Tribal MAT
A unified response to the opioid crisis in California Indian Country

Project ECHO
University of California Los Angeles Integrated Substance Abuse Programs

HCV: Expanding Access to Cure

Norah Terrault, MD, MPH
Professor of Medicine
Chief of Gastroenterology and Liver Diseases
Keck Medicine of University of Southern California

Keck Medical Center of USC
Keck Medicine of USC

Tuesday, November 19th, 2019

World Health Organization

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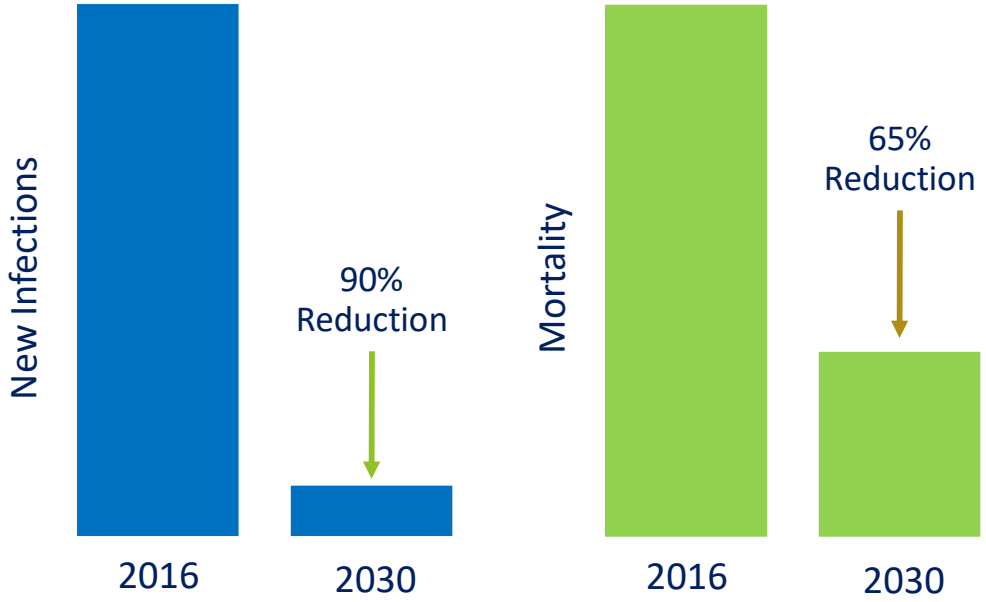
Viral Hepatitis Elimination by 2030

WHO Global Hepatitis Strategy, 2016-2021



In May 2016, the World Health Assembly endorsed the *Global Health Sector Strategy (GHSS)* on viral hepatitis 2016–2021. The GHSS calls for the elimination of viral hepatitis as a public health threat by 2030 (reducing new

- Ambitious goals
- Recent projections for US indicates we are off track by 20+ years

H. Razavi, Presented AASLD/EASL HCV Conference, 2019

Newly Reported HCV Infections Among Individuals Age 15-19 Yrs in 8 California Counties in 2018

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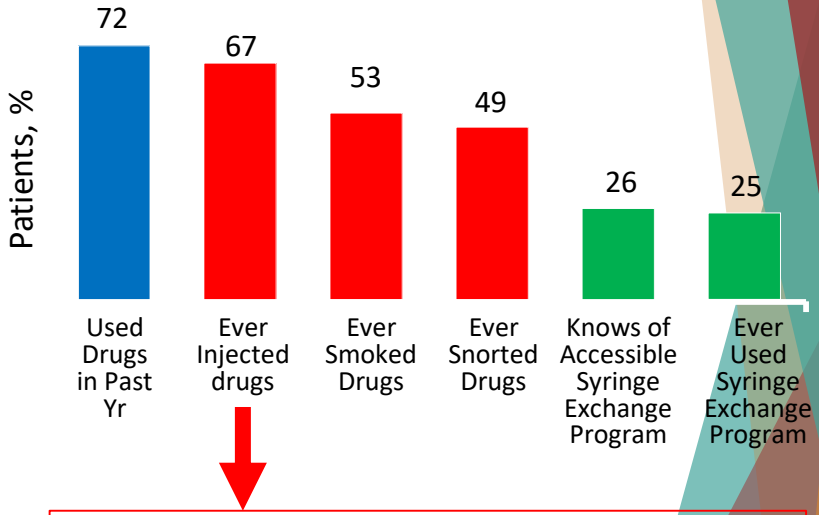
- **8 participating CA counties: Imperial, Lake, Monterey, Orange, Placer, Riverside, San Luis Obispo, and Santa Cruz**
  - N = 472 patients eligible
- **Responded to patient questionnaire: n = 114 (24%)**
  - Median age 26 yrs
  - 68% White
  - 48% female

Self-Reported Drug-Related Risk Factors Among HCV Cases Who Ever Used Any Drug (n = 61)



83% witnessed overdose
63% ever had naloxone access while injecting
44% needed naloxone during overdose but did not have it

Ohringer. AASLD 2019. Abstr 166.

