



Creating Action Steps for Linking Underserved Populations with Hepatitis C Care

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Learning Objective **1**

Apply CDC universal screening guidelines to improve diagnosis of HCV and linkage to treatment.

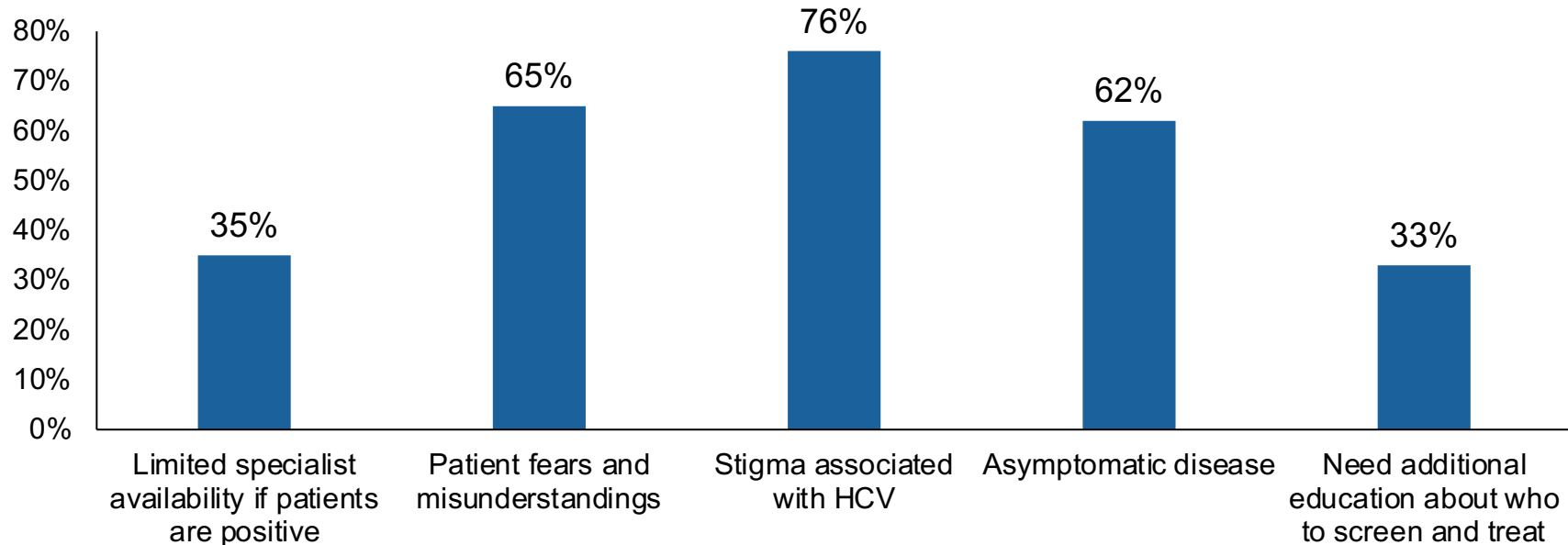


Audience Response

Identify the top 3 barriers to screening patients with HCV:

- A. Limited specialist availability if patients are positive
- B. Patient fears and misunderstandings
- C. Stigma associated with HCV
- D. Asymptomatic disease
- E. Need additional education about who to screen and treat

Identify the Top 3 Barriers to Screening Patients with HCV



The Faces of HCV

The CDC estimates that for every reported case, there are 13.9 actual cases

137,713 new cases of chronic HCV in 2018¹

36.3% baby boomers (1945-1965)¹

23.1% GenX (1966-1980)¹

36.5% millennials (1981-1996)¹

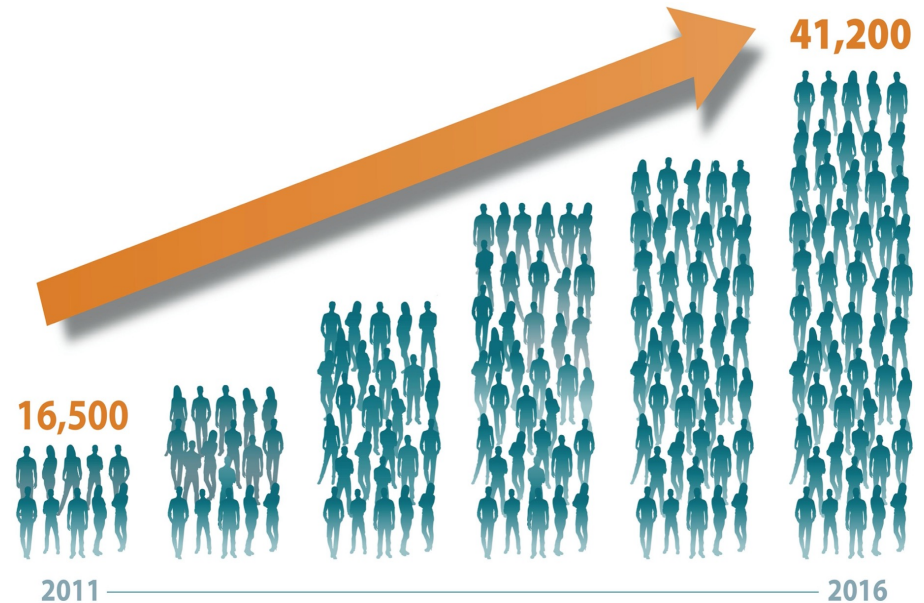
HCV deaths per year > HIV, tuberculosis, and 58 other infections combined²

