

Role of the Primary Care Provider in HCV Elimination

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Disclosure

- Dr. Jorge Mera does not have any conflicts of interest to disclose

Outline

- Case presentation
- HCV epidemiology overview
- HCV elimination overview
- Role of the primary care provider in HCV elimination
- Evaluation and treatment of HCV
- Conclusions

Mr. S

- **Reason for consultation:** Patient referred to your practice for MAT and HCV evaluation after being induced with buprenorphine/naloxone in the ED.
- **HPI:** Mr. **S** is a pleasant 24 yo male who had a MVA 6 years ago, suffered a right femur fracture and was placed on OxyContin for pain control. Two years ago his new medical provider refused to refill the pain medication. He initially got OxyContin from friends but later had to purchase them in the streets and started injecting it. One year ago he started injecting heroin since it was cheaper. He has been sharing needles and syringes since the pharmacy will not sell them to him.
Three days ago he presented to the ED with opioid withdrawal symptoms (Nausea, vomiting, diarrhea, restlessness, abdominal pain). The ED medical provider induced him with Bup/Nal and gave him a 4 day prescription of Bup/Nal, enough until he could be evaluated and placed on MAT. During the ED visit an HCV test was positive.
- **PE:** Vital signs are normal, BMI 26. Except for track marks in his arms the physical exam is unremarkable.

Mr. S “continued”

- **Labs**

- RNA Viral load positive, 3.4 million copies /mL, Genotype pending.
- ALT 72 IU/L, AST 65 IU/, Creatinine 0.9 mg/dL, GFR 69 ml/min, Hg 13.4 g/dL, **Platelets 288 x 10³/mcL**, Albumin 4.5 g/dL, Total Bilirubin 0.7 mg/dL, INR 1.0.
- Hep A Ab (-), **HBsAg (-), HBsAb (-), HBcAb (-)**

- **Questions:**

- What is his liver fibrosis stage
- As a primary care provider what can you do for this patient?
- How will this impact HCV elimination in your community?

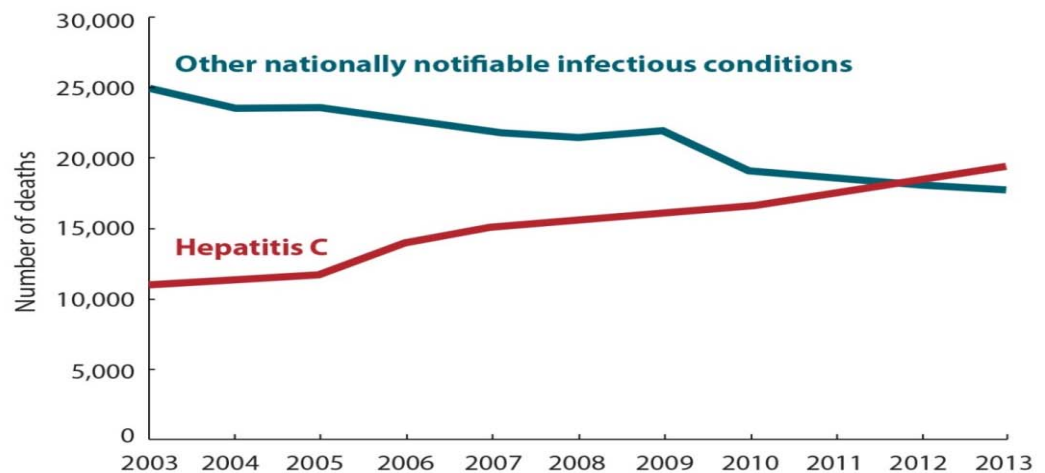
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Increasing Deaths Due to Hepatitis C

More people are dying of HCV than all 60 other nationally notifiable infectious diseases combined.

Annual number of hepatitis C-related deaths vs. other nationally notifiable infectious conditions in the US, 2003-2013



Source: Centers for Disease Control and Prevention

HCV in the USA

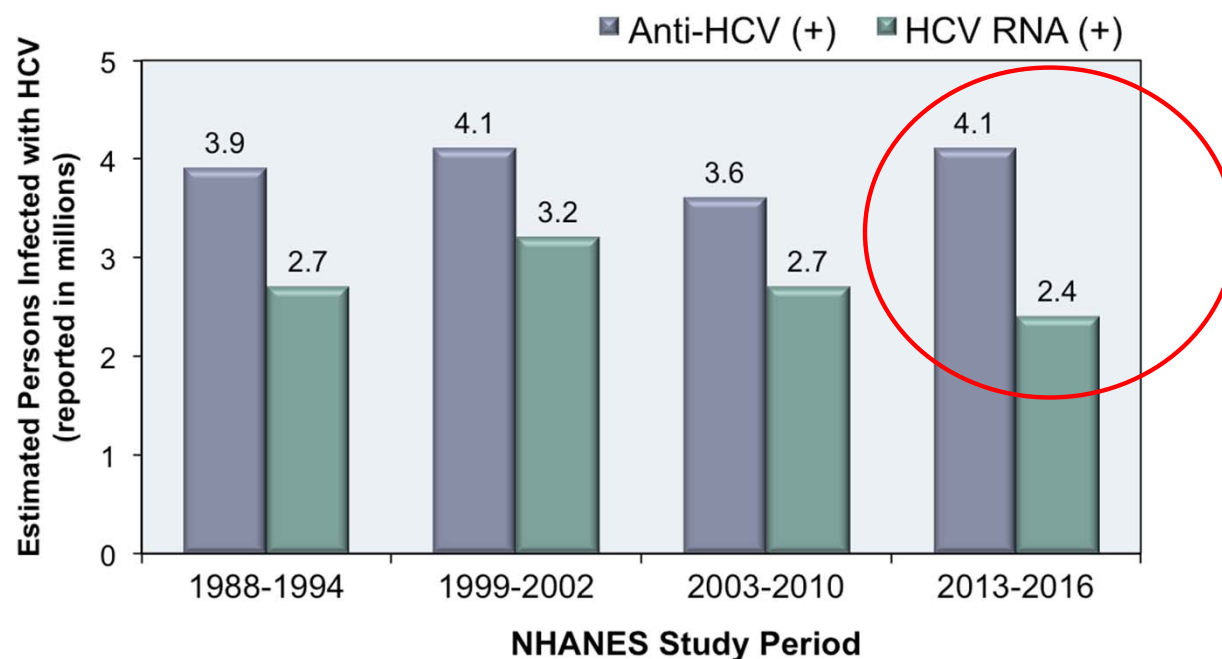
- An estimated 2.4 million people in the United States are living with HCV
- In 2017, a total of 3,186 cases of acute hepatitis C were reported to CDC. After adjusting for under-ascertainment and under-reporting, an estimated 44,300 acute hepatitis C cases occurred in 2017.
- HCV disease and complications are estimated to account for over 15,000 US deaths annually

Actual number of acute hepatitis C cases submitted to CDC by states and estimated* number of acute hepatitis C cases — United States, 2010–2017



Source: CDC, National Notifiable Diseases Surveillance System.

Estimated Number of Persons Infected with HCV in the United States



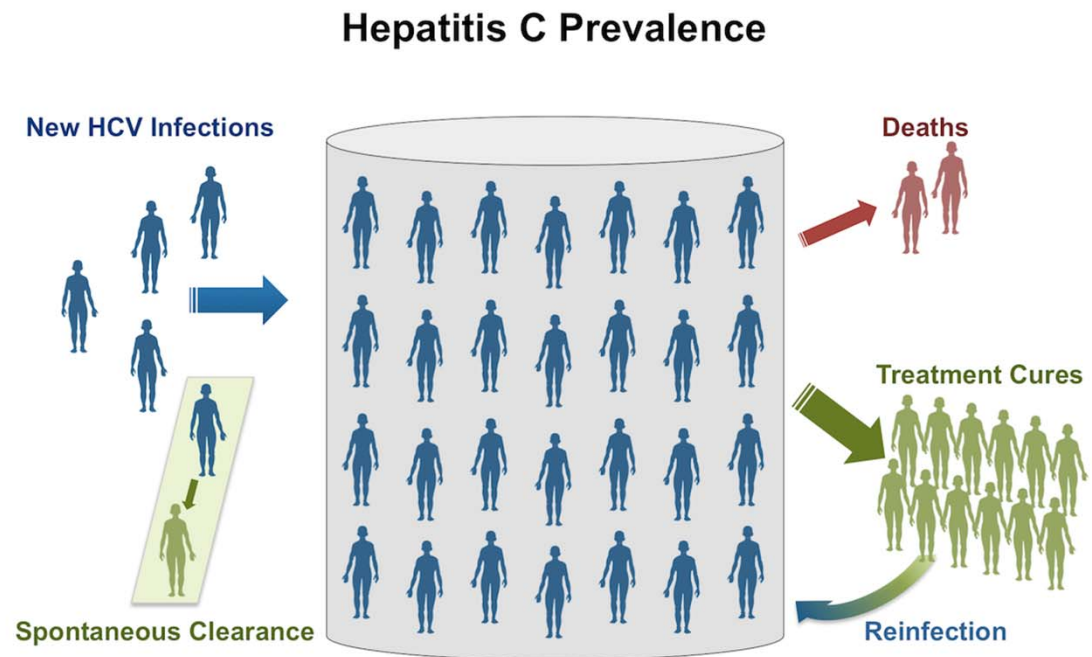
This graphic shows data representing seroprevalence (anti-HCV) and chronic infection (HCV RNA) from four distinct NHANES studies. The numbers on the bar graph represent millions of persons