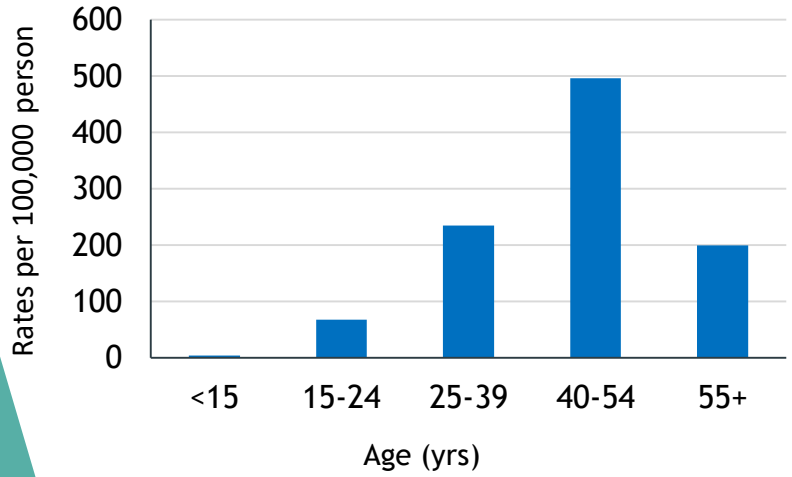
Limited Awareness of Risk and Access to Preventive Services Among Newly Identified HCV Cases

Characteristics of Newly Identified Patients N=114	(%)
Not currently seeing HC provider for HCV	58
Never taken antiviral medications for HCV	96
Acute case with jaundice or elevated LFTs and ≥ 1 symptom	16
Thought they were at risk for HCV before diagnosis	33
Ever been incarcerated for > 24 hrs Received tattoo/piercing while incarcerated Injected while incarcerated (shared injection equipment)	27 29 39
Exchanged sex for drugs, money, or housing in past yr	4

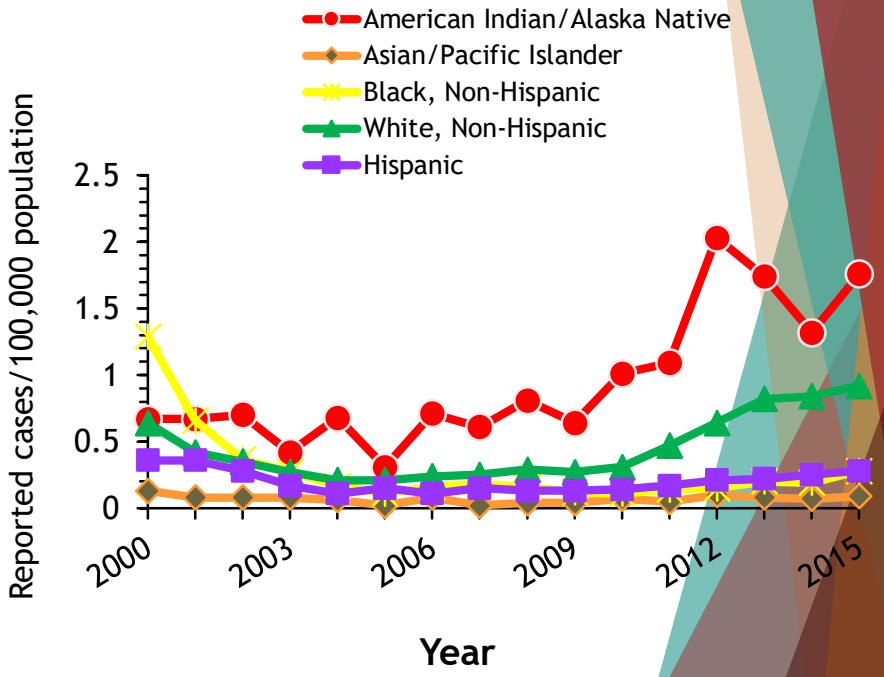
Ohringer. AASLD 2019. Abstr 166.

Acute and Chronic HCV Among AI/AN's (IHS 2005-2015)

- Estimated 120,000 persons chronic HCV in tribal health
- Predominantly among 40-54 yo

