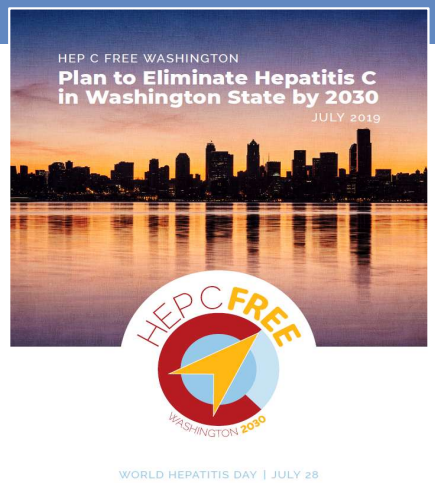
PCSS Providers Clinical Support System

Treating Hepatitis C Among People Who Use Drugs

Judith Tsui, MD, MPH
Associate Professor
University of Washington
May 10th, 2022

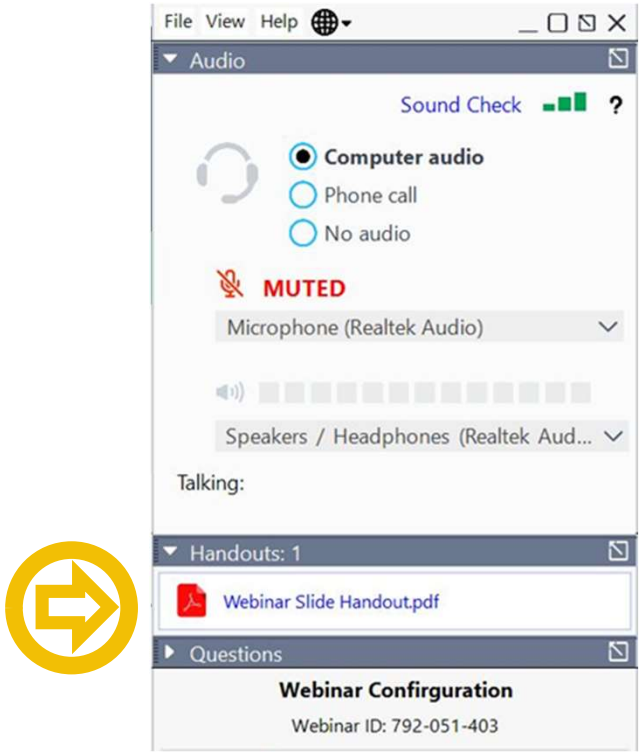


Slide deck created by: Dr. Jocelyn James and Dr. Judith Tsui
in collaboration with Washington State Department of Health

How to Download Handouts

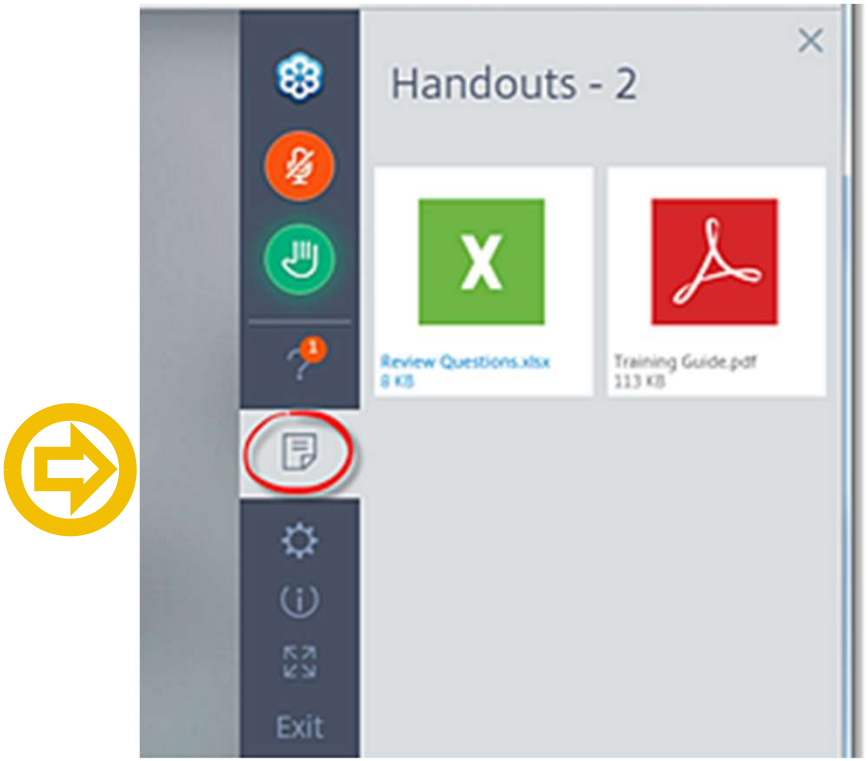
Desktop

Use the “Handouts” area of the attendee control panel.