Source: (1) Denniston MM, Jiles RB, Drobeniuc J, Kleven RM, Ward JW, McQuillan GM, Holmberg SD. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. *Ann Intern Med.* 2014;160:293-300. (2) Hofmeister MG, Rosenthal EM, Barker LK, et al. Estimating Prevalence of Hepatitis C Virus Infection in the United States, 2013-2016. *Hepatology.* 2018 Nov 6. [Epub ahead of print]

[Hepatitis C Online](https://www.hepatitisc.uw.edu)
<https://www.hepatitisc.uw.edu>

Dynamics of HCV Prevalence in the United States

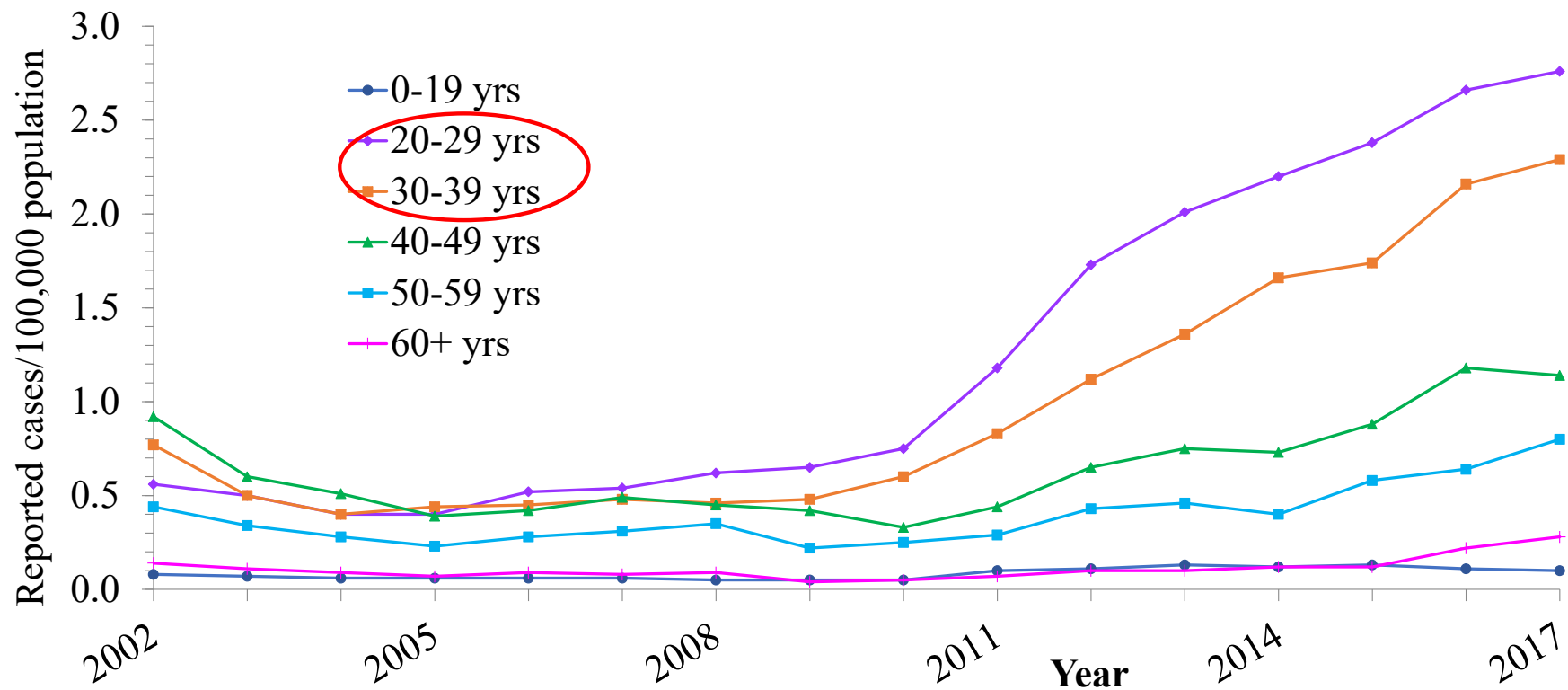
This illustration shows the dynamics of HCV prevalence in the United States (persons living with chronic HCV infection) is impacted by multiple factors, including number of new infections, spontaneous resolution of new infections, deaths, and treatment-related HCV cure. Persons cured of HCV can become reinfected. In addition, a small number of persons have spontaneous resolution of chronic HCV infection.



Source: Illustration by David H. Spach, MD

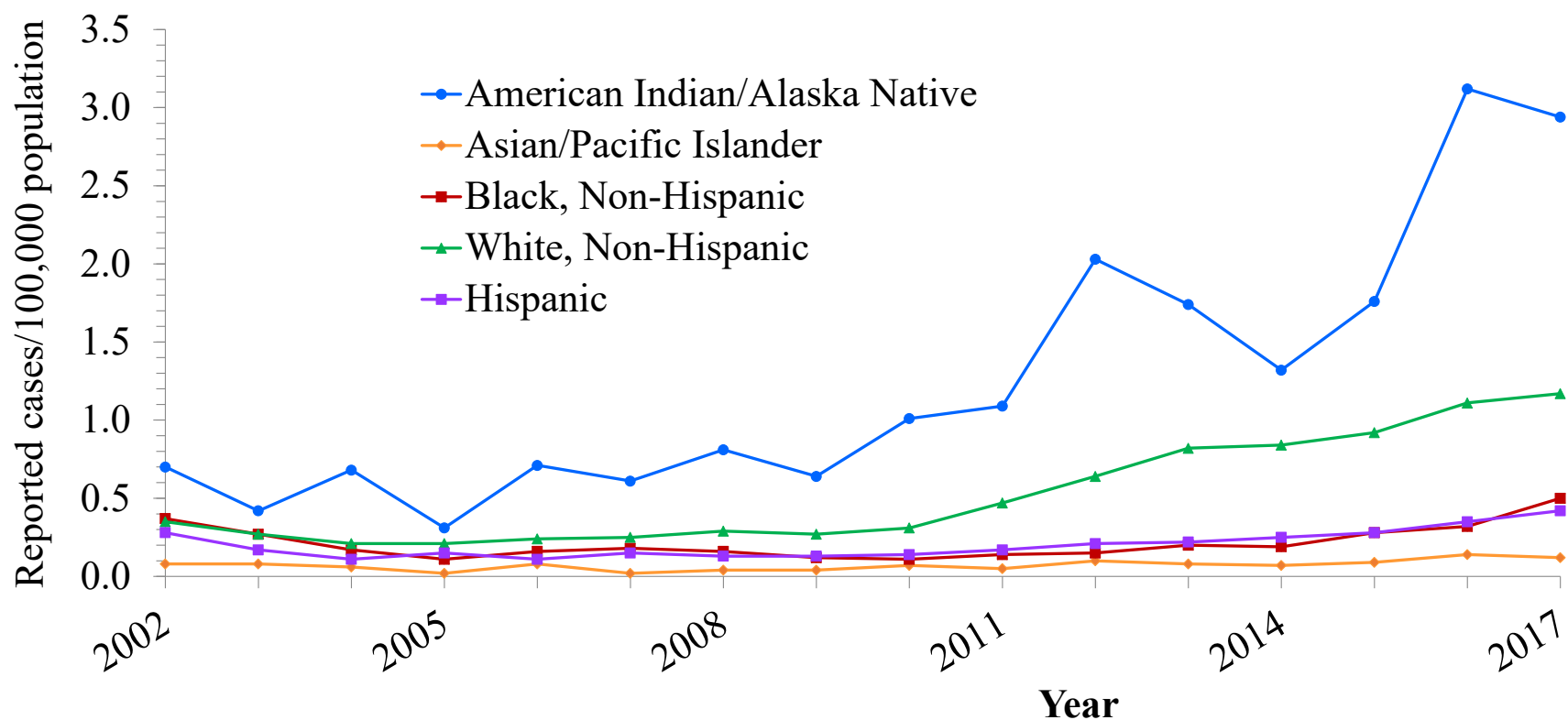
[Hepatitis C Online](https://www.hepatitisc.uw.edu)
<https://www.hepatitisc.uw.edu>

Rates of reported acute hepatitis C, by age group United States, 2002–2017



Source: CDC, National Notifiable Diseases Surveillance System.