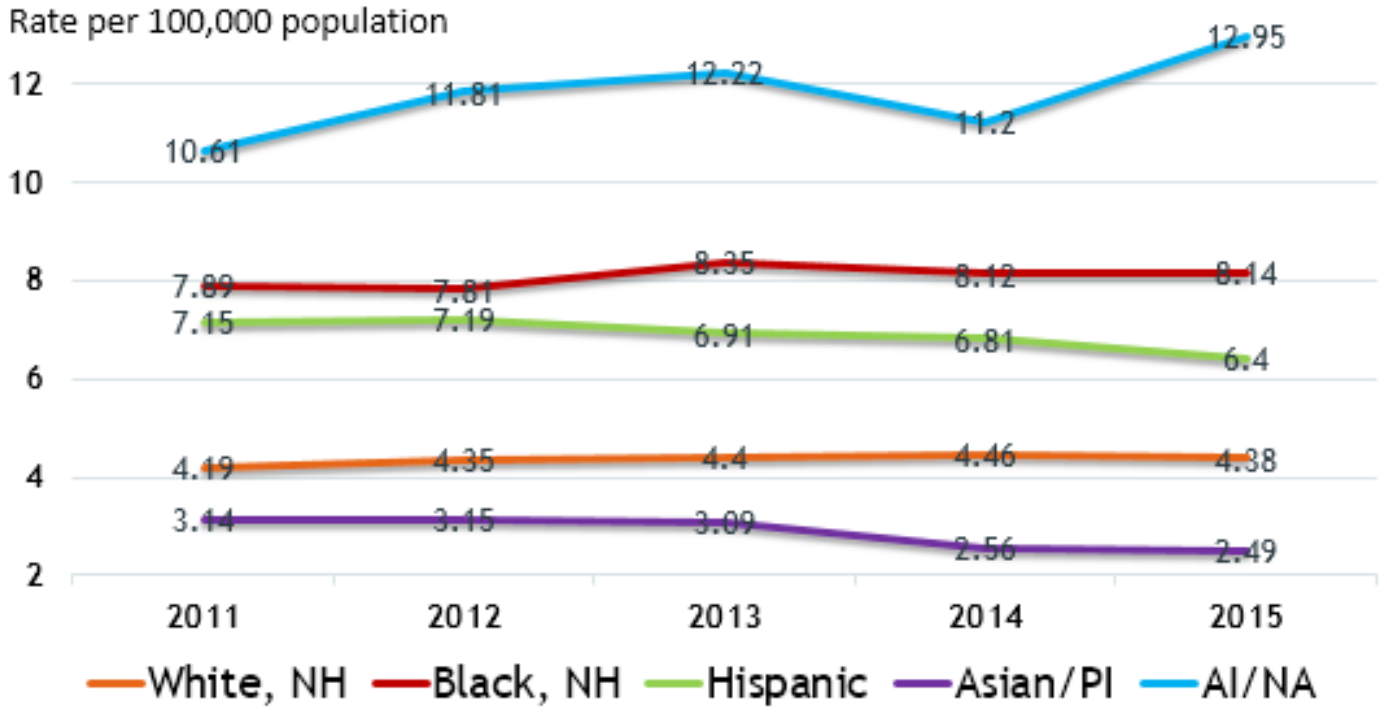


- Incidence of acute HCV, 2000–2015



Edlin B, Hepatology 2016;62:1353–1363
Reilly B, J Community Health (2018) 43:1115–1118
CDC Viral Hepatitis Surveillance 2000-2015

Mortality Rates in HCV-Positive Persons: AI/AN Highest in U.S.

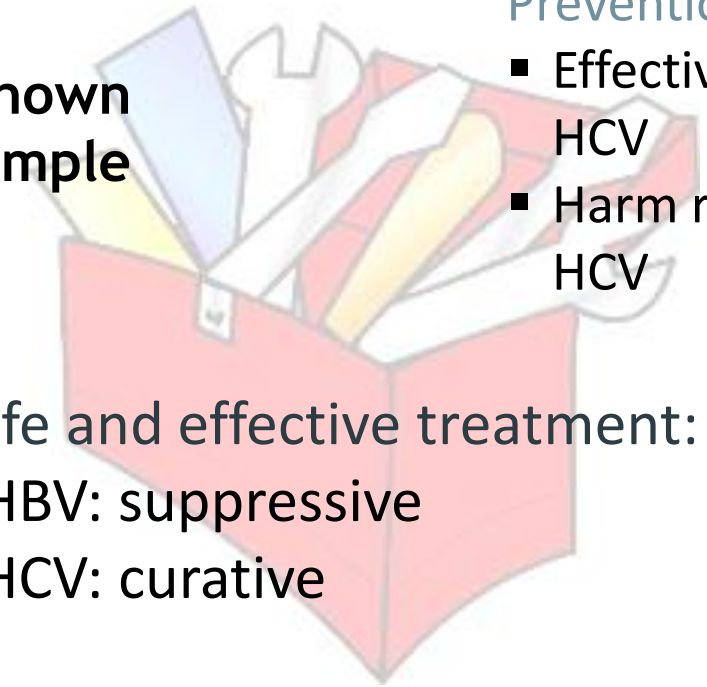


CDC Surveillance for Viral Hepatitis – United States, 2015

We Have the Many Tools to Achieve Elimination of HBV and HCV

Diagnosis:

