Il paziente coinfetto HIV-HCV

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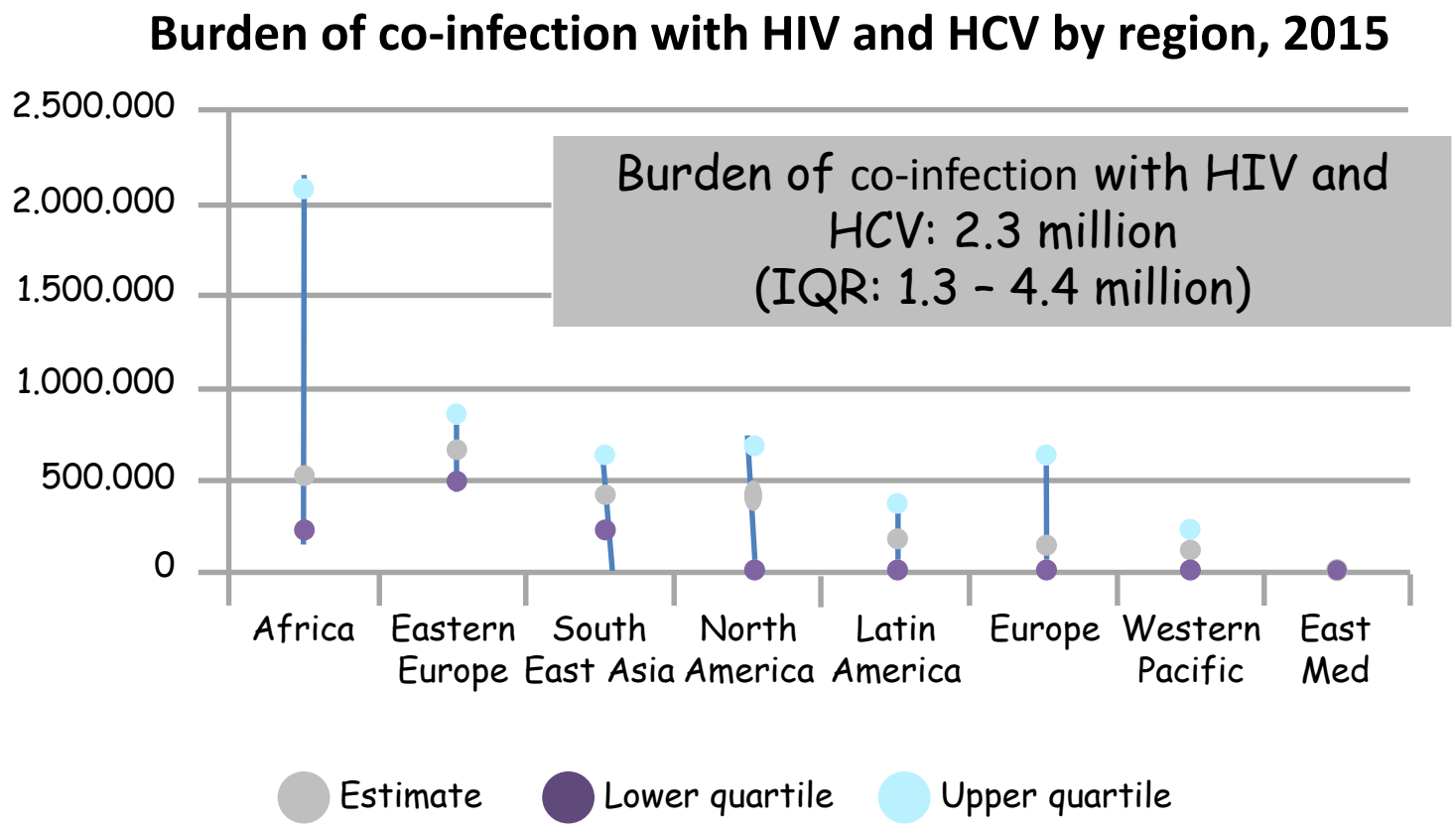
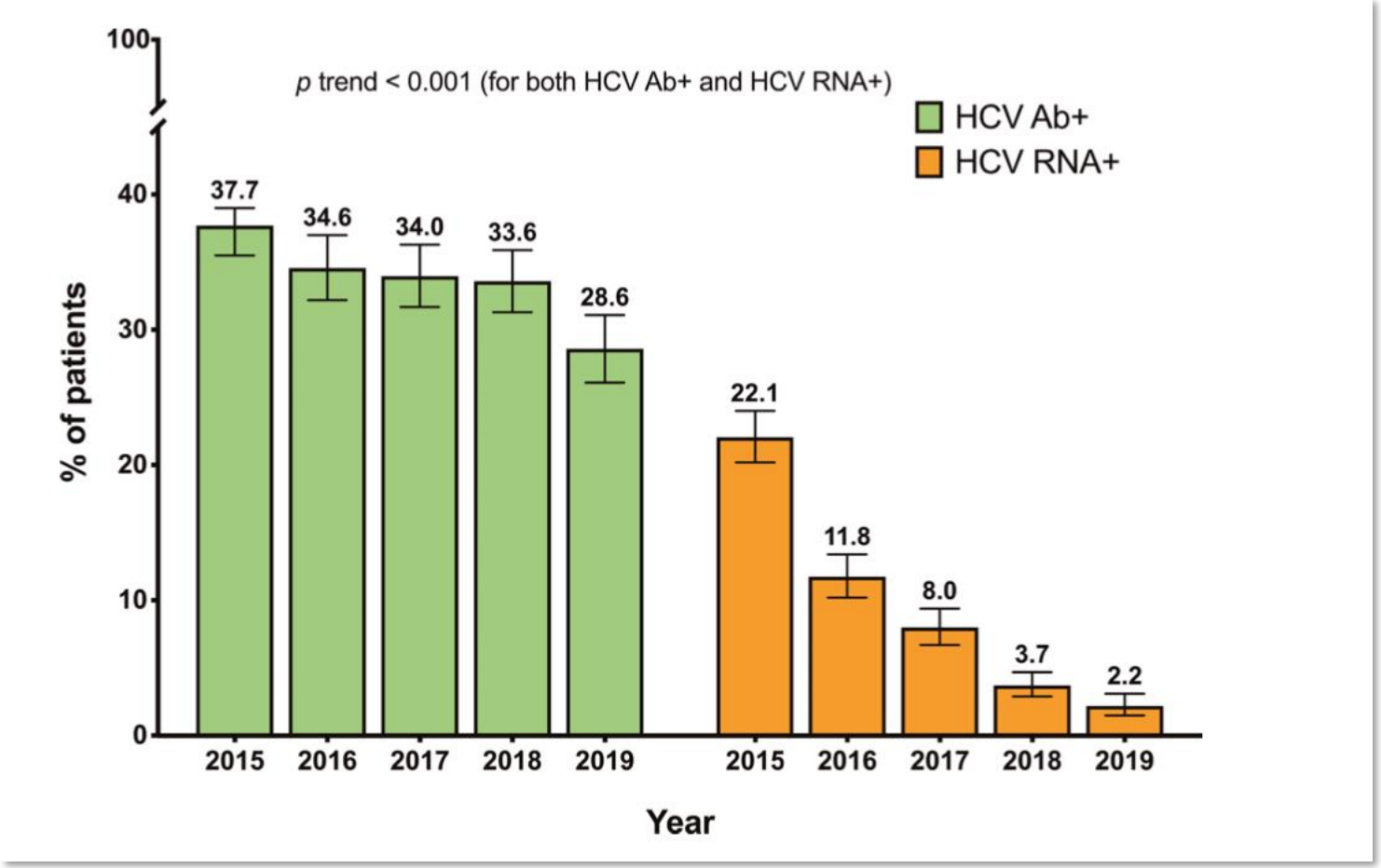
Prevalence of HIV/HCV co-infection:

WHO global systematic review of prevalence of HIV/HCV Ab co-infection based on prevalence studies in HIV+ persons stratified by risk group (where available) or general population surveys reporting HIV/HCV infection:



Platt L et al the Lancet 2016 July Vol 16

Prevalence of hepatitis C virus (HCV) seropositivity and active HCV infection in the annual cross-sectional studies carried out by GeSIDA from 2015 to 2019.



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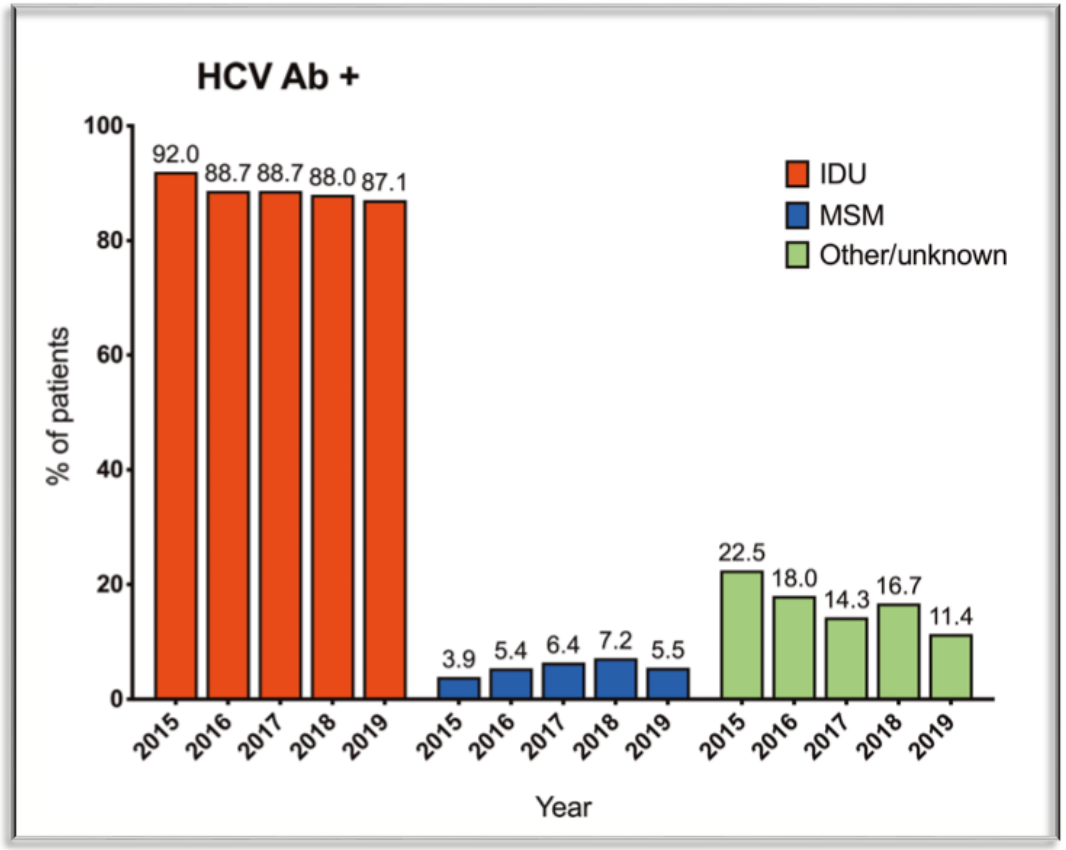

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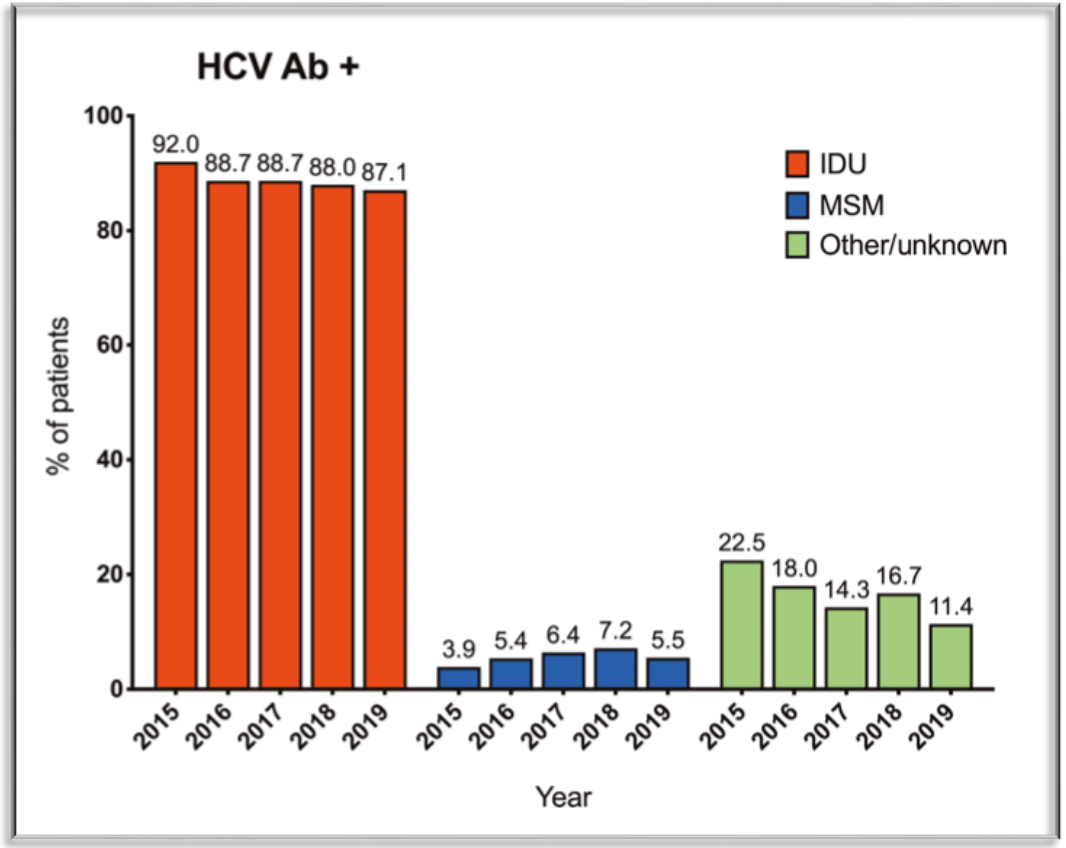

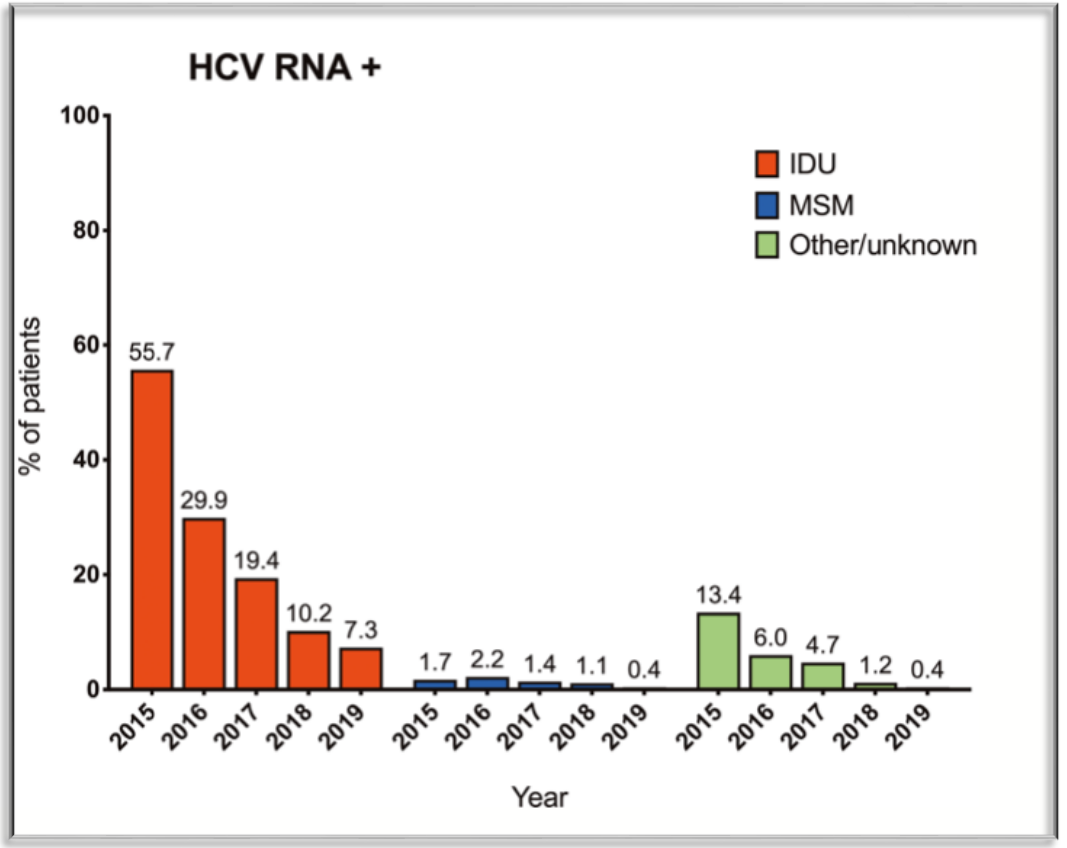

Fanciulli C et al *HIV Medicine.* 2022;23:705–716.

