Hepatitis C Treatment in People Who Inject Drugs (PWID)

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Empire Liver FOUNDATION

Training Development and Funding

This training is funded by the NYC City Council

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Overarching Learning Objectives

By the end of this presentation, participants will be able to:

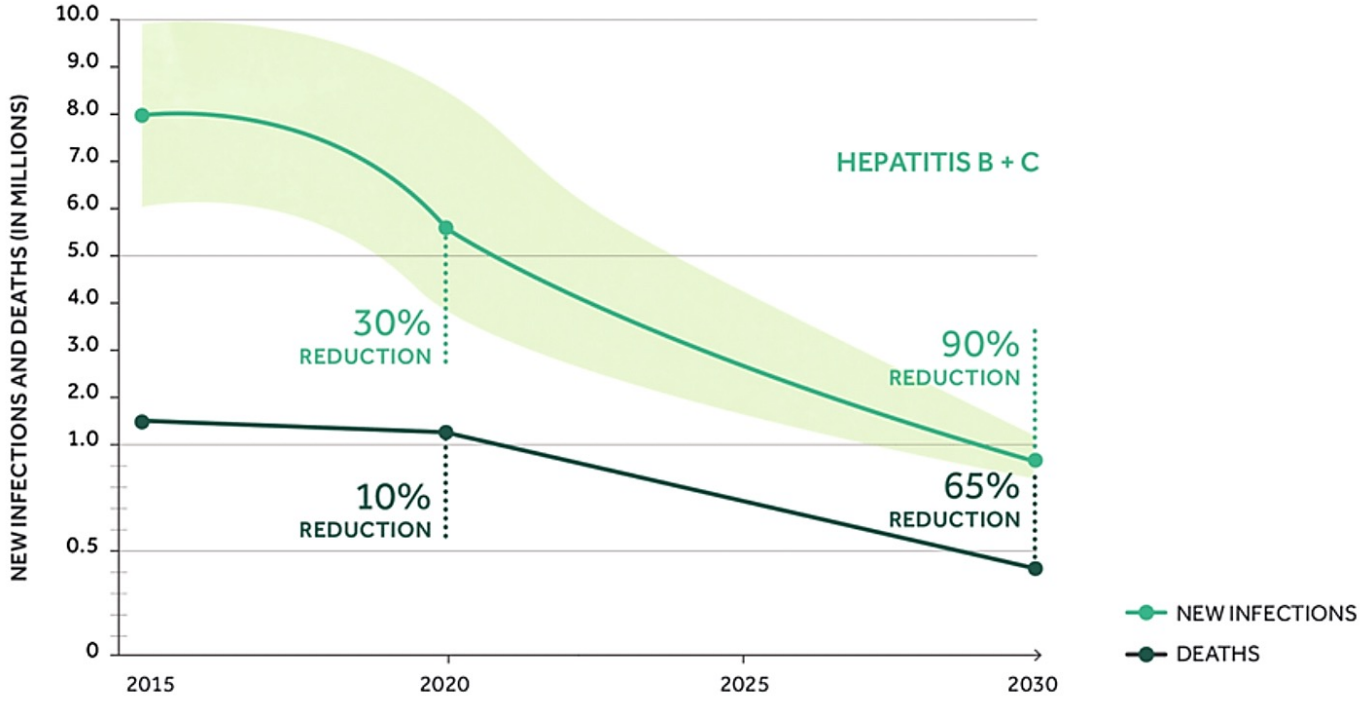
1. Describe the importance of interprofessional collaboration in effectively meeting the healthcare, educational, and psychosocial needs of patients living with hepatitis B or C infection.
2. Describe the epidemiology and natural history of hepatitis B and hepatitis C infection.
3. Use updated guidelines to identify patients at risk for hepatitis B and/or hepatitis C infection and provide screening according to these guidelines.
4. Select appropriate antiviral treatments for people living with hepatitis B or hepatitis C, including special populations such as people with advanced liver disease or HIV co-infection.
5. Explain the efficacy and safety of current and emerging therapies for hepatitis B and C, including use in special populations such as people who use drugs or alcohol or have substance use disorders.
6. Illustrate how to counsel patients diagnosed with hepatitis B or C regarding risks and benefits of therapies and involve them in shared treatment decisions.

Objectives

- Review the evidence on the effectiveness of treating chronic hepatitis C (HCV) infections in people who inject drugs (PWID) and the impact on health
- Discuss the role and responsibilities of the primary care and HCV providers in successfully curing HCV in PWID
- Review prevention and harm reduction strategies while on HCV treatment
- Discuss the current algorithm for simplified treatment of HCV

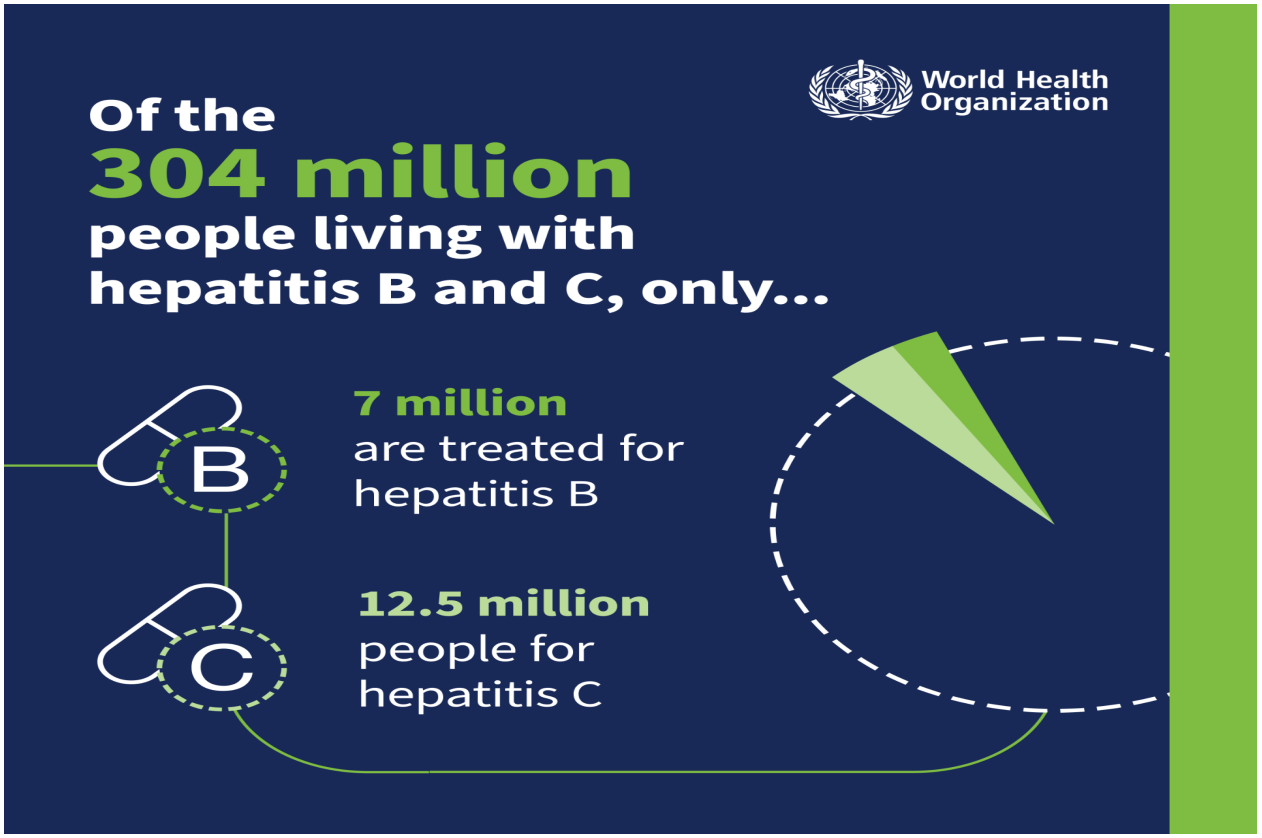
WHO HCV Elimination Goals

Targets for reducing new cases of and deaths from chronic viral hepatitis B and C



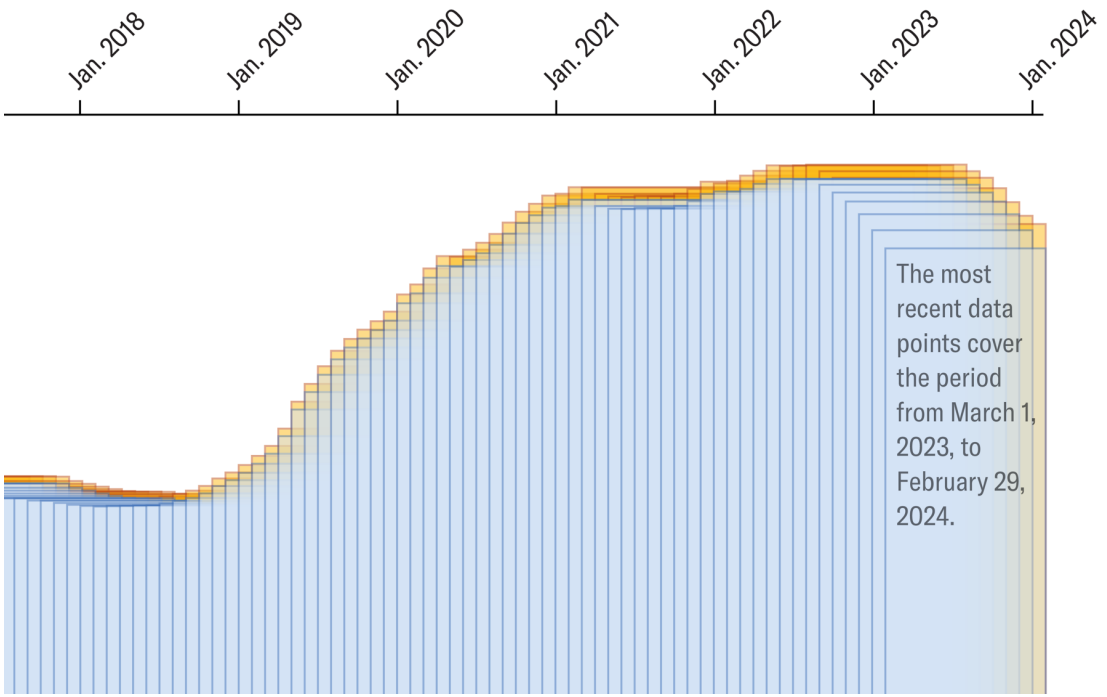
https://www.researchgate.net/figure/World-Health-Organization-2020-and-2030-targets-for-the-reduction-of-chronic-viral_fig3_327523536

WHO Statistics on Hepatitis Treatment Worldwide



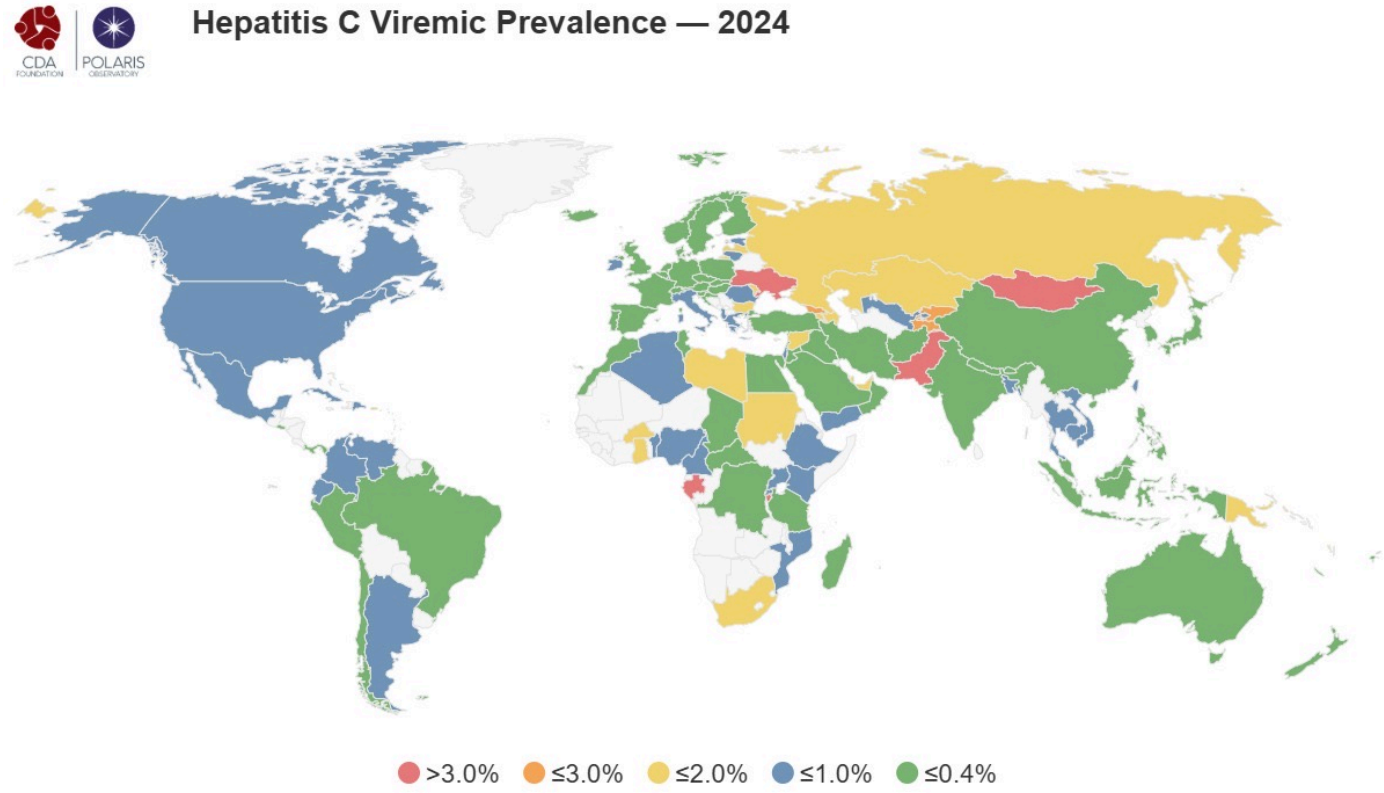
who_global-hepatitis-sm_05_low.png (1920×1920)