Instant Join Viewer

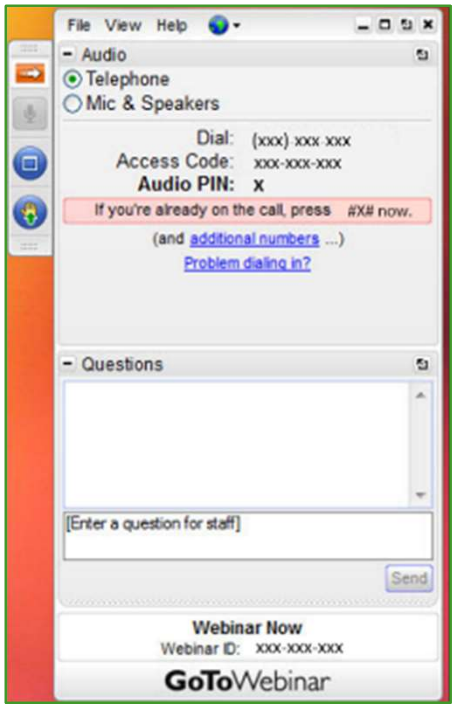
Click the “Page” symbol to display the “Handouts” area.



How to Participate in Q&A

Desktop

Use the “Questions” area of the attendee control panel.



Instant Join Viewer

Click the “?” symbol to display the “Questions” area.

Webinar Faculty

Judith Tsui, MD, MPH

Associate Professor
University of Washington

PCSS Providers Clinical Support System

About Me…

- Addiction Medicine/Primary Care physician
  - Treated hepatitis C since 2003
  - Buprenorphine prescriber since 2008
  - Certified in Addiction Medicine since 2013
- Clinical work/research focused on persons with opioid use disorders and persons who inject drugs
  - Currently practice at Harborview Medical Center and Evergreen Treatment Services in Seattle, WA
- Research funded by NIH (NIDA and NIAAA)
  - Disclosure: content does not officially represent NIH/NIDA

Disclosures

- Dr. Judith Tsui, faculty for this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

Target Audience

- The overarching goal of PCSS is to train healthcare professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well for the prevention and treatment of substance use disorders.

Educational Objectives

- At the conclusion of this activity participants should be able to:

1. Explain hepatitis C elimination campaigns and the importance of extending access to treatment for people who use drugs (PWUD).
2. Understand barriers/challenges to hepatitis C care which are specific to PWUD, as well as unique models to overcome.
3. Use adult HCV screening methods and evaluate treatment methods if a patient has hepatitis C.
4. Work with healthcare team to identify methods to use direct-acting antivirals (DAAs) with clients and know key steps in treatment.

Intended Audience

- Clinicians and providers who care for persons who use drugs (who are at-risk for hepatitis C), including:
  - Physicians
  - Physician Assistants
  - Nurses
  - Pharmacists
  - Social Workers
  - Counselors
  - Peer Support Specialists

HCV Background

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

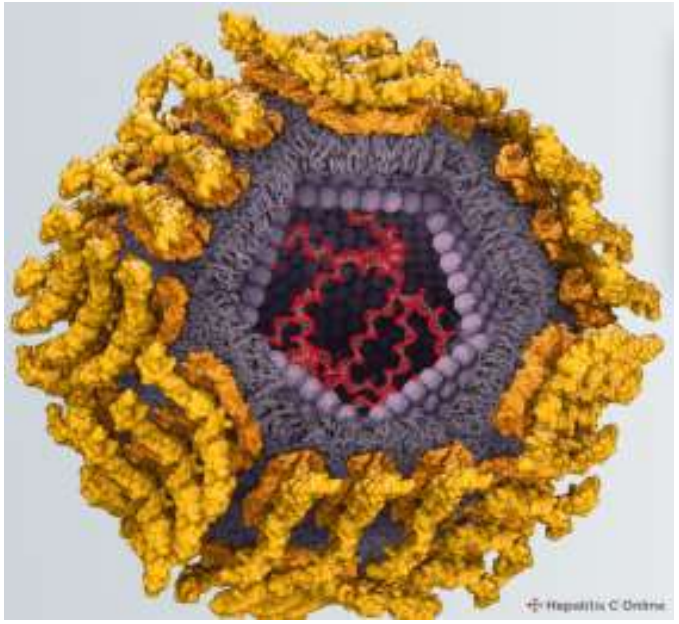
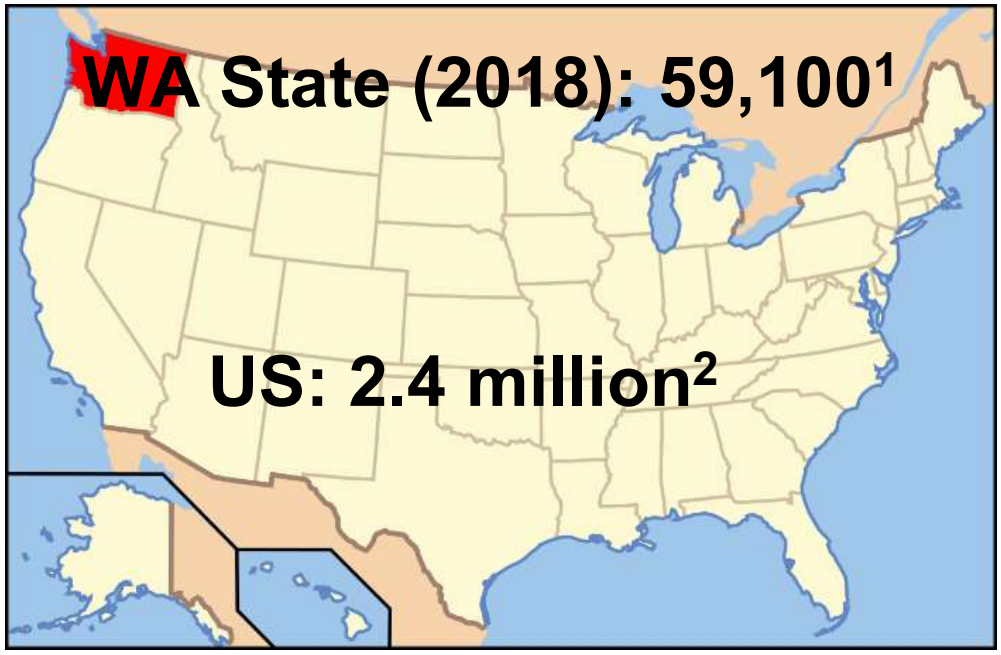


