Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

I dati della coorte Icona

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Disclosure statement

- Personal fees for consultancy and lectures from Abbvie, Angelini, Bristol Myers Squibb, Gilead, Janssen, Merck, ViiV.
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- Research grants from Gilead, Janssen, ViiV.

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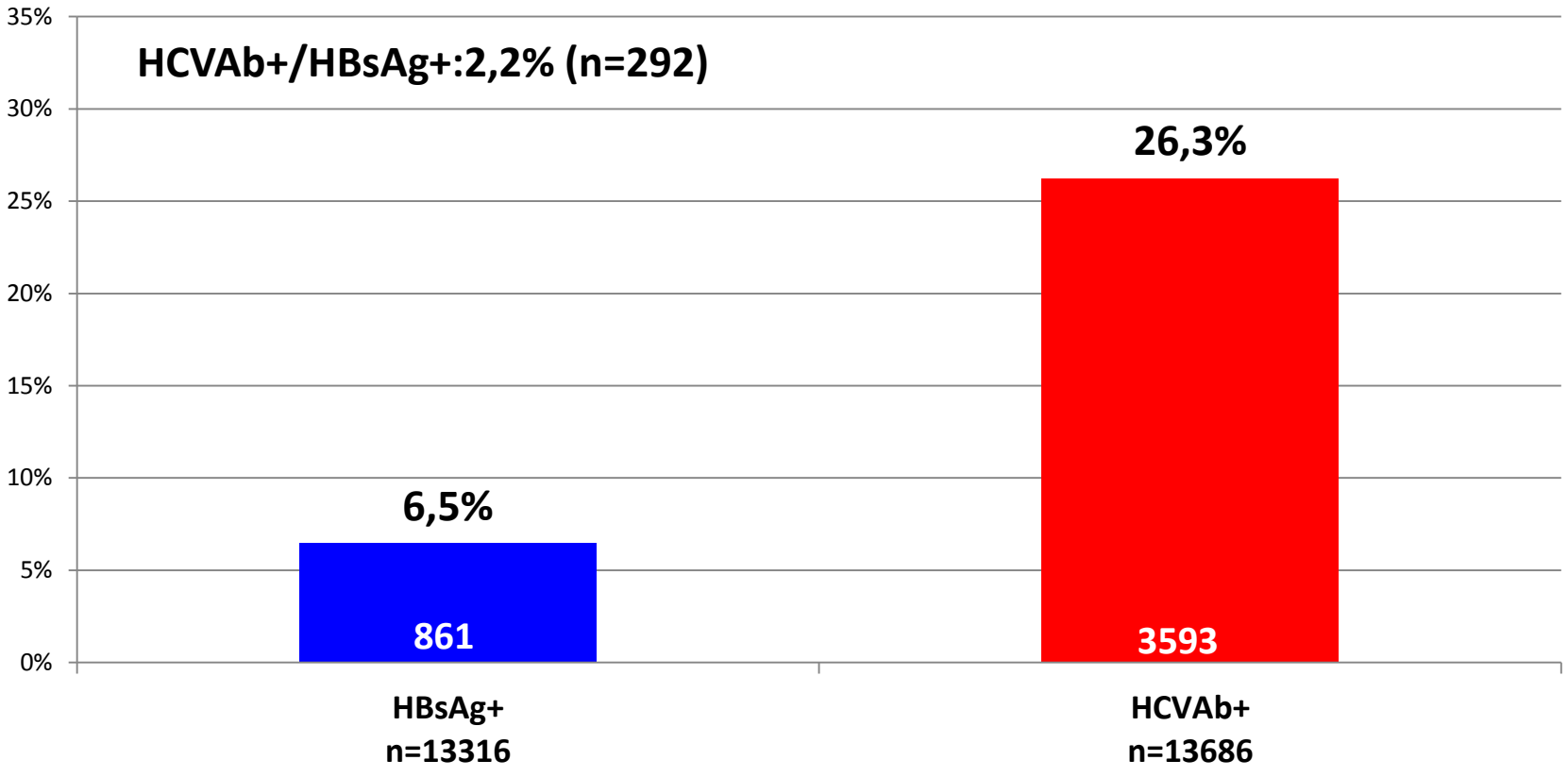
Italian Cohort I. C. O. N. A. Naive Antiretrovirals

HBsAg and HCVAb positivity in ICONA patients



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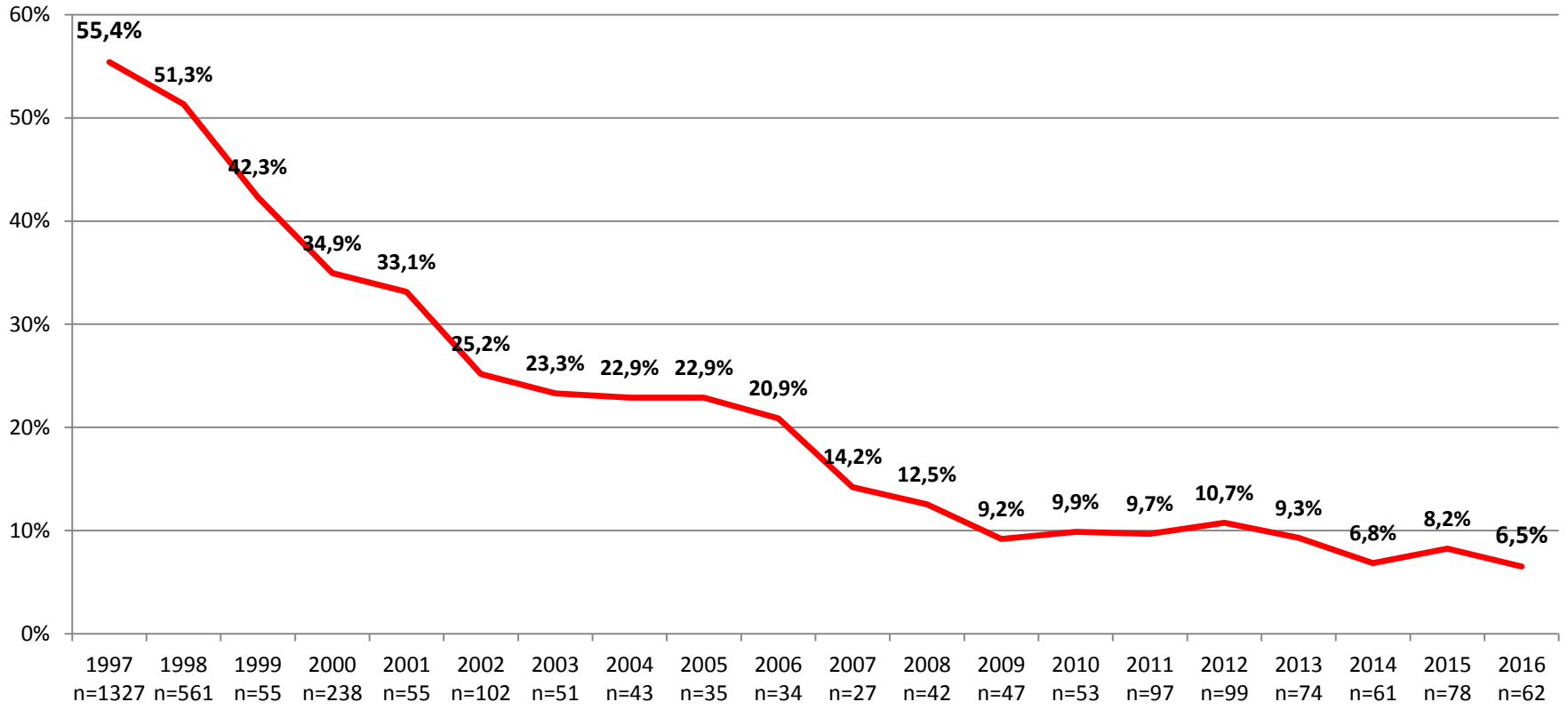
Proportion of patients with HCVAb pos test within 1 year from enrolment, according to calendar year of enrolment



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Italian Cohort I.C.O.N.A. Naive Antiretrovirals

Patients
enrolled in ICONA cohort
HCV-RNA pos at/later
than Dec 2013
(n=917)

HEPAICONA Patients:
-HIV/HCV coinfected
-HCV RNA pos -DAA
naives
(n=1887)

ICONA/HEPAICONA
Patients:
HCV-RNA pos at/later
than Jan 2013
(n=2804)