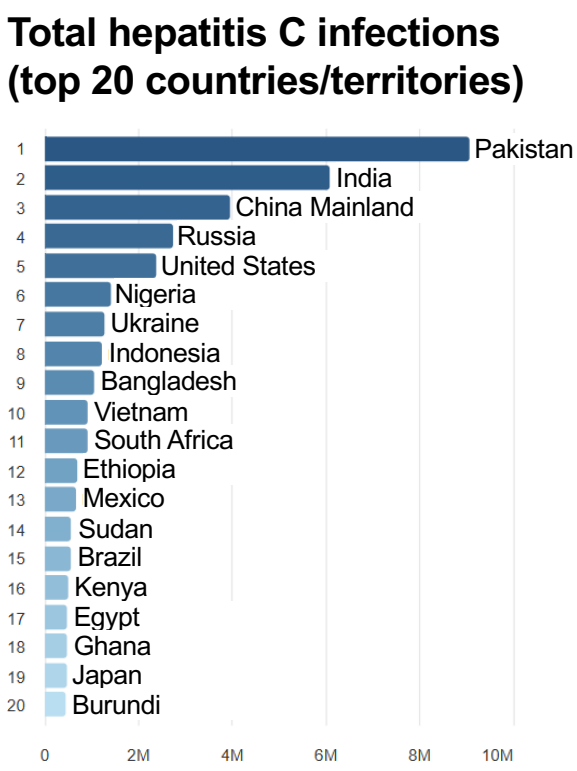
Overdoses in the US Are Declining to Pre-COVID-19 Levels, but Disparities Persist



Overdose Deaths Are Finally Starting to Decline. Here's Why. | Scientific American

Hepatitis C Worldwide Viremic Prevalence, 2024

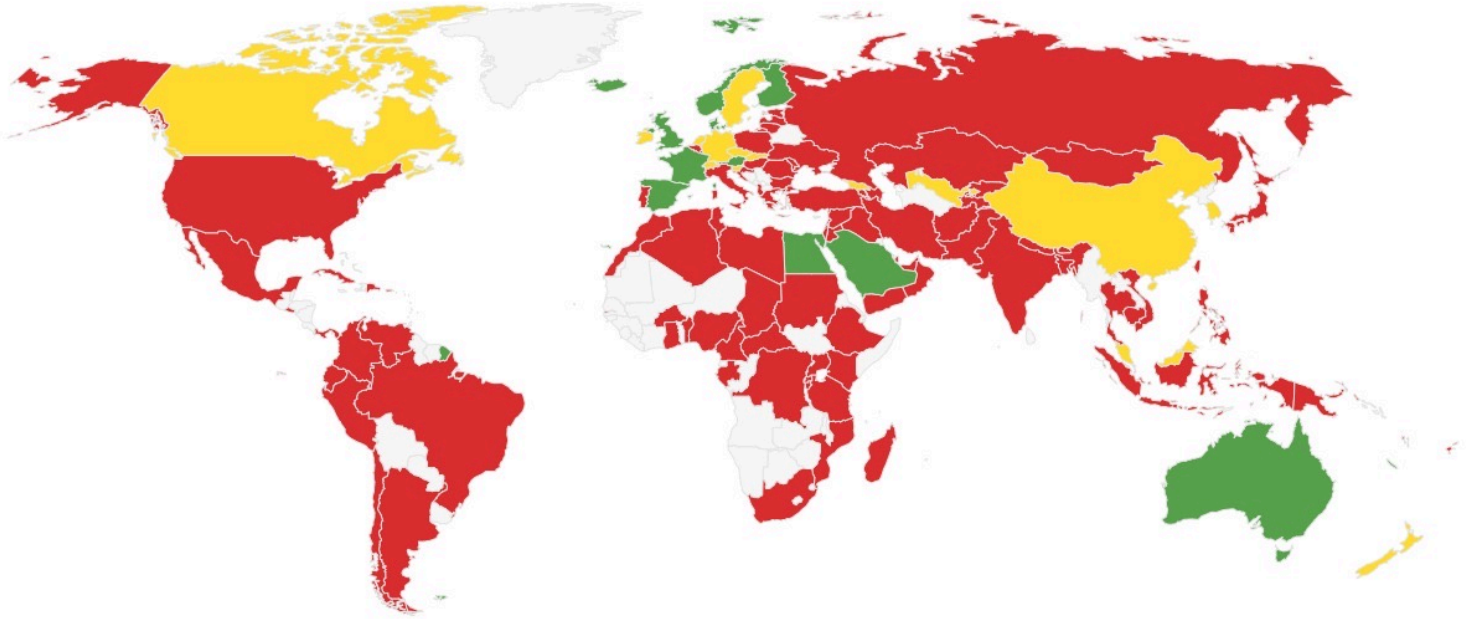




Are We on Track to Meet WHO's Hepatitis C Elimination Goals?

Locations Achieving Relative or Absolute Impact and Programmatic Targets — HCV

By Country/Territory — Trending 2023 Data



From the Polaris Observatory (https://cdafound.org/polaris/) © Natural Earth

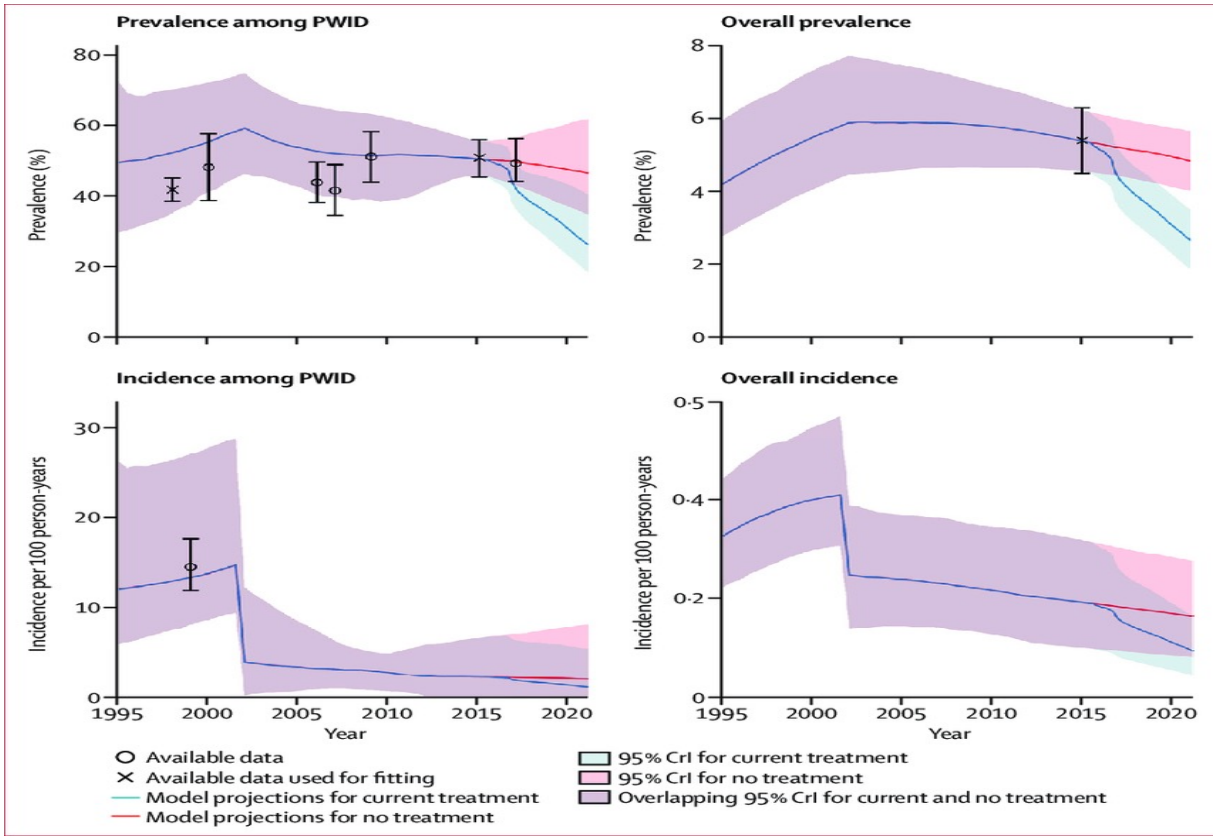
Incidence and Prevalence of HCV in the US

- An estimated 4 million people in the US are living with hepatitis C (HCV)
  - In 2023,
  - 4,966 reported acute HCV cases
  - 69,000 estimated acute HCV infections
  - 11,194 reported HCV-related deaths
- The rate of acute HCV is highest among non-Hispanic American Indian/Alaska Native (AI/AN) persons
- The rate of HCV-related deaths is highest among non-Hispanic AI/AN and non-Hispanic Black persons

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report – United States, 2023. https://www.cdc.gov/hepatitis-surveillance-2023/about/index.html Published April 2025.

Thanks to Boatemaa Ntiti-Reid (NASTAD) for the slide

Estimated Incidence and Prevalence of HCV Among PWID



Walker, JG, et al. Lancet Glob Health, 2020

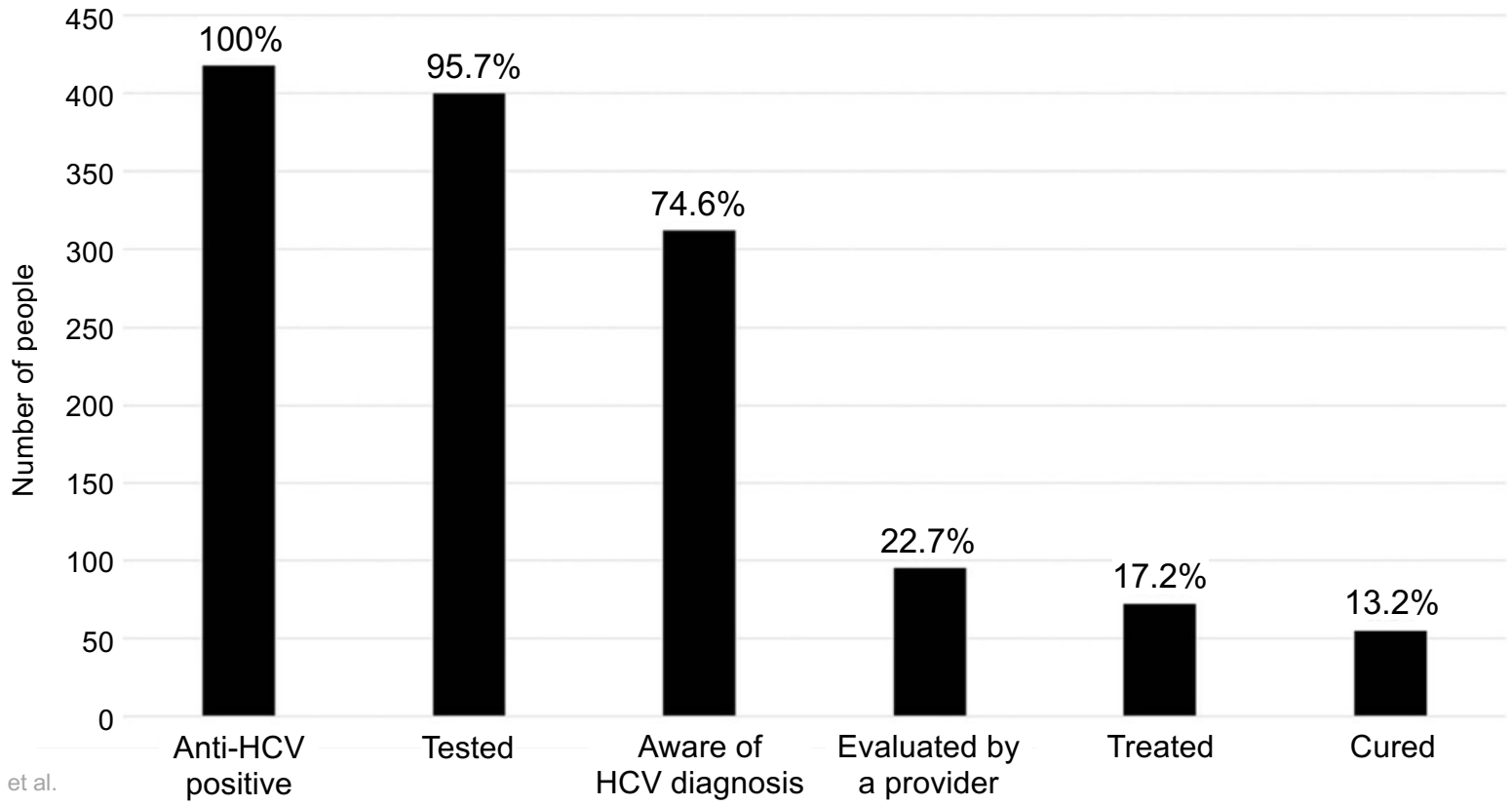
Acquisition/Transmission of Untreated HCV Among PWID

