

L'epatite C nei consumatori di sostanze: epidemiologia, importanza del trattamento con farmaci DAA (Direct-Acting Antivirals) in una prospettiva di eliminazione del virus

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Outline

5 3 SETTEMBRE 2020

Epatite C e consumatori
di sostanze

- Epidemiology
- Therapy
- Reinfection
- Barriers
- Future perspectives

Outline

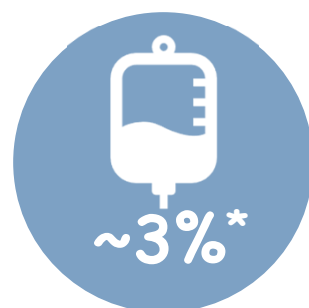
- **Epidemiology**
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Epidemiology

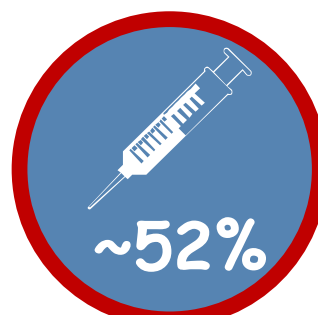
Global HCV Prevalence Among Patient Groups:



General population¹⁻³



Baby boomers^{1-2,4}



PWID or former PWID^{1-2,5}



Men who have sex with men^{1-2,6}



Prisoners^{1,2,7}



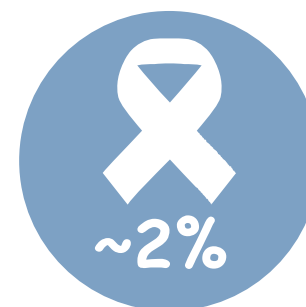
Hemodialysis patients^{1-2,8}



Migrant communities^{1-2,9}



Patients from geographically hard to reach areas^{1-2,10}



HIV/HCV co-infection^{1-2,11}

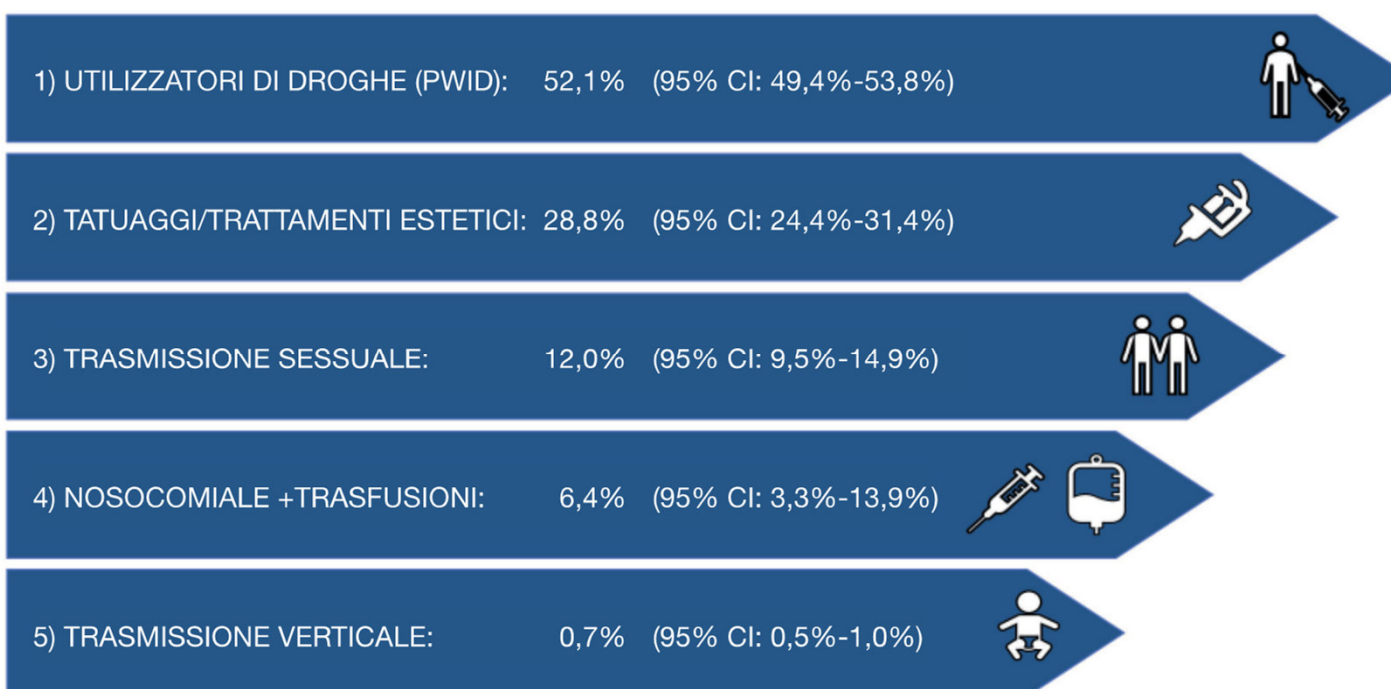


Adolescents^{1-2,12}

* Data from the US;
† data from Europe.
PWID, people who inject drugs.

1. Lazarus JV, et al. *Semin Liver Dis* 2018; 2. Lazarus JV, et al. *J Hepatol* 2017; 3. Polaris Observatory. *Lancet* 2017; 4. Winetsky D, et al. *Open Forum Infect Dis* 2019; 5. Degenhardt L, et al. *Lancet Glob Health* 2017; Midgard H, et al. *J Hepatol* 2016; 65; 7. Zampino R, et al. *World J Hepatol* 2015; 8. Etik DO, et al. *World J Hepatol* 2015; 9. Falla AM, et al. *BMC Infect Dis* 2018; 10. Shiha G, et al. *Lancet* 2018; 11. Platt L, et al. *Lancet Infect Dis* 2016; 12. Indolfi G, et al. *Lancet Gastroenterol Hepatol* 2019.

Estimated prevalence of undiagnosed hepatitis C virus infected individuals in Italy: a mathematic model to accurately measure HCV prevalence with a route of transmission granularity



Screening and treatment difficulties in hepatitis C virus-infected patients with substance use disorders or dual diagnoses, despite centralized management in an addiction and dual diagnosis center

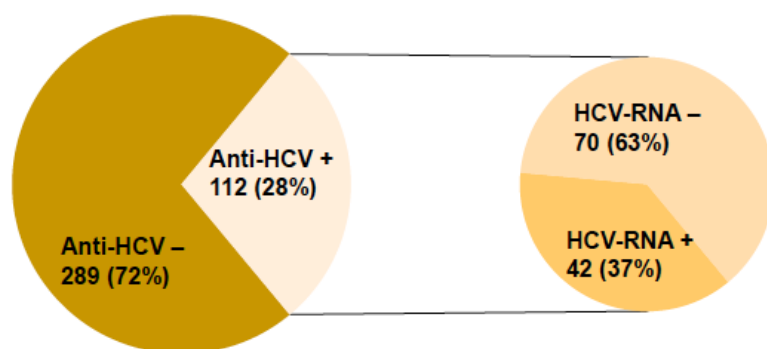
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Epatite C e consumatori di sostanze

Baseline characteristics of screened patients (N=401)

Males	301 (75%)
Mean age, years	45.4±11.5
Dual diagnosis	253 (63%)
Age of SUD onset	20.9 ± 9.4
Injected drug use	93 (23%)
Polyconsumption ≥3 SUD	195 (49%)

Prevalence of anti-HCV and HCV-RNA



Of the 70 anti-HCV positive patients with undetectable HCV-RNA, 34 (48.6%) had been previously treated for HCV infection. Eight (19%) of the 42 patients testing HCV-RNA positive did not know that they were infected.

Baseline characteristics of HCV-RNA positive patients (N=42)

ALT, IU/mL	75.5±63.9
Platelets, x10E9/L	224.5±71.5
FIB-4	1.7±1.1
FIB-4>3.25	5 (12%)
HCV Genotype:	
1a	16 (38%)
1b	7 (17%)
2	1 (2%)
3	13 (31%)
4	3 (7%)
Ungenotyping	2 (5%)
HCV-RNA log UI/l	5.9±1.1

Screening and treatment difficulties in hepatitis C virus-infected patients with substance use disorders or dual diagnoses, despite centralized management in an addiction and dual diagnosis center

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Epatite C e consumatori di sostanze