- **Risk groups known**
- **Diagnosis is simple**



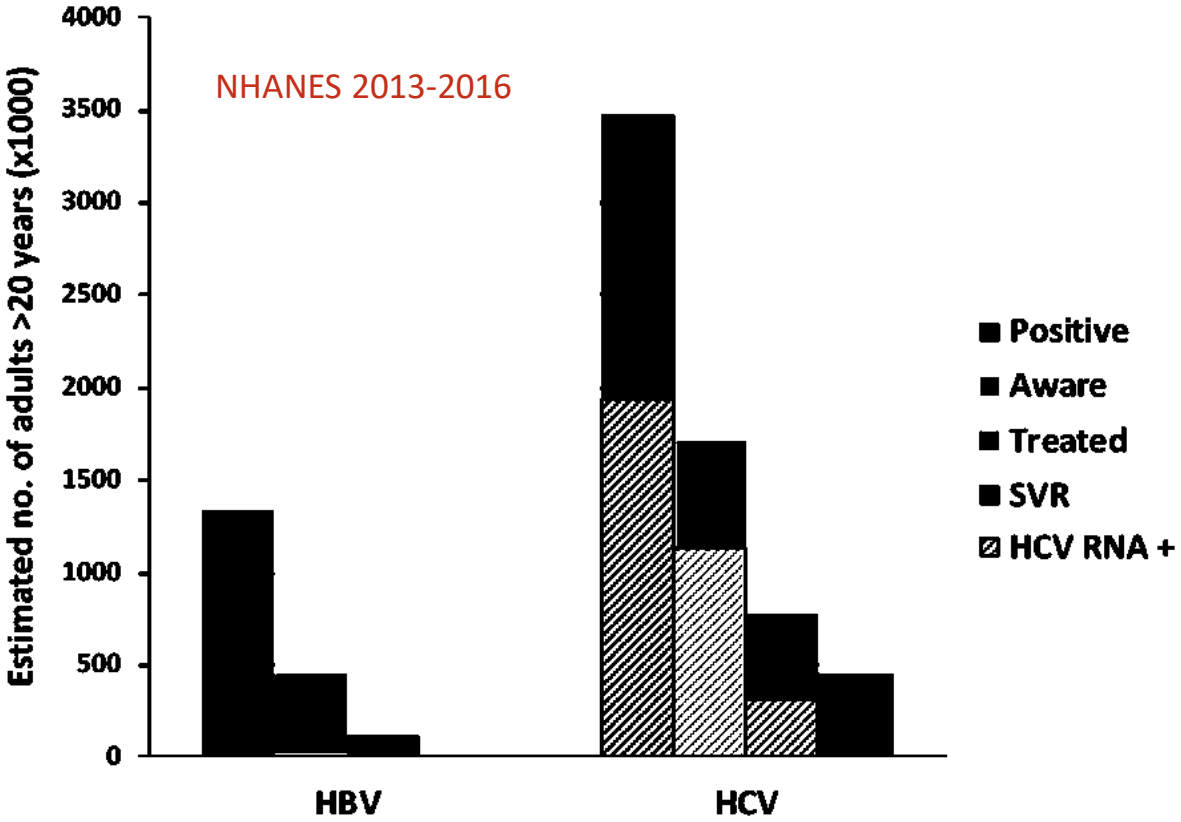
Prevention:

- Effective, durable vaccine for HCV
- Harm reduction works for HCV

Safe and effective treatment:

- HBV: suppressive
- HCV: curative

Gaps in the Cascade of Care



HBV:

- 32% aware
- 28% of aware on treatment

HCV:

- **49% aware**
- **45% of aware persons treated**
- **59% of treated patients achieved SVR**

Zhou K & Terrault N, CGH 2019

- Adults born between 1945-1965
- Risk-based:
  - IDU
  - Receipt of blood products prior to 1992 (clotting factors prior to 1987)
  - Hemodialysis
  - HIV+
  - ALT elevated
  - Recognized exposure: needlesticks, children of HCV+ moms

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA
Infectious Diseases Society of America

AASLD-IDSA

- **All pregnant women**
- **Opt-out screening in jails/prisons**

The Second Wave of HCV in the U.S.

AASLD/IDSA: One-time screening for all persons ≥18 years of age

- ~30,000 new HCV infections per year, increasing since 2006
- Parallels the rise in opioid abuse with new consequences

California Department of Public Health. Chronic hepatitis C infections in California: cases newly reported through 2015. June 2017.

Many DAA Options Provide Cure Across a Broad Spectrum of Patients

What defines cure?

- SVR12 = undetectable HCV RNA 12 weeks after completion of treatment
- ~95% of patients achieve SVR12 with initial treatment

AASLD-IDSA Guidance, accessed November 2019

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C who do not have cirrhosis and have not previously received hepatitis C treatment

↓

- **Cirrhosis assessment**

  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.

  - FIB-4 >3.25
  - APRI >2.0
  - Platelet count <150,000/mm³
  - Fibroscan™ stiffness >12.5 kPa

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- HIV or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m²)
- Currently pregnant

- **Pretreatment laboratory testing**

  Within 6 months of initiating treatment

  - Complete blood count (CBC)
  - Hepatic function panel (ie, albumin, total protein, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
  - Calculated glomerular filtration rate (eGFR)

  Anytime prior to starting antiviral therapy

  - Quantitative HCV RNA (HCV viral load)
  - HIV antigen/antibody test
  - Hepatitis B surface antigen (HBsAg)