>70% of all new hepatitis C infections occur in **people who inject drugs**[1]

Each PWID can **spread HCV to ~20 others,** predominantly in the first 3 years of infection[2]

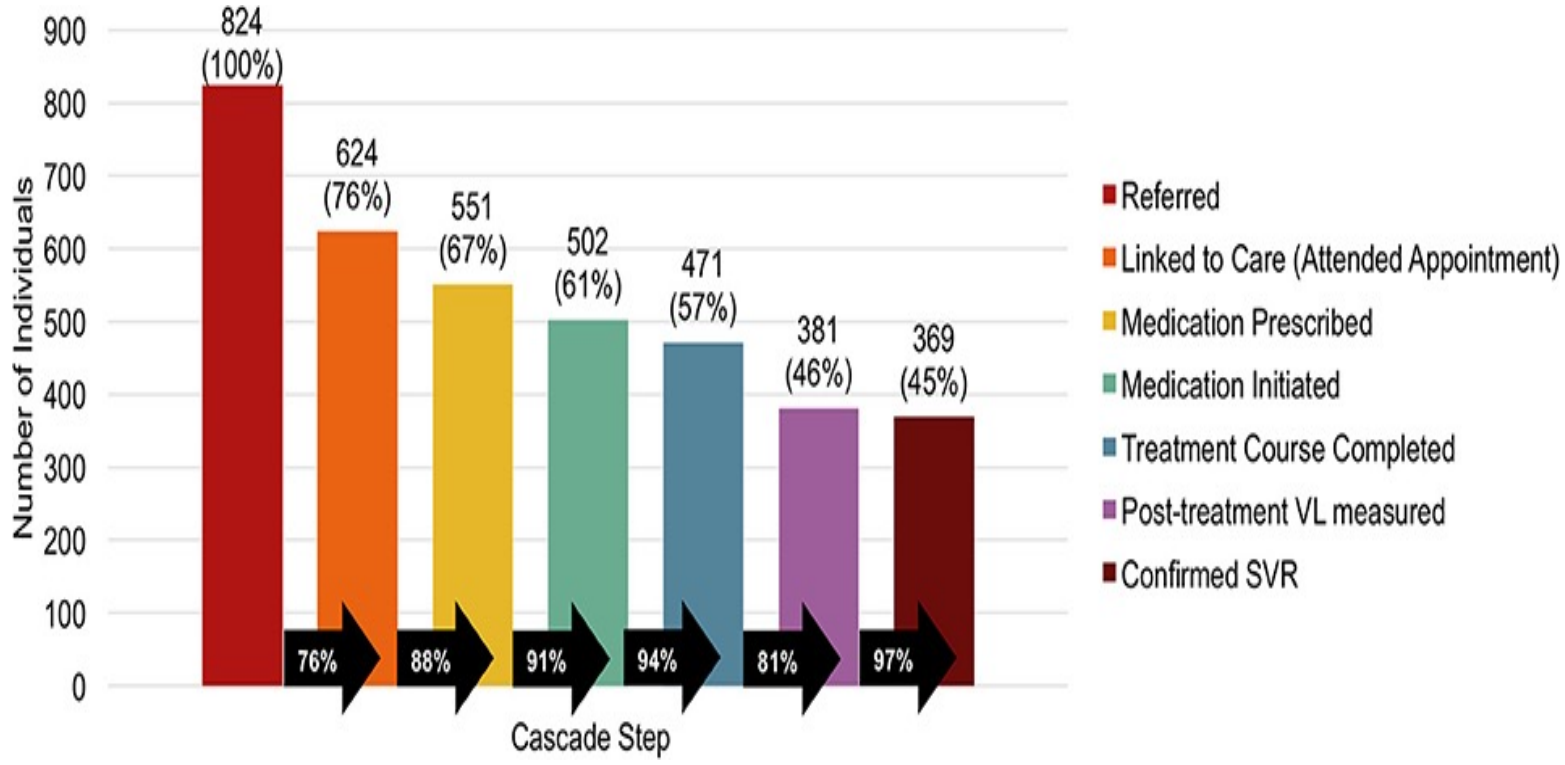
ABBV-US-00437-MC.pdf, 2021

Treatment Initiation Among PWID is Still Low….



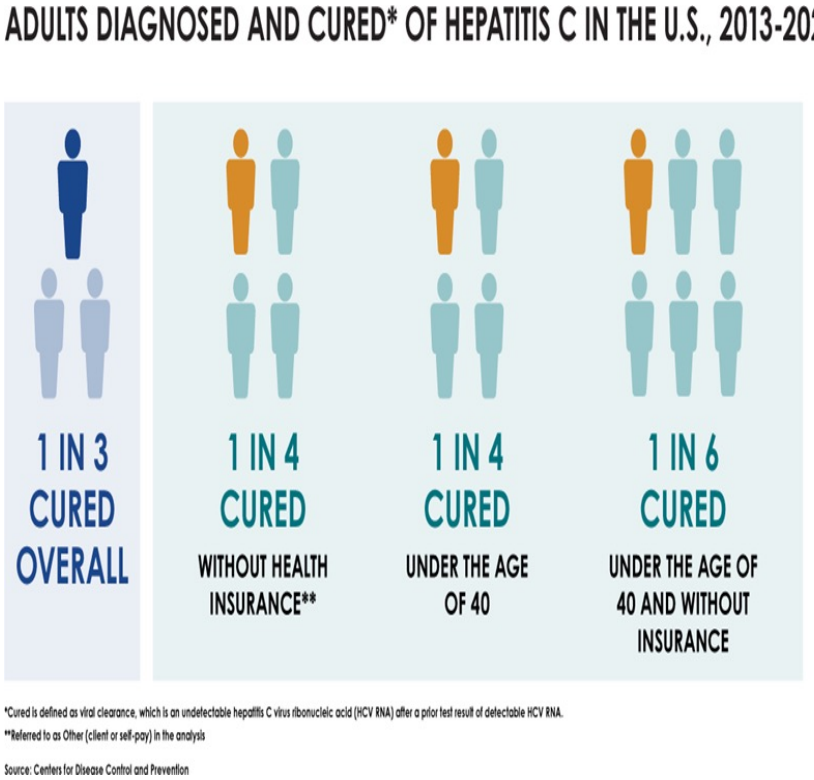
Falade-Nawulia, O, et al. *Liver Int*, Oct 2020.

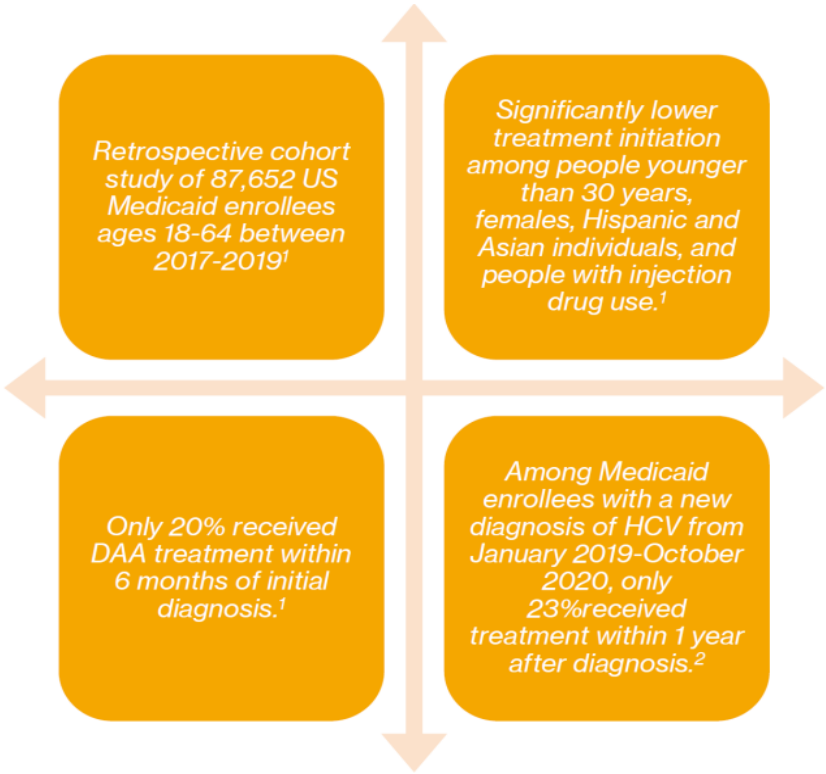
HCV Cascade of Care with an Embedded Nurse Navigator Model



Sherbuk, JE, et al. Front Public Health, 2019

HCV Treatment Rates in the US





JAMA Network Open, 2023
Thompson, WW, et al. MMWR, 2022
Thanks to Anthony Martinez for the slide

Barriers to HCV Care for PWID

- Provider did not recommend treatment or did not refer for treatment because of lack of knowledge or implicit bias
- Competing priorities for the patient – active substance use, mental health concerns, and other health conditions
- The provider's and the patient's lack of knowledge about HCV treatment
- Need for additional phlebotomy, which can be traumatic for patients
- Lack of provider follow up, lack of closed loop referrals
- Lack of insurance coverage for medications or a prior authorization requirement
- Transportation/logistical concerns

HCV Case Study

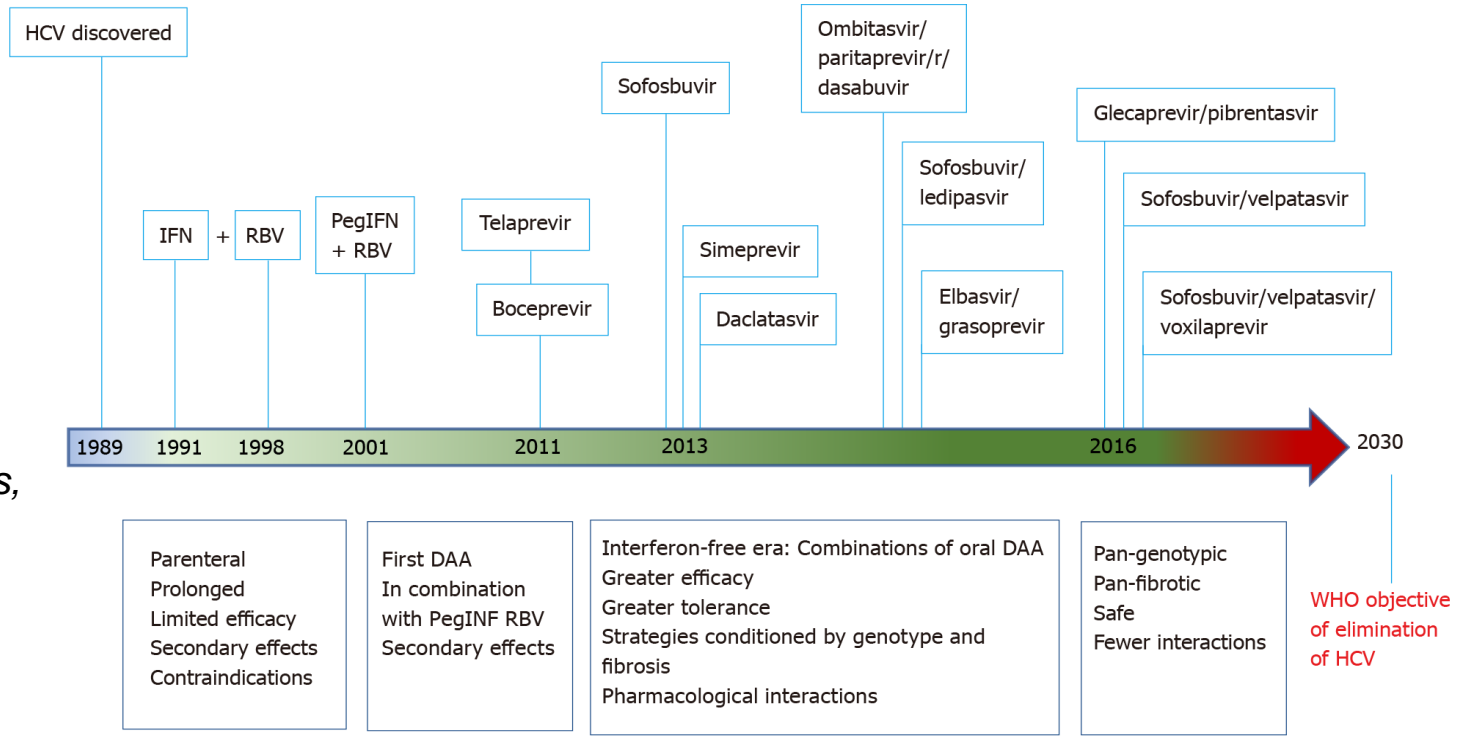
58-year-old female presents to the clinic because she was told that she had a positive HCV antibody when rapid tested at a syringe services program

- Past medical history: HTN, asthma
- The patient is currently injecting fentanyl several times daily, binge drinks alcohol on the weekend with her male partner (who also has HCV)
- HCV viremia was confirmed
- Estimated liver fibrosis per bloodwork (proprietary Fibrotest, etc.): F2
- The patient asks: Is there treatment for HCV? Can I be treated?