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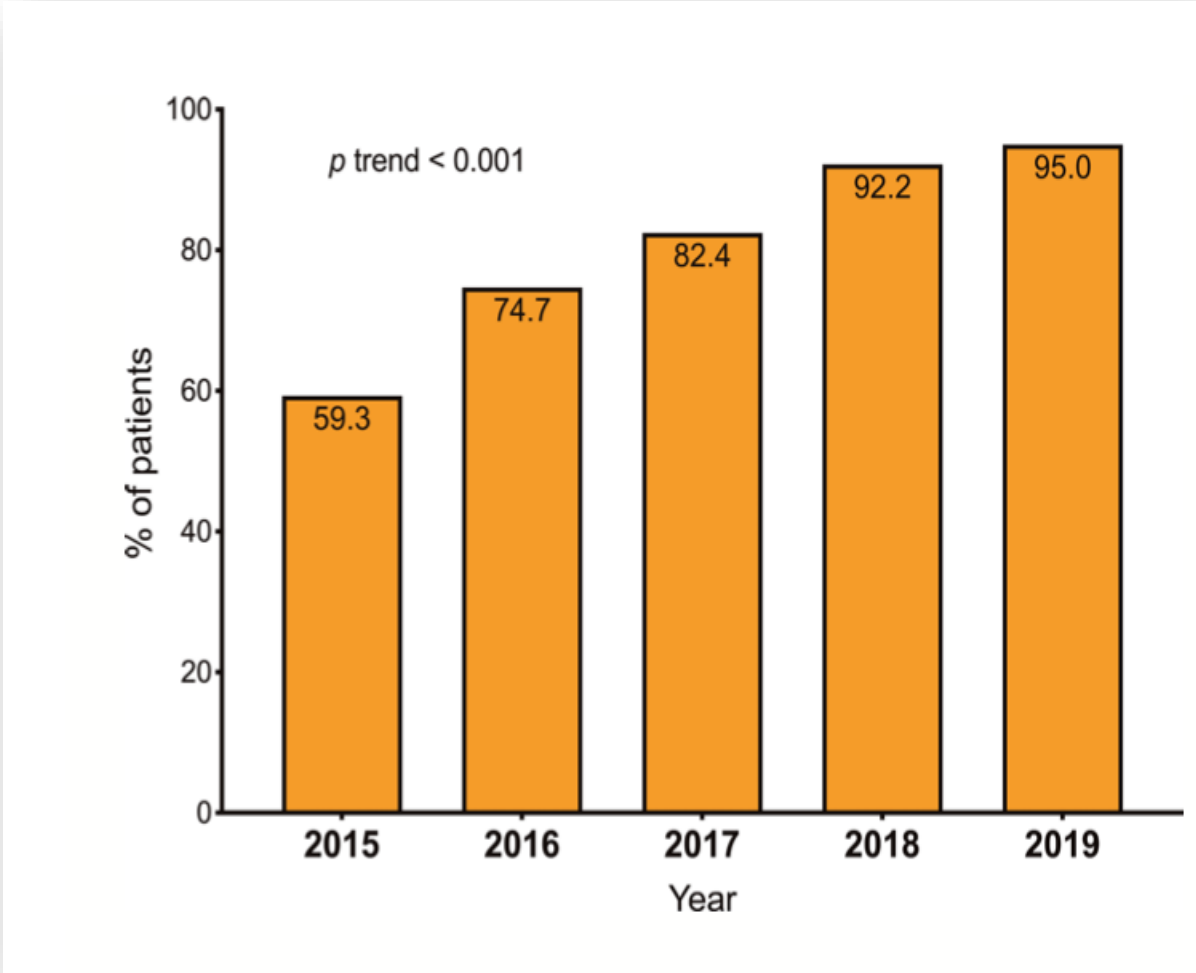
Uptake of anti-hepatitis C virus (HCV) treatment in the annual cross-sectional studies carried out by GeSIDA from 2015 to 2019



Fanciulli C et al *HIV Medicine.* 2022;23:705–716.

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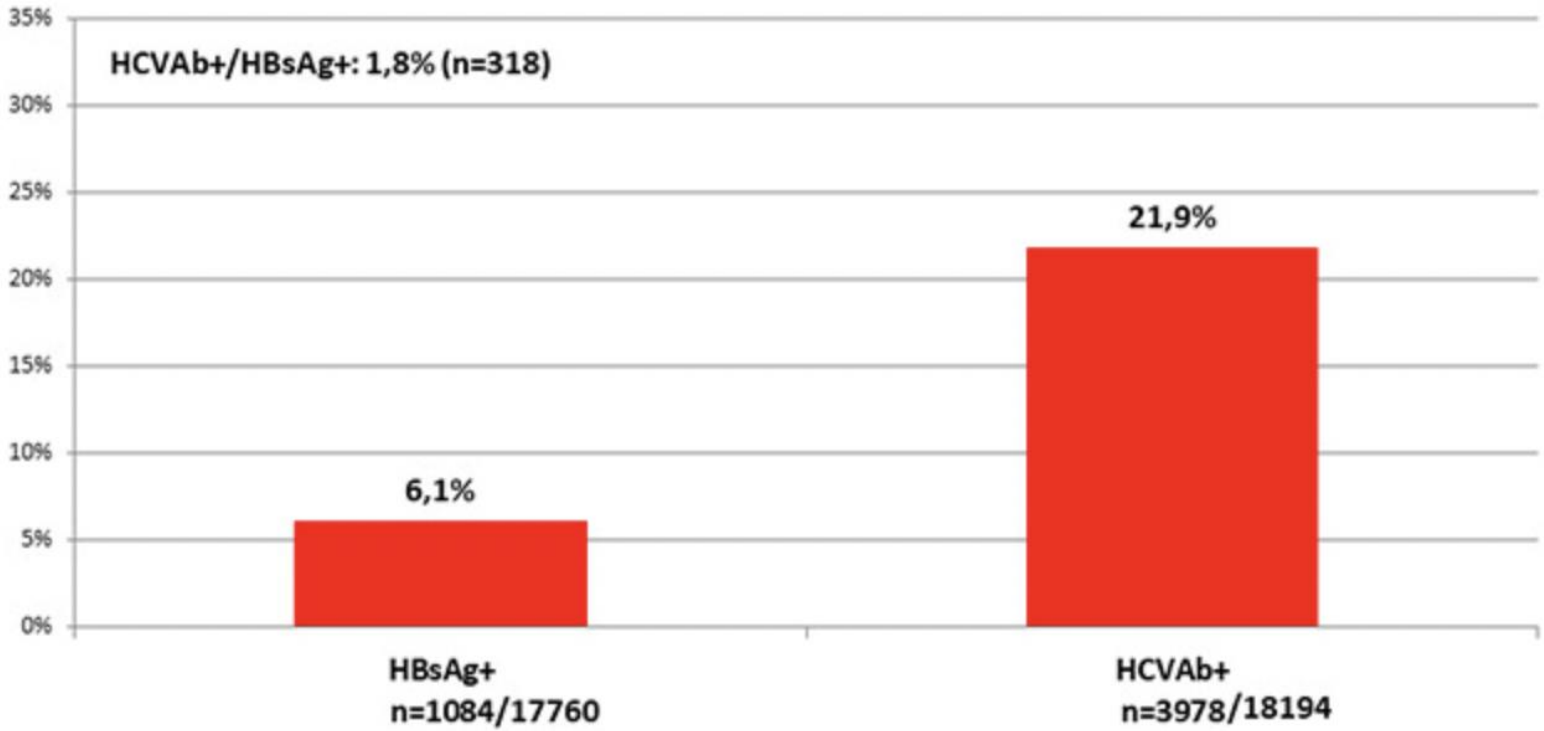
HBsAg and HCVAb positivity in ICONA patients



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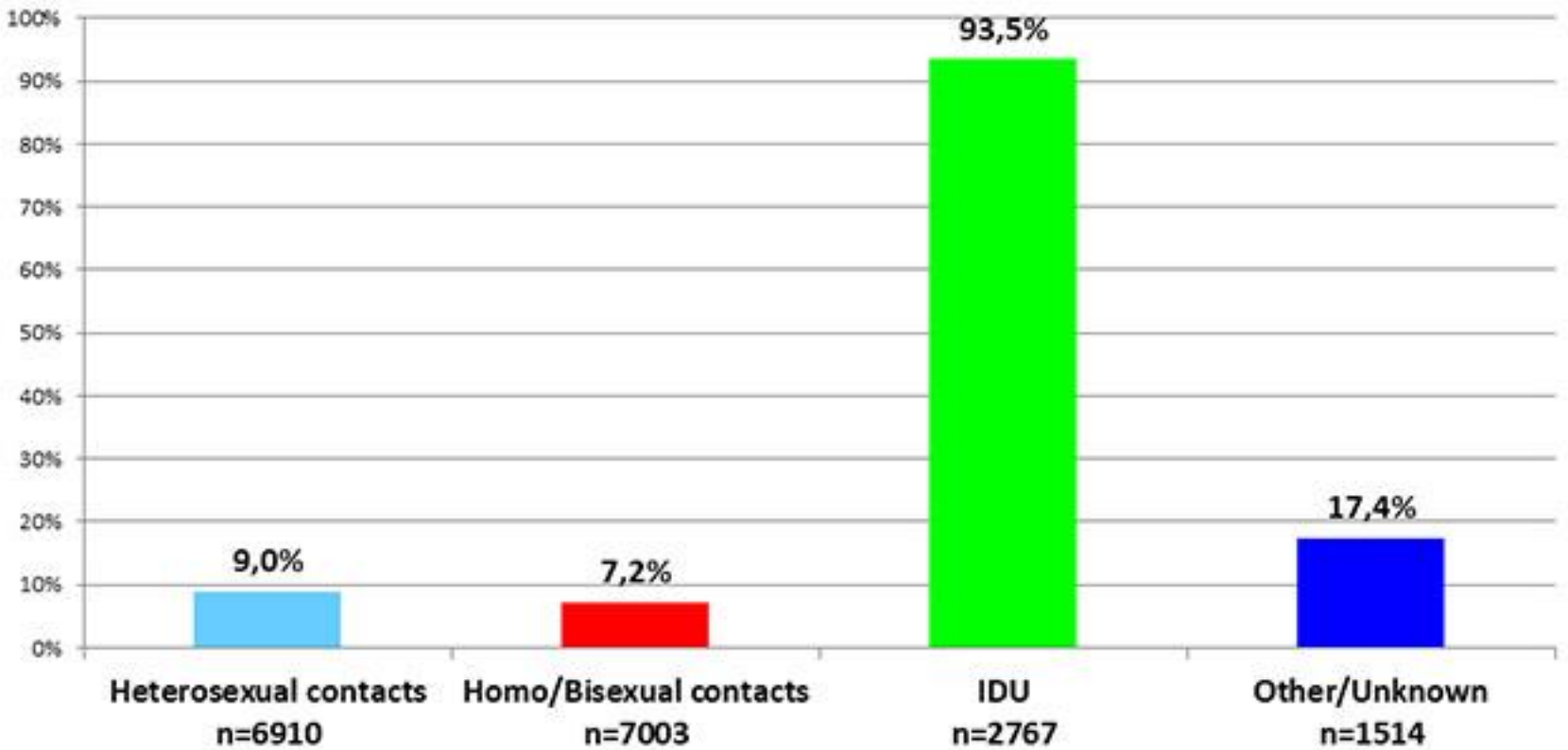
HCVAb positivity according to mode of HIV transmission in 18.194 ICONA patients



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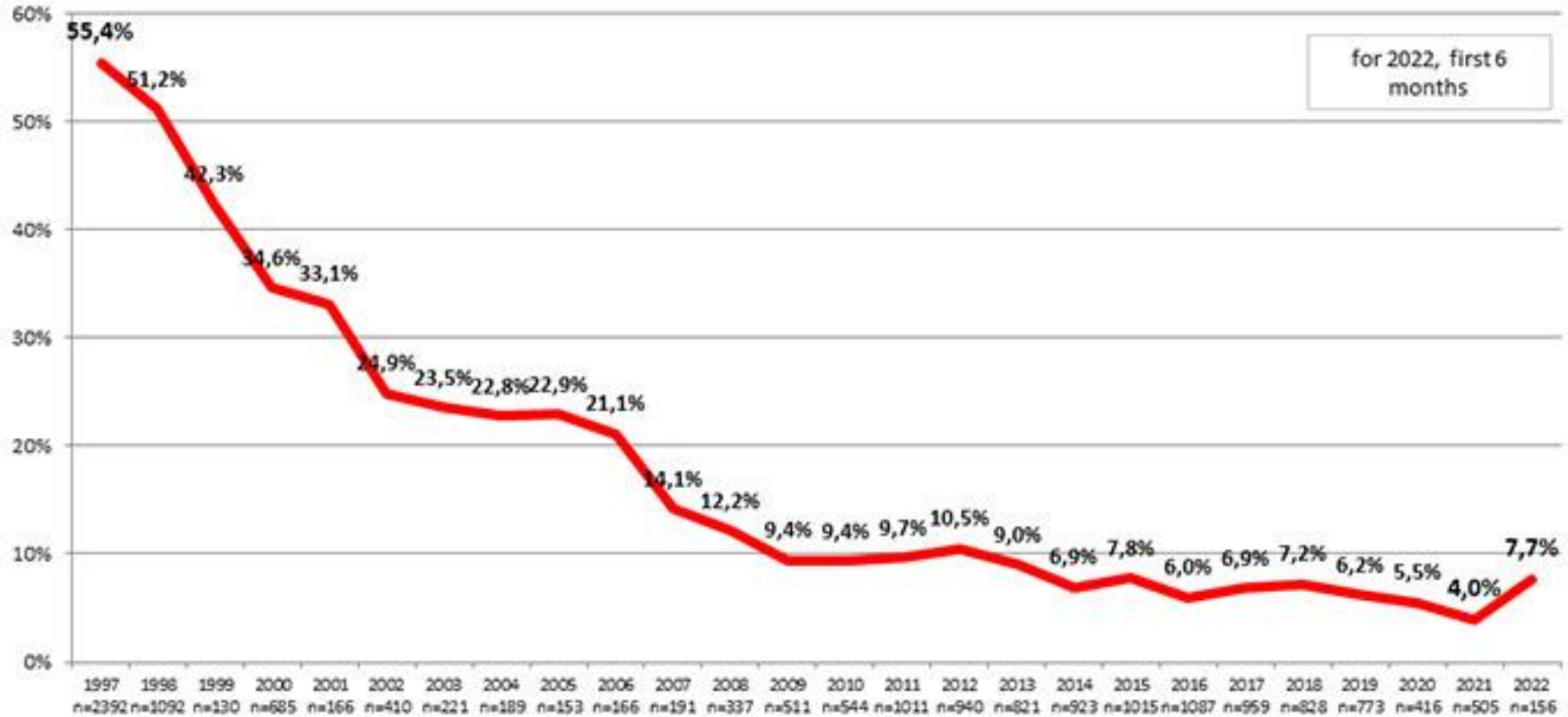
Proportion of patients with HCVAb pos test within 1 year from enrolment, according to calendar year of enrolment



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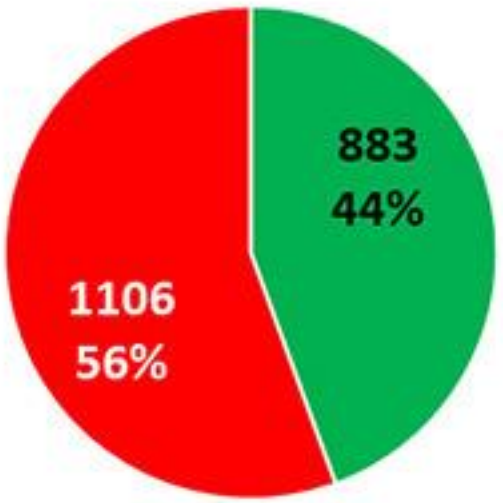
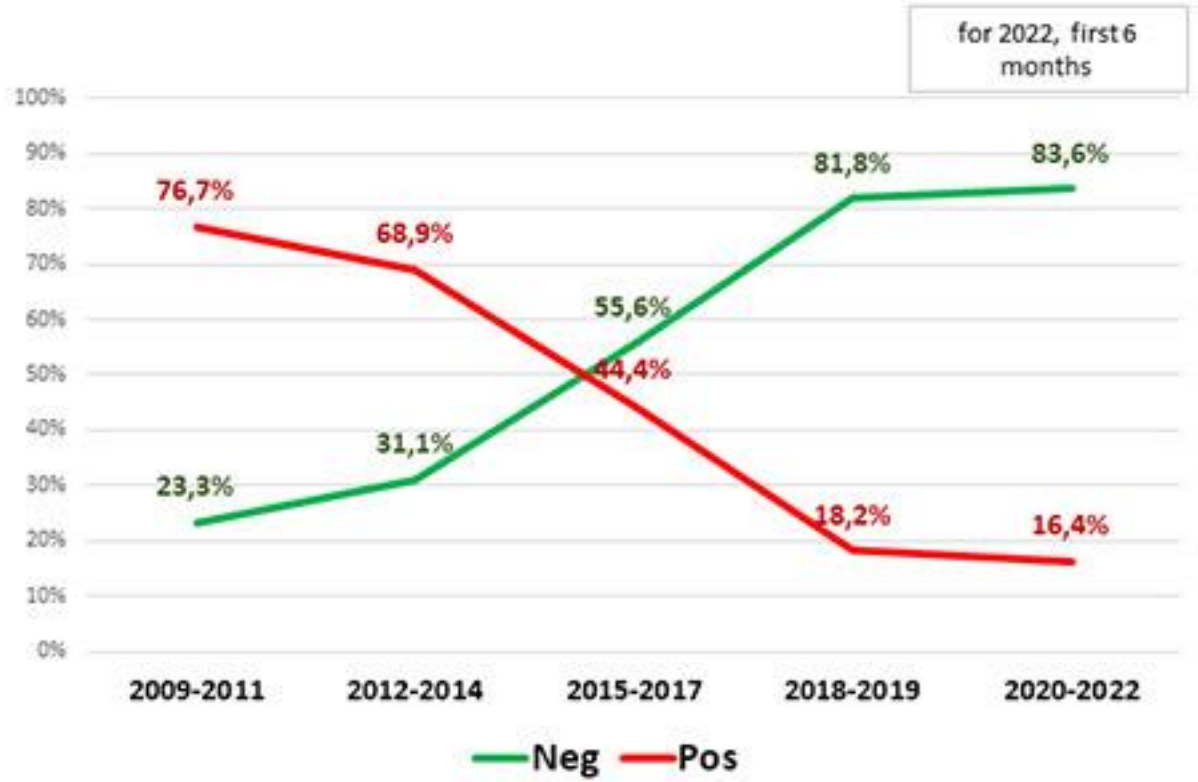
Prevalence of HCV-RNA pos in HCVAb pos patients according to calendar year of follow up in ICONA