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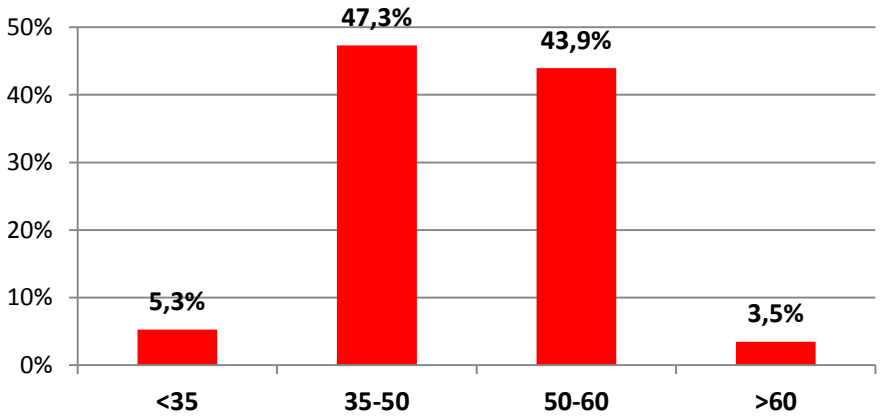
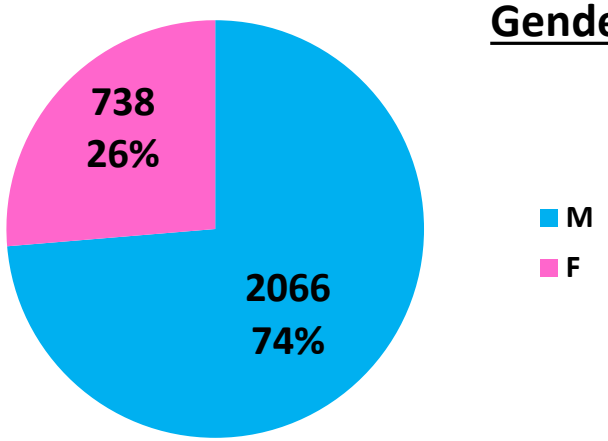
Demographic characteristics of 2804 HepaICONA+ICONA Patients

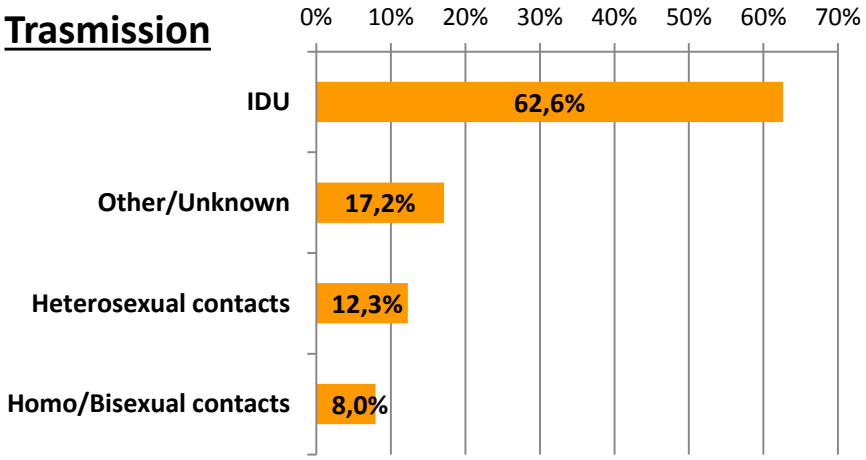
Age



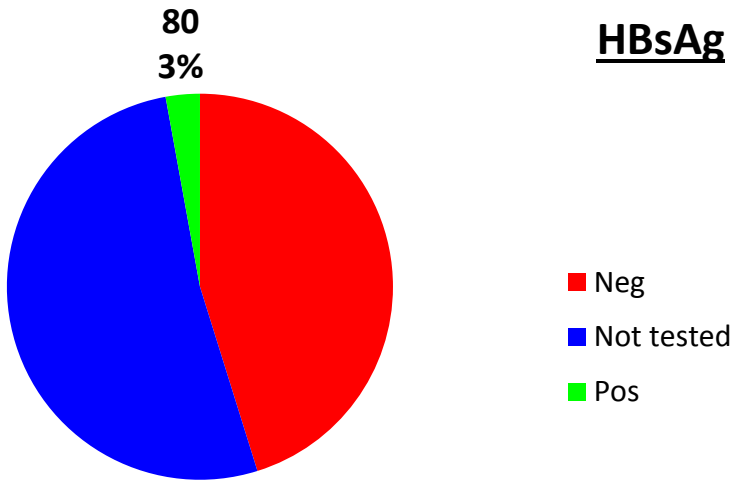
Gender



Mode of HIV Trasmission



HBsAg



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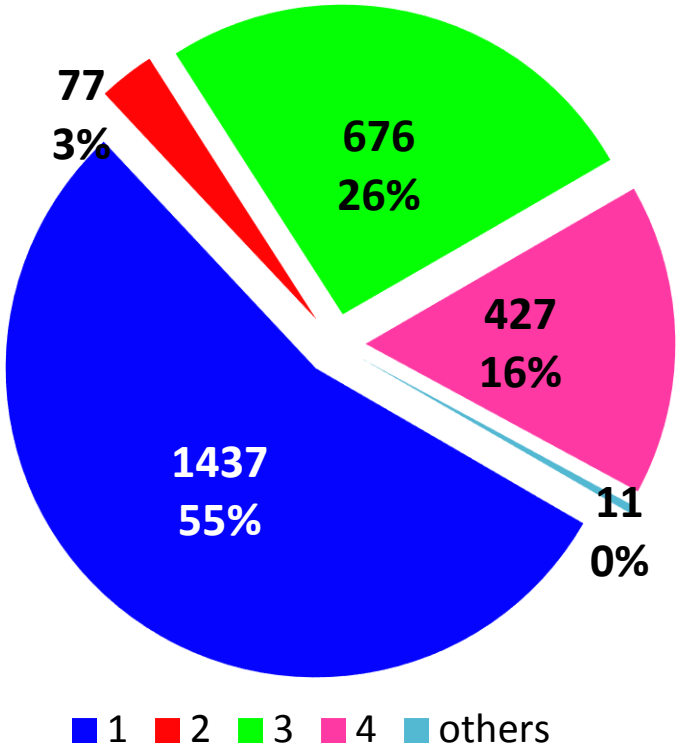
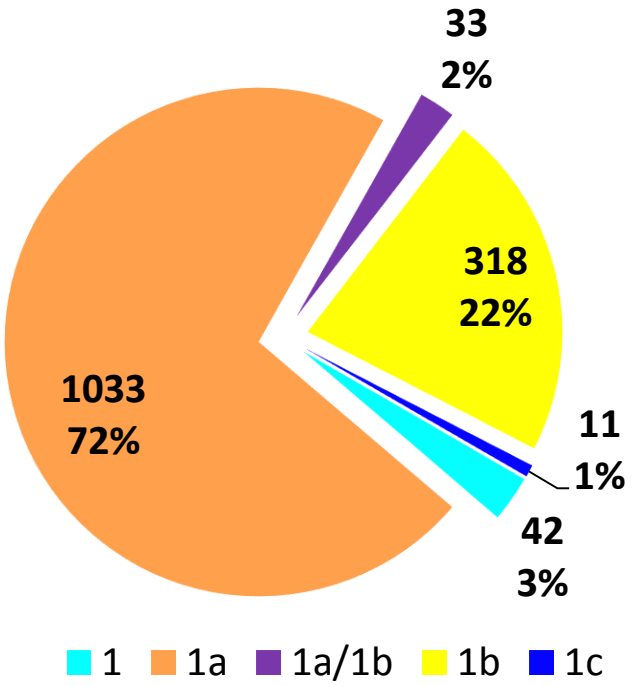
Proportion of HCV genotypes in 2628 Icona/HepaIcona patients