Figure credit: hepatitisc.uw.edu.

HCV is Common and Deadly

Prevalence of chronic HCV infection



- Many persons with HCV (~1/2) are unaware of their infection[3]
- In U.S., ***deaths from HCV outnumber those from HIV plus 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.

PCSS Providers Clinical Support System

HCV in the U.S.: Routes of Transmission

- Injection drug use: majority of cases
- Blood transfusion prior to 7/1992
- Receipt of solid organ transplantation or factor concentrates made before 1987
- Healthcare exposure
- Sex (especially male-to-male sex)
- Unregulated tattoos
- Maternal-child transmission
- Sharing personal items in contact with blood

Highest risk: sharing needles and syringes

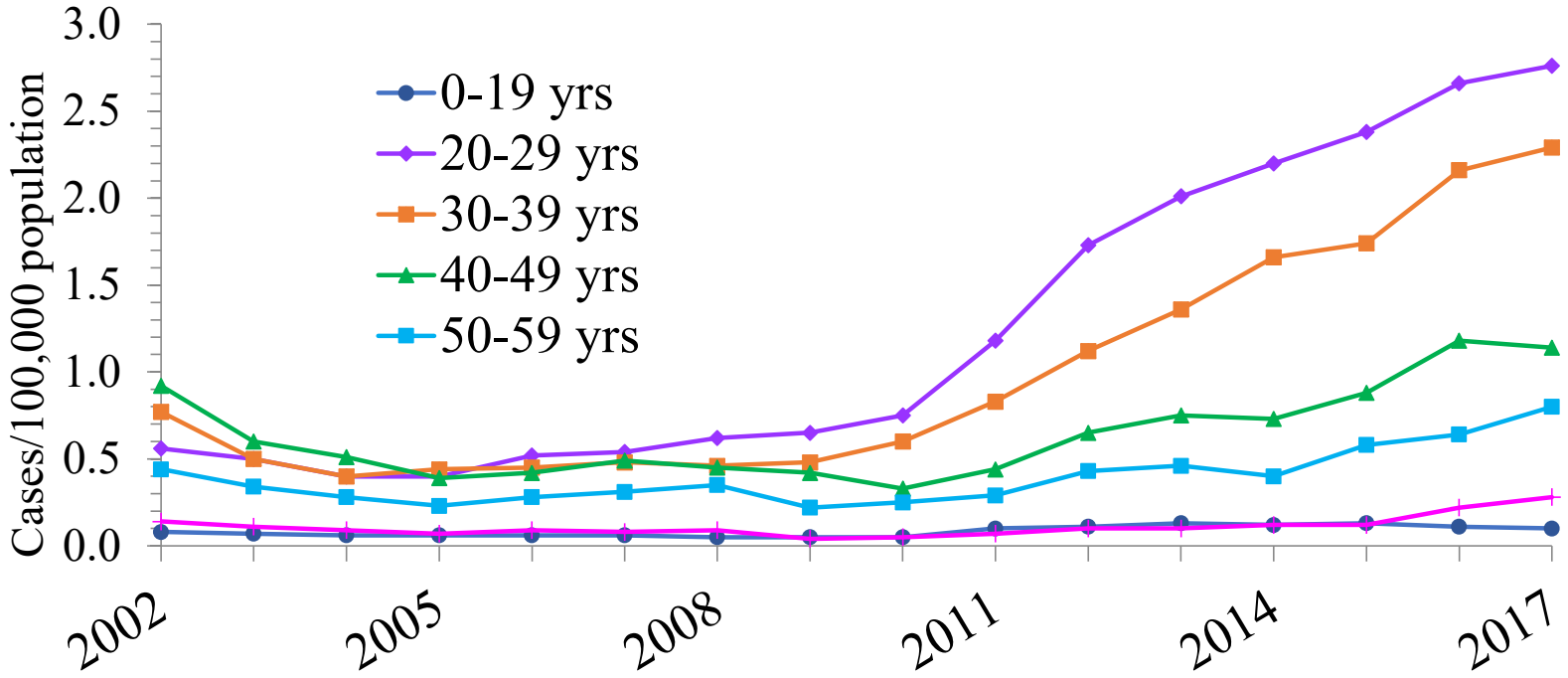
Can also occur with sharing injection paraphernalia such as water, cookers, and cotton filters

