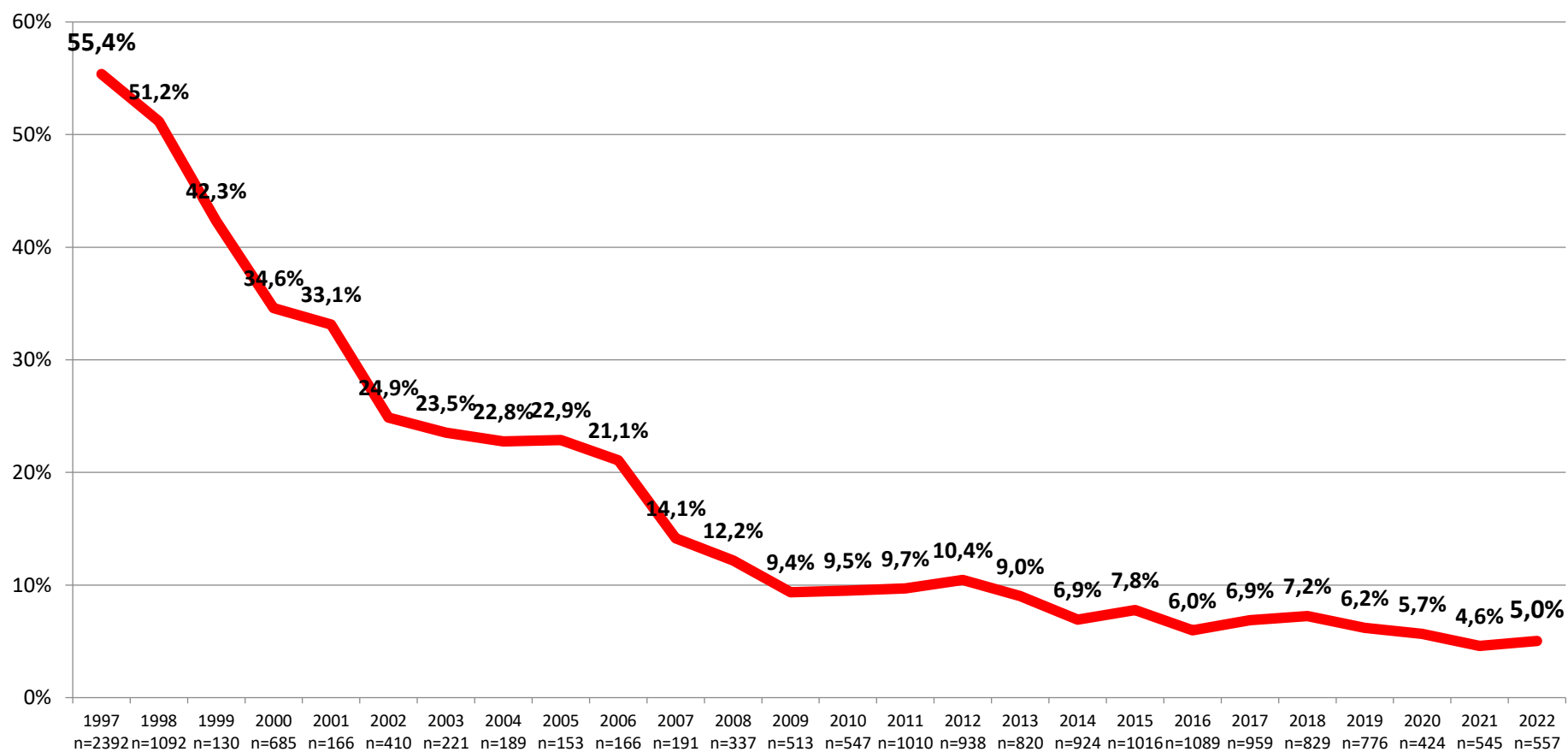
0.046

^xinteraction test exposure group and calendar year of ART start: p<0.01

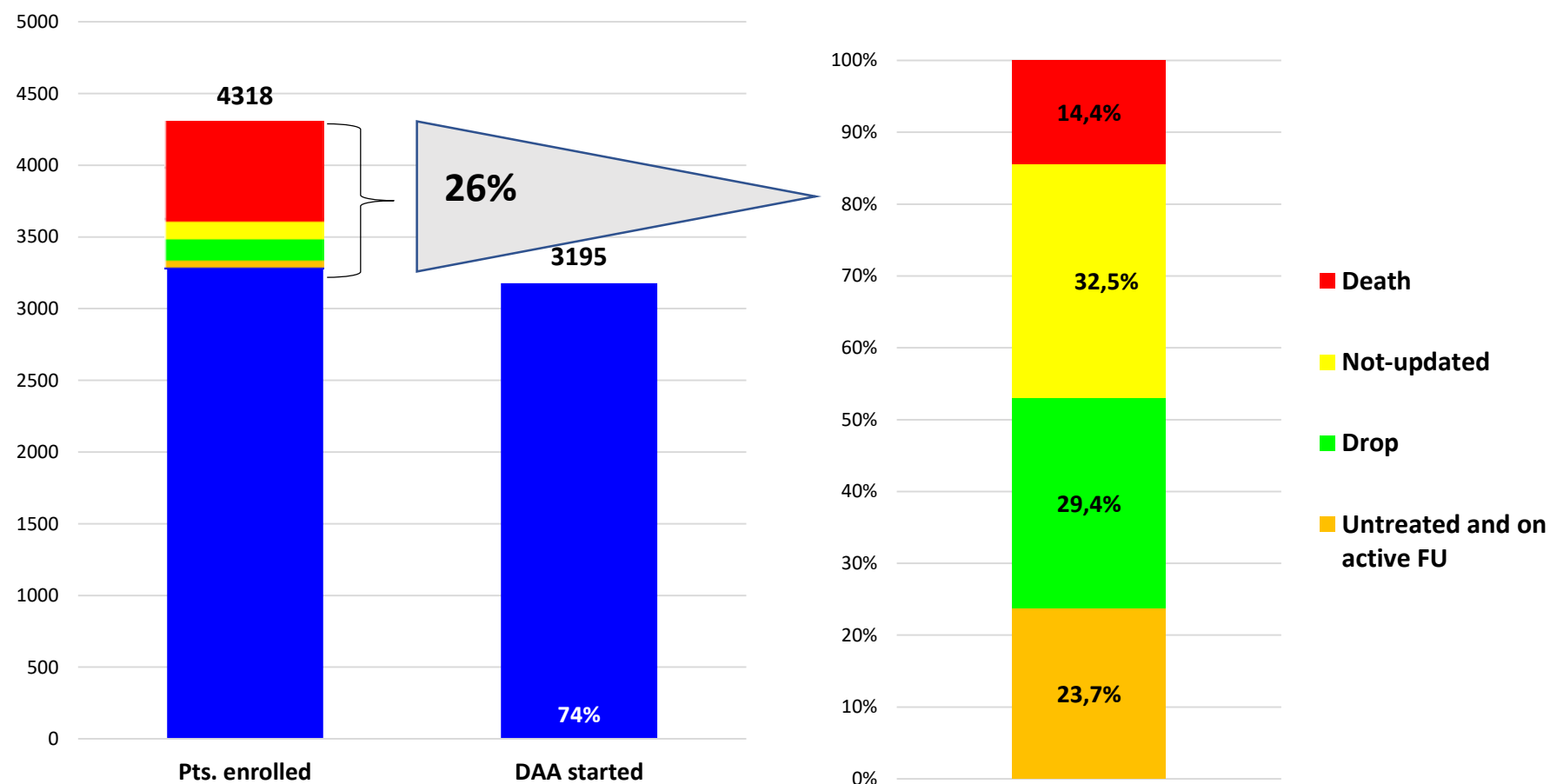
Conclusions

- ❖ In more recent years, LD subjects and, particularly AIDS presenters, despite an early ART initiation, remained at a higher risk of poorer outcomes in terms of both survival and treatment durability compared with the rest of ART-naïve subjects.
- ❖ Public health strategies to implement early HIV diagnosis are urgently needed to constrain the mortality gap of this vulnerable population.

