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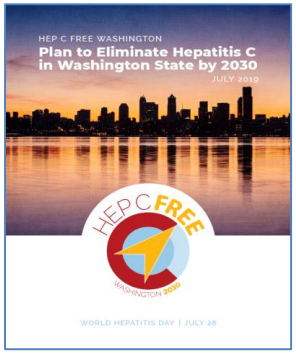

TREATING HEPATITIS C AMONG PEOPLE WHO USE DRUGS

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UW Medicine
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Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

SPEAKER DISCLOSURES

- ✓ No conflicts of interest

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BY THE END OF THIS SESSION, PROVIDERS WILL…

1. Be aware of hepatitis C elimination campaigns and that prior authorization requirements and provider restrictions have been lifted
2. Understand why treating people who use drugs (PWUD) is important
3. Understand that all adults should be screened for hepatitis C and that (nearly) all patients with infection should be treated
4. Be familiar with direct-acting antivirals (DAAs) and key steps in treatment
5. Be excited to treat hepatitis C and know where to get help

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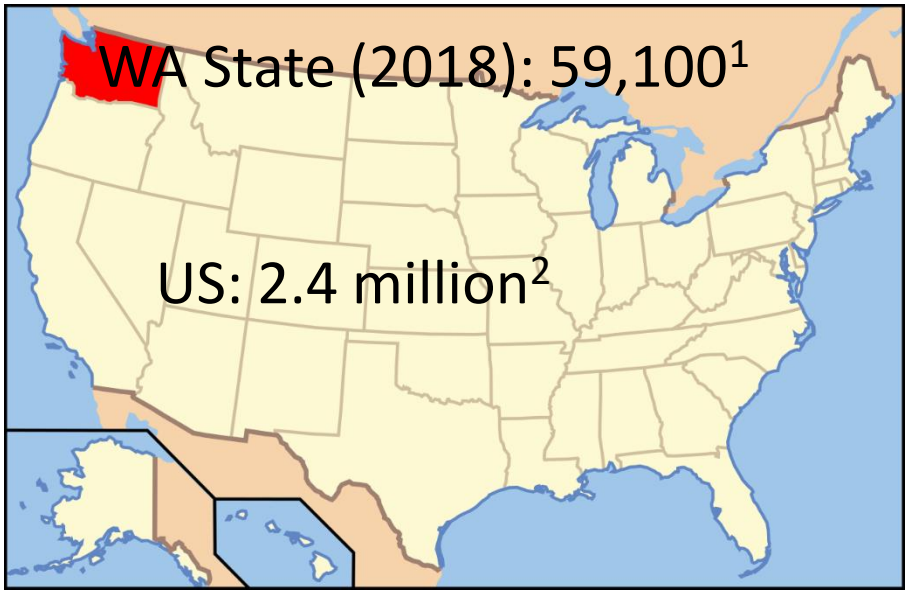
HCV BACKGROUND

- RNA virus identified in 1988
- Most common blood-borne infection in US
- Not vaccine preventable
- Most people exposed to HCV will develop chronic infection

Figure credit: hepatitisc.uw.edu.

HCV IS COMMON AND DEADLY

Prevalence of chronic HCV infection



- Approximately 56% of those with HCV are aware of infection[3]
- In U.S., **deaths from HCV outnumber those from HIV and from 60 other infectious conditions combined[4]**

[1]Department of Health data; [2]Hofmeister MG et al, Hepatology 2018; [3]Kim HS et al, J Viral Hepat 2019 May;26(5):596-602; [4] Ly et al, Clin Infect Dis 2016 May 15;62(10):1287-1288.

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HCV IN THE U.S. - 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