Last HCV-RNA test



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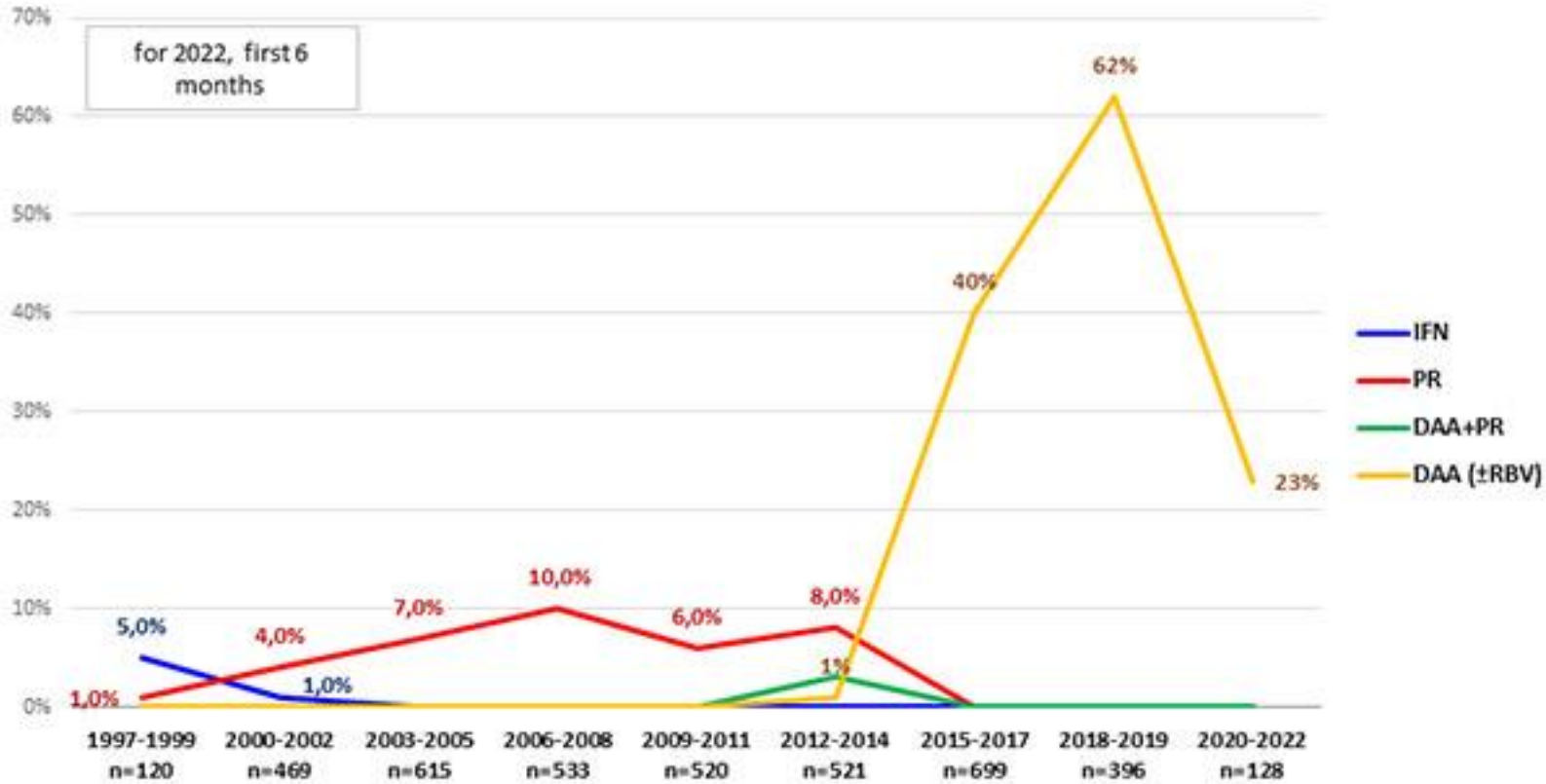
Proportion of HCV-RNA+ patients starting any anti-HCV treatment for the first time, according to drug compound and period of starting



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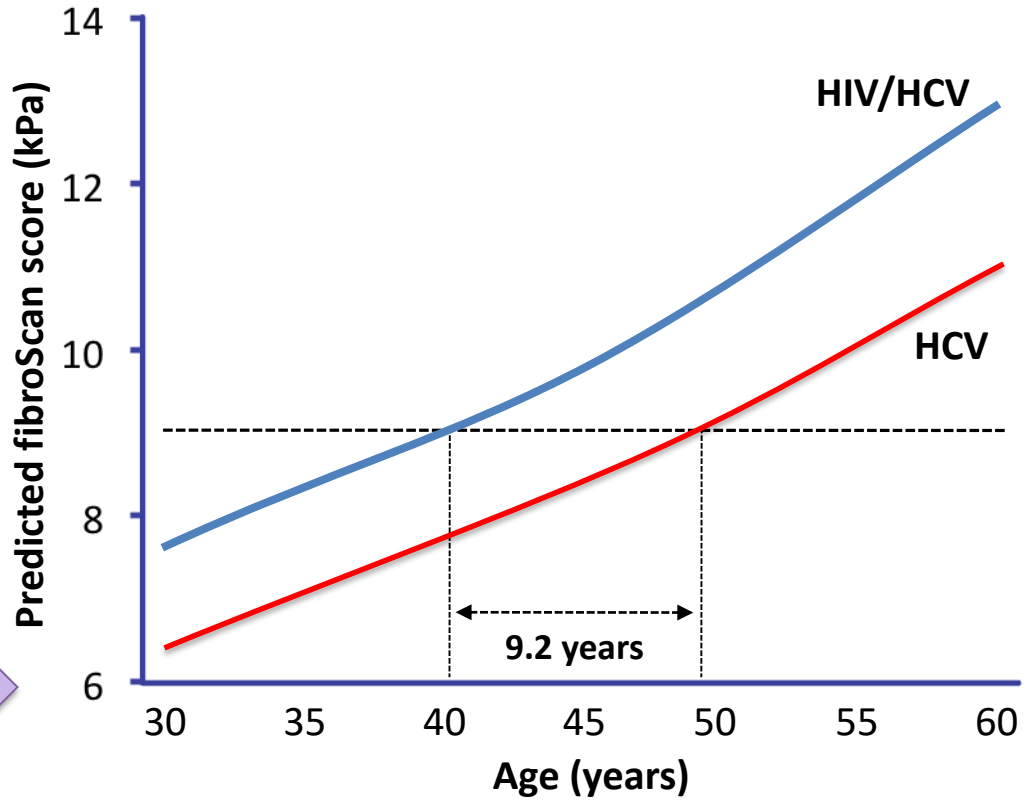
ALIVE Study: HIV, Age, and Severity of HCV-Related Liver Diseases

Prospective cohort of 1176 HCV-infected IDUs, including 394 patients co-infected with HIV

Fibrosis was significantly greater in HIV/HCV co-infected versus HCV mono-infection (P<0.001)

HIV/HCV co-infected patients have liver fibrosis similar to HCV mono-infected patients who are nearly 10 years older

Liver fibrosis and age: HIV/HCV versus HCV infection



ALIVE = AIDS Linked to the IntraVenous Experience; IDU = injection drug user.

Kirk GD, *et al. Ann Intern Med* 2013; **158:**658-666.

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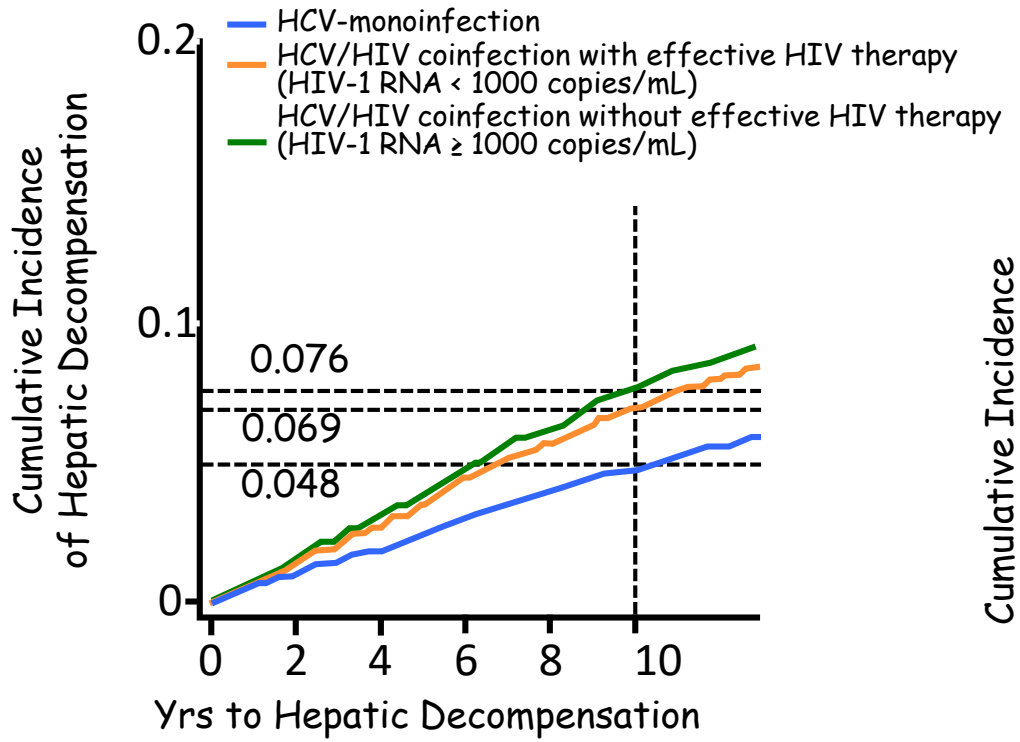
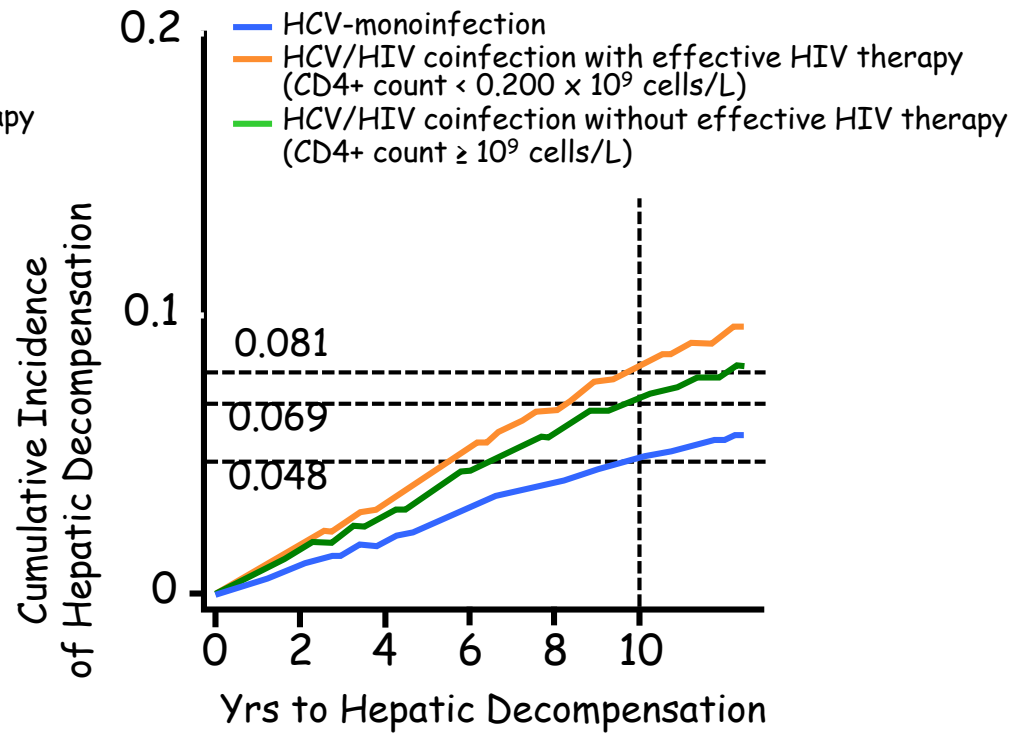
Disease Progression in HCV Monoinfection vs HCV/HIV Coinfection With or Without HIV Suppression

Time to Decompensation by Maintained HIV RNA Level



Time to Decompensation by Maintained CD4+ Cell Count



Lo Re III V, et al. Ann Intern Med. 2014;160:369-379.

Antiretroviral therapy for HIV and intrahepatic hepatitis C virus replication

Jeffrey R. Quinn[a], Ashish Goyal[b], Ruy M. Ribeiro[b], Guido Massaccesi[a], Justin R. Bailey[a], David L. Thomas[a] and Ashwin Balagopal[a]

Objective: HIV alters host responses to hepatitis C virus (HCV). However, the impact of antiretroviral therapy (ART) on HCV is rarely understood in relevant tissues and never before within individual hepatocytes.

Design: HIV and HCV kinetics were studied before and after ART initiation among 19 HIV/HCV co-infected persons. From five persons with the largest decline in plasma HCV RNA, liver tissues collected before and during ART, when plasma HIV RNA was undetectable, were studied.

Methods: We used single-cell laser capture microdissection and quantitative PCR to assess intrahepatic HCV. Immunohistochemistry was performed to characterize intrahepatic immune cell populations.

Results: Plasma HCV RNA declined by 0.81 (0.52–1.60) $\log_{10}$ IU/ml from a median (range) 7.26 (6.05–7.29) $\log_{10}$ IU/ml and correlated with proportions of HCV-infected hepatocytes ($r = 0.89$, $P = 2 \times 10^{-5}$), which declined from median (range) of 37% (6–49%) to 23% (0.5–52%) after plasma HIV clearance. Median (range) HCV RNA abundance within cells was unchanged in four of five participants. Liver T-cell abundance unexpectedly decreased, whereas natural killer (NK) and NK T-cell infiltration increased, correlating with changes in proportions of HCV-infected hepatocytes ($r = -0.82$ and $r = -0.73$, respectively). Hepatocyte expression of *HLA-E,* an NK cell restriction marker, correlated with proportions of HCV-infected hepatocytes ($r = 0.79$).

Conclusion: These are the first data to show that ART control of HIV reduces the intrahepatic burden of HCV. Furthermore, our data suggest that HIV affects the pathogenesis of HCV infection by an NK/NK T-cell-mediated mechanism that may involve HLA-E and can be rescued, at least in part, by ART.

AIDS 2022, **36**:337–346

Impact of co-infection by hepatitis C virus on immunological and virological response to antiretroviral therapy in HIV-positive patients

Table 2

Impact of coinfection by HCV on immunological Response at 48 weeks from ART initiation.

			Univariable analyses		Multivariable analyses*	
	n	Mean of increase in CD4 T-cell count, cells/μL, CI 95%	Difference in mean CD4 T-cell count increase, cells/μL, 95% CI	*P*	Difference in mean CD4 T-cell count increase, cells/μL, 95% CI	*P*
HCV (–)	4382	229.7 (224.2–235.2)	0		0	
HCV (+)	688	161.9 (149.7–174.2)	−67.8 (−87.4 to −48.1)	<.001	−44.5 (−64.3 to −24.8)	<.001

Table 3

Impact of Co-infection by HCV on Virological Response at 48 weeks from ART initiation.