Factors related to the presence of anti-HCV and HCV-RNA

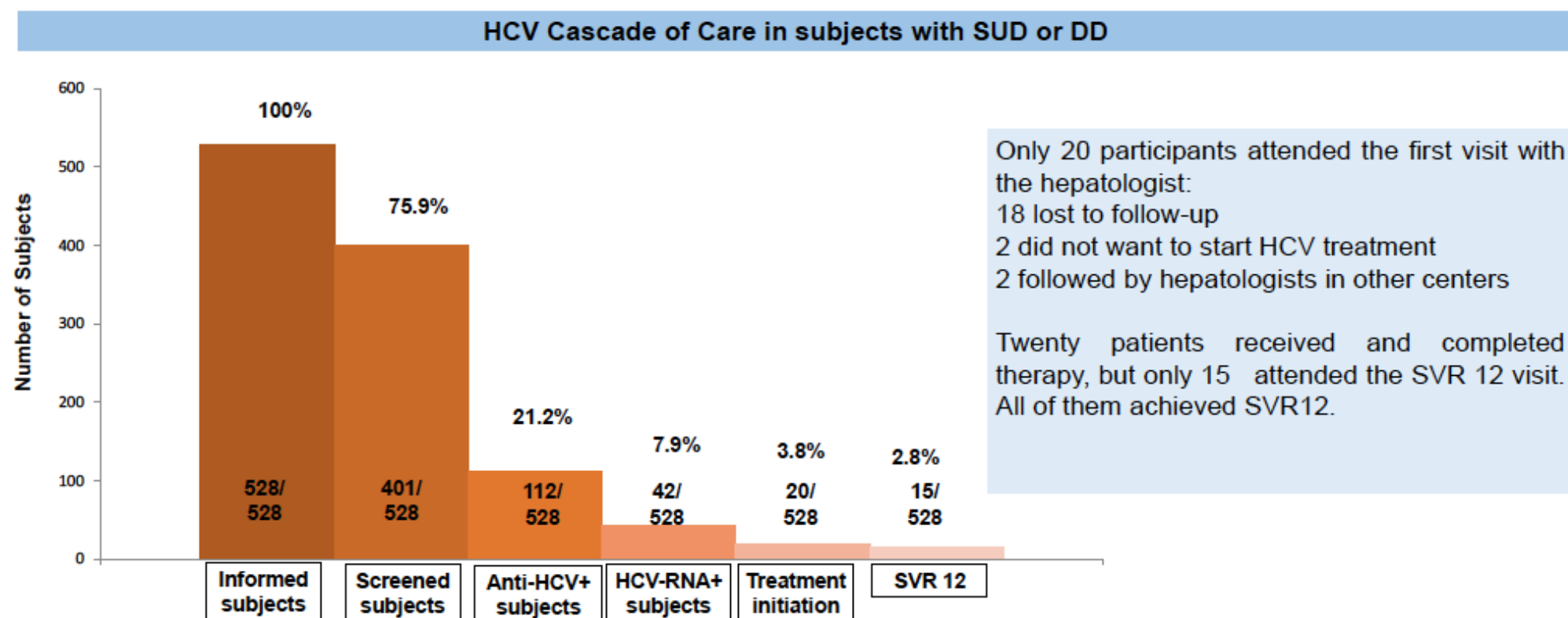
	Anti-HCV -ve N=289	Anti-HCV+ve N=112	p	HCV-RNA-ve N=70	HCV-RNA+ve N=42	p
Males %	72.7	81.3	0.075	88.6	69	0.010
Mean age, years	45.9±12.6	44.1±8.3	0.178	46.1±8.3	41.1±7.3	0.001
Dual diagnosis %	64.7	58.9	0.282	62.9	52.4	0.257
Criminal records %	26.6	72.3	<0.0001	74.3	69	0.549
Age of SUD onset	22.7±10.3	16.4±4.2	<0.0001	16.6±4.5	15.9±3.6	0.659
Previous medical treatment for SUD %	80.8	91.9	0.007	98.6	58.7	0.007
Injected drug use %	4.2	72.3	<0.0001	70	76.2	0.478
Polyconsumption ≥3 SUD %	33.7	88.3	<0.0001	90	85.4	0.464
Benzodiazepine use disorders %	22	54.1	<0.0001	58.6	46.3	0.212
Cocaine use disorder %	46.2	90.1	<0.0001	91.4	87.8	0.537

Marcos-Fosch. Et al presented during EASL 2020

Screening and treatment difficulties in hepatitis C virus-infected patients with substance use disorders or dual diagnoses, despite centralized management in an addiction and dual diagnosis center

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Epatite C e consumatori di sostanze

Factors related to access to treatment			
	Treatment N=20	No treatment N=22	p
Males %	78.9	60.9	0.178
Mean age, years	42.1±7.2	40.1±7.5	0.383
Dual diagnosis %	42.1	52.2	0.367
Low academic level	22.7	52.6	0.047
Unemployed %	73.7	95.7	0.056
Injected drug use %	78.9	73.9	0.496
Cocaine last month, gr/week	0.55±1.8	2.64±3.74	0.014

HCV-RNA positive patients who rejected DAA treatment reported use of a larger amount of cocaine during the last month and had lower academic level than those who started DAA treatment.

The presence of DD does not seem to increase the risk of HCV infection in comparison with SUD alone and does not hinder access to treatment. Centralized management with multidisciplinary teams is required for these patients, but it does not suffice to ensure linkage to care and should be accompanied by preventive efforts and identification of risk factors to achieve the WHO objective.

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Farmaci antivirali per HCV

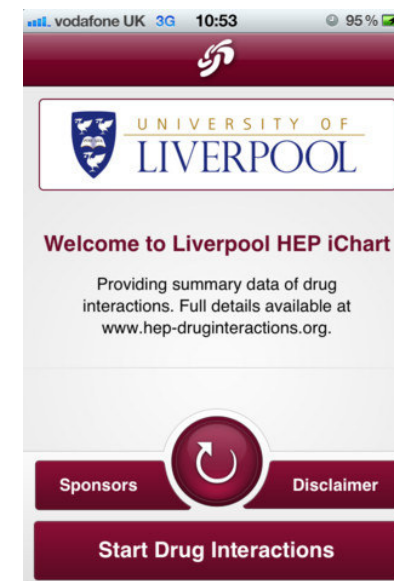
Genotipo	Regimi Pangenotipici			Regimi Genotipo dipendenti
	SOF/VEL	GLE/PIB	SOF/VEL/VOX*	GZR/EBR
Genotipo 1	Sì	Sì	Sì	Sì
Genotipo 2	Sì	Sì	Sì	No
Genotipo 3	Sì	Sì	Sì	No
Genotipo 4	Sì	Sì	Sì	Sì
Genotipo 5	Sì	Sì	Sì	No
Genotipo 6	Sì	Sì	Sì	No

OST and HCV Therapy: Drug-Drug Interactions

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Epatite C e consumatori di sostanze

- Do not coadminister
- Potential weak interaction
- No interaction expected



	EBR/GZR	GLE/PIB	SOF/VEL	SOF/VEL/VOX
Buprenorphine				
Methadone				
Naloxone				
Naltrexone				

RD and HCV Therapy: Drug-Drug Interactions

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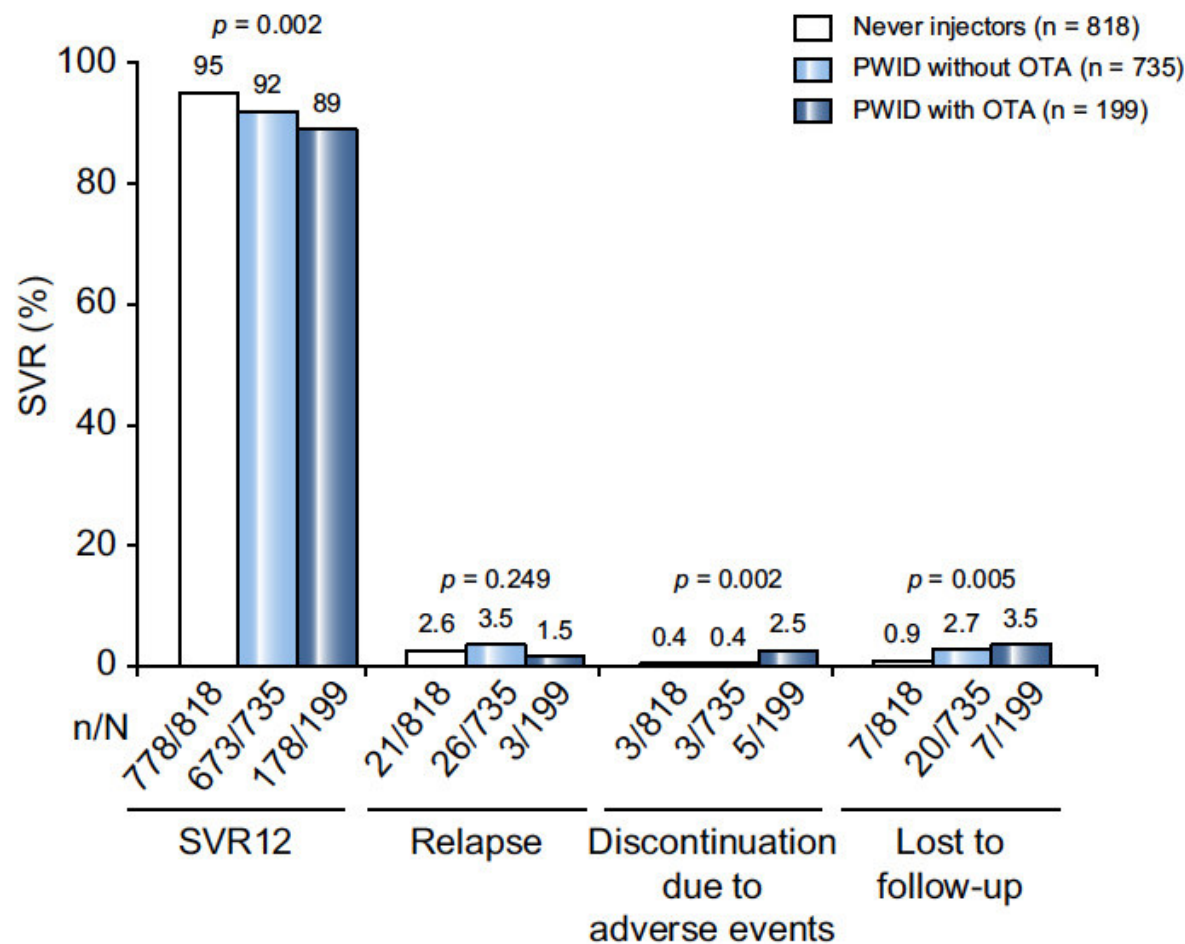
Epatite C e consumatori di sostanze

