

Prevention and Treatment of Hepatitis C Infection Among People Who Use Drugs

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Disclosures

Slides adapted from talk developed by Dr. James and Dr. Judith Tsui in collaboration with the Washington State Department of Health.

Session Objectives

- Describe epidemic of hepatitis C (HCV) infection among people who use drugs and importance of treating this population in order to eliminate hepatitis C as a public health threat
- Address common myths about HCV treatment among people use drugs
- Describe key features of a typical treatment course for HCV infection

Outline

- Background
- Changing epidemiology of HCV associated with opioid use epidemic
- Health consequences of chronic HCV
- Health benefits of cure of HCV
- Treatment as prevention for people who use substances
- Basics of HCV treatment
- Screening and prevention of HCV

Which of the following best describes your professional role?

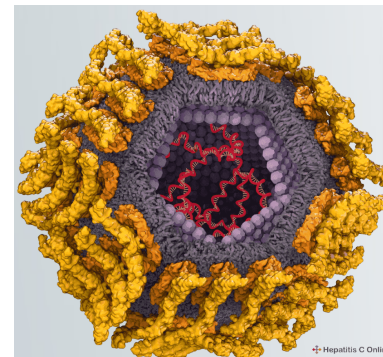
- A. Administrator
- B. Counselor / case worker / social worker
- C. Nurse
- D. Physician or other prescribing provider
- E. Other

Patient Case

- 51 yo woman with opioid use disorder on methadone maintenance, chronic hepatitis C, tobacco use, presenting to establish care. Due to severe L hip pain, her substance use has escalated in the last month. She now muscled heroin and smokes methamphetamine daily.
- She has heard there are great medications for hepatitis C now, but her priority is to get control over her heroin use.
- How would you approach the topic of hepatitis C treatment? What would you recommend? What other information would you most want to know?

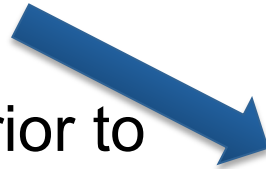
Background and Epidemiology of HCV

- RNA virus identified in 1988
- Most common blood-borne infection in US: 2.4 million chronically infected¹
- 56% aware of infection²
- Not vaccine preventable
- Most people exposed to hepatitis C virus will develop chronic infection



HCV in the US: Routes of Transmission

- **Injection drug use: 60% of cases**
- Blood transfusion prior to 7/1992
- Receipt of solid organ transplantation or factor concentrates made before 1987
- Male-to-male sex
- Body tattoos
- Intranasal cocaine use



Highest risk: sharing needles and syringes

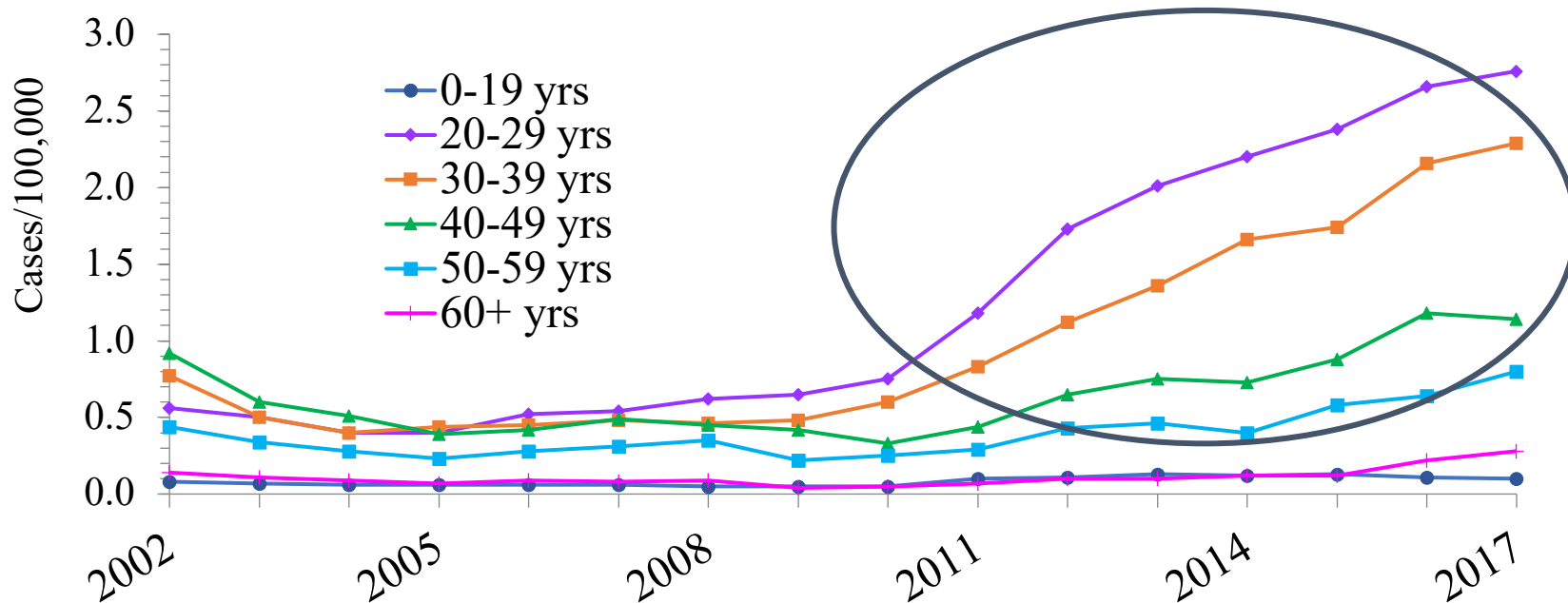
Can also occur with sharing injection paraphernalia such as water, cookers, and cotton filters