Proportion of patients with HCVAb pos test within 1 year from enrolment, according to calendar year of enrolment



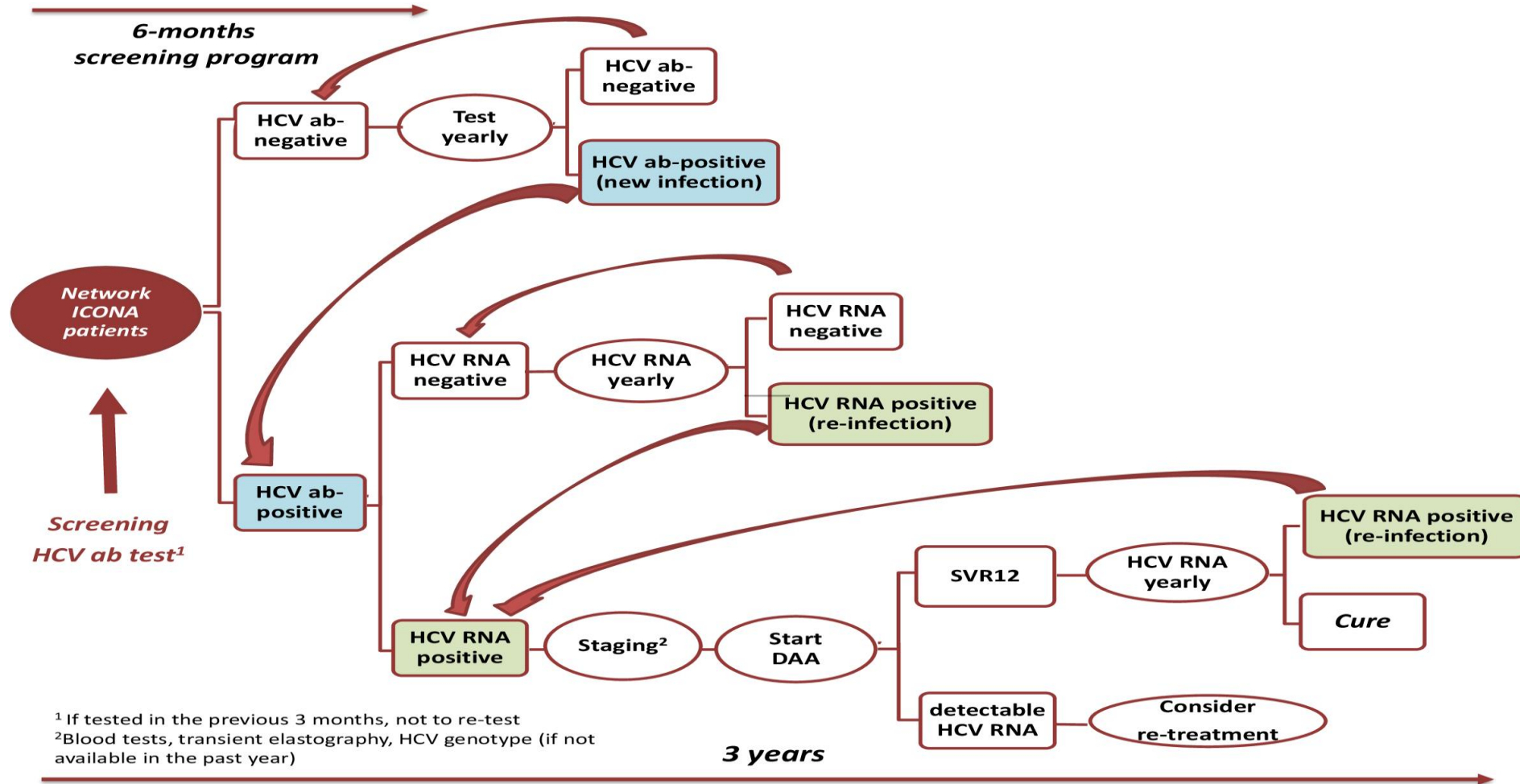
Proportion of untreated HCV patients in IcoNa/HepalcoNa