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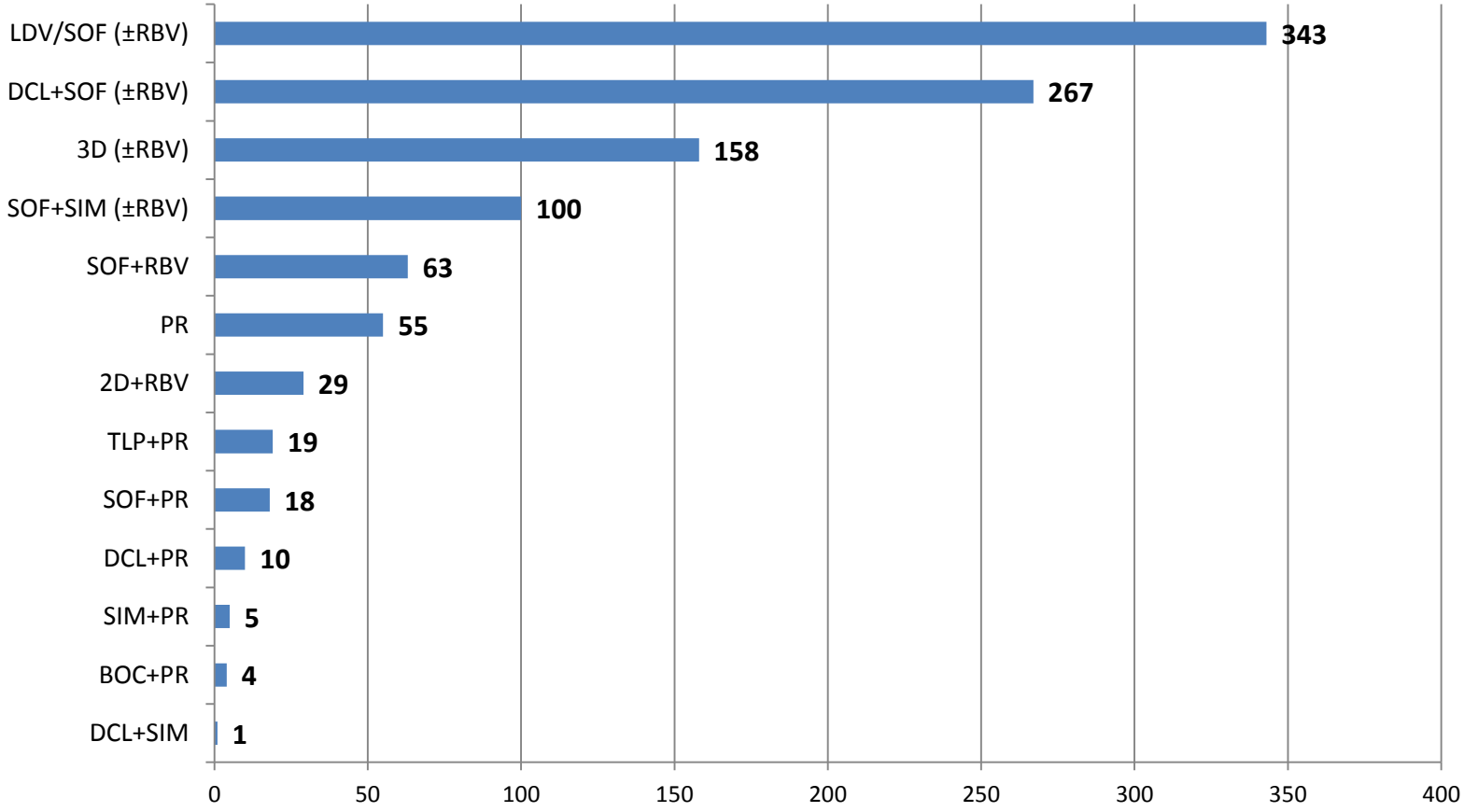
Distribution of anti-HCV treatment regimens in HepaICONA and Icona patients, after Jan 2013 (n=1072 in 1030 patients)



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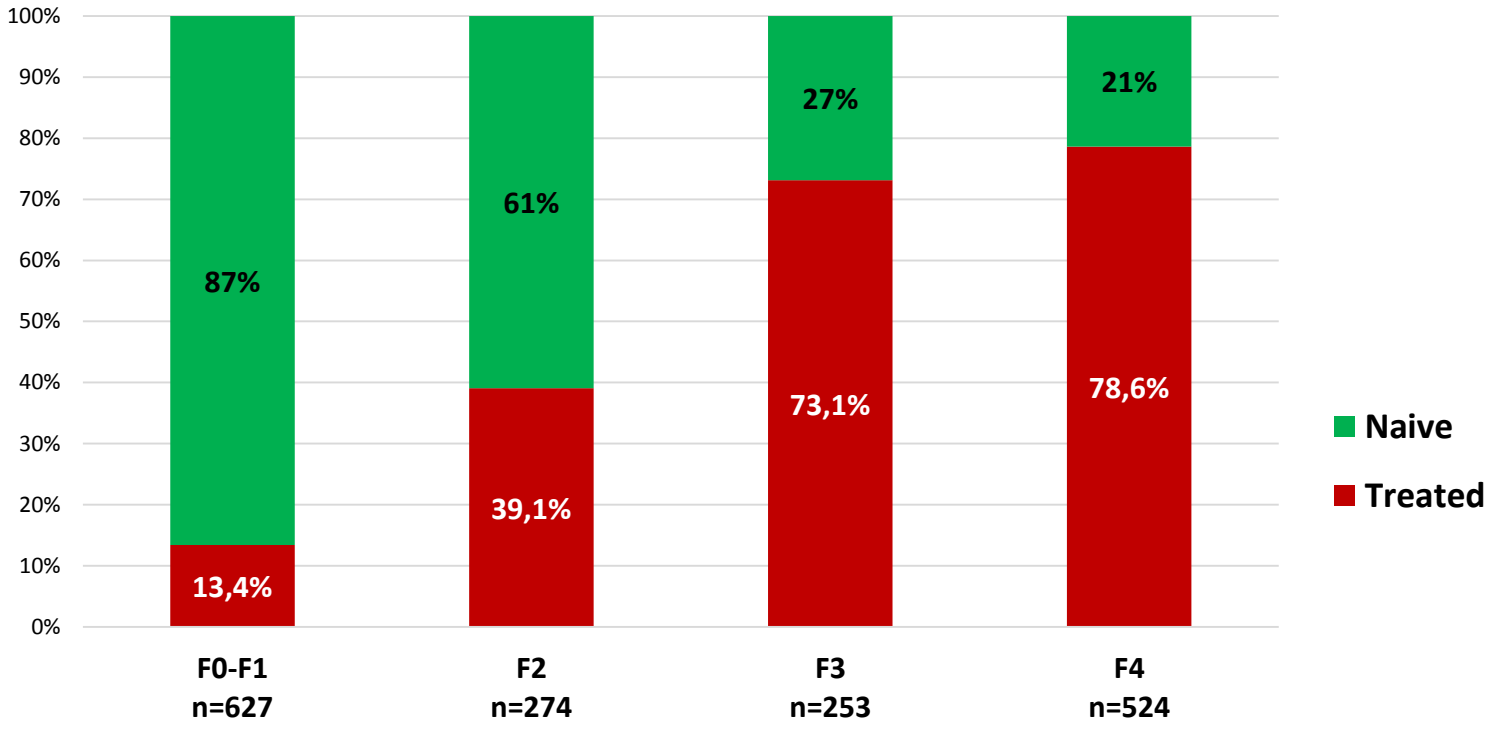
Prevalence of start of any anti-HCV treatment according to last fibrosis stage in Icona/Hepaicona patients (1678 patients with fibroscan test available)



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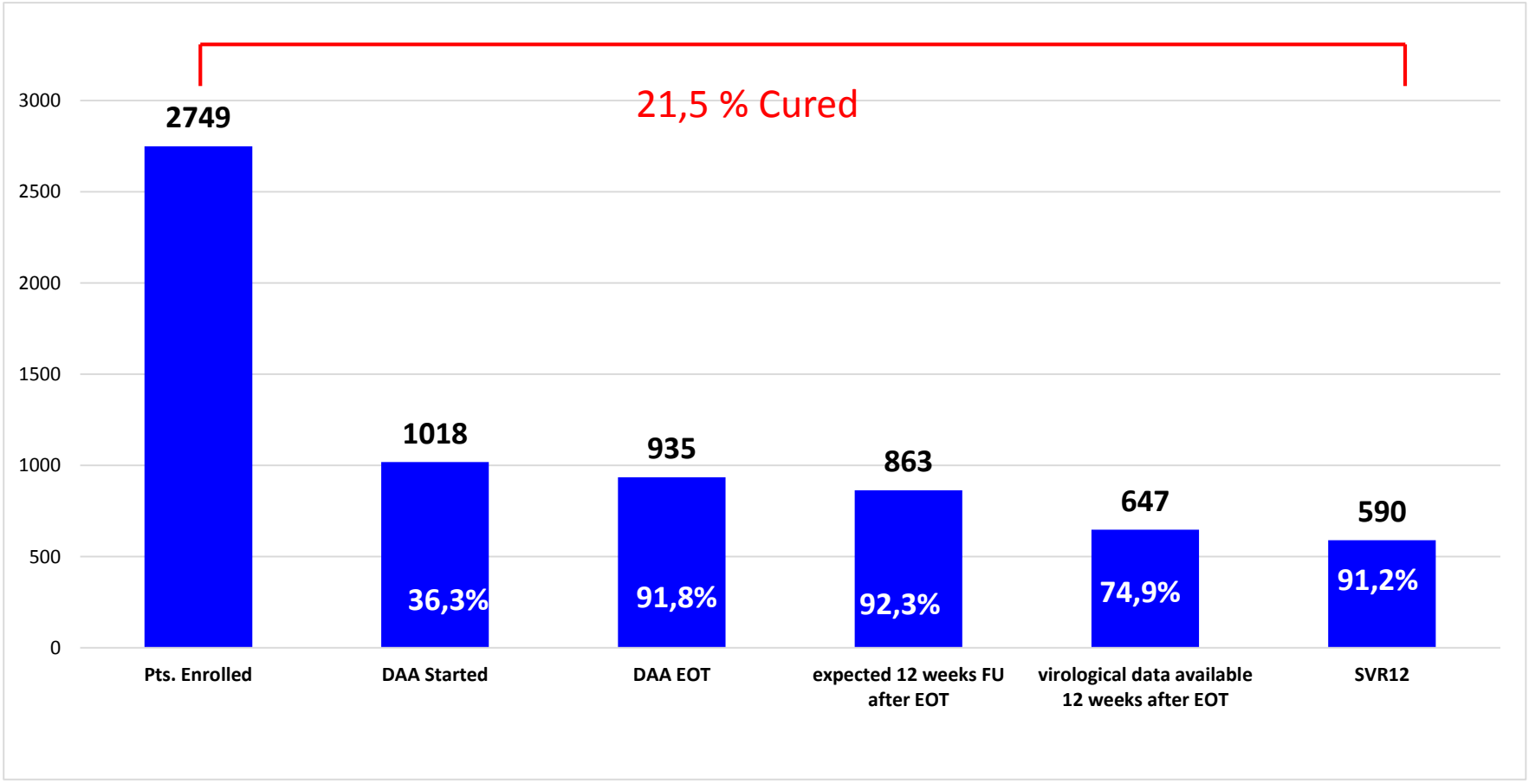
Outcome of DAA regimens started in Icona/Hepaicona