  Before initiating antiviral therapy

  - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

AASLD-IDSA Guidance, accessed November 2019

Treatment Simplification

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RECOMMENDED REGIMENS*

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

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

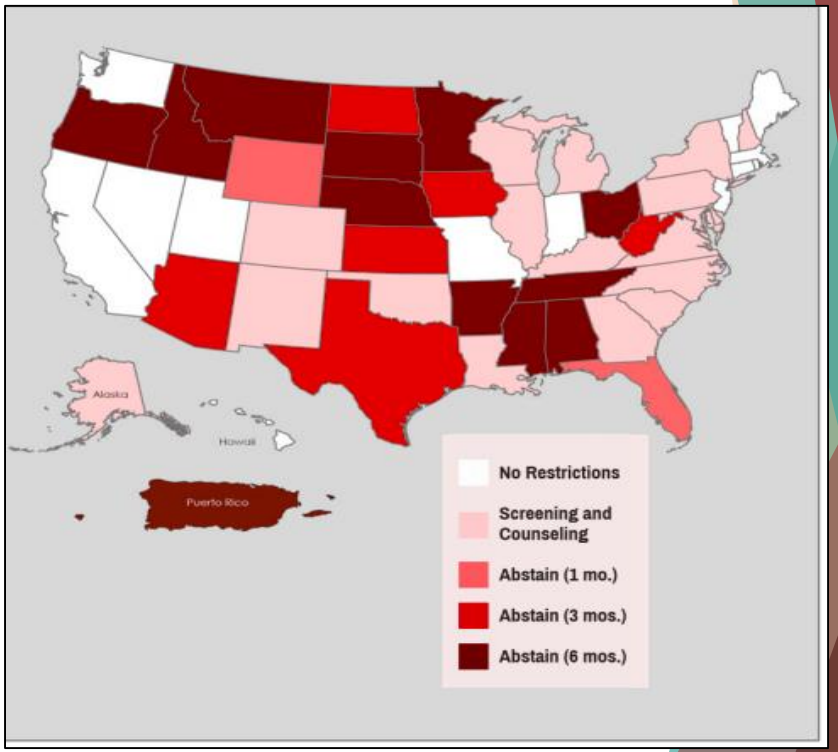
- Select based on drug-drug interactions, patient preference (pill #, packaging, # wks)
- Insurance preference

ON-TREATMENT MONITORING

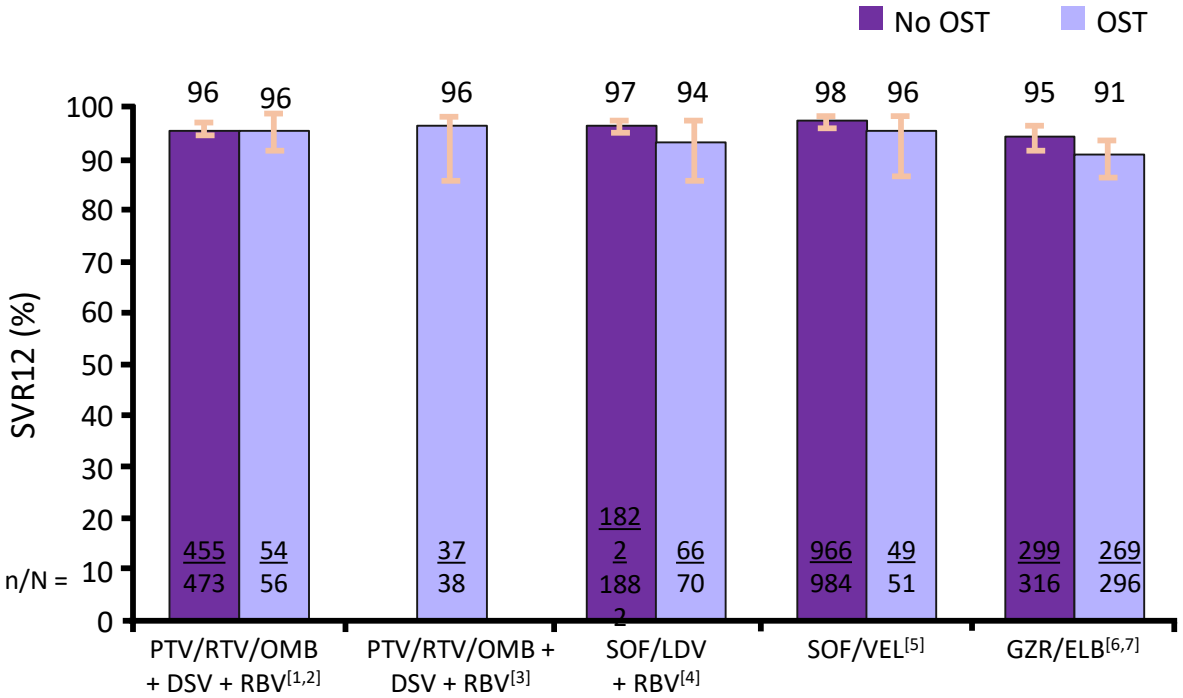
- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No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

Patients Using Drugs/Alcohol Denied Access to HCV Treatment in Some States

- Medicaid reimbursement criteria for DAAs based on required drug/alcohol abstinence period
- In California, this should not be a barrier to accessing HCV treatment



DAA Therapy in PWID: OST vs Non-OST



In clinical trials:

Rates of SVR are comparable in patients on OST and those not

OST: opiate substitution therapy

Feld JJ, et al. N Engl J Med. 2014; Puoti M, AASLD 2014; Lalezari J, J Hepatol. 2015; Grebely J, Clin Infect Dis. 2016; Zeuzem S, Ann Intern Med. 2015; Dore GJ, Ann Intern Med. 2016.