www.cdc.gov/hepatitis/hcvcfaq

PCSS Providers Clinical Support System

Opioid Epidemic and HCV

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



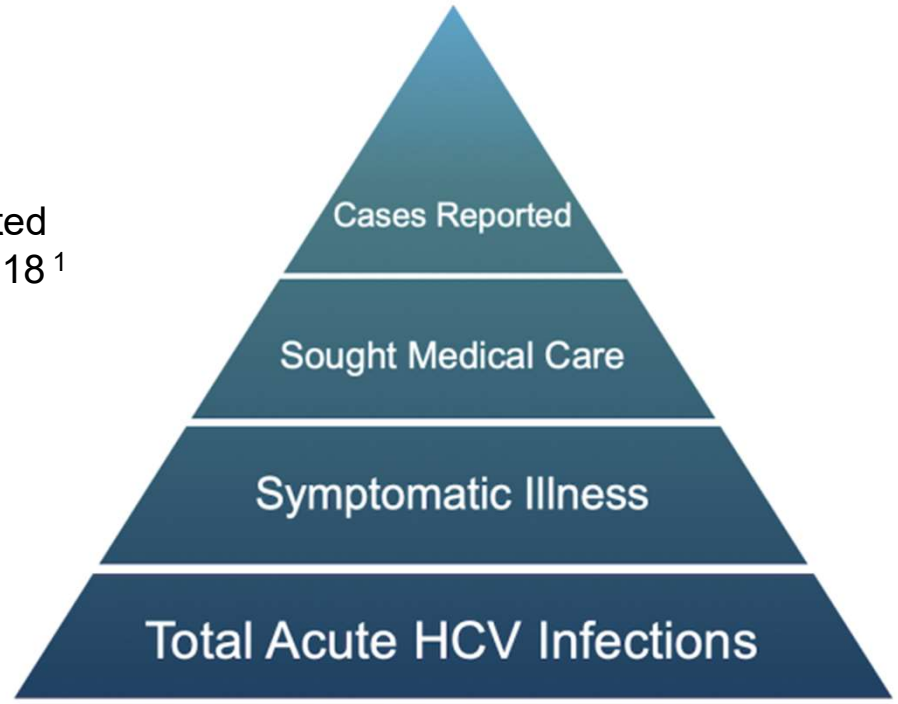
Rates of reported acute hepatitis C by age group, US, 2002-2017 (CDC Viral Hepatitis Surveillance Data)

PCSS Providers Clinical Support System

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]

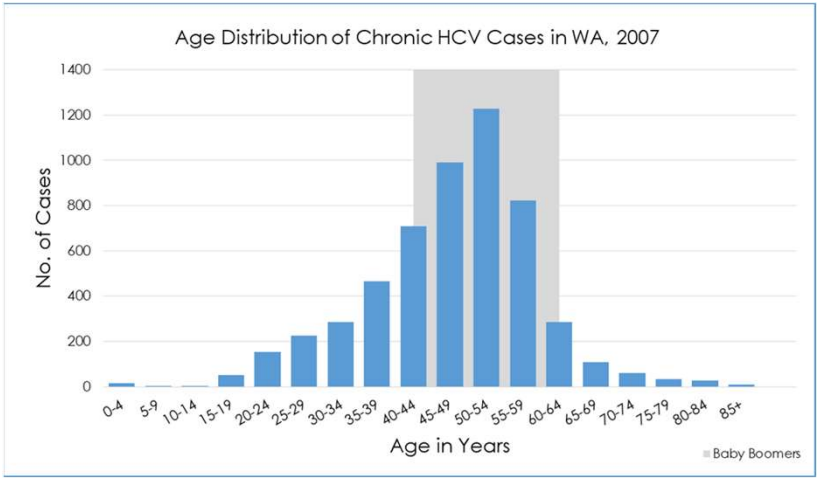
Figure source: modified from hepatitisc.uw.edu from Klevens et al, Am J Public Health 2014

PCSS Providers Clinical Support System

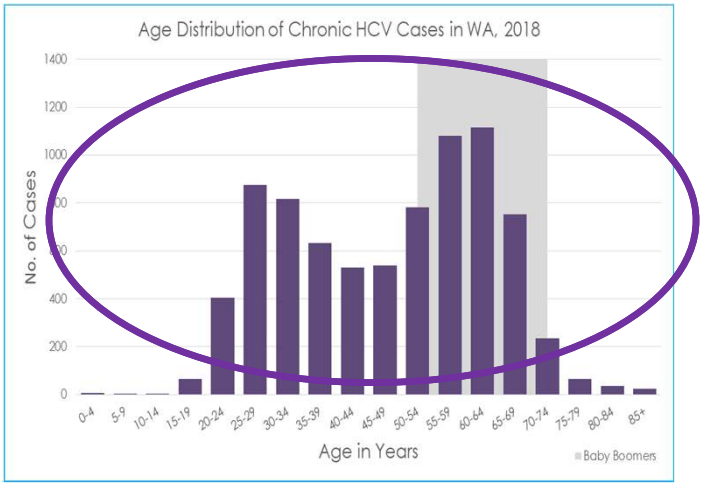
Shifting Epidemiology Due to Opioid Use Disorders/Injecting Drugs