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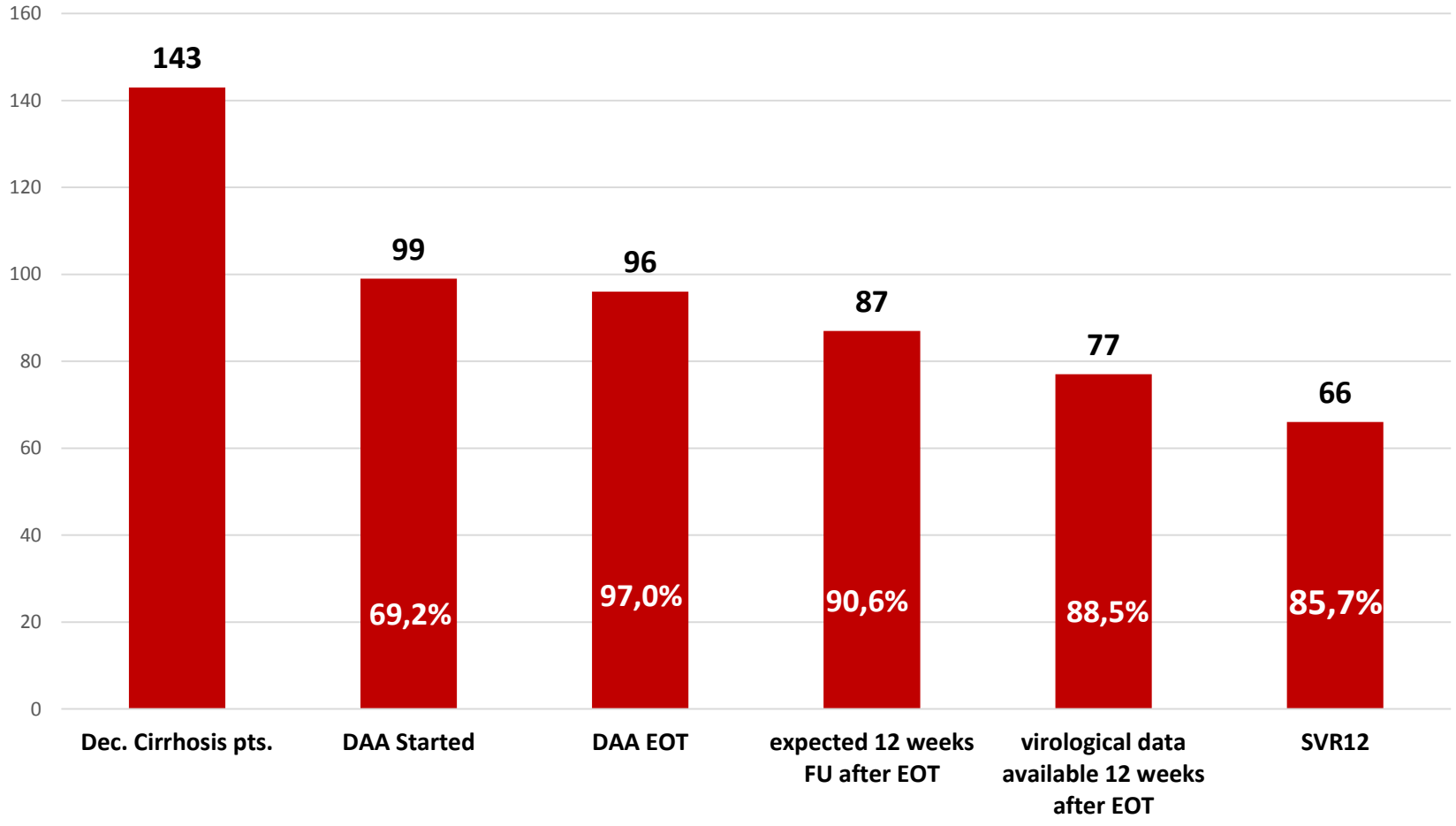
Outcome of Icona and Hepaicona patients with decompensated cirrhosis starting a DAA (n=99)



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Data from accepted papers

Clinical Microbiology and Infection 23 (2017) 267.e1–267.e4

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Research note

Incidence and progression to cirrhosis of new hepatitis C virus infections in persons living with human immunodeficiency virus☆

M. Puoti [1], P. Lorenzini [2], A. Cozzi-Lepri [3], A. Gori [4], C. Mastroianni [5], G. Rizzardini [6], G. Mazzarello [7], A. Antinori [2], A. d'Arminio Monforte [8], E. Girardi [2,*], the Icona Foundation Study Group [9]