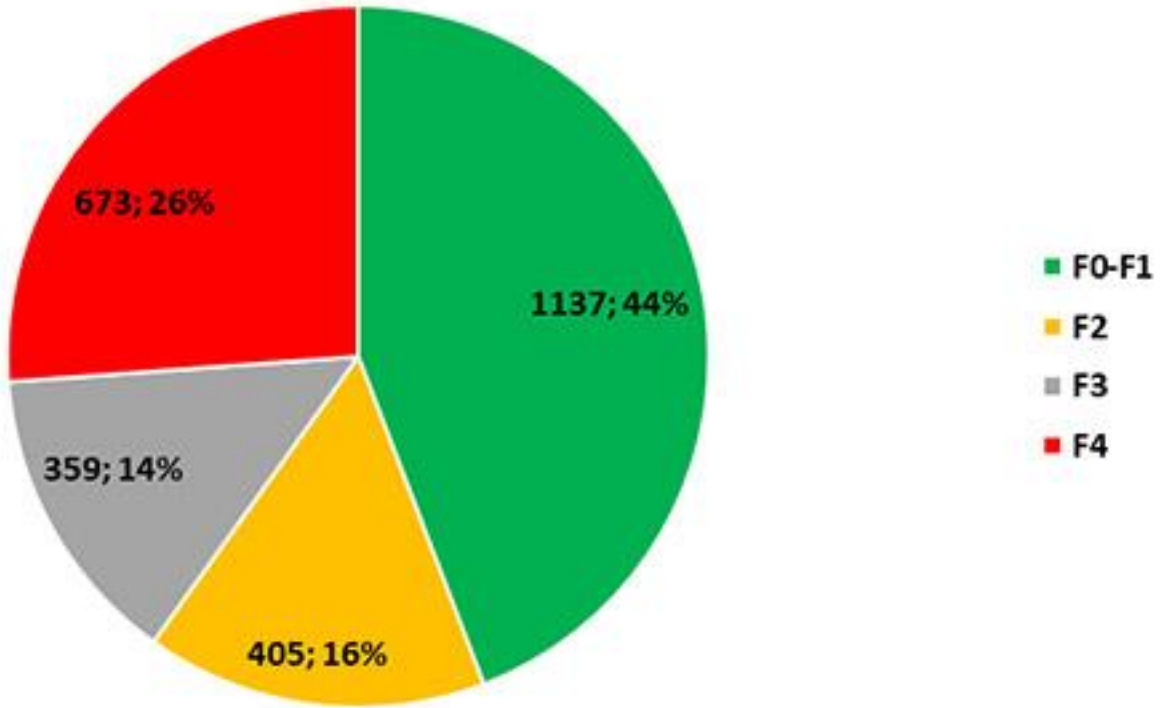
			Univariable analyses		Multivariable analyses*	
	n	Patients (%) who achieved virological response	OR of virological response (95% CI)	*P*	OR of virological response (95% CI)	*P*
HCV (–)	4382	3811 (87.0)	1		1	
HCV (+)	688	539 (78.3)	0.54 (0.44–0.66)	<.001	0.62 (0.44–0.88)	<.01

Portocarrero Nuñez et al. Medicine (2018) 97:38

HEPAicona Hepatitis Icona Cohort

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Transient Elastography Stiffness strata in Icona/Hepaicona patients at start of any anti-HCV treatment (n=2574)



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PITER
Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

RESULTS

Main baseline characteristics of HIV/HCV co-infected and HCV mono-infected patients (1)

	HCV/HIV co-infected (N=197*)		HCV mono-infected (N=2726*)		
Quantitative variables	Median	Range	Median	Range	p**
Age	52	32 - 66	62	20 - 86	< 0.001
ALT	55.5	0.0 - 301.0	62.0	0.0 - 969.0	> 0.05
AST	53.0	0.0 - 371.0	56.0	0.0 - 652.0	> 0.05
Glycemia	98.5	64.0 - 373.0	98.0	0.9 - 351.0	> 0.05

* For some variables inconsistencies are due to missing values

** p value Mann–Whitney rank-sum test

Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

RESULTS

Main baseline characteristics of HIV/HCV co-infected and HCV mono-infected patients with liver cirrhosis (1)

	HCV/HIV co-infected (N=92*)		HCV mono-infected (N=1284*)		
Quantitative variables	Median	Range	Median	Range	p**
Age	52	36 - 55	63	28 - 86	< 0.001
ALT	57.0	0.0 - 284.0	74.0	0.0 - 797.0	< 0.05
AST	59.0	0.0 - 371.0	72.0	0.0 - 652.0	> 0.05
Glycemia	99.0	68.0 - 373.0	101.0	1.0 - 351.0	> 0.05

HEPAicona Hepatitis Icona Cohort

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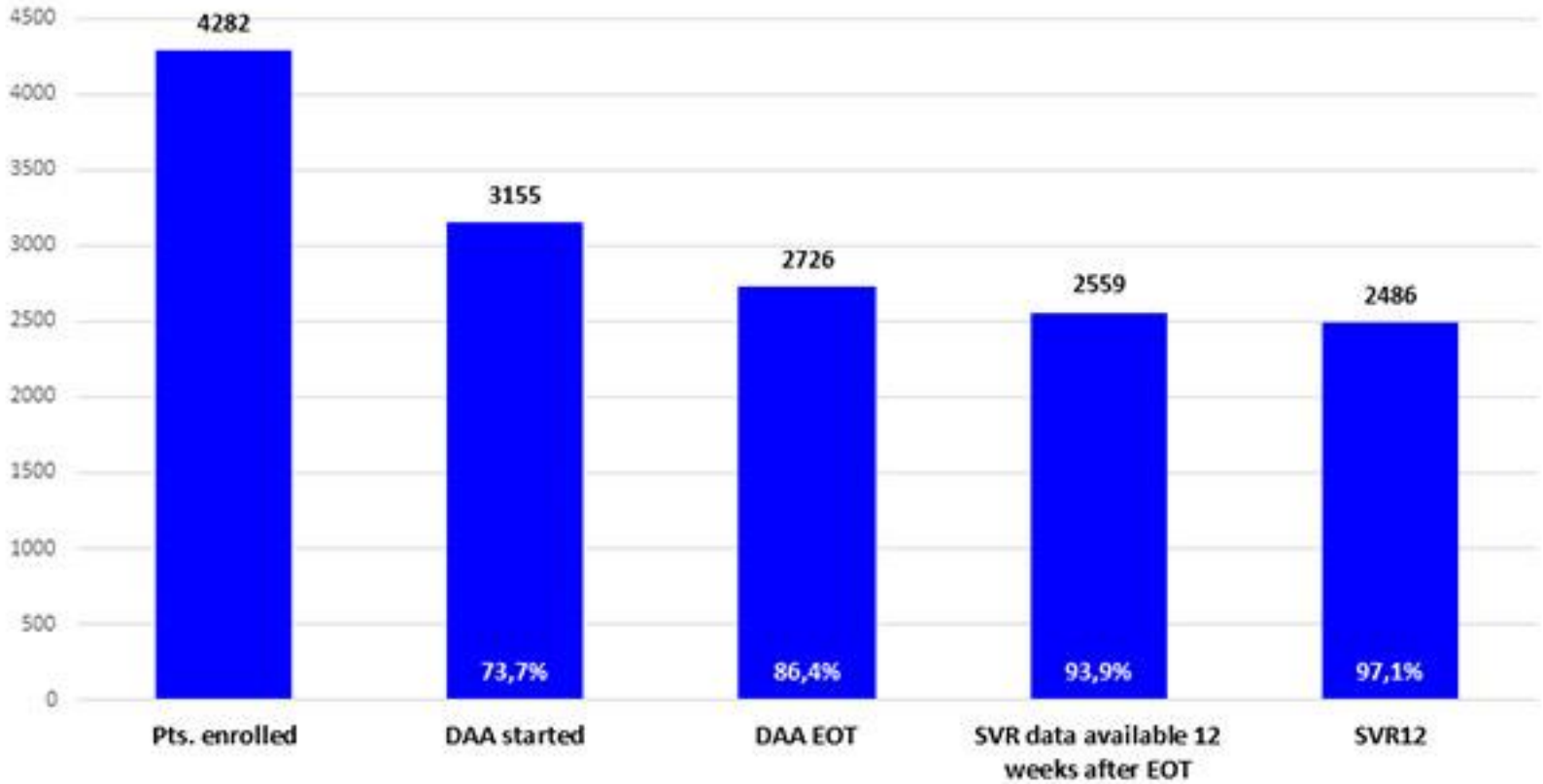
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Outcome of anti-HCV therapies started in Icona/Hepaicona



* 58 patients starting Peg-Interferon+Ribavirin

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HEPAicona Hepatitis Icona Cohort

Fondazione Icona
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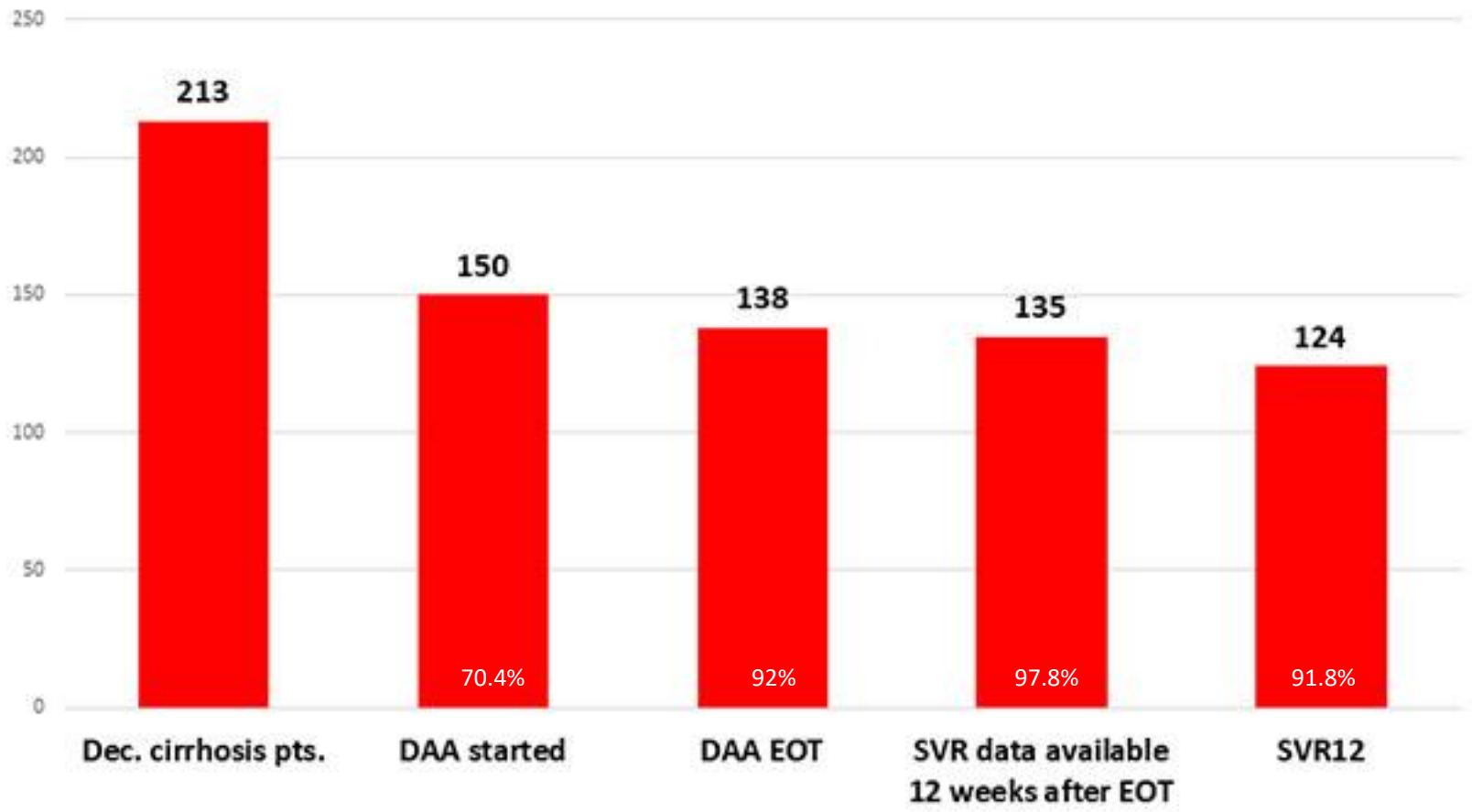
Outcome of DAA-cohort patients with decompensated cirrhosis starting DAA



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Drug-drug Interactions between Viral Hepatitis Drugs and ARVs

EACS European AIDS Clinical Society

Viral hepatitis drugs		ATV/c	ATV/r	DRV/c	DRV/r	LPV/r	DOR	EFV	ETV	NVP	RPV	FTR	MVC	BIC	CAB oral	CAB/ RPV	DTG	EVG/c	RAL	TAF	TDF
HCV DAAs	elbasvir/ grazoprevir	↑	↑376% ↑958%	↑	↑66% ↑650%	↑271% ↑1186%	↓4% ↑7%	↓54% ↓83%	↓	↓	↑7% ↓2%	↔ ↑	↔	↔	↔	↔	↓2% ↓19%	↑118% ↑436%	↓19% ↓11%	↔	↓7% ↓14%
	glecaprevir/ pibrentasvir	↑	↑553% ↑64%	↑	↑397%	↑338% ↑146%	↔	↓	↓	↓	E 84%	↑	E	E	↔	↔	↔	↑205% ↑57% E47%	E47%	↔	E29%
	sofosbuvir	↔	↔	↑	↑34%	↔	↔	↓6%	↔	↔	↑9%	↑	↔	↔	↔	↔	↔	↔	↓5% D27%	↔	↓6%
	sofosbuvir/ ledipasvir	↑ a	↑8% ↑113%a	↑ a	↑34% ↑39%a	↔ a	↑4% ↓8%	↓6% ↓34%a	↔	↔	↑10% ↑8%a	↑	E	↑7% ↓13%	↔	↔	↔	↑36% ↑78%a	↓5% ↓9% D~20%	E32%	E a
	sofosbuvir/ velpatasvir	↔ a	↑22% ↑142%a	↔ a	↓28% ↓16%a	↓29% ↑2%a	↔	↓3% ↓53%	↓	↓	↑16% ↓1%	↑	E	↔	↔	↔	↓8% ↓9%	↑ a	↑24% ↓2%	↔	E a
	sofosbuvir/ velpatasvir/ voxilaprevir	↑	↑40% ↑93% ↑331%	↑ a	↓28% ↓5% ↑143%b	↑	↔	↓	↓	↓	↔	↑	E	↑9% ↓4% ↓9%	↔	↔	↔	↑22% ↑16% ↑171%a	↔	E	E a
HDV	Bulevirtide	↑	↑	↑	↑	↑	E	↑	↑	↔	E	↔	E	↔	↔	E	↔	↑	↔	↔	↔

Legend

↑	Potential elevated exposure of the hepatitis therapy
↓	Potential decreased exposure of the hepatitis therapy
↔	No significant effect
D	Potential decreased exposure of ARV drug
E	Potential elevated exposure of ARV drug

EACS Guidelines 2021

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www.hep-druginteractions.org

UNIVERSITY OF LIVERPOOL

Interaction Report

Report ID:
Date Produced: 08 December 2021

Hepatitis Treatment	Co-medications
Glecaprevir/Pibrentasvir Sofosbuvir/Velpatasvir/Voxilaprevir	Doravirine/Lamivudine/Tenofovir-DF Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (EVG/c/FTC/TAF)

This report lists the summaries of potential interactions (i.e. "red", "amber" and “yellow” classifications) for the drugs in the table above.

Interactions with a "green" or "grey" classification (i.e. no clinically significant interaction or no clear data) have been checked and are listed at the end of this report, but summaries are not shown. Please note that some co-medications with a green classification may require dose adjustment due to hepatic impairment.

For full details of all interactions, see www.hep-druginteractions.org .

Description of the interactions

Potential clinically significant interaction - likely to require additional monitoring, alteration of drug dosage or timing of administration (AMBER)

Sofosbuvir/Velpatasvir/Voxilaprevir + Doravirine/Lamivudine/Tenofovir-DF
Coadministration has not been studied. Doravirine and lamivudine are not expected to inhibit or induce any relevant metabolic enzymes or transporters of sofosbuvir/velpatasvir/voxilaprevir. However, sofosbuvir/velpatasvir/voxilaprevir has been shown to increase tenofovir exposure due to inhibition of P-gp inhibition by velpatasvir and voxilaprevir. Tenofovir exposure (AUC and Cmax) increased by ~40% during co-treatment with sofosbuvir/velpatasvir/voxilaprevir and tenofovir-DF (with darunavir/ritonavir/emtricitabine). Patients receiving sofosbuvir/velpatasvir/voxilaprevir concomitantly with tenofovir-DF should be monitored for tenofovir-associated adverse reactions.