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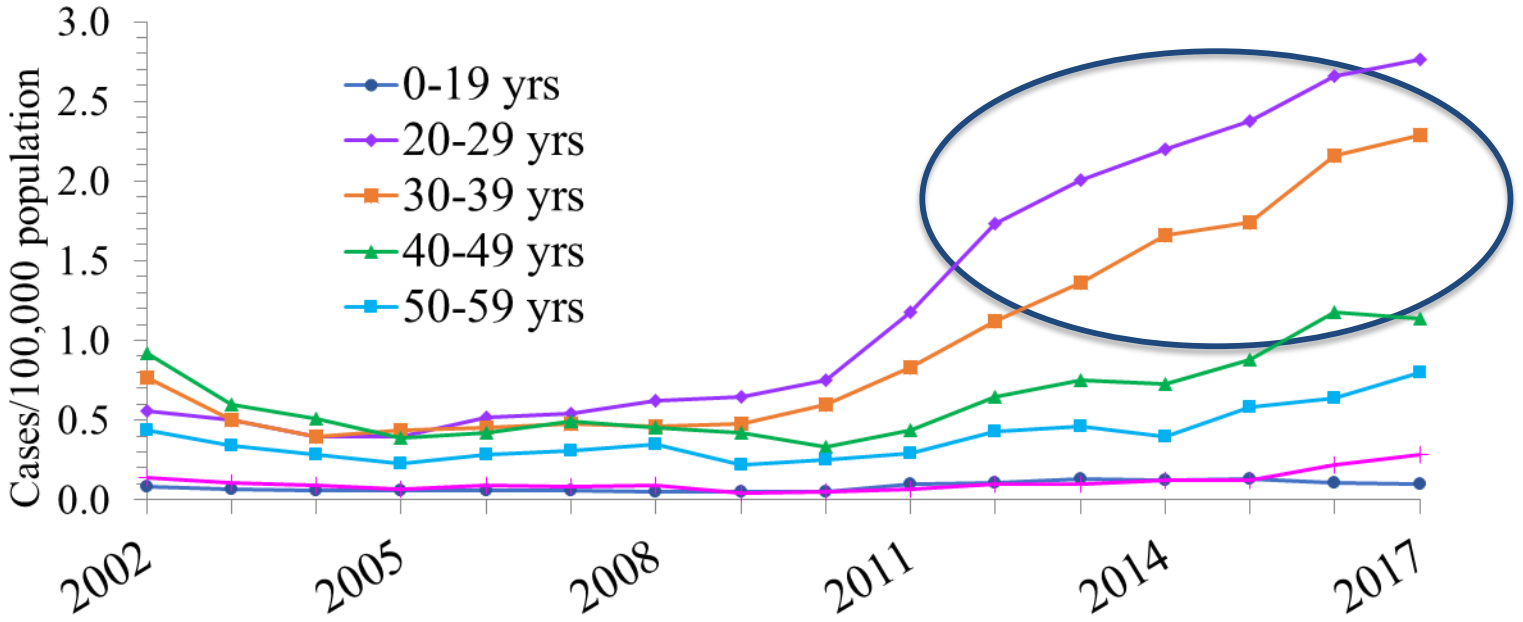
OPIOID EPIDEMIC AND HCV

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



Rates of reported acute hepatitis C by age group, US, 2002-2017 (CDC Viral Hepatitis Surveillance Data)

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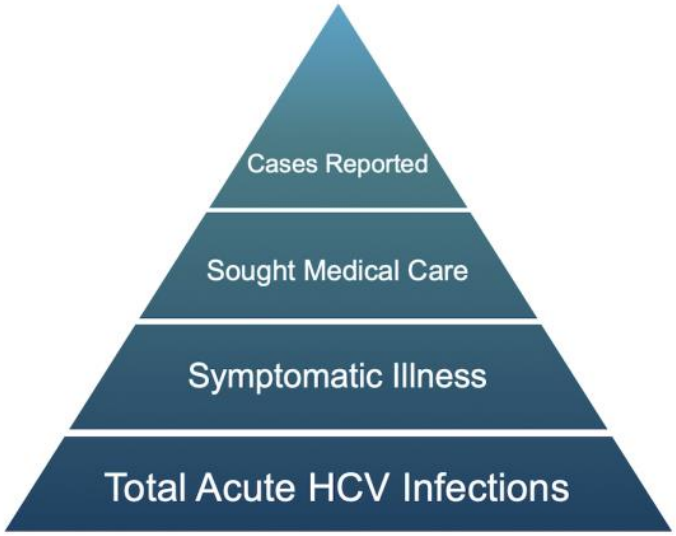
OPIOID EPIDEMIC AND HCV

- **Reported acute infections are only the "tip of the iceberg"**

3,621 acute cases reported in U.S. in 2018 [1]



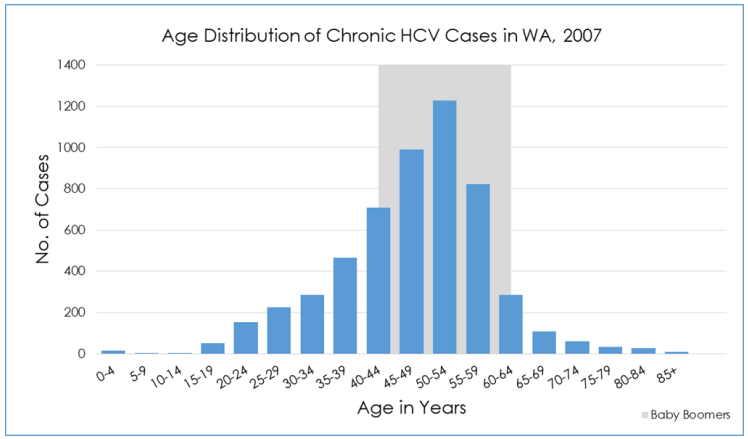
Estimated 50,300 actual new cases[1]