Opioid Epidemic and HCV

- **Emerging epidemic** of HCV infections among young people who inject drugs
- Closely related to opioid epidemic

Figure source: modified from hepatitis.cw.edu from Kleven et al, Am J Public Health 2014



Opioid Epidemic and HCV

- Reported acute infections are only the tip of the iceberg

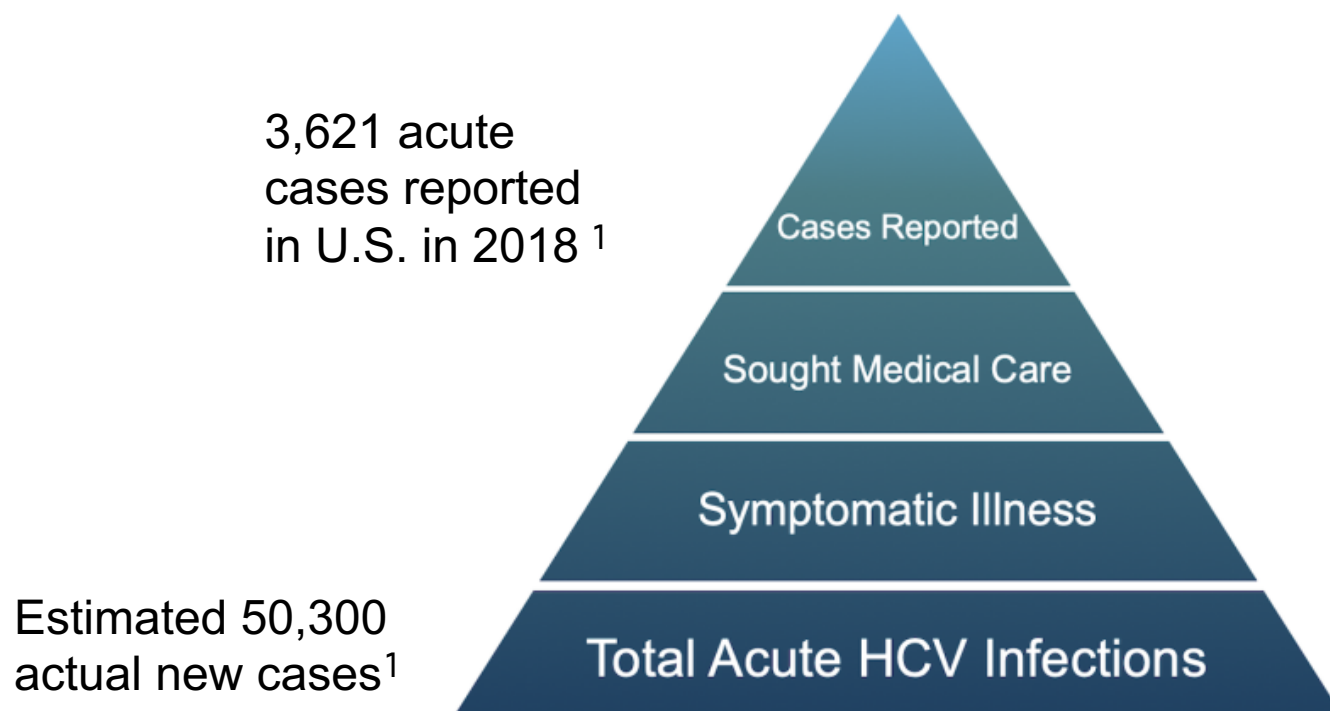
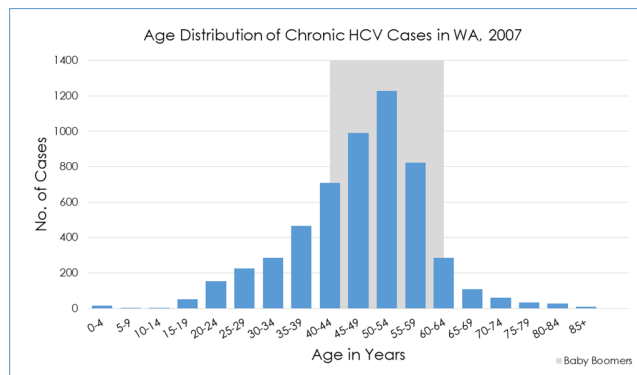


Figure source: modified from hepatitisc.uw.edu from Klevens et al, Am J Public Health 2014. ¹ Centers for Disease Control

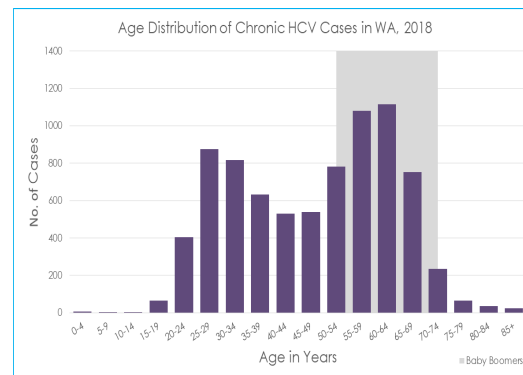
Example from Washington State

- As throughout US, there are now **two epidemics: baby boomers and young people who inject drugs**
- In 2018 there were 118 new reports of acute HCV, the highest in 20 years