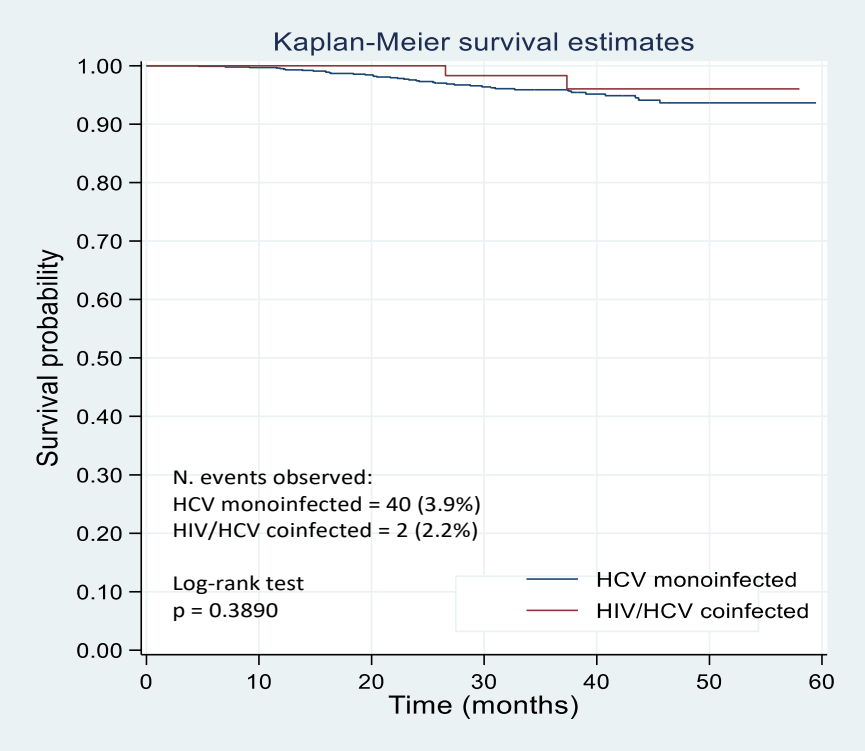
No clinically significant interaction expected (GREEN)

Glecaprevir/Pibrentasvir + Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (EVG/c/FTC/TAF)

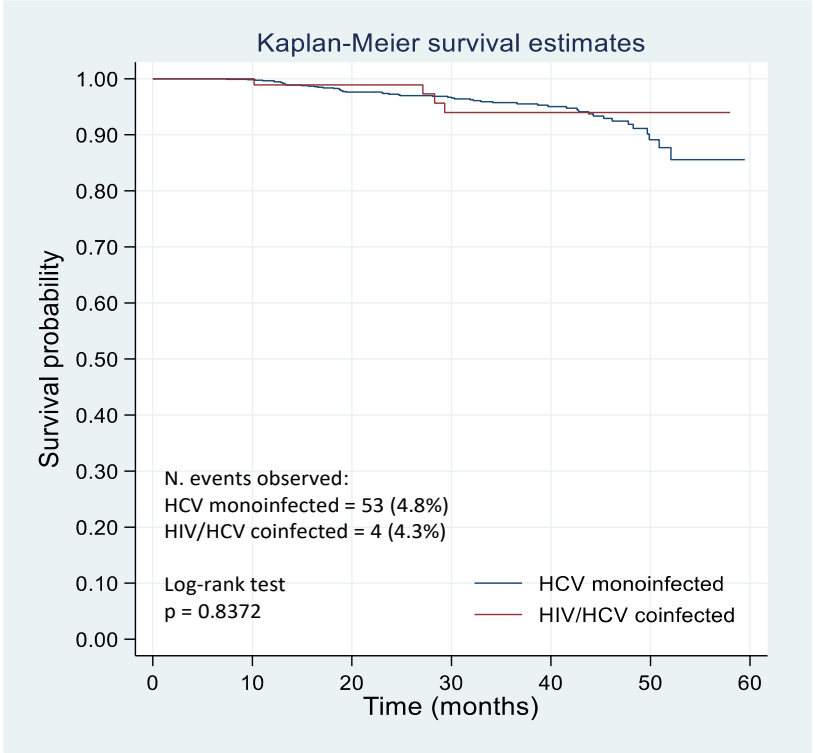
Sofosbuvir/Velpatasvir/Voxilaprevir + Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir alafenamide (EVG/c/FTC/TAF)

Glecaprevir/Pibrentasvir + Doravirine/Lamivudine/Tenofovir-DF

Liver related outcomes following viral eradication



Kaplan-Meier curves for *de novo* HCC occurrence by HCV monoinfected and HIV/HCV coinfected groups



Kaplan-Meier curves for *decompensating event* by HCV monoinfected and HIV/HCV coinfected groups

Predictors of clinical outcomes following SVR12

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Variables associated with *de-novo* HCC occurrence

Baseline factors	Crude HR (95% CI)	Adjusted HR (95% CI)
HIV infection	0.54 (0.13 - 2.24)	0.60 (0.08 4.77)
Age (increasing years)	**1.06 (1.03 - 1.10)**	**1.08 (1.04 - 1.13)**
Sex (ref. female)	**2.68 (1.28 - 5.60)**	**2.76 (1.28 - 5.96)**
BMI: overweight/obese (ref. under-normalweight)	1.07 (0.58 - 1.98)	
Current alcohol use (ref. never)	1.73 (0.70 - 4.32)	
Past alcohol use (ref. never)	**2.13 (1.09 - 4.16)**	
ALT (increasing IU/L)	1.00 (0.99 - 1.00)	
AST (increasing IU/L)	1.00 (0.99 - 1.01)	
Platelets (ref. >100,000/µL)	1.50 (0.81 - 2.79)	
Albumin (decreasing g/dL)	**4.53 (2.24 - 9.13)**	**3.94 (1.81 - 8.58)**
Bilirubin (increasing mg/dL)	1.15 (0.94 - 1.42)	
INR (increasing unit)	1.17 (0.36 - 3.81)	
Genotype (3 vs others)	1.68 (0.75 - 3.79)	**5.05 (1.75 - 14.57)**
Diabetes	0.95 (0.44 - 2.06)	
Anti-HBc+	**2.07 (1.12 - 3.84)**	**1.99 (1.01 - 3.95)**
HBsAg+	Not estimable**	
Previous Interferon	0.94 (0.50 - 1.79)	

Variables associated with decompensating event

Baseline factors	Crude HR (95% CI)	Adjusted HR (95% CI)
HIV infection	0.90 (0.32 - 2.49)	0.55 (0.07 - 4.32)
Age (increasing years)	**1.03 (1.00 - 1.05)**	**1.03 (1.00 - 1.07)**
Sex (ref. female)	1.58 (0.91 - 2.77)	**2.13 (1.06 - 4.26)**
BMI: overweight/obese (ref. under-normalweight)	0.93 (0.71 - 1.20)	
Current alcohol use (ref. never)	1.36 (0.56 - 3.29)	
Past alcohol use (ref. never)	**2.17 (1.24 - 3.82)**	1.84 (0.97 - 3.50)
ALT (increasing IU/L)	1.00 (0.99 - 1.00)	
AST (increasing IU/L)	1.00 (0.99 - 1.01)	
Platelets (ref. >100,000/µL)	**1.95 (1.16 - 3.29)**	1.73 (0.93 - 3.20)
Albumin (decreasing g/dL)	**4.66 (2.54 - 8.56)**	**3.75 (1.89 - 7.46)**
Bilirubin (increasing mg/dL)	0.99 (0.69 - 1.42)	
INR (increasing unit)	**2.11 (1.27 - 3.50)**	
Genotype (3 vs others)	1.26 (0.57 - 2.79)	
Diabetes	1.57 (0.88 - 2.81)	
Anti-HBc+	0.47 (0.22 - 1.00)	
HBsAg+	1.03 (0.14 - 7.48)	
Previous Interferon	0.74 (0.41 - 1.32)	
HCC	1.85 (0.67 - 5.13)	

HIV coinfection was not associated with a higher probability of developing liver complications in cirrhotic patients, after viral eradication

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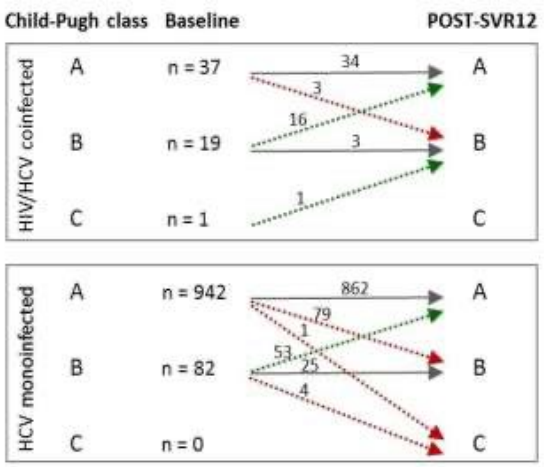
Baseline characteristics		HCV/HIV co-infected (N=108*) N.	%	HCV mono-infected (N=1242*) N.	%	p**
Previous decompensations	Yes	15	13.9	133	10.7	0.31
	No	93	86.1	1109	89.3	
Child-Pugh Score	A-5	39	52.7	762	69.5	**< 0.001**
	A-6	14	18.9	242	22.1	
	B-7	12	16.2	58	5.3	
	B-8	8	10.8	28	2.6	
	B-9	0	0.0	6	0.6	
	C-10	1	1.4	0	0.0	

Baseline factors associated with a more advanced liver disease before treatment (C-P class B/C vs A)

Baseline factors	Adjusted O.R.	95% CI
Age (increasing years)	1.00	0.98 -1.02
Sex (ref. female)	1.07	0.69 - 1.67
Current/past alcohol use (ref. never)	0.87	0.56 - 1.37
HCV-genotype (3 vs others)	1.48	0.80 - 2.76
HBsAg+	2.27	0.57 - 8.99
HIV+	**3.73**	**2.00 - 6.98**

Changes in the severity of liver disease in terms of C-P class improvement or worsening following viral eradication



Child-Pugh class changes

AA 34/37 (92%)
AB 3/37 (8.1%)
BA 16/19 (84.2%)
BB 3/19 (15.8%)
CB 1/1 (100%)

IMPROVEMENT 17/20 (85%)
WORSENING 3/56 (5.3%)

AA 862/942 (91.5%)
AB 79/942 (8.4%)
AC 1/942 (0.1%)
BA 53/82 (64.6%)
BB 25/82 (30.5%)
BC 4/82 (4.8%)

IMPROVEMENT 53/82 (64.6%)
WORSENING 84/1024 (8.2%%)

Variables associated with Child-Pugh class worsening following viral eradication

Baseline factors	Crude HR	95% CI	Adjusted HR	95% CI
HIV infection	0.68	0.21 - 2.15	0.51	0.15 - 1.73
Age (increasing years)	1.00	0.98 - 1.02	1.00	0.98 - 1.02
Sex (ref. female)	**1.77**	**1.12 - 2.81**	**2.00**	**1.18 - 3.36**
BMI: overweight/obese (ref. under-normalweight)	0.88	0.58 - 1.34	0.79	0.51 - 1.22
Current/past alcohol use (ref. never)	0.99	0.63 - 1.55	0.76	0.47 - 1.24
ALT (increasing IU/L)	1.00	0.99 - 1.00	1.00	0.99 - 1.01
AST (increasing IU/L)	1.00	0.99 - 1.00	0.99	0.98 - 1.00
Platelets (ref. >100,000/µL)	**2.01**	**1.31 - 3.08**	**1.75**	**1.08 - 2.85**
Albumin (decreasing g/dL)	1.57	0.99 - 2.43	1.35	0.82 - 2.23
Bilirubin (increasing mg/dL)	0.98	0.87 - 1.12	0.84	0.60 - 1.18
INR (increasing unit)	**2.15**	**1.45 - 3.19**	**2.41**	**1.51 - 3.84**
HCV-genotype (3 vs others)	1.51	0.80 - 2.84	1.54	0.75 - 3.17
Diabetes	1.14	0.69 - 1.89	0.93	0.55 - 1.57
Anti-HBc+	1.02	0.63 - 1.65	1.05	0.63 - 1.76
Previous Interferon treatment	0.82	0.52 - 1.29	0.77	0.48 - 1.23
Esophageal varices	**1.85**	**1.20 - 2.85**	1.47	0.89 - 2.42
HCC	**2.32**	**1.20 - 4.49**	1.88	0.87 - 4.08
Previous decompensating event	**1.97**	**1.17 - 3.31**	1.12	0.60 - 2.11

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Article

Impact of HCV Eradication on Lipid Metabolism in HIV/HCV Coinfected Patients: Data from ICONA and HepaICONA Foundation Cohort Study

Martina Spaziante [1], Gloria Taliani [2,3,*], Giulia Marchetti [4], Alessandro Tavelli [5], Miriam Lichtner [6], Antonella Cingolani [7], Stefania Cicalini [8], Elisa Biliotti [2], Enrico Girardi [1], Andrea Antinori [8], Massimo Puoti [9], Antonella d'Arminio Monforte [4] and Alessandro Cozzi-Lepri [10]

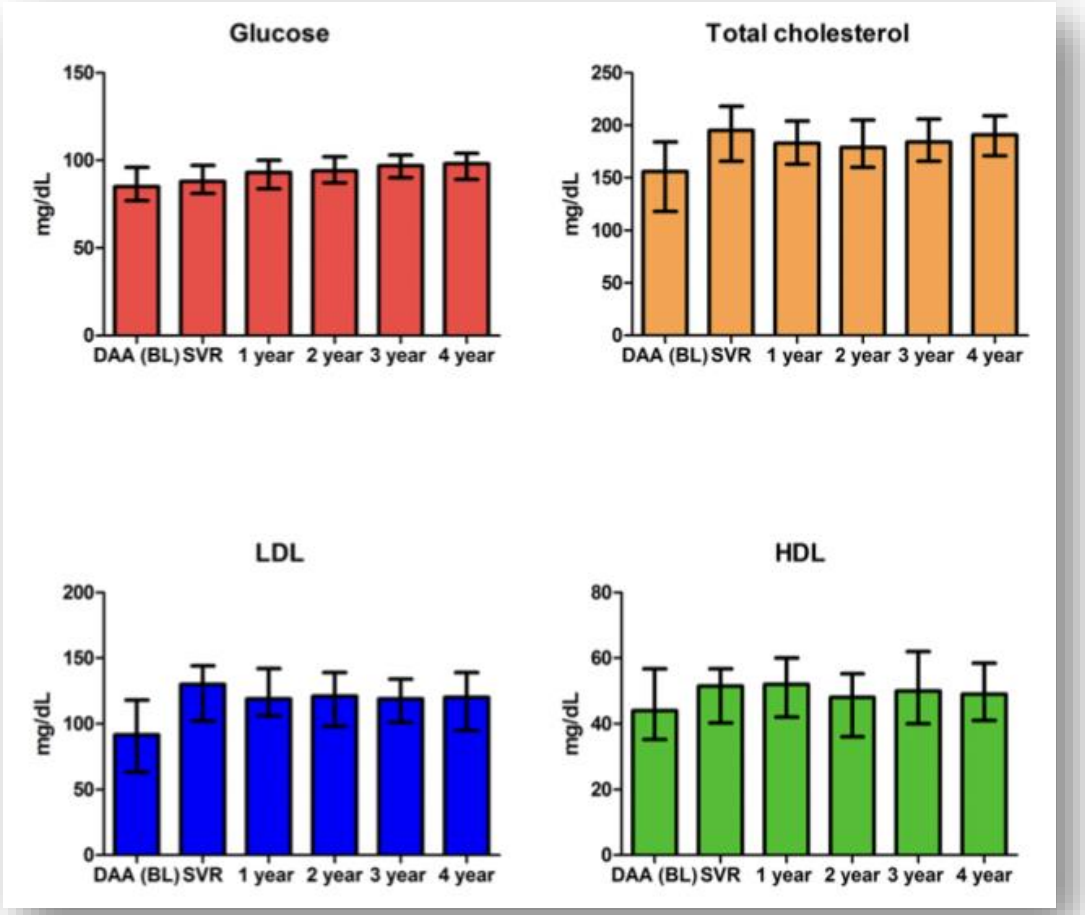
Abstract: Objectives: HCV shows complex interactions with lipid metabolism. Our aim was to examine total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) changes in HIV/HCV coinfected patients, after achieving sustained virological response (SVR), according to different HCV genotypes and specific antiretroviral use. Methods: HIV/HCV coinfected patients, enrolled in the ICONA and HepaICONA cohorts, who achieved DAA-driven SVR were included. Paired t-tests were used to examine whether the pre- and post-SVR laboratory value variations were significantly different from zero. ANCOVA regression models were employed to estimate the causal effect of SVR and of PI/r use on lipid changes. The interaction between the effect of eradication and HCV genotype was formally tested. Results: six hundred and ninety-nine HIV/HCV coinfected patients were enrolled. After HCV eradication, a significant improvement in liver function occurred, with a significant decrease in AST, ALT, GGT, and total plasmatic bilirubin. TC and LDL-C significantly increased by 21.4 mg/dL and 22.4 mg/dL, respectively ($p < 0.001$), after SVR, whereas there was no evidence for a change in HDL-C ($p = 0.45$) and triglycerides ($p = 0.49$). Notably, the TC and LDL-C increase was higher for participants who were receiving darunavir/ritonavir, and the TC showed a more pronounced increase among HCV genotype 3 patients (interaction-p value = 0.002). Conclusions: complex and rapid changes in TC and LDL-C levels, modulated by HCV genotype and PI/r-based ART combinations, occurred in HIV/HCV coinfected patients after SVR. Further studies are needed to evaluate the clinical impact of these changes on the long-term risk of cardiovascular disease.