Evolution of HCV Therapies

One of the most exciting advances in clinical medicine in decades:

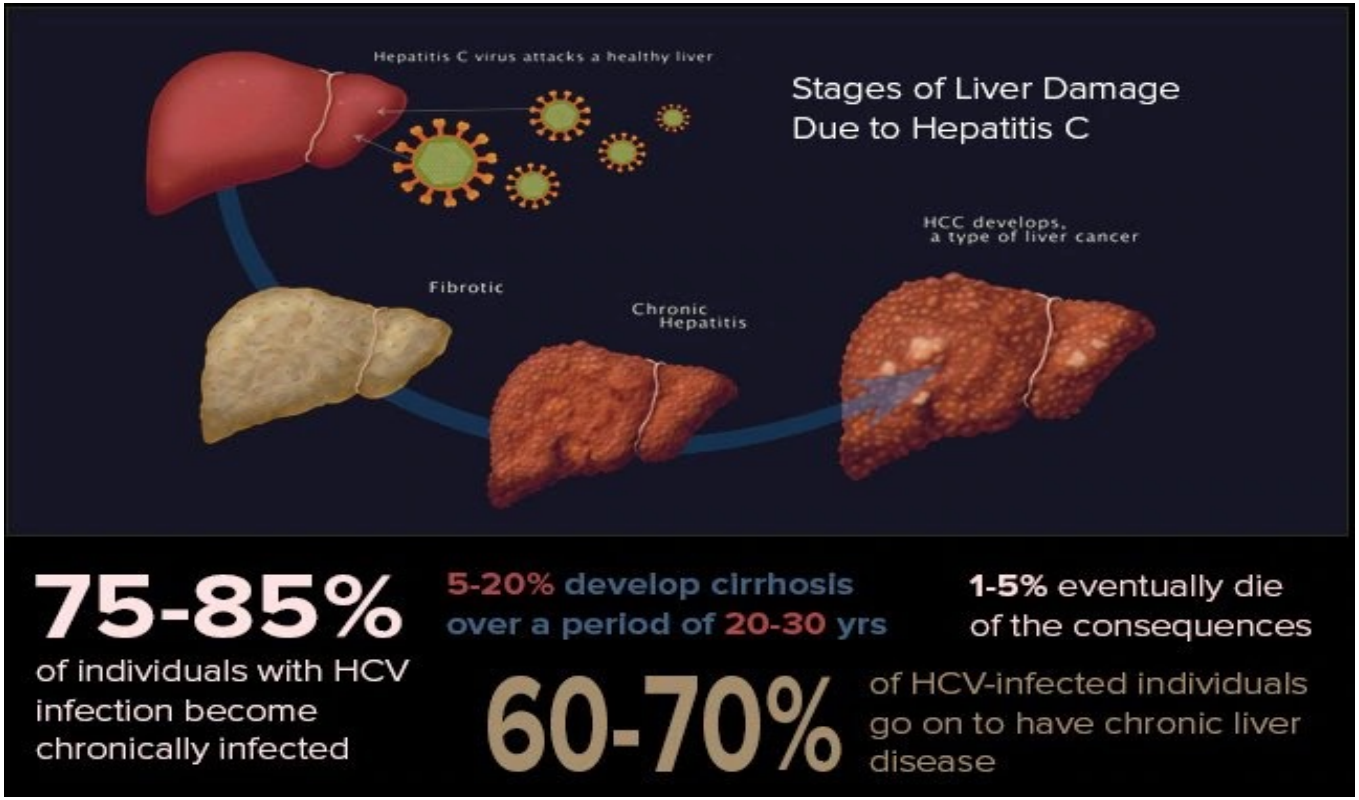
Direct acting antivirals (DAAs) have cure rates>95% in 8-12 weeks, with few side effects



IFN: Interferon; RBV: Ribavirin; Peg: Pegylated; DAA: Direct-acting antiviral

Gonzalez, GR, et al. *World Journal of Gastroenterology*, 12/21/21

What Happens if HCV Isn't Treated?



Hepatitis C: Cure Is About More Than the Liver
Duchini, A. Medscape, 2017

Benefits of HCV Treatment with DAAs on Mortality Among PWID

Implications

Direct-acting antiviral treatment for HCV

84%
Reduction in
mortality related to extrahepatic manifestations

For healthcare providers

- DNA treatment results in a significant reduction in EHM-related mortality in the overall population and among PWID
- Engagement in care may provide **additional benefits**
- Can be motivating for both providers and patients to treat hepatitis C infection

For patients

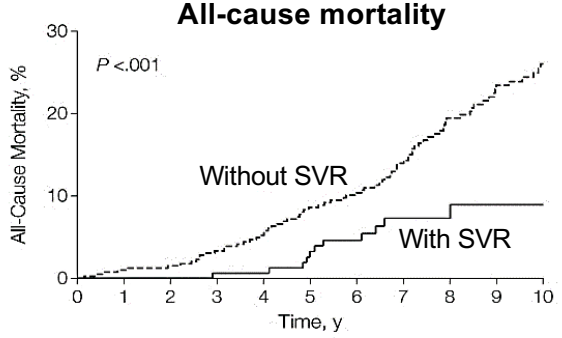
- HCV treatment can not only cure them of HCV but also provides **non-liver related benefits**; reducing mortality risk from heart, kidney, metabolic and neurologic disorders
- Being aware of all these benefits of treating hepatitis C can increase their motivation to start and finish treatment

NATAP, AASLD Conference Poster, 2021

Why Should We Treat PWID With DAAs?

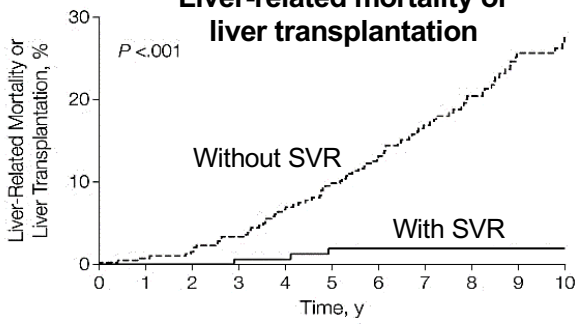
Individual: Reduction in Mortality

All-cause mortality



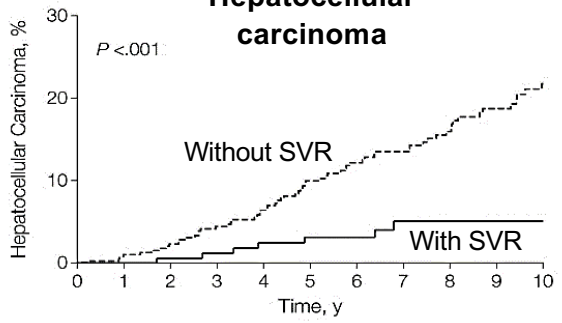
No. at risk											
Without SVR	405	393	382	363	344	317	295	250	207	164	135
With SVR	192	181	168	162	155	144	125	88	56	40	28

Liver-related mortality or liver transplantation



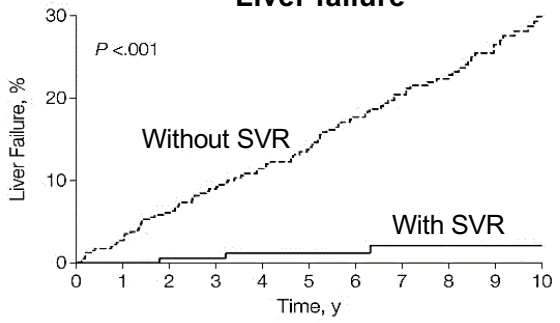
No. at risk											
Without SVR	405	392	380	358	334	305	277	229	187	146	119
With SVR	192	181	168	162	155	144	125	88	56	40	28

Hepatocellular carcinoma



No. at risk											
Without SVR	405	390	375	349	326	294	269	229	191	151	122
With SVR	192	181	167	161	152	142	124	86	54	39	27

Liver failure

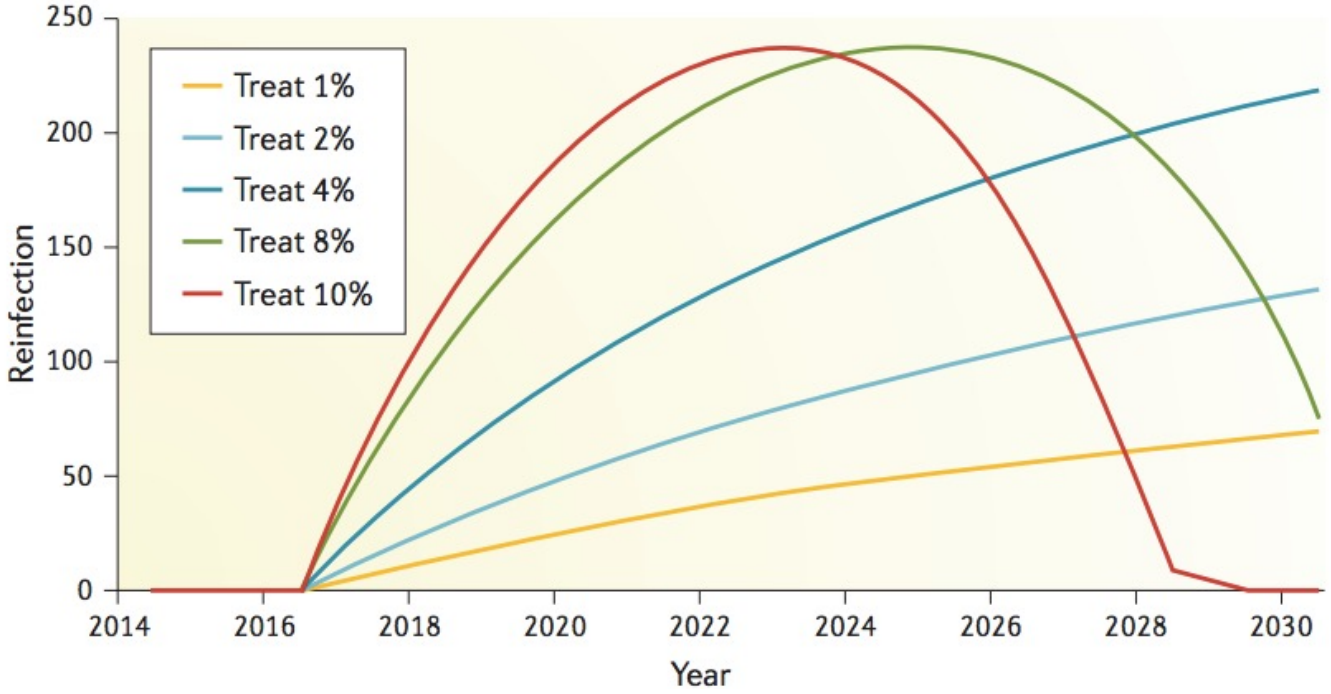


No. at risk											
Without SVR	405	384	361	337	314	288	259	216	184	143	113
With SVR	192	180	166	160	152	141	123	88	56	40	28

van der Meer et al. JAMA, 2012

Why Should We Treat PWID With DAAs?

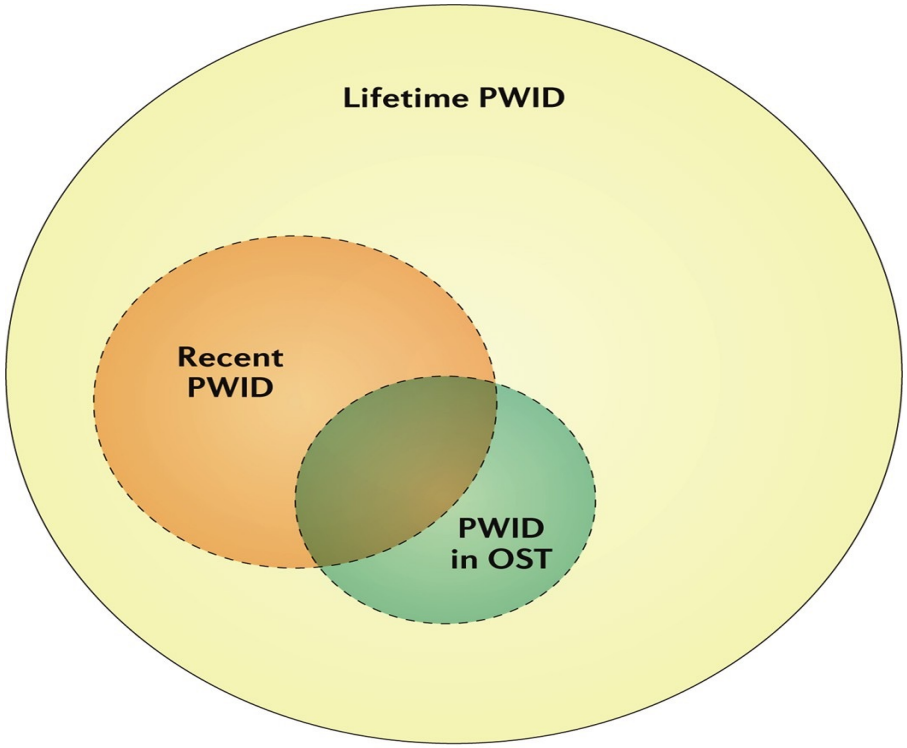
Public Health: Reduce Transmission



Razavi et al. 4th International Network of Hepatitis in Substance Users

What is the Evidence to Show that DAAs Are Effective in PWID?