	GZR/ EBR	SOF/ VEL	GLE/PI B	SOF/VEL /VOX
Amfetamine	●	●	●	●
Cannabis	●	●	●	●
Cocaina	●	●	●	●
Diamorfina	●	●	●	●
Diazepam	●	●	●	●
Gamma-idrossibutirrato	●	●	●	●
Chetamine	●	●	●	●
MDMA (ecstasy)	●	●	●	●
Metamfetamine	●	●	●	●
Fenciclidina (PCP)	●	●	●	●
Temazepam	●	●	●	●

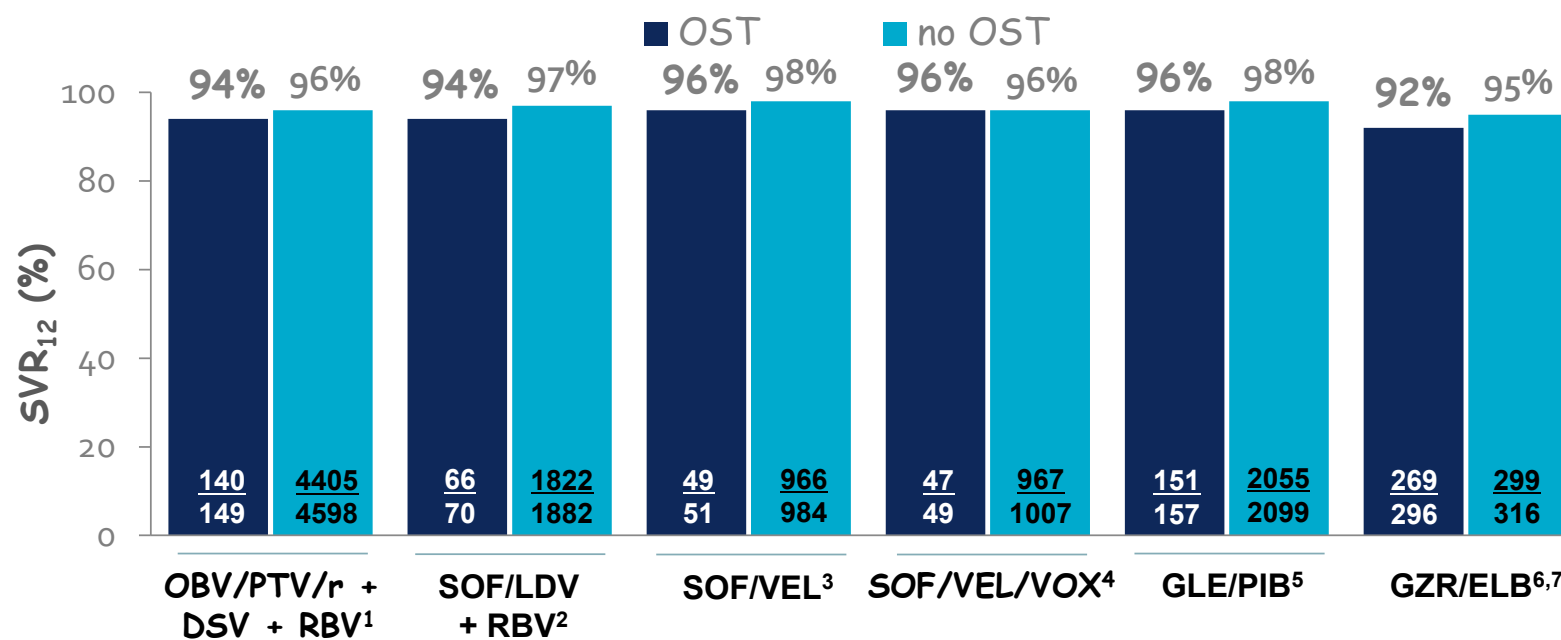
● = potenziali controindicazione

● = nessuna controindicazione

Response to direct-acting antiviral therapy among ongoing drug users and people receiving opioid substitution therapy

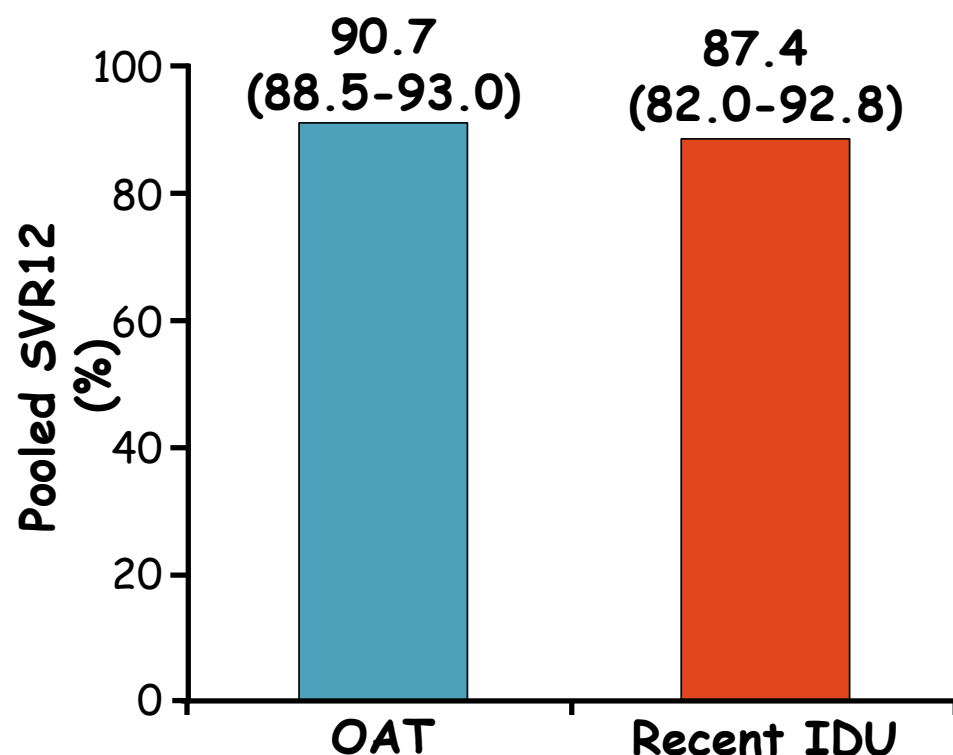


Hepatitis C Virus Infection in Persons Receiving Opioid Agonist Therapy



1) Grebely J, et al *ILC* 2017 (FRI-236). 2) Grebely *CID* 2016. 3) Grebely *CID* 2016. 4) Grebely J, *ILC* 2017 (FRI-235). 5) Grebely J, *INHSU* 2017. 6) Zeuzem, S. *Ann Intern Med* 2015. 7) Dore, GJ *Ann Intern Med* 2016. 8) Grebely J, Hajarizadeh B, and Dore GJ *Nat Rev in Gastroenterology & Hepatology* 2017.