Viruses 2021, 13, 1402.

Long-term outcomes in GT3 HCV/HIV co-infected subjects treated with DAAs: impact on metabolic profile

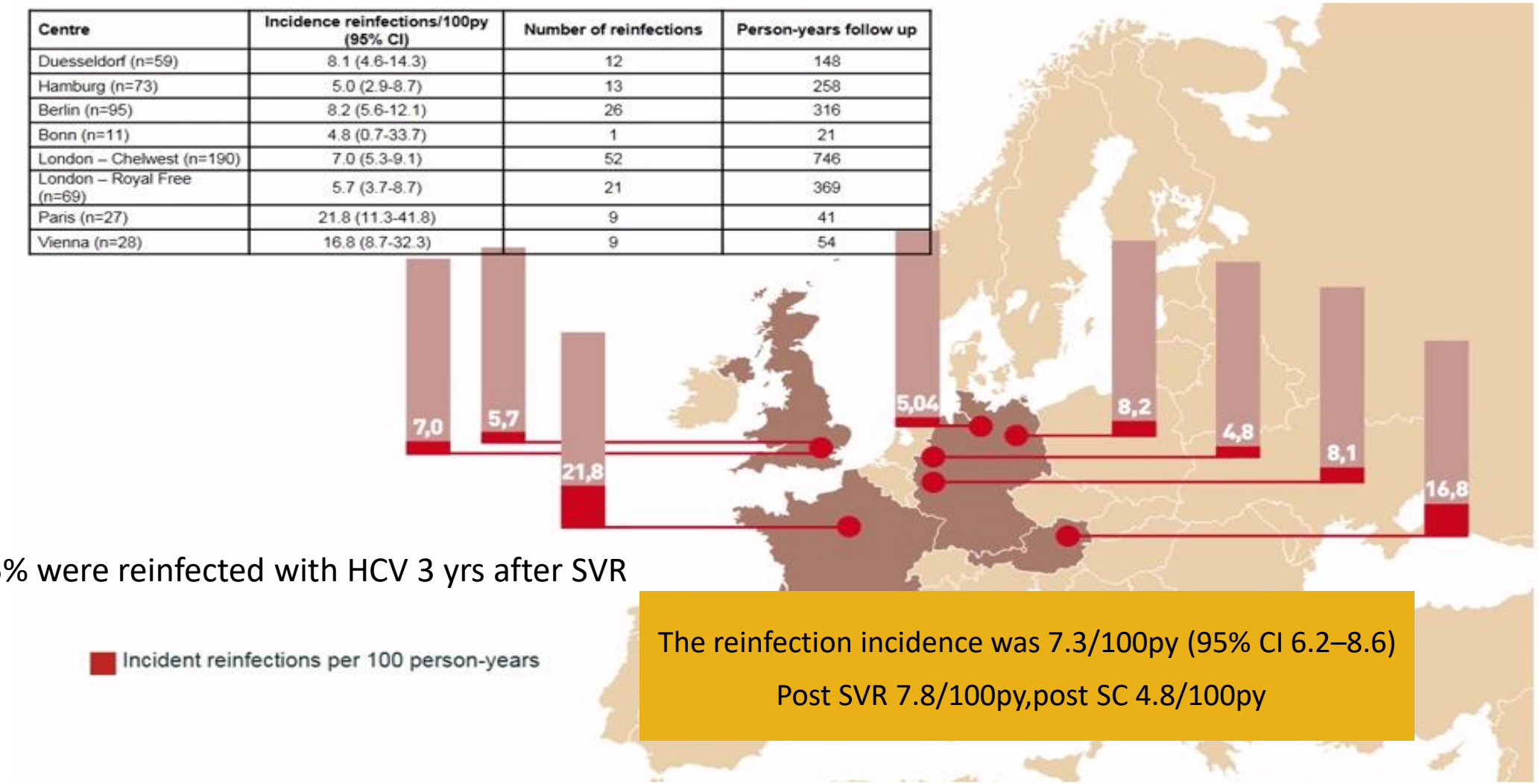
Siribelli Alessia, Ceccarelli Daniele, Messina Emanuela, Bertoni Costanza, Lolatto Riccardo, Morsica Giulia, Uberti-Foppa Caterina, Castagna Antonella, Hasson Hamid

Parameter	DAA BL	SVR	VARIATION AFTER 48 WEEKS FROM BL	VARIATION AFTER 96 WEEKS FROM BL	VARIATION AFTER 144 WEEKS FROM BL	VARIATION AFTER 192 WEEKS FROM BL
Triglycerides mg/dL	104 [79.0;141]	112 [88.2;149]	4.00 [-24.00;38.8] p: 0,5468	6.00 [-28.00;42.0] p: 0,2064	1.50 [-21.75;53.0] p: 0,1246	3.00 [-26.75;45.0] p: 0,4516
PLT 10^3/mm^3	167 [132;220]	195 [149;227]	23.0 [2.75;43.2] p: 0,0000	30.5 [3.50;49.5] p: 0,0000	27.0 [5.50;48.2] p: 0,0000	41.5 [14.0;63.8] p: 0,0000
CKD EPI	93.0 [81.0;102]	85.0 [74.0;98.0]	-6.00 [-15.00;-1.00] p: 0,0000	-12.00 [-18.00;-6.00] p: 0,0000	-11.00 [-20.00;-3.00] p: 0,0000	-14.00 [-19.00;-7.00] p: 0,0000
FIB 4	2.31 [1.44;4.14]	1.68 [1.22;2.29]	-0.79 [-1.90;-0.14] p: 0,0000	-0.70 [-2.06;-0.17] p: 0,0000	-0.67 [-1.30;-0.10] p: 0,0000	-0.66 [-2.42;-0.20] p: 0,0000
Stiffness kPa	8.20 [5.60;13.3]	4.10 [4.05;5.35]	-0.25 [-2.42;0.88] p: NA	-2.20 [-5.77;2.75] p: NA	2.20 [-1.30;19.7] p: NA	-2.10 [-2.10;-2.10] p: NA
CAP	229 [200;272]	204 [192;254]	-9.00 [-23.50; - 5.00] p: NA	11.0 [-42.50;32.0] p: NA	-42.00 [-83.50; -0.50] p: NA	-
AFP ng/mL	3.75 [2.50;6.43]	2.80 [2.10;3.95]	-1.90 [-4.55; 0.50] p: 0,0000	-1.45 [-4.80;-0.60] p: 0,0001	-1.60 [-3.80;-0.45] p: 0,0003	-1.40 [-5.30;-0.55] p: 0,0002



HCV reinfection among HIV+ MSM: Europe

Centre	Incidence reinfections/100py (95% CI)	Number of reinfections	Person-years follow up
Duesseldorf (n=59)	8.1 (4.6-14.3)	12	148
Hamburg (n=73)	5.0 (2.9-8.7)	13	258
Berlin (n=95)	8.2 (5.6-12.1)	26	316
Bonn (n=11)	4.8 (0.7-33.7)	1	21
London – Chelwest (n=190)	7.0 (5.3-9.1)	52	746
London – Royal Free (n=69)	5.7 (3.7-8.7)	21	369
Paris (n=27)	21.8 (11.3-41.8)	9	41
Vienna (n=28)	16.8 (8.7-32.3)	9	54



25% were reinfected with HCV 3 yrs after SVR

The reinfection incidence was 7.3/100py (95% CI 6.2–8.6)

Post SVR 7.8/100py,post SC 4.8/100py

Ingiliz P et al. J. Hepatol 2017

Incidence of HCV Reinfection in MSM With HIV in Western Europe (2002-2014)

Baseline Characteristics	Incident Infection	1st Reinfection	2nd Reinfection
Included in study, n	NA	606	70
Reinfections, n (%)	606	149 (24.6)	30 (42.9)
Reinfection genotype, n (%) ▪ 1 ▪ 2 ▪ 3 ▪ 4 ▪ Mixed genotype 1/3	 376 (70.5) 13 (2.4) 46 (8.6) 96 (18) 3-2 (0.4)	 104 (73.2) 1(0.7) 12 (8.5) 25 (17.6) NR	 23 (85.2) 0 (0) 1 (3.7) 3 (11.1) NR
Genotype switches, %	NA	71/136 (52)	12/54 (54)
Spontaneous clearing, %	NA	(15.6)	(28.6)
SVR, %	NA	70	92
Median age, yrs (IQR)	39 (24-44)	41 (37-45)	42 (40-48)

Ingiliz. J Hepatology. 2017;66:282.

Reinfection by hepatitis C virus following effective all-oral direct-acting antiviral drug therapy in HIV/hepatitis C virus coinfected individuals

Juan Berenguer, Angela Gil-Martin, Inmaculada Jarrin, Maria L. Montes, Lourdes Dominguez, Teresa Aldamiz-Echevarria, Maria J. Tellez, Ignacio Santos, Jesus Troya, Juan E. Losa, Regino Serrano, Maria T. De Guzman, Maria J.Calvo, Juan J.Gonzalez-Garcia, the Madrid-CoRe Study Group

Reinfections HIV/HCV 17/2359 (0.72%) overall,
12/177 (6.78%) MSM
5/1459 (0.34%) PWID.

HIV transmission category	Number	Number of reinfections	Years of Follow-up	Rate of reinfection per 100 pY (95%CI)
All categories	2359	17	3546	0.48 (0.30-0.77)
PWID	1459	5	2329	0.21 (0.09-0.52)
MSM	177	12	202	5.93 (3.37-10.44)
Other/unknown	723	0	1015	-

Reinfection a median of 15 weeks after SVR

Berenguer J et al. AIDS 2019

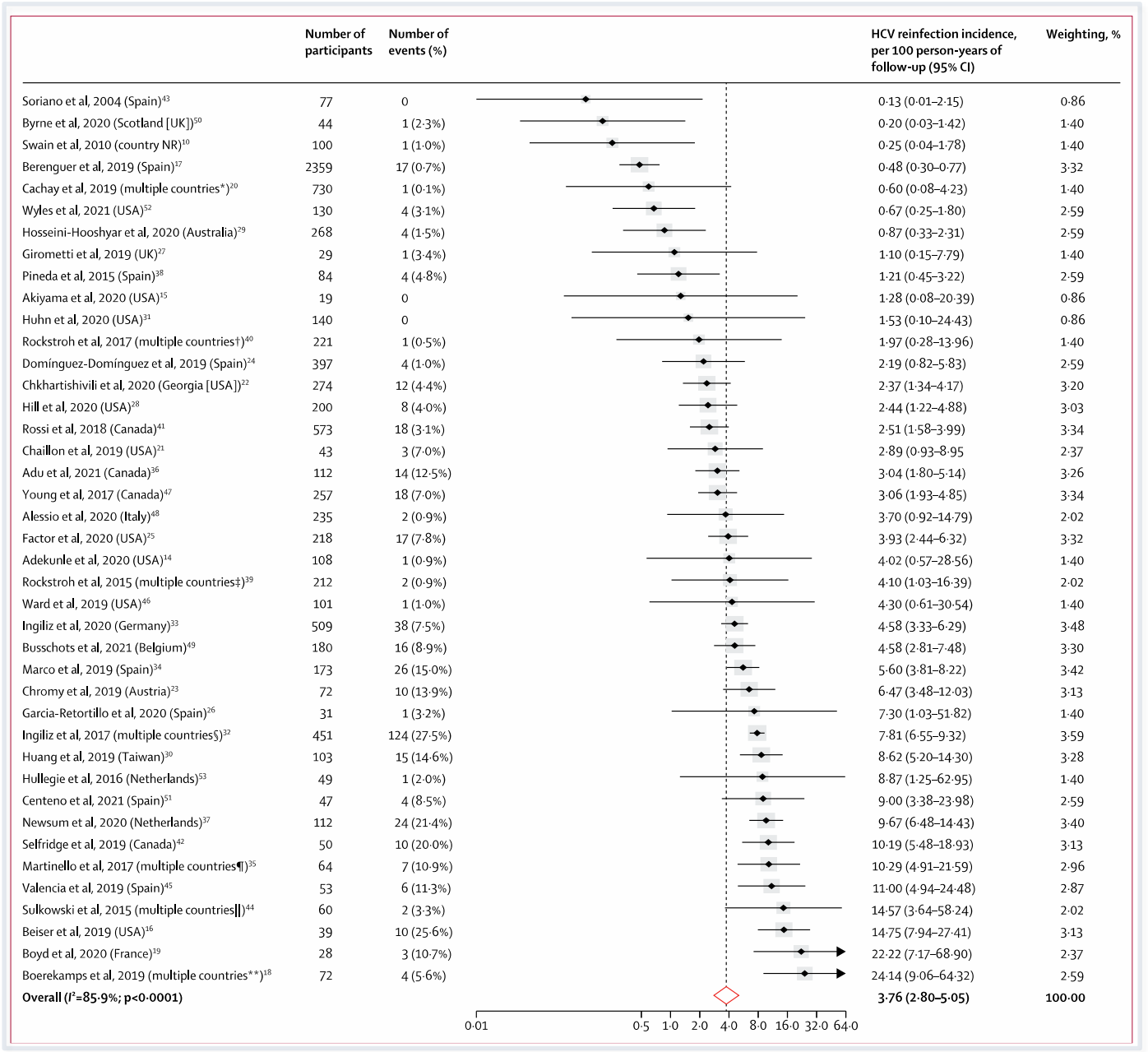
Risk of hepatitis C reinfection following successful therapy among people living with HIV: a global systematic review, meta-analysis, and meta-regression

Samira Hosseini-Hooshyar, Behzad Hajarizadeh, Sahar Bajis, Matthew Law, Naveed Z Janjua, Daniel S Fierer, David Chromy, Jürgen K Rockstroh, Thomas C S Martin, Patrick Ingiliz, Chien-Ching Hung, Gregory J Dore, Marianne Martinello, Gail V Matthews**

41studies with a total of 9024 partecipants

Incidence of reinfection

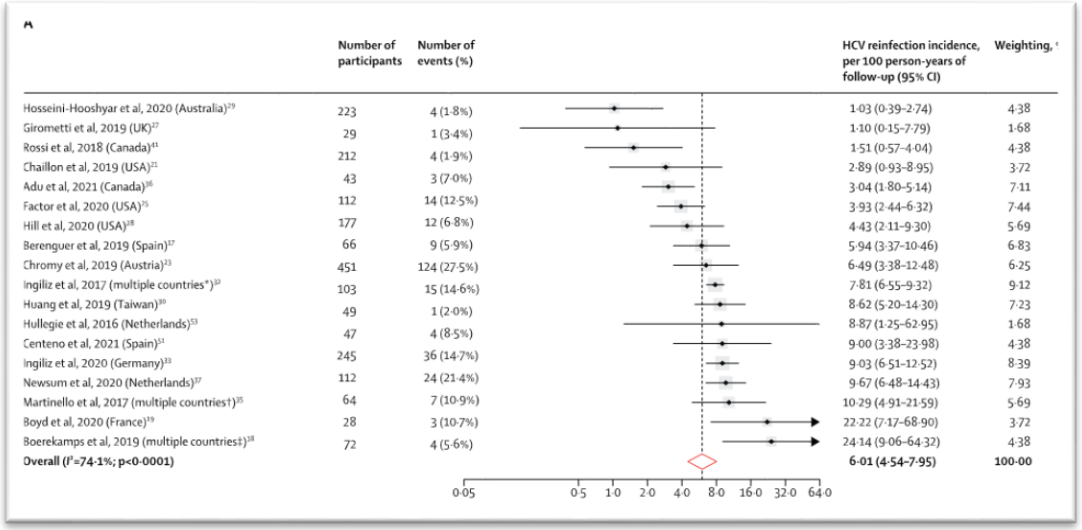
HIV overall	3.76 cases/100py follow-up
MSM	6.01
PWID	3.29



Risk of hepatitis C reinfection following successful therapy among people living with HIV: a global systematic review, meta-analysis, and meta-regression