HIV = human immunodeficiency virus

1. Ryerson AB, et al. *MMWR*. 2020;69(14):399-404. 2. Rojas SA, Godino JG, Northrup A, Shasira M, Tam A, Asmus L, Frenette C, Ramers CB. *Hepatol Commun*. 2021;5(3):412-423.

In the Shadow of the Opioid Epidemic

- IDU now primary risk factor: 70%-80% new HCV infections¹
- Oral to IV opioids = ↑ HCV
- White adults, 20s-30s, ↑ nonurban areas²
- HCV ↑ 400% in people age 18-29³
- Transmission via shared needles, syringes, other equipment
- HCV survives on cookers, cotton filters for **days**, longer in needle



IDU= intravenous drug use; IV = intravenous

1. Liang JT, et al. *N Engl J Med.* 2018;378:1169-1171. 2. Centers for Disease Control and Prevention [CDC] Website. Last reviewed 2019. <https://www.cdc.gov/hepatitis/statistics/2017surveillance/index.htm>. 3. Hellard M, et al. *Int J Drug Policy.* 2015;26(10):958-962.

Cohorts at Risk

- ✓ ● Boomers most likely to be engaged in healthcare system
- ✓ ● Young PWID may present in the ED
- ✓ ● Women of childbearing age and pregnant women may present to OB/GYN¹
- ✓ ● Children seen in pediatrics, typically not screened. ~ 23,000 to 46,000 children in the US with HCV²
- ✓ ● Prison population

ED = emergency department; PWID = persons who inject drugs

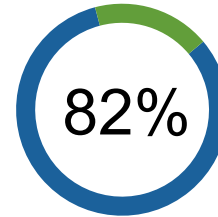
1. Centers for Disease Control and Prevention [CDC] Website. 2020.

<https://www.cdc.gov/hepatitis/statistics/SurveillanceRpts.htm>. 2. American Liver Foundation Website. 2020. <https://liverfoundation.org/hepatitis-c-in-children/>.

Kentucky Study: Pregnant Women and HCV Linkage to Care

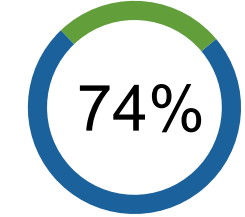
- Kentucky law: HCV screening for pregnant women
- University of Louisville initiative: RN-led linkage-to-care navigation program for mothers + infants
- Study results: 97 HCV+ women delivered
 - 89 (91.8%) HCV RNA+
 - Demographics: 88% white, 12% black
 - 25.8% report methamphetamine use, 19.8% heroin
- 81.4% linked to care:
 - Women newly diagnosed and/or without prenatal less likely to link to care
 - No difference with substance abuse, current IDU, insurance, marital status, and other factors

History of IDU



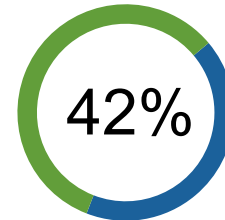
■ Ever injected drugs
■ Never injected drugs