Rates of reported acute hepatitis C, by race/ethnicity United States, 2002–2017



Source: CDC, National Notifiable Diseases Surveillance System.

HCV IN OKLAHOMA

OSDH Home > Organization > Office of Communications > News Releases > 2017 News Releases > Chronic Hepatitis C Infection Disproportionately Affecting Oklahomans [email](#) | [print](#)

Chronic Hepatitis C Infection Disproportionately Affecting Oklahomans; OSDH Encourages Testing

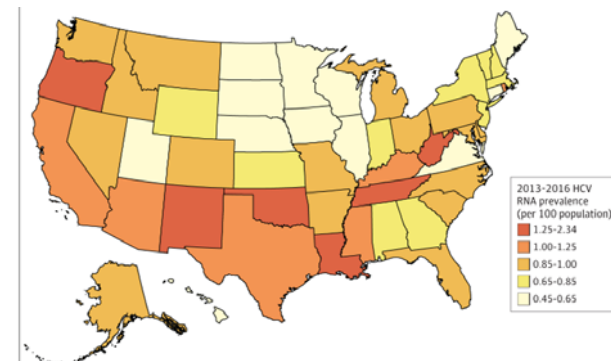
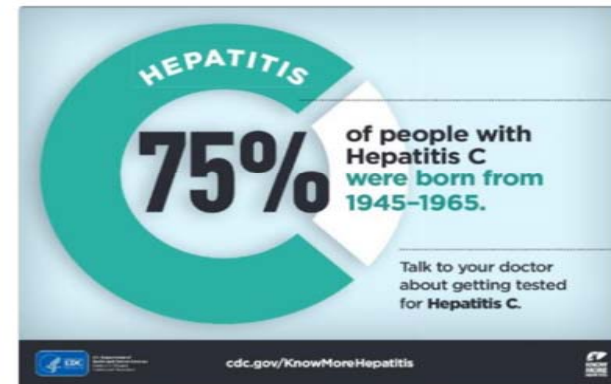
For Release: April 26, 2017 – Jamie Dukes, Office of Communications (405) 271-5601 [@](#)

According to a newly released study, there are an estimated 94,200 Oklahomans living with Hepatitis C virus infection. Estimates were developed by researchers at Emory University in conjunction with the Centers for Disease Control and Prevention to better understand the number of people in each state living with Hepatitis C.

"Far too many individuals are unaware of their risk of infection and importance to get tested," said Kristen Eberly, director of the OSDH HIV/STD Service. "Although the ongoing opioid epidemic has contributed to recent increases in HCV infections among adults under age 40, it's also important for Oklahomans to understand hepatitis C poses a serious health concern for people of all ages, including infants born to infected mothers."



OK Dept of Health @HealthyOklahoma · 15h
More than 94,000 Oklahomans are living with Hep C, but may not know it. Should you be tested? Find out here: go.usa.gov/x58dU



HCV: Transmission

- **Blood**

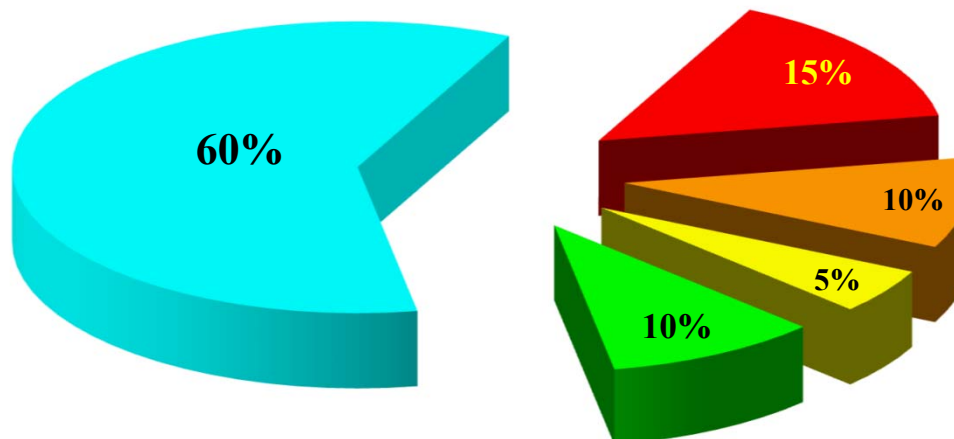
- IVDU is the leading cause in the United States
 - Snorting
- Percutaneous injuries
- Dental
- Tattooing
- Blood transfusion (Before 1992)

- **Sexual contact**

- Rare in heterosexual
- More frequent in HIV + MSM

- **Mother-to-child**

- The rate is 1.7% - 4.3 %
- *Increased in IVDU, HIV co-infection, VL (?)*



PWID

Sexual

Transfusion

Other*

Unknown



*Nosocomial; Health-care work; Perinatal

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance—United States, 2016.
Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2018.
Available at: <https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm>.

HCV and Injection Drug Use

**Today > 80% of HCV
Transmission Occurs in PWID**



Paraphernalia

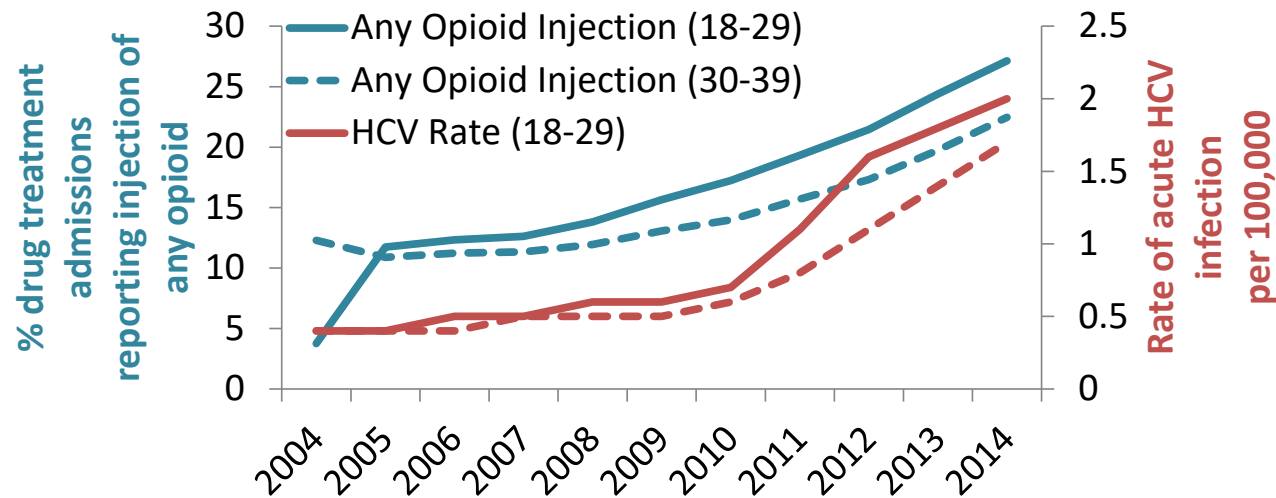


Needle
Syringe
Cooker
Table
Tourniquet

Palmateer N, Hutchinson S, McAllister G et al. Risk of transmission associated with sharing drug injecting paraphernalia: analysis of recent hepatitis C virus (HCV) infection using cross-sectional survey data. J Viral Hepatol 2014 Jan;21(1):25-32

What is Driving the HCV Epidemic in the USA?