Figure source: modified from hepatitisc.uw.edu from Klevens et al, Am J Public Health 2014

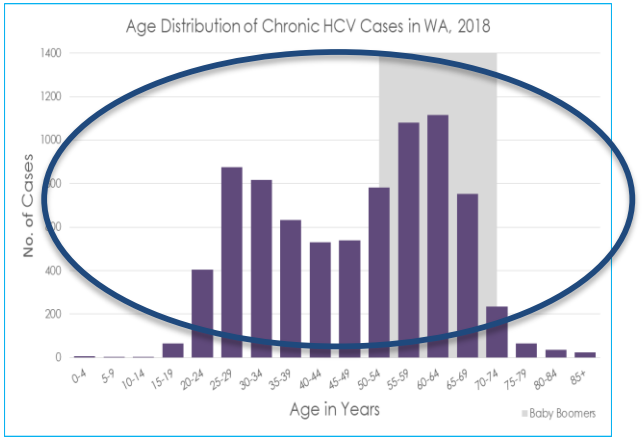
WHAT ABOUT IN WASHINGTON STATE?

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

Chronic HCV in WA State



2007



2018

Source: WA State Dept of Health

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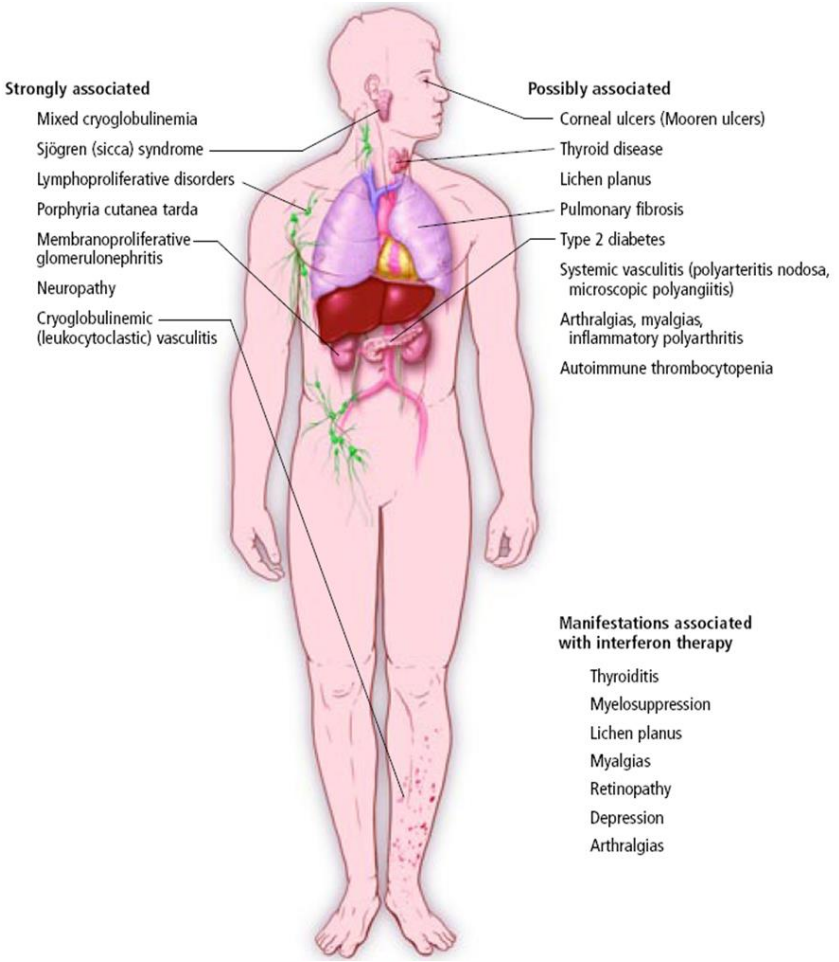
LIVED EXPERIENCE WITH HCV

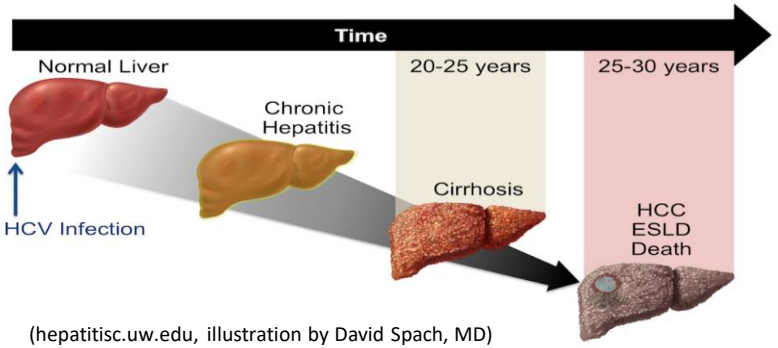


- Symptoms: range from none at all to systemic, hepatic, and a variety of extra-hepatic symptoms
- Patients frequently report fatigue, sleep problems, depression, and anxiety[1]
- Stigma and illness-related uncertainty contribute to chronic stress[2]