HCV DAA Therapy Is Effective Among PWID, Even in the "Real-World"



Recent IDU

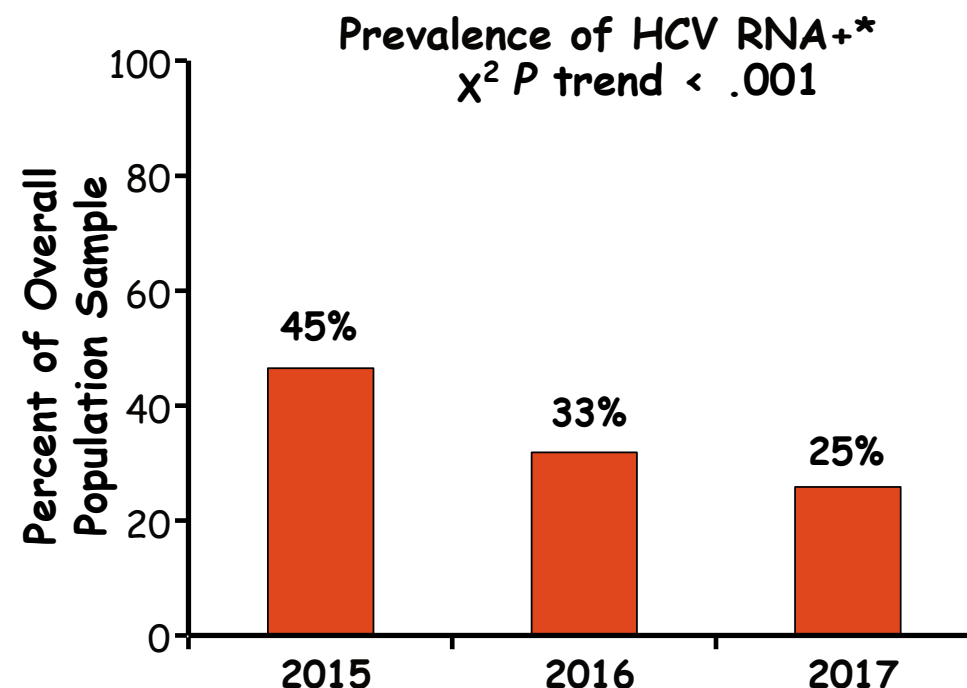
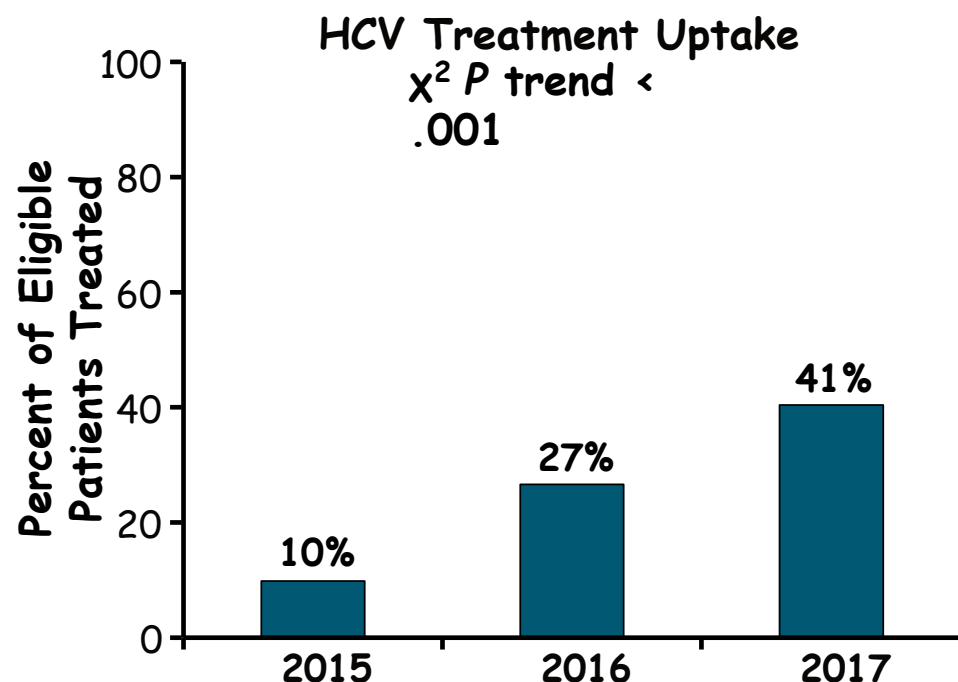
Study	SVR, % (95% CI)
Bielen 2017	81.3 (60.8-94.2)
Boglione 2017	93.9 (89.1-96.6)
Boscaillou 2017	80.4 (73.0-86.2)
Conway 2017	96.7 (88.8-99.1)
Grebely 2018	94.2 (87.9-97.3)
Mazhnaya 2017	64.0 (44.5-79.8)
Milne 2017	87.4 (80.2-92.2)
Valencia 2017	74.4 (59.8-85.1)
Overall	87.4 (82.0-92.8)

- In meta-regression, clinical trials significantly associated with higher SVR rates vs observational studies
 - aOR: 2.18 (95% CI: 1.27-3.75; $P = .006$)
- Difference due to loss to follow-up, not virologic failure

Hajarizadeh. Lancet Gastroenterol Hepatol. 2018;3:754

High HCV Treatment Uptake Among People With Ongoing IDU and Evidence of Treatment as Prevention

- Australian Annual Needle Syringe Program Survey (n = 2000-2500)
- Anti-HCV prevalence declined from 57% (2015) to 49% (2017; χ^2 P trend < .001)

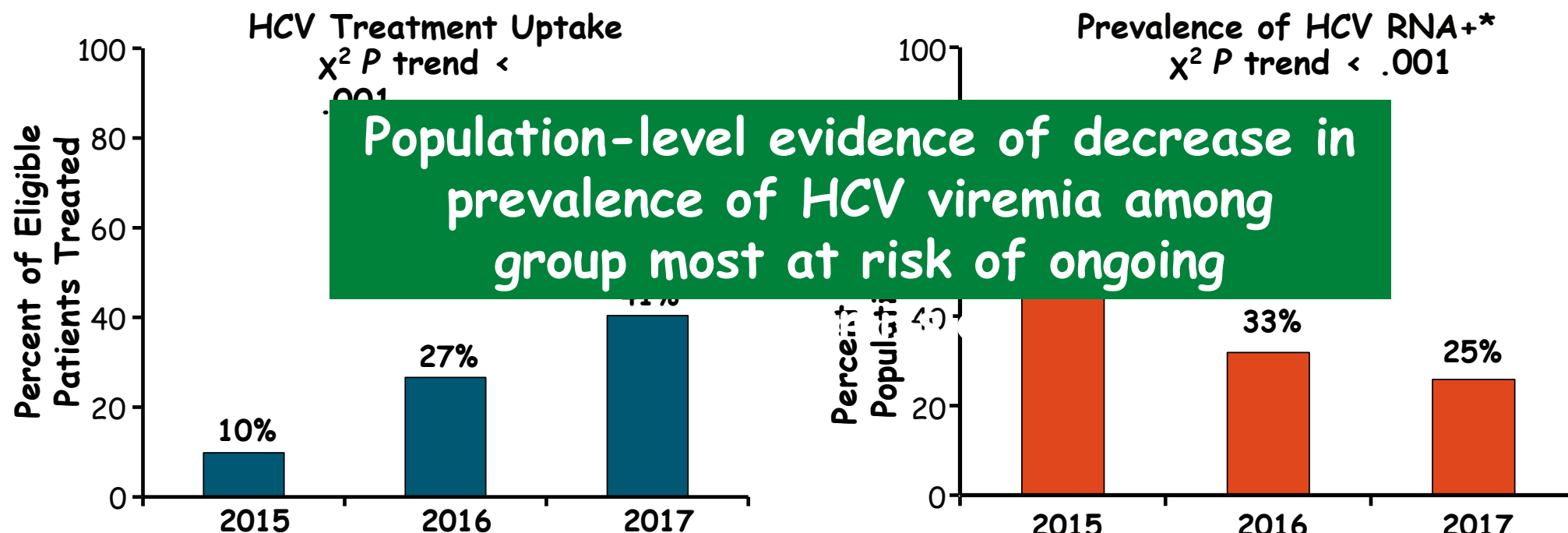


*Untreated + treated (VF) + treated (reinfection).

Iversen. J Hepatol. 2019;70:33.