Chronic HCV in WA State

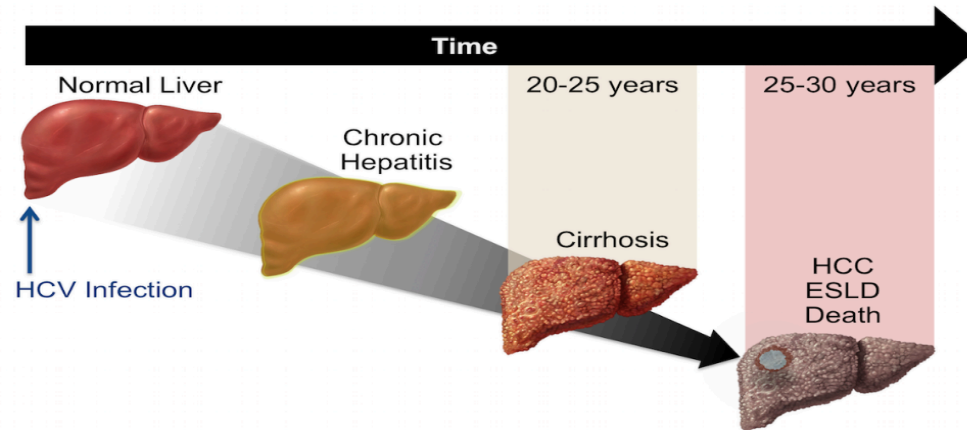


2007



2018

Health Consequences of Chronic HCV



- 15-30% of those with chronic HCV will develop cirrhosis, which can lead to
 - Liver failure
 - Hepatocellular carcinoma: 3-5% per year
 - Death: since 2017, deaths from HCV > deaths from HIV
- **Alcohol use** increases each of these risks AND affects transplant candidacy