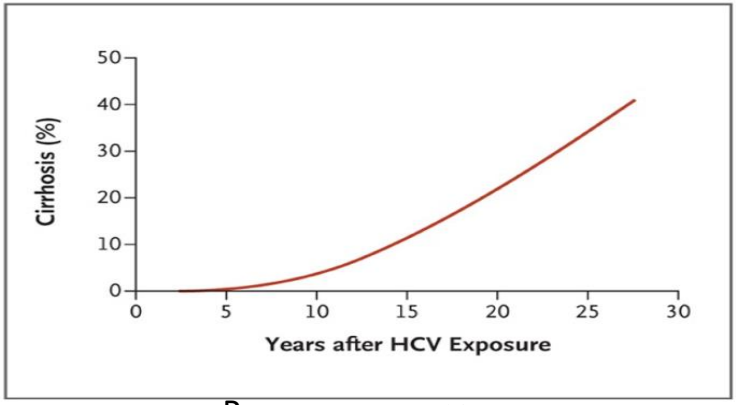
[1]Evon et al, PLoS One 2018;13(8):e0196908; [2]Goutzamanis et al, BMC Infectious Diseases 2018

NATURAL HISTORY OF CHRONIC HCV

- 15-30% of those with chronic HCV will develop cirrhosis, which can lead to:
  - Hepatocellular carcinoma (3-5% incidence per year)
  - Liver failure
  - Death
- Alcohol use increases each of these risks AND affects transplant candidacy



(hepatitisc.uw.edu, illustration by David Spach, MD)



Rosen H.R, NEJM 2011

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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)

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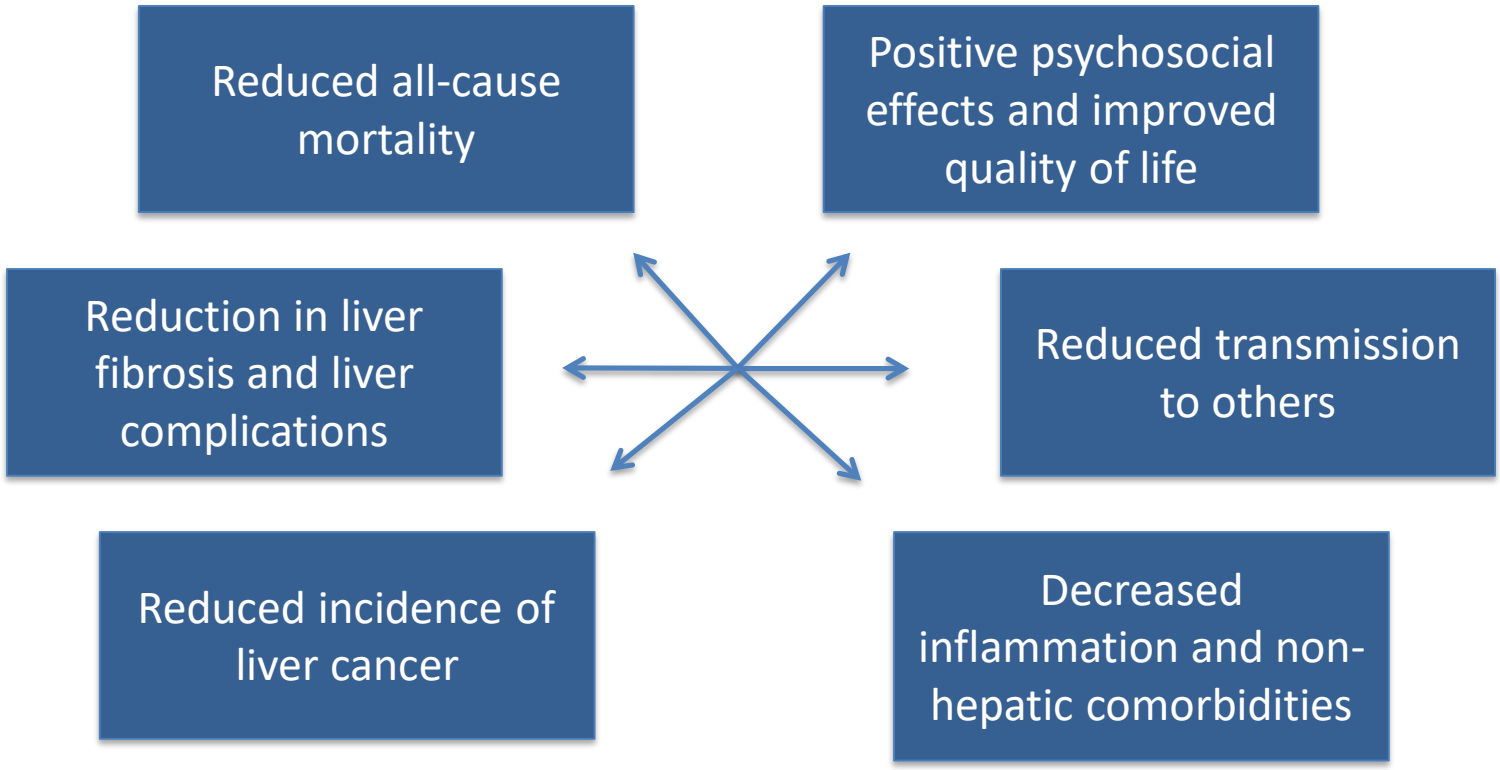
BENEFITS OF CURE OF HCV