Rates of HCV Infections are Rising Among Younger PWIDs

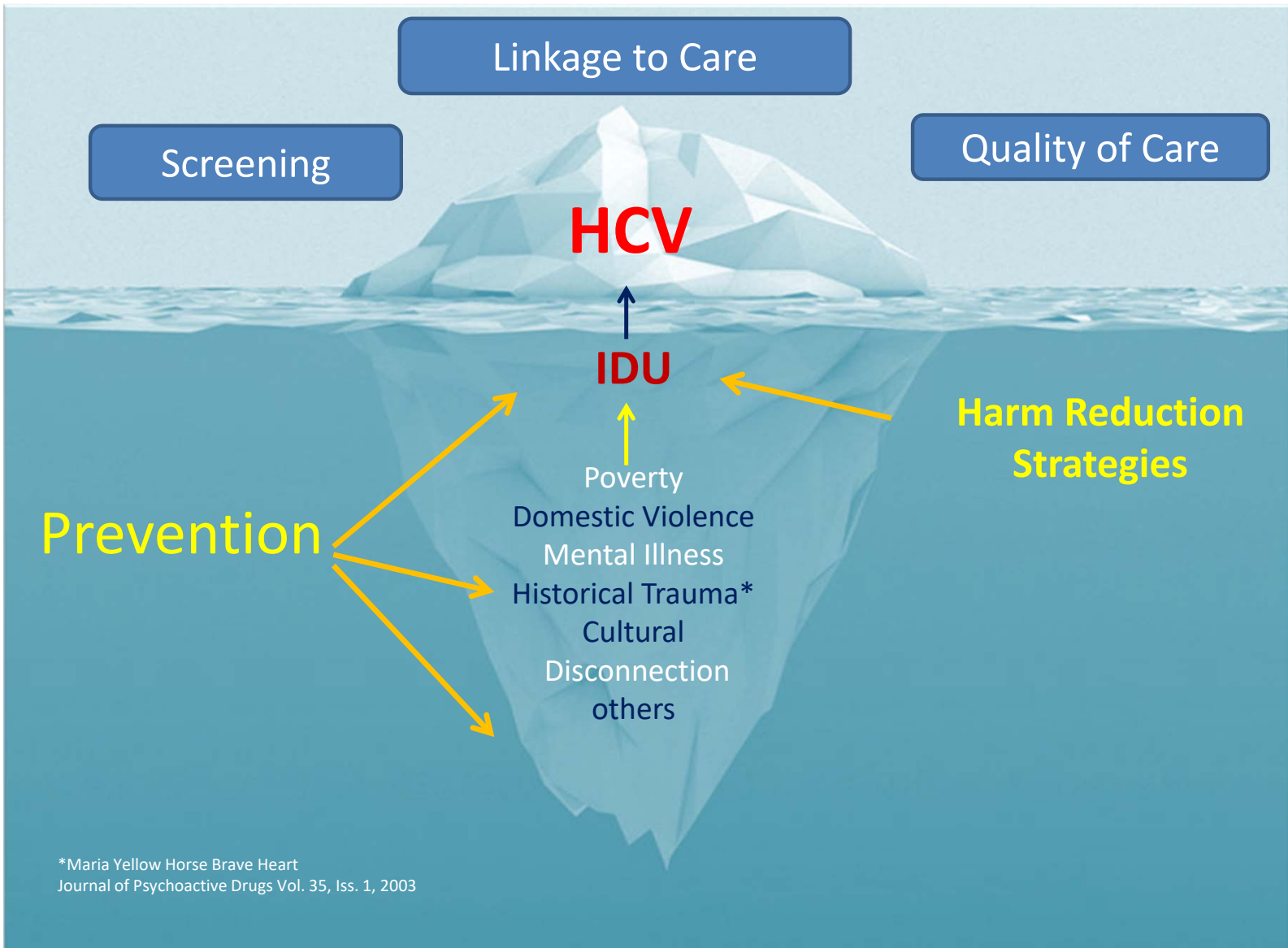


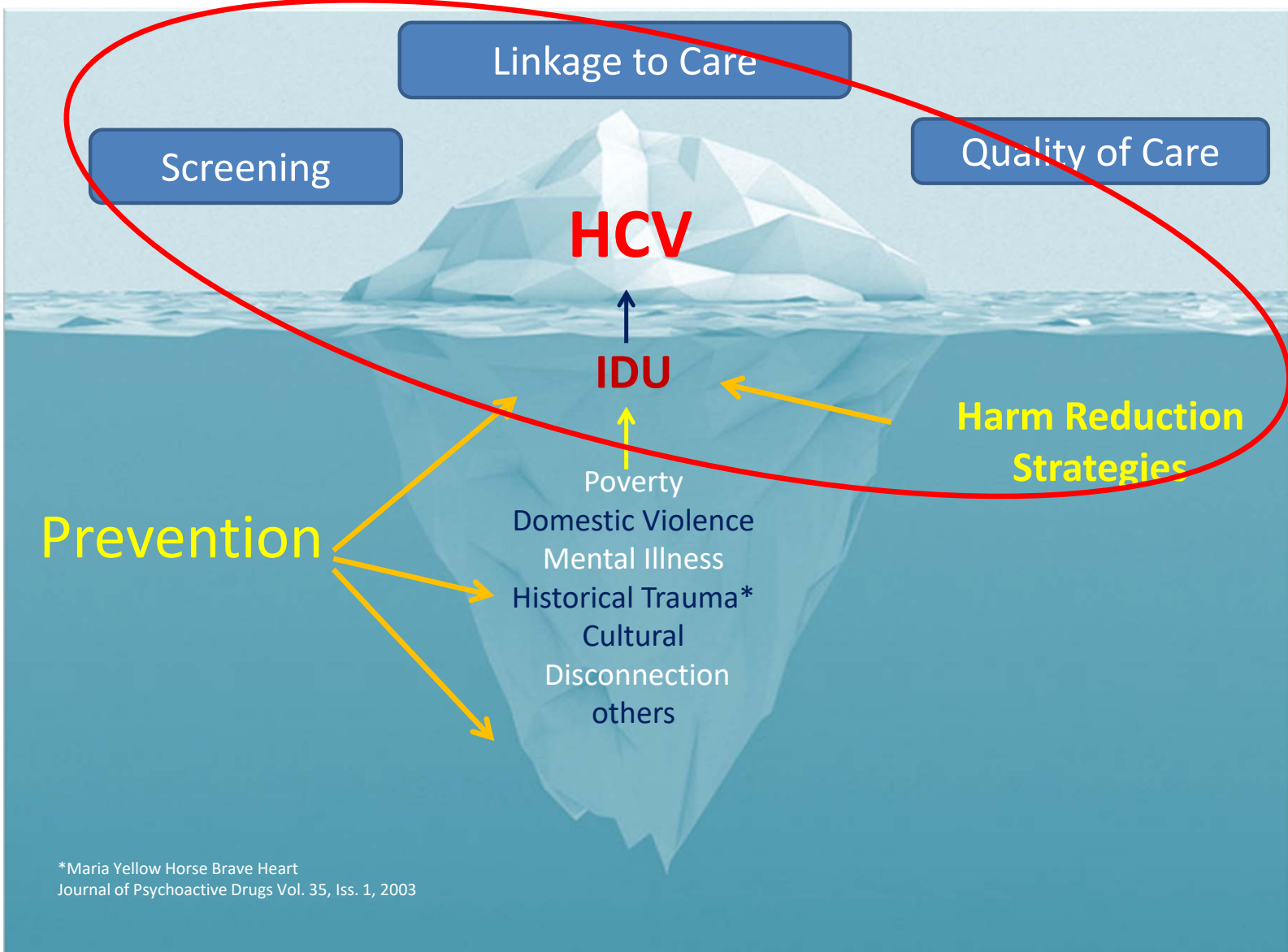
- Among people aged 18-29, HCV increased by 400% and admission for opioid injection by 622%¹
- Among people aged 30-39, HCV increased by 325% and admission for opioid injection by 83%¹
- HCV seroprevalence among PWIDs is ~55% in North America²

1. Zibbell JE, et al. *Am J Public Health*. 2018 Feb;108(2):175-181;
2. Degenhardt L, et al. *Lancet Glob Health* 2017;5:e1192-e1207.