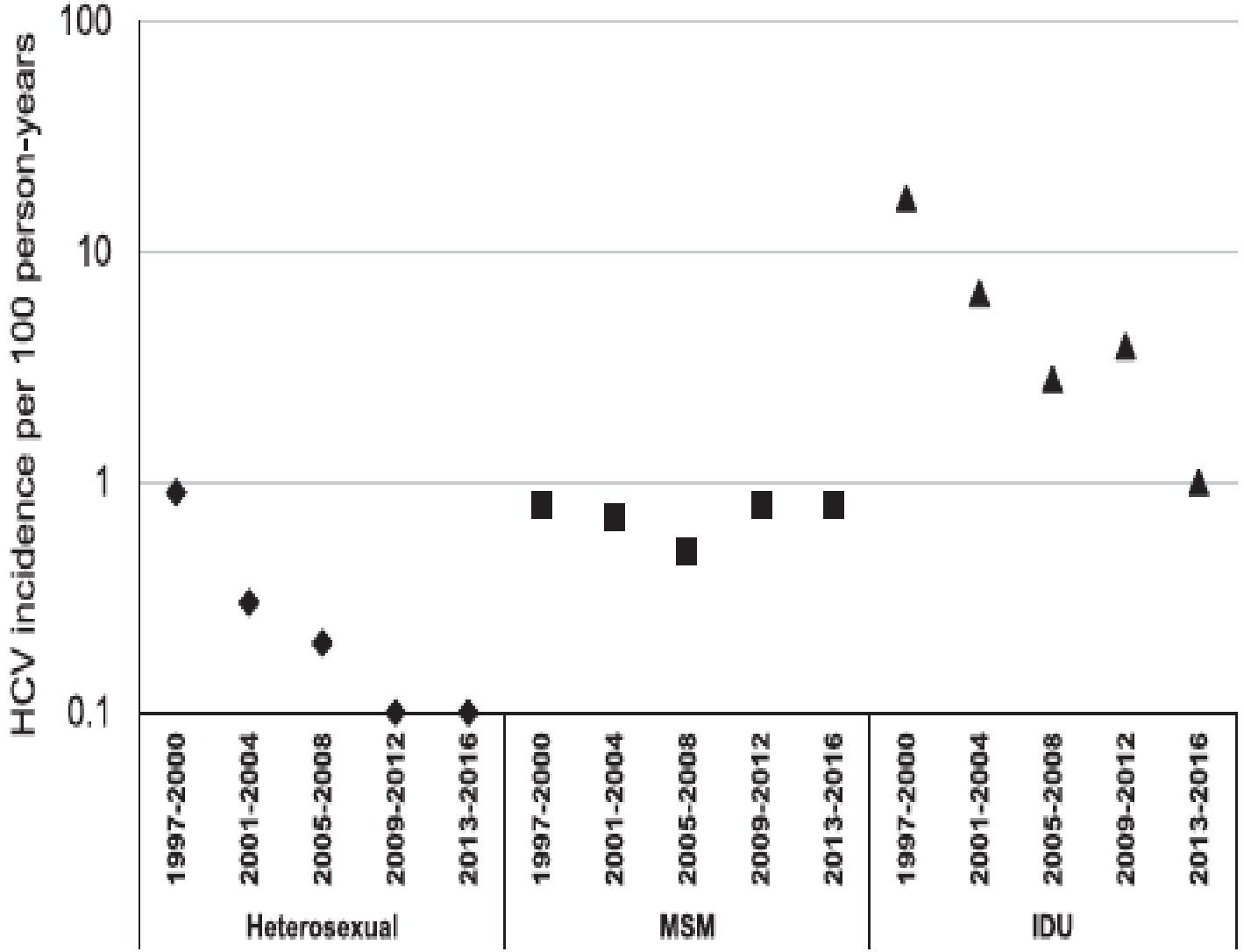
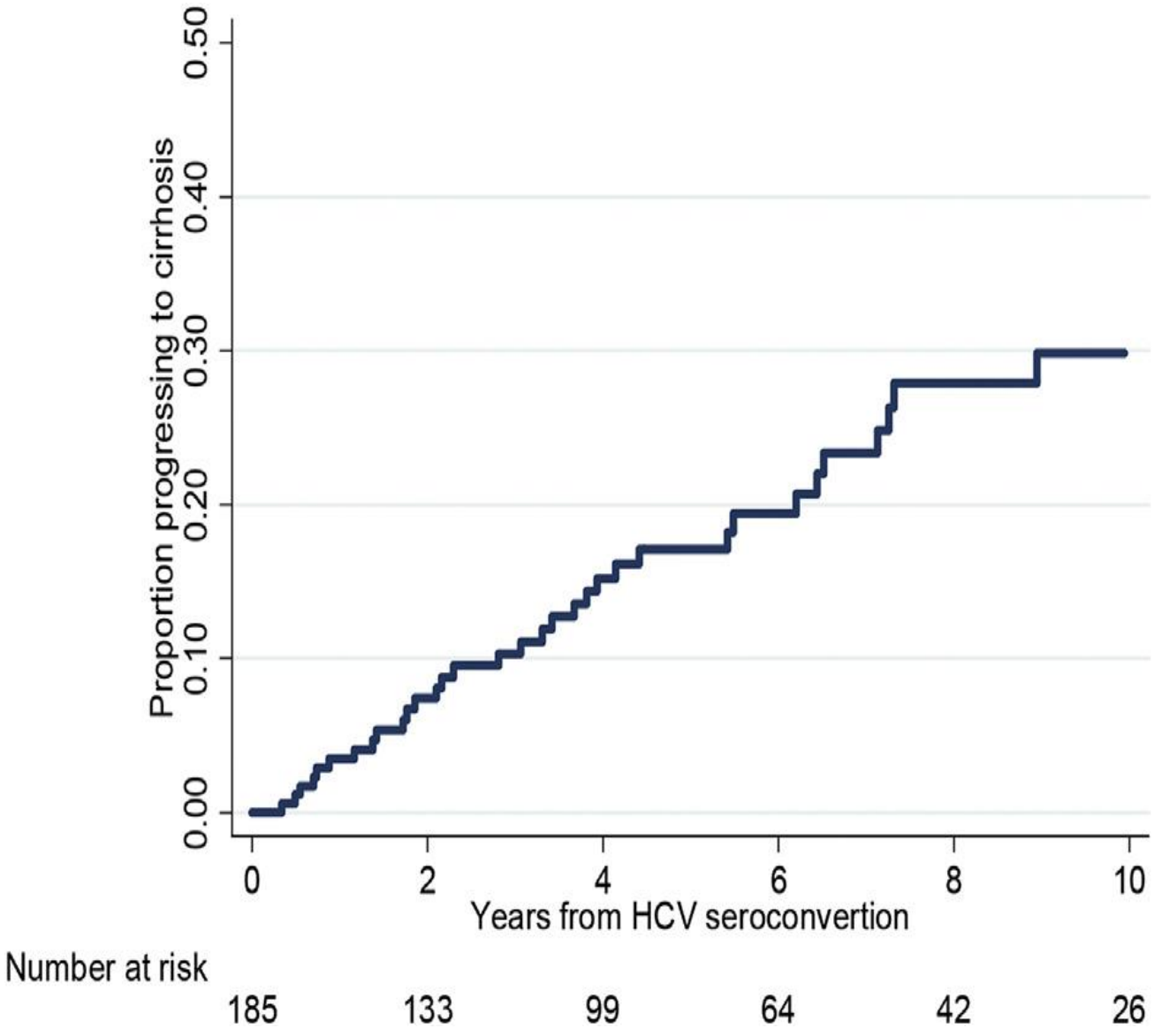


Figure 1. Incidence rates of hepatitis C virus seroconversion by calendar year and human immunodeficiency virus risk factor

Kaplan Meier estimate of the probability of progressing to HCV related severe fibrosis/cirrhosis in persons living with HIV HCV seroconversion in the Icona cohort



Incidence rate of seroconversion was 0.6/100 person-years overall, and drug users (7.2 per 100 PYFU) and men-who-have-sex-with-men (0.7 per 100 PYFU) were at highest risk.

In multivariable analysis, being IDU (RR 21.56, 95% CI 14.07-33.06) or MSM (RR 2.24, 95% CI 1.43-3.51) compared to heterosexuals were associated with a higher risk of seroconversion

The cumulative risk of progression to severe fibrosis/cirrhosis was 30% by 10 years after seroconversion.

New HCV infections have a rapidly progressive course in this population. Persons with HIV and HCV superinfection should be prioritized for treatment with anti-HCV direct-acting antivirals

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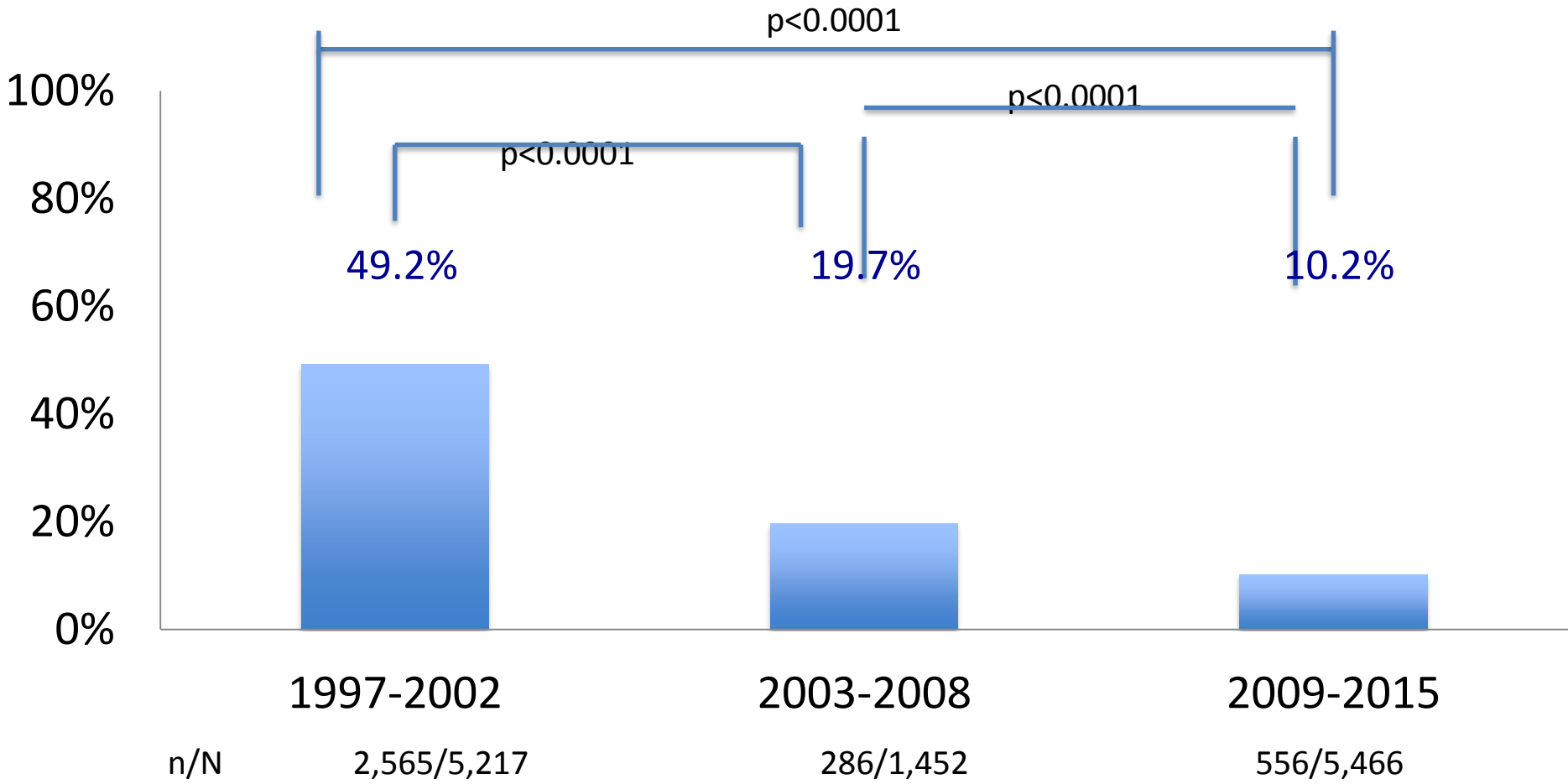
Evolution and determinants of the prevalence of HCV infection and HCV genotype distribution among HIV-infected patients entering in care between 1997 and 2015 in Italy: data from a prospective nationwide cohort (ICONA)