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PSYCHOSOCIAL BENEFITS

- Improved self-efficacy and empowerment
- Relief from stigma and from illness-related uncertainty, stress[1]
- 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]

[1]Goutzamanis et al, BMC Infectious Diseases 2018; [2]Batchelder et al, Drug and Alcohol Depend 2015

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?

  To eliminate HCV, treating people who use drugs is **critical**

http://www.hcvguidelines.org/full-report/when-and-whom-initiate-hcv-therapy

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TREATMENT AS PREVENTION FOR HCV AMONG PWID

Treating populations that actively transmit HCV

Reduces new infections

Reduces prevalence over time

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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…

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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

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Annals of Internal Medicine ORIGINAL RESEARCH

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[1] enrolled in opioid agonist treatment
- Participants had to be at least 80% adherent to OAT visits
- Primary outcome: proportion of patients with SVR 12
- Results:
  - 301 patients, 76% men, 80% white, >46% with positive urine screens
  - 91.5% had SVR 12

[1]Genotypes 1, 4, 6

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 HCV[1] and injection drug use within 6 months
- Therapy was given in one-week electronic blister packs
- Primary outcome: proportion of patients with SVR 12
- Results:
  - 103 patients, mostly male, 59% receiving opioid agonist treatment, 74% had injected in last month
  - 97% completed treatment, 94% had SVR 12, drug use did not affect SVR

[1]Genotypes 1-6; Grebely, Lancet Gastroenterol Hepat 2018

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COUNTERING MYTH #2

- *Rate of reinfection among people who use drugs is low...*
  - And substantially lower than rates of first infection[1,2]
  - Hepatitis C treatment has been associated with reduced opioid injecting/sharing[3]
- Rate of reinfection is *decreased…*
  - When people receive medications for opioid use disorder[1]
  - When people use syringe service programs
- Some degree of reinfection suggests you are treating the right population

[1]Hajaridazeh, J Hepatol 2020; [2]Morris, Clin Infect Disease 2017; [3]Artenie, Clin Infect Disease 2020

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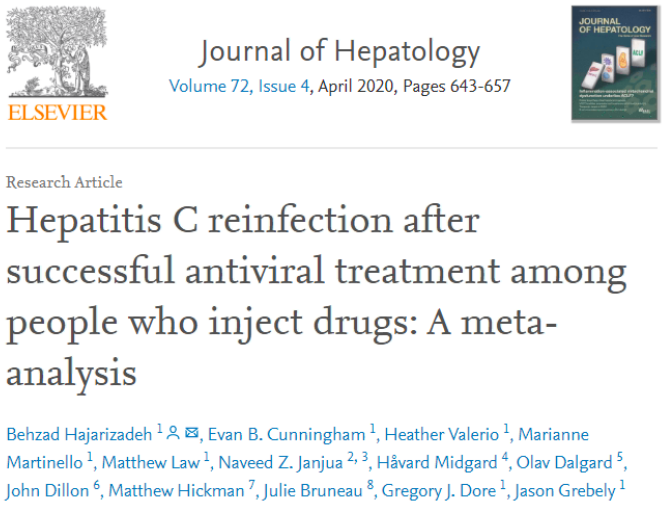
META-ANALYSIS OF RATE OF HCV REINFECTION