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- **HCV elimination overview**
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Feasibility Criteria for Elimination

In General ¹	Hepatitis C Virus	Check list
No non- human reservoir and the organism can not multiply in the environment	No non human reservoir	
There are simple and accurate diagnostic tools	Serology widely available	
Practical interventions to interrupt transmission	Treatment as prevention Needle and syringe programs Medication assisted programs	
The infection can in most cases be cleared from the host	Treatment is 95% curative	

Adapted from Hopkins D. **Disease Eradication**. N Engl J Med 2013;368:54-63

HCV Elimination: Definitions and Goals

- **Traditional Definition: Eradication vs Elimination vs Control**
- **Present Definition:** Elimination of hepatitis C as a *public health problem (previously known as “Control”)*
- **Goals:**
 - **National Viral Hepatitis Action Plan 2017-2020¹**
 - Decrease in new infections by 60 % by the year 2020
 - Decrease in mortality by 25 % by the year 2020
 - ***National Academy of Sciences²***
 - Decrease the incidence of new infections by 90% by the year 2030
 - Decrease in mortality by 65 % by the year 2030

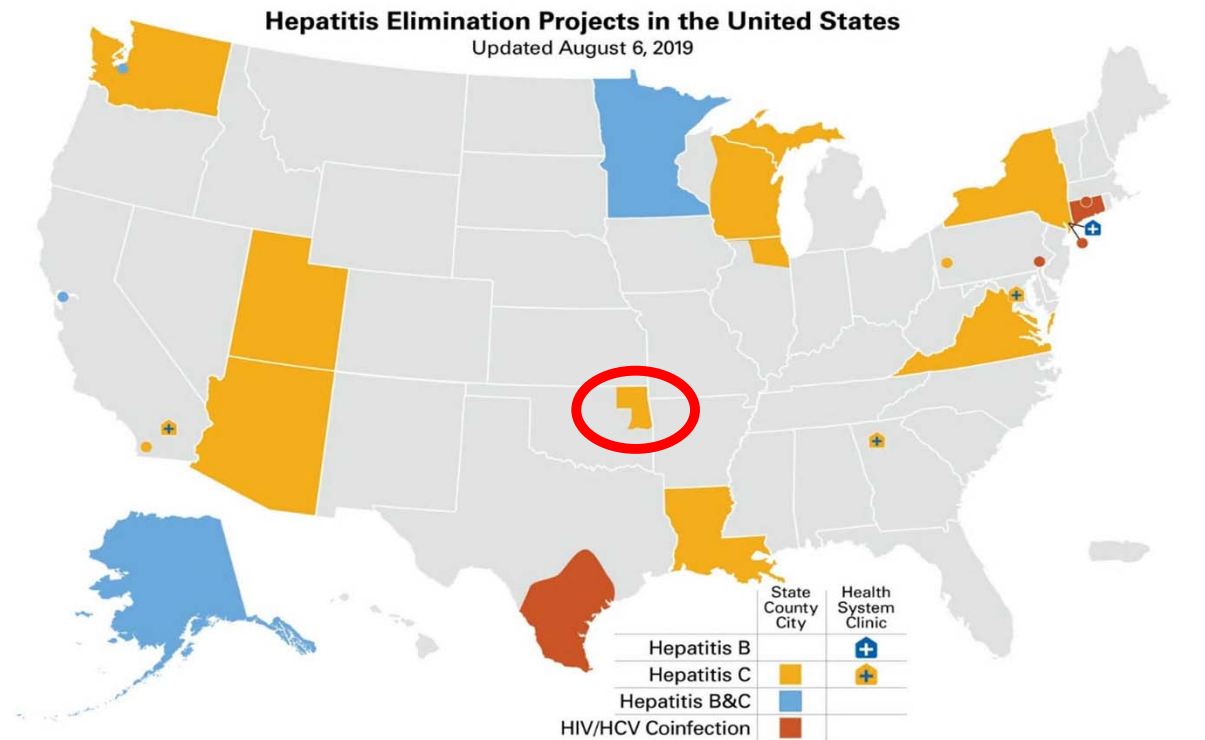
1. <https://www.cdc.gov/hepatitis/hhs-actionplan.htm> 2. National Academies of Sciences, Engineering, and Medicine. 2017. *A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report*. Washington, DC: The National Academies Press

Key Concepts to Guide HCV Elimination

- **Decrease the burden of HCV related liver diseases by treating the chronically infected population**
 - Birth cohort (patients born between 1945-1965)
 - Anyone infected for 20 + years or with multiple liver comorbidities

- **Decrease new infections by preventing transmission**
 - **Mainly target the younger population who are PWID**
 - *Treatment as prevention* /MAT/Needle and syringe programs
 - Corrections system is an opportunity
 - Address sexual transmission in MSM

HCV/HBV Elimination Projects in the USA



<https://www.hhs.gov/hepatitis>

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How Can PCP Contribute to HCV Elimination?

- Universal Screening
- Be an advocate
 - For MAT programs
 - For Syringe and Service Programs
- Treat patients with chronic infections to prevent morbidity and mortality
- Treat patients who are injecting drugs to prevent new infections

Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965



Rationale

- 45%-85% of infected persons are undiagnosed
- Limitations of current risk-based strategies
- 75% of chronic infections are in persons born from 1945-1965

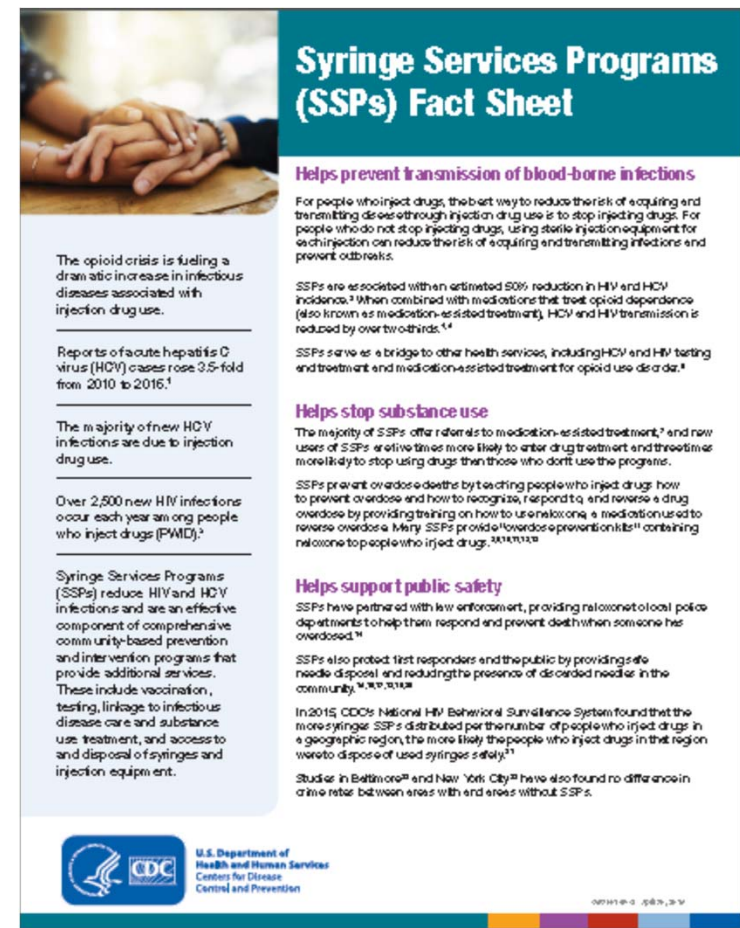
Cost-effectiveness: HCV Testing Expansion

- *“In addition to risk-based testing, one time HCV testing of persons 18 and older appears to be cost-effective, leads to improved clinical outcomes and identifies more persons with HCV than the current birth cohort recommendations. These findings could be considered for future recommendation revisions.*

Barocas JA et al. **Population-level Outcomes and Cost-Effectiveness of Expanding the Recommendation for Age-based Hepatitis C Testing in the United States** *Clinical Infectious Diseases*, 2018 67 (4);549–556

Myths and misconceptions of SSPs

- SSPs increase high-risk practices
- SSPs promote syringes in the community
- SSPs enable drug use
- SSPs increase crime



Syringe Services Programs (SSPs) Fact Sheet

Helps prevent transmission of blood-borne infections

For people who inject drugs, the best way to reduce the risk of acquiring and transmitting disease through injection drug use is to stop injecting drugs. For people who do not stop injecting drugs, using sterile injection equipment for each injection can reduce the risk of acquiring and transmitting infections and prevent outbreaks.

SSPs are associated with an estimated 50% reduction in HIV and HCV incidence.¹ When combined with medications that treat opioid dependence (also known as medication-assisted treatment), HCV and HIV transmission is reduced by over two thirds.^{1,4}

SSPs serve as a bridge to other health services, including HCV and HIV testing and treatment and medication-assisted treatment for opioid use disorder.⁴

Helps stop substance use

The majority of SSPs offer referrals to medication-assisted treatment,² and new users of SSPs are five times more likely to enter drug treatment and three times more likely to stop using drugs than those who do not use the program.³

SSPs prevent overdose deaths by teaching people who inject drugs how to prevent overdose and how to recognize, respond to, and reverse a drug overdose by providing training on how to use naloxone, a medication used to reverse overdose. Many SSPs provide naloxone to people who inject drugs, containing naloxone to people who inject drugs.^{3,4,5,6,7,8,9}


Helps support public safety

SSPs have partnered with law enforcement, providing naloxone to local police departments to help them respond and prevent death when someone has overdosed.¹⁰

SSPs also protect first responders and the public by providing safe needle disposal and reducing the presence of discarded needles in the community.^{4,5,6,7,8,9,11}

In 2015, CDC's National HIV Behavioral Surveillance System found that the more syringes SSPs distributed per the number of people who inject drugs in a geographic region, the more likely the people who inject drugs in that region were to dispose of used syringes safely.¹²

Studies in Baltimore¹³ and New York City¹⁴ have also found no difference in crime rates between areas with and areas without SSPs.