Smoking Status



■ Smoker
■ Non-Smoker

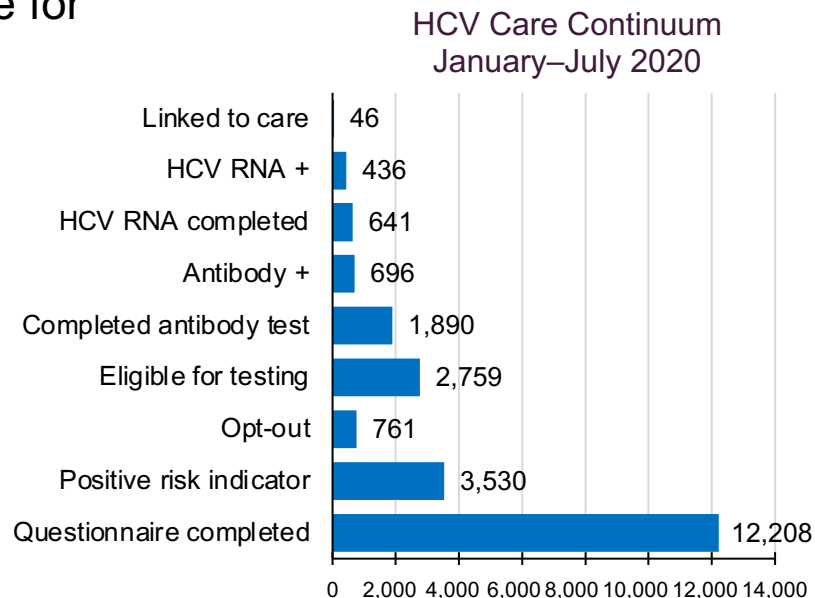
Substance Use During Pregnancy



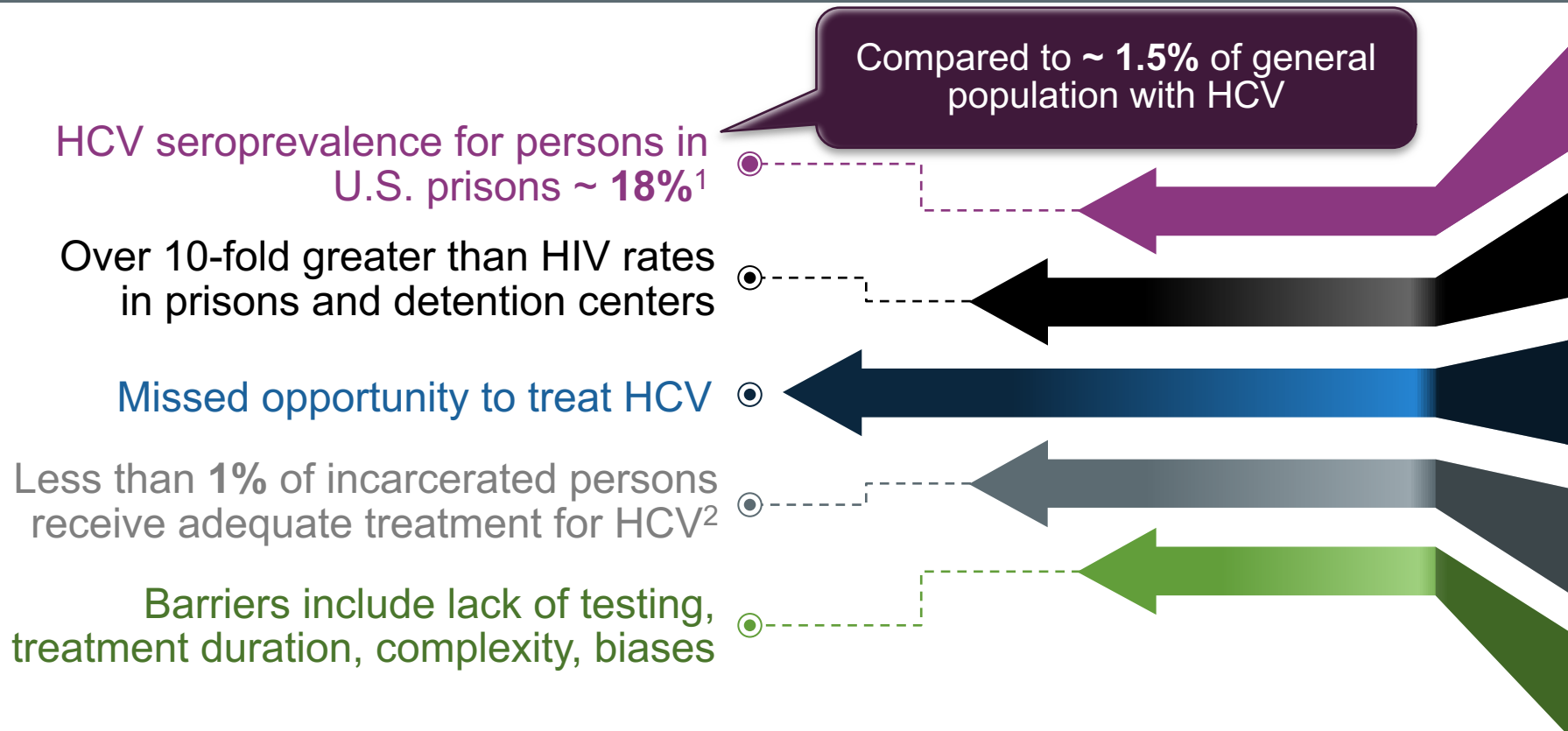
■ Illicit drug use ■ No illicit drug use