- 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



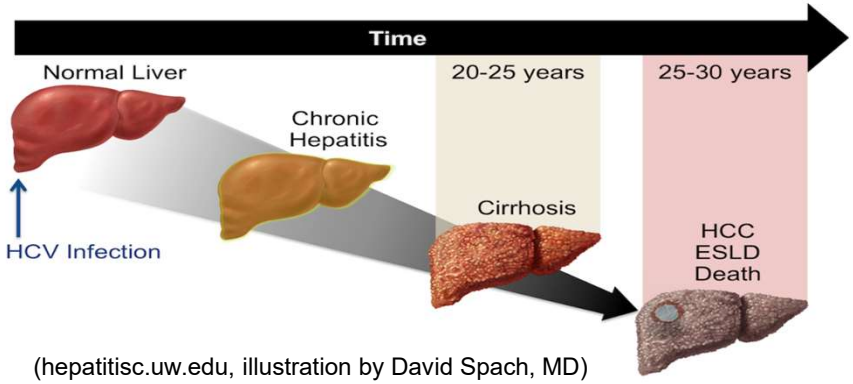
2018

Source: WA State Dept of Health

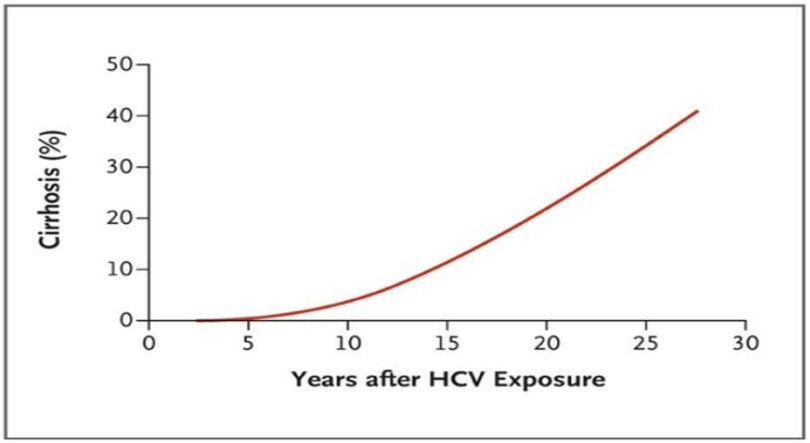
PCSS Providers Clinical Support System

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

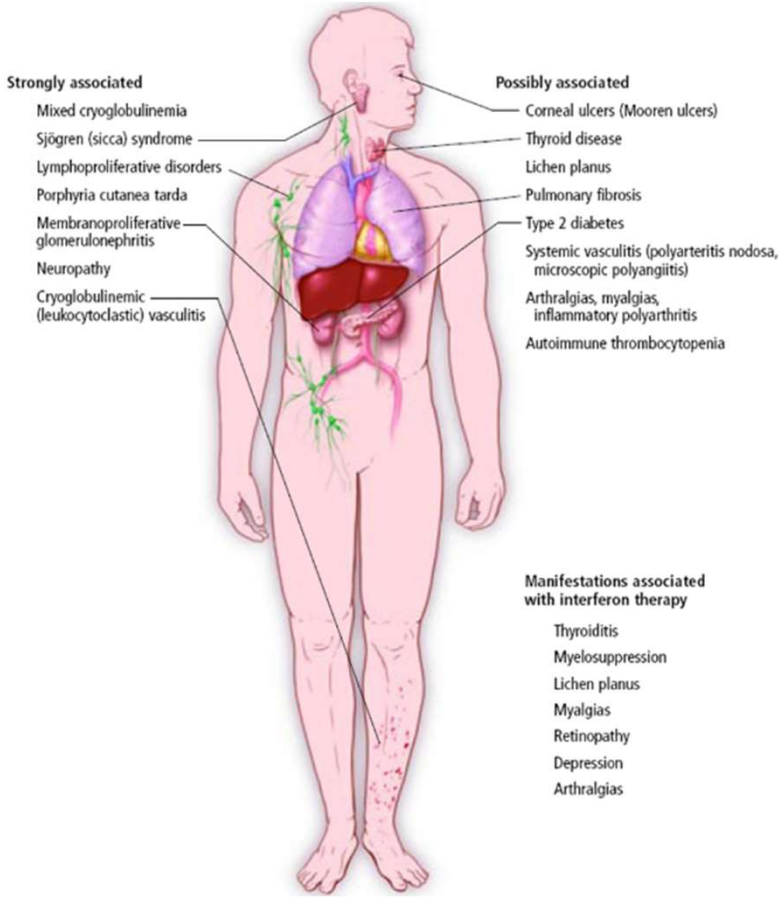


(hepatitisc.uw.edu, illustration by David Spach, MD)



Rosen H.R, NEJM 2011

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

Benefits of Cure of HCV

- Reduced all-cause mortality
- Positive psychosocial effects and improved quality of life
- Reduction in liver fibrosis and liver complications
- Reduced transmission to others
- Reduced incidence of liver cancer
- Decreased inflammation and non-hepatic comorbidities

PCSS Providers Clinical Support System

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

PCSS Providers Clinical Support System

Treatment as Prevention for HCV among PWID

Treating populations that actively transmit HCV

Reduces new infections

Reduces existing disease (i.e. prevalence) over time

PCSS Providers Clinical Support System

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

PCSS Providers Clinical Support System

Myths

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

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

Though previously assumed true and incorporated into guidelines and coverage requirements, these assumptions have been largely disproven…

Definitions

Cure of HCV = Sustained Virologic Response (aka SVR)

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)

Countering Myth #1: "People who use substances can't be cured"

- 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, or to impose criteria for abstinence.