 U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

000110-0-0809-000

SSPs FACTS

- **SSP prevent transmission of blood-borne infections in PWID**
 - SSPs are associated with an estimated 50% reduction in HIV and HCV incidence in PWID.¹
 - The best way to reduce the risk of blood borne infections through IDU is to stop injecting drugs.
 - For people who do not stop injecting drugs, using sterile injection equipment for each injection can reduce the risk of acquiring and transmitting infections
 - When combined with MAT, HCV and HIV transmission is reduced by over two-thirds.^{1,2}
- **Helps stop substance use**
 - SSPs are a bridge to other health services, including HCV and HIV care and MAT for opioid use disorder.³
 - New users of SSPs are five times more likely to enter drug treatment and three times more likely to stop using drugs than those who don't use the programs.
 - SSPs prevent drug over dose deaths by teaching PWID how to prevent and treat drug overdose⁴⁻⁹

1) Platt L, Minozzi S, Reed J, et al. Cochrane Database Syst Rev. 2017;9:CD012021. 2) Fernandes RM, Cary M, Duarte G, et al. BMC Public Health. 2017;17(1):309. 3) [HIV and Injection Drug Use – Vital Signs – CDC. Centers for Disease Control and Prevention](#). Published December 2016. 4) Seal KH, Thawley R, Gee L. J Urban Health. 2005;82(2):303–311. 5) Galea S, Worthington N, Piper TM, Nandi VV, Curtis M, Rosenthal DM. Addict Behav. 2006;31(5):907-912. 6) Tobin KE, Sherman SG, Beilenson P, Welsh C, Latkin CA. Int J Drug Policy. 2009;20(2):131-136. 7) Doe-Simkins M, Walley AY, Epstein A, Moyer P. Am J Public Health. 2009;99(5):788-791. 8) Bennett AS, Bell A, Tomedi L, Hulsey EG, Kral AH. J Urban Health. 2011;88(6):1020-1030. 9) Leece PN, Hopkins S, Marshall C, Orkin A, Gassanov MA, Shahin RM. Can J Public Health. 2013;104(3):e200-204.

SSPs FACTS

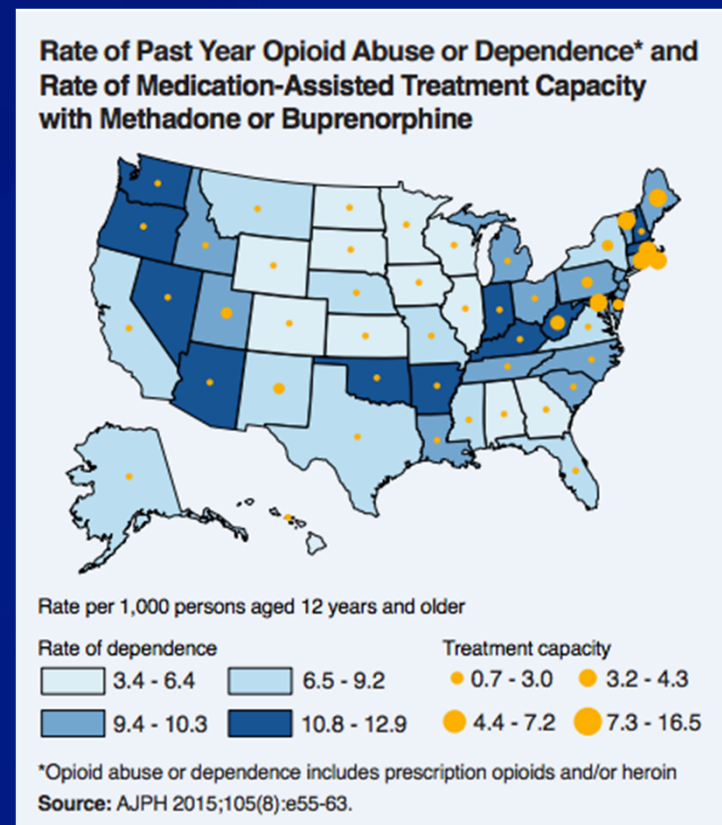
- **Helps support public safety**

- SSPs have partnered with law enforcement, providing naloxone to local police departments to help them respond and prevent death due to OD.¹
- SSPs also protect first responders and the public by providing safe needle disposal and reducing the presence of discarded needles in the community.²⁻⁸
- In 2015, CDC's National HIV Behavioral Surveillance System found that the more syringes SSPs distributed per the number of people who inject drugs in a geographic region, the more likely the people who inject drugs in that region were to dispose of used syringes safely.⁹
- Studies in Baltimore¹⁰ and New York City¹¹ have also found no difference in crime rates between areas with and areas without SSPs.

1) Childs R. [FDA website pdf icon\[PDF – 1 MB, 24 pages\]external icon](#). 2) Tookes HE, Kral AH, Wenger LD, et al. Drug Alcohol Depend. 2012;123(1-3):255-259. 3) Riley ED, Kral AH, Stopka TJ, Garfein RS, Reuckhaus P, Bluthenthal RN. J Urban Health. 2010;87(4):534-542. 15) 4) Klein SJ, Candelas AR, Cooper JG, et al. 5) Public Health Rep. 2008;123(4):433-440. 6) Montigny L, Vernez Moudon A, Leigh B, Kim SY. Int J Drug Policy. 2010; 21(3):208-214. 7) Doherty MC, Junge B, Rathouz P, Garfein RS, Riley E, Vlahov D. Am J Public Health. 2000;90(6):936-939. 8) Bluthenthal RN, Anderson R, Flynn NM, Kral AH. Drug Alcohol Depend. 2007;89(2-3):214-222. 9) Centers for Disease Control and Prevention. —National HIV Behavioral Surveillance: Injection Drug Use, 20 U.S. Cities, 2015. 10) [HIV Surveillance Special Report 18. Revised edition pdf icon\[PDF – 2 MB, 38 pages\]](#). Published May 2018. 11) Marx MA, Crape B, Brookmeyer RS, et al. Am J Public Health. 2000;90(12):1933-1936.

Unmet Opioid Treatment Need

- In 2014, opioid injection accounted for 360,707 admissions for drug treatment
 - 22.3% of all admissions
- In 2015, nearly 2.4 million Americans had an opioid use disorder
- Close to 80% of these individuals did not receive treatment.



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What Are We Trying To Prevent?