B. Rossetti[1,2], F. Bai[3], A. Tavelli[4], M. Galli[5], A. Antinori[6], F. Castelli[7], G. Pellizzer[8], A. Cozzi Lepri[9], S. Bonora[10], A. d'Arminio Monforte[3], M. Puoti[11], A. De Luca[1,12]
for ICONA Foundation study group

In press, CMID 2017

Prevalence of HCV-Ab positive status according to calendar year of enrollment



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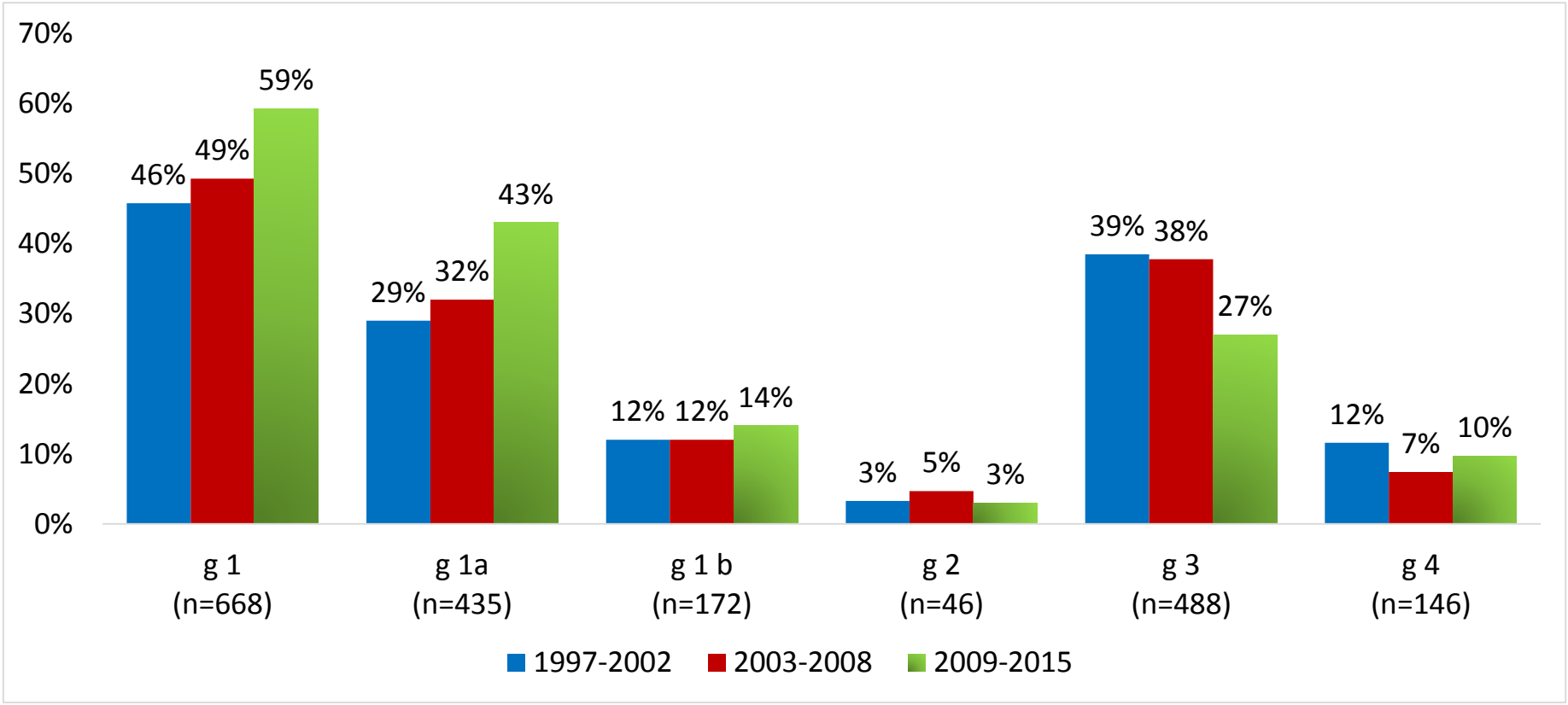
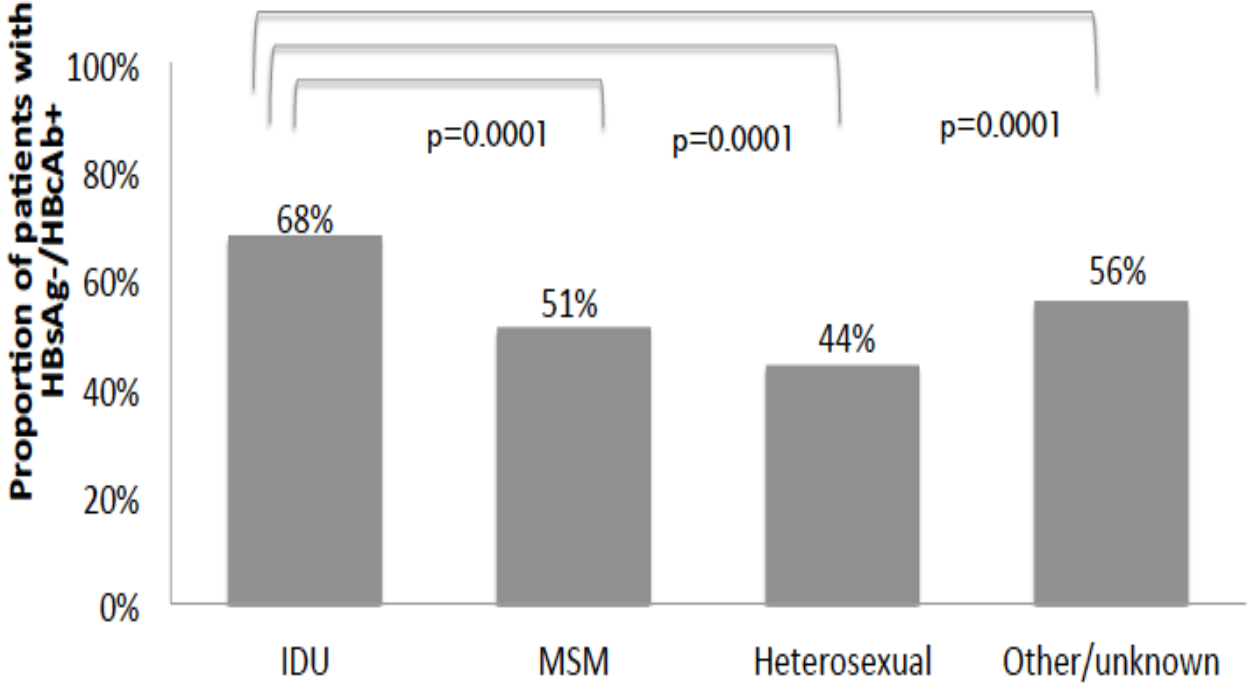
Italian Cohort I. C. O. N. A. Naive Antiretrovirals

HCV genotype distribution according to calendar year of enrollment (N=1,359*)



*1 not specified: 61 (4.5%); mixed 11 (0.8%)