NoCo Project



Conceived by Professor Mauro Moroni
Fondazione Icona

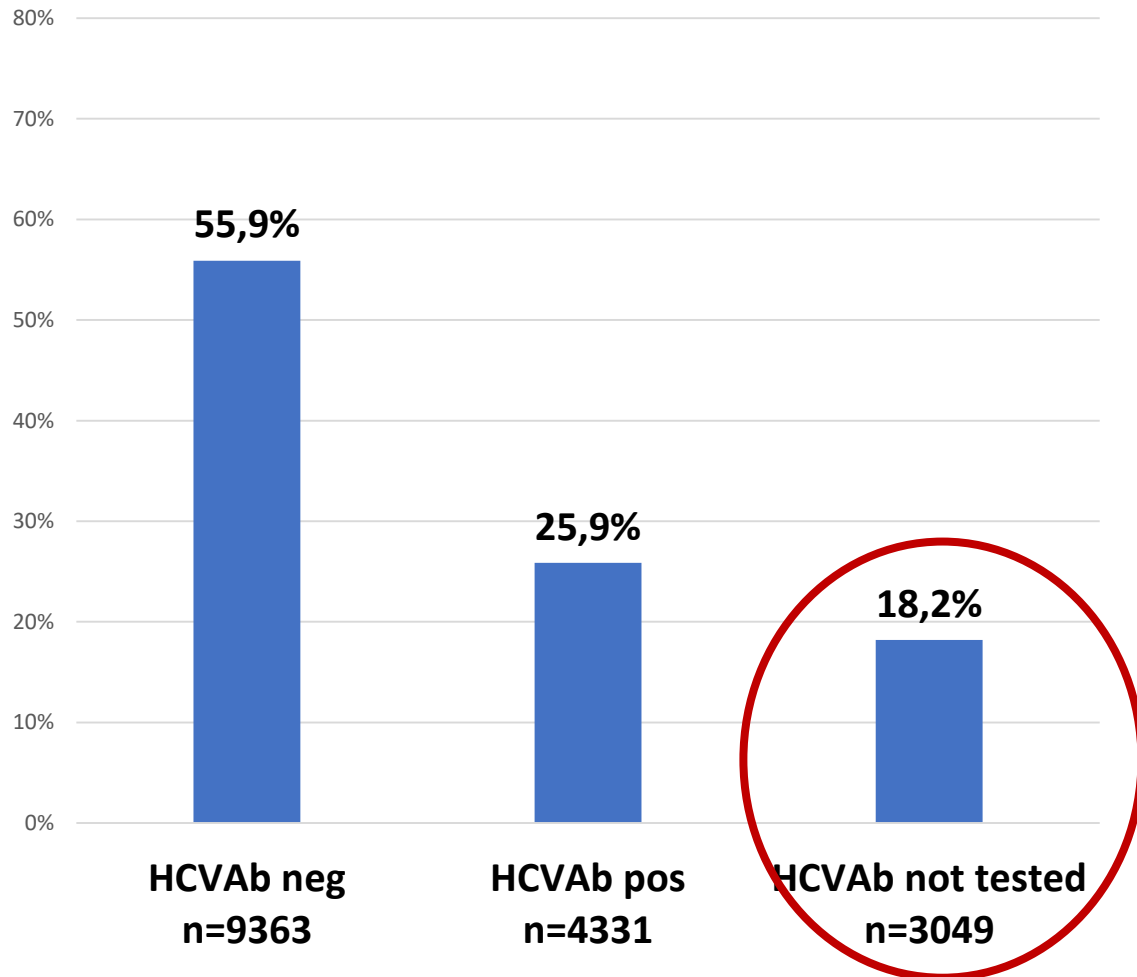


A d'Arminio Monforte, Liver International 2023

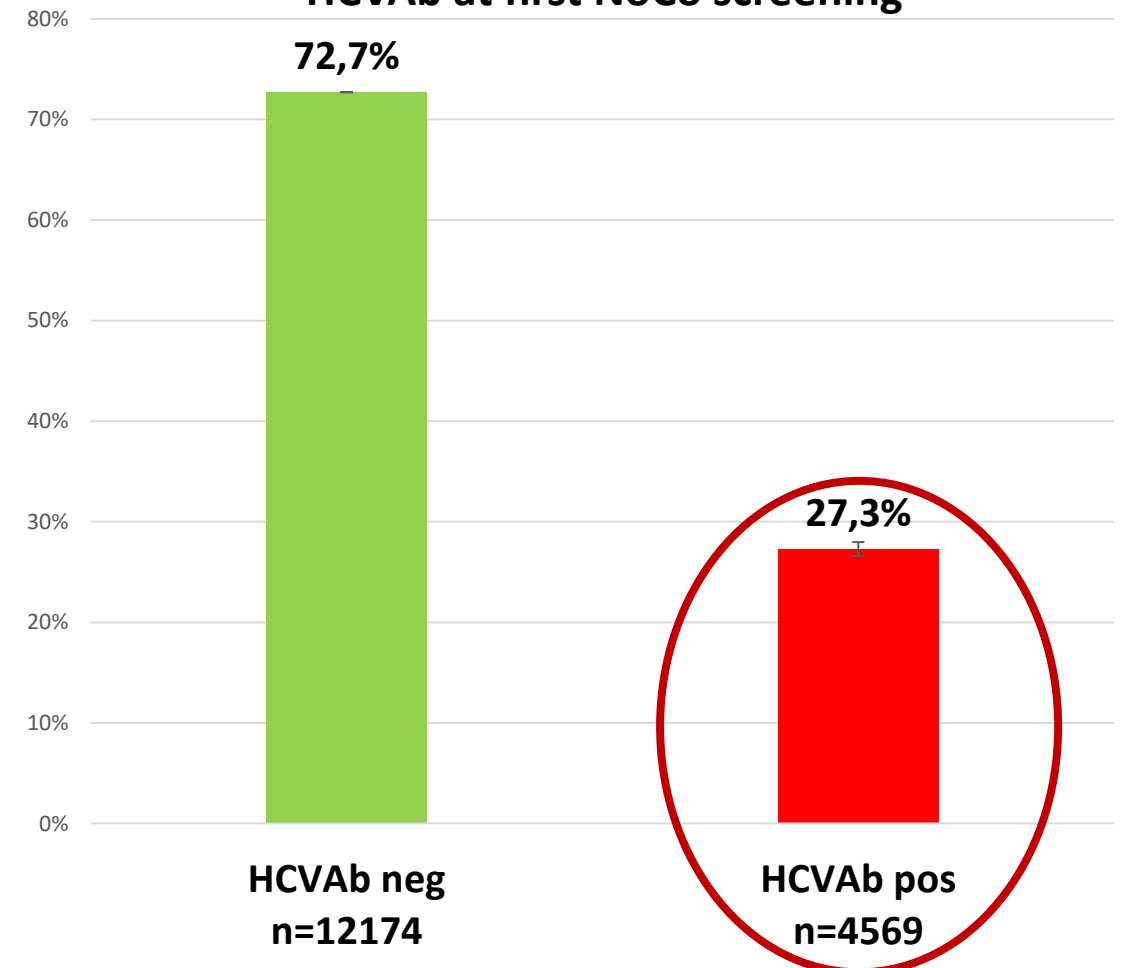


NoCo Study: HCV Ab at baseline in 16,743 PLWH

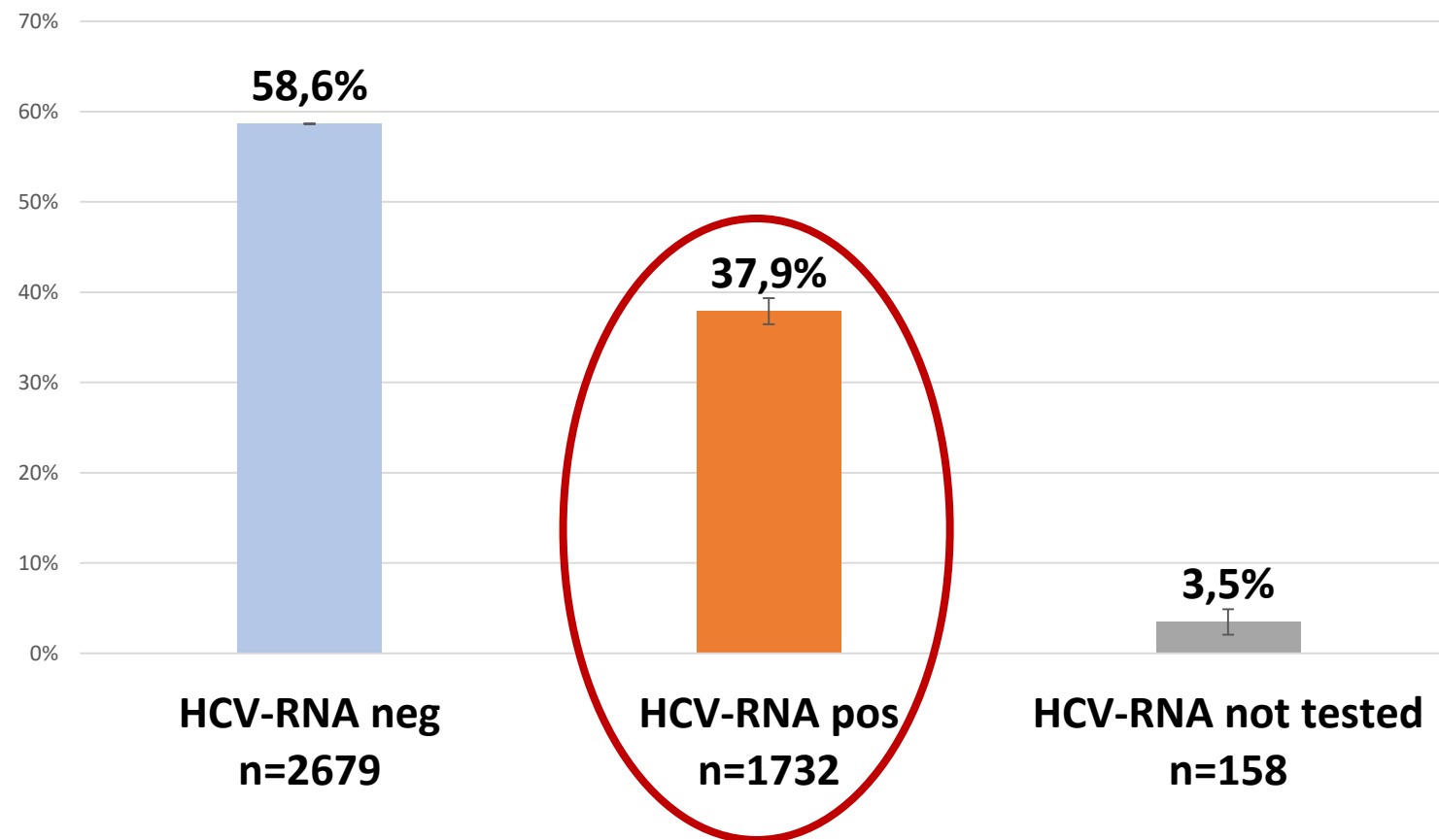
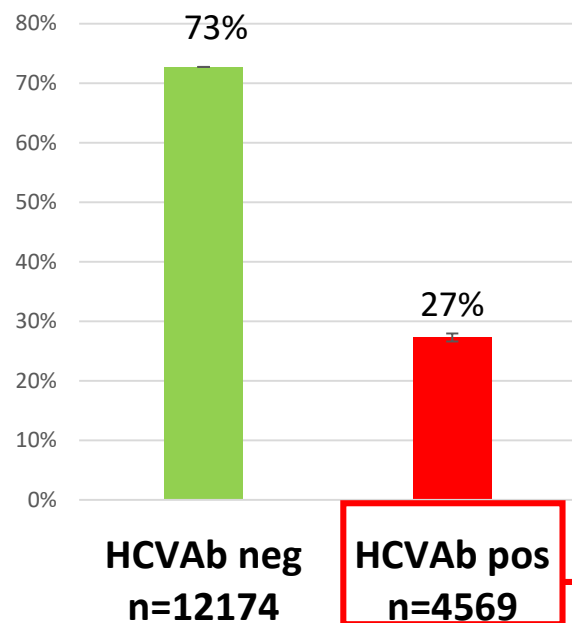
HCV Ab status pre-enrollment