Worse Outcomes in People Co-infected with HIV and HCV

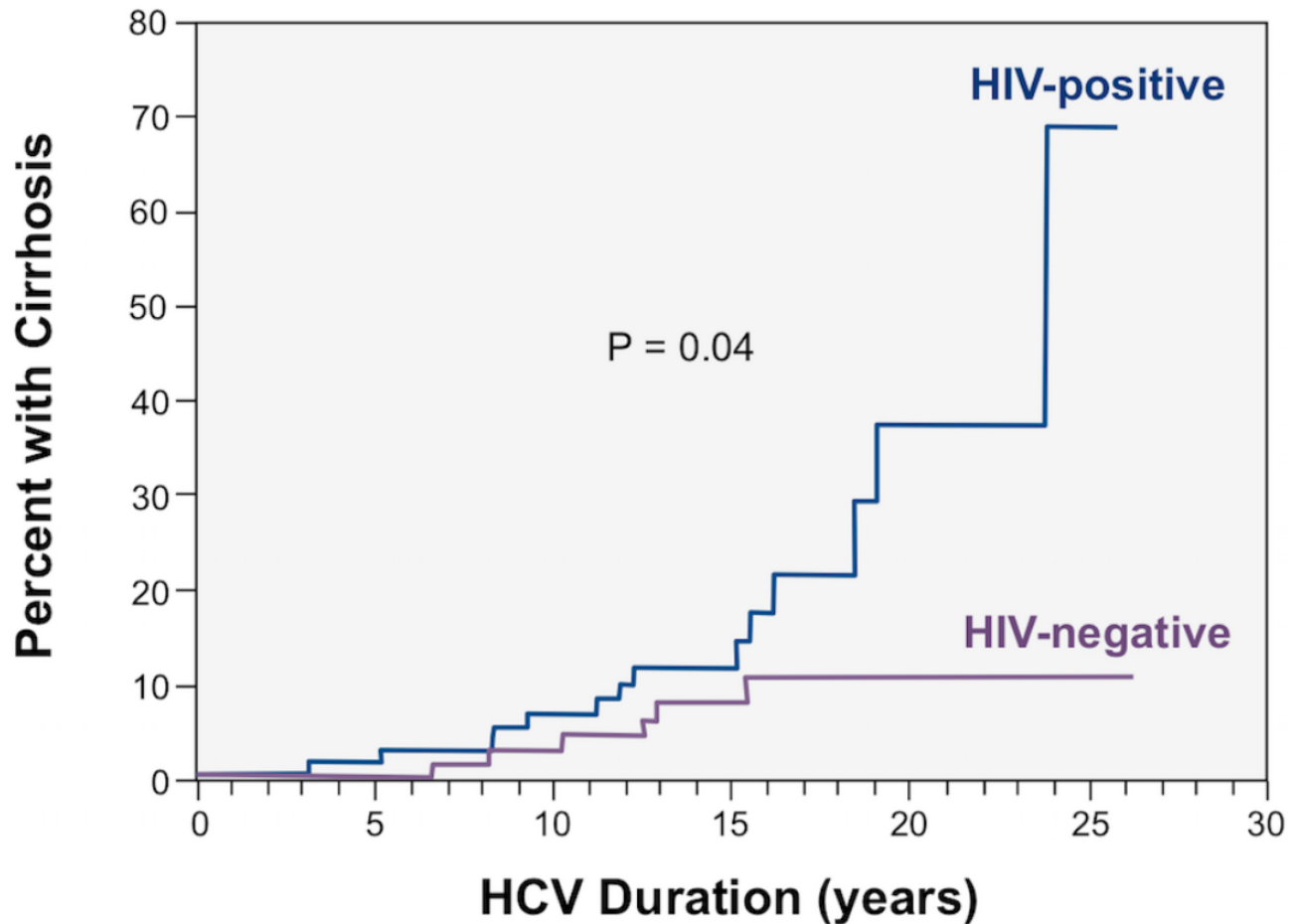


Image credit:
Hepatitis C Online:
hepatitisc.uw.edu

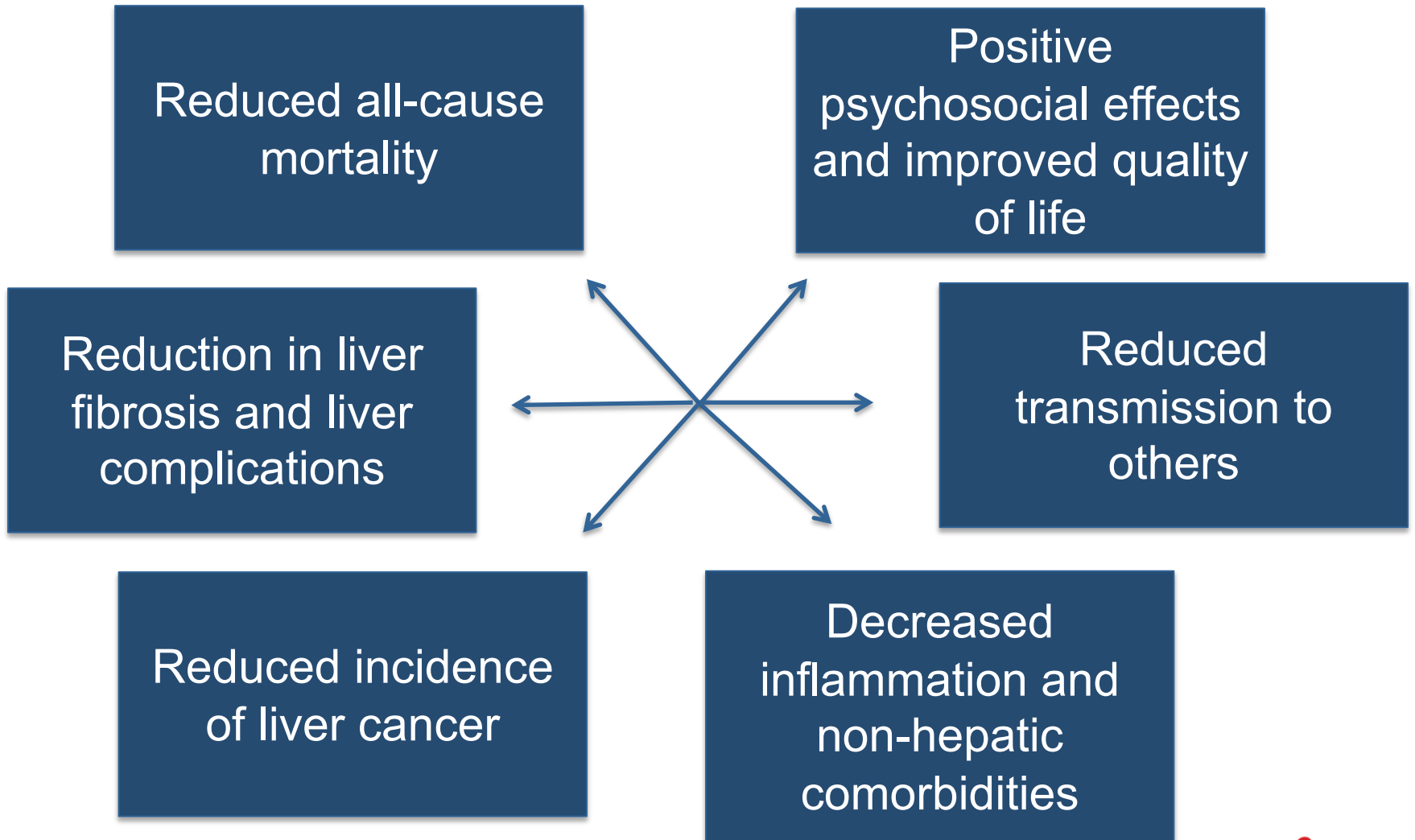
Definitions

Cure of HCV = SVR 12

No detectable HCV virus (HCV RNA) at 12 or more weeks after completion of treatment

DAA= direct-acting antiviral medication (to treat hepatitis C infection)

Benefits of Cure of HCV




Psychosocial Benefits

- Improved self-efficacy and empowerment
- Relief from stigma and illness-related uncertainty/stress
- Positive impacts on substance use
 - *“Clearing HCV will help in defeating the bigger problems, because it’s like trying to get up when you’ve got 100 bricks on ya. But then if I took half the bricks off from the Hep C, then now I’ve got a bit more movement and I can start taking the bricks off.”¹*
 - *“Everything changed. I stopped drug use. I stopped everything because I said if I beat the Hep C, I could beat that too. Praise God up to today, I feel so good.”²*

Which People with HCV Should Be Treated?

- Nearly everyone:

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING 
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that 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.	I, A

- What about people who use drugs?