Prevalence of HCV-Ab positive status according to HIV risk group



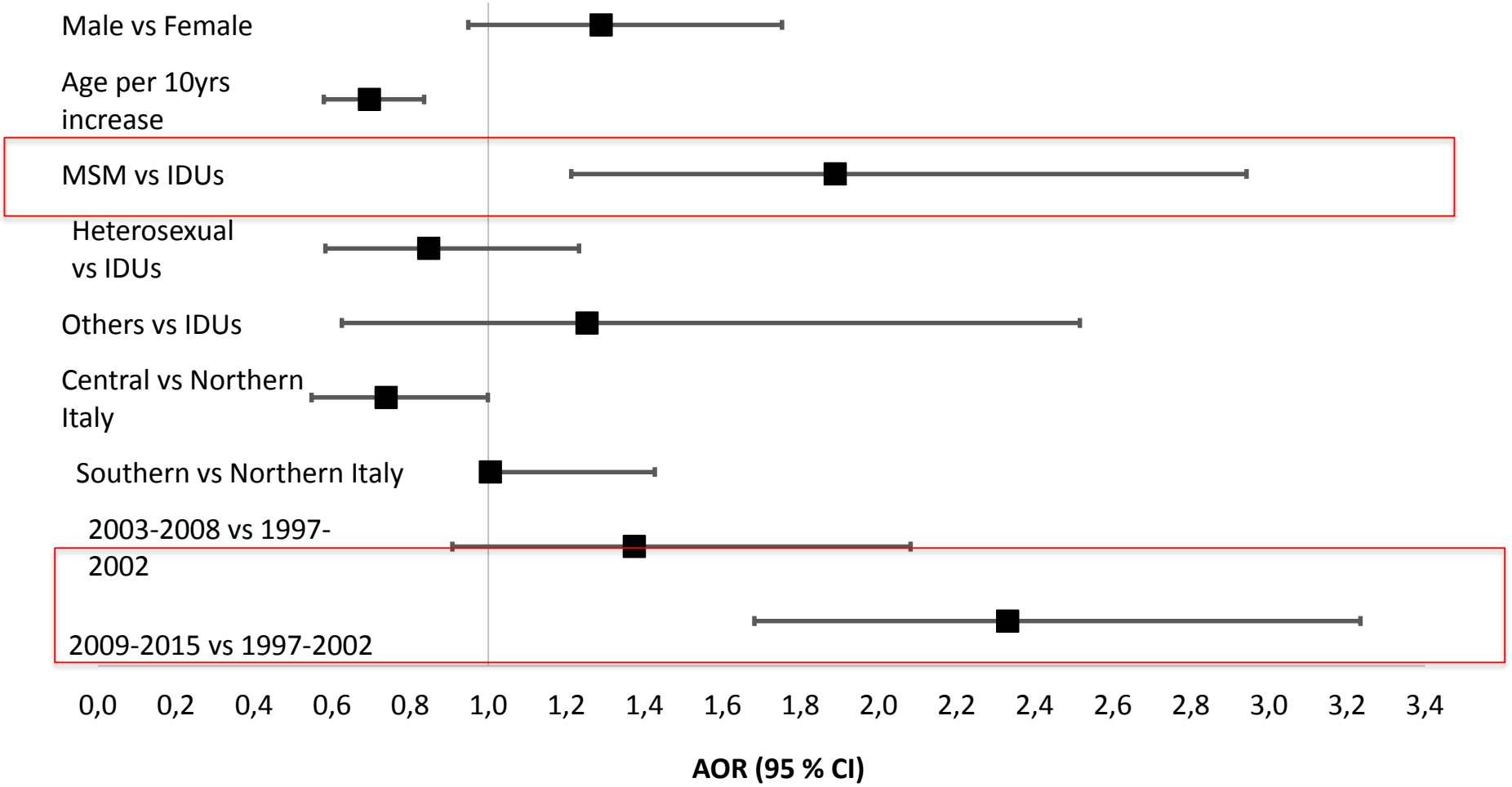
*Other comparisons between groups are non statistically different

Factors associated with HCV-Ab positive status

Variable	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	**P**	**AOR**	**95% CI**	**P**
Female gender	1			1		
Male gender	0.940	0.858-1.030	0.183	0.811	0.685-0.957	0.013
Age, for 10 years older	1.523	1.466-1.581	<0.0001	1.039	0.971-1.112	0.276
Risk factor						
IDU	1		<0.0001	1		<0.0001
MSM	0.008	0.007-0.010	<0.0001	0.012	0.010-0.015	<0.0001
Heterosexual	0.012	0.01-0.014	<0.0001	0.013	0.011-0.016	<0.0001
Other/Unknown	0.016	0.012-0.02	<0.0001	0.021	0.015-0.026	<0.0001
Country region						
North	1		<0.0001	1		0.098
Center	0.758	0.692-0.831	<0.0001	0.851	0.734-0.986	0.031
South and Islands	1.474	1.319-1.647	<0.0001	0.951	0.788-1.148	0.601
Foreign born	1			1		
Italian	4.271	3.625-5.032	<0.0001	1.449	1.163-1.807	0.001
Calendar period of enrollment						
1997-2002	1		<0.0001	1		<0.0001
2003-2008	0.254	0.220-0.292	<0.0001	0.497	0.407-0.608	<0.0001
2009-2015	0.117	0.106-0.130	<0.0001	0.229	0.196-0.268	<0.0001
HBsAg-	1			1		
HBsAg+	1.464	1.252-1.713	<0.0001	1.181	0.916-1.521	0.201

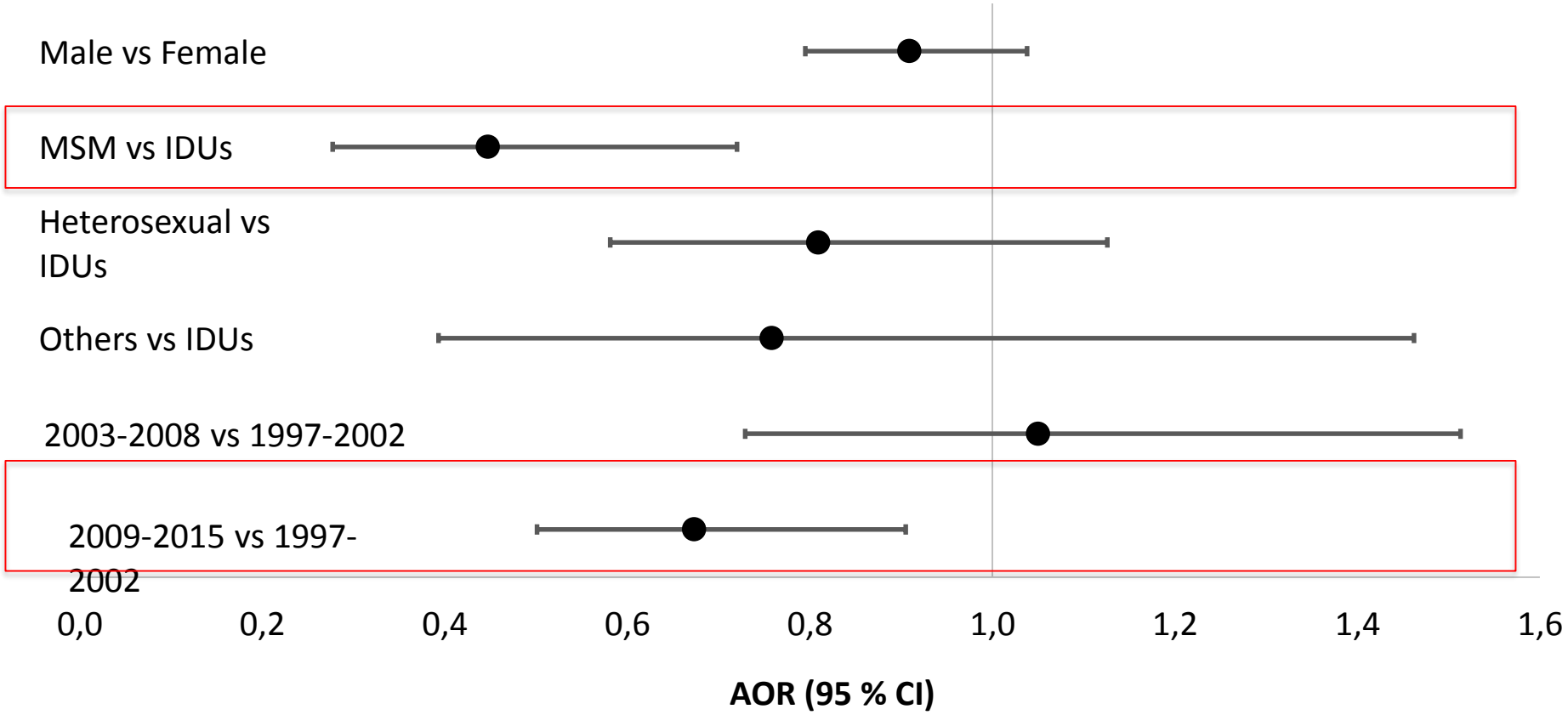
✓ **Female sex versus male AOR +1.191, CI 95% 1.014-1.398 p= 0.033, excluding MSM**