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



ELSEVIER

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 Hajarizadeh [1], Evan B. Cunningham [1], Heather Valerio [1], Marianne Martinello [1], Matthew Law [1], Naveed Z. Janjua [2, 3], Håvard Midgard [4], Olav Dalgard [5], John Dillon [6], Matthew Hickman [7], Julie Bruneau [8], Gregory J. Dore [1], Jason Grebely [1]

Population	# Studies	Person-years f/u	Rates of reinfection per 100 person-years
Injecting or non-injecting drug use	33	5,061	5.9 (95% CI 4.1-8.5)
Injecting drug use	31	4,648	6.2 (95% CI 4.3-9.0)
Opioid agonist treatment	25	2,507	3.8 (95% CI 2.5-5.8)

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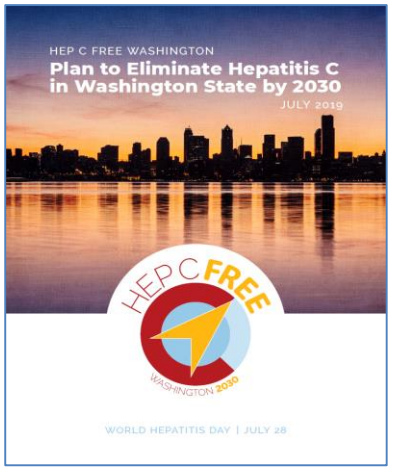
HEPATITIS C: THE FUTURE

- 2016: the WHO announces plan for elimination of HCV by 2030
  - Defined as 80% reduction in incidence, 65% reduction in mortality
- 2016: WA HCA removes disease severity restrictions
- 2018: Gov. Inslee announces “Hep C Free WA” initiative
  - PWID identified as a **priority population** for treatment
  - Removes prescriber restrictions

There is a great opportunity to treat HCV here, now

Inslee unveils first-in-nation approach to eliminate hepatitis C in Washington by 2030

WA Governor's Office Follow
Sep 28, 2018 · 4 min read



WHO: World Health Organization; HCA: Healthcare Authority

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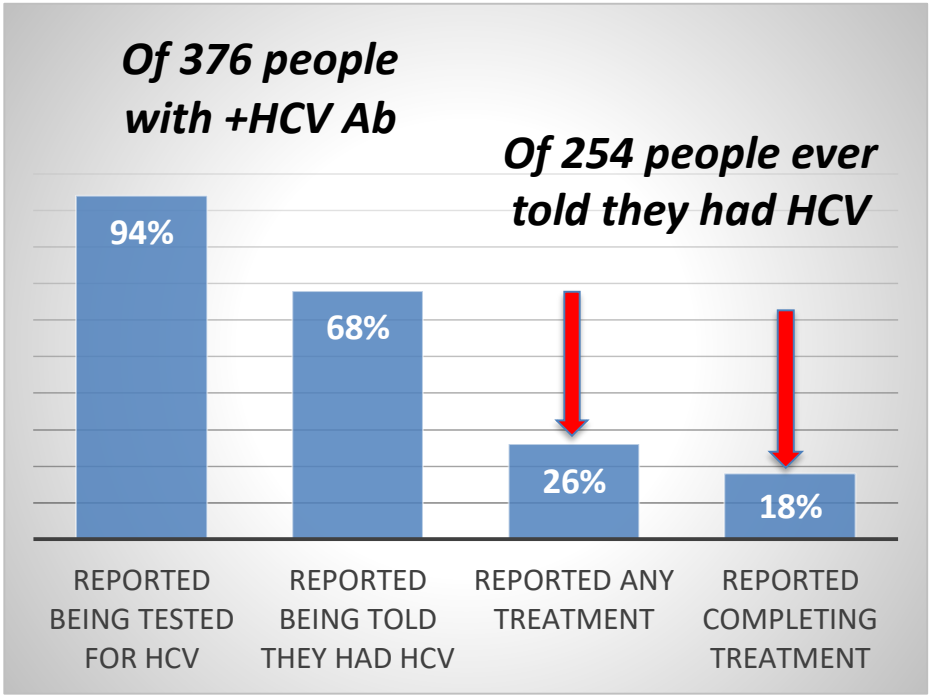
WA HEALTH CARE AUTHORITY'S MEDICAID PHARMACY POLICY FOR HCV TREATMENT

- Aligns with national expert (AASLD/IDSA) HCV guidance
  - No sobriety requirement
  - Evidence of fibrosis not required
  - Any licensed prescriber allowed to screen and treat
  - Not necessary to document chronic hepatitis C infection: a single detectable RNA is sufficient
  - Prior Authorization not required for AbbVie's Mavyret product

But…There Are Ongoing Treatment Gaps

- Study of PWID in Seattle area found that only 26% of those who knew they had HCV reported any treatment
- **Urgent need to**
  - **connect people diagnosed with HCV to "rapid start" of treatment**
  - **offer treatment in settings in which PWID are seen**