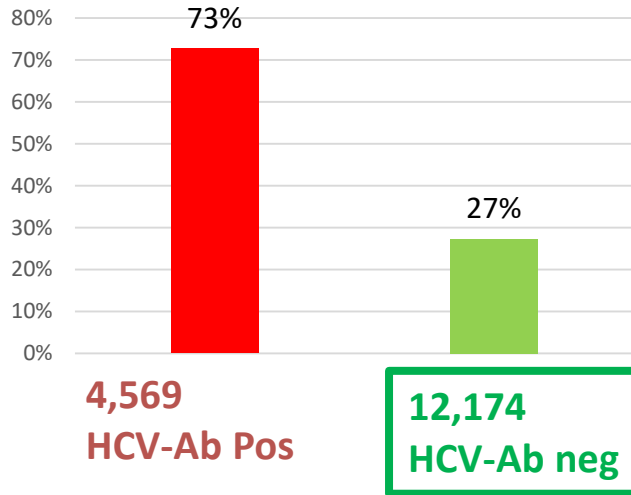
HCVAb at first NoCo screening



Active HCV infection: first NoCo screening



HCV seroconversions during NoCo Study: Incidence and KM probabilities



4890 HCV-Ab neg PLWH
with at least a 2nd screening (40.2%)

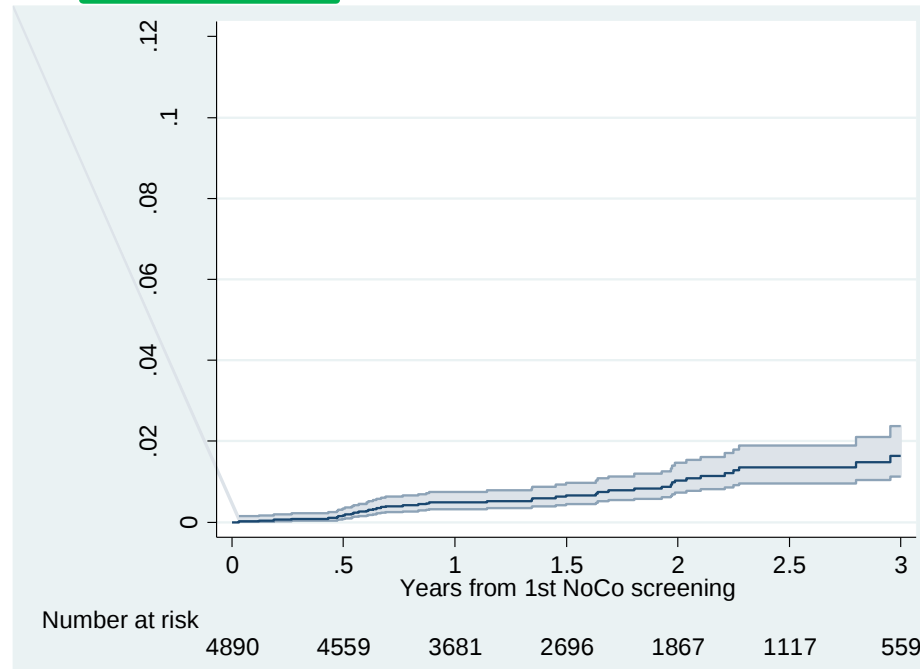
Median FU (IQR) = 1.64 yrs (1.00-2.43)

42 HCV seroconversions (0.86%)

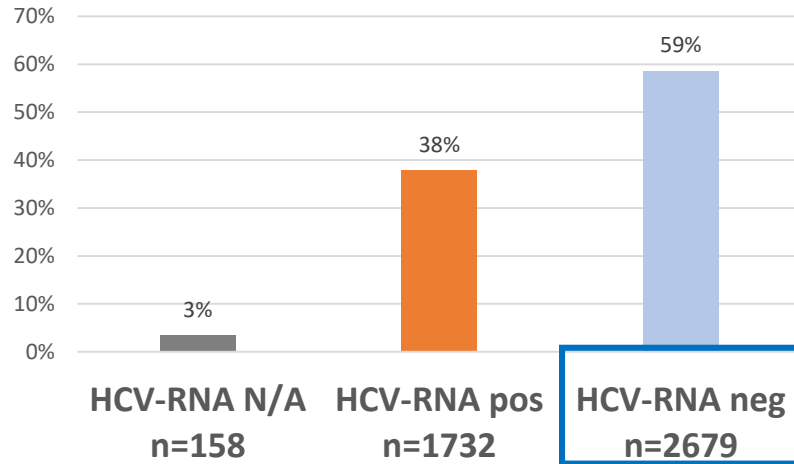
Incidence Rate: 0.48 x 100 PYFU
(95% CI: 0.36-0.65)

KM estimated probability of HCV SC:

- 1-yr: 0.5% (0.3-0.7)
- 2-yr: 1.0% (0.7-1.5)



HCV re-infections during NoCo Study: Incidence and KM probabilities

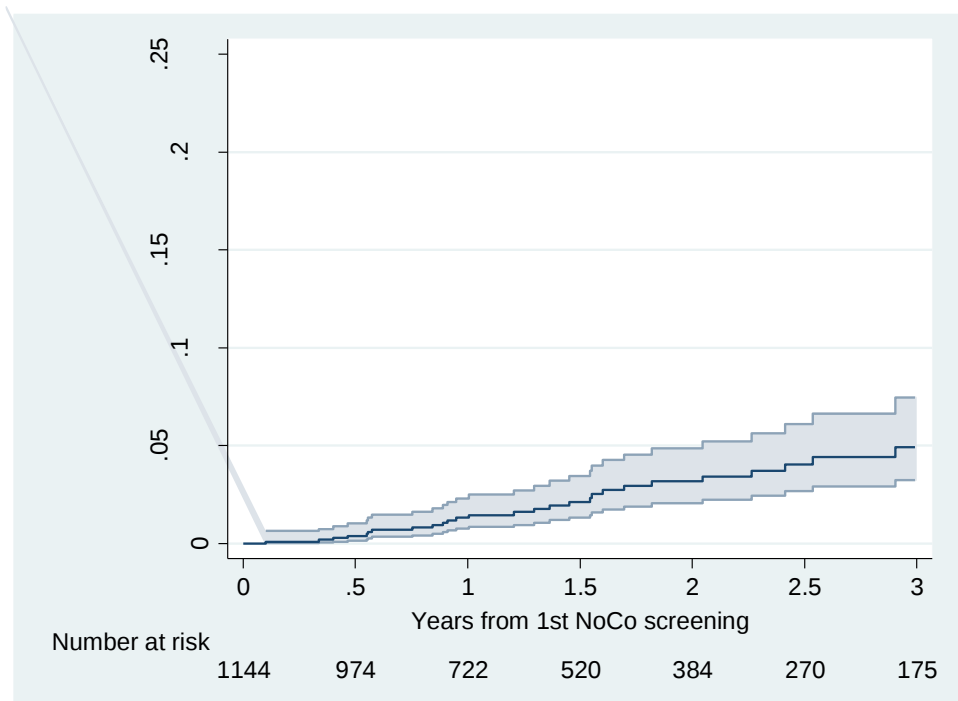


1,144 HCV-RNA neg with at least a
2nd HCV RNA test (42.7%)

Median FU(IQR)= 1.3 yrs (0.7-2.4)