Factors associated with genotype 1a (N=435)



*Variables are mutually adjusted

Factors associated with genotype 3 (N=488)



*Variables are mutually adjusted

Conclusions

- ✓ Prevalence of HCV infection is significantly declining in PLWHA, independently of risk factors
- ✓ After adjusting for risk factors and calendar year of enrollment, HCV co-infection is more frequent in female patients and in natives
- ✓ In recent years the relative frequency of genotype 3 in co-infected patients is declining, while genotype 1a is increasing, mainly driven b y younger patients and MSM

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Italian Cohort I. C. O. N. A. Naive Antiretrovirals

Access and response to direct antiviral agents (DAA) in HIV-HCV co-infected patients in Italy

A d'Arminio Monforte, A Cozzi-Lepri, F Ceccherini-Silberstein, A De Luca, S Lo Caputo, A Castagna, C Mussini, A Cingolani, A Tavelli, M Shanynde, A Gori, E Girardi, M Andreoni, A Antinori, M Puoti for the ICONA Foundation Study Cohort.

In press PlosOne 2017

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Aim

We aimed:

- to estimate the rate of access to DAA in a real-life setting of HIV-HCV co-infected people on care in Italy;
- to identify factors associated with faster DAA initiation;
- to describe the use and/or change of concomitant antiretroviral agents;
- to describe the regimens used in relation to HCV-genotype and liver disease stage;
- to identify the variables associated with the risk of treatment failure and of lack of SVR12.

2,607 HIV-HCV co-infected patients

1,090 (41%) eligible to DAA reimbursement

920 (761 -69.8%- patients eligible, and 159 -10.5%- not eligible), started DAA in a median FU of 38 (30-41) months

61/606 patients (10.1%) experienced TF: 50 had detectable HCV-RNA 12 weeks after a full course of treatment and 11 had suspended treatment prematurely

RATE OF SVR12: 92% (545/595)
RATE OF TREATMENT SUCCESS: 90%

Table 2 Relative hazards of starting DAA from fitting a Cox regression model

	Relative hazards of starting DAA			
	Unadjusted RH (95% CI)	**p-value**	**Adjusted* RH (95% CI)**	**p-value**
Age, years				
>50 years vs. below	1.15 (0.98, 1.36)	0.092	1.07 (0.88, 1.30)	0.496
Gender				
Female vs. Male	0.90 (0.76, 1.07)	0.253	0.99 (0.80, 1.23)	0.926
Employment				
Unemployed	1.00		1.00	
Employed	1.56 (1.26, 1.93)	<.001	1.45 (1.12, 1.89)	0.005
Other/unknown	1.66 (1.19, 2.30)	0.003	1.55 (1.07, 2.26)	0.021
CD4 count, cells/mm3				
per 100 higher	1.00 (0.98, 1.02)	0.862	0.98 (0.95, 1.01)	0.170
HIV-RNA, copies/mL				
0-50 vs. >50	1.20 (0.98, 1.46)	0.073	1.19 (0.91, 1.58)	0.208
Time from HIV diagnosis, years				
per 10 longer	0.83 (0.76, 0.91)	<.001	0.83 (0.74, 0.93)	0.002
HCV genotype				
1a	1.00		1.00	
1b	1.03 (0.81, 1.30)	0.837	0.93 (0.71, 1.23)	0.631
2	0.59 (0.34, 1.02)	0.059	0.48 (0.25, 0.93)	0.029
3	0.86 (0.72, 1.03)	0.099	0.72 (0.59, 0.90)	0.003
4	1.08 (0.87, 1.34)	0.479	1.00 (0.78, 1.29)	0.971
Other/unknown	0.75 (0.45, 1.26)	0.275	1.10 (0.58, 2.10)	0.770
HCV-RNA, log10 IU/l				
per log higher	0.88 (0.81, 0.95)	0.002	0.89 (0.81, 0.97)	0.011
Fib4,				
0-1.45	1.00		1.00	
1.46-3.25	1.23 (0.97, 1.56)	0.091	1.01 (0.75, 1.37)	0.931
3.25+	1.06 (0.84, 1.34)	0.638	0.82 (0.58, 1.16)	0.255
Decompensated cirrhosis				
Yes vs. No	1.28 (1.01, 1.64)	0.044	1.26 (0.93, 1.70)	0.137
Previous failure of HCV treatment				
Yes vs. No	1.64 (1.42, 1.90)	<.001	1.52 (1.27, 1.82)	<.001

*adjusted for all factors examined in table and stratified by cohort

Table 4

Variation of HIV-related markers (CD4 counts and HIV-RNA copy levels) from DAA initiation to 12 weeks after end of treatment, according to use of ribavirin

HIV lab markers	RBV in DAA	RBV-free DAA		RBV in DAA	RBV-free DAA	
	Unadjusted Mean (95% CI)		p-value	Adjusted*& Mean (95% CI)		p-value
CD4 count at EOT						
cells/mm3	481 (454, 507)	616 (588, 644)	<.001	480 (453, 507)	616 (588, 644)	<.001
CD4 count 12 weeks after EOT						
cells/mm3	623 (589, 656)	663 (628, 699)	0.108	624 (590, 657)	665 (629, 700)	0.100
HIV-RNA at EOT						
log10 copies/mL	0.50 (0.38, 0.62)	0.66 (0.54, 0.78)	0.067	0.48 (0.37, 0.60)	0.67 (0.55, 0.79)	0.033
HIV-RNA 12 weeks after EOT						
log10 copies/mL	0.56 (0.43, 0.69)	0.63 (0.50, 0.76)	0.458	0.56 (0.43, 0.69)	0.63 (0.50, 0.77)	0.443

*adjusted for gender, age, HCV genotype, decompensate cirrhosis and diabetes

&HIV-RNA also adjusted for CD4 count at DAA initiation and viceversa

ART and DAA

In the 3 months before starting DAA, ART was switched in:

- 118/328 (36.0%) PI/r-based regimen (113 to INI, 5 to RPV)
- 36/175 (21%) NNRTI-based regimen (30 to INI)
- 5/272 (2%) INI-including regimen (4 to RPV)

).

Table 5. Odds ratios of_ a) virological failure (non-SVR12). B) treatment failure (TF) from fitting a logistic regression model

a) non-SVR12

Characteristics	Virological failure N= 50	SVR N= 545	OR of DAA failure from fitting a logistic regression model: Unadjusted OR (95% CI)	p-value	Adjusted* OR (95% CI)	p-value
Sub-optimal DAA						
No	35 (70.0%)	467 (85.7%)	1.00		1.00	
Yes	15 (30.0%)	78 (14.3%)	2.57 (1.34, 4.92)	0.005	2.52 (1.24, 5.12)	0.011
Decompensated cirhrosis						
No	42 (84.0%)	494 (90.6%)	1.00		1.00	
Yes	8 (16.0%)	51 (9.4%)	1.85 (0.82, 4.14)	0.138	1.79 (0.77, 4.16)	0.177

b) TF

Characteristics	Treatment failure N= 61	No TF N= 545	OR of DAA failure from fitting a logistic regression model: Unadjusted OR (95% CI)	p-value	Adjusted* OR (95% CI)	p-value
Sub-optimal DAA						
No	44 (72.1%)	467 (85.7%)	1.00		1.00	
Yes	17 (27.9%)	78 (14.3%)	2.31 (1.26, 4.25)	0.007	2.19 (1.13, 4.22)	0.020
Decompensated cirrhosis						
No	51 (83.6%)	494 (90.6%)	1.00		1.00	
Yes	10 (16.4%)	51 (9.4%)	1.90 (0.91, 3.97)	0.088	1.84 (0.85, 3.95)	0.120

Based on reported data, how many HIV-HCV coinfected patients are still to be treated in Italy? by E Girardi

115000 HIV pos diagnosed pts (end 2016, COA data)

26% HCV coinfected=29923

16000 undiagnosed 7% coinfected=1120

Estimated total HIV-HCV coinfected: 29923+1120=31043

HCV-RNA pos 76% (Icona data) =23592

Eligible to DAA 41% (Icona)= 9672

Already treated, estimated (Icona) 70%

Estimated eligible still to be treated=2901

Estimated total (including F0-F2) =16800

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