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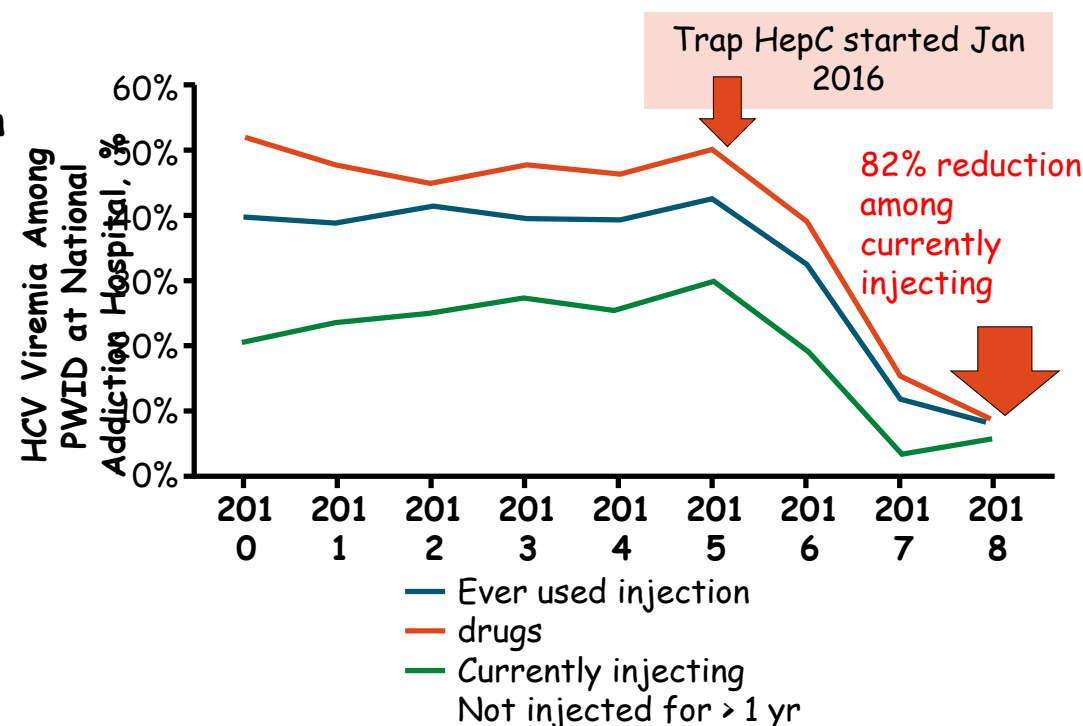
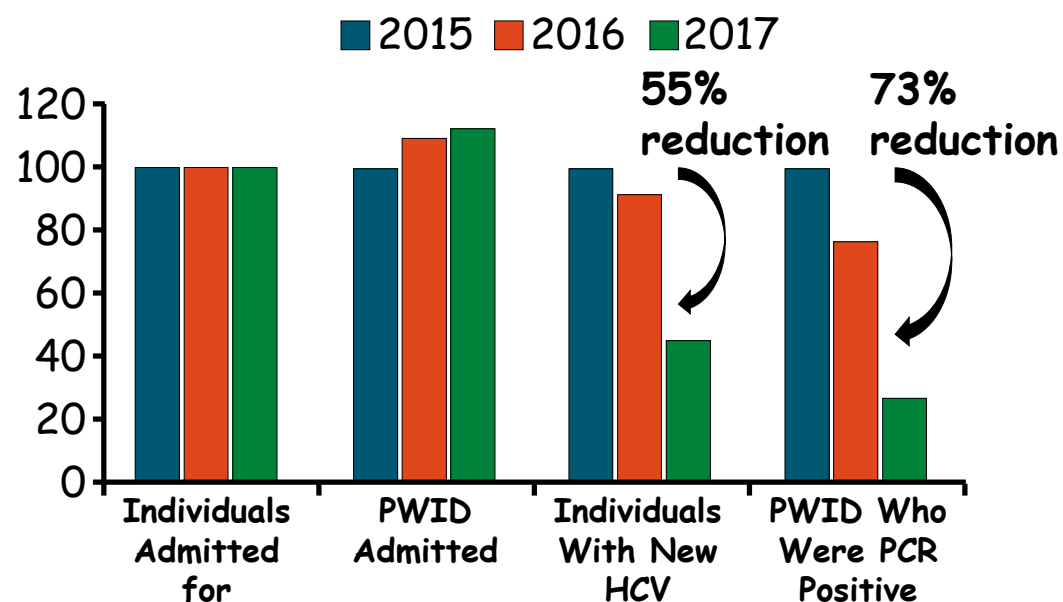
*Untreated + treated (VF) + treated (reinfection).

Iversen. J Hepatol. 2019;70:33.

Trap Hep C: HCV Treatment as Prevention Program in Iceland Reduced Incidence in 2 Yrs

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Epatite C e consumatori di sostanze



- Major scale up with reasonable cure rates
 - Overall SVR: 89%; SVR for patients who completed treatment: 95%
- Dramatic reduction in community viral load and HCV incidence

Follow-up post SVR

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Epatite C e consumatori
di sostanze

- SVR12 = viral eradication
- And after SVR?
 - Cirrhosis
 - Reinfection
 - Abnormal LFTs

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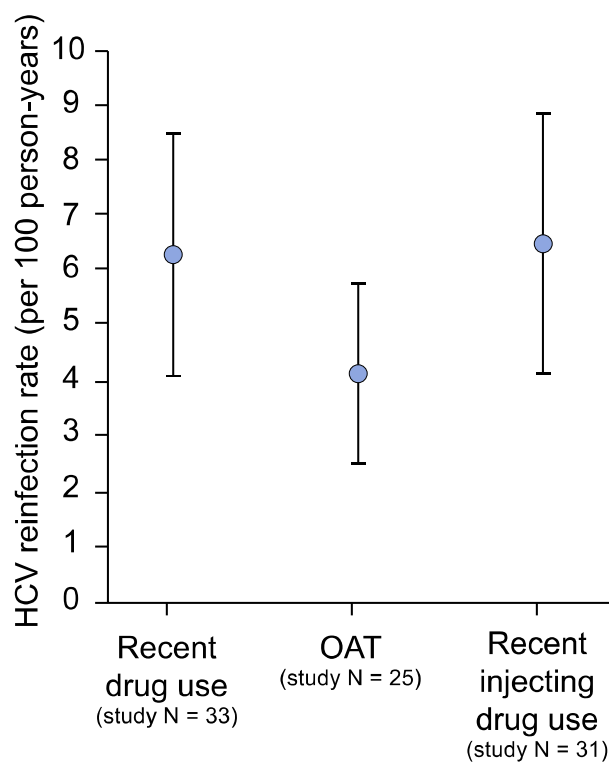
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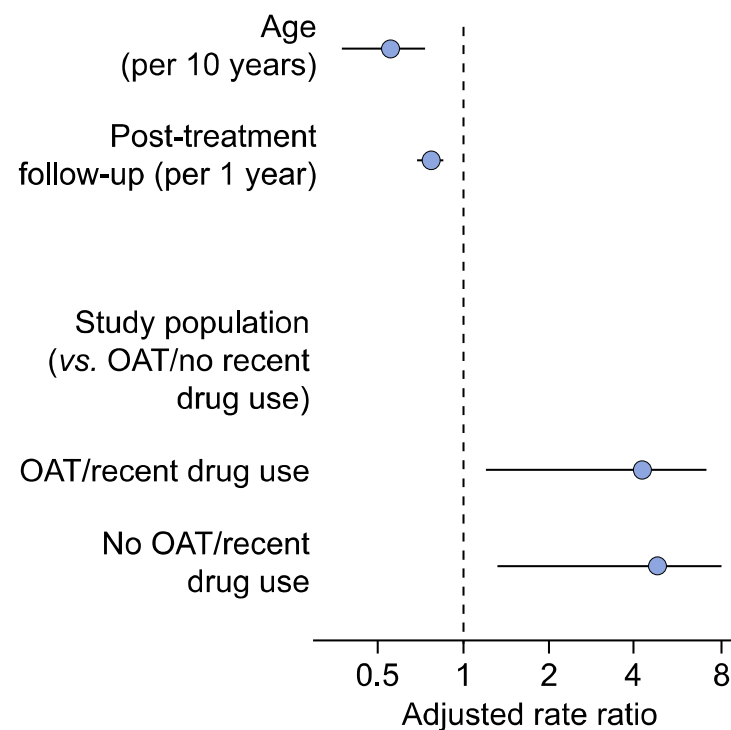
Reinfection

- Discuss methods of risks reduction
- Propose a new therapy without stigmatizing or discriminating

HCV Reinfection Rates After SVR Among PWIDs



HCV infection rate in various study populations, based on recent drug use & OAT status