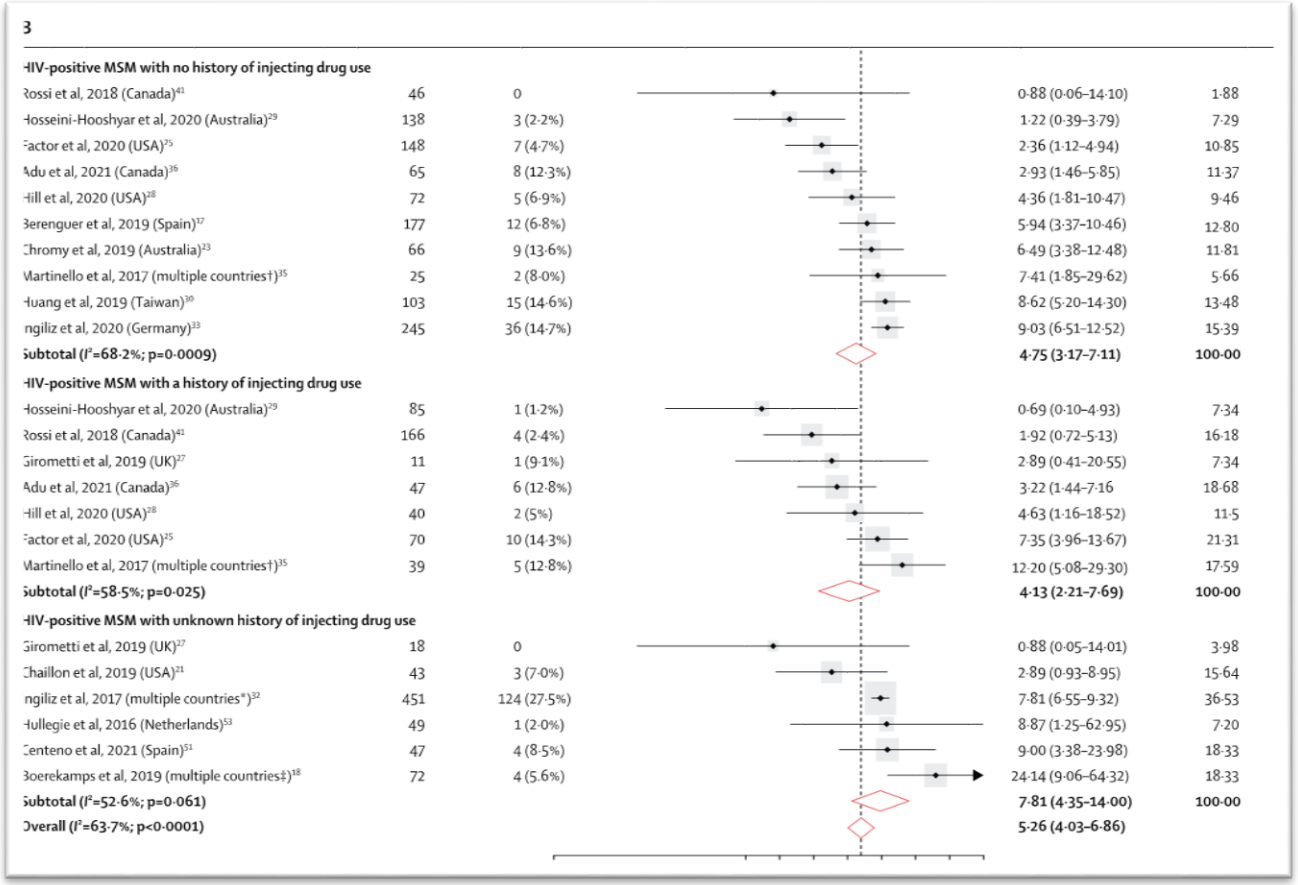
Samira Hosseini-Hooshyar, Behzad Hajarizadeh, Sahar Bajis, Matthew Law, Naveed Z Janjua, Daniel S Fierer, David Chromy, Jürgen K Rockstroh, Thomas C S Martin, Patrick Ingiliz, Chien-Ching Hung, Gregory J Dore, Marianne Martinello, Gail V Matthews**

HCV Reinfection incidence among MSM HIV+: 6.01



	Number of participants	Number of events (%)	HCV reinfection incidence, per 100 person-years of follow-up (95% CI)	Weighting, %
Hosseini-Hooshyar et al, 2020 (Australia)[29]	223	4 (1·8%)	1·03 (0·39–2·74)	4·38
Girometti et al, 2019 (UK)[27]	29	1 (3·4%)	1·10 (0·15–7·79)	1·68
Rossi et al, 2018 (Canada)[41]	212	4 (1·9%)	1·51 (0·57–4·04)	4·38
Chaillon et al, 2019 (USA)[21]	43	3 (7·0%)	2·89 (0·93–8·95)	3·72
Adu et al, 2021 (Canada)[36]	112	14 (12·5%)	3·04 (1·80–5·14)	7·11
Factor et al, 2020 (USA)[25]	177	12 (6·8%)	3·93 (2·44–6·32)	7·44
Hill et al, 2020 (USA)[28]	66	9 (5·9%)	4·43 (2·11–9·30)	5·69
Berenguer et al, 2019 (Spain)[17]	451	124 (27·5%)	5·94 (3·37–10·46)	6·83
Chromy et al, 2019 (Austria)[23]	103	15 (14·6%)	6·49 (3·38–12·48)	6·25
Ingiliz et al, 2017 (multiple countries*)[32]	49	1 (2·0%)	7·81 (6·55–9·32)	9·12
Huang et al, 2019 (Taiwan)[39]	47	4 (8·5%)	8·62 (5·20–14·30)	7·23
Hullegie et al, 2016 (Netherlands)[53]	245	36 (14·7%)	8·87 (1·25–62·95)	1·68
Centeno et al, 2021 (Spain)[51]	112	24 (21·4%)	9·00 (3·38–23·98)	4·38
Ingiliz et al, 2020 (Germany)[33]	64	7 (10·9%)	9·03 (6·51–12·52)	8·39
Newsum et al, 2020 (Netherlands)[37]	28	3 (10·7%)	9·67 (6·48–14·43)	7·93
Martinello et al, 2017 (multiple countries†)[35]	72	4 (5·6%)	10·29 (4·91–21·59)	5·69
Boyd et al, 2020 (France)[19]			22·22 (7·17–68·90)	3·72
Boerekamps et al, 2019 (multiple countries‡)[18]			24·14 (9·06–64·32)	4·38
Overall (I^2=74·1%; p<0·0001)			**6·01 (4·54–7·95)**	**100·00**

0·05 0·5 1·0 2·0 4·0 8·0 16·0 32·0 64·0

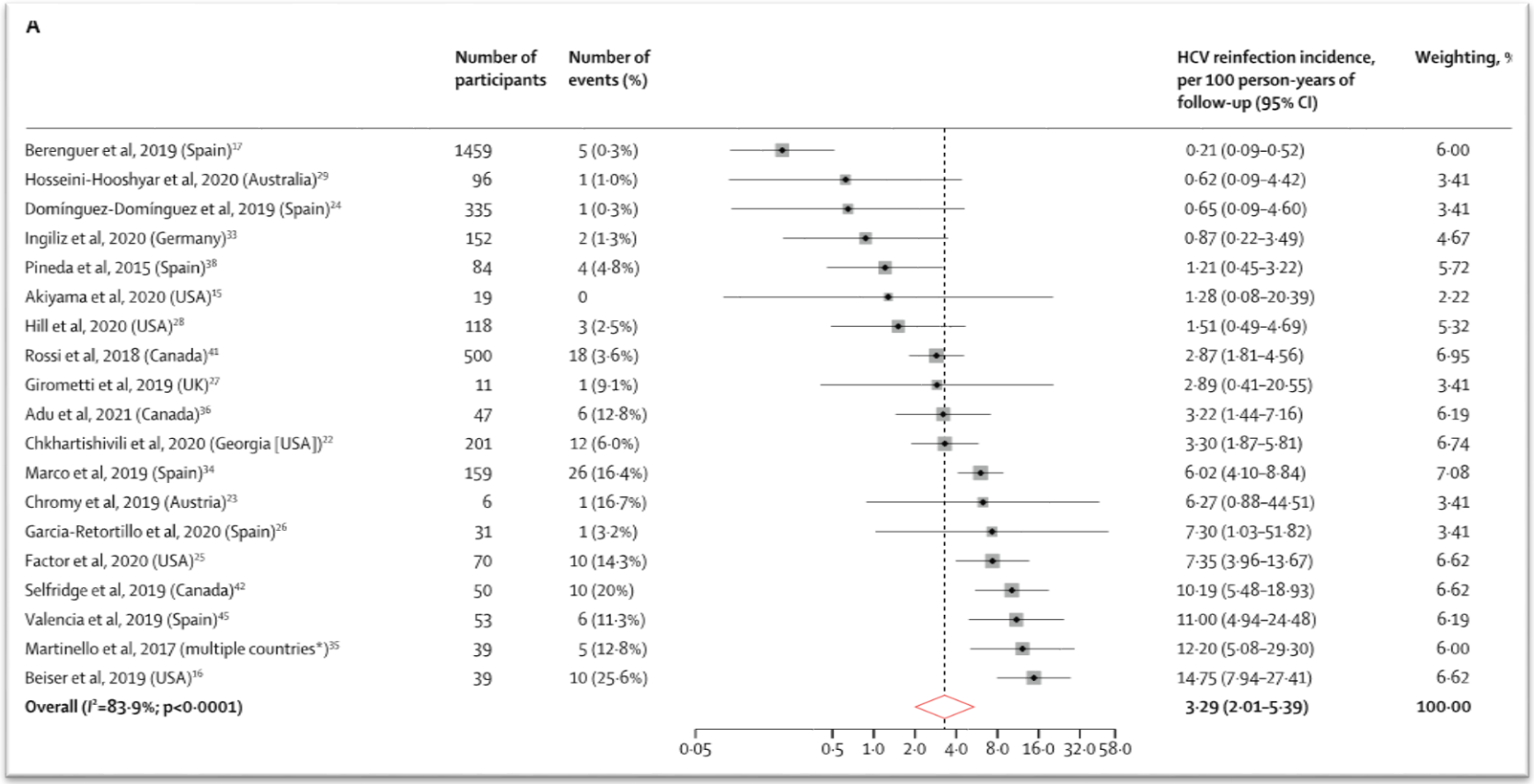


HIV-positive MSM with no history of injecting drug use				
Rossi et al, 2018 (Canada)[41]	46	0	0·88 (0·06–14·10)	1·88
Hosseini-Hooshyar et al, 2020 (Australia)[29]	138	3 (2·2%)	1·22 (0·39–3·79)	7·29
Factor et al, 2020 (USA)[25]	148	7 (4·7%)	2·36 (1·12–4·94)	10·85
Adu et al, 2021 (Canada)[36]	65	8 (12·3%)	2·93 (1·46–5·85)	11·37
Hill et al, 2020 (USA)[28]	72	5 (6·9%)	4·36 (1·81–10·47)	9·46
Berenguer et al, 2019 (Spain)[17]	177	12 (6·8%)	5·94 (3·37–10·46)	12·80
Chromy et al, 2019 (Australia)[23]	66	9 (13·6%)	6·49 (3·38–12·48)	11·81
Martinello et al, 2017 (multiple countries†)[35]	25	2 (8·0%)	7·41 (1·85–29·62)	5·66
Huang et al, 2019 (Taiwan)[39]	103	15 (14·6%)	8·62 (5·20–14·30)	13·48
Ingiliz et al, 2020 (Germany)[33]	245	36 (14·7%)	9·03 (6·51–12·52)	15·39
Subtotal (I^2=68·2%; p=0·0009)			**4·75 (3·17–7·11)**	**100·00**
HIV-positive MSM with a history of injecting drug use				
Hosseini-Hooshyar et al, 2020 (Australia)[29]	85	1 (1·2%)	0·69 (0·10–4·93)	7·34
Rossi et al, 2018 (Canada)[41]	166	4 (2·4%)	1·92 (0·72–5·13)	16·18
Girometti et al, 2019 (UK)[27]	11	1 (9·1%)	2·89 (0·41–20·55)	7·34
Adu et al, 2021 (Canada)[36]	47	6 (12·8%)	3·22 (1·44–7·16	18·68
Hill et al, 2020 (USA)[28]	40	2 (5%)	4·63 (1·16–18·52)	11·5
Factor et al, 2020 (USA)[25]	70	10 (14·3%)	7·35 (3·96–13·67)	21·31
Martinello et al, 2017 (multiple countries†)[35]	39	5 (12·8%)	12·20 (5·08–29·30)	17·59
Subtotal (I^2=58·5%; p=0·025)			**4·13 (2·21–7·69)**	**100·00**
HIV-positive MSM with unknown history of injecting drug use				
Girometti et al, 2019 (UK)[27]	18	0	0·88 (0·05–14·01)	3·98
Chaillon et al, 2019 (USA)[21]	43	3 (7·0%)	2·89 (0·93–8·95)	15·64
Ingiliz et al, 2017 (multiple countries*)[32]	451	124 (27·5%)	7·81 (6·55–9·32)	36·53
Hullegie et al, 2016 (Netherlands)[53]	49	1 (2·0%)	8·87 (1·25–62·95)	7·20
Centeno et al, 2021 (Spain)[51]	47	4 (8·5%)	9·00 (3·38–23·98)	18·33
Boerekamps et al, 2019 (multiple countries‡)[18]	72	4 (5·6%)	24·14 (9·06–64·32)	18·33
Subtotal (I^2=52·6%; p=0·061)			**7·81 (4·35–14·00)**	**100·00**
Overall (I^2=63·7%; p<0·0001)			**5·26 (4·03–6·86)**	

Risk of hepatitis C reinfection following successful therapy among people living with HIV: a global systematic review, meta-analysis, and meta-regression

Samira Hosseini-Hooshyar, Behzad Hajarizadeh, Sahar Bajis, Matthew Law, Naveed Z Janjua, Daniel S Fierer, David Chromy, Jürgen K Rockstroh, Thomas C S Martin, Patrick Ingiliz, Chien-Ching Hung, Gregory J Dore, Marianne Martinello, Gail V Matthews**

HCV Reinfection incidence among PWID HIV+: 3.29

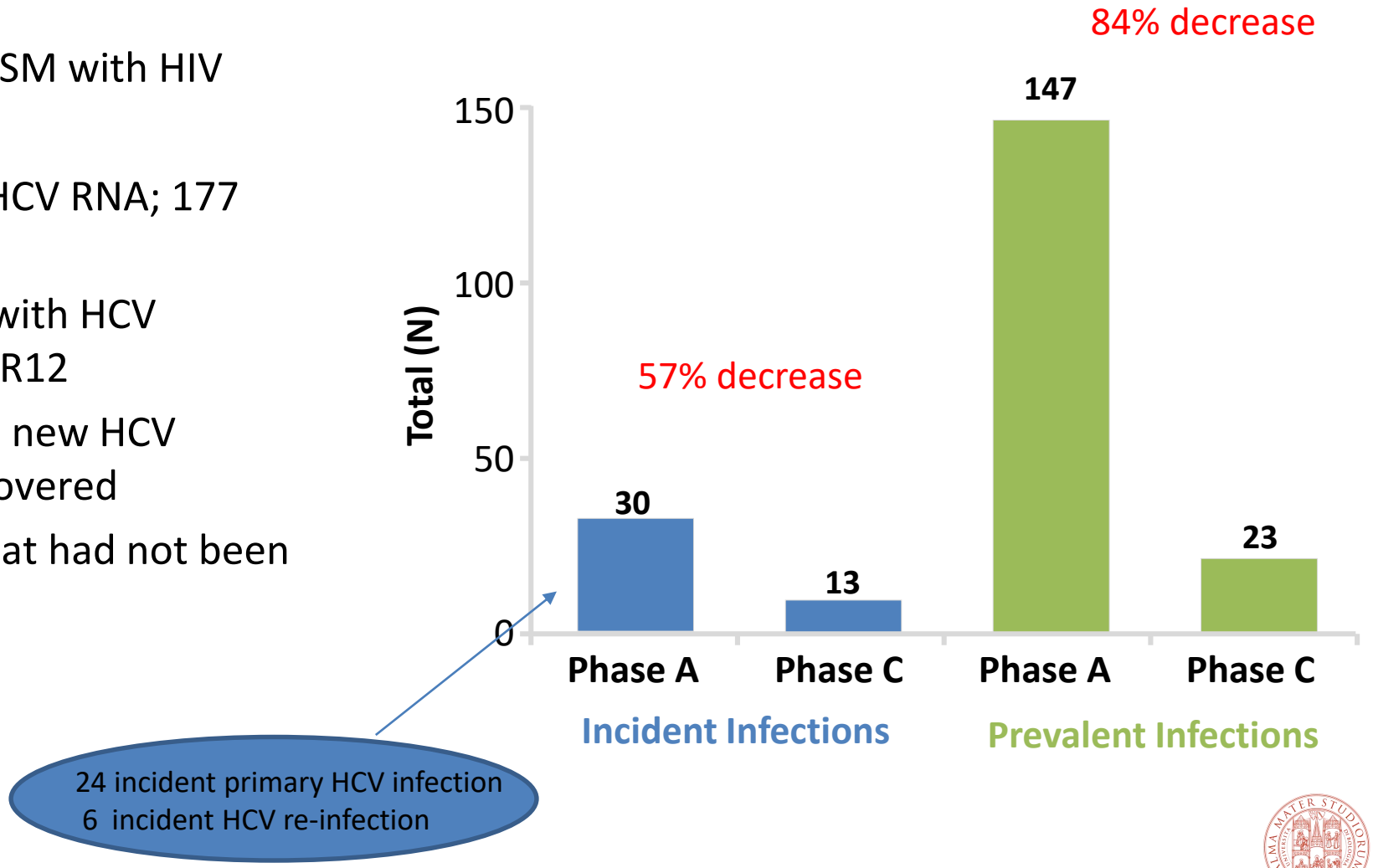


Swiss HCVree Trial: Treatment as Prevention in MSM With HIV Infection

- Systematic HCV screening of MSM with HIV

  (N = 4640)

  - **Phase A:** Test all MSM for HCV RNA; 177 with HCV infection (4.8%)
  - **Phase B:** 150/177 persons with HCV received DAAs; 99% had SVR12
  - **Phase C:** At rescreening, 13 new HCV infections (0.4%) were discovered
    - 23 chronic infections that had not been treated during phase A