ANCHOR Substudy: Colocation of HCV and Buprenorphine Treatment

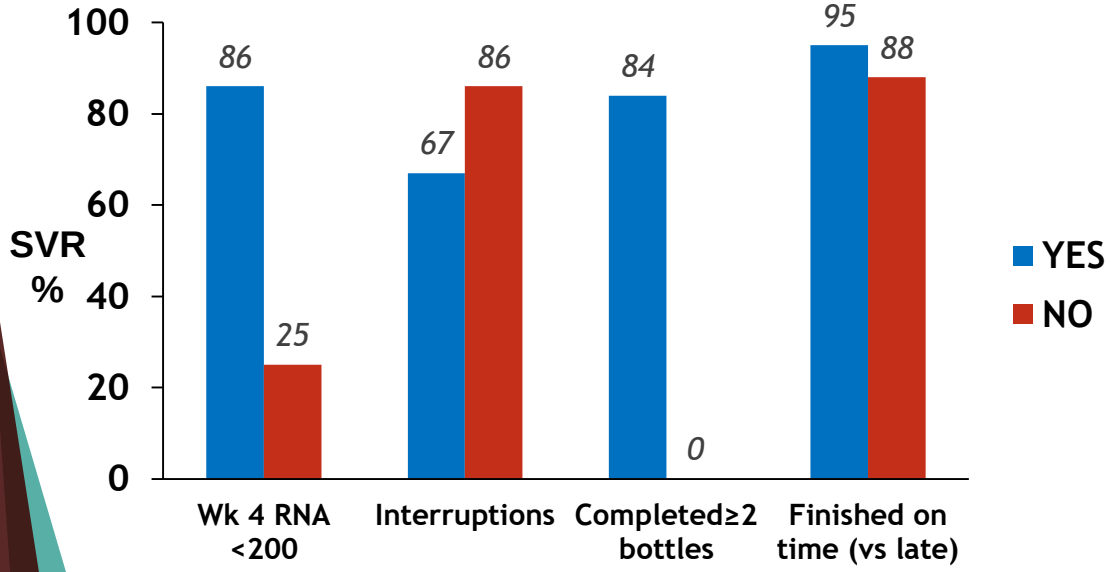
- **Substudy of single-arm HCV treatment trial in Washington, DC**
  - **Endpoints: adherence to SOF/VEL, SVR12 rate; risk behaviors, HCV reinfection, HIV acquisition**

*Buprenorphine started between Wk 0-24 of SOF/VEL treatment initiation with follow-up for 1 yr at same center and with same provider as HCV treatment.

Rosenthal E, et al. EASL 2018. Abstract PS-092.

Anchor Study: SOF/VEL in PWIDs

Active injection drug use within 3 m treated with SOF/VEL x 12w, n=66



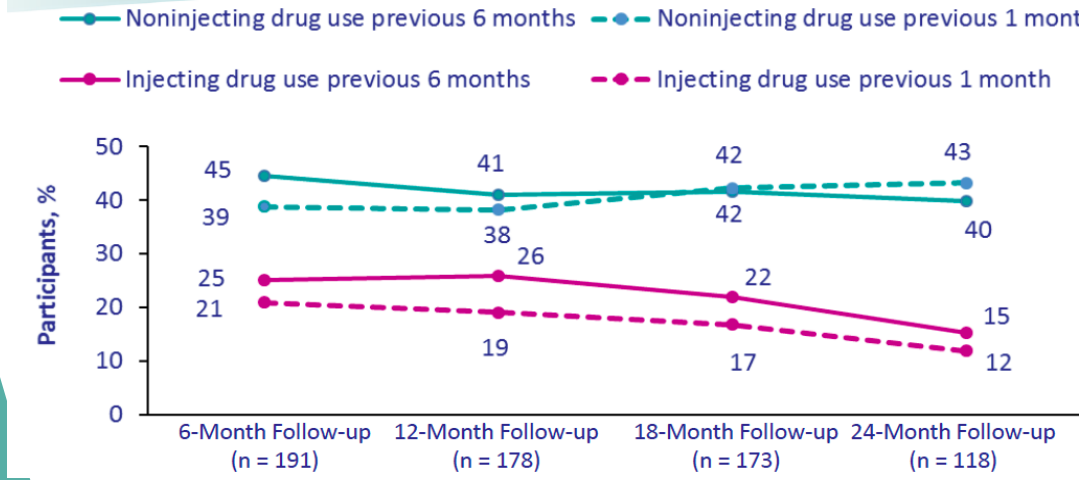
- 78% achieved SVR
- **SVR lower if:**
  - HCV RNA>200 IU/mL at week 4
  - <8 weeks of therapy total
- Finishing late – even 14d late – no effect on SVR