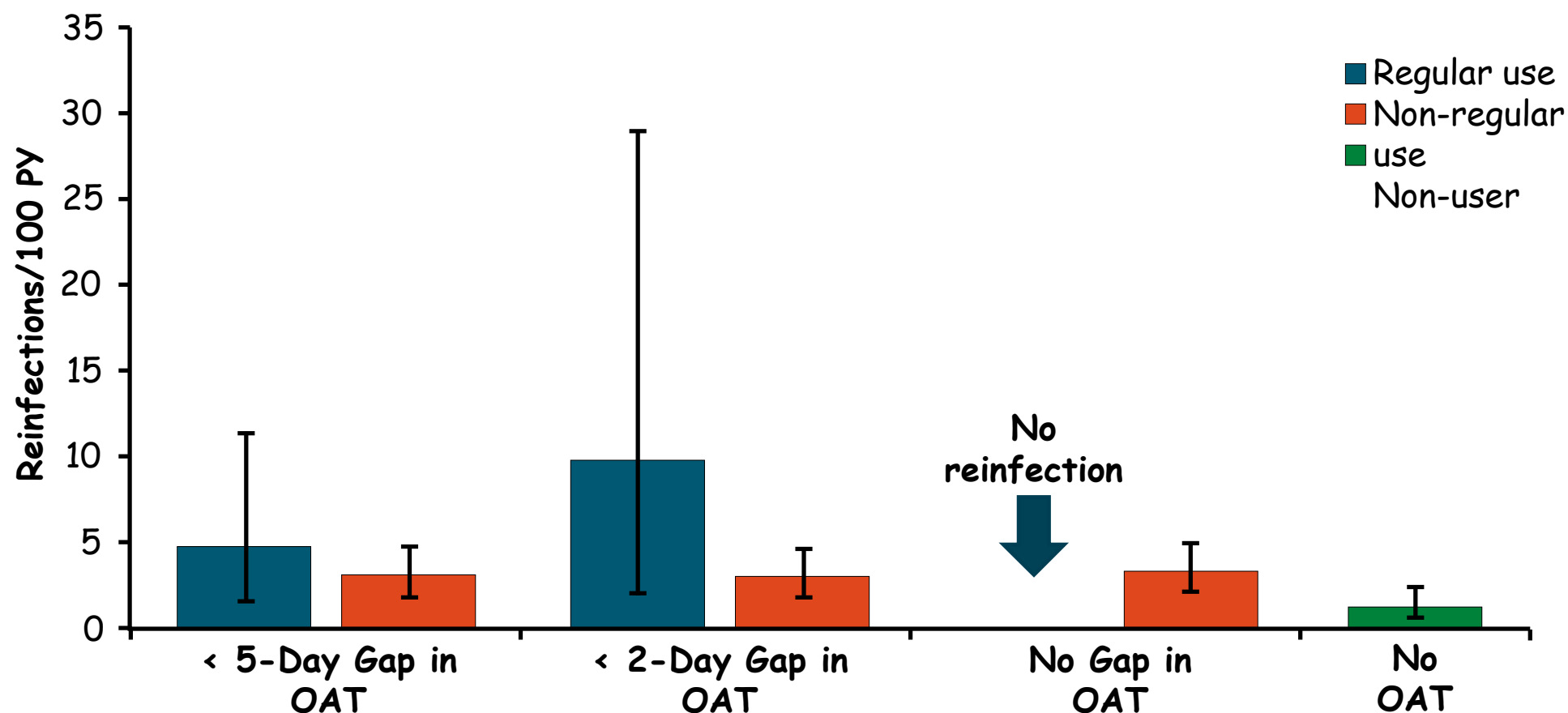


Study-level factors associated with HCV reinfection rate

BC Hepatitis Testers Cohort: HCV Reinfection Rate in PWID by OAT Interruption

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Epatite C e consumatori di sostanze

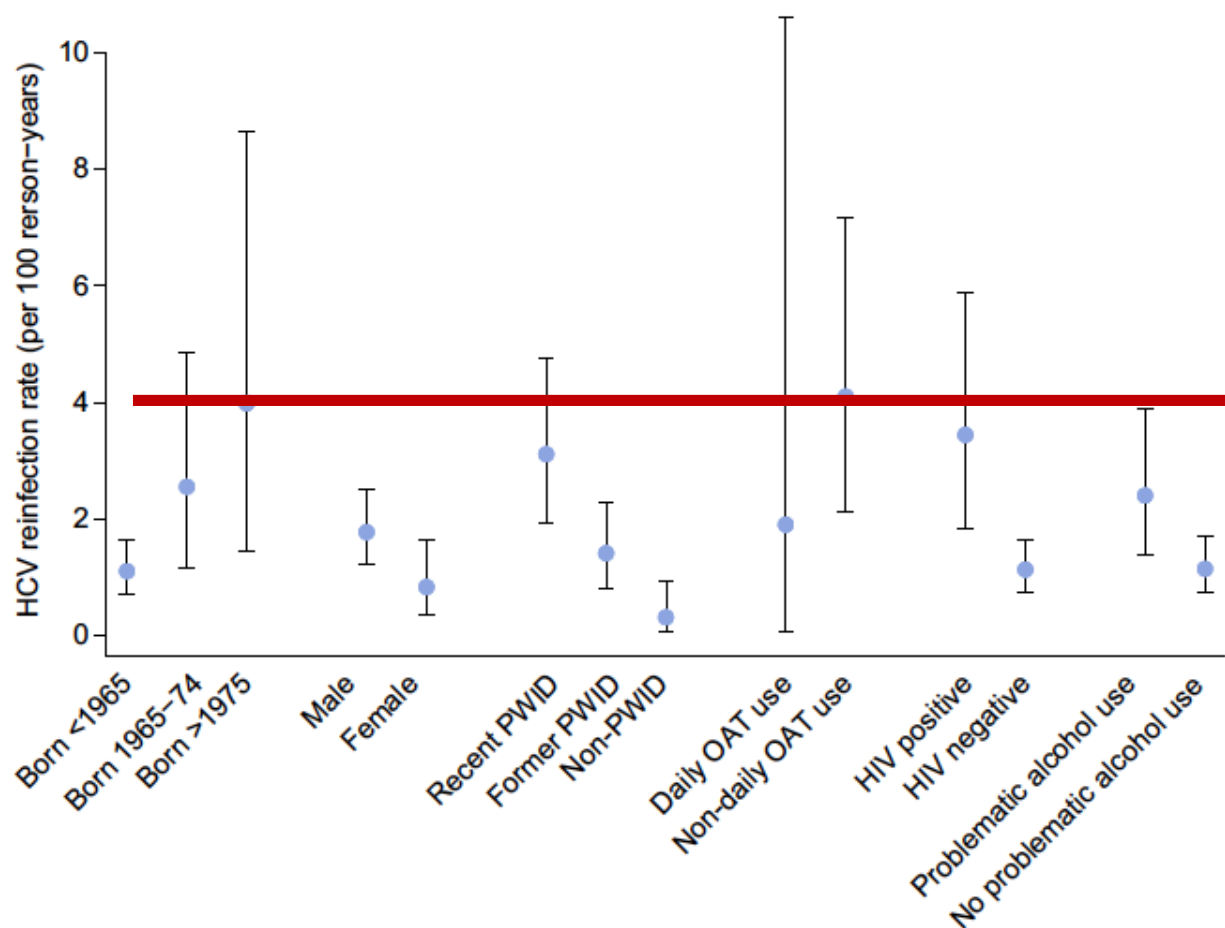


Janjua. AASLD 2019. Abstr 282.

Hepatitis C virus reinfection after successful treatment with direct-acting antiviral therapy in a large population-based cohort

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Epatite C e consumatori di sostanze

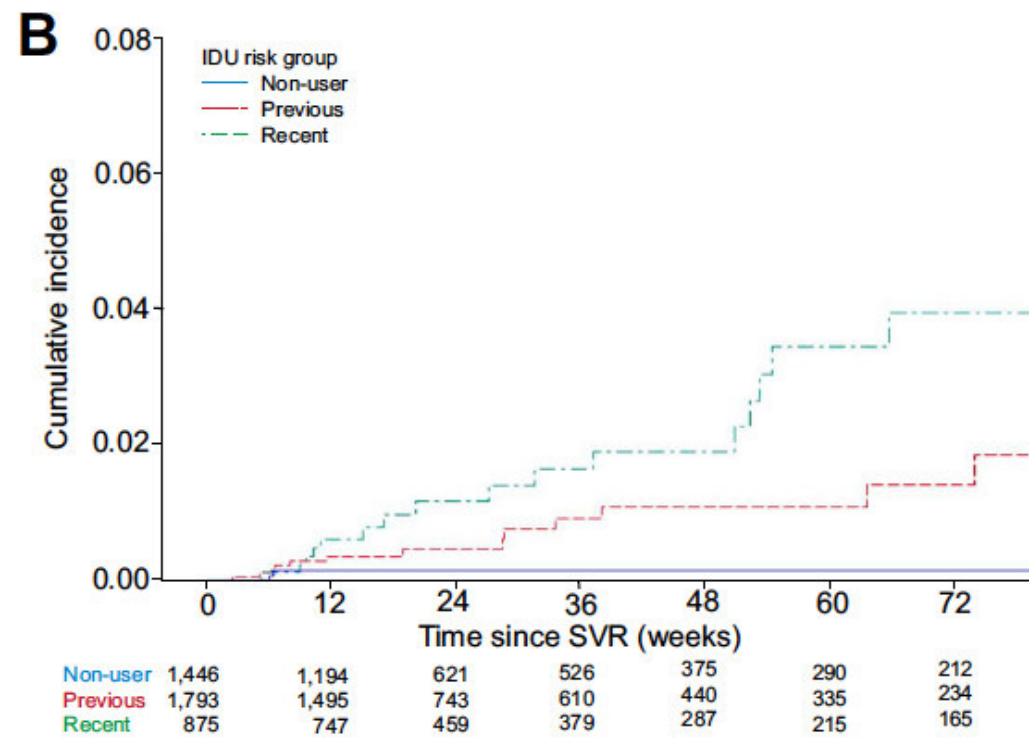
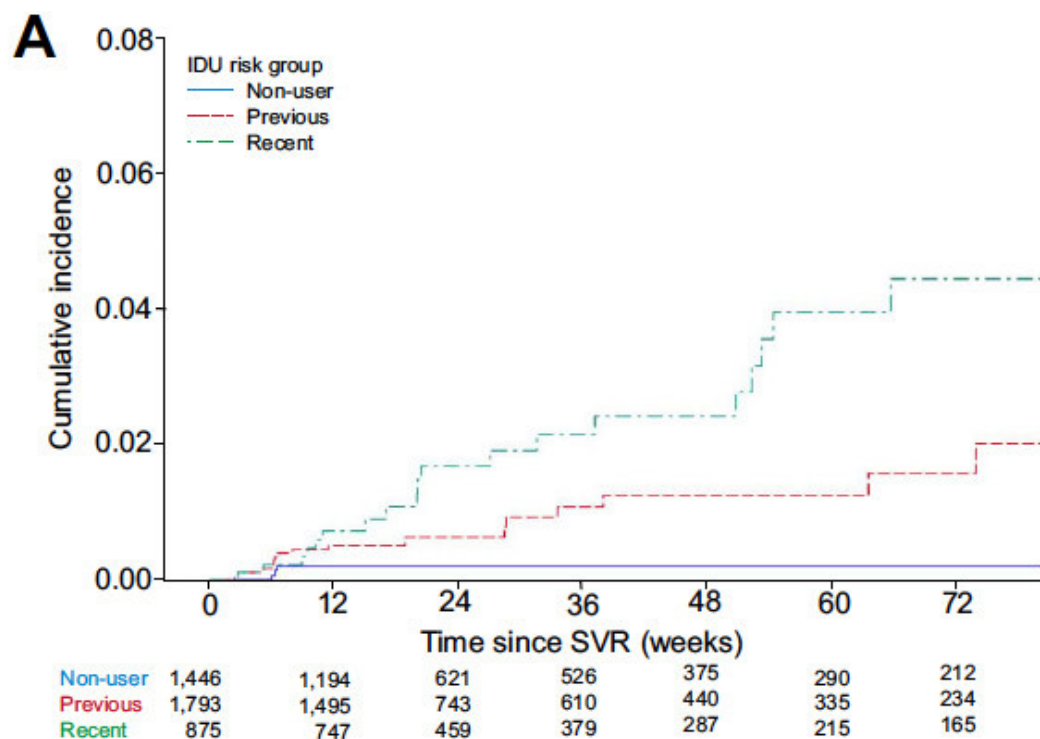