Ascites

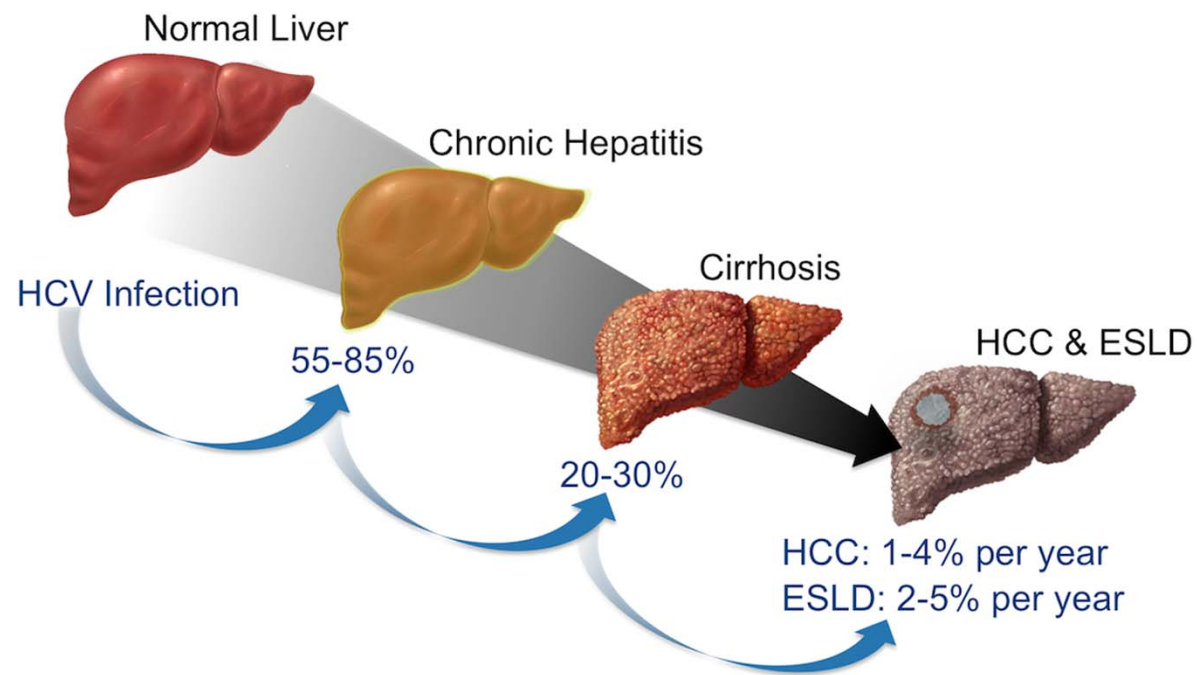


Esophageal Varices



End Stage Liver Disease/Liver Cancer

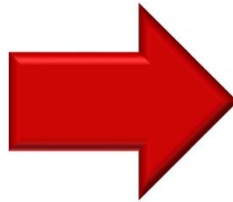
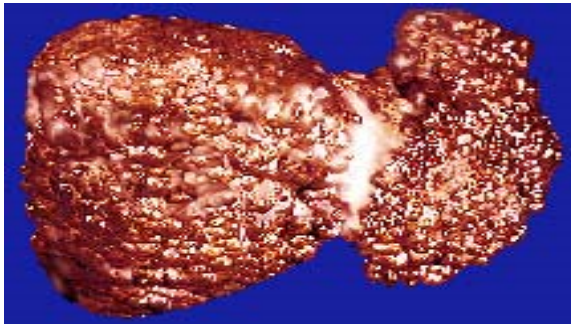
Natural History Following Initial Infection with HCV



Abbreviations: ESLD = end-stage liver disease HCC = hepatocellular carcinoma Source: Lingala S, Ghany MG. Natural History of Hepatitis C. Gastroenterol Clin North Am. 2015;44:717-34.

What Does HCV Treatment Accomplish?

- **SVR (cure) of HCV** is associated with:
 - 70% Reduction of Liver Cancer
 - 50% Reduction in All-cause Mortality
 - 90% Reduction in Liver Failure



- Lok A. NEJM 2012; Ghany M. Hepatol 2009; Van der Meer AJ. JAMA 2012

HCV Evaluation and Treatment: Laboratory Workup

- Hepatitis C RNA and genotype
- Hepatitis Serology
 - Hep A Total antibody
 - Hep B surface antibody, Hep B surface antigen, Hep B core antibody
- HIV serology
- CBC with differential
- Comprehensive metabolic panel
- Urinary drug screen
- If the patient has Cirrhosis
 - PT/INR
 - Alpha Fetoprotein Tumor Marker (AFP)
 - Fibrotest/Fibrosure

Liver Fibrosis Stages

- F0: No fibrosis
- F1: Periportal Fibrosis
- F2: Periportal Septae
- F3: Portal Central Septae
- F4: Cirrhosis

Verizon LTE 3:37 PM

HCV Score Calculator About

AGE Enter Number...

AST / SGOT (IU/L) Enter Number...

ULN AST / SGOT (IU/L) Enter Number...

PLATELET COUNT (10⁹/L) Enter Number...

ALT Enter Number...

CREATININE Enter Number...

TOTAL BILIRUBIN Enter Number...

SERUM ALBUMIN Enter Number...

INR Enter Number...

ASCITES NONE

HEPATITIS STATUS NONE

CALCULATE

APRI: **A**ST to **P**latelet **R**atio Index

$$\text{APRI} = \frac{\text{AST Level (IU/L)}}{\text{AST (Upper Limit of Normal) (IU/L)}} \times \frac{100}{\text{Platelet Count (10}^9\text{/L)}} = \frac{126}{39} \times \frac{100}{155} = 2.084$$

An APRI score greater than 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

Lin ZH, Xin YN, Dong QJ, et al. Hepatology. 2011;53:726-36 University of Washington: Hepatitis C Online www.hepatitisc.uw.edu/
Sterling RK, Lissen E, Clumeck N, et. al. Hepatology 2006;43:1317-1325 University of Washington: Hepatitis C Online www.hepatitisc.uw.edu/

FIB-4 Index

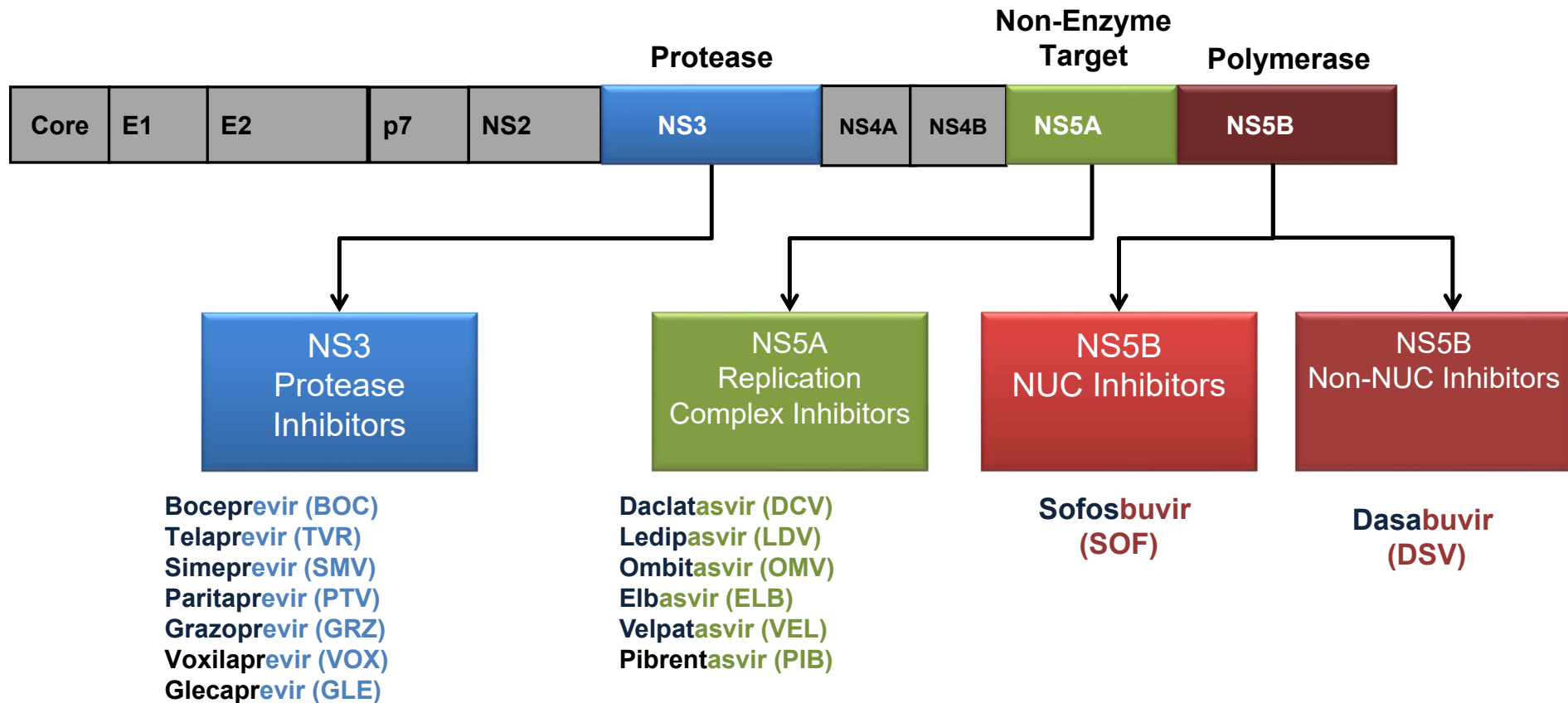
$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \frac{56 \times 129}{196 \times \sqrt{96}} = 3.76$$

A FIB-4 score <1.45 has a negative predictive value of 90% for advanced fibrosis A FIB-4 >3.25 has a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Why is it Important to Stage Liver Fibrosis?