38 /1,144 (3.3%) PLWH turned HCV-RNA pos

- 10 relapses after DAA
- 28 confirmed HCV-reinfections



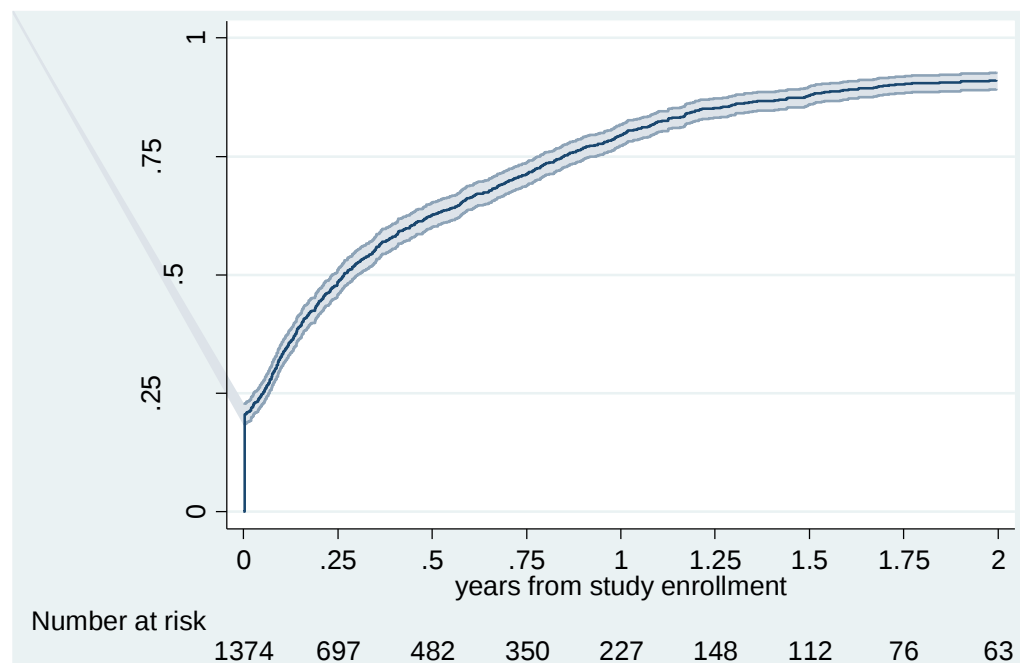
KM estimated probability of HCV SC:

- 1-yr: 1.3% (0.7-2.3)
- 2-yr: 3.2% (2.0-4.8)

DAA uptake and response

1,374/1,732 (79.3%) HCV viremic subjects at baseline had a follow-up thereafter

1,184 subjects started DAA



	Probability of DAA-update (95%CI)
1-year	79.5% (95%CI: 77.3-81.7)
2-year	79.5% (95%CI: 77.3-81.7)

SVR12 in 874, 95.5%

Predictors of SVR12 by fitting a logistic regression

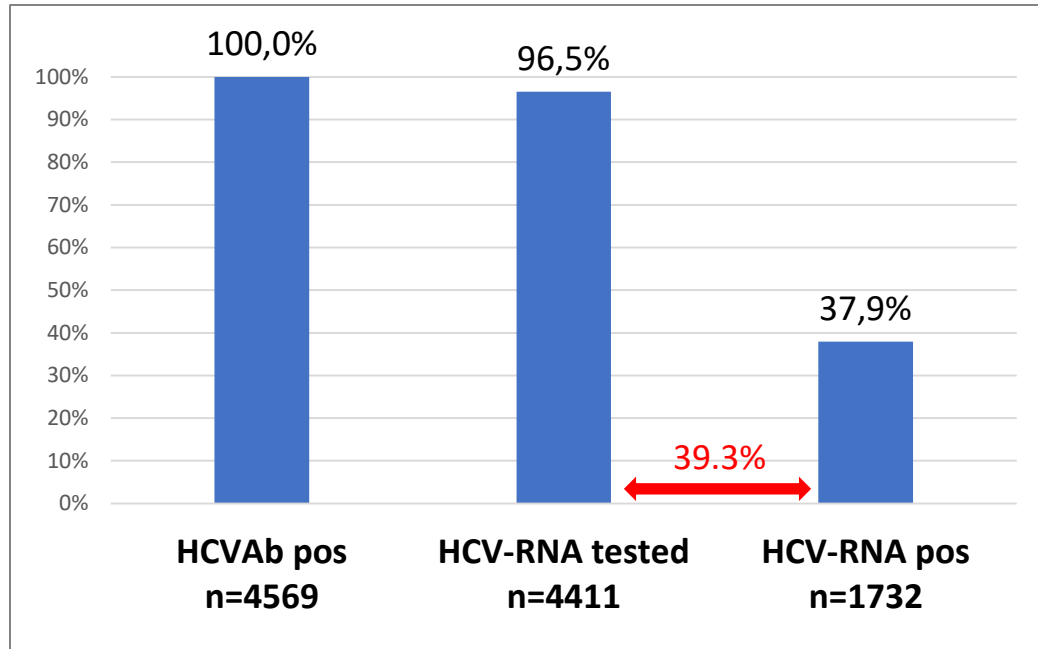
	aOR* 95%CI			p
Mode of HIV Transmission				
Heterosexual	1.00			
IDU	0.70	0.25	1.96	0.500
MSM	8.14	0.93	70.84	0.058
Other/Unknown	0.32	0.09	1.13	0.076
HIV-RNA>50 copies/ml	1.41	0.32	6.22	0.646
CD4<200 cells/mmc	0.18	0.06	0.52	0.001
FIB-4, per 1 more				
<1.45	1.00			
1.45-3.25	1.04	0.49	2.24	0.913
>3.25	0.46	0.19	1.11	0.085
Missing FIB4	1.03	0.13	8.20	0.976
HCV Genotype				
G1 or G4				
G2 or G3	1.09	0.52	2.29	0.820
Other/Multiple/Missing	0.89	0.19	4.06	0.879
Regimen				
GCV/PBV	1.00			
SOF/VEL	0.80	0.38	1.67	0.556
Other Regimen	0.46	0.14	1.56	0.213
Missing	0.43	0.05	3.76	0.448