Studies Show High Cure Rates in PWUD

Population	Outcome
CO-STAR[1]: 301 persons in treatment for OUD (methadone and buprenorphine) treated with elbasvir/grazoprevir	91.5% rate of SVR, no difference in adherence or cure among those with + urines; around 90% adherence despite ~50% +urines
SIMPLIFY[2]: 103 persons who had injected drugs within 6 months treated sofosbuvir/velpatasvir	97% completed tx, 94% had SVR 12, drug use did not affect SVR 12
HERO study[3]: 755 persons who injected within 3 months treated with sofosbuvir/velpatasvir and randomized to patient navigation (PN) vs directly-observed treatment (DOT)	In both groups, >80% initiated treatment: of those, 92% had SVR 12 (no difference between arms); 74% adherence (non-adherence associated with no SVR)
PREVAIL study[4]: 145 PWID treated on-site at a methadone program with different DAA regimens via electronic blister packs	Overall, 96% had SVR 12 with average daily adherence 74% adherence; among those with ≥50% adherence, 99% achieved SVR 12 *(even with suboptimal adherence patients are cured!)*

[1] Dore G, Annal Int Med 2016; [2] Grebely, Lancet Gastroenterol Hepat 2018; [3] Litwin, A Multisite Randomized Pragmatic Trial of Patient-Centered Models of Hepatitis C Treatment for People Who Inject Drugs: The HERO Study. Oral presentation at AASLD 2020, Nov 11-16
[4]Norton B OFID 2020

PCSS Providers Clinical Support System

Countering Myth #2:
"Persons who use drugs are likely to be reinfected"

- *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]
- *Reinfection can be prevented…*
  - 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

PCSS Providers Clinical Support System

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

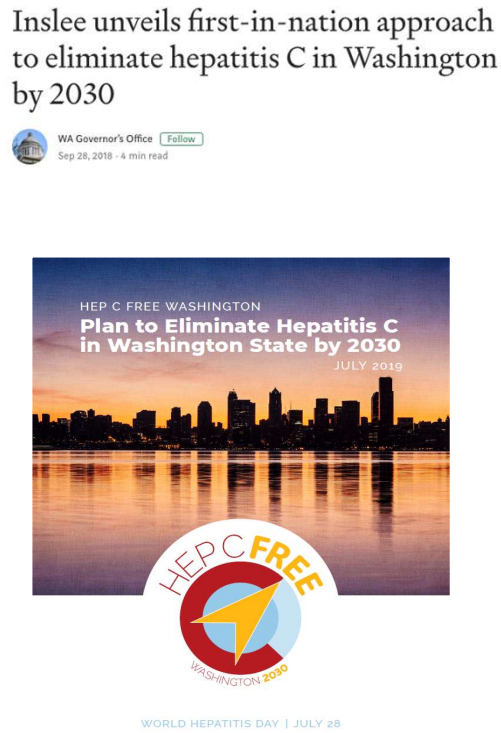
Population	# Studies	Person-years f/u	Rates of reinfection per 100 person-years
Injecting or non-injecting drug use	33	5,061	5.9 (95% CI 4.1-8.5)
Injecting drug use	31	4,648	6.2 (95% CI 4.3-9.0)
Opioid agonist treatment	25	2,507	3.8 (95% CI 2.5-5.8)

Hajarizadeh, et al, 2020

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[1]
  - Many high-income countries are not expected to achieve elimination before 2050, including the USA[2]; only 3 states projected to succeed (WA, SC, CT)[3]
- 2018: Gov. Inslee announces "Hep C Free WA" initiative
  - PWID identified as a **priority population** for treatment
  - WA Health Care Authority removes remaining restrictions to DAAs