- Treatment **will be different** between those patients with decompensated and NOT decompensated cirrhosis
- **All patients** with liver fibrosis (F3 or F4) will need screening for
 - hepatocarcinoma
 - Esophageal varices
 - Hepatic encephalopathy
- Patients with decompensated cirrhosis **need** to be referred to a liver transplant center

Direct Acting Antiviral Agents (DAAs): Keeping them Straight



HCV Therapies – Direct Acting Antivirals (DAAs)

Medication	NS5B Inh	NS5A Inh	NS3/4A PI	Other
Epclusa®	sofos bu vir	velpat as vir		
Mavyret®		pibrent as vir	glecapr ev ir	

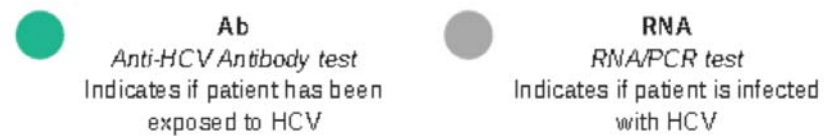
NS5B Inh – Nonstructural protein 5B Polymerase Nucleotide Analog Inhibitor

NS5A Inh – Nonstructural protein 5A Inhibitor

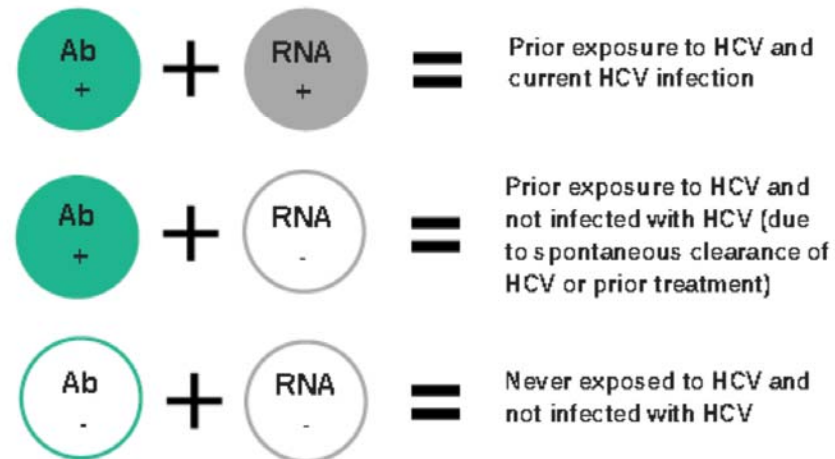
NS3 PI – Nonstructural protein 3/4A Protease Inhibitor

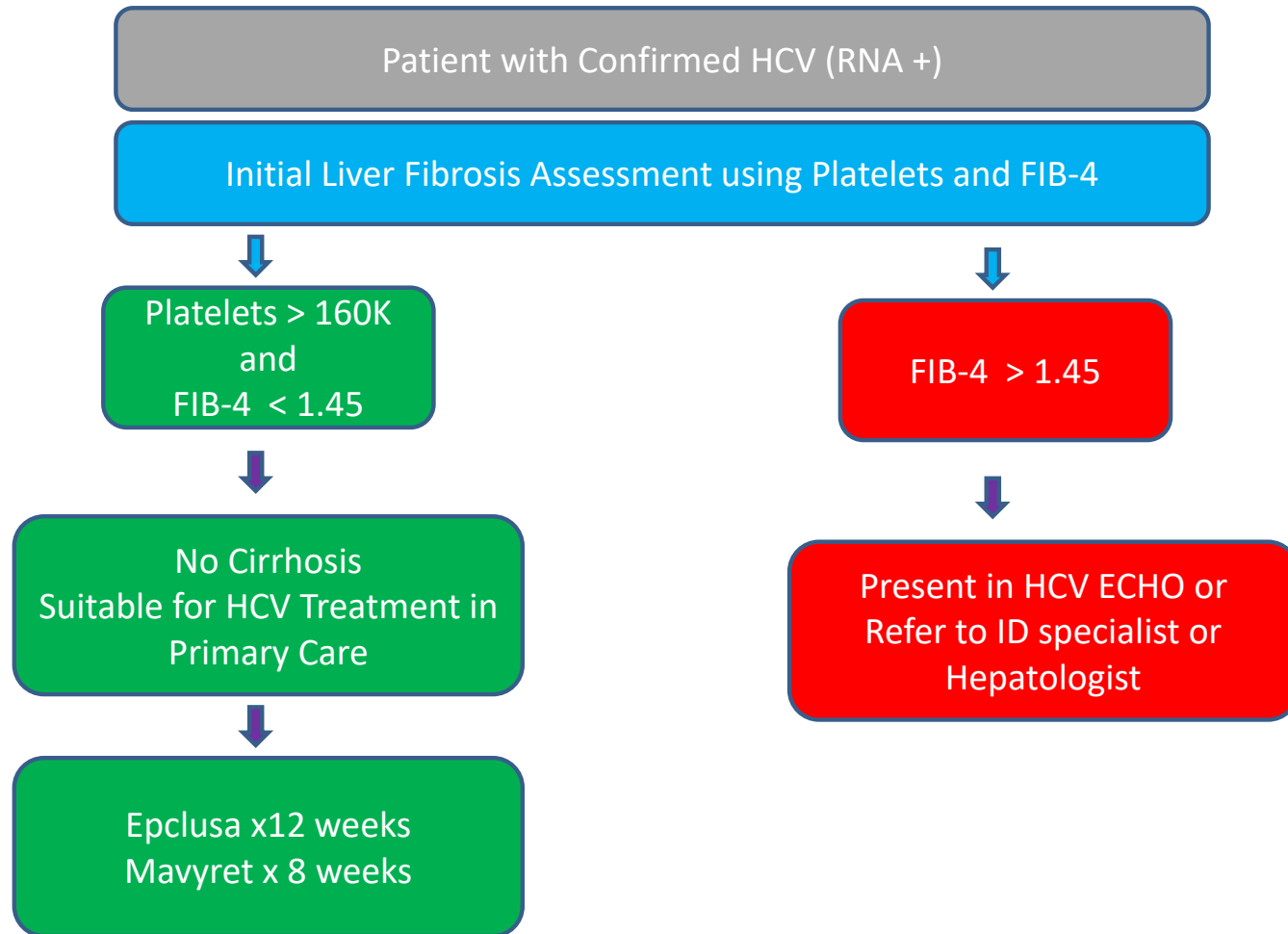
HCV Tests Interpretation

Legend:



Hepatitis C Test Results Interpretation





Mr. S “continued”

- **Labs**

- RNA Viral load positive, 3.4 million copies /mL, Genotype 1a.
- ALT 72 IU/L, AST 65 IU/, Creatinine 0.9 mg/dL, GFR 69 ml/min, Hg 13.4 g/dL, **Platelets 288 x 10³/mcL**, Albumin 4.5 g/dL, Total Bilirubin 0.7 mg/dL, INR 1.0.
- Hep A Ab (-), **HBsAg (-), HBsAb (-), HBcAb (-)**

- **Questions:**

- What is his liver fibrosis stage
- As a primary care provider what can you do for this patient?
- How wil this impact HCV elimination in your community?

Mr. S

Verizon LTE 12:18 PM 77%

HCV Score Calc... About

AGE	24
AST / SGOT (IU/L)	65
ULN AST / SGOT (IU/L)	39
PLATELET COUNT (10 ³ /L)	288
ALT	72
CREATININE	0.9
TOTAL BILIRUBIN	0.7
SERUM ALBUMIN	4.5
INR	1
ASCITES	NONE
CALCULATE	



Verizon LTE 1:13 PM 68%

HCV Score Calc...

APRI INDEX	0.58
CHILD PUGH	5(A)
FIB-4	0.64
MELD	6
tap result for more information	
RESET	

What can you do for HCV Elimination?

- Since FIB-4 is less than 1.45 the patient does not have cirrhosis:
 - Sofosbuvir/Velpatasvir x 12 wk
 - Glecaprevir/Pibrentasvir x 8 wk
- Continue Buprenorphine/naltrexone
- Educate about injection with sterile equipment if he has a relapse
- Advocate for SSPs

MOVING KNOWLEDGE INSTEAD OF PATIENTS



Helpful Resources

- <http://www.npaihb.org>
 - Text HCV 97779
- <http://www.hcvguidelines.org/>
- <http://www.hepatitisc.uw.edu/>
 - On-line curriculum on liver disease and HCV, includes clinical studies, clinical calculators, slide lectures
- ECHO guidelines

Conclusions

- Elimination of HCV is possible by the year 2030
- Effective interventions are available
- Primary care providers play a major role in:
 - Decreasing morbidity and mortality by treating HCV
 - Decreasing transmission by:
 - Having an MAT waver and prescribing buprenorphine/naloxone
 - Advocating for SSPs
- Planning and commitment can accelerate the process

Thank You

GV (Wado)

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