Outcomes of HCV care in the NoCo Study



Conceived by Professor Mauro Moroni

Fondazione Icona



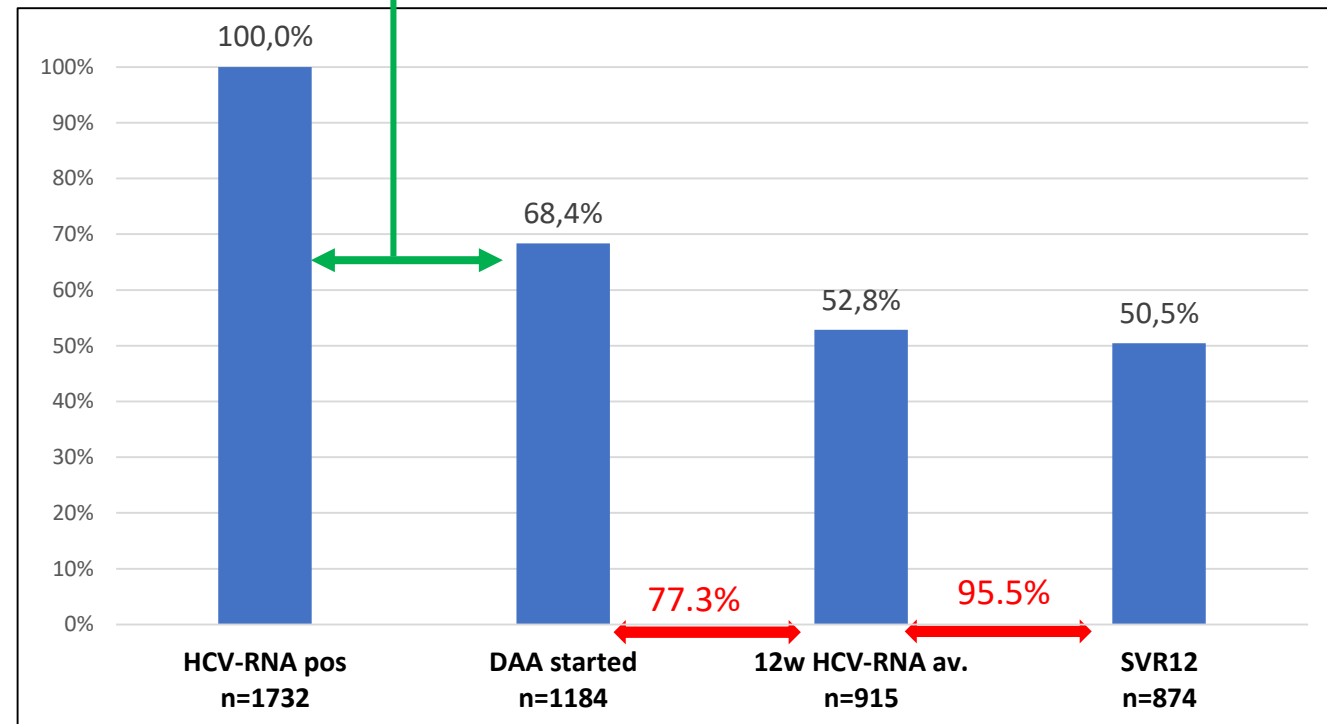
548 not starting DAA or not updated

22 deaths

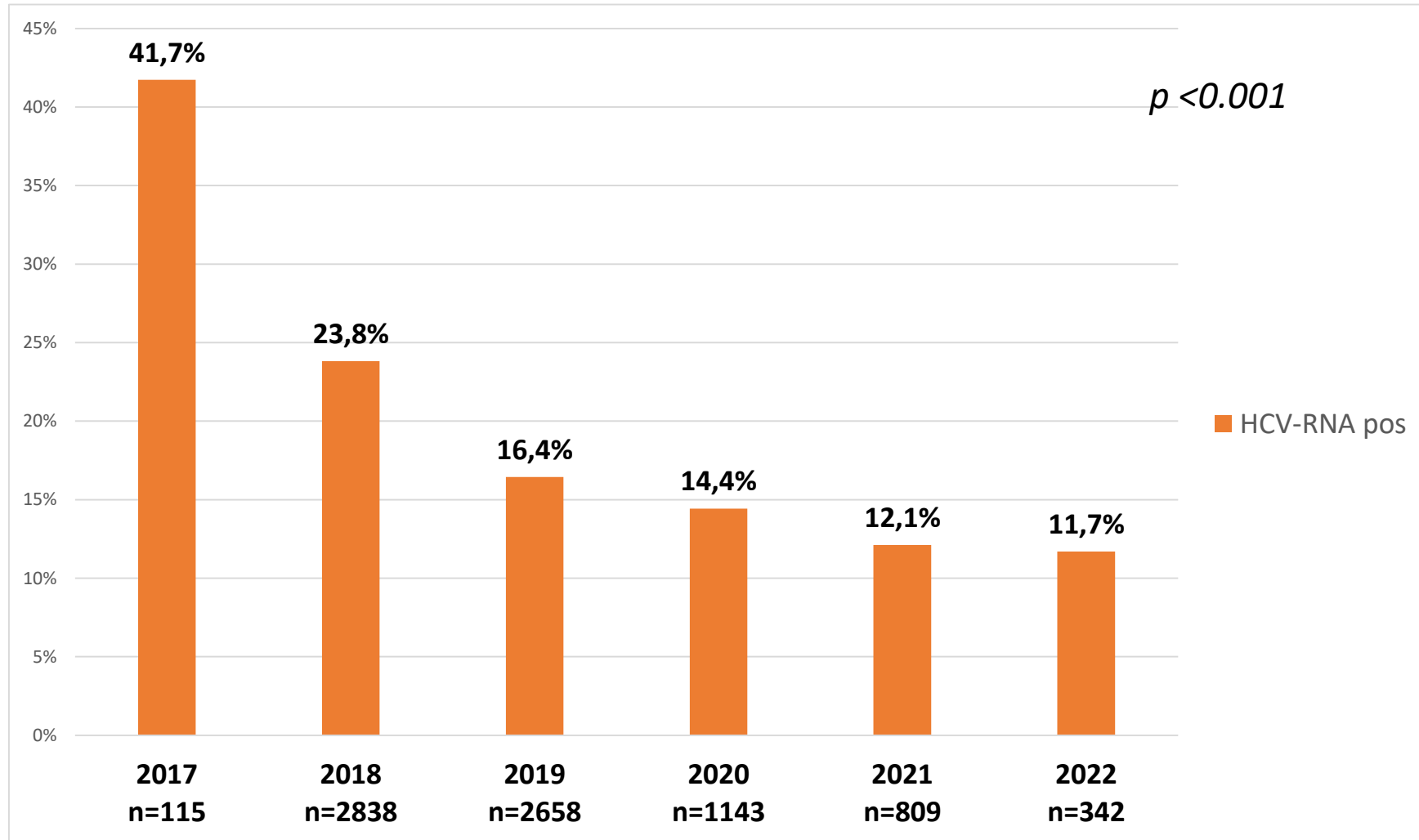
29 drop

174 updated in 2021-2022 not started DAA

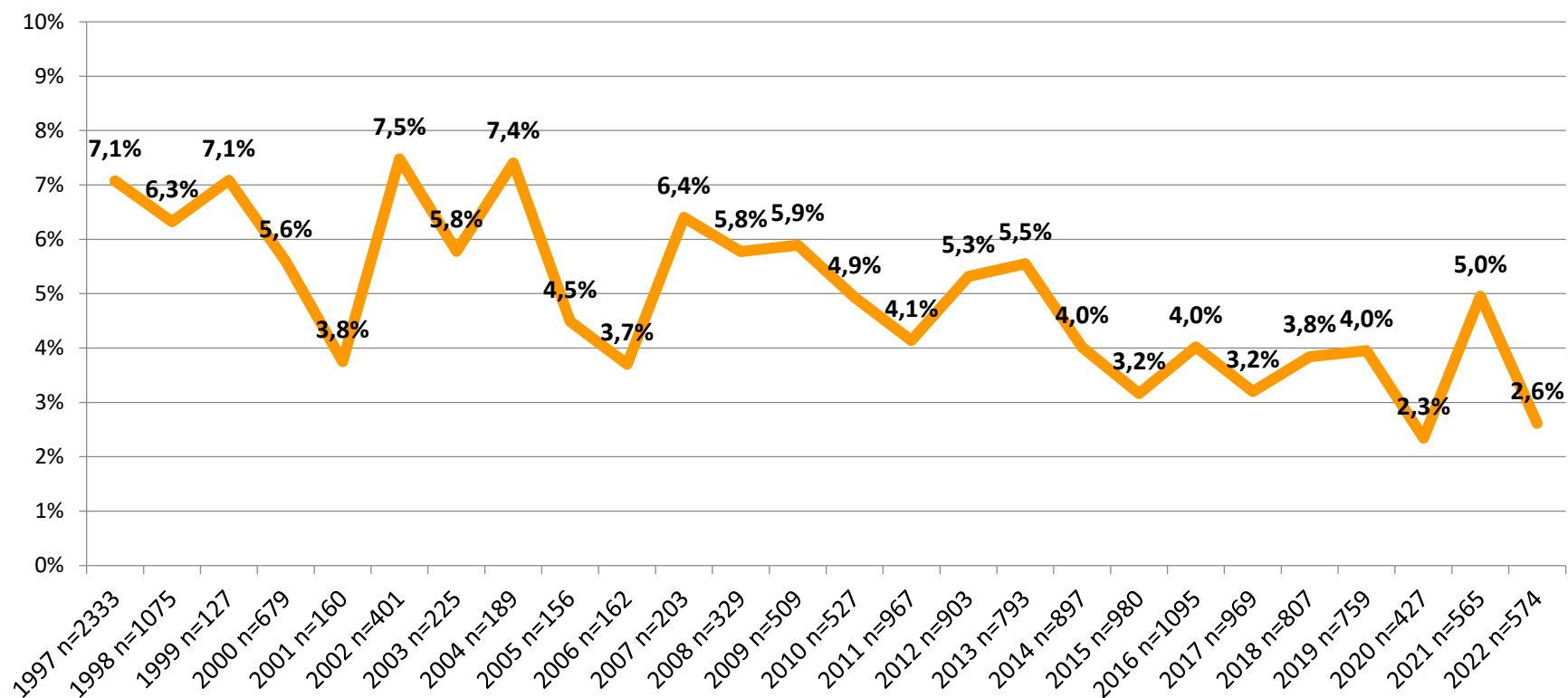
323 not updated (2021-2022) not started DAA