Rossi C. et al J Hep 2018

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Rossi C. et al J Hep 2018

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Passaggi essenziali nel trattamento dell'infezione da HCV nei PWID



... The Barriers Faced At Each Stage of the Patient Journey Can Vary by Patient Type

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Epatite C e consumatori di sostanze

At risk
or
infected



System
Entry^{1,2}

Screening
/Diagnosis^{1,2}



Link to
Care^{1,2}



On
Treatment^{1,2}



e.g. Limited connection with healthcare system for PWID²

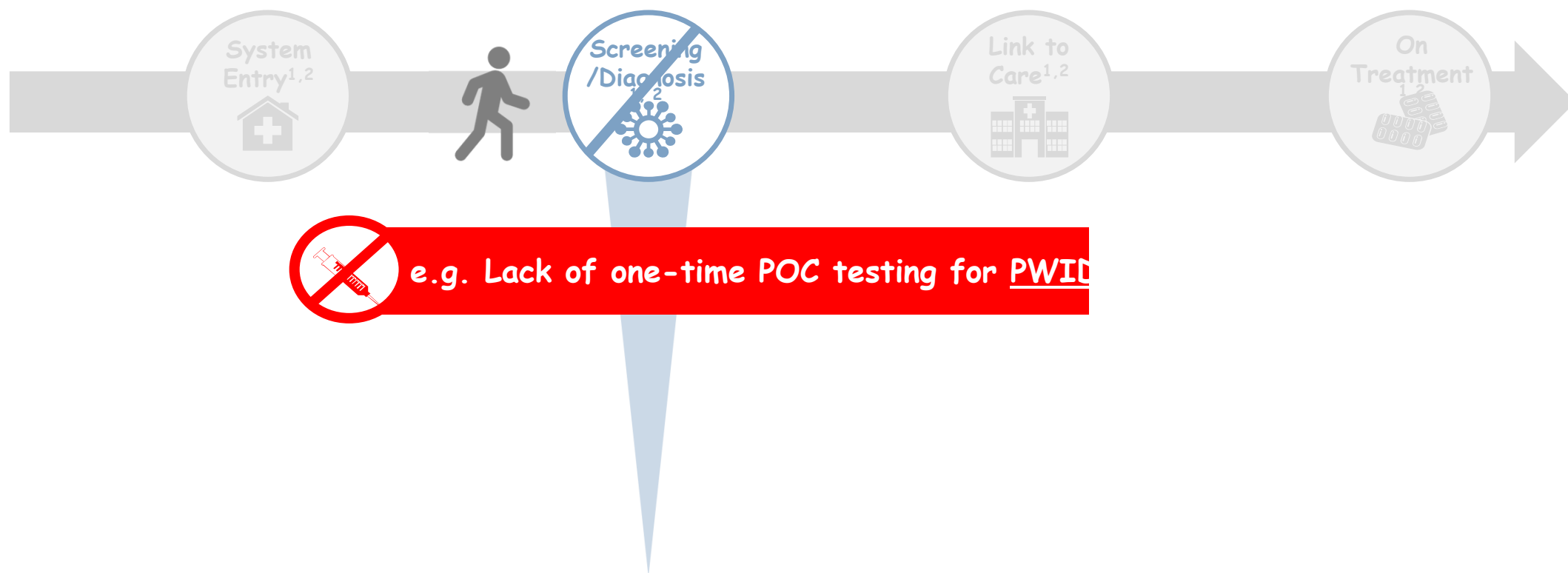
1. WHO Guidelines on Hepatitis B and C Testing, 2017. Available at: <https://www.who.int/hepatitis/publications/guidelines-hepatitis-c-b-testing/en/> (accessed Nov 2019);
2. Grebely J, et al. *J Int AIDS Soc*.

PWID, people who inject drugs.

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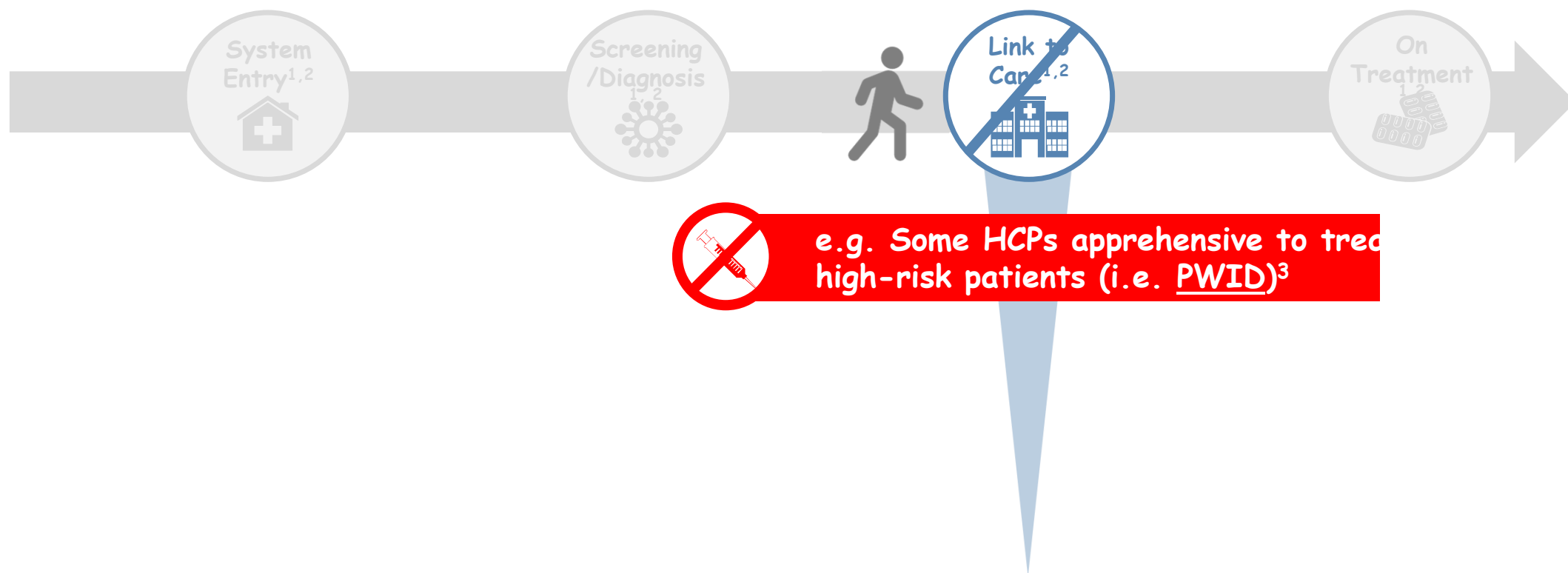
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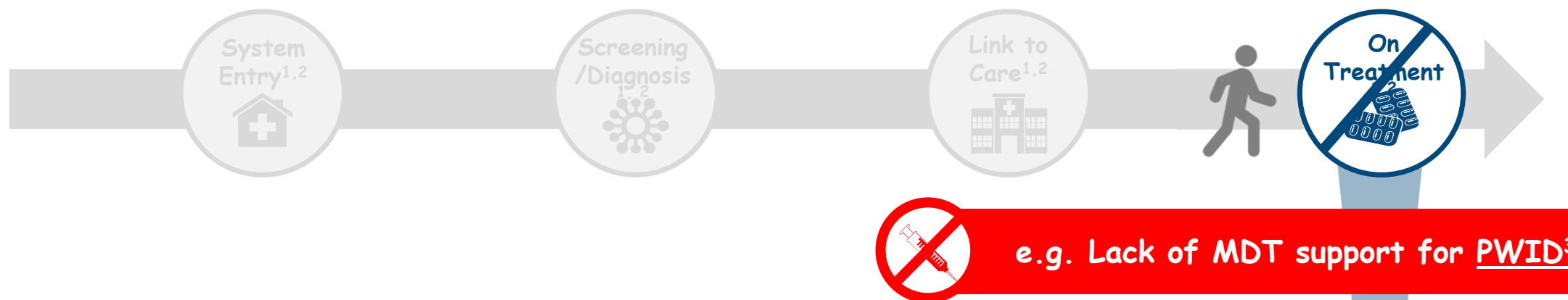
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Epatite C e consumatori di sostanze



MDT, multidisciplinary team; PWID, people who inject drugs;
SVR, sustained viral response; SVR12, defined as an undetectable
HCV RNA viral load 12 weeks after treatment completion.