There is a great opportunity to treat HCV here, now



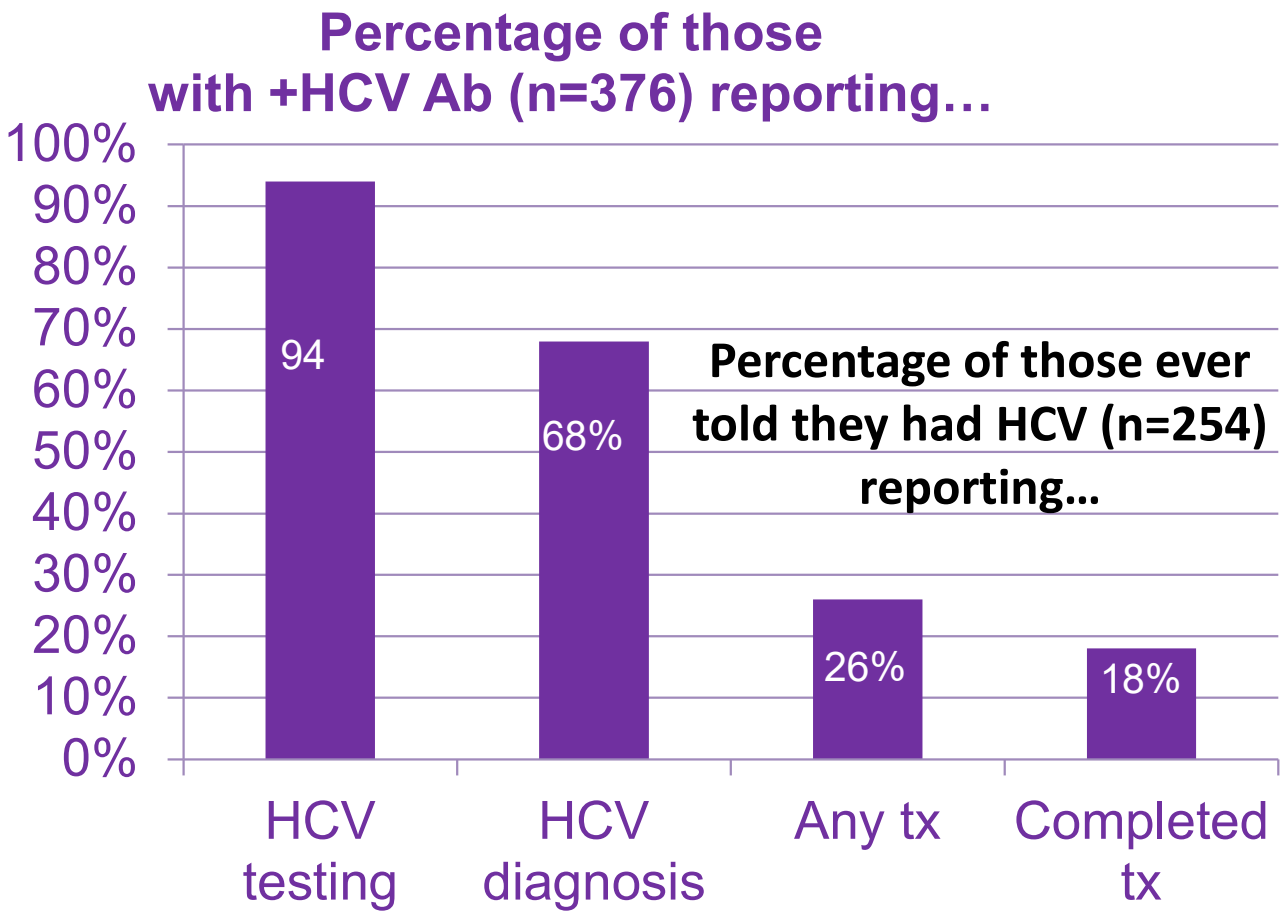
1. WHO: World Health Organization; HCA: Healthcare Authority
2. Razavi H Liver Int 2020
3. Sulkowski M Adv Ther 2021

WA Health Care Authority's Medicaid Pharmacy Policy for Curative HCV Treatment

- Aligns with national expert (AASLD/IDSA) HCV guidance
  - No requirement for abstinence
  - Evidence of fibrosis not required
  - Any licensed prescriber can treat
  - Not necessary to document chronic infection with multiple consecutive tests: a single detectable RNA is sufficient
  - Prior authorization not required for glecaprevir/pibrentasvir

But…There Are Ongoing Treatment Gaps

- Data from 2018 show an ongoing gap from screening to treatment among persons who inject drugs (PWID) in Seattle[1]
- **Indicate an urgent need to offer treatment without delays in settings where PWID are seen.**



HCV Care Continuum among Seattle PWID, National HIV Behavioral Surveillance Survey, 2018

[1] Corcorran, Tsui et al., Drug and Alcohol Dependence 2021

PCSS Providers Clinical Support System

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

PCSS Providers Clinical Support System

HCV Treatment: The Big Picture

- In most patients with hepatitis C, treatment is straight-forward and simple and can be done by PCPs with prescribing capacity (MD/NP/PA)
  - Studies demonstrate equivalent or better outcomes[1-4]
- In people with advanced liver disease or certain other conditions (hepatitis B co-infection, HIV, transplant, liver cancer), treatment is more complicated and should be done by or in consultation with specialists

[1]Kattakuzhy S, Annal of Int Med 2017; [2]Lasser K, Annals Fam Med 2017; [3]AWade AJ, Clin Inf Dis 2020; [4] Radley A, Lancet Gastroent Hep 2020

PCSS Providers Clinical Support System

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®)

Screening for Hepatitis C Virus Infection

- **New USPSTF recommendation to screen all asymptomatic adults age 18-79 for HCV: *Anti-HCV antibody followed by confirmatory PCR for viral detection***
- 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.

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)* 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

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

* Within 6 months of starting treatment

When to Refer

Reasons to refer:

- Decompensated cirrhosis: ascites, jaundice, variceal hemorrhage, encephalopathy (Child's Class B or C)
- Hepatocellular carcinoma
- Post-transplant
- 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)			

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

Consider involving a SW, case manager or patient navigator when referring patients to facilitate engagement/follow-up.

*Guidelines for retreatment are evolving—refer to IDSA/AASLD guideline for updates.

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

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
- For patients who need addition monitoring, engagement of various members of care team (pharmacist, SW, case manager) can be helpful

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.