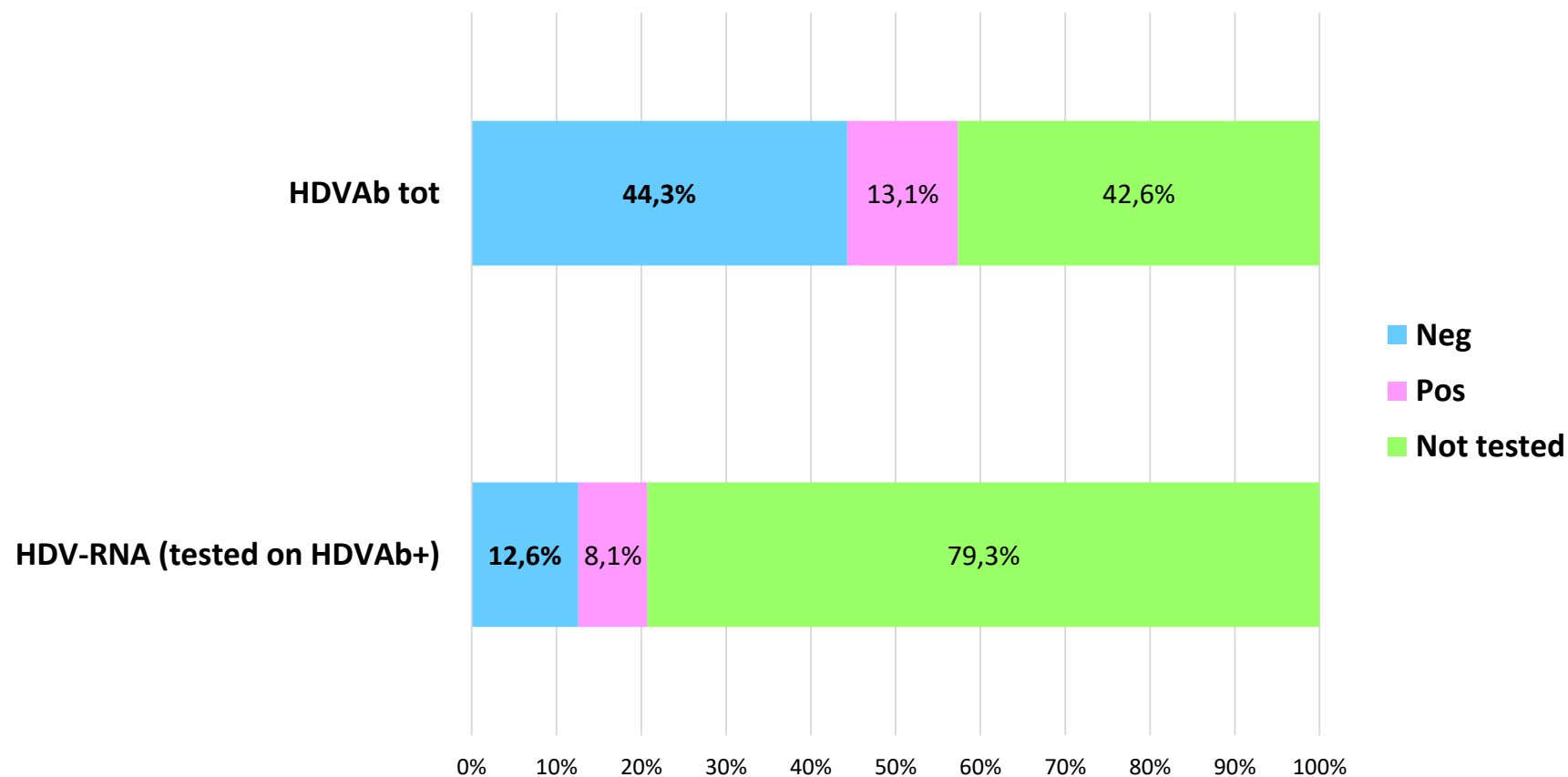
Active HCV infection according to calendar year of Follow Up



Proportion of patients with an HBsAg positive test within 1 year from enrolment, according to calendar year of enrolment



Delta prevalence of anti-delta in HBsAg positive individuals (n=1034)



Hepatitis Delta Virus (HDV) infection. Data from the ICONA cohort

18,285/20,012 (91.4%) tested for HBsAg

1,025/18,285 (5.6%) HBsAg positive

809/1,025 (79.0%) tested for anti-HDV

152/809 (18.8%) anti-HDV positive

93/152 (61.2%) tested for HDV-RNA

63/93 (67.7%) HDV-RNA positive

Prevalence, incidence and Adjusted SHR (ASHR) of SLRE according to HDV status from fitting unadjusted and adjusted Fine-Gray regression model (using death as competing event)

	N			IR x1000PYFU	CIF 5-years
	PLWH	SLRE	Prevalence (95%CI)	(95%CI)	
HDV Ab neg	612	15	2.4% (1.4-4.0)	3.6 (2.0-6.0)	1.9% (0.9-3.5)
HDV Ab pos / HDVRNA missing	50	6	12.0% (4.5-24.3)	17.2 (6.3-37.5)	10.2% (3.1-22.2)
HDV Ab pos / HDV-RNA neg	29	4	13.8% (3.9-31.7)	13.7 (3.8-35.1)	12.0% (3.0-27.7)
HDV Ab pos / HDV-RNA pos	59	12	20.3% (11.0- 32.8)	23.7 (12.2-41.4)	13.6% (6.0-24.4)
HDV-RNA>1.000 IU/ml	43	8	18.6% (8.4-33.4)	23.7 (10.2-46.7)	13.8% (5.0-27.0)
HDV-RNA≤1.000 IU/ml	14	3	21.4% (4.6-50.8)	21.4 (4.4-62.8)	15.4% (2.5-38.8)

	ASHR*	95%CI	p
HDV Ab neg	1		
HDV Ab pos / HDVRNA missing	3.22	1.23-8.45	0.018
HDV Ab pos / HDVRNA neg	3.09	0.99-9.59	0.051
HDV Ab pos / HDVRNA pos	4.54	2.07-9.96	<.001

* Adjusted for baseline CD4, age, alchool use and HCV status

Prevalence, incidence and Adjusted SHR (ASHR) of SLRE according to HDVAb/HCVAb at baseline from fitting unadjusted and adjusted Fine-Gray regression model (using death as competing event)

	N PLW H	SLRE	Prevalence (95%CI)	IR x1000PYFU (95%CI)	CIF 5-years
HDVAb+ HCVAb+	101	20	19.8% (12.5-28.9)	23.6 (14.4-36.4)	14.8% (8.3-23.1)
HDVAb+ HCVAb-	37	2	5.4% (0.6-18.2)	6.7 (0.8-24.3)	3.9% (0.3-16.6)
HDVAb- HCVAb+	133	9	6.7% (31.5-12.4)	8.6 (3.9-16.3)	3.7% (1.2-8.5)
HDVAb- HCVAb-	455	6	13.2% (4.8-28.5)	2.1 (0.7-4.4)	1.3% (0.5-3.0)

	AHSR*	95%CI	p
HDVAb- HCVAb-	1		
HDVAb+ HCVAb+	11.88	4.64-30.39	<.001
HDVAb+ HCVAb-	3.75	0.73-19.12	0.112
HDVAb- HCVAb+	4.11	1.45-11.65	0.008

** Adjusted for baseline CD4, age, alcohol use*

Conclusions

- ❖ One fifth of the HBsAg positive PWH harbor HDV infection, and are at high risk of progression to advanced liver disease.
- ❖ HCV plays a pivotal role for worse outcome.
- ❖ This population needs urgently effective treatment.

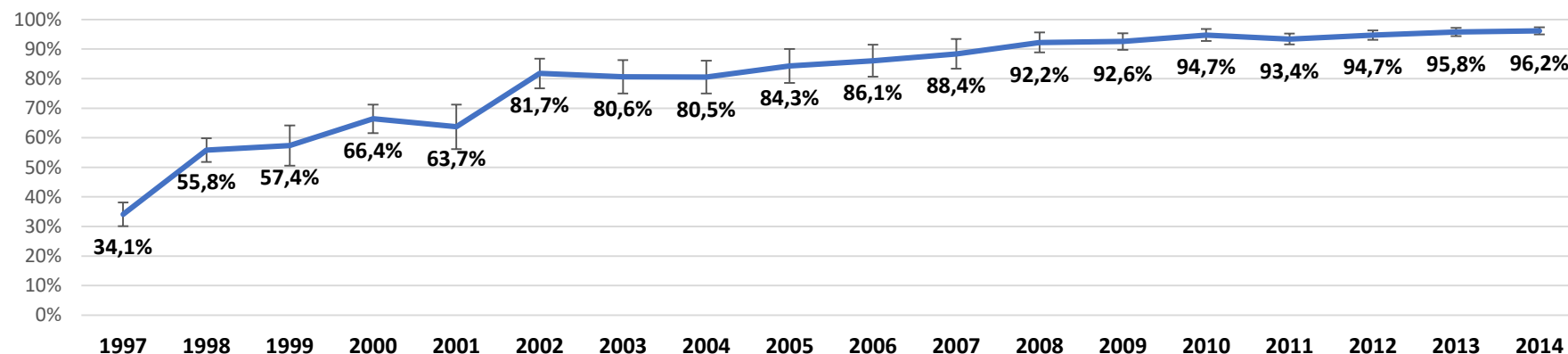
Demographic characteristics of 10.941 patients at last follow up in 2021-2023