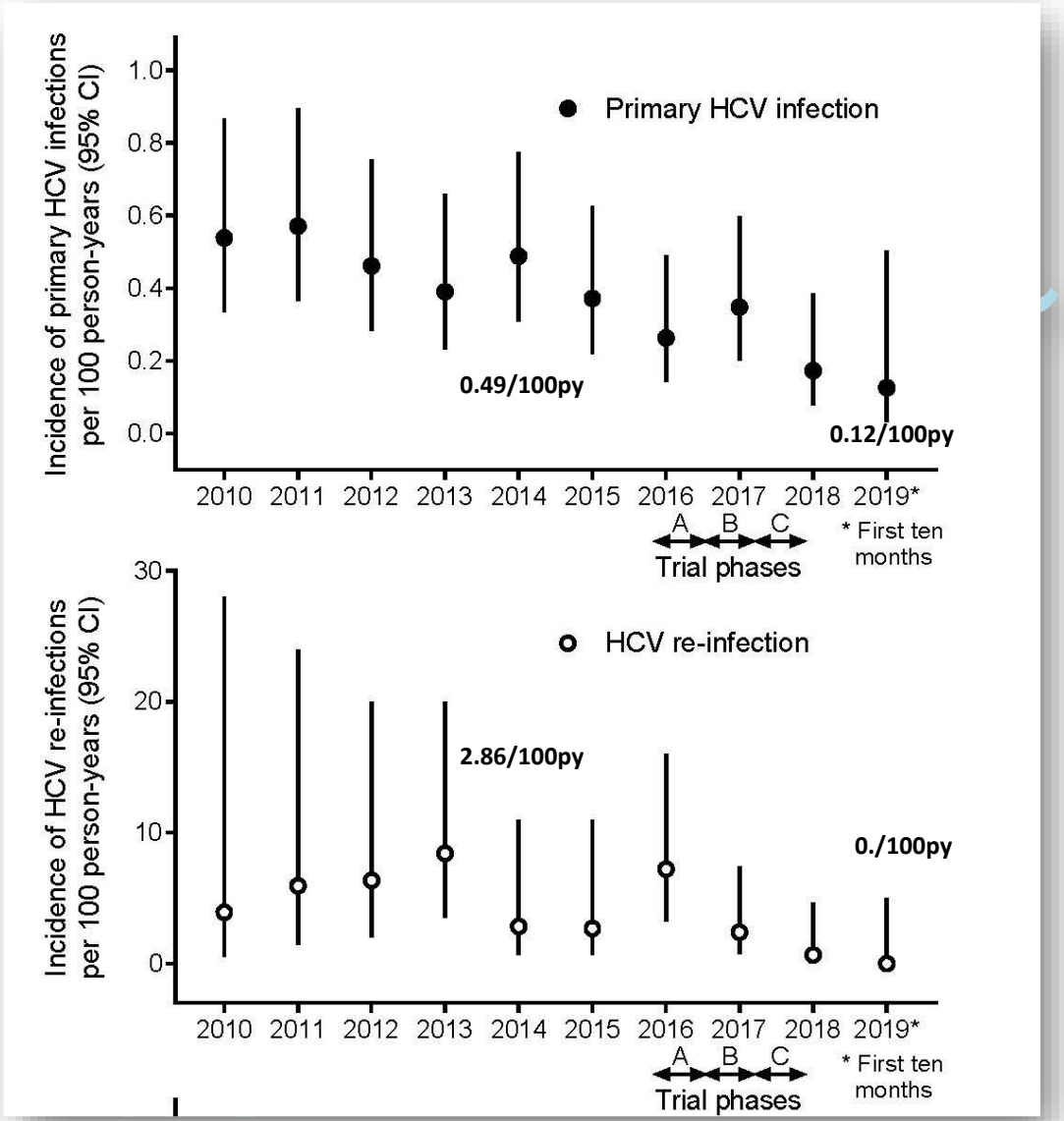


Braun. Clin Infect Dis. 2021 Oct 5;73:e2194.

Swiss HCVree Trial: Treatment as Prevention in MSM With HIV Infection

Mean follow-up 6.53y (IQR 3.75-9.3)

Incidence rate of Hepatitis C virus

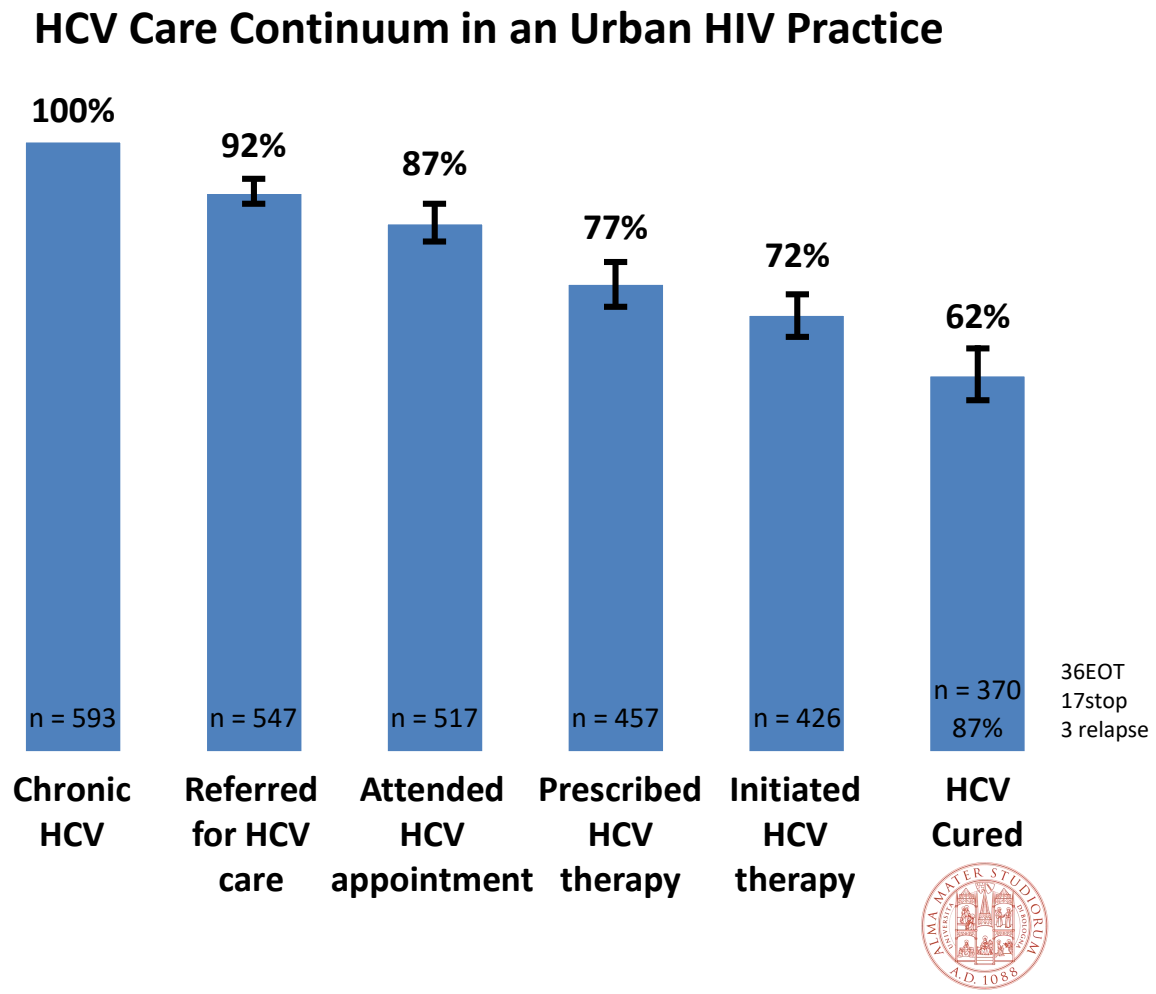


Braun. Clin Infect Dis. 2021 oct 5,;73:e2194.

HCV Elimination in PWH Requires Focus on HIV Care Continuum

- Referral to HCV care, treatment start, and cure status assessed in patients with HIV clinic visits in ≥2 consecutive yr in Baltimore, Maryland
  - HIV/HCV coinfection identified in 593 people
- Incomplete engagement in HIV care was negatively associated with HCV treatment

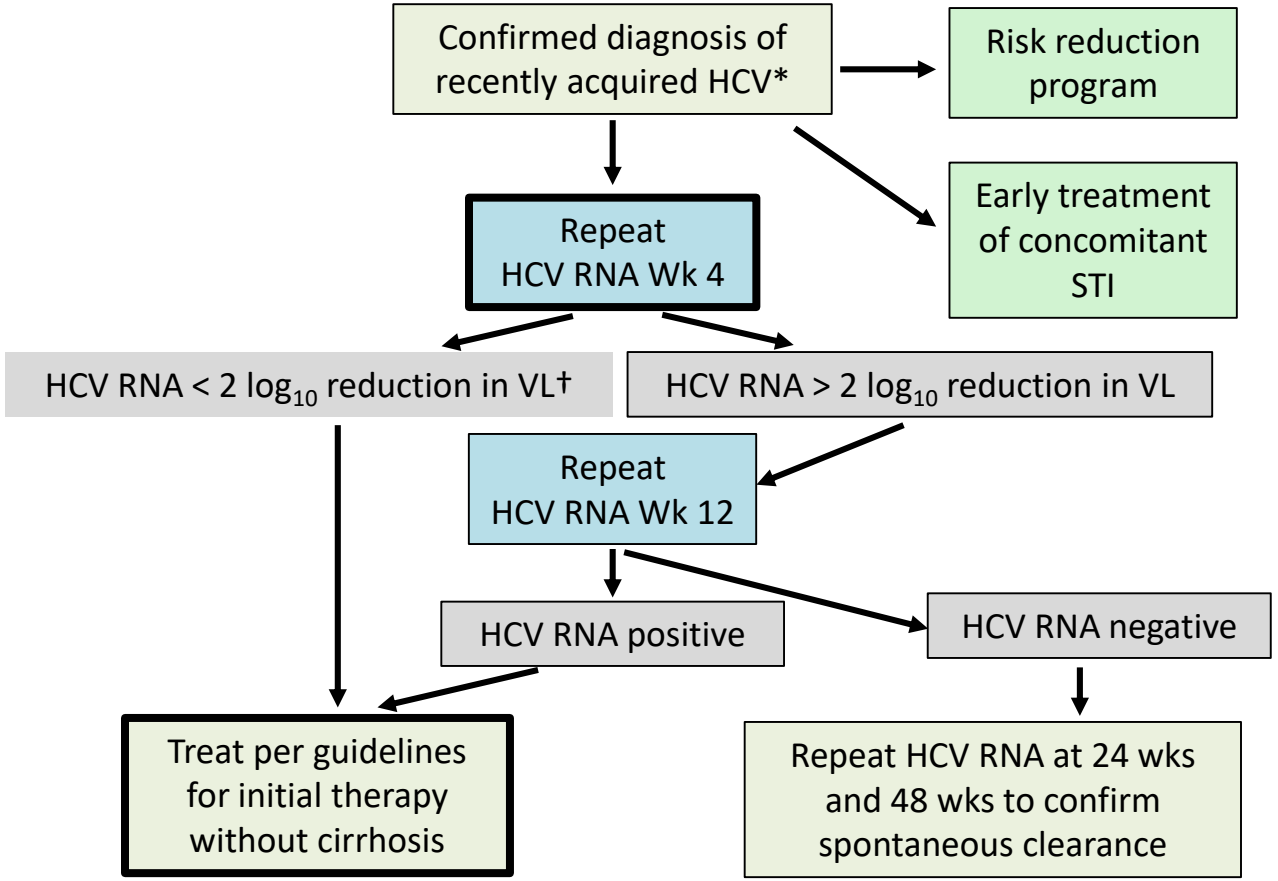
Factors Negatively Associated With HCV Tx Start	HR (95% CI)
Insured by state Medicaid	0.75 (0.61-0.92)
HIV-1 RNA >400 copies/mL	0.29 (0.18-0.49)
HIV clinic visits missed, % ▪ 1-24 ▪ 25-49 ▪ ≥50	 0.72 (0.54-0.97) 0.66 (0.49-0.89) 0.39 (0.25-0.60)



Falade-Nwulia. Open Forum Infect Dis. 2019;6:ofz426.

EACS Guidelines: Algorithm for Management of Recently Acquired HCV Infection in PWH

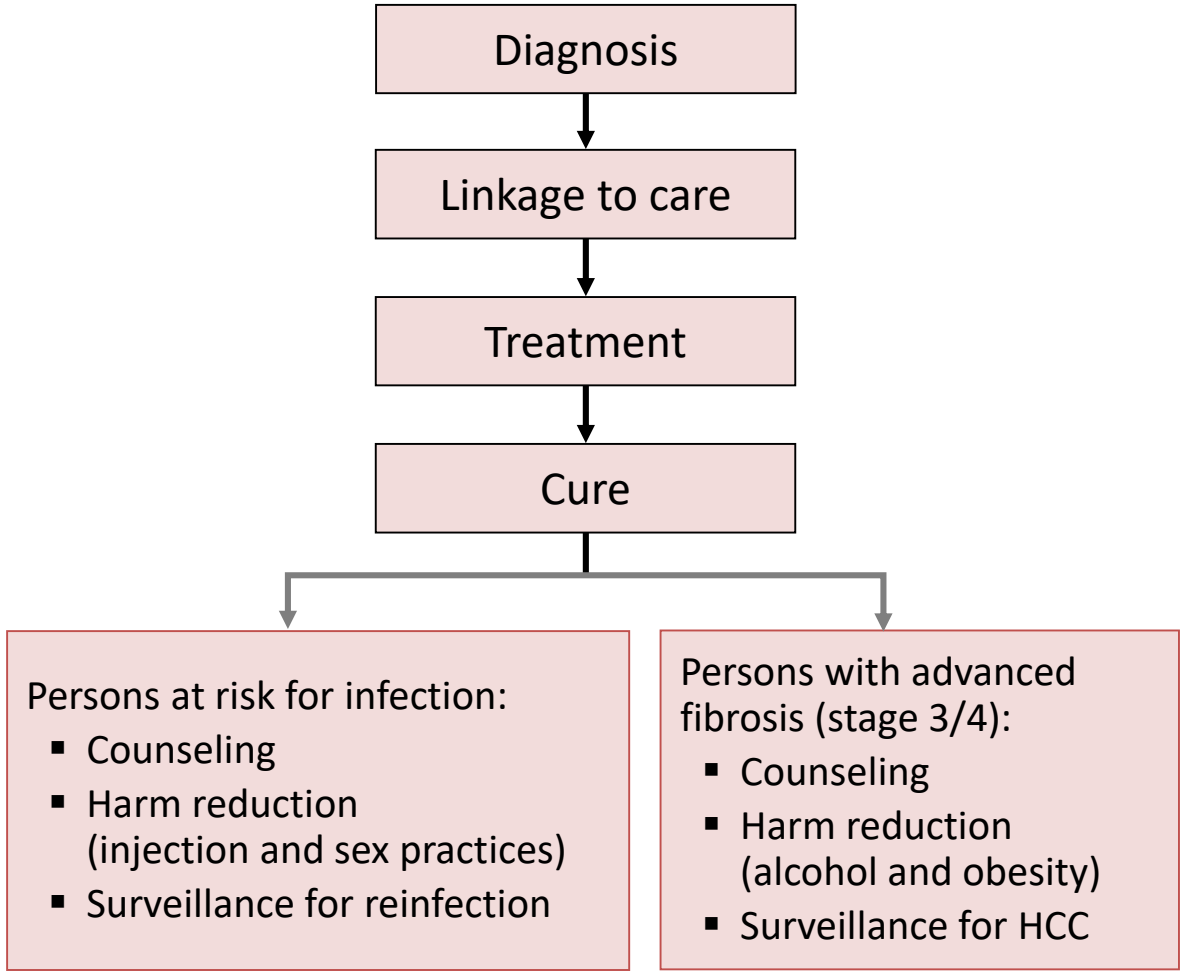
- If HCV RNA is reduced more than 100-fold 4 wks after diagnosis, defer treatment and repeat HCV RNA at Wk 12
- In cases of spontaneous clearance, repeat HCV RNA at Wk 24 and Wk 48 to confirm spontaneous clearance



*Where available initiate DAA-based treatment immediately in persons with risk of onward transmission.
†HCV-RNA < 2 $\log_{10}$ reduction at Wk 4 is considered as chronic HCV infection.

EACS Guidelines v10. 2021.

HCV Care Continues Past Achievement of SVR



Characteristic	Follow up After SVR
No advanced fibrosis (Metavir stage F0-F2), no or low risk of HCV reinfection	▪ Standard medical care, as in someone without HCV
Advanced fibrosis (Metavir stage F3 or F4)	▪ Ultrasound surveillance for HCC every 6 mos ± AFP
Moderate to high risk of HCV reinfection	▪ Harm reduction ▪ HCV RNA every 12 mos

Falade-Nwulia O, et al. J Hepatol. 2017;66:267-269. AASLD/IDSA HCV Guidelines. 2017.