PCSS Providers Clinical Support System

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

PCSS Providers Clinical Support System

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

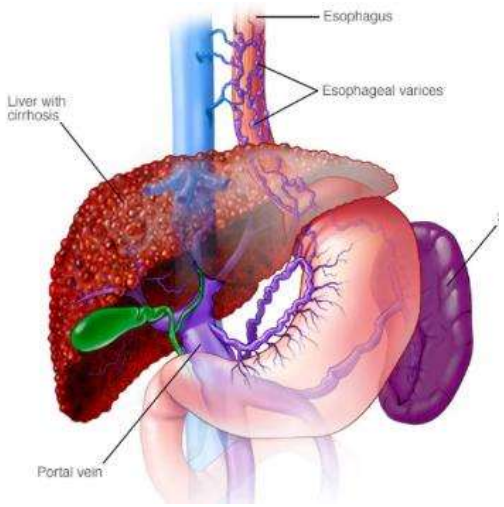
- Avoid excessive alcohol (those with cirrhosis should avoid alcohol completely)
- *Cure does not prevent reinfection: screen annually with HCV RNA if ongoing risk factors*

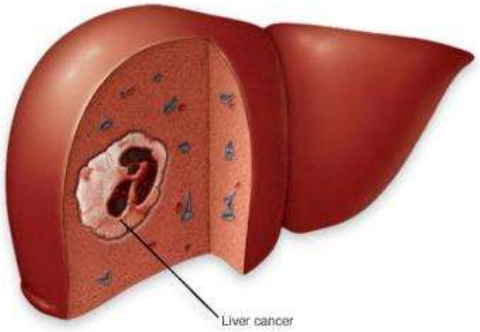
IDSA/AASLD Guideline: hcvguidelines.org

PCSS Providers Clinical Support System

Patients with Cirrhosis Need Follow Up Care

Screen for esophageal varices if appropriate





Screen for liver cancer

Offer help with drinking for those who need it (consider pharmacotherapy, referrals to psychologist, support groups, peer specialists, etc.)

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 SSPs 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

PCSS Providers Clinical Support System

Back to Screening

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

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

PCSS Providers Clinical Support System

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

Get Started!

- Key resources:
  - IDSA/AASLD guidelines: https://www.hcvguidelines.org/
  - UW HCV training: https://www.hepatitisc.uw.edu/
  - Project ECHO: for UW contact Pam Landinez at landinez@uw.edu; U Utah https://physicians.utah.edu/echo/
  - UCSF phone consultation, 9 am-8 pm ET: (844) HEP-INFO or (844) 437-4636; https://nccc.ucsf.edu/clinician-consultation/hepatitis-c-management/
  - U. of Liverpool medication interaction checker: https://www.hep-druginteractions.org/checker
  - Consult with your local/specialty pharmacist

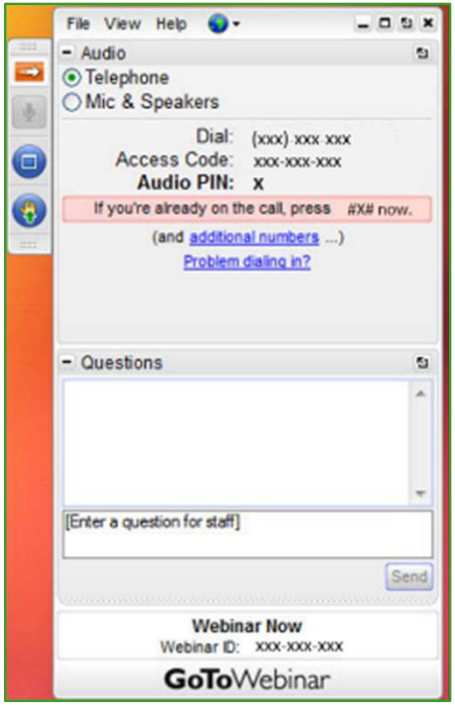
Tips

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

Presenter Q&A

Desktop

Use the “Questions” area of the attendee control panel.



Instant Join Viewer

Click the “?” symbol to display the “Questions” area.

Thank You!

- Questions and discussion

PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.
- PCSS Mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medications for opioid use disorder (MOUD)**.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

For more information visit:

https://pcssNOW.org/mentoring/

PCSS Providers Clinical Support System

PCSS Discussion Forum

Have a clinical question?

Ask a Colleague

A simple and direct way to receive an answer related to medications for opioid use disorder. Designed to provide a prompt response to simple practice-related questions.

http://pcss.invisionzone.com/register

PCSS Providers Clinical Support System

PCSS is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with:

Addiction Technology Transfer Center	American Society of Addiction Medicine
American Academy of Family Physicians	American Society for Pain Management Nursing
American Academy of Pain Medicine	Association for Multidisciplinary Education and Research in Substance use and Addiction
American Academy of Pediatrics	Council on Social Work Education
American Pharmacists Association	International Nurses Society on Addictions
American College of Emergency Physicians	National Association for Community Health Centers
American Dental Association	National Association of Social Workers
American Medical Association	National Council for Mental Wellbeing
American Osteopathic Academy of Addiction Medicine	The National Judicial College
American Psychiatric Association	Physician Assistant Education Association
American Psychiatric Nurses Association	Society for Academic Emergency Medicine

PCSS Providers Clinical Support System

Educate. Train. Mentor

@PCSSProjects

www.facebook.com/pcssprojects/

www.pcssNOW.org

pcss@aaap.org

Funding for this initiative was made possible (in part) by grant no. 1H79TI081968 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.