HCV CARE CONTINUUM AMONG SEATTLE PWID, NATIONAL HIV BEHAVIORAL SURVEILLANCE SURVEY, 2018

[1]Corcorran et al, Drug and Alcohol Dependence, Volume 220, 2021

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INTEREST IN HCV TREATMENT IS HIGH AMONG 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

Alcohol and Drug Abuse Institute: adai.uw.edu/wa-state-syringe-exchange-health-survey-2019-results

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HCV TREATMENT: THE BIG PICTURE

- In most patients with hepatitis C, treatment is straight-forward 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

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DIRECT-ACTING ANTIVIRALS 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 sustained viral response at 12 weeks (SVR 12), now considered “cure” Comparable effectiveness in those with substance use
Examples (pan-genotypic)	Glecaprevir/pibrentasvir (Mavyret®) Sofosbuvir/velpatasvir (Epclusa®)

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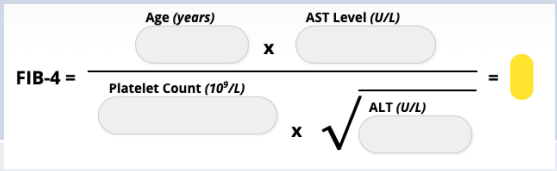
PRETREATMENT ASSESSMENT

Required	*Complete blood count (CBC), *Comprehensive metabolic panel (CMP), HCV RNA, HIV, HBsAg
Consider according to level of clinical concern for cirrhosis, based on… • existing lab and imaging data • **(likely) duration of infection** • cumulative alcohol exposure • signs/symptoms of cirrhosis	International normalized ratio (INR) FibroTest/FibroSure®, ActiTest Transient elastography (*FibroScan)* Abdominal ultrasound 
Treat as cirrhosis if any of the following	FIB-4 > 3.25 Platelet count < 150,000/mm^3 *FibroScan* > 12.5 kPa Liver nodularity and/or splenomegaly on imaging Prior liver biopsy showing cirrhosis

* Within 6 months of starting treatment

IDSA/AASLD Guideline: hcvguidelines.org

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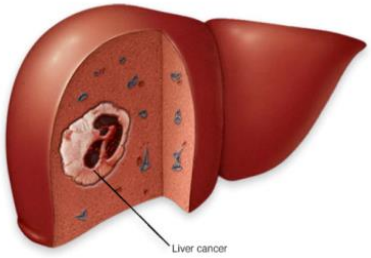
WHEN TO REFER

Reasons to refer:

- Decompensated cirrhosis:
  - ascites, jaundice, variceal hemorrhage, encephalopathy (CTP B or C)
- Hepatocellular carcinoma
- Post-transplant



Relative, depend on setting/comfort:

- HBV and/or HIV
- *Prior treatment with DAAs

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)			

*Guidelines for retreatment are evolving—refer to IDSA/AASLD guideline for updates. CTP: Child-Turcotte-Pugh.

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

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SIMPLIFIED HCV TREATMENT ALGORITHM: PATIENTS *WITHOUT CIRRHOSIS*

Key Steps:

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

Treatment:

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

Monitoring:

No lab monitoring required

Offer visits for support, assessment of symptoms

hcvguidelines.org

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CAVEATS : MONITORING DURING TREATMENT

- Monitor for hypoglycemia in people with DM
- Monitor INR closely in those on warfarin
- There are rare reports of hepatitis B reactivation among people with isolated anti-HBc:
  - Consider monitoring AST/ALT mid-treatment in those with anti-HBc

PATIENTS WITH COMPENSATED (CHILDS A) 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**; refer to specialist as needed

*If treating with sofosbuvir/velpatasvir. **Hepatic panel every 4 weeks; monitor for jaundice, ascites, encephalopathy.

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POTENTIAL DRUG INTERACTIONS

- Not all interactions require medication adjustment: helpful to consult with pharmacist

Glecaprevir/pibrentasvir (Mavyret®)

- Ethinyl estradiol containing medications (oral contraceptives)
- Statins
- DOACs (dabigatran) and antiarrhythmics (amiodarone, digoxin)
- Anticonvulsants (carbamazepine, phenytoin)
- Rifampin
- Antiretrovirals
- St. John's Wort

Sofosbuvir/velpatasvir (Epclusa®)

- Acid reducers (PPIs>H2B>antacids)
- Statins
- Antiarrhythmics (amiodarone, digoxin)
- Anticonvulsants (carbamazepine, phenytoin, phenobarbital)
- Antiretrovirals
- Rifampin
- St. John's Wort