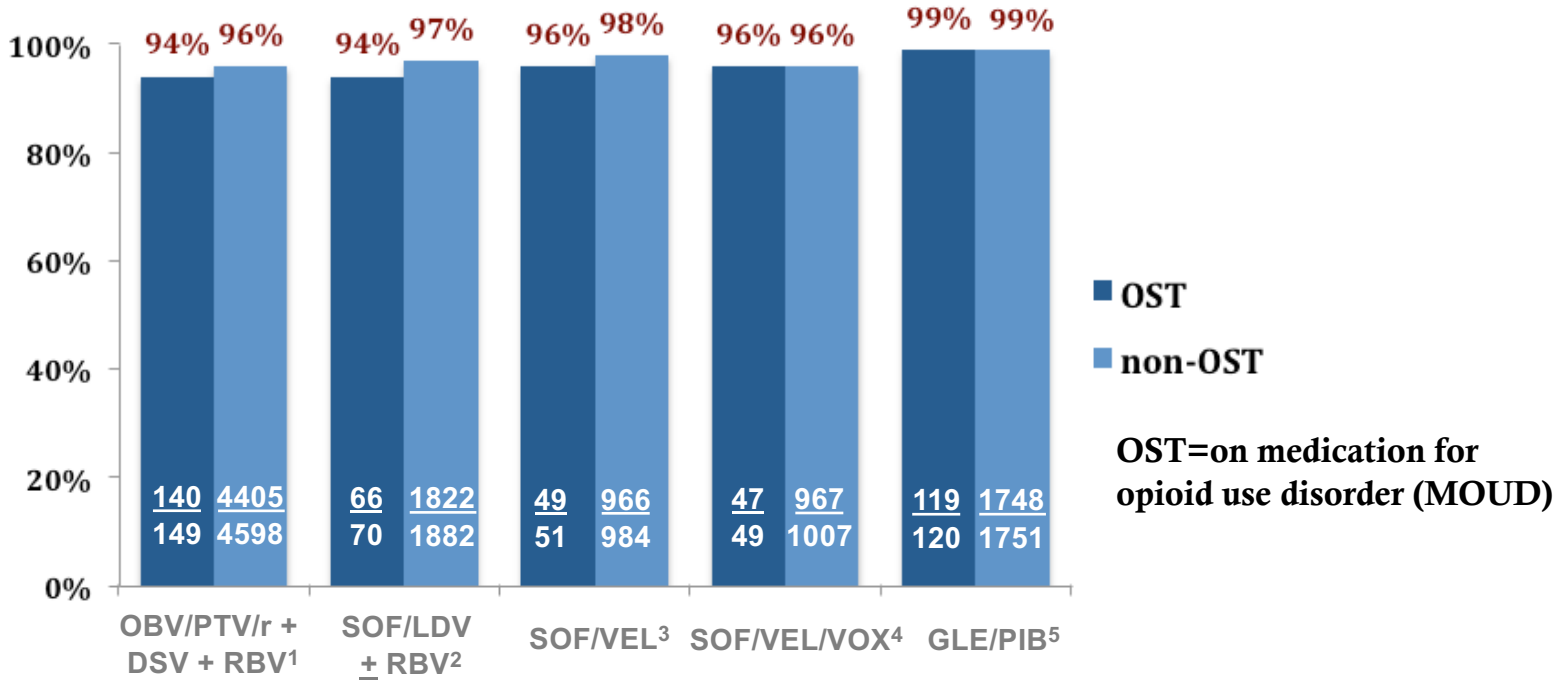
Most PWUD/PWID Were Excluded from DAA Clinical Trials



Nature Reviews | Gastroenterology & Hepatology

Grebely, J, et al. Nat Rev Gastroenterol Hepatol, 2017

People Receiving Medication for Opioid Use Disorder (MOUD): Post-Hoc Analysis of Phase II/III Trials for HCV Treatment

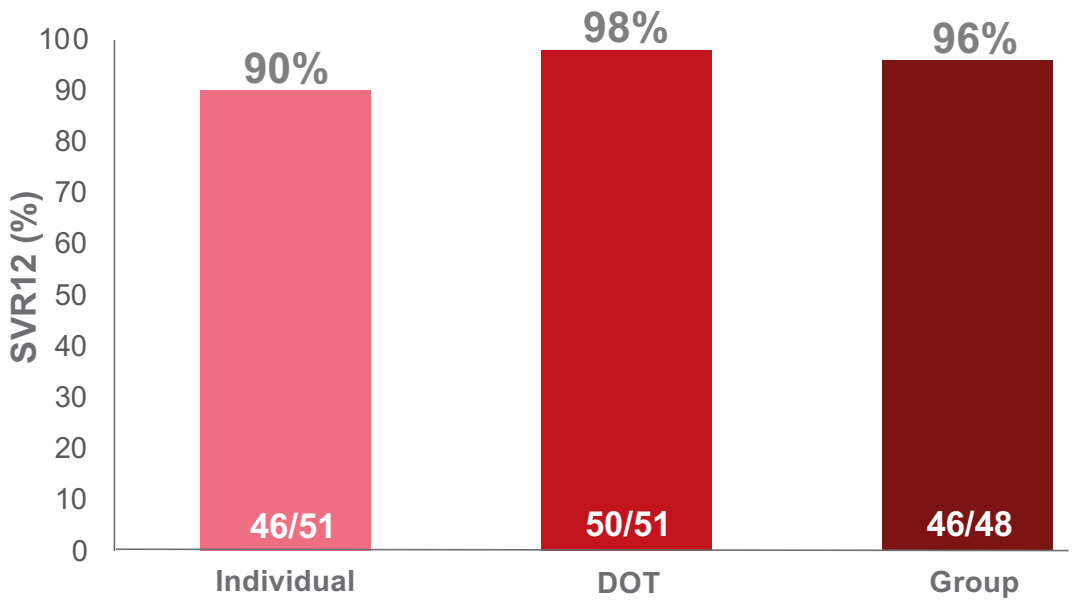


1)Grebely J, ILC 2017, Amsterdam, The Netherlands, April 19-23rd, 2017. 2) Grebely CID 2016. 3) Grebely CID 2016.
4) Grebely J, ILC 2017, Amsterdam, The Netherlands, April 19-23rd, 2017. 5) Zeuzem, S. Ann Intern Med 2015. 6) Dore, GJ Ann Intern Med 2016. Zeuzem 2016; Puoti, 2017

PREVAIL Study – Sustained Viral Response (SVR) 12

Patient Characteristics:

- 85% with genotype 1a, 27% with cirrhosis, 11% were treatment-experienced, 14% PWH
- 98% on methadone for OUD, *65% with recent drug use in last 6 months*

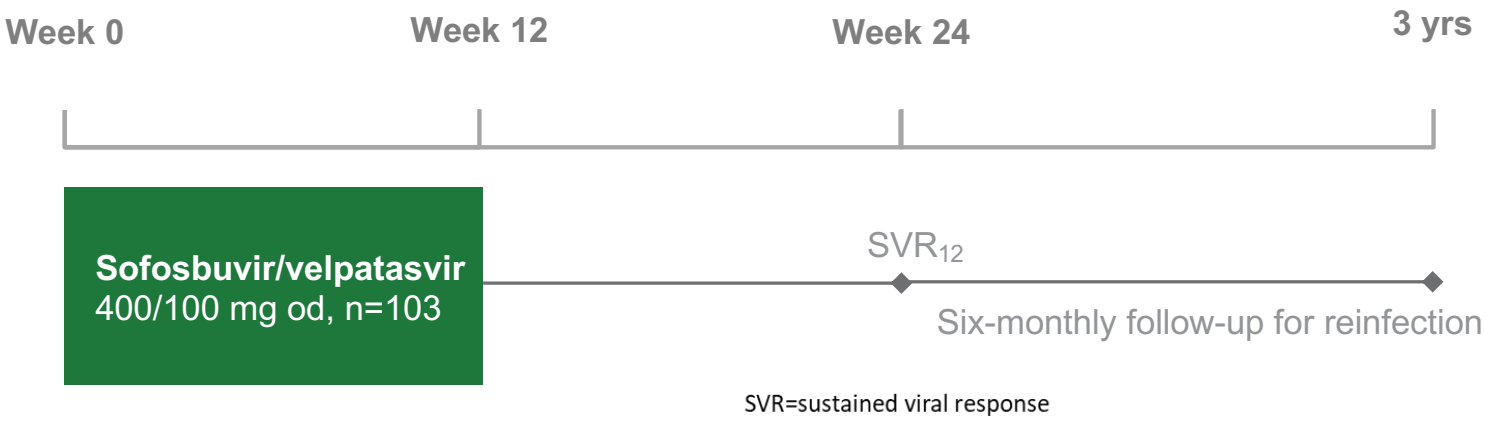


DOT=directly observed treatment
PWH=people with HIV

Litwin AL, et al. ILC 2017, Amsterdam, The Netherlands, April 19-23rd, 2017 (PS-130)

HCV Treatment in Recent PWID – The SIMPLIFY Study

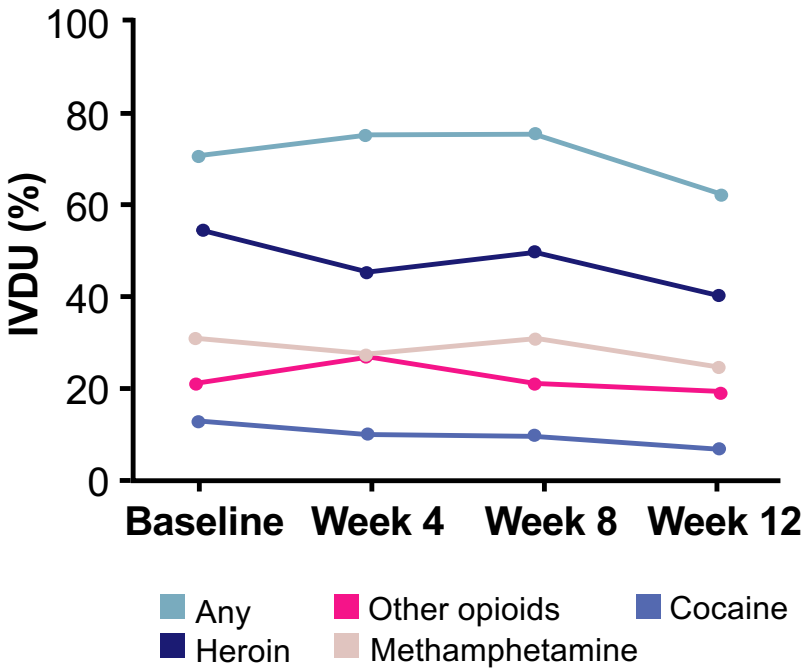
- An international open-label trial, N=103
- Electronic blister packs were used to monitor adherence
- 100% of the participants were people with recent injecting drug use (within the past six months)
- 74% were persons with injection use within the last month



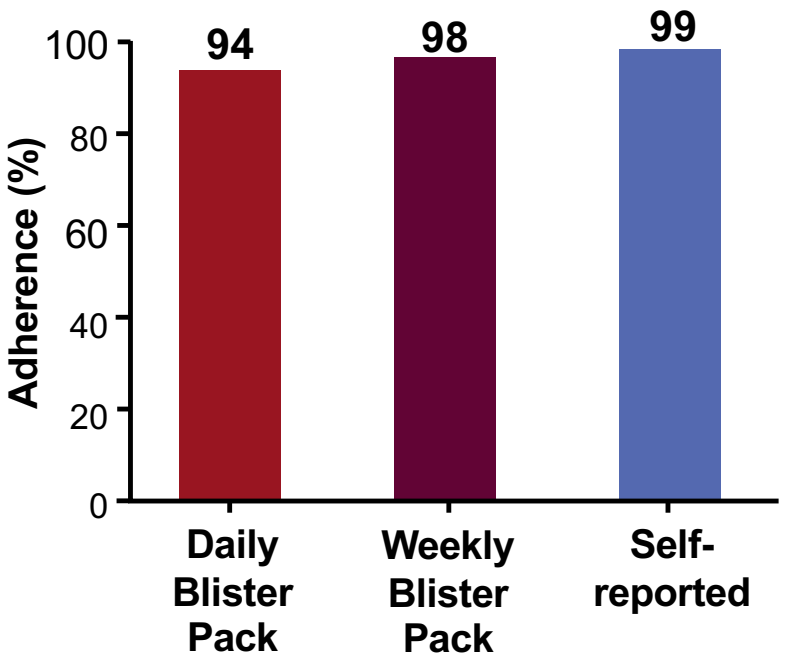
Grebely. Lancet Gastroenterol Hepatol. 2018;3:153. Grebely. Clin Infect Dis. 2016;63:1479.