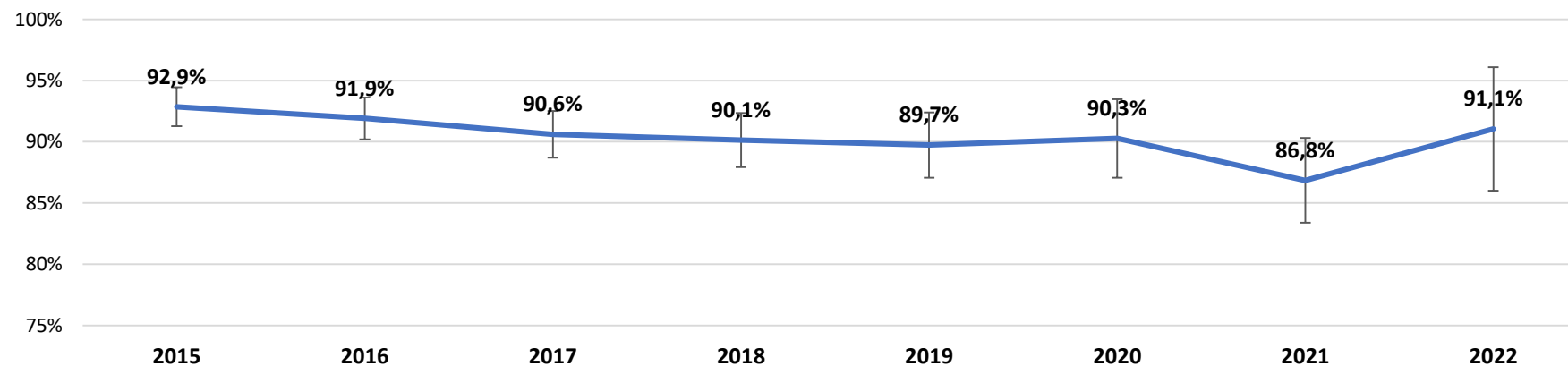
Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

VL<50	9642 (88.1%)
Median VL	19
CD4<200	611 (5.5%)
CD4<350	1445 (13.2%)
Median CD4 (cell/μL)	710
Median CD4 (%)	33.4
Median age	49
Age>60	1920 (17.5%)
Gender M	8762 (80%)
Gender F	2179 (19.9%)
Risk: Heterosexual contacts	4299 (39.2%)
Risk: Homo/Bisexual contacts	4954 (45.2%)
Risk: IDU/ex IDU	704 (6.4%)
Risk: Other/Unknown	946 (8.6%)
Risk: Not compiled	38 (0.3%)
Italians	8877 (81.1%)
Migrants	2064 (18.8%)
Line: 2	2332 (21.3%)
Line: ≥ 3	5708 (52.1%)
Line: Naïve	173 (1.5%)
INSTI	7682 (70.2%)

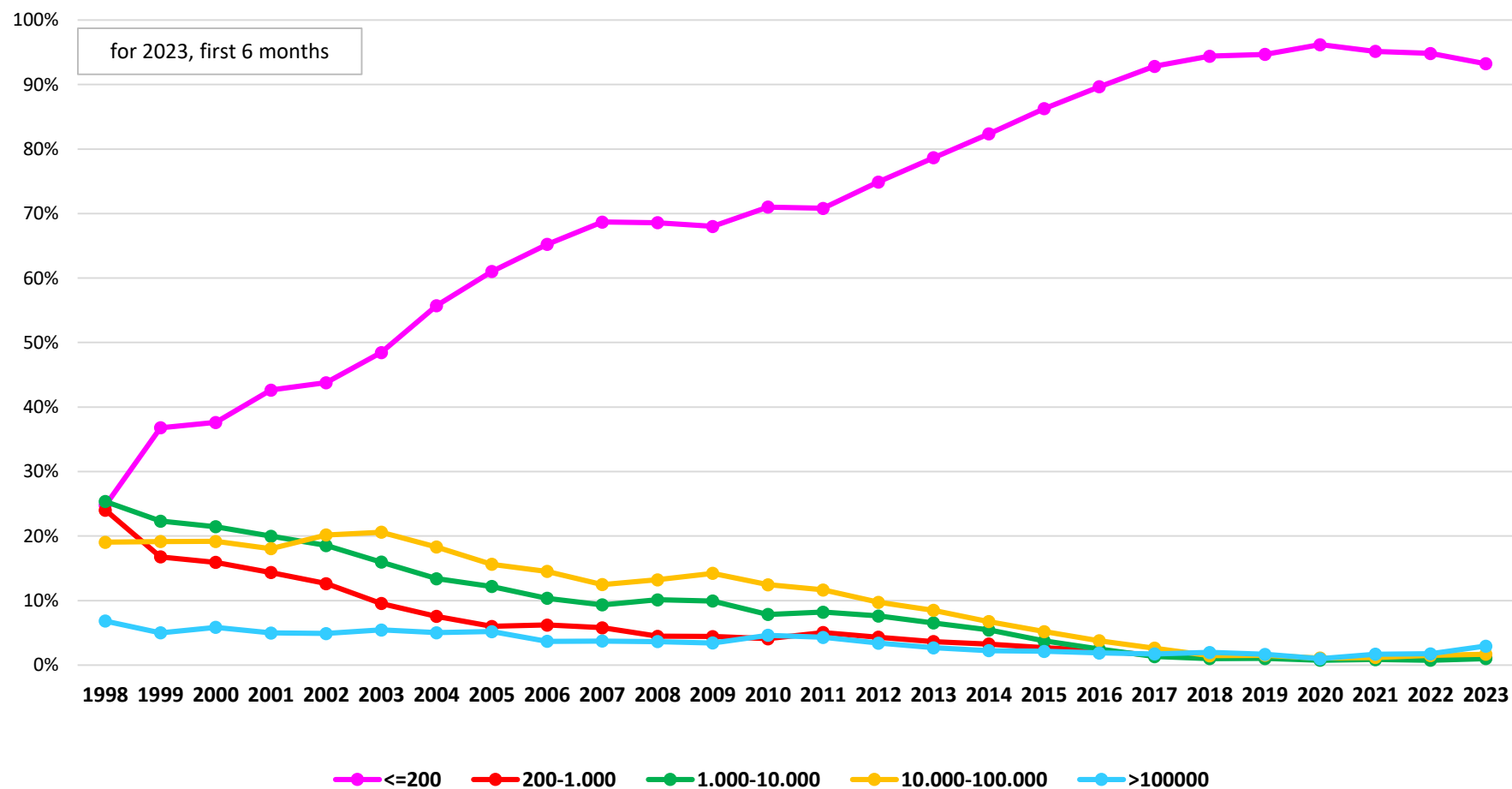
Proportion of patients with a VL≤200 copies/mL at 12 months from starting their first cART from ART-naïve from 1997 to 2014



Proportion of patients with a VL≤50 copies/mL at 12 months from starting their first cART from ART-naïve from 2015



HIV-RNA strata (copies/mL) in all patients in follow-up according to calendar year



Fotografia delle PLHIV in ICONA: conclusioni

- ❖ Analogamente ai dati COA segnaliamo una mancata diminuzione delle nuove diagnosi negli ultimi anni
- ❖ In più del 50% dei casi si tratta di late presenters, a trasmissione sessuale
- ❖ Mentre la epatite da HCV è in diminuzione nella gran maggioranza guarita con DAA, la epatite da HBV è stazionaria, e la epatite da HDV viene frequentemente non ricercata
- ❖ Le PLWH in trattamento sono in più del 90% dei casi a VL undetectable e quindi NON TRASMETTONO L'INFEZIONE DA HIV PER VIA SESSUALE

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