1. WHO Guidelines on Hepatitis B and C Testing, 2017. Available at:
<https://www.who.int/hepatitis/publications/guidelines-hepatitis-c-b-testing/en/> (accessed Nov 2019);

2. WHO Global Hepatitis Report, 2017. Available at: <https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/> (accessed Nov 2019);

3. Grebely J, et al. *J Int AIDS Soc* 2017;

4. Aspinall EJ, et al. *J Viral Hepat* 2016; 5. Franco RA, et al. *Hepatoma Res*.

Le barriere nella presa in carico e trattamento dei PWID



Correlate al Paziente

- Mancata o scarsa conoscenza sulla malattia e delle terapie
- Disturbi comportamentali
- Difficoltà sociali ed economiche
- Relazione negativa con i medici e l'équipe
- Stigma
- Scarsa motivazione ad essere trattato



Correlate al Medico

- Scarsa conoscenza sulle nuove terapie
- Preoccupazione sull'aderenza al trattamento e sulle reinfezioni
- Mancanza di coordinamento tra specialisti
- Mancanza di comunicazione tra specialisti

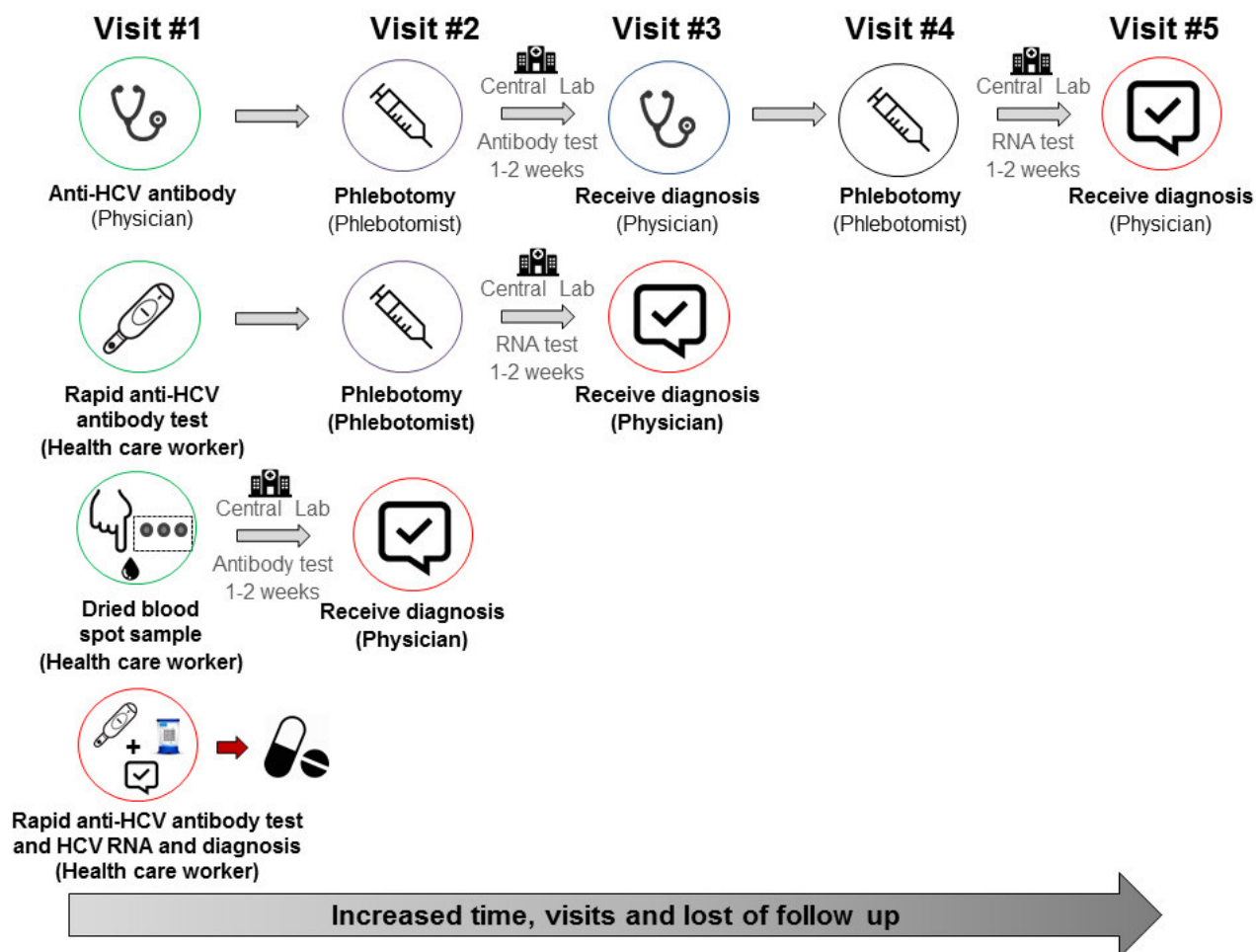


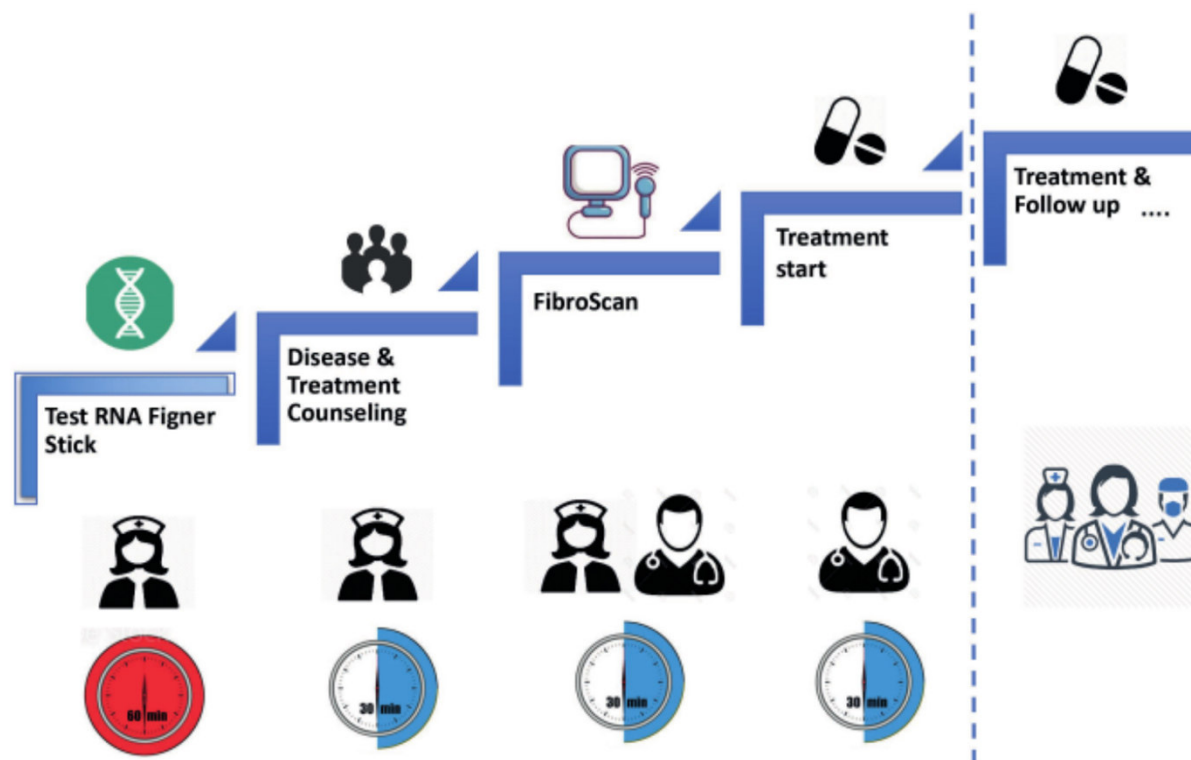
Correlate alla Struttura

- Mancanza di risorse
- Mancanza di collaborazione tra specialisti
- Distanza tra i centri specialistici
- Mancanza di punti prelievi tra i Ser.D.
- Mancanza di procedure e linee guida

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Conclusions

- Higher prevalence of HCV positive
- Available therapy for all PWID
- Monitor risk of reinfection
- Overcome barriers