The SIMPLIFY Study: Injection Drug Use and Treatment Adherence

Self-Reported Injection Drug Use During Therapy[1]



Overall Treatment Adherence[2]



1. Gilead Sciences. EPCLUSA US full Prescribing Information. 2. Cunningham. Int J Drug Policy. 2018;62:14.

Reinfection is Expected Among Some PWID, but Rates are Low

Perceived risk of reinfection may hinder willingness of HCPs to provide treatment[2,3]

Persons who have been successfully cured can no longer transmit the virus to others.[1]

AASLD/IDSA guidelines state: ***"Active or recent drug use*** *or concerns regarding reinfection* ***<u>are not</u> contraindications*** *to treatment"*[1]

Resolved infection ***does not*** *confer immunity.* **Reinfection is possible in *anyone*** after viral cure or spontaneous clearance **if exposed to HCV**[4,5]

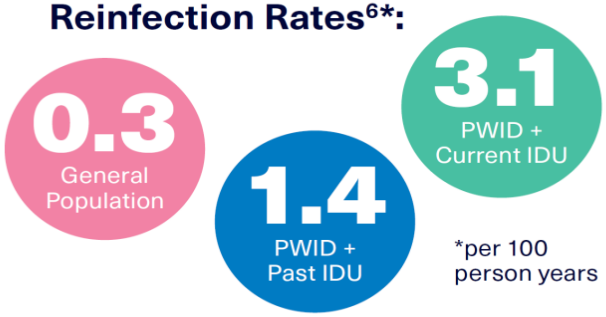
What is reinfection?

Detectable virus following a cure or spontaneous clearance.[4]* Reinfection rates are higher in active PWID without harm reduction.[4,5]

How is it different from virologic failure?

Relapse generally occurs within 4 weeks after completing treatment and is driven by reemergence of the same HCV GT/strain.[4]

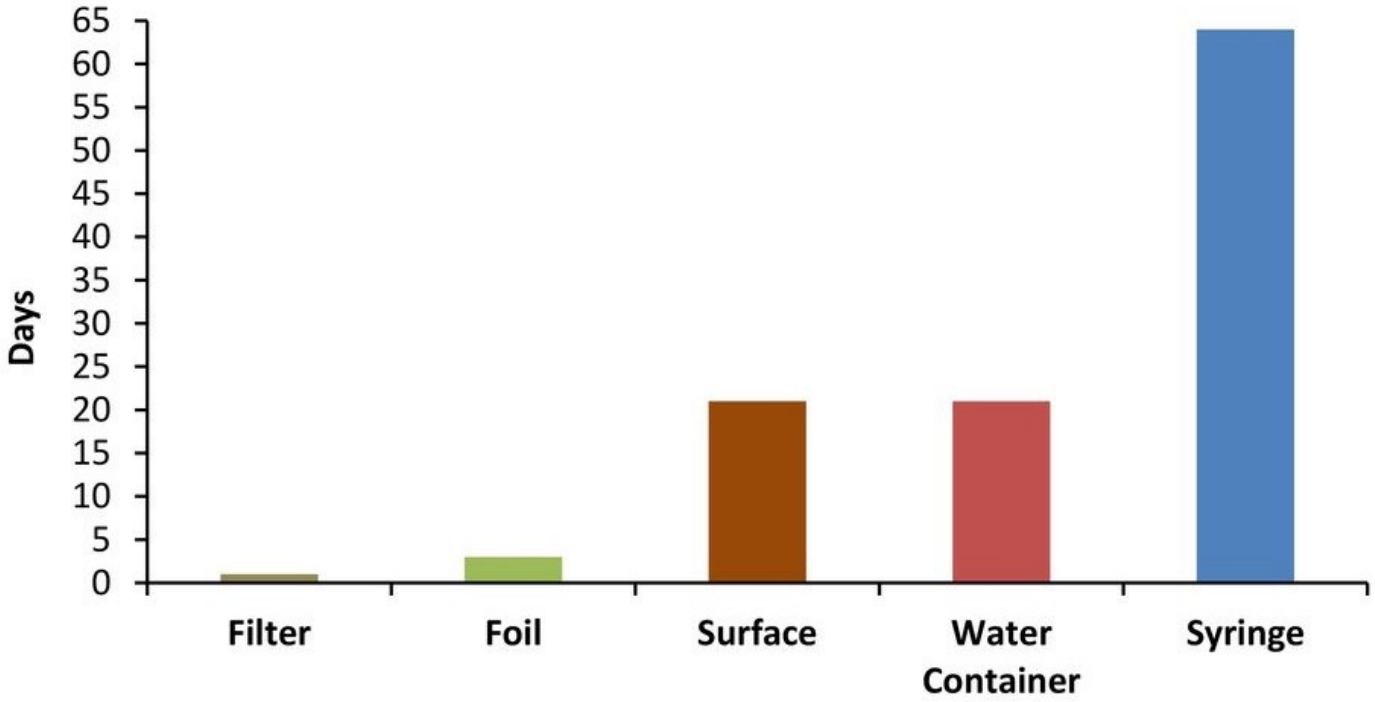
Reinfection Rates[6]*:



*Cure is defined as undetectable virus ≥12 weeks after HCV treatment, also known as sustained virologic response.

ABBV-US-00437-MC.pdf, 2021

How Long Can HCV Survive on Inanimate Objects?



HCV-contaminated solution needs to be heated for almost **90 seconds** and reach temperatures of **144°F** for the virus to be at undetectable levels.

Paintsil, et al. *JID*. 2010; Doerrbecker, et al. *JID*. 2011; Thibault, et al. *JID*. 2011; Doerrbecker, et al. *JID*. 2012; Paintsil, et al. *JID*. 2014.

Harm Reduction Strategies to Reduce the Risk of HCV Transmission With Injection Drug Use

Possible means of HCV transmission with injection drug use	Safer drug use equipment provided by syringe services programs/harm reduction programs
Shared and reused syringes	• Sterile, single-use syringes • Sharps containers
Sharing cookers	Single-use cookers
Sharing cotton filters	Single-use cotton filters
Multiple people using one water container	Single-use sterile water containers

Examples of Safer Drug Use Equipment Provided by Syringe Services Programs/Harm Reduction Programs

Sterile syringes provided for single use

Cotton filters provided for single use

Cookers provided for single use

Sterile water containers provided for single use

a.l.p.h.a. (https://alphaidaho.org/services/syringe-exchange-services/)

What are Overdose Prevention Centers (OPCs)?

OnPoint NYC, East Harlem
104-106 E 126th St., #1A
New York, NY 10035

OnPoint NYC, Washington Heights
500 W 180th St.
New York, NY 10033

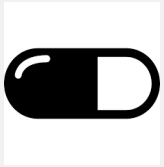
- The OPCs in NYC were the first sanctioned OPCs to open in the US and have been operational since November 2021
- OPCs are places where people who use drugs (PWUD) can use substances under the supervision of trained staff
- OPCs reduce potential substance-related harms, such as the risk of fatal overdose and transmission of HCV and HIV, and provide health services and supports to PWUD

DAAs and Harm Reduction Strategies Work Together as Prevention for HCV

- Curing HCV infection in PWID will help prevent new HCV infections
  - It will reduce the number of individuals with active HCV and decrease the HCV viral load in the community
- With fewer people with active HCV, syringe and other drug equipment access and MOUD utilization will be more effective
- However, HCV treatment alone will not control HCV infection in PWID
- Combined HCV prevention – syringe and other drug equipment access and MOUD access – must be continued (and expanded). Low threshold access to harm reduction services and MOUD is crucial.

Test and Treat Model of Care

TEST: Simplified HCV screening and diagnosis

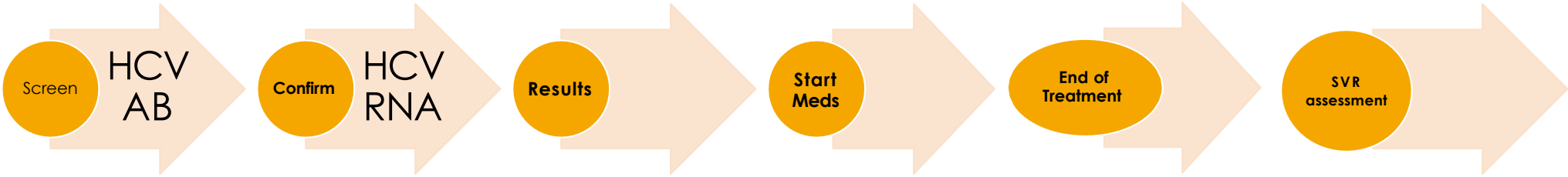


TREAT: Simplified, short-duration, pan-genotypic treatments, immediate initiation

CURE: Retreat as needed

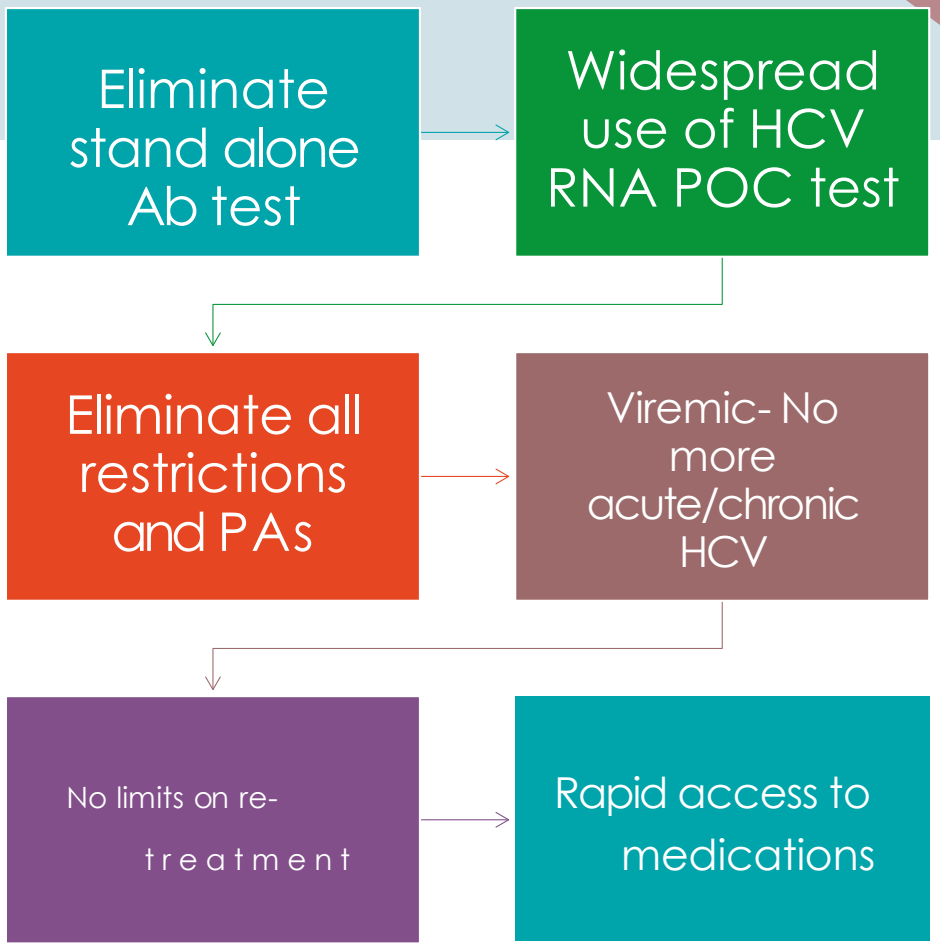
thanks to Anthony Martinez for the slide

Speed Is The Key



thanks to Anthony Martinez for the slide

Test And Treat Key Elements



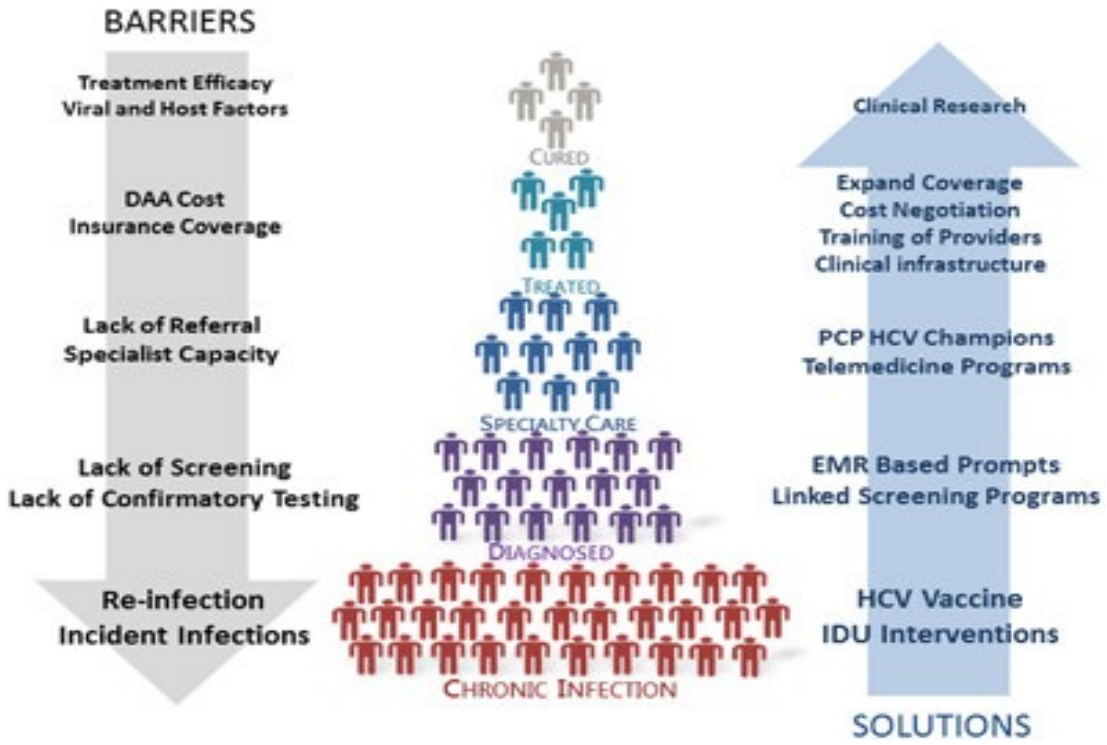
thanks to Anthony Martinez for the slide

Ab=antibody
HCV RNA POC=HCV virus point of care test
PA=prior authorization

Current HCV Treatment: How Can We Improve the Care Cascade?

Treatment in the Past		Current Treatment
Small numbers		Potential for large numbers
Advanced liver disease		Covered if no liver disease
Specialist prescriber with extensive paperwork		Non-specialist MD/NP prescribers & minimal paperwork
Complex drug regimens requiring teams		Simple drug regimens under solo providers
Frequent monitoring, often side-effects		Little or no monitoring, minimal side-effects
Response-guided therapy & long treatments		Few on-treatment decisions & shorter therapy length

Current HCV Treatment: How Can We Improve the Care Cascade?



Konerman, MA and Lok, AS. Clin Transl Gastroenterol, 2016

Screening/Testing/ Diagnosing and Treating HCV

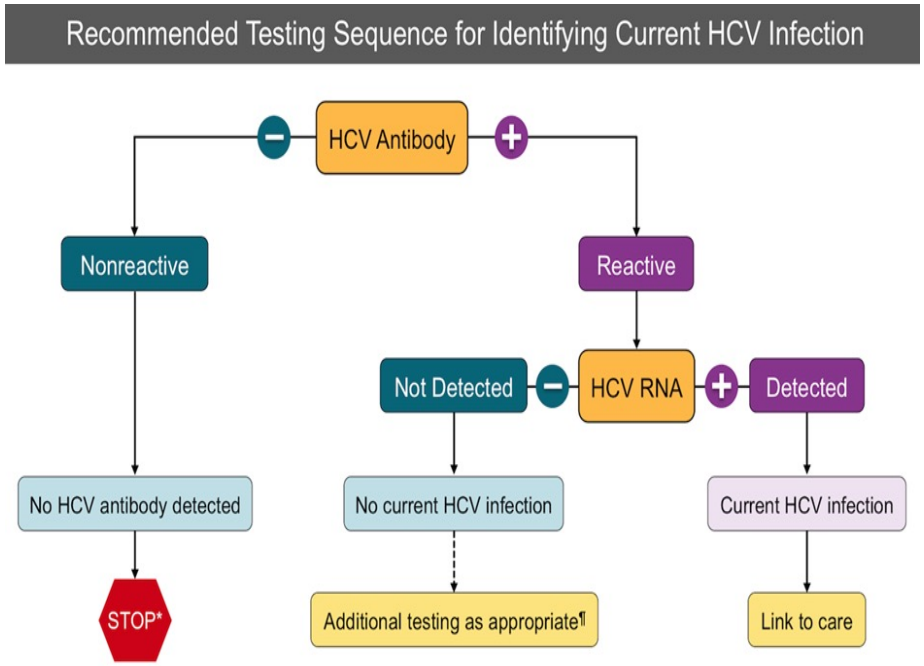
Recommendations for HCV Testing

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy.	I, B
Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP).	IIa, C

AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

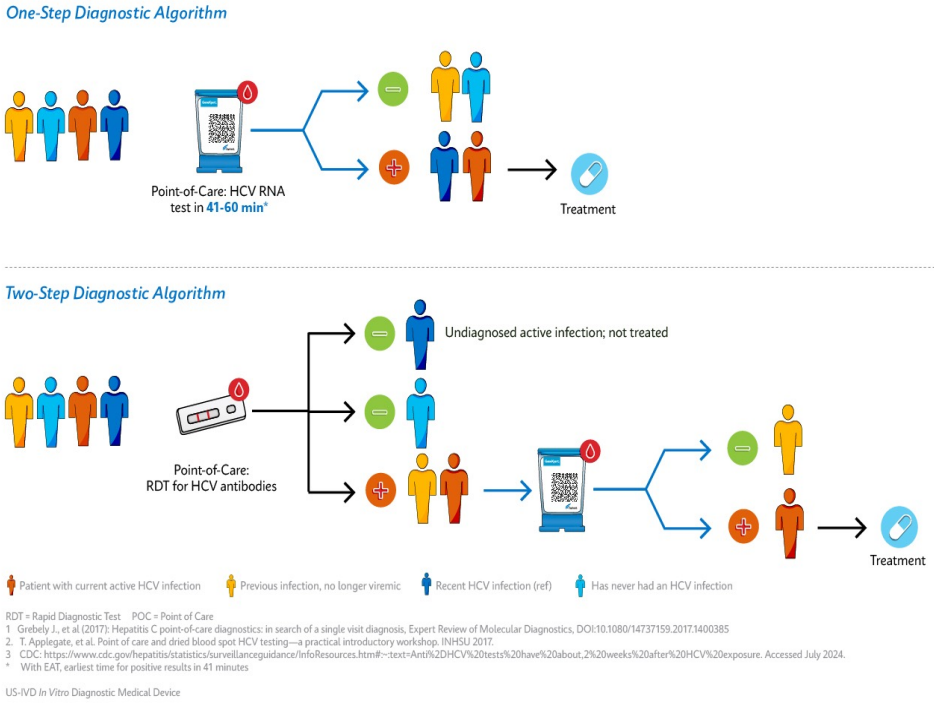
A Paradigm Shift: One-Step HCV Diagnostic Testing

Traditional HCV Screening Algorithm



CDC, MMWR, 2013

New Paradigm: One Step HCV Diagnostic Algorithm



Xpert® HCV Info

Simplified HCV Treatment for Treatment-Naïve Adults Without Cirrhosis

Who Is Eligible for Simplified Treatment

Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

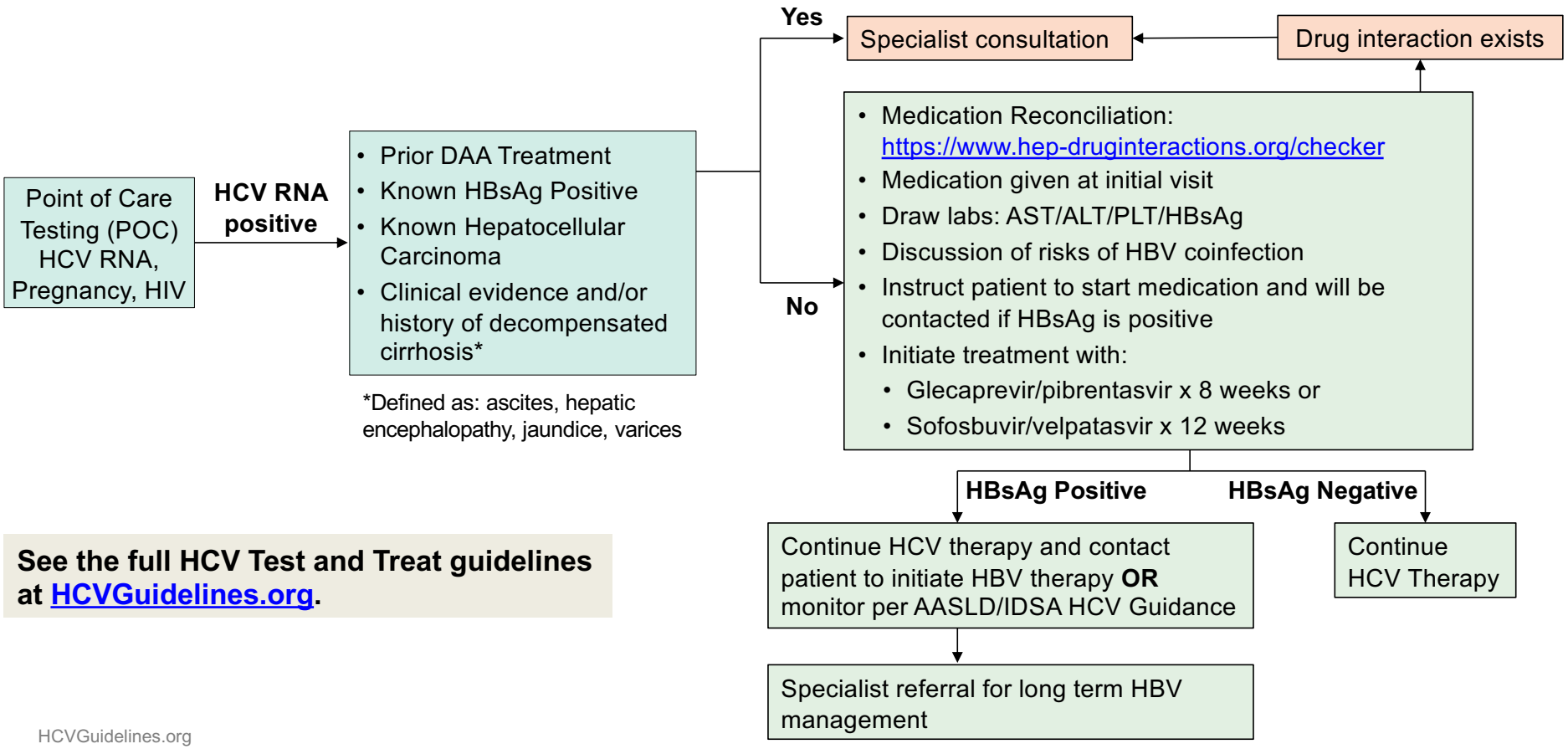
Who Is *NOT* Eligible for Simplified Treatment (Without Cirrhosis)

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(see HCV guidance for treatment recommendations for these patients)

AASLD/IDSA HCV Guidance Update for Simplified Treatment:
HCV Test and Treat Follow-Up Visit



See the full HCV Test and Treat guidelines at HCVGuidelines.org.

Assess for Liver Fibrosis/Rule Out Cirrhosis

- Assessment for liver fibrosis/rule out cirrhosis: refer for specialized liver care as needed
- **A liver biopsy has not been needed for many years**
- You can calculate a FIB-4 score (https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4): presumed cirrhosis>3.25 OR prior testing that showed:
- Fibroscan (transient elastography) stiffness >12.5 kPa
- Non-invasive, proprietary blood tests that estimate liver fibrosis, e.g., Fibrosure, Fibrotest-Actitest, Enhances Liver Fibrosis (ELF) test, Fibrometer
- Clinical evidence consistent with cirrhosis (though not diagnostic of cirrhosis): platelets <150K, nodularity of liver on imaging and/or splenomegaly
- Prior liver biopsy demonstrating cirrhosis
- ***Individuals with F3 or F4/cirrhosis need hepatocellular carcinoma (HCC) surveillance with an abdominal ultrasound +/- AFP every 6 months for life, regardless of HCV treatment and cure***

Starting HCV Treatment

Considerations:

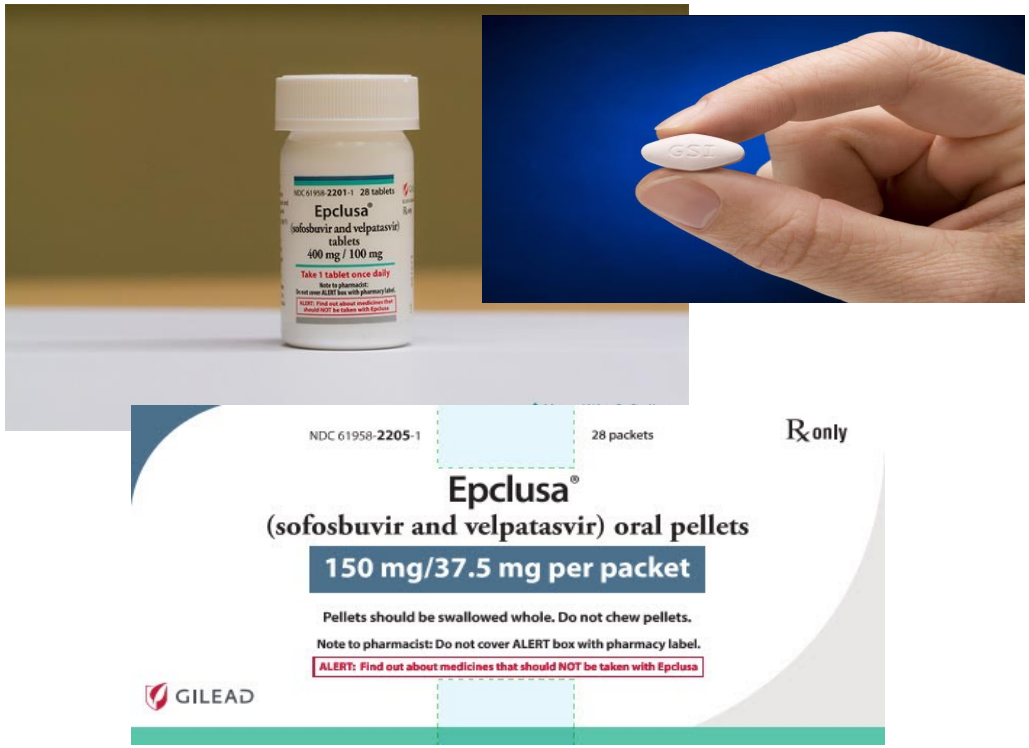
- Medication access: which medication/s are covered by their insurance? Can the patient safeguard their medications?
- Medication-medication interactions: AASLD guidance (https://www.hcvguidelines.org)
- Liverpool HEP drug interactions checker (https://www.hep-druginteractions.org/checker)
- Treat (preferably) or refer (link to appropriate care with a closed loop referral)

How to improve chances of sustained virologic response (SVR)/cure:

- Medication education: dosing (daily), potential side effects, adherence
- Harm reduction: prevent reinfection, treat partners, offer MOUD, offer new works, naloxone, support goals regarding alcohol use

Simplified HCV Treatment: Pangenotypic Medications

Glecaprevir (300mg)/pibrentasvir (120mg) x 8 weeks with food



Sofosbuvir (400mg)/velpatasvir (100mg) x 12 weeks

Monitoring

Can We Shorten the Time to Cure?

SVR12

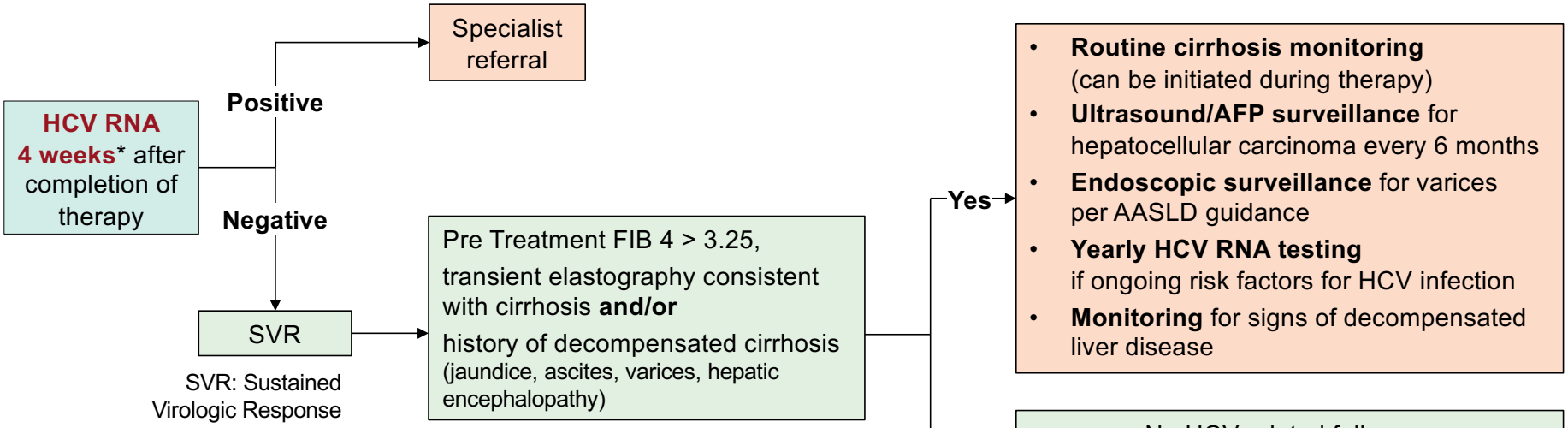
- Many get lost to follow up
- Hard to track people down for SVR 12 assessment
- Potential to return to use and reacquire HCV
- Heightened anxiety while waiting could be a trigger for return to use

SVR4

- Shortens care cascade by 2 months
- Easier to retain in care for a month
- Knowledge of cure can serve as reinfection/return to use deterrent
- Entire patient journey reduced to 3 months start to finish (for 8-week G/P regimen)

Source: Anthony Martinez

AASLD/IDSA HCV Guidance Update for Simplified Treatment:
HCV Test and Treat Follow-Up Visit



*Quantitative PCR testing using venipuncture is recommended, but point-of-care qualitative tests can be used to determine sustained virologic response (SVR) in certain settings where venipuncture may be unavailable

See the full HCV Test and Treat guidelines at HCVGuidelines.org.

Post-Treatment Follow-up Considerations

- Check for SVR 4 weeks after treatment completion (with an HCV viral load)
- If elevated liver function tests persist after SVR (HCV cure), check for other causes of elevated liver function tests
- Retest with a POC HCV RNA test or HCV viral load if the individual has ongoing risk factors for HCV reinfection
- If an individual acquires HCV again, then just **RE-TREAT** them!!
- Other HCV treatment medication options exist for patients previously treated, who fail treatment, or reacquire HCV

Practical Tips for HCV Treatment

- Work with a specialty pharmacy to assist with any prior authorizations (inform patients as this likely isn't their usual pharmacy)
- Be organized when communicating with the specialty pharmacy. Have the patient's insurance information, address (as needed), and a contact phone number for the patient
- Plan for any labs needed before, during, or post-treatment with an order set
- Prepare individuals for a realistic timeline for treatment and post-treatment follow-up
- Consider having medications delivered to the clinic for weekly, biweekly, or monthly pick-up depending on the needs of your individual patient
- Educate patients regarding the concept of reinfection and how to avoid reinfection

Utilizing Harm Reduction Strategies in the Clinic Setting

- Never withhold HCV treatment due to current substance use
- Offer buprenorphine (MOUD) to individuals using opioids who are interested
- Refer to an opioid treatment program (OTP) if a patient wants to use methadone to treat opioid use disorder
- Write a prescription for needles/syringes, alcohol wipes, sharps container, etc.
  - Refer to syringe services programs/harm reduction programs for other works (cotton, cooker, etc.); familiarize yourself with the SSPs/harm reduction programs near your clinic
- Offer a naloxone kit or a prescription for naloxone; inform patients regarding the importance of airway/breathing with rescue breaths in case of overdose

Utilizing Harm Reduction Strategies in the Clinic Setting

- With respect to alcohol use
  - Offer treatment with medication for alcohol use disorder (AUD) with acamprosate or naltrexone (if the patient does not use opioids) if the patient is interested
  - Alcohol use or AUD is not a contraindication for HCV treatment
  - Assist the patient with reduction of alcohol use if they are interested
- Discuss harm reduction strategies to avoid HCV reinfection
- Treat sexual, household, or substance-sharing partners together

Case Study Revisited

- The patient was treated with sofosbuvir/velpatasvir for 12 weeks
- She was cured of her HCV!
- She then decided to start MOUD for her OUD and was prescribed buprenorphine
- She has reduced her alcohol use
- Her male partner was also treated for his HCV and cured
  - He is still injecting fentanyl, but is using the SSP and is not sharing needles
- If either reacquires HCV, treat them ASAP

Takeaway Messages

- Offer DAAs to all persons with active HCV
- DAA treatment should be combined with comprehensive harm reduction strategies and substance use disorder treatment strategies, if the individual is willing
- Treating HCV reduces individual harms, has public health benefits, and is cost effective, even with HCV reinfection

Takeaway Messages

- Reinfection in some patients is inevitable (if you never see an HCV reinfection, it means that you are not treating a population of active PWUD)
- Treatment in treatment naïve patients without cirrhosis is simplified, refer others to a higher level of care as needed
- Linkage to care and lost to follow-up need to be addressed so everyone who needs HCV treatment successfully accesses HCV treatment

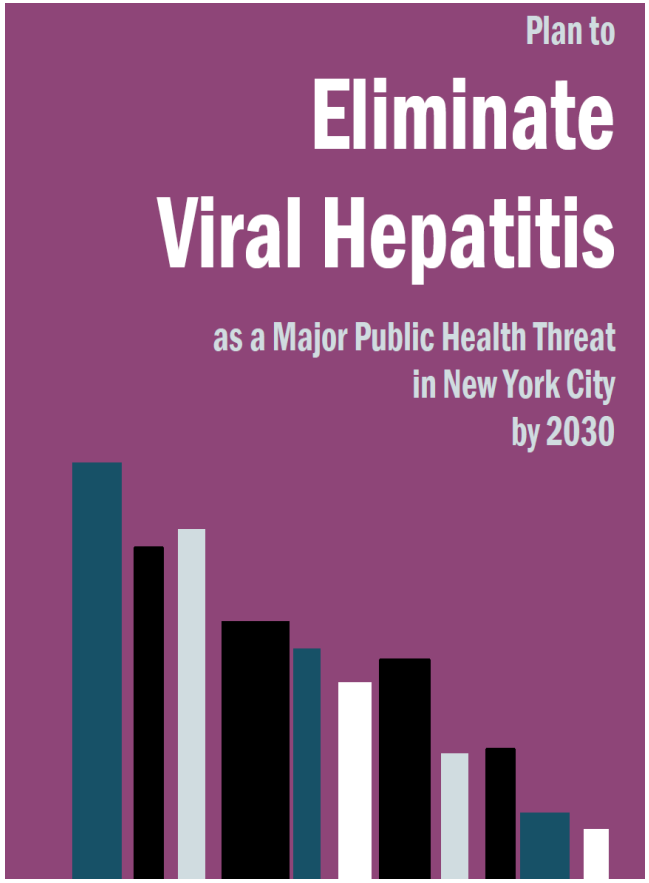
HCV Guidelines and Resources

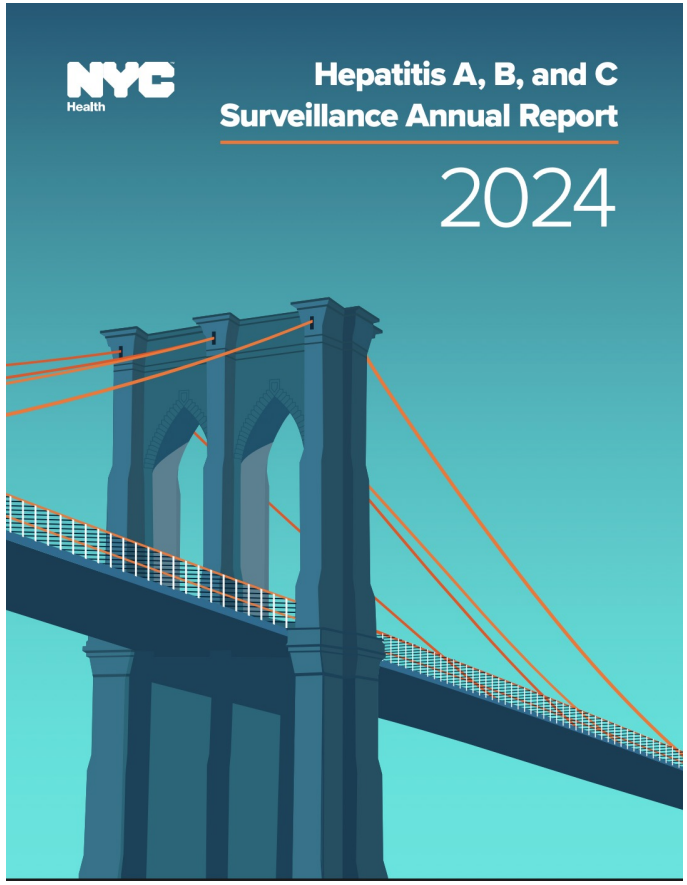
- Treatment Guidelines - HCVguidelines.org
  - Includes a simplified treatment algorithm for use by primary care providers
- Medication-Medication Interactions - https://www.hepdruginteractions.org/

HCV Resources in NYC

- NYS HCV CEI Clinical Consultation Hotline:
  (866) 637-2342 (clinicians will answer questions)
  - Hep C Task Force
  - Clinical Resources
  - Capacity Building Tools
  - Advocacy Committee
- Hepatitis C patient information page: www.nyc.gov/health/hepc
  - Free or low-cost testing and treatment

Elimination Plan and Annual Report





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