★ Treating people who use drugs is **critical** to achieving elimination of HCV ★

IDSA/AASLD Guideline Update

Recommendations for Screening and Treatment of HCV Infection in People Who Inject Drugs (PWID)

RECOMMENDED	RATING i
Annual HCV testing is recommended for PWID with no prior testing, or past negative testing and subsequent injection drug use. Depending on the level of risk, more frequent testing may be indicated.	IIa, C
Substance use disorder treatment programs and needle/syringe exchange programs should offer routine, opt-out HCV-antibody testing with reflexive or immediate confirmatory HCV-RNA testing and linkage to care for those who are infected.	IIa, C
PWID should be counseled about measures to reduce the risk of HCV transmission to others.	I, C
PWID should be offered linkage to harm reduction services including intranasal naloxone, needle/syringe service programs, medications for opioid use disorder, and other substance use disorder treatment programs.	I, B
Active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment.	IIa, B

Treatment as Prevention in HCV

Treating populations that actively transmit HCV



Reduces new infections



Reduces prevalence over time

Common Myths

#1 People who use substances can't be effectively treated / cured

#2 People who use substances are likely to get reinfected anyway

Though previously assumed true and incorporated into guidelines and coverage requirements, **these myths have been debunked...**

Countering Myth #1

- Studies from various settings show **good adherence** and **high cure rates** among people who use drugs, including those with injection drug use
- There are **NO data to support pretreatment screening** for illicit drug or alcohol use to select a population more likely to be successful with hepatitis C treatment

Elbasvir–Grazoprevir to Treat Hepatitis C Virus Infection in Persons Receiving Opioid Agonist Therapy

A Randomized Trial

Gregory J. Dore, MD; Frederick Altice, MD; Alain H. Litwin, MD; Olav Dalgard, MD; Edward J. Gane, MD; Oren Shibolet, MD; Anne Luetkemeyer, MD; Ronald Nahass, MD; Cheng-Yuan Peng, MD; Brian Conway, MD; Jason Grebely, PhD; Anita Y.M. Howe, PhD; Isaias N. Gendrano, MPH; Erluo Chen, MPH; Hsueh-Cheng Huang, PhD; Frank J. Dutko, PhD; David C. Nickle, PhD; Bach-Yen Nguyen, MD; Janice Wahl, MD; Eliav Barr, MD; Michael N. Robertson, MD; and Heather L. Platt, MD; on behalf of the C-EDGE CO-STAR Study Group*

- Randomized, double-blind, placebo-controlled trial of elbasvir/grazoprevir for treatment-naïve patients with genotype 1, 4, or 6 enrolled in opioid agonist treatment
- Participants had to be at least 80% adherent to OAT visits
- Primary outcome: proportion of patients with SVR12
- Results:
 - 301 patients, 76% men, 80% white, 7% coinfecting with HIV, >46% with positive urine screens
 - **91.5% had SVR 12**

Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY)

- Open-label international trial of sofosbuvir/velpatasvir among people with hepatitis C, genotypes 1-6, and with injection drug use within 6 months
- Therapy was given in one-week electronic blister packs
- Primary outcome: proportion of patients with SVR12
- Results:
 - 103 patients, mostly male, 59% of whom were receiving opioid agonist treatment, 74% of whom had injected in last month
 - 97% completed treatment, **94% had SVR 12**, drug use did not affect SVR

Countering Myth #2

- *Rate of reinfection among people who use drugs is low*
 - Compared to rates of first infection: hepatitis C treatment has been associated with reduced needle sharing
- Rates of reinfection are *decreased...*
 - When people receive **medications for opioid use disorder**
 - When people use **syringe service programs**
- **Some degree of reinfection suggests you are treating the right population**

Meta-Analysis of Rate of HCV Reinfection



Journal of Hepatology
Volume 72, Issue 4, April 2020, Pages 643-657



Research Article

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

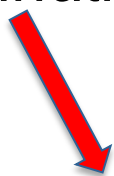
Behzad Hajarizadeh¹✉, Evan B. Cunningham¹, Heather Valerio¹, Marianne Martinello¹, Matthew Law¹, Naveed Z. Janjua^{2,3}, Håvard Midgard⁴, Olav Dalgard⁵, John Dillon⁶, Matthew Hickman⁷, Julie Bruneau⁸, Gregory J. Dore¹, Jason Grebely¹

- Studied 1) people who recently used drugs, and 2) those on opioid agonist treatment
- 36 studies; 6,311 person-years follow up

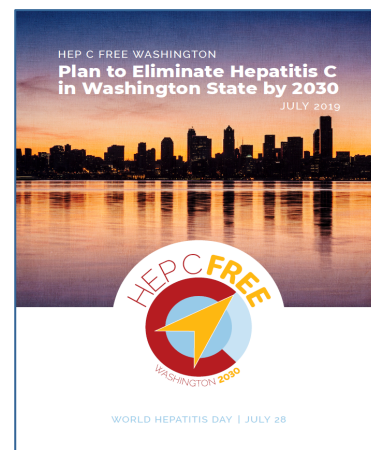
Population	# Studies	Rates of reinfection per 100 person-years
Any drug use	33	5.9 (95% CI 4.1-8.5)
Injecting drug use	31	6.2 (95% CI 4.3-9.0)
Opioid agonist treatment	25	3.8 (95% CI 2.5-5.8)

The Future of HCV

- **2016**: the World Health Organization announces plan for *elimination* of HCV by 2030



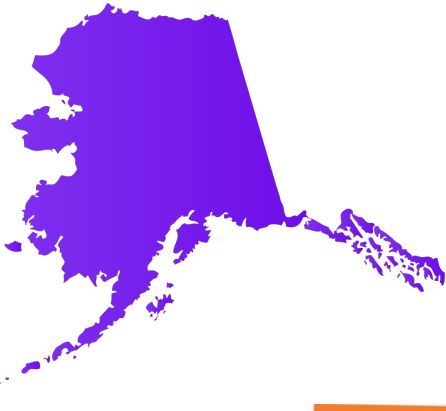
80% reduction in incidence
65% reduction in mortality