- High SVR rates despite imperfect adherence
- **Missed doses and finishing late had little effect on SVR**

y et al AASLD 2018, Abstract 18

HCV Reinfection and Injecting Risk Behavior in Patients on OST Post EBR/GZP Treatment

- Assessments every 6 months
- Compared viral sequences at baseline and at recurrence to see if reinfection
- Urine drug screen
- Participant-reported behaviors
- Behavioral questionnaire: self-reported drug use



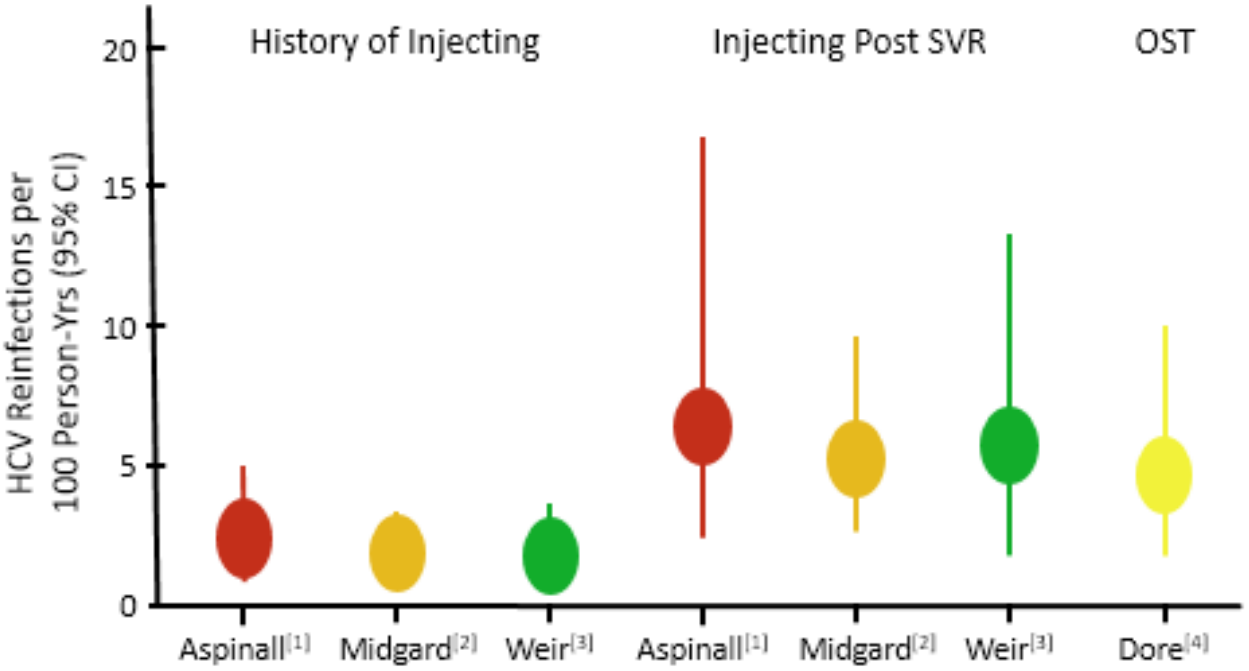
Reinfection rate was 2.3/100 person-yrs

Persistent reinfection rate of 1.6/100 person-yrs

C-EDGE Follow-up Study

Dore et al HEPATOLOGY. 2017 66(1). 195

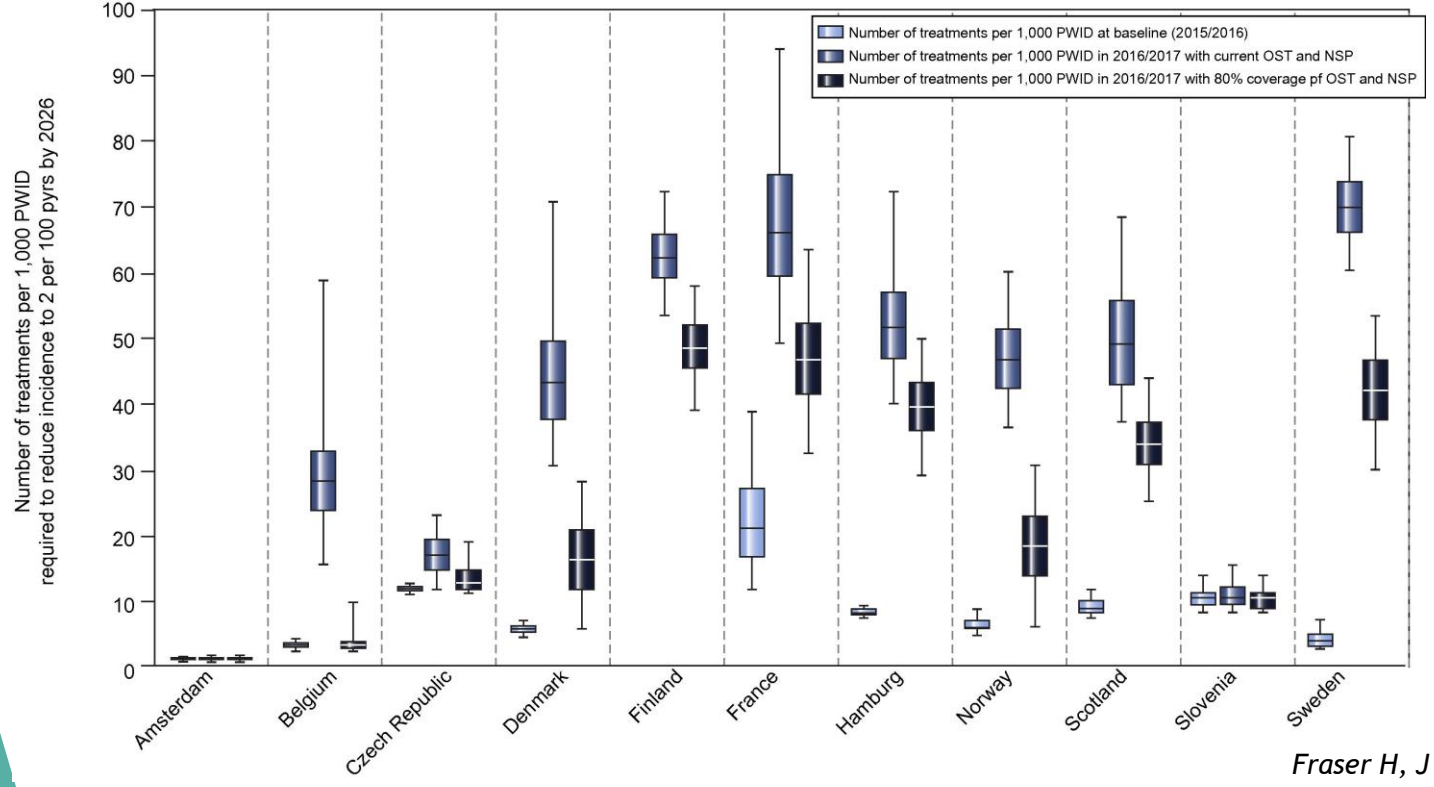
HCV Reinfection by Study Population



"If there are no cases of reinfection, then you are not treating a current PWID population"

1. Aspinall EJ, et al. Clin Infect Dis. 2013 2. Midgard H, et al. International Liver Congress 2015;3. Weir A, et al. Drug Alcohol Depend. 2016;4. Dore GJ, et al. Ann Intern Med. 2016.

Maximum Reductions in New HCV Infections if Treatment Partnered with Harm Reduction



Fraser H, J Hepatol, 2018:68:402-411

Specific Issues of Treating HCV in PWIDs

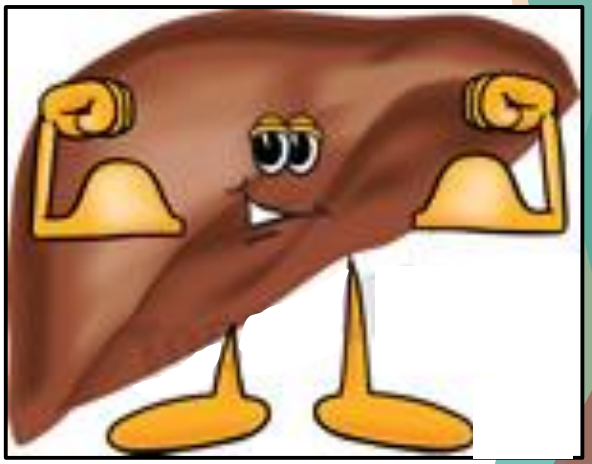
- **High priority group for the "treat to prevent transmission" strategy**