Hepatitis C Drug Interaction Checker: hep-druginteractions.org

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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 (those with cirrhosis should avoid alcohol completely)
- Cure does not prevent reinfection: screen annually if ongoing risk factors

IDSA/AASLD Guideline: hcvguidelines.org

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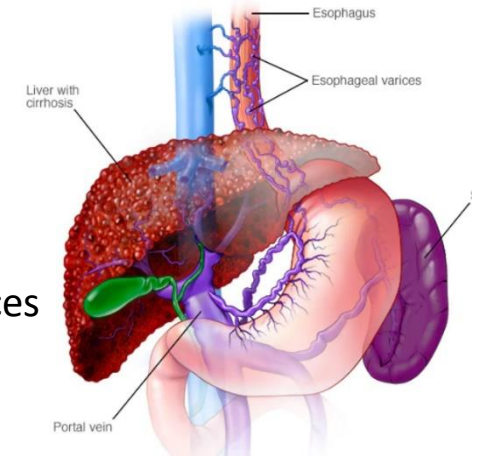
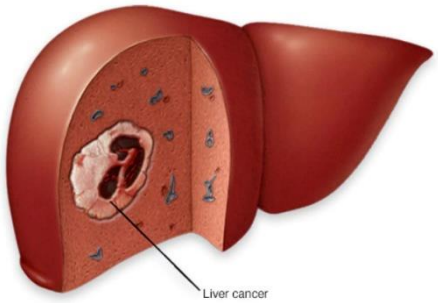
PATIENTS WITH CIRRHOSIS NEED FOLLOW UP

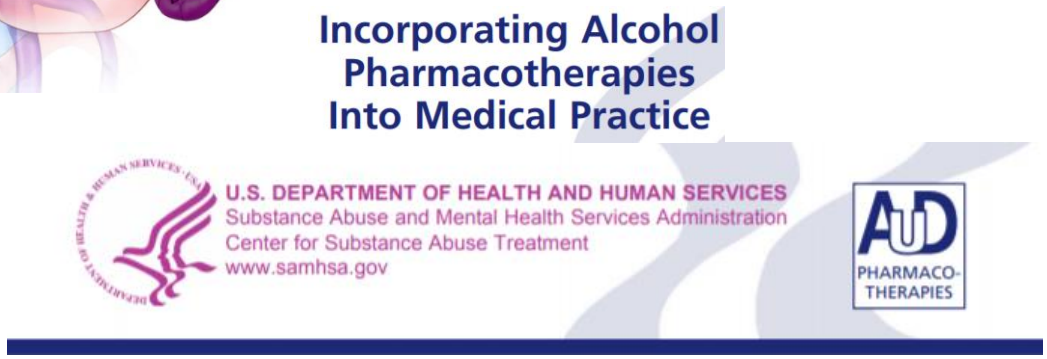
Screen for esophageal varices if appropriate





Screen for liver cancer

Offer help with drinking for those who need it



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REMEMBER… KEY POINTS ABOUT REINFECTION

Cured patients remain vulnerable to reinfection	**Screen those with risk factors with HCV RNA** **Try to minimize shame around reinfection**
Reinfection risk is reduced by use of NSPs and medications for OUD	**Offer harm reduction services, encourage meds for OUD**
Some degree of reinfection is a sign that you are treating the right population	**Don't let reinfection risk be a barrier to treatment**

Hajarizadeh, J Hepatol 2019

NSP: needle and syringe exchange programs

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BACK TO SCREENING

- New USPSTF recommendation to screen all asymptomatic adults age 18-79 for HCV: *Anti-HCV antibody followed by confirmatory PCR*
- **Those at high risk (e.g. past/current injection drug use) should be periodically rescreened: expert recommendation to rescreen annually**

USPSTF, HCV Guidance, 2020 and Centers for Disease Control and Prevention.

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DON'T FORGET IMMUNIZATION!

- Recommend hepatitis A and B vaccination for people with OUD, whether or not they have HCV
  - Periodic outbreaks make this particularly important
- Those with cirrhosis, tobacco use, and/or heavy alcohol (among other conditions) should also receive pneumococcal vaccination

HCV TREATMENT: TAKE-HOME POINTS

- Simplified pathway w/ limited monitoring for most patients
- Adherence support helpful but DAAs are “forgiving” of imperfect adherence
- SVR 12 check is key
- Easy, fun, gratifying to cure people of an important disease
- Part of primary care, especially for people with OUD

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GET STARTED!

- 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

TIPS

- Start with one straight-forward case
- Find a local expert and/or connect with ECHO
- Identify a trusted pharmacist
- Decide your scope of practice and when to refer

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THANK YOU!

- Questions and discussion

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