- **2018**: Gov. Inslee announces first state initiative to eliminate HCV: “Hep C Free WA”
 - Identifies people who inject drugs as **priority population** for treatment
 - Removes prescriber restrictions

HCV Restrictions/Requirements

Screening and referral if active alcohol or substance use



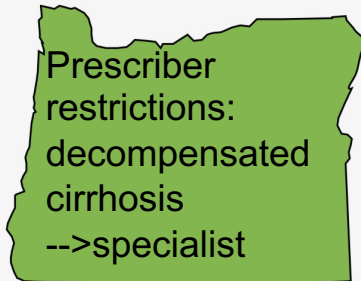
None



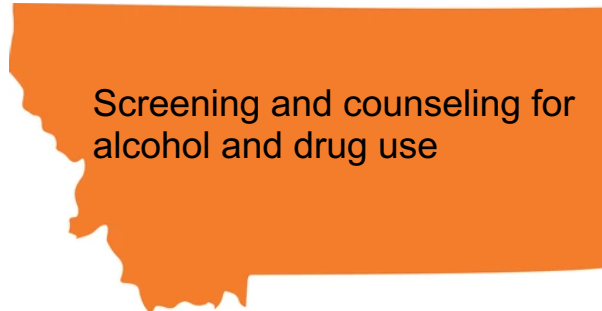
Consider SUD in adherence counseling



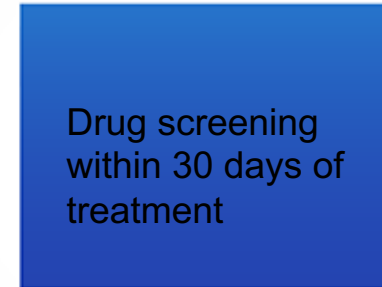
Prescriber restrictions: decompensated cirrhosis -->specialist



Screening and counseling for alcohol and drug use

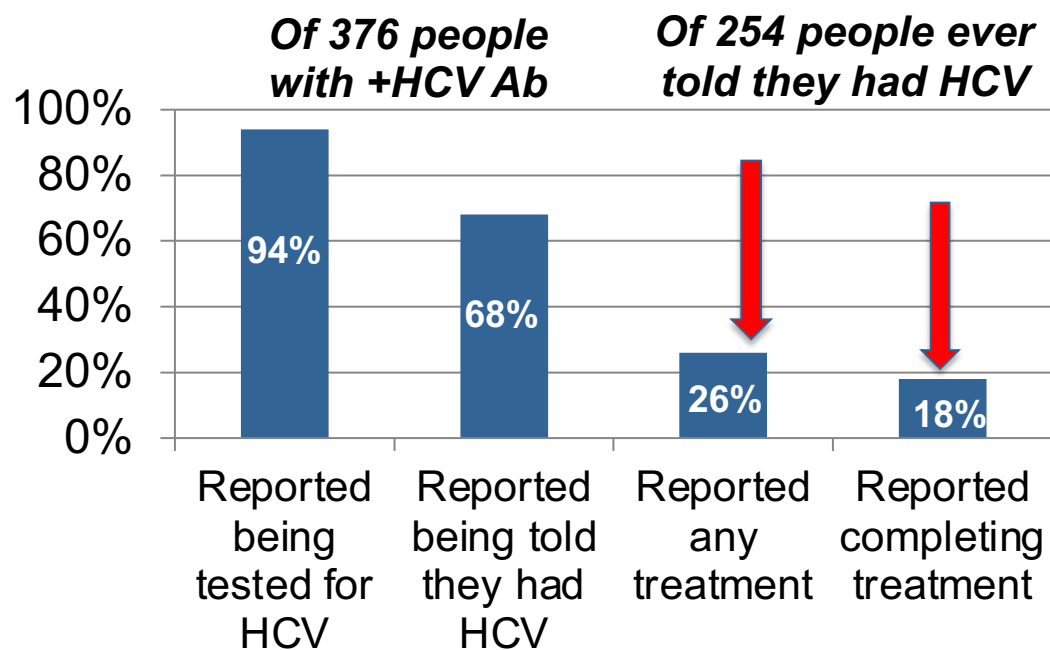


Drug screening within 30 days of treatment



How Are We Doing?

- There is still a **large cliff from screening to treatment among people who inject drugs**
- This 2018 Seattle, WA, data from National HIV Behavioral Surveillance Survey mirrors the region and nation



Interest in HCV Treatment is High in PWID

- **58%** of respondents to a state syringe exchange survey from 2019 **reported HCV testing** in the last year
- Of those diagnosed with HCV,
 - **28%** had received any treatment
 - **68%** reported interest in treatment



Photo: Hepatitis Education Project

Hepatitis C Treatment: The Big Picture

- In most patients with hepatitis C, treatment is straightforward and simple and can be done by PCPs/pharmacists
- In people with advanced liver disease or certain other conditions (transplant, liver cancer), treatment is more complicated and should be done by or in consultation with specialists
- Distinguishing these two groups is an important task and starts with a good clinical history