HCV Exposure and Outcomes in Young Adults Seen in the ED

- ED triage: nurse-administered questionnaire for adults age 18-45
- HCV antibody with reflex to RNA
 - At least one positive indicator
 - Did not opt out
 - Had blood drawn as part of care
 - No HCV antibody result within 90 days
- Results:
 - 3,530 with at least one indicator
 - 1,890 people tested
 - 638 HCV antibody positive = 36.8% HCV exposure (navigator education)
 - 436 HCV RNA+ = 23% infection (linked to care; median age 34; 71.6% male)
 - HCV RNA+ African-American patients less likely to link to care
 - Patients with Medicaid insurance more likely to link to care



Ghost Population: Incarcerated People

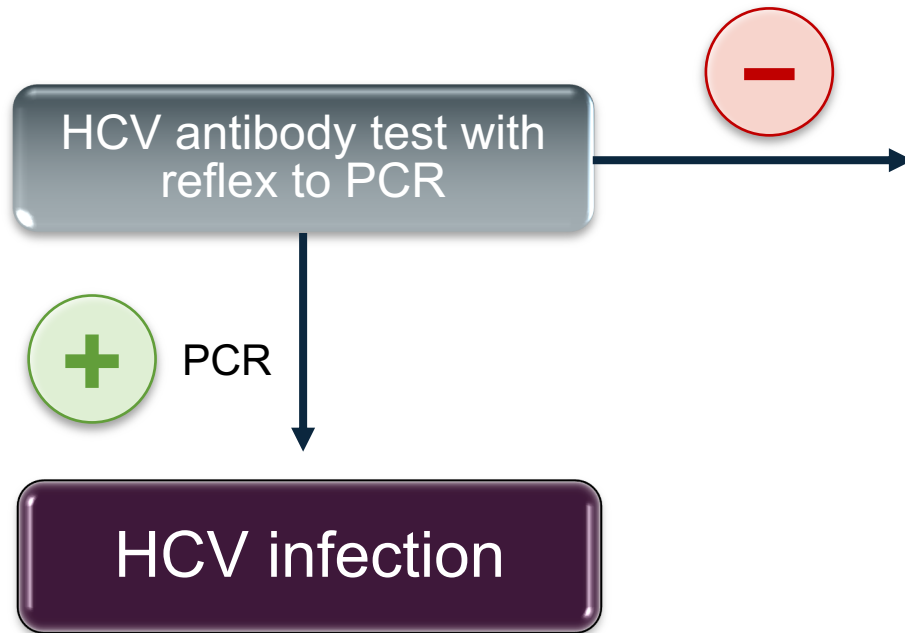


1. Spaulding A, et al. *AIDS Rev.* 2017;19(3):134-147. 2. Beckman AL, et al. *Health Affairs.* 2016;35(10):1893-1901.

CDC Recommends Universal HCV Screening for U.S. Adults

Universal Screening	One-Time Screening Regardless of Age or Setting Prevalence	Routine Periodic Testing
<ul style="list-style-type: none">• HCV screening at least once in lifetime (except in settings in which HCV infection prevalence < 0.1%) for all:<ul style="list-style-type: none">○ Adults age ≥ 18○ All pregnant women during <i>each</i> pregnancy	<ul style="list-style-type: none">• Persons with HIV• Persons who inject drugs and share needles, syringes, or other drug preparation equipment• Persons with select medical conditions, including those who ever received maintenance hemodialysis• Persistently abnormal ALT levels• Recipients of transfusions or organ transplants, including clotting factor concentrates produced < 1987, blood transfusion or blood components < July 1992, organ transplant < July 1992, or were notified that they received blood from a donor who later tested positive for HCV infection• Health care, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood	<ul style="list-style-type: none">• Persons who currently inject and share needles, syringes, or other drug equipment• Persons with select medical conditions, including if ever received maintenance hemodialysis• Any person who requests HCV testing should receive it, regardless of disclosure of risk; many may be reluctant to disclose stigmatizing risks

A Simplified Approach to HCV Screening and Diagnosis



Annual screening for persons at recurrent risk

- Confirm patient understands how HCV is spread
- Drug and alcohol treatment, counseling, and harm reduction services should be provided if appropriate

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Learning Objective **2**

Expand treatment for HCV in primary care settings using simplified algorithms for screening, treatment, and patient monitoring.