- **Rapid scale-up:** A slow scale-up will create HCV "susceptible" PWID without reduction in viremic pool
- **Co-management is highly desirable:** HCV and drug use disorder
- **SVR rates are acceptable** - comparable to non-PWIDs **-- as long as the total treatment course is completed.**
- **There will be cases of HCV reinfection:** be prepared to retreat
- **Harm reduction optimization (SSP, OST access) is important:** to reduce reinfections and new infections

What to do after Cure?

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.

"Keep the Liver in Good Shape"



Prevention of fatty liver

- Optimize weight
- Prevent/treat diabetes
- Treat dyslipidemia

Safe levels of alcohol

- None if advanced fibrosis

Summary of HCV Management

- ~50% undiagnosed → universal screening recommended
- Treatment is simplified with 2 pan-genotypic regimens
  - ≥95% cured with initial treatment
- For persons who inject drugs, important to couple HCV treatment with harm reduction
  - Colocalization of care best model
  - HCV cure rates in PWIDs on or off OST are similar – key is completion of treatment
- Care after cure
  - Counsel to reduce risk of infection and maintain good liver health

Thank-You!

Terrault@usc.edu

Helpful Videos on HCV

https://www.aaip.org/programs/capacity-building-assistance/hepatitis-c-testing-treatment-awareness/

https://vimeo.com/364921289