Direct-Acting Antivirals (DAAs) for HCV

Typical treatment duration	8-12 weeks
Usual pill burden	1-3 pills taken once daily
Tolerability	Very well-tolerated overall Headache, fatigue, and nausea are relatively common but rarely interfere with treatment course
Effectiveness	>95% rate of cure Comparable effectiveness in those with substance use
Examples (pan-genotypic)	Glecaprevir/pibrentasvir (Mavyret®) Sofosbuvir/velpatasvir (Epclusa®)

Pretreatment Assessment

<p>Required</p>	<p>*Complete blood count (CBC), *Comprehensive metabolic panel (CMP), HCV RNA, HIV, HBsAg</p>
<p>Consider based on level of clinical concern for cirrhosis, based on...</p> <ul style="list-style-type: none"> ○ Review of existing data ○ (likely) duration of infection ○ cumulative alcohol exposure ○ signs/symptoms of cirrhosis 	<p>International normalized ratio (INR) FibroTest/FibroSure®, ActiTest Transient elastography (<i>FibroScan</i>) Abdominal ultrasound</p> <div data-bbox="1093 761 1833 979" style="border: 1px solid black; padding: 10px; margin: 10px auto; width: fit-content;"> $\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \text{Yellow}$ </div>
<p>Treat as cirrhosis if any of the following</p>	<p>FIB-4 > 3.25 Platelet count < 150,000/mm³ <i>FibroScan</i> > 12.5 kPa Liver nodularity and/or splenomegaly on imaging Prior liver biopsy showing cirrhosis</p>

Know When to Refer

Definite:

- Decompensated cirrhosis
- Hepatocellular carcinoma
- Post-transplant

Relative:

- Hepatitis B and/or HIV
- Prior treatment with DAAs

Image credit:
Hepatitis C
Online:
hepatitisc.uw
.edu

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			

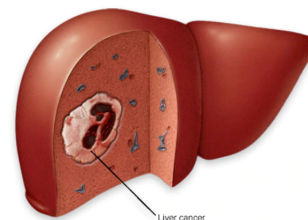


Image credit:
Mayo Clinic

Simplified HCV Treatment: No Cirrhosis

Key Steps:

- Review medications, drug-drug interactions
 - Update labs
- Educate re: medication administration, adherence, and preventing reinfection

Treatment:

- Glecapresvir/pibrentasvir for 8 wks (3 pills daily), or
- Sofosbuvir/velpatasvir for 12 wks (1 pill daily)

Monitoring:

No lab monitoring required
Offer visits for support, assessment of symptoms

Treating Patients with Compensated Cirrhosis

- There is also a simplified algorithm, **with some key differences:**

Check liver ultrasound to exclude liver cancer prior to treatment

Basic labs within 3 months

Check genotype*

Monitor for decompensation**

*If treating with sofosbuvir/velpatasvir.

**Hepatic panel every 4 weeks; monitor for jaundice, ascites, encephalopathy.

Post-Treatment

Test for cure! Check HCV RNA 12 or more weeks after completing treatment



If RNA detectable, refer to specialist for retreatment

Check AST and ALT

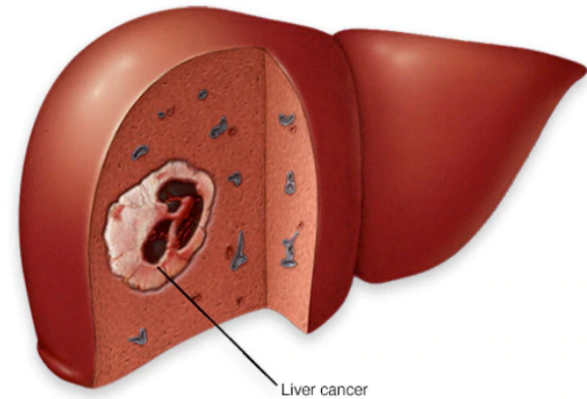
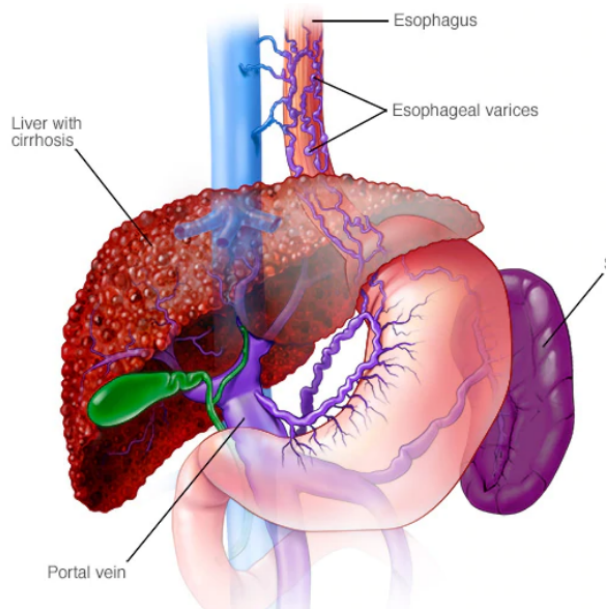


If elevated despite undetectable RNA, assess for other causes of liver disease

Provide Counseling

- Avoid excessive alcohol
- Cure does not prevent reinfection: screen annually if ongoing risk factors

