An Update on The Elimination of HCV

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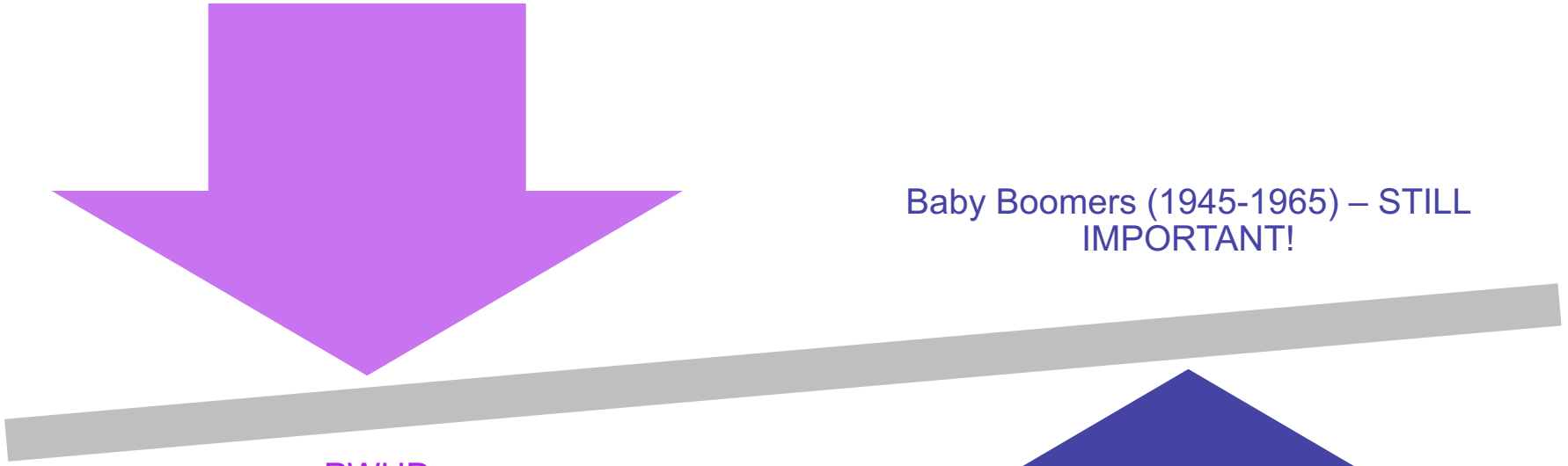
HCV In 2023



Baby Boomers (1945-1965) – STILL IMPORTANT!

- PWUD
- Justice Involved
- WOCBA
- Children born to HCV + mothers
- Indigenous
- Migrants
- -Unstably Housed

Injection Drug Use/ Opiate Crisis

Injection Drug Use Is the Most Important Risk Factor for HCV Infection[1-7]

Young PWUD with propensity to share needles and preparation equipment

HCV often acquired shortly after individuals begin injecting

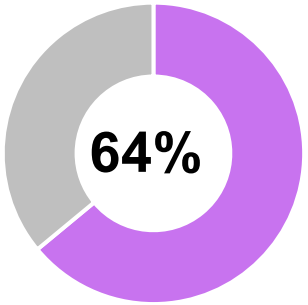
HCV can survive on cookers and cotton filters for days, and longer in needle barrel

10

HCV transmitted at a tenfold rate relative to HIV

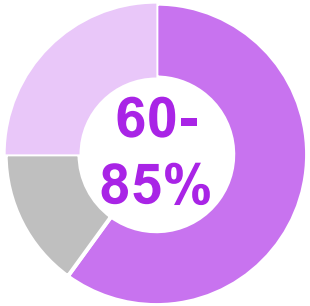
80

HCV is prevalent in 60-80% or more in people with IDU



of PWUDs in the **United States** are chronically infected

PWUD make up between 60% and 85% of all new HCV infections in **USA**



1. https://www.hhs.gov/sites/default/files/viral-hepatitis-action-plan.pdf; 2. https://hepfree.nyc/wp-content/uploads/2017/08/hcv-and-young-pwid-consultation-report.pdf;
3. Paintsil E, et al. *J Infect Dis.* 2010;202:984-90; 4. Doerrbecker J, et al. *J Infect Dis*. 2013;207:281-7; 5. Clausen LN, et al. *World J Gastroenterol*.2014;20:12132-43.
6. Nelson PK, et al. *Lancet*. 2011;378:571-83. 7. Lourenço L, et al. *Can Commun Dis Rep*. 2021;47(12):561-70.

Syringe Sharing Among People Who Inject Drugs in 23 US Cities, 2018

Sharing needles, syringes, or other drug injection equipment puts people who inject drugs (PWID) at high risk for HIV and other infections.

of PWID shared syringes

Syringe sharing is more common among young people.

of people aged 18 to 24 shared syringes

of people aged 25 to 29 shared syringes

of people aged 30 to 39 shared syringes

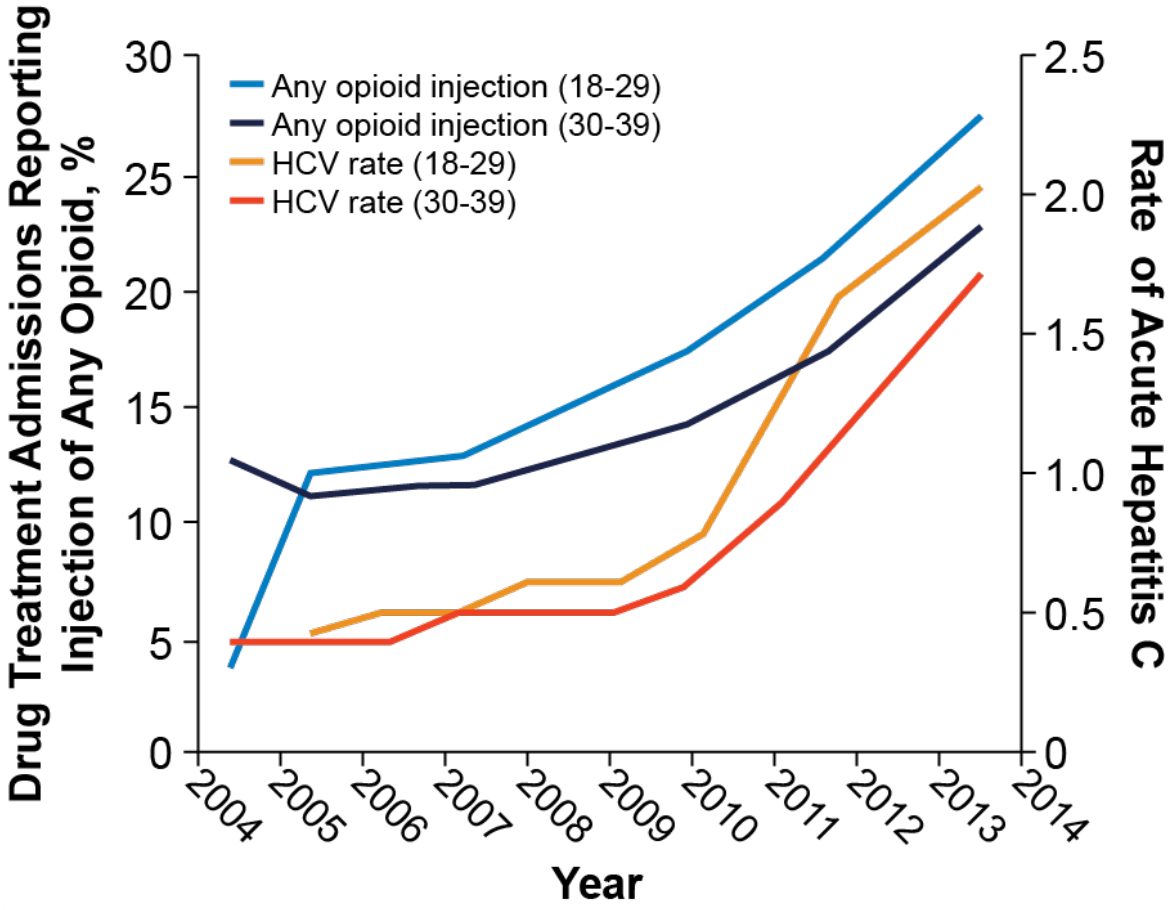
of people aged 40 to 49 shared syringes

of people aged 50 and older shared syringes

CDC. HIV Infection risk, prevention, and testing behaviors among persons who inject drugs-National HIV Behavioral Surveillance: Injection drug use – 23 U.S. Cities, 2018. HIV Surveillance Special Report 2020;24.

Increase in Hepatitis C Infections Linked to Worsening Opioid Crisis[1]

Hepatitis C and Opioid Injection Rose Dramatically in Younger Americans From 2004-2014



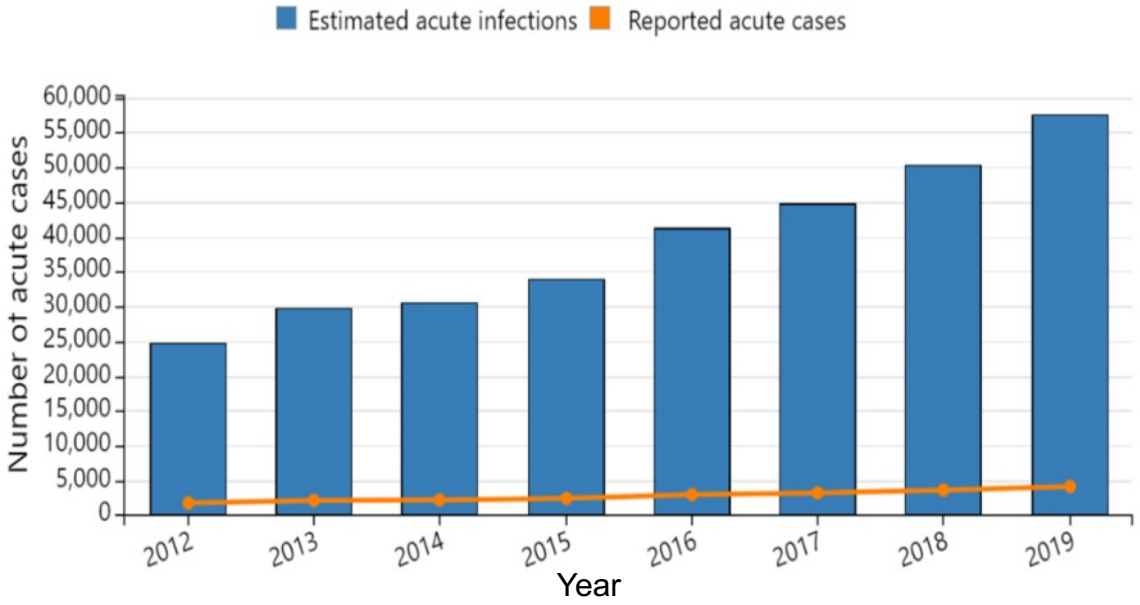
Among people **ages 18-29,** admission for injection opioid use increased by **622%**

HCV incidence increased by **400%** **in the** same cohort

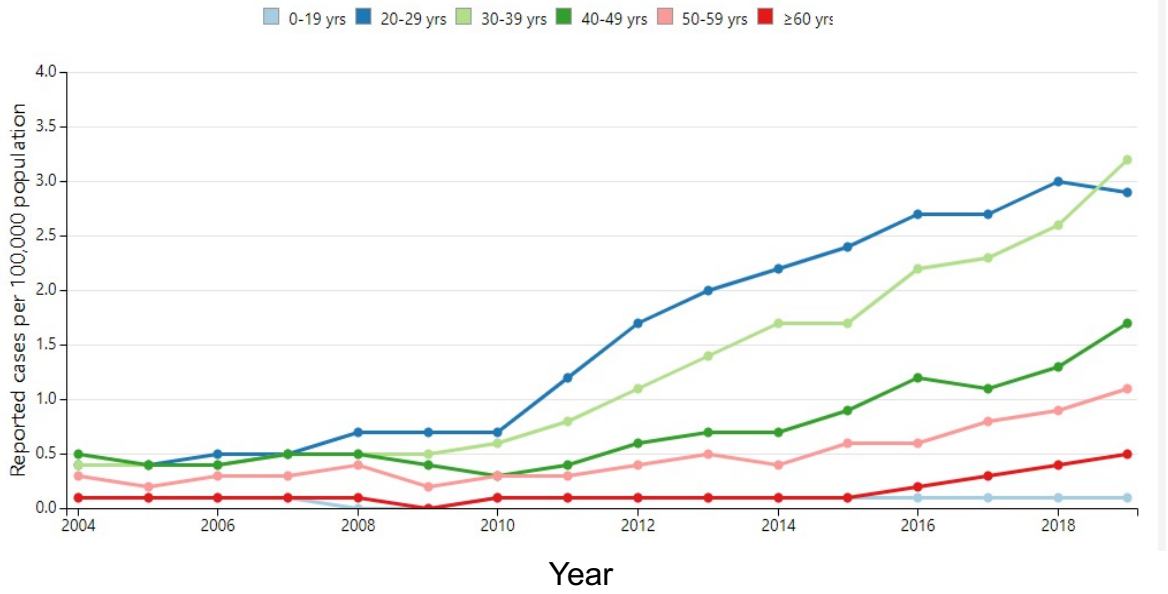
1. https://www.cdc.gov/nchhstp/newsroom/2017/hepatitis-c-and-opioid-injection-press-release.html.

HCV Infection in the United States: Incidence

Number of Reported Acute HCV Infection Cases and Estimated Infections — US, 2012–2019



Rates of Reported Acute HCV infection, by Age Group — US, 2004–2019

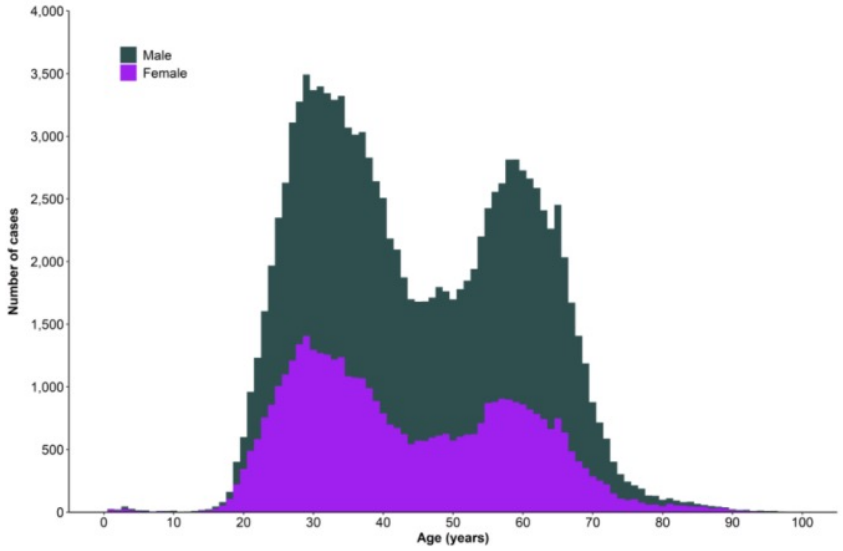


- Surge in HCV infections in the United States is intricately connected with the ongoing opioid epidemic and its associated injection drug use
  - Regions of the United States east of the Mississippi River have been most heavily impacted, with a particularly high intensity of new HCV cases in the central Appalachian region

https://www.cdc.gov/hepatitis/statistics/2019surveillance/HepC.htm

HCV and Women of Child-Bearing Age (WOCBA)

Number of newly reported chronic HCV infection cases, by sex and age — US, 2019[1]



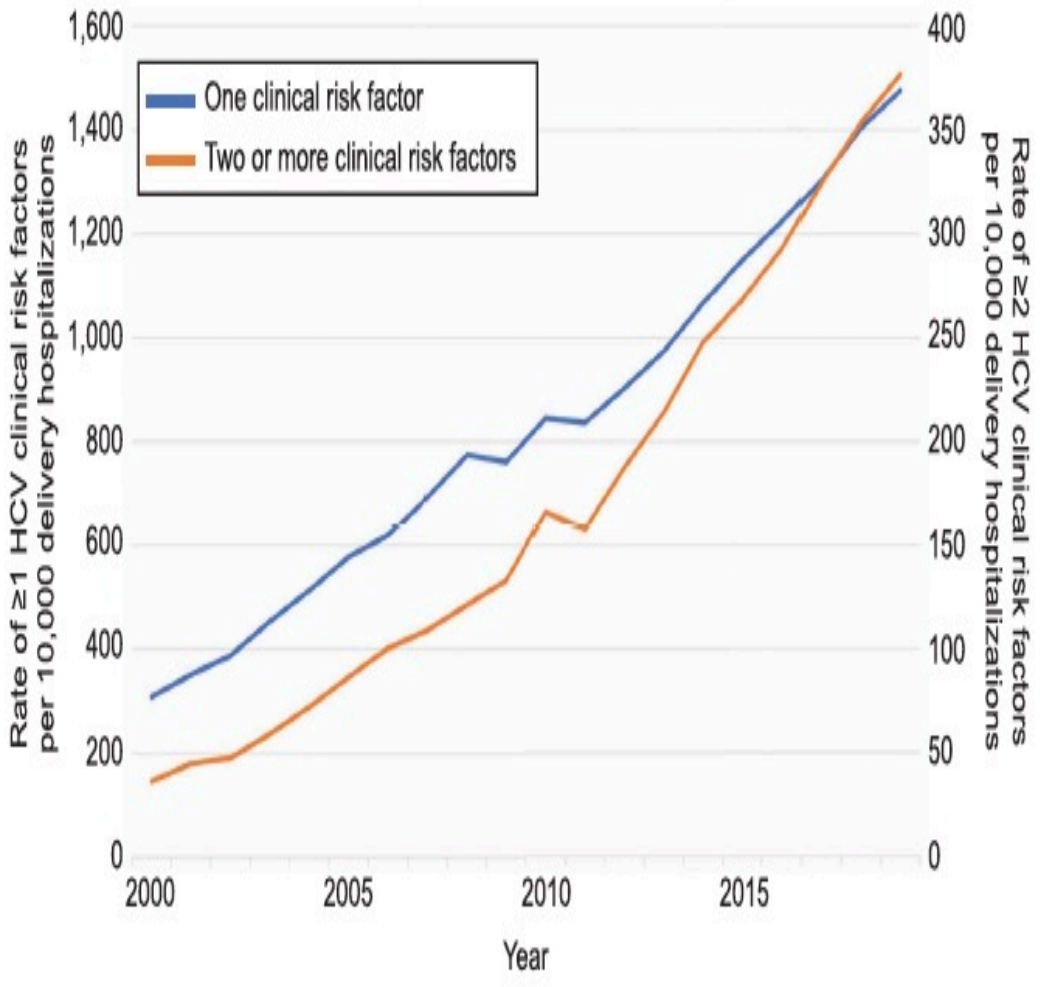
Changing HCV Prevalence Among Pregnant Women[2,]

- During 2000–2019, prevalence of HCV diagnosed during pregnancy increased **10 fold** from .05% in 2000 to .49% in 2019
- Prevalence increased **161%** between 2009-2017
- 494 cases per 100,000

Meta-analysis of 17 studies looked at HCV vertical transmission risk in women with chronic HCV: risk was 5.8% in HIV-negative women; risk doubled to 10.8% in HIV-positive women[3]

1. https://www.cdc.gov/hepatitis/statistics/2019surveillance/Figure3.8.htm. 2. *Arditi et al Deliveries Among Patients With Maternal Hepatitis C OBSTETRICS & GYNECOLOGY VOL. 141, NO. 4, APRIL 2023*
3. Society for Maternal-Fetal Medicine (SMFM). *Am J Obstet Gynecol*. 2017;217(5):B2-B12.

Trends In Clinical Risk Factors Among Patients with Delivery Hospitalizations



- Substance use (exclusive of opiates)
- Opiate use
- STI
- Smoking
- Mental Health Dx

Arditi et al Deliveries Among Patients With Maternal Hepatitis C *OBSTETRICS & GYNECOLOGY* VOL. 141, NO. 4, APRIL 2023

Table 3. Comparison of Adverse Outcomes for Patients With and Without a Diagnosis of Hepatitis C Virus Infection (Weighted)*

	HCV Infection Diagnosis		Unadjusted Model		Adjusted Model	
Adverse Outcome	Yes	No	OR	95% CI	aOR	95% CI
Non–transfusion-related SMM	525,531 (0.7)	2,598 (1.4)	2.10	1.92–2.29	1.83	1.67–2.00
Preterm birth	4,950,079 (6.5)	19,699 (10.8)	1.75	1.69–1.82	1.89	1.82–1.96
Cesarean delivery	23,638,014 (30.9)	67,955 (37.3)	1.33	1.30–1.37	1.26	1.22–1.30
HDP	6,016,056 (7.9)	16,450 (9.0)	1.16	1.12–1.21	1.01	0.97–1.05

HCV, hepatitis C virus infection; OR, odds ratio; aOR, adjusted odds ratio; SMM, severe maternal morbidity; HDP, hypertensive disorders of pregnancy.

Data are n (%) unless otherwise specified.

* The table demonstrates counts and estimates from weighted data. The adjusted models include all of the demographic (maternal race, age category, payer status, median income quartile by ZIP code), clinical (asthma, obesity, chronic hypertension, pregestational diabetes, gestational diabetes, prior cesarean delivery, multiple gestation), and hospital factors (location, region) in Table 1.

SMM = severe maternal morbidity HDP = Hypertensive Disorders of Pregnancy

PWUD and HIV

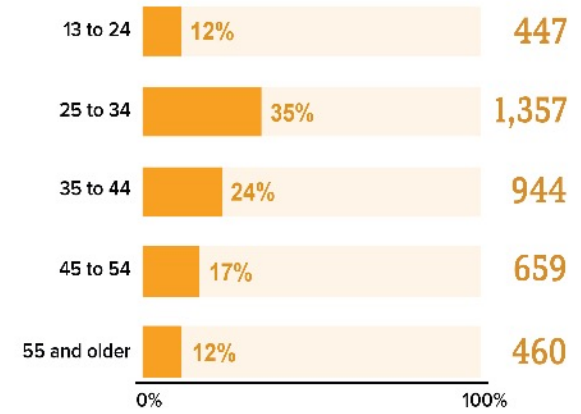
Outbreaks have been linked to IDU in Indiana, West Virginia, Massachusetts, Florida, and Washington State.

10% of new cases remain IDU-related and the opioid crisis – driven by illicitly manufactured fentanyl that requires frequent injection

Proportion of new human immunodeficiency virus (HIV) cases attributed to injection drug use (IDU) has declined overall.

New HIV Diagnoses Among People Who Inject Drugs in the US and Dependent Areas by Age, 2018*

People aged 13 to 34 made up nearly half of all new HIV diagnoses among people who inject drugs.



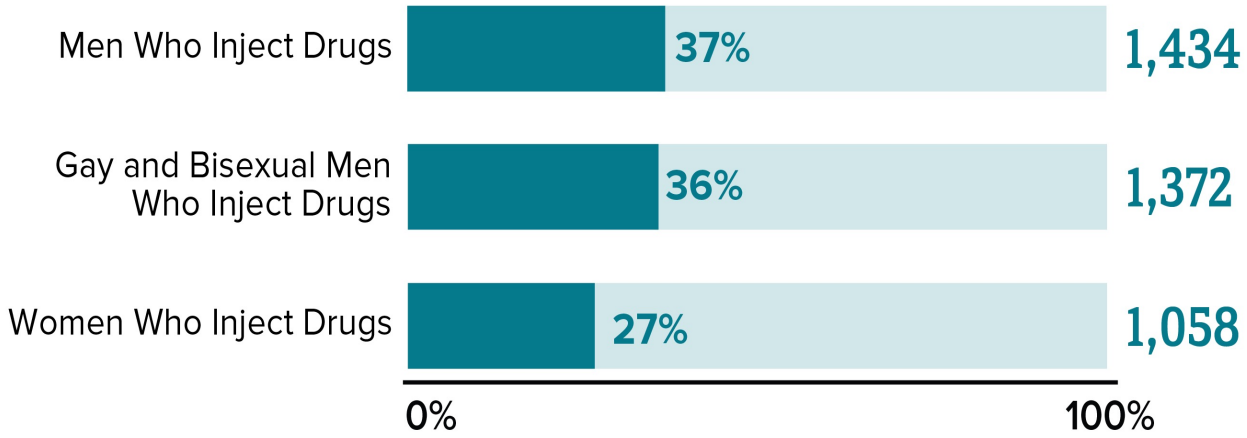
The numbers have been statistically adjusted to account for missing transmission categories. Values may not equal the total number of PWID who received an HIV diagnosis in 2018.

* Includes infections attributed to male-to-male sexual contact *and* injection drug use (men who reported both risk factors).

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

New HIV Diagnoses Among People Who Inject Drugs in the US and Dependent Areas by Sex, 2018*

Among people who inject drugs, most new HIV diagnoses were among men.



* Based on sex assigned at birth and includes transgender people.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

The Effect of COVID-19 on HCV[1-3]

30% Increase in drug overdose deaths between December 2019 and December 2020; United States eclipsed 100,000 in November 2021

73% Reduction in HCV screening/testing reported by local health departments[a]

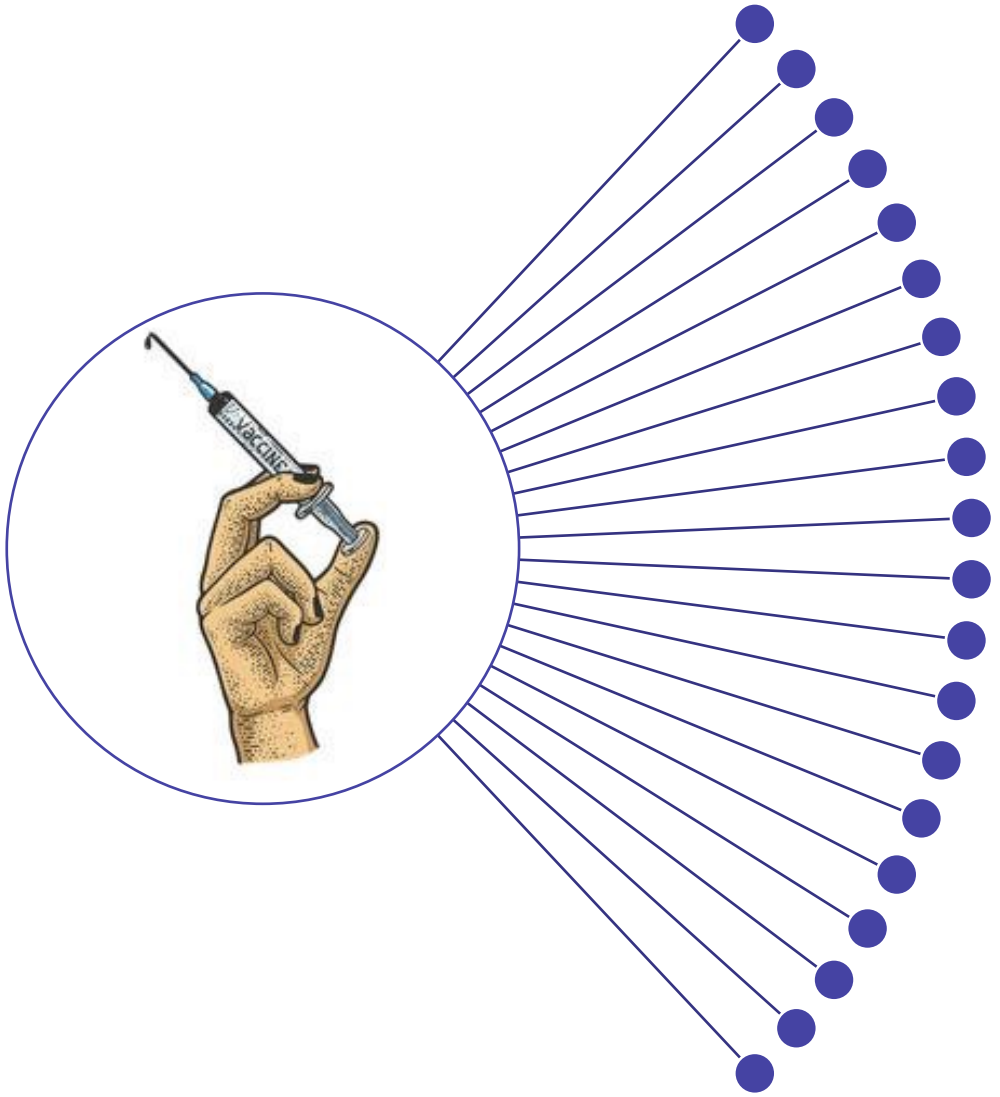
22% Decrease in HCV treatment occurred from 2019 to 2020[b]

[a] Represents percentage of local health departments offering the service. [b] Data do not include Department of Corrections and Veterans Affairs

1. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. 2. https://hepvu.org/state-of-viral-hepatitis-during-covid-19/.
3. IMS Monthly Data (Week of January 4, 2019 through January 1, 2021).

Treatment As Prevention

Left untreated,
one active injector
potentially will **infect up to 20 others** with HCV within the first 3 years of diagnosis[1,2]



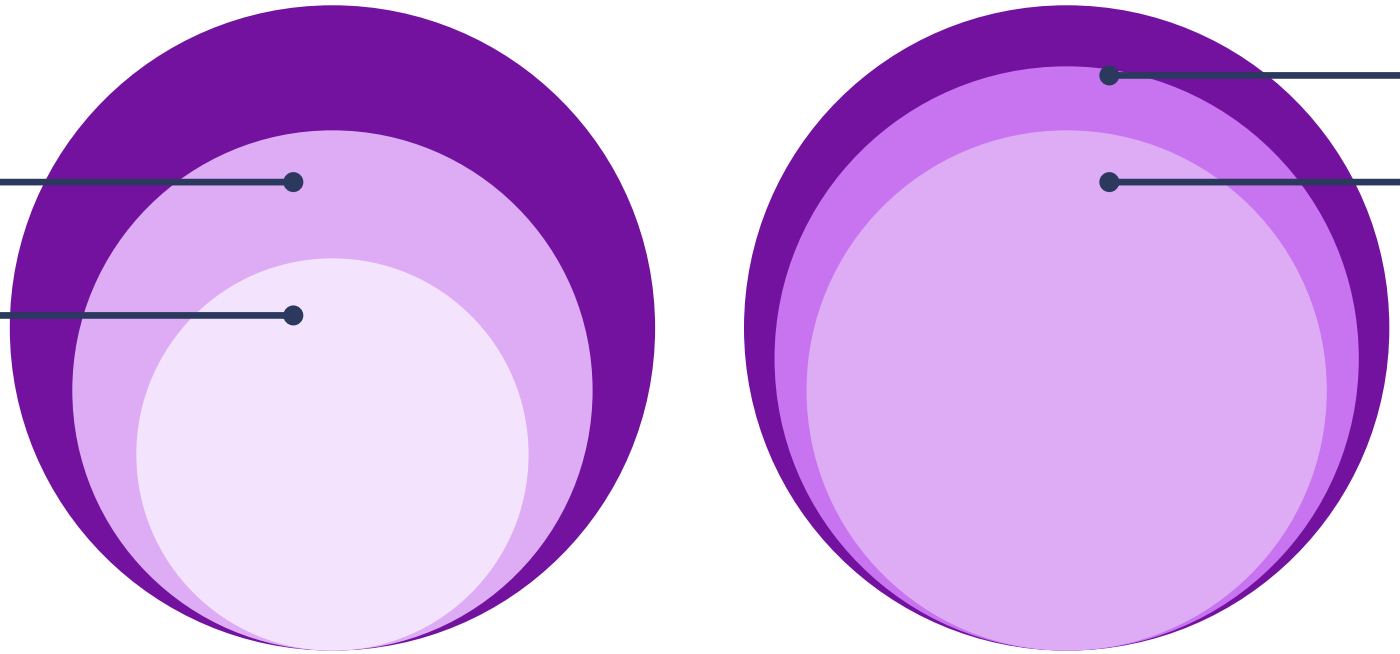
1. NIH National Institute on Drug Abuse. Heroin Research Report. Updated June 2021. Accessed November 2, 2021. https://www.drugabuse.gov/download/37596/heroin-research-report.pdf 2. NIH National Institute on Drug Abuse. Viral Hepatitis—A Very Real Consequence of Substance Use. Updated August 3, 2020. Accessed November 9, 2021. https://www.drugabuse.gov/drug-topics/viral-hepatitis-very-real-consequence-substance-use

WHO Elimination Target

The WHO has developed set targets relative to 2015 benchmark levels with the goal of eliminating HCV as a public threat by 2030:

Reducing new HCV infections by **80%**

Reducing HCV-related deaths by **65%**

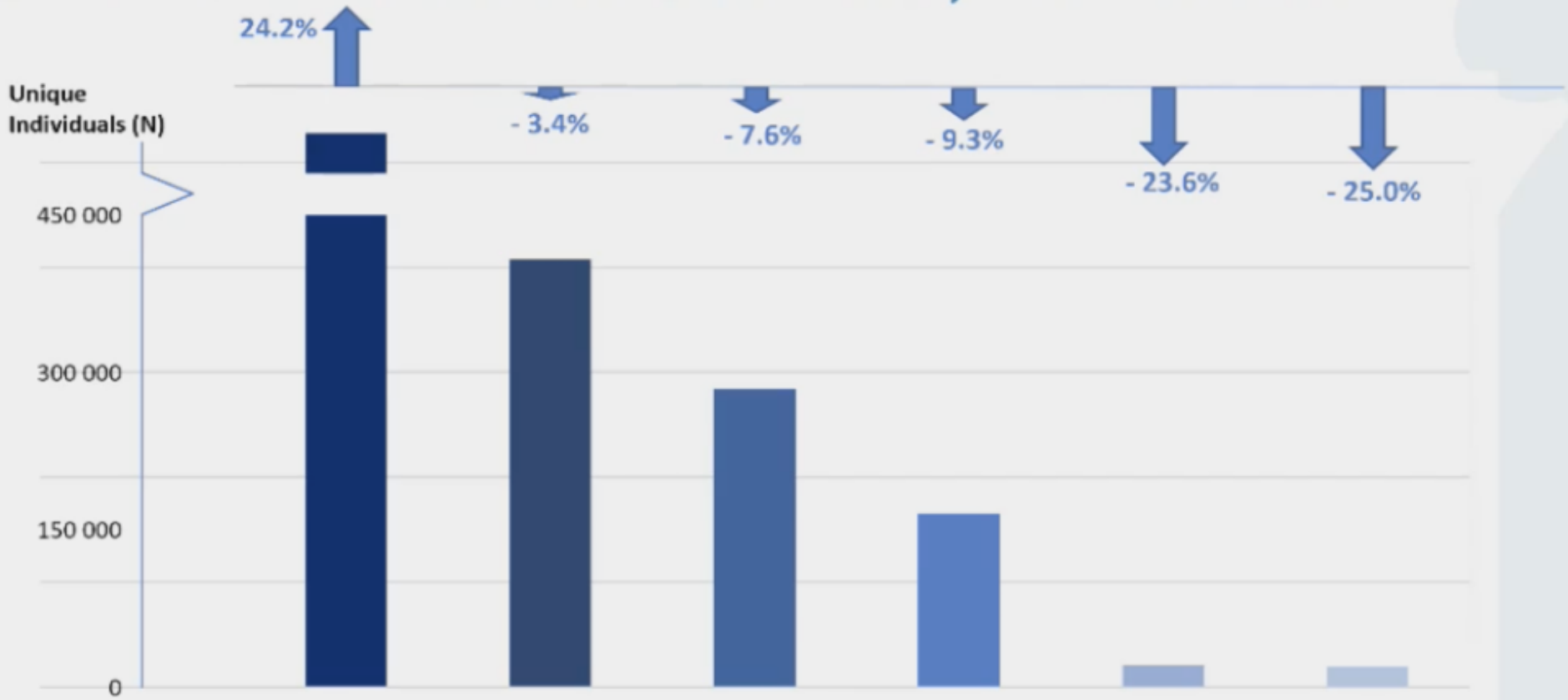


90% **Diagnosing** of the HCV-infected population

80% **Treating** of the eligible population

World Health Organization. Global health sector strategy on viral hepatitis, 2016–2020. WHO REFERENCE NUMBER: WHO/HIV/2016.06

Changes in HCV Treatment and Cure, 2021 vs 2019



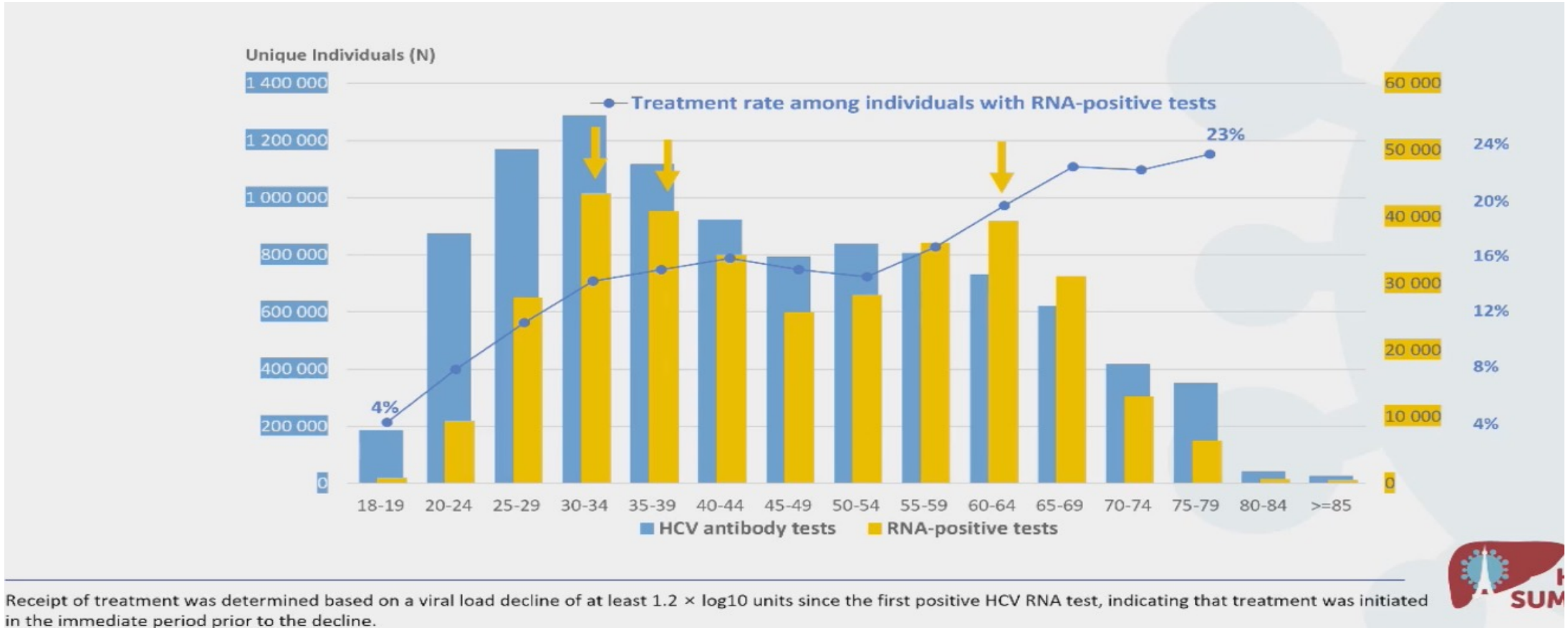
	HCV Ab tested	HCV Ab+	HCV RNA	HCV RNA+	Treated	Cured
Frequency (2021)	10,167,524	407,795	284,220	165,142	21,136	19,584
Proportion	100.0%	4.0% of Ab tested	100.0%	58.1% of RNA tested	12.8% of RNA+	92.7%* of treated

Figure is only showing HCV RNA tested, RNA+, treated (among those tested RNA+ in 2021), and cured individuals who had an Ab+ test in 2021.
HCV Treated and cured individuals were identified using validated imputation algorithms.
*Cure rate may be underestimated because patients diagnosed toward the end of 2021 may not have enough follow-up data to predict treatment initiation and cure.

GLOBAL HEPATITIS SUMMIT 2023

Hepatitis C Care Cascade and Progress Toward Elimination in the United States, 2021, Ward et al; Global Hepatitis Summit 2023

Age Distribution for Individuals with HCV Antibody Screening and RNA-Positive Tests Among Adults in the US in 2021



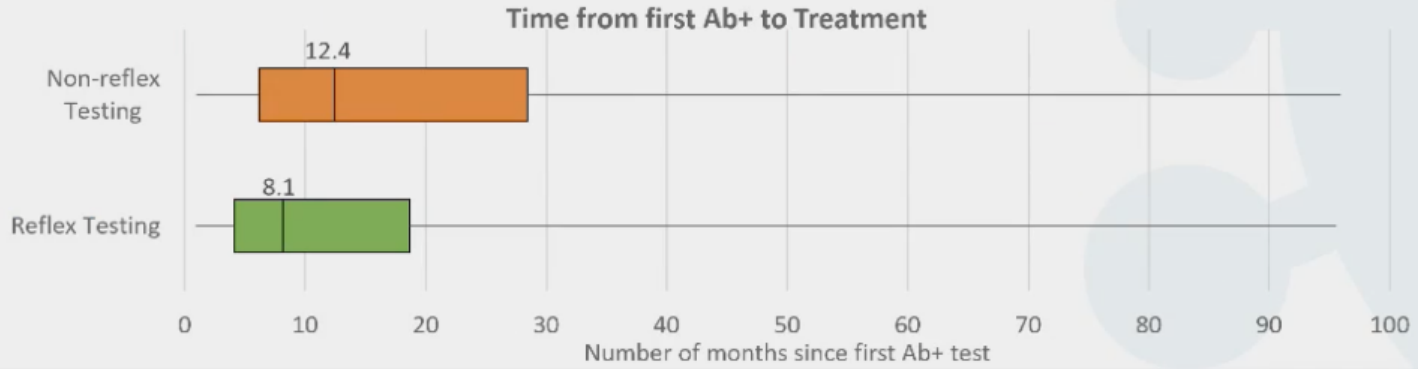
Receipt of treatment was determined based on a viral load decline of at least 1.2 × log10 units since the first positive HCV RNA test, indicating that treatment was initiated in the immediate period prior to the decline.

Hepatitis C Care Cascade and Progress Toward Elimination in the United States, 2021, Ward et al; Global Hepatitis Summit 2023

Association of Reflex Testing and Receipt of HCV Treatment, 2014-2021

- Received HCV treatment
  - 30% among persons having reflex HCV RNA testing
  - 8% among persons for whom HCV Ab and RNA testing were ordered separately

- Median time from first HCV Ab+ test to treatment
  - 8.1 mos. median, 14.5 mos. mean among persons having reflex HCV RNA
  - 12.4 mos. median, 19.9 mos. mean HCV Ab and RNA testing ordered separately



*Percent treated for individuals for whom Ab and RNA testing were ordered separately may be underestimated due to inclusion of those who may not have a confirmed RNA+ test result. Reflex testing (HCV Antibody with reflex to RNA test) was identified by matching the test date (date the specimen was drawn) of the Antibody test with that of the RNA test. Reflex testing analyses are only available with data from one large US national laboratory.
Receipt of treatment was determined based on a viral load decline of at least 1.2 × log10 units since the first positive HCV RNA test, indicating that treatment was initiated in the immediate period prior to the decline. Time to treatment analysis was limited to individuals with an Ab+ test at least 28 days prior to the viral load decline.

GLOBAL HEPATITIS SUMMIT 2023

Hepatitis C Care Cascade and Progress Toward Elimination in the United States, 2021, Ward et al; Global Hepatitis Summit 2023

Barriers to HCV Treatment Uptake

Systemic

- Lack of insurance
- Lack of provision of services
- PA process complicated
- Transportation

Patient

- Fear of side effects, stigmatization
- Mistrust of health care system
- IFN “PTSD”
- Lack of HCV-related knowledge / perceived need for treatment / lack of symptoms

Provider

- Concerns regarding adherence, reinfection
- Discomfort with coexisting mental health diagnoses or active drug use
- Lack of HCV Tx knowledge

Progress Toward HCV Elimination in the United States[1]

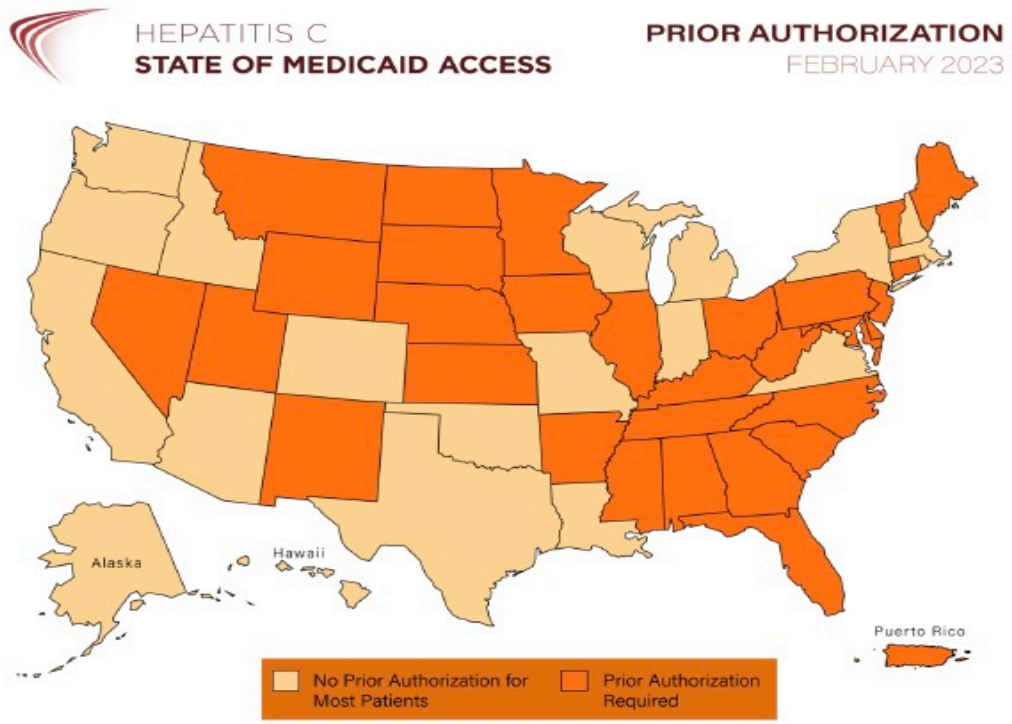
Only 3 states (6%) are on track to achieve elimination **by 2030**

18 states (35%) are not expected to meet these targets before **2040**

Nine states (17%)

Had treatment restrictions based on liver fibrosis severity in 2017 and none of these states were expected to achieve HCV elimination by 2030

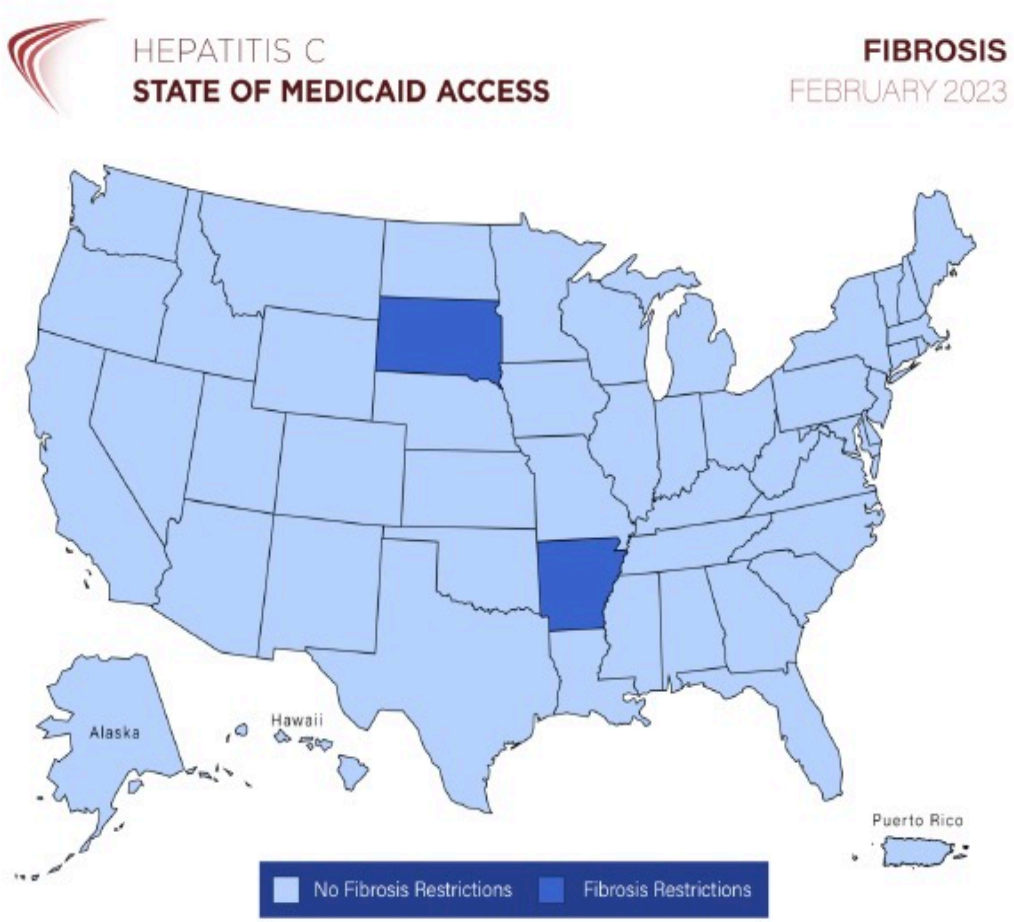
Current Hepatitis C Treatment Restrictions for Medicaid, 2023



No Prior Authorization for Most Patients (21): Alaska, Arizona, California, Colorado, DC, Hawaii, Idaho, Indiana, Louisiana, Massachusetts, Michigan, Missouri, New Hampshire, New York, Oklahoma, Oregon, Rhode Island, Texas, Virginia, Washington, Wisconsin

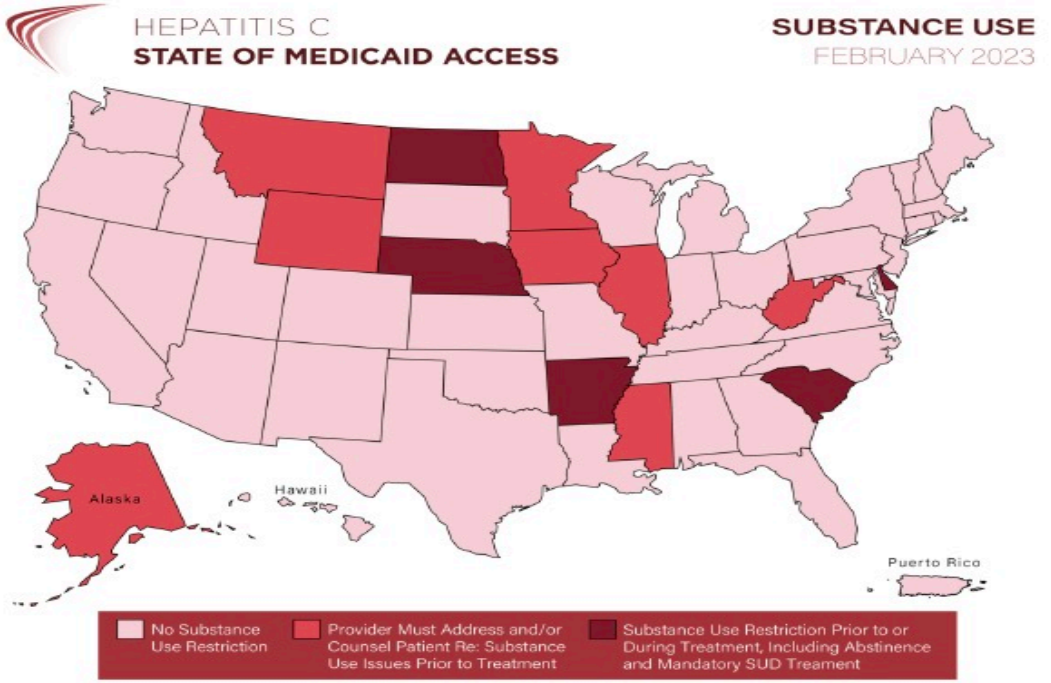
Prior Authorization Required (31): Alabama, Arkansas, Connecticut, Delaware, Florida, Georgia, Illinois, Iowa, Kansas, Kentucky, Maine, Maryland, Minnesota, Mississippi, Montana, Nebraska, Nevada, New Jersey, New Mexico, North Carolina, North Dakota, Ohio, Pennsylvania, Puerto Rico, South Carolina, South Dakota, Tennessee, Utah, Vermont, West Virginia, Wyoming

Citation: Center for Health Law and Policy Innovation & National Viral Hepatitis Roundtable, Hepatitis C: State of Medicaid Access



No Fibrosis Restrictions (50):
Alabama, Alaska, Arizona, California, Colorado, Connecticut, DC, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming

Fibrosis Restrictions (2):
Arkansas, South Dakota



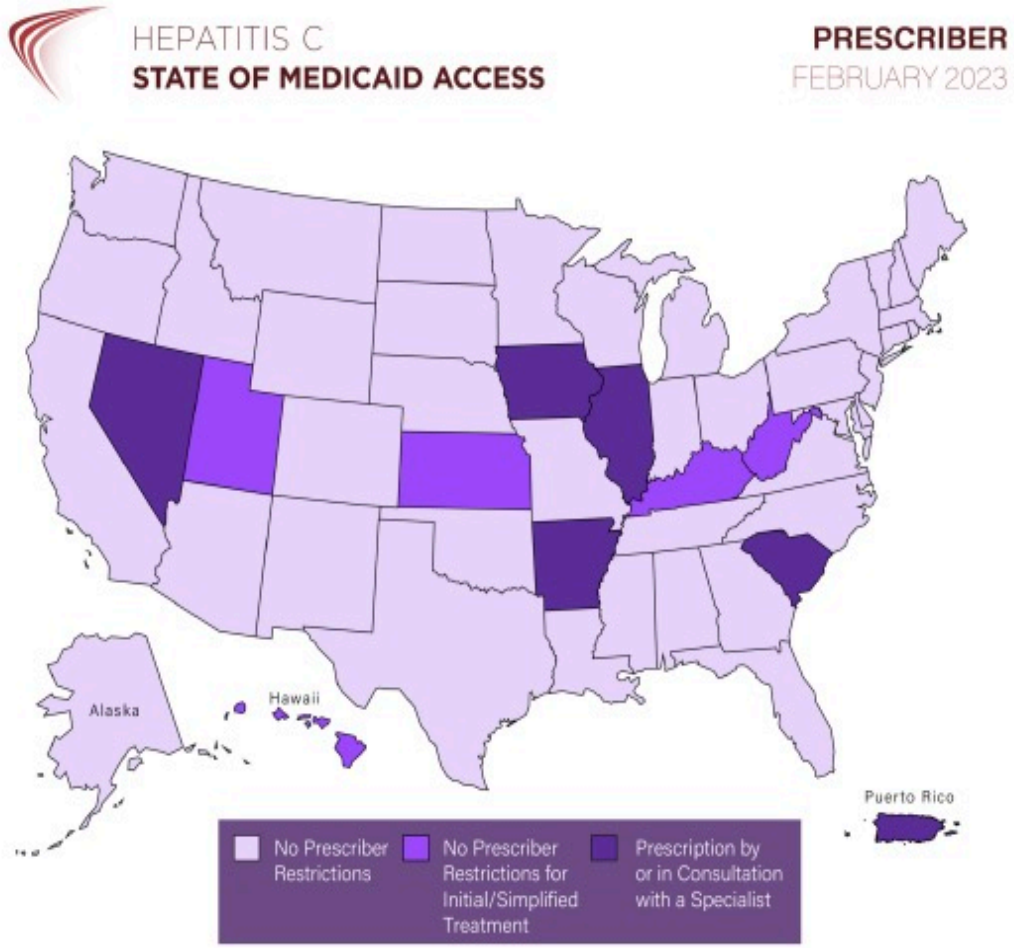
No Substance Use Restriction (39): Alabama, Arizona, California, Colorado, Connecticut, DC, Florida, Georgia, Hawaii, Idaho, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, Wyoming

Provider Must Address and/or Counsel Patient About Substance Use Issues Prior to Treatment (8): Alaska, Illinois, Iowa, Minnesota, Mississippi, Montana, West Virginia, Wisconsin

Substance Use Restriction Prior to or During Treatment, Including Abstinence and Mandatory SUD Treatment (5): Arkansas, Delaware, Nebraska, North Dakota, South Carolina

Citation: Center for Health Law and Policy Innovation & National Viral Hepatitis Roundtable, Hepatitis C: State of Medicaid Access (2023), www.stateofhepc.org

PRESCRIBER RESTRICTIONS



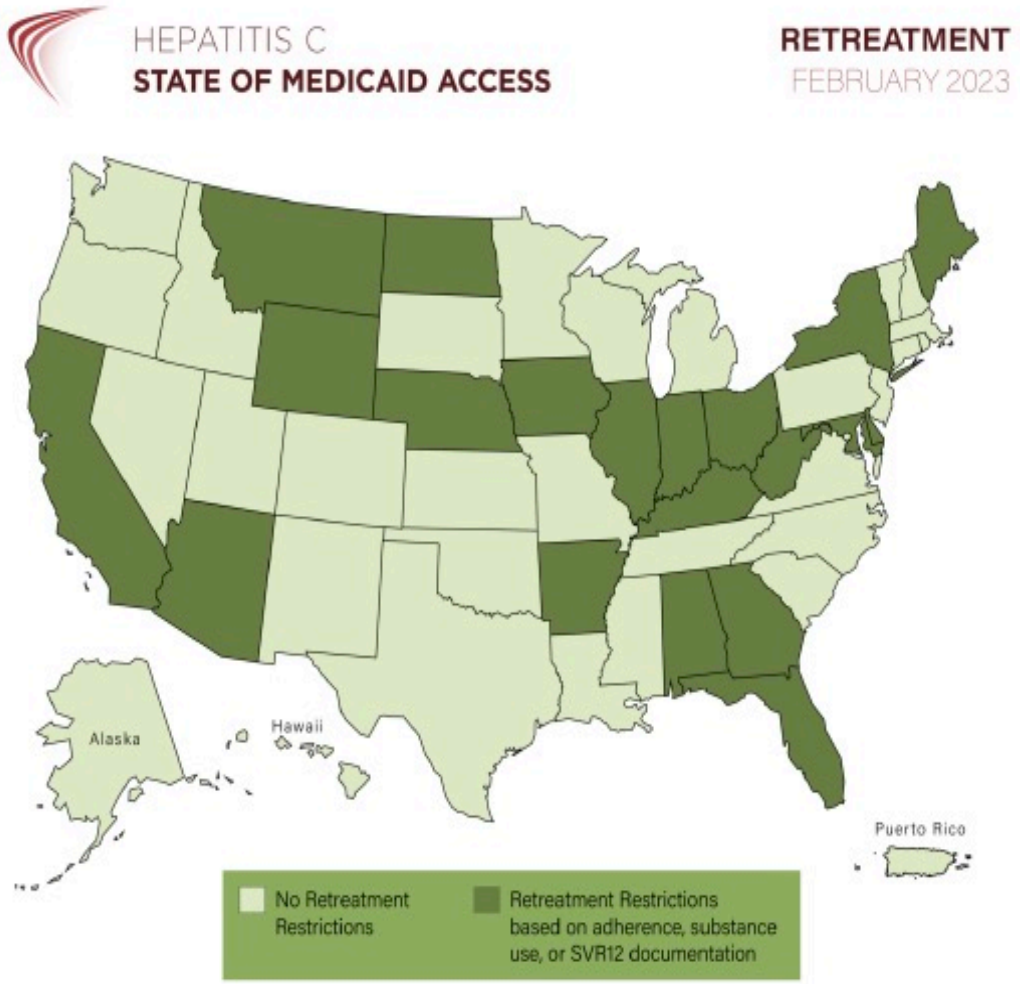
No Prescriber Restrictions (41): Alabama, Alaska, Arizona, California, Colorado, Connecticut, DC, Delaware, Florida, Georgia, Idaho, Indiana, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Dakota, Tennessee, Texas, Vermont, Virginia, Washington, Wisconsin, Wyoming

No Prescriber Restrictions for Initial/Simplified Treatment (5): Hawaii, Kansas, Kentucky, Utah, West Virginia

Prescription by or in Consultation with a Specialist (6): Arkansas, Illinois, Iowa, Nevada, Puerto Rico, South Carolina

Citation: Center for Health Law and Policy Innovation & National Viral Hepatitis Roundtable, Hepatitis C: State of Medicaid Access (2023), www.stateofhepc.org

RETREATMENT RESTRICTIONS



No Retreatment Restrictions (32): Alaska, Colorado Connecticut, DC, Hawaii, Idaho, Kansas, Louisiana, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Washington, Wisconsin

Retreatment Restrictions based on adherence, substance use, or SVR12 documentation (20): Alabama, Arizona, Arkansas, California, Delaware, Florida, Georgia, Illinois, Indiana, Iowa, Kentucky, Maryland, Maine, Montana, Nebraska, New York, North Dakota, Ohio, West Virginia, Wyoming

Citation: Center for Health Law and Policy Innovation & National Viral Hepatitis Roundtable, Hepatitis C: State of Medicaid Access (2023), www.stateofhepc.org

US National HCV Elimination Plan

March 9, 2023

A National Hepatitis C Elimination Program in the United States

A Historic Opportunity

Rachael L. Fleurence, MSc, PhD[1]; Francis S. Collins, MD, PhD[1]

Author Affiliations | Article Information

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Highlights of the White House Plan

Proposed a plan to eliminate hepatitis C in five years in the United States through a mandatory authorization:

1. Supporting the development of point-of-care diagnostic tests to enable a test-to-treat model;
2. Broadening access to curative hepatitis C medications, primarily through a national subscription model; and
3. Expanding infrastructure needed to reach, test, and treat all affected individuals.

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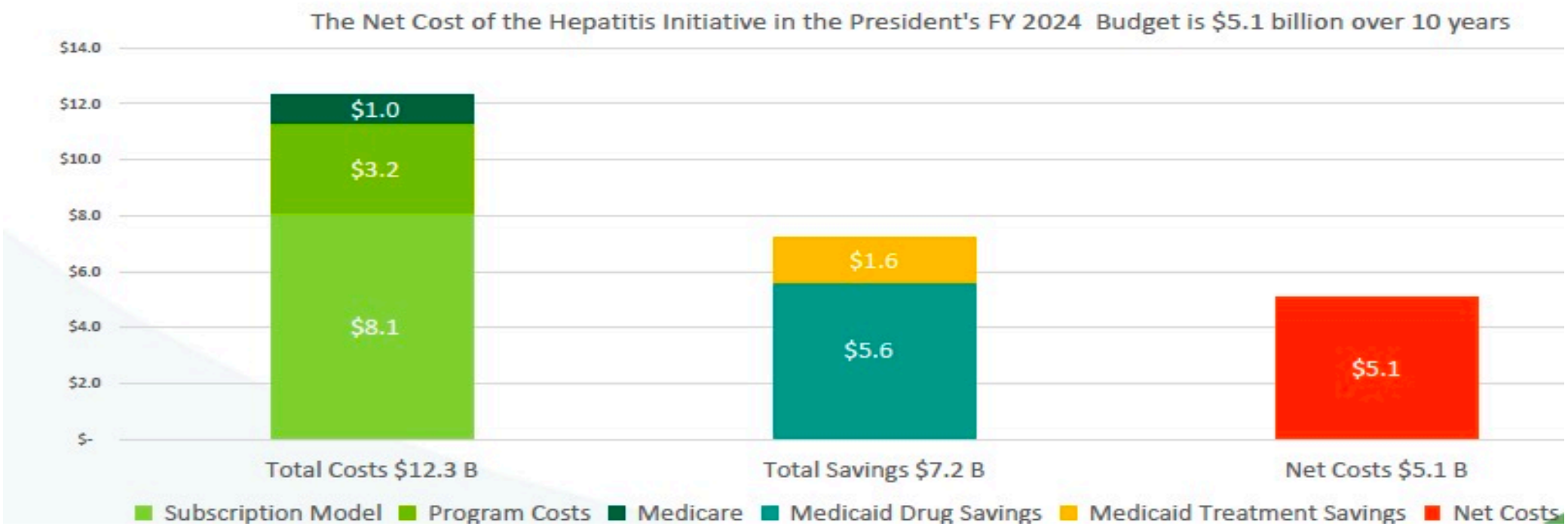
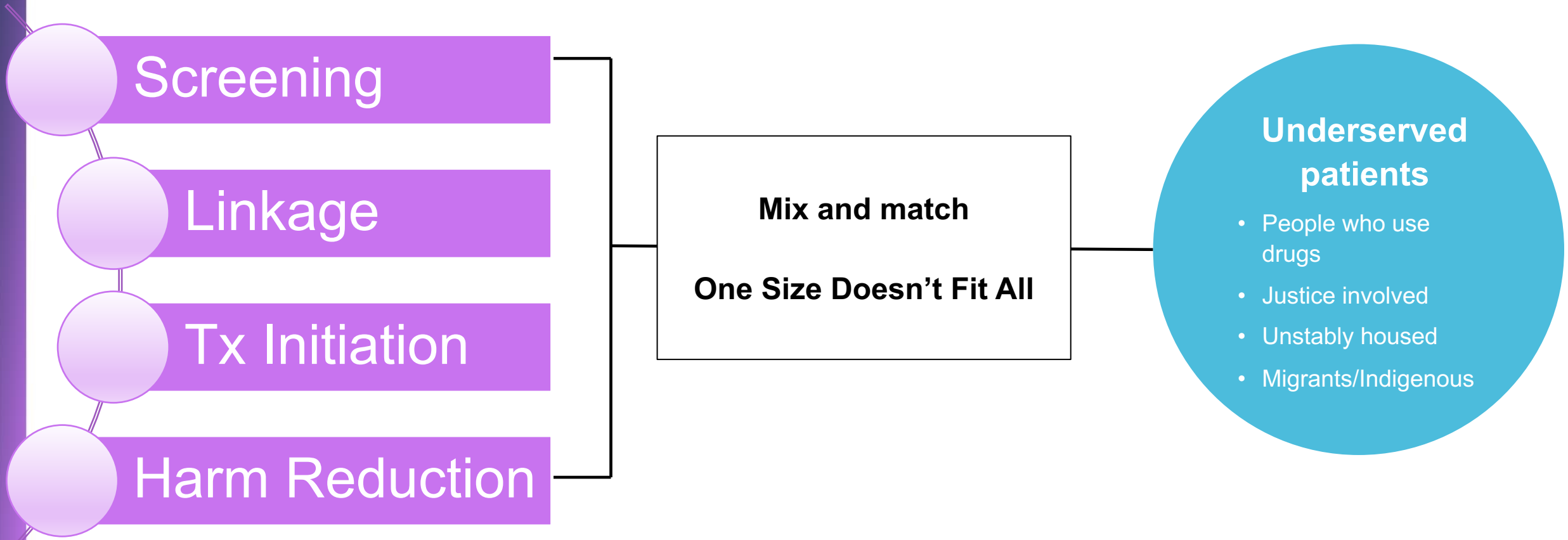
White House Plan Cost Estimate



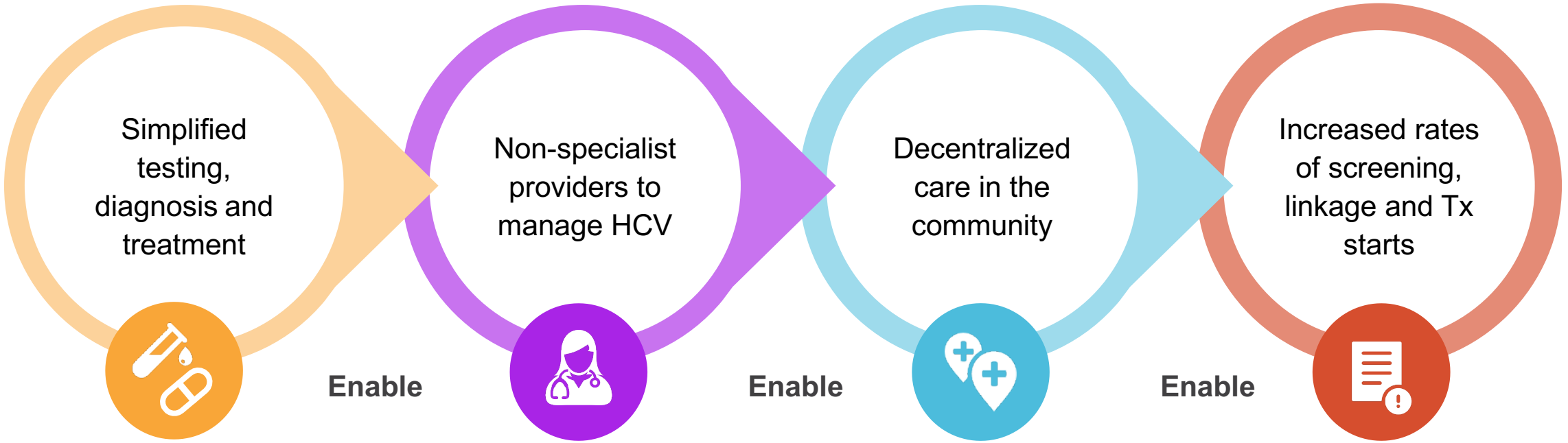
In order to achieve the $7 billion dollar cost savings, need to treat >300,000 patients annually x 5 years
What will an effective program look like?

Pillars For HCV Elimination



What does Simplified Care Delivery Entail?

Simplified Care delivery



Adapted from World Health Organization. *Updated recommendations on simplified service delivery and diagnostics for hepatitis C infection*, 2022.

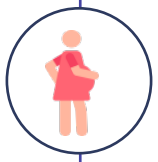
HCV Screening and Initial Evaluation

2020 CDC Recommendations for HCV Screening Among Adults in the United States[1]

Universal screening

Screen at least once in a lifetime for **all adults ≥18 years** (except in settings where HCV RNA-positivity is <0.1%)

Pregnancy

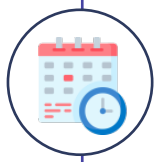


Screen **all pregnant women during each pregnancy** (except in setting where HCV RNA-positivity is <0.1%)

Exposure

One-time testing among people with recognized conditions or exposures, regardless of age or setting prevalence)

Periodic testing



Routine **periodic testing** for people with ongoing risk factors

1. Schillie S, et al. *MMWR Recomm Rep*. 2020;69:1-17.

HCV Simplified Algorithm[1]

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

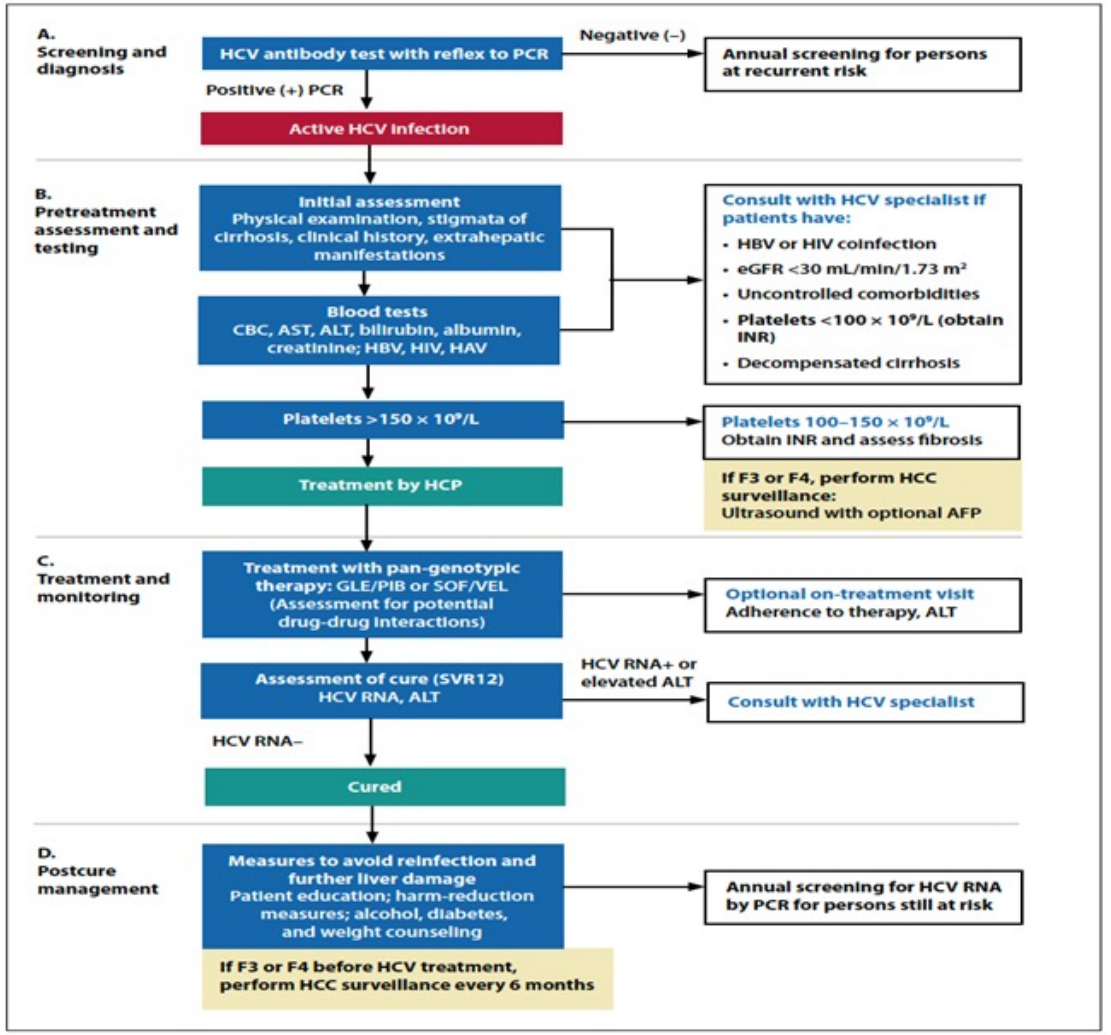
Adults with chronic hepatitis C (any genotype)
who do not have cirrhosis
and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

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

- CBC with diff
- Comprehensive Metabolic Panel
- CBC, CMP, PT/INR
- HCV genotype
- HCV RNA
- HIV serology
- HBV surface antibody (HBV SAb)
- HBV surface antigen (HBV SAg)
- HBV core antibodies
- HAV IgG or total Ab



1. hcvguidelines.org

HBV Assessment

BOXED WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN HCV/HBV COINFECTED PATIENTS

Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with DAAs. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Cases have been reported in patients who are HBsAg positive, in patients with serologic evidence of resolved HBV, and also in patients receiving certain immunosuppressant or chemotherapeutic agents; the risk of HBV reactivation associated with treatment with HCV direct-acting antivirals may be increased in patients taking these other agents. Monitor HCV/HBV coinfected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.

There is a **1.4%** prevalence of HCV/HBV co-infection in the United States[1]

HBsAg anti-HBc anti-HBs	negative negative negative	Susceptible
HBsAg anti-HBc anti-HBs	negative positive positive	Immune due to natural infection
HBsAg anti-HBc anti-HBs	negative negative positive	Immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	Acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	Chronically infected
HBsAg anti-HBc anti-HBs	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

1. Tyson GL, et al. *Hepatology*. 2013;58(2):538-45.

Noninvasive Assessment of Hepatic Fibrosis

AST to Platelet Ratio Index (APRI) Calculator[1]

$$\text{APRI} = \frac{\text{AST level (IU/L)}: 120 \;/\; \text{AST (upper limit of normal; IU/L)}: 40}{\text{Platelet count } (10^9/\text{L}): 100} \times 100 = \mathbf{3.000}$$

FIB-4 Index Calculator[2]

$$\text{FIB-4} = \frac{\text{Age (years)}: 57 \times \text{AST level (IU/L)}: 19}{\text{Platelet count } (10^9/\text{L}): 220 \times \sqrt{\text{ALT (IU/L)}: 16}} = \mathbf{1.23}$$

- Provides information regarding liver stiffness, which correlates with the degree of hepatic fibrosis and also the degree of steatosis[3]
- Does not replace US for HCC surveillance
- Does not diagnose “abnormal LFTs”

1. Wai CT, et al. *Hepatology*. 2003;38(2):518–26; 2. Vallet-Pichard A, et al. *Hepatology*. 2007;46(1):32–6; 3. Sandrin L, et al. *Ultrasound Med Biol*. 2003;29(12):1705-13.

HCV Therapy

When and in Whom to Initiate HCV Therapy[1,a]

Treatment is recommended for *all patients with acute or chronic HCV infection*, except those with a short life expectancy who cannot be remediated by HCV therapy, liver transplantation, or another directed therapy.

Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.

Active substance use, substance use disorders, or injection-drug use are not contraindications to HCV treatment!

[a] Rating: Class I, Level A.

1. https://www.hcvguidelines.org.

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis: Regimens & Monitoring[1]

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

1. https://www.hcvguidelines.org/

Clinical Snapshot of Recommended Regimens or Most People with HCV[1,2]

Agent	Composition	Duration	Dosing	Contraindications
Sofosbuvir/ velpatasvir (± ribavirin) **Geno 1-6**	Sofosbuvir, a HCV nucleotide analog NS5B polymerase inhibitor; velpatasvir, an HCV NS5A inhibitor	12 weeks	1 tablet daily	• Ribavirin combination regimen contraindicated in patients for whom ribavirin is contraindicated.
Glecaprevir/ pibrentasvir **Geno 1-6**	Glecaprevir, a HCV NS3/4A protease inhibitor; pibrentasvir, an HCV NS5A inhibitor	8 weeks	3 tablets dosed once daily with food	• Patients with moderate or severe hepatic impairment (Child-Pugh B or C) or those with any history of prior hepatic decompensation • Coadministration with atazanavir or rifampin

1. https://hcp.epclusa.com/efficacy 2. https://www.mavyret.com/hcp/mavyret-efficacy

Drug-Interaction Potential Between Selected HIV Antiretroviral and Preferred HCV Direct-Acting Antiviral Agents

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Atazanavir + RTV or COBI	x	√	√	x	x
Darunavir + RTV or COBI	x	√	√	x	≈
Lopinavir/ritonavir	x	≈	√	x	x
Doravirine	√	√	√	√	√
Efavirenz	x	x	≈	x	x
Rilpivirine	√	√	√	√	√
Raltegravir	√	√	√	√	√
Elvitegravir/COBI/FTC/TAF	√	√	√	x	√
Dolutegravir	√	√	√	√	√
Bictegravir/FTC/TAF		√	√	√	√
Tenofovir DF	√	≈	≈	√	≈
Tenofovir AF	√	√	√	√	√
Abacavir	√	√	√	√	√
Lamivudine	√	√	√	√	√

No clinically significant interaction expected | Potential weak interaction | Potential interaction | Do not coadminister

HEP Drug Interactions. https://www.hep-druginteractions.org/.

Common Drug-Drug Interactions

SOF/VEL

Avoid

- Amiodarone
- Topotecan
- Carbamazepine, phenytoin, phenobarb, oxcarbazepine
- Rifampin
- Atorvastatin
- St John’s Wort

G/P

Avoid

- Carbamazepine, phenytoin, phenobarb, oxcarbazepine
- Rifampin
- Atorvastatin, lovastatin, simvastatin
- St John’s Wort
- Oral estrogen (for now)

Efficacy Overview of Recommended Regimens for Most People With HCV[1-6]

Sofosbuvir/Velpatasvir

In pivotal clinical trials

98% overall cure rate

in GT 1-6 TN/TE NC/CC adult patients
(n = 1,015/1,035; ASTRAL-1, -2, -3 studies)

Real-world integrated analysis

99% overall cure rate

in effectiveness population in GT 1-6 TN/TE NC/CC patients
(n = 5,141/5,196; pooled analysis of 12 clinical cohorts and studies in Canada, Europe, and the USA, PP)

Glecaprevir/Pibrentasvir

Overall treatment-naïve efficacy

Proven 8-week efficacy in treatment-naïve patients without cirrhosis or with compensated cirrhosis

98% cure rate

(SVR12) based on integrated pooled analysis of GT 1-6 TN, NC, and CC patients across 8 clinical trials that included US study locations (n = 1,218/1,248, ITT)

8-week real-world evidence

Results from two TRIO Health Network studies

99% cure rate

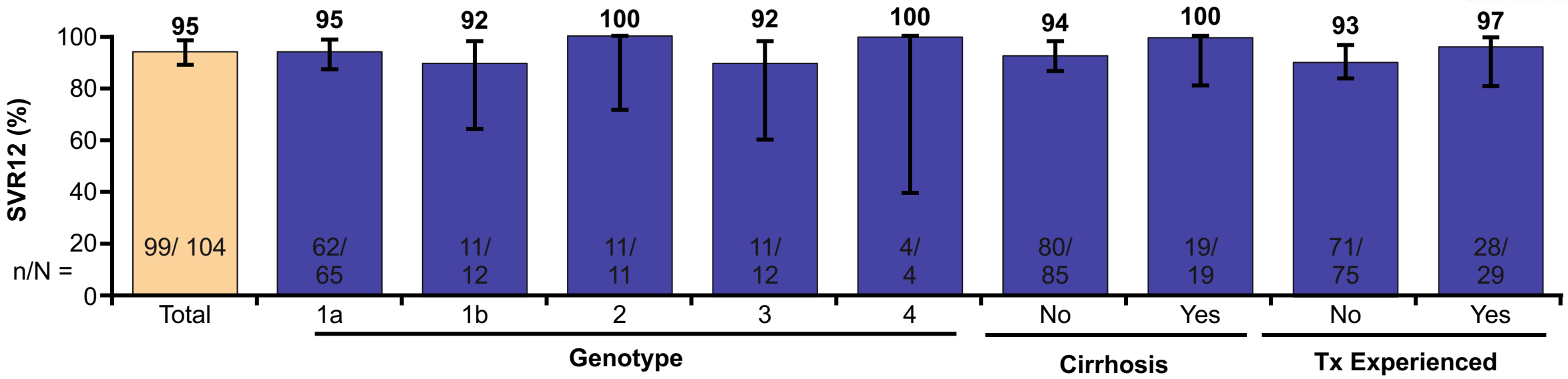
in per protocol population

In GT 1-4 and 6, TN, NC (n = 537/540) and TN, CC (n = 70/71) patients treated for 8 weeks

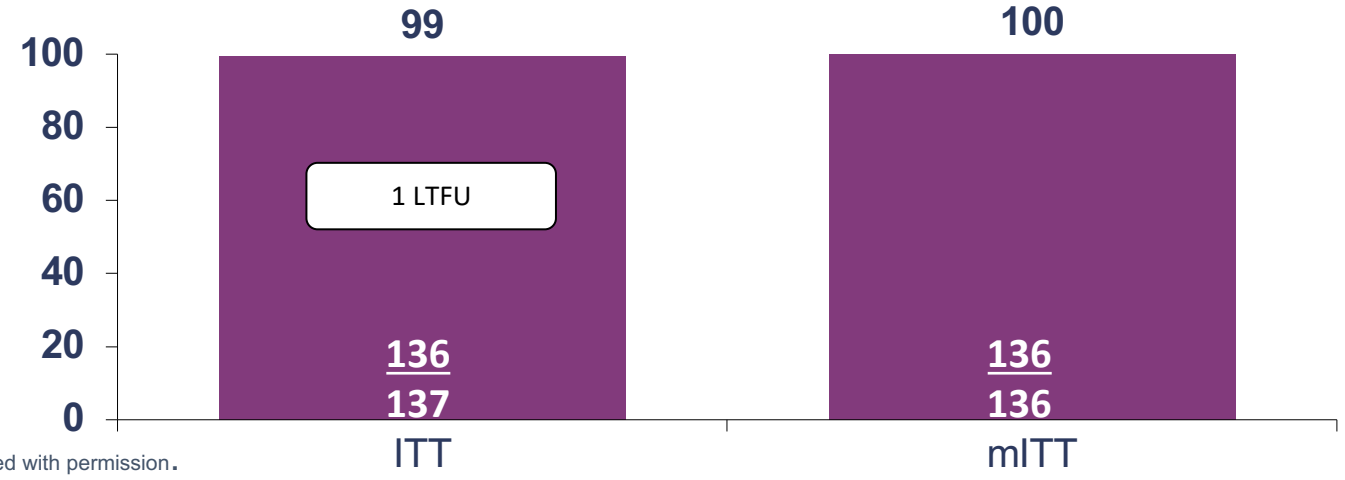
1. Gilead Sciences Canada, Inc. EPCLUSA product monograph. Date of revision: Aug. 8, 2022; 2. Mangia A, et al. *Liver Int*. 2020;40:1841-52;
3. AbbVie Corporation. MAVIRET product monograph. Date of revision: Apr. 7, 2022; 4. Zuckerman E, et al. *Clin Gastroenterol Hepatol*. 2020;18:2544-53;
5. Curry MP, et al. *GastroHep*. 2020;2:64-71; 6. Flamm SL, et al. *Adv Ther*. 2020;37:2267-74.

HIV/HCV Coinfected Individuals Have Similar Cure Rates

Sofosbuvir/Velpatasvir x 12 weeks



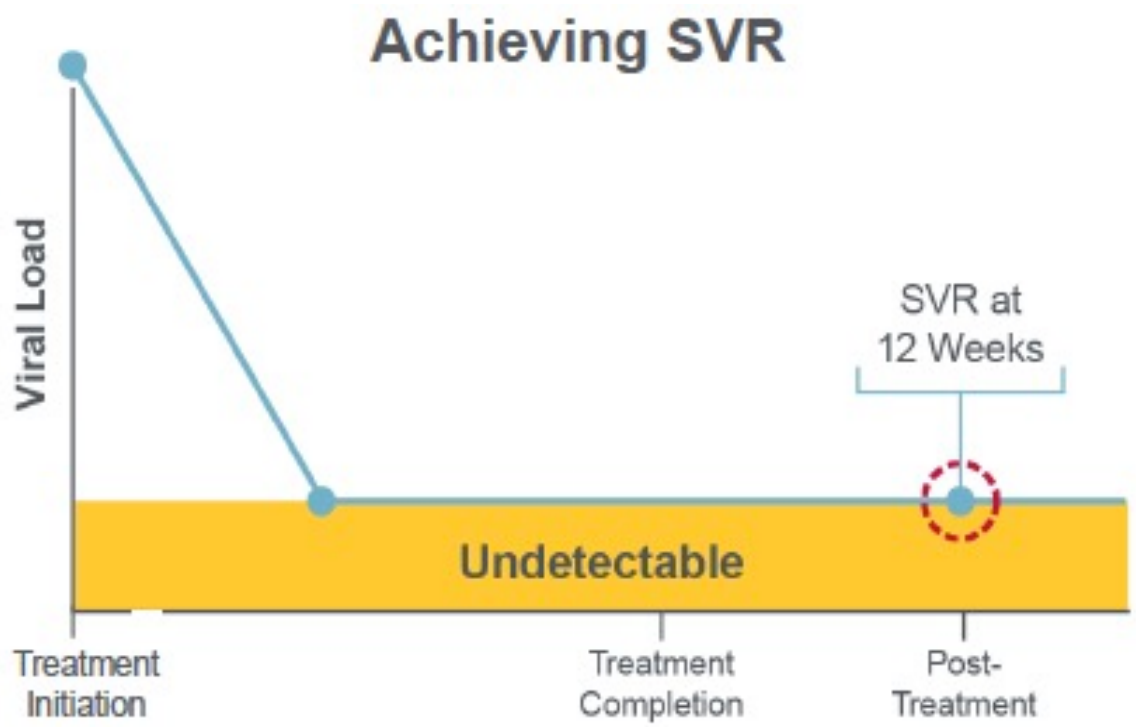
Glecaprevir/Pibrentasvir for 8 weeks



Wyles D, et al. EASL 2016. Abstract PS104. Reproduced with permission.

Post-Treatment Assessment of Cure: Sustained Virologic Response[1]

- Unlike HIV and HBV, HCV is an RNA virus and is curable; do not use words such as “dormant” or “remission”
- Assessment of qualitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm undetectable HCV RNA and transaminase normalization
- Assessment for other causes of liver disease recommended for patients with increased transaminase levels after achieving SVR



1. https://www.hcvguidelines.org.

HCV Care Models for Elimination

Mix-and-Match Approach: Settings, Services, Providers

Settings

- Sexual health clinics
- NSP services
- Substance use clinics
- Primary healthcare/GPs
- Community health centers
- Prisons – State / Federal; Jail

Services

Screening

Confirmed viral load

Treatment

Follow-up

Providers

- Other specialists
- Primary care providers
- Addiction medicine providers
- Nurse Practitioners, Physician Assistants, Pharmacists
- Peer support workers
- Others

Clinical Models to Improve Linkages to HCV/Addiction Care and Treatment Uptake

Conventional referral

- System is difficult to navigate for many
- Transportation
- Need a multidisciplinary approach
- Utilization of case managers
- Peer navigators

Telemedicine

- Useful to deliver services to any setting (prison, rural, substance abuse clinics)
- Provide specialty care where not otherwise available
- Supportive data in both addiction and HCV settings
- Slows cascade

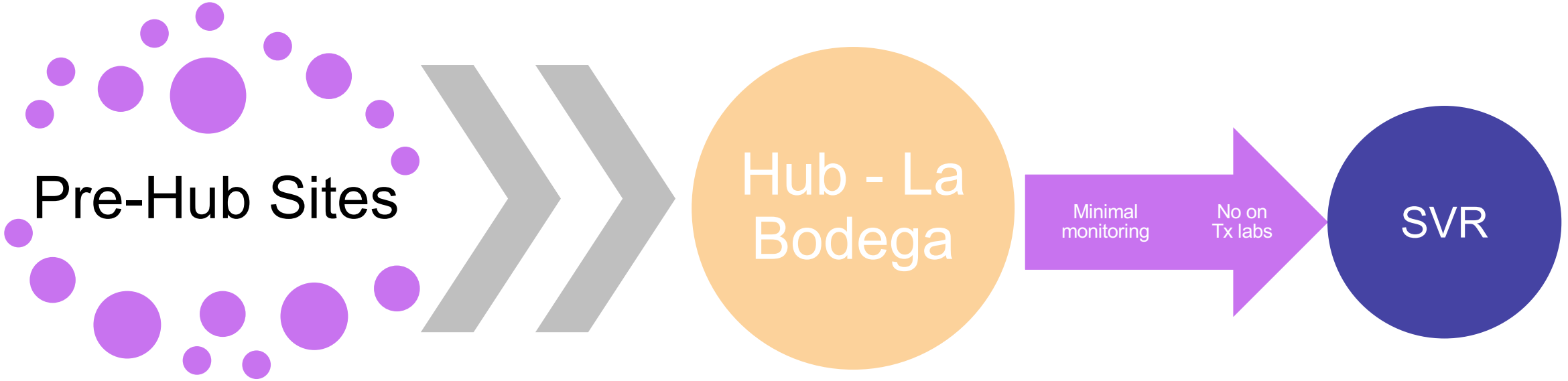
Colocalization

- One-stop shopping
- Multiple services offered in one location
- Minimizes loss to follow-up
- Streamlines care

La Bodega

- Conventional Hepatology
- Conventional Addiction Medicine
- Combined Hep/Addiction

La Bodega Buffalo, NY – Modified rapid start/test and treat model



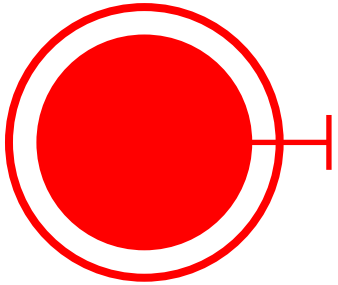
- Community addiction clinics; SEPs
- High Risk OB / Peds (foster care system)
- Prison / Jail
- STI clinics
- ER
- Primary care
- Street Medicine

- Individualized screening protocol: POC AB test; conventional Ab w/PCR reflex
- Single number and email for referral
- Bodega staff schedules / navigates system

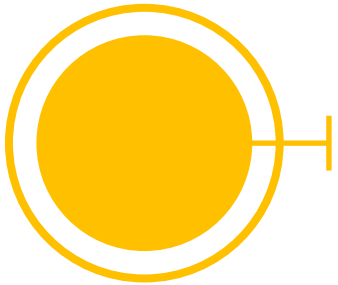
- On-site lab draw
- Colocalized MAT – rapid start
- Immediate HCV Tx
- On-site pharmacy
- Counseling services
- PrEP, HIV, Primary Care

- Staff assists with refills based on triage system – red, yellow, green

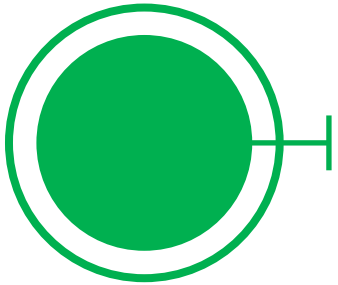
La Bodega Triage System



Full support required – meds delivered to clinic or held at clinic; frequent check-ins and reminders via phone, text, social media



Intermediate support – meds delivered to the patient; Bodega staff tracks refills, deliveries; less frequent check in



Minimal support required – script written, see you in 5-6 months!

La Bodega Buffalo

A hybrid model of outreach, referral, colocalization, and telemedicine, implemented state-wide and nationally

Key success factors of the model
Meets the patients AND the providers where they are.

Facilitating linkage

- Low threshold – no wait time
- Flexible and forgiving schedule
- Eases burden on referring provider
- “Show up and we will see you”

Transportation

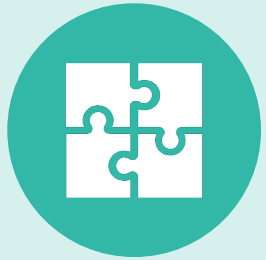
- Arranged immediately if needed
- Public transportation vouchers provided
- Telemed if needed
- Medicaid cabs
- “We go get you”

System navigation

- Appointments and follow-ups made for patients within days
- No formal referral process or labs needed from providers
- “Call this number”

Handpicked, dedicated team

- Multidisciplinary team
- Case manager, counselor, social worker, nurses, PA and secretaries
- No titles / hierarchy



Mix-and-match approach

- Multiple micro-models in place within a global structure, based on local resource availability
- “One size does not fit all”

La Bodega Outcomes (Active PWUD)

Colocalized model, 2014–2020 n = 1133 (Total PWUD 1600)

Regimen	Full adherence	Variable adherence	Treatment failure	SVR
8-weeks Glecaprevir/pibrentasvir (n=403) Sofosbuvir/ledipasvir (n=65)	423 (90.4%)	45 (9.6%)	28 (6.0%)	440 (94.0%)
12-weeks Elbasvir/grazoprevir (n=83) Glecaprevir/pibrentasvir (n=52) Sofosbuvir/ledipasvir (n=189) Sofosbuvir/velpatasvir (n=301) Sofosbuvir/velpatasvir/voxilaprevir (n=40)	607 (91.3%)	58 (8.7%)	40 (6.0%)	625 (94.0%)
		P=0.75		P=0.90

- PWUD had high rates of SVR (94%), high rates of adherence (91%) to HCV treatment, low rates of reinfection (2/1000 PY = 1.4%)
- Adherence and SVR rates were similar with 8- and 12-week therapies
- 8000 visits annually, 80% show rate and 85% rate of retention in care, 100% uptake in OAT initiation

A colocalised, hybrid model of care is an effective and flexible strategy, helping to increase HCV screening and treatment uptake among people with addiction disorders

VARIABLE ADHERENCE TO HCV TREATMENT AMONG PEOPLE WHO INJECT DRUGS TREATED WITH 8 VERSUS 12 WEEKS OF ANTIVIRAL THERAPY RESULTED IN HIGH RATES OF SVR12 AND REINFECTION RATE WAS LOW, The Liver Meeting American Association For The Study Of Liver Disease, Washington, DC, 2022. Abstract # 38479

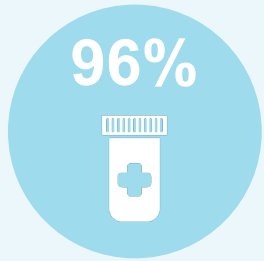
La Bodega Telemedicine Outcomes

Telemedicine among PWID in response to COVID-19, March 2020 – June 2020

visits conducted by **video call or telephone**

of all visits were conducted by **video at the end of Week 2**

patients were seen for an initial HCV evaluation



initiated HCV treatment (n=49)
SVR 100%

Benefits
Facilitates linkage to care; flexibility; good for no-shows

Limitations
Telemedicine can slow down the HCV management cascade from linkage totreatment initiation due to **delays in obtaining lab data**

La Bodega Harm Reduction Measures

Safe Injection tool kit

- Sharps container
- Clean syringes x 10
- Sterile cookers x 3
- Clean water source
- Sterile tie downs
- BandAids
- Alcohol Prep Pad
- Safe Filter material

Harm Reduction kit

- Case Fentanyl Test Strips x 100
- Case worker / Never Use Alone contact info
- FTS x 3 & Instructions
- Safe Injection Tool Kit
- Case Narcan Nasal Spray 4mg x 12
- Sterile tie downs x 5
- Alcohol Prep Pad
- Condoms / lip balm / sanitizer
- Discreet hold all bag

- Uninterrupted MAT/MOUD/OAT
- Ongoing harm reduction education
- Overall retention in care = 90%

La Bodega – Outreach, Education and Advocacy

- HCV mini-residency for Addiction Medicine Providers
- Bodega rotation part of GME curriculum for GI, ID, Addiction med fellows; IM and FM residents; med students
- Implementation of screening (and Tx in collab with family med) for all children of HCV+ moms
- Implementation of universal screening in the foster care system
- Local, state and federal advocacy efforts

Variable Adherence

Adherence is an EVERYONE issue, not unique to PWUD!

Variable Adherence

SOF/VEL - SIMPLIFY prospective in PWID)[1]

- >90% adherence (</= 8 dosages missed) = 96% SVR (69/103)
- <90% adherence (>8 doses missed) = 91% SVR (31/34)

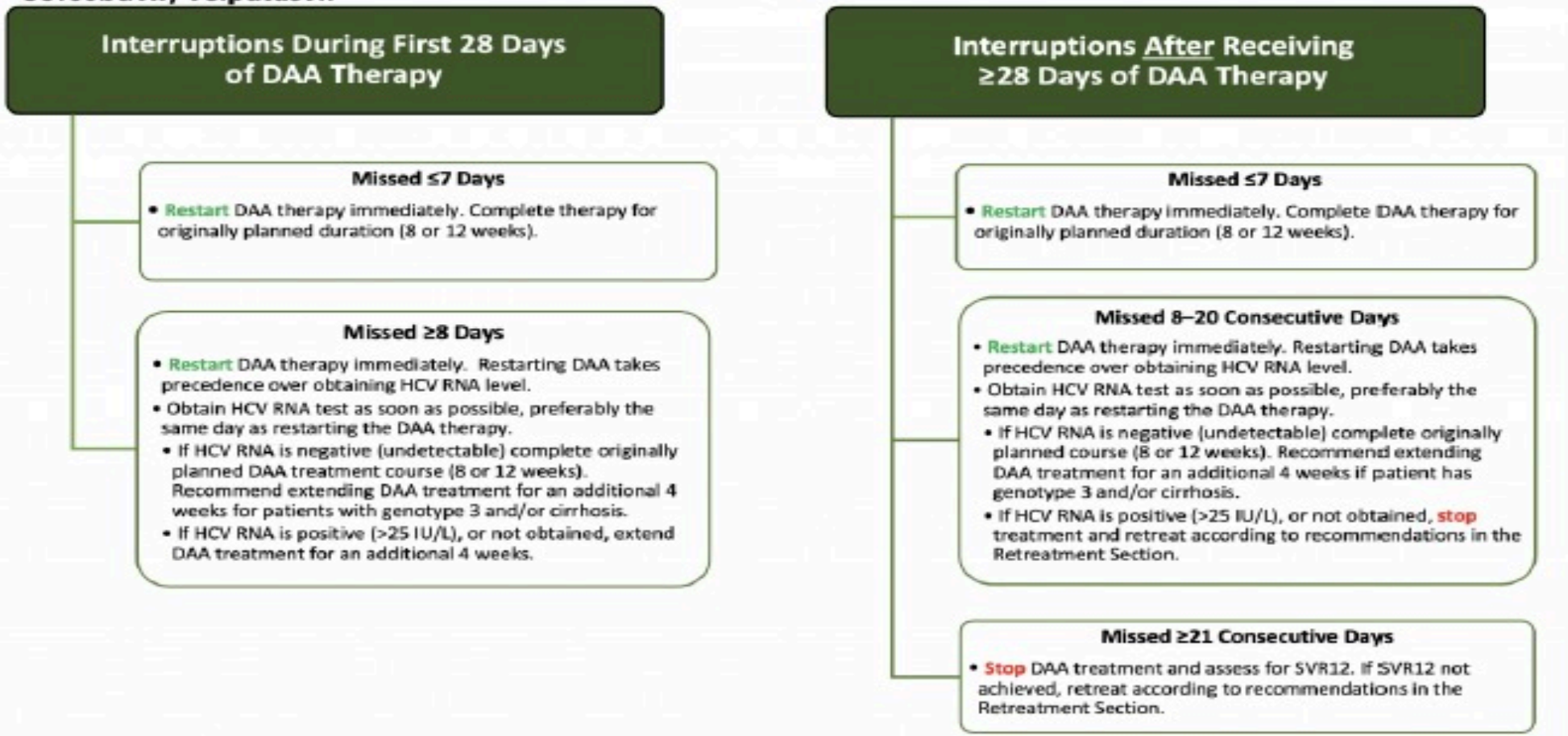
GLE/PIB- retrospective[2]

- Data on 8-week regimen from 10 phase 3 clinical trials
- <90% adherence = 100% SVR (weeks 0-4 n=21/21, weeks 5-8 n=76/76
- >90% adherence = 99% SVR (weeks 0-4 n=1155/1162, weeks 5-8 n=1136/1143)

1. Cunningham EB, et al. *Int J Drug Policy*. 2018; 62:14-23; 2. Zamor PJ, et al. *Am J Gastroenterol*. 2021; 116(9):1896-904.

Management of Missed Dosages

Figure 1. Recommended Management of DAA Treatment Interruptions for Treatment-Naive Patients, Without Cirrhosis or With Compensated Cirrhosis, Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir



DAA, direct-acting antiviral; HCV RNA, hepatitis C virus ribonucleic acid; SVR12, sustained virologic response 12 weeks after end of treatment.

https://www.hcvguidelines.org/evaluate/monitoring

HCV Re-Infection

Hepatitis C reinfection after successful antiviral treatment among people who inject drugs: A meta-analysis

- Thirty-six studies were included (6,311 person-years of follow-up)
- **Overall rate of HCV reinfection was 5.9/100 person-years (95% CI 4.1–8.5) among people with recent drug use (injecting or non-injecting)**
- 6.2/100 person-years (95% CI 4.3–9.0) among people recently injecting drugs
- 3.8/100 person-years (95% CI 2.5–5.8) among those receiving OAT

Stratified analysis

- **1.4/100 person-years (95% CI 0.8–2.6) among people receiving OAT with no recent drug use**
- 5.9/100 person-years (95% CI 4.0–8.6) among people receiving OAT with recent drug use
- 6.6/100 person-years (95% CI 3.4–12.7) among people with recent drug use not receiving OAT

Hajarizadeh B, et al. *J Hepatol*. 2020;72(4):643-57.

HCV Reinfection After Successful DAA Treatment: Analysis of the British Columbia Testers Cohort

- Retrospective analysis of HCV reinfection rates after DAA treatment
- N=7472
- Individuals followed from date of SVR until earliest reinfection, death, or last HCV RNA measurement
- Reinfection defined as a single positive HCV RNA measurement after SVR attained

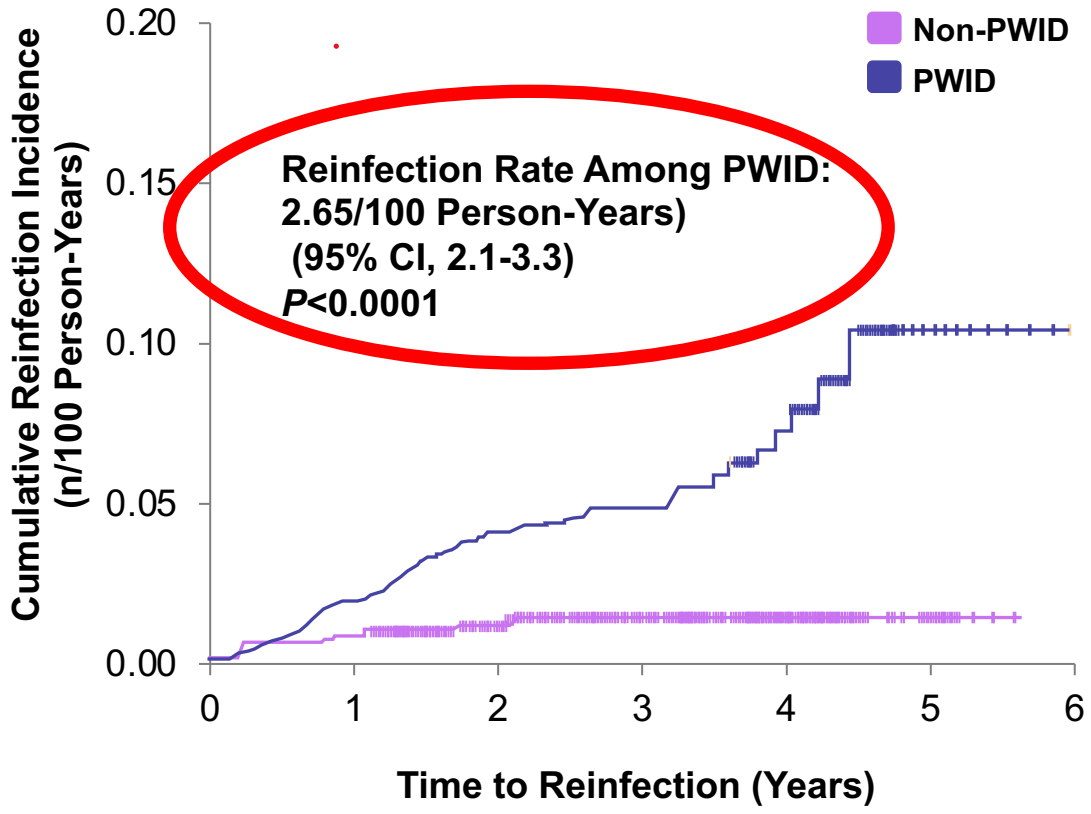
Baseline Characteristics

		PWID	
	Total (n=7472)	Yes (n=2360)	No (N=5112)
Median age (years)	58	54	60
Male (%)	65	65	64
Genotype (%)			
1	69	64	71
2	9	7	10
3	18	25	15
Birth cohort (%)			
<1945	4	1	5
1945-1964	72	57	78
1965-1974	15	26	11
≥1975	9	17	6
Major mental illness (%)	34	64	20
Bipolar disorder	7	17	3
Psychosis	11	28	4
Problematic alcohol use (%)	27	57	14
HIV coinfection (%)	9	20	5

Janjua N, et al. *Hepatology*. 2021;74(1 Suppl):592A-593A. Abstract 967.

HCV Reinfection After Successful DAA Treatment: Analysis of the British Columbia Testers Cohort (Cont'd)

Incidence of HCV Reinfection



Factors Associated With HCV Reinfection*

	Adjusted HR (95% CI)
Age (ref: 50-59), years	
20-29	3.4 (1.2-10.0)
30-39	2.3 (1.3-4.3)
40-49	1.1 (0.6-2.0)
≥60	0.4 (0.2-0.9)
Male (ref: female)	2.2 (1.2-3.8)
Stimulant use (ref: no)	0.8 (0.5-1.4)
Opioid use history (ref: no)	1.8 (1.0-3.1)
Antipsychotic treatment (ref: no)	0.5 (0.3-0.8)
HIV coinfection (ref: no)	1.9 (1.2-3.1)
Benzodiazepine (ref: no)	1.0 (0.4-2.3)

*Multivariate model. Covariates: age, sex, HIV coinfection, injection drug use, alcohol use disorder, and major mental illness.

Janjua N, et al. *Hepatology*. 2021;74(1 Suppl):592A-593A. Abstract 967.

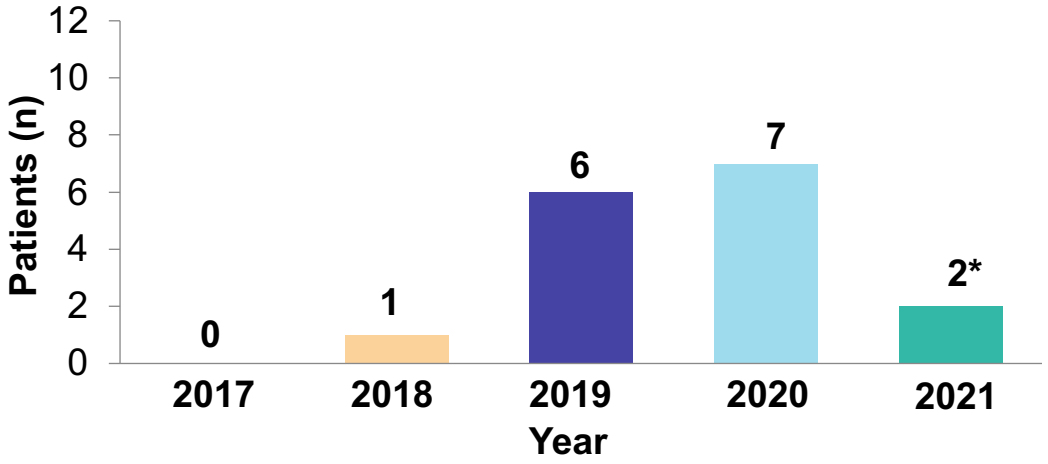
Long-Term Evaluation of HCV Reinfection Rates in Inner City Vulnerable Populations

- Retrospective analysis of longitudinal data from a single center to evaluate HCV reinfection rate among active PWID, January 2017-October 2021
- 16 reinfection events among 350 individuals with documented SVR (4.6%)
- Demographic characteristics among reinfections similar to those of entire cohort except higher rate of being unstably housed

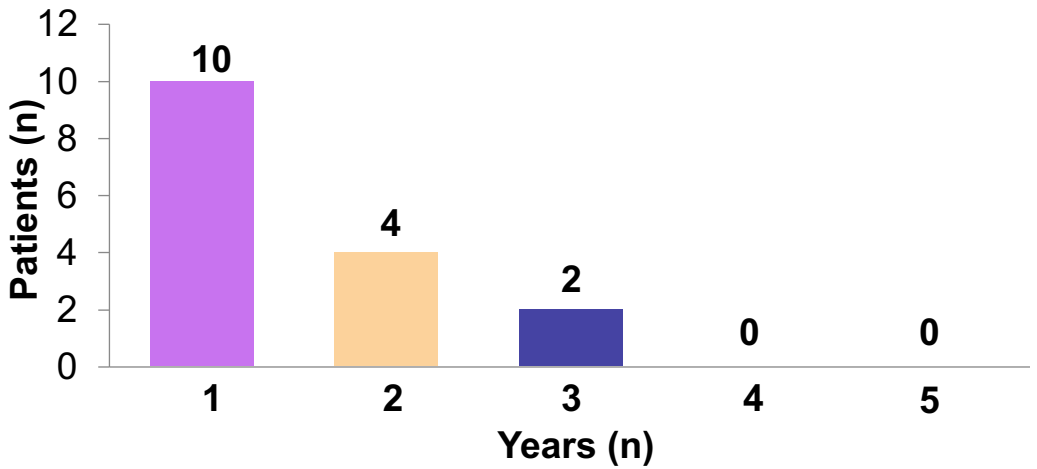
Summary of Reinfections

Years of Follow-Up (n)	Reinfection Events (n)	Individuals in Follow-Up in Time Period (n)	Reinfection Rate (n/100 Person-Years)
0-2	14	350	4.57
≥2	2	336	0.55

Median time to reinfection: 0.62 years



HCV Reinfections by Calendar Year

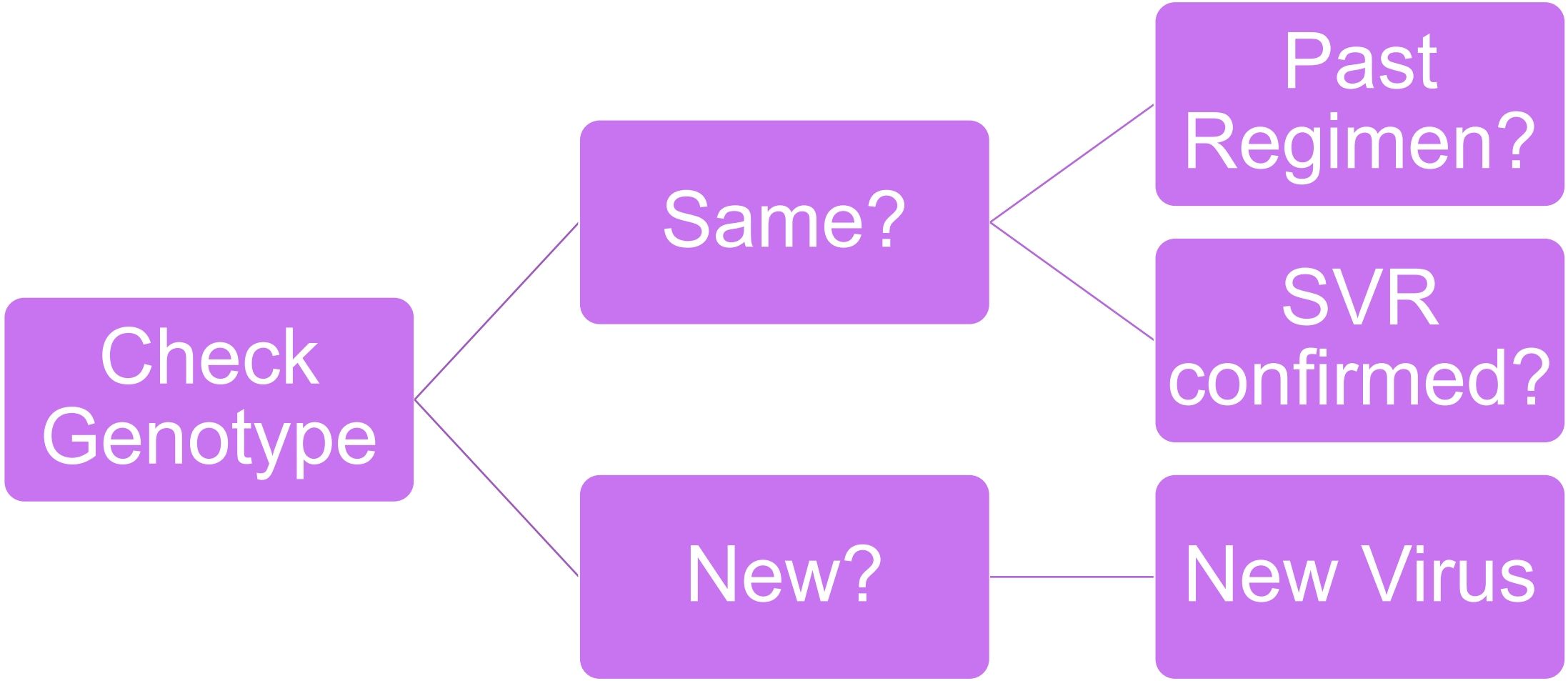


HCV Reinfections by Year of Follow-Up

*Through October 11.

Conway B, et al. *Hepatology*. 2021;74(1 Suppl):594A. Abstract 970.

HCV Re-Treatment



SOF Based Failure

Recommended and alternative regimens listed by evidence level and alphabetically for:

Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)[b]	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) except for NS3/4 protease inhibitor inclusive combination DAA regimen failures[c] • **Not** recommended for genotype 3 infection with sofosbuvir/NS5A inhibitor experience.	16 weeks	I, A

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Genotype 3: Add weight-based ribavirin if cirrhosis is present and there are no contraindications.
[c] This regimen is not recommended for patients with prior exposure to an NS5A inhibitor plus NS3/4 PI regimens (eg. Elbasvir/grazoprevir).

Glecaprevir/Pibrentasvir Treatment Failures

Recommended regimens listed by evidence level and alphabetically for:

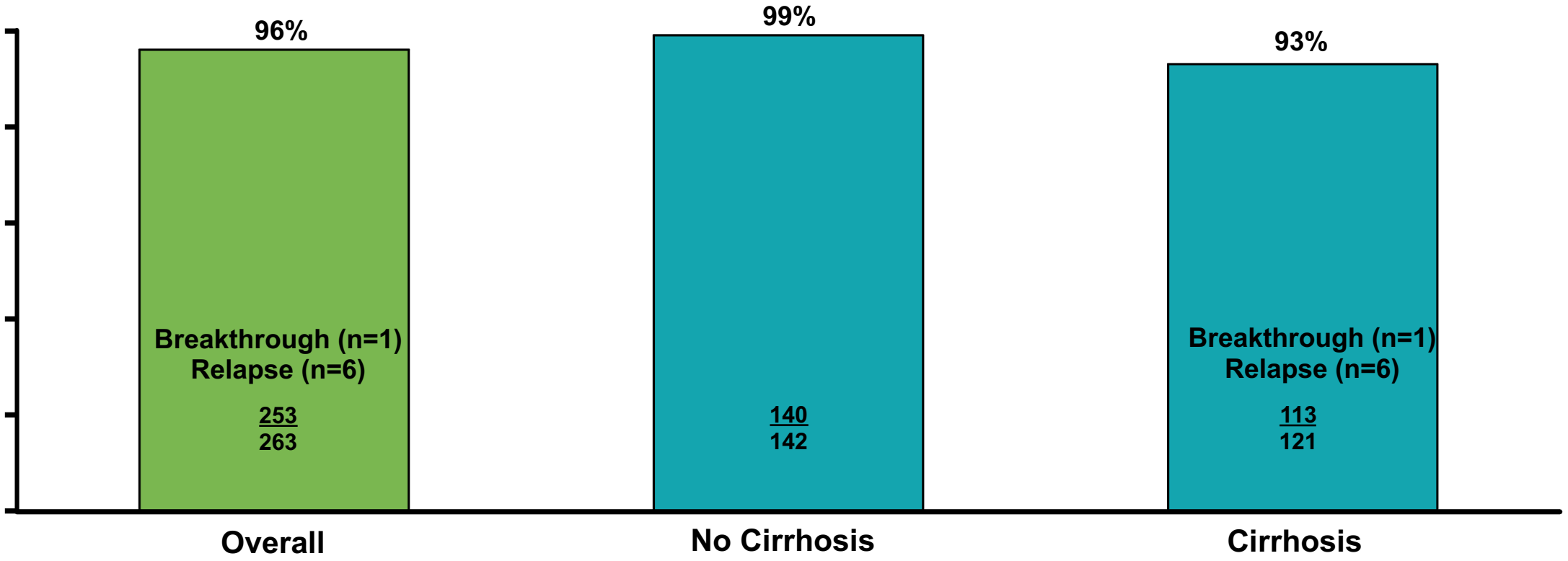
Glecaprevir/Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) plus daily sofosbuvir (400 mg) and weight-based ribavirin	16 weeks	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	IIa, B
For patients with compensated cirrhosis, addition of weight-based ribavirin is recommended.	12 weeks	IIa, C

[a] For decompensated cirrhosis, please refer to the appropriate section.

Overall Cure Rates in NS5A inhibitor – Experienced patients

Sofosbuvir/Velpatasvir/Voxilaprevir (Genotypes 1-6)

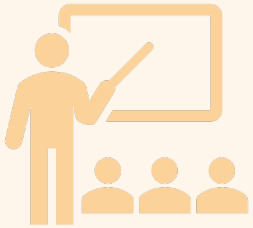


No placebo patients achieved an SVR12.
*P<0.001 for superiority versus pre-specified goal of 85% for sofosbuvir/velpatasvir/voxilaprevir.

Bourlière M, et al. Hepatology. 2016;64(suppl S1):102A. Abstract 194.

Preventing Reinfection

Harm Reduction



Education

Screening

Recommendation for Testing for Reinfection in PWID	
RECOMMENDED	**RATING**
At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated.	IIa, C

American Association for the Study of Liver Diseases–Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Updated: January 21, 2021. Accessed August 10, 2021. www.hcvguidelines.org

Conclusions

Need to eliminate all restrictions- fibrosis, sobriety, provider type, re-Tx and PA process

Need more providers – NP, PA, pharmacists, community health workers etc

Need universal, incentivized screening; POC tests help but need a deployment and reimbursement plan

Reimbursement ability in the addiction setting is a must

To achieve 100% linkage to care and treatment initiation- need a mix-and-match approach, One size won't fit all.

HARM REDUCTION, HARM REDUCTION, HARM REDUCTION

Thank You!

- Angela
- Crystal
- Irish Phil
- Joe B
- Emily
- Scott
- Kath
- Amy
- Cellina
- Stan
- Steve-O
- Steve 2
- Andrea