Patients with Cirrhosis Require Follow Up



Incorporating Alcohol Pharmacotherapies Into Medical Practice



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Treatment
www.samhsa.gov



Coinfection with HCV and HIV

- Co-infection leads to accelerated rates of fibrosis
- **Rates of cure are comparable** in those with coinfection vs monoinfection
- Treatment regimens are generally equivalent, though in some circumstances, 8-week regimens should be extended to 12 weeks
- **Drug-drug interactions are key**
 - IDSA/AASLD guideline provides examples of HIV and hepatitis C medications that can be used together
 - If considering other combinations, expert consultation is needed
 - Resources: hcvguidelines.org, <https://aidsinfo.nih.gov/guidelines>, www.hep-druginteractions.org

DAAs and Antiretroviral Medications

		Ledipasvir/ Sofosbuvir (LDV/SOF)	Sofosbuvir/ Velpatasvir (SOF/VEL)	Elbasvir/ Grazoprevir (ELB/GRZ)	Glecaprevir/ Pibrentasvir (GLE/PIB)	Sofosbuvir/ Velpatasvir/ Voxilaprevir (SOF/VEL/VOX)
Protease Inhibitors	Boosted Atazanavir	A	A			
	Boosted Darunavir	A	A			
	Boosted Lopinavir	ND, A	A			ND
NNRTIs	Doravirine		ND		ND	ND
	Efavirenz				ND	ND
	Rilpivirine					
	Etravirine	ND	ND	ND	ND	ND
Integrase Inhibitors	Bictegravir			ND	ND	
	Cobicistat-boosted elvitegravir	C	C			C
	Dolutegravir					ND
	Raltegravir					ND
	Maraviroc	ND	ND	ND	ND	ND
NRTIs	Abacavir		ND	ND		ND
	Emtricitabine					
	Lamivudine		ND	ND		ND
	Tenofovir disoproxil fumarate	B, C	B, C			C, D
	Tenofovir alafenamide	D	D	ND		D

Green indicates coadministration is safe; **yellow** indicates a dose change or additional monitoring is warranted; and **red** indicates the combination should be avoided.

ND: No data

A: Caution only with tenofovir disoproxil fumarate

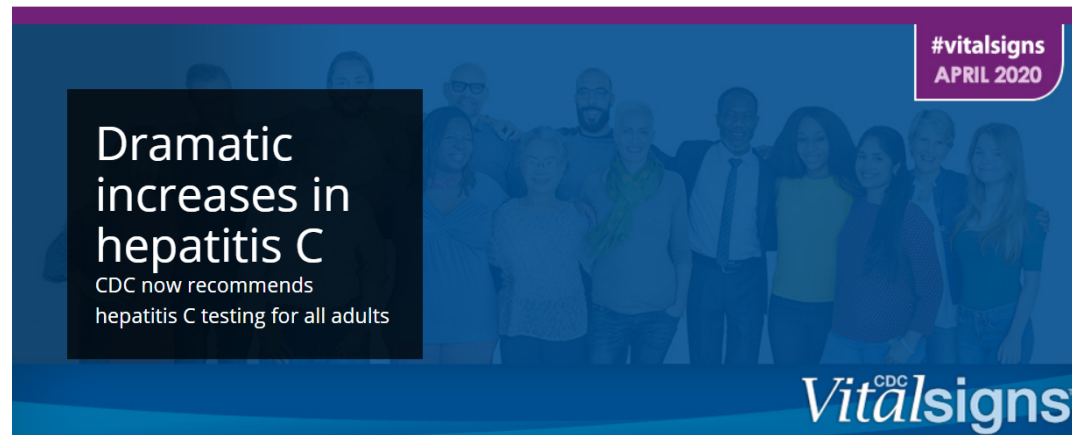
B: Increase in tenofovir depends on which additional concomitant antiretroviral agents are administered.

C: Avoid tenofovir disoproxil fumarate in patients with an eGFR <60 mL/min; tenofovir concentrations may exceed those with established renal safety data in individuals on ritonavir- or cobicistat-containing regimens.

D: Studied as part of fixed-dose combinations with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir plus TAF, emtricitabine, elvitegravir, and cobicistat.

New Recommendation for Universal Screening

- New USPSTF recommendation to screen all asymptomatic adults age 18-79 for hepatitis C
- Those at high risk should be periodically rescreened



4 in 10

About 4 in 10 people with hepatitis C do not know they are infected.

4x

New hepatitis C cases are 4 times as high as they were 10 years ago.

20-39

Younger adults 20-39 years old have the highest rates of new hepatitis C cases.

HCV Prevention

Treatment as
prevention

Medications for opioid
use disorder

Education/harm
reduction

Syringe service
programs

Patient Case: Considerations

- How concerned are you for advanced fibrosis?
 - Duration infection, alcohol history, symptoms and data
- How relevant is the public health argument to treat ASAP to reduce transmission?
- How does hepatitis C treatment fit with her goals?
 - It may improve quality of life/symptoms
 - It may increase self-efficacy, reduce risk behavior, improve SUD
 - Important to treat when she feels she can be successful, but also keep in mind, DAAs are forgiving of imperfect adherence

Key Resources

- HCVguidelines.org: IDSA/AASLD guideline
- Hepatitisc.uw.edu: excellent free online training
- Project ECHO, weekly videoconferences : contact Pam Landinez at landinez@uw.edu
- UCSF phone consultation, 9 am-8 pm ET: (844) HEP-INFO or (844) 437-4636
- U. of Liverpool medication interaction checker: hep-druginteractions.org

Panel Discussion

- What do you find most rewarding about providing hepatitis C treatment?
- What challenges have you encountered while treating hepatitis C among people who use drugs?
- What advice would you offer others interested in treating hepatitis C?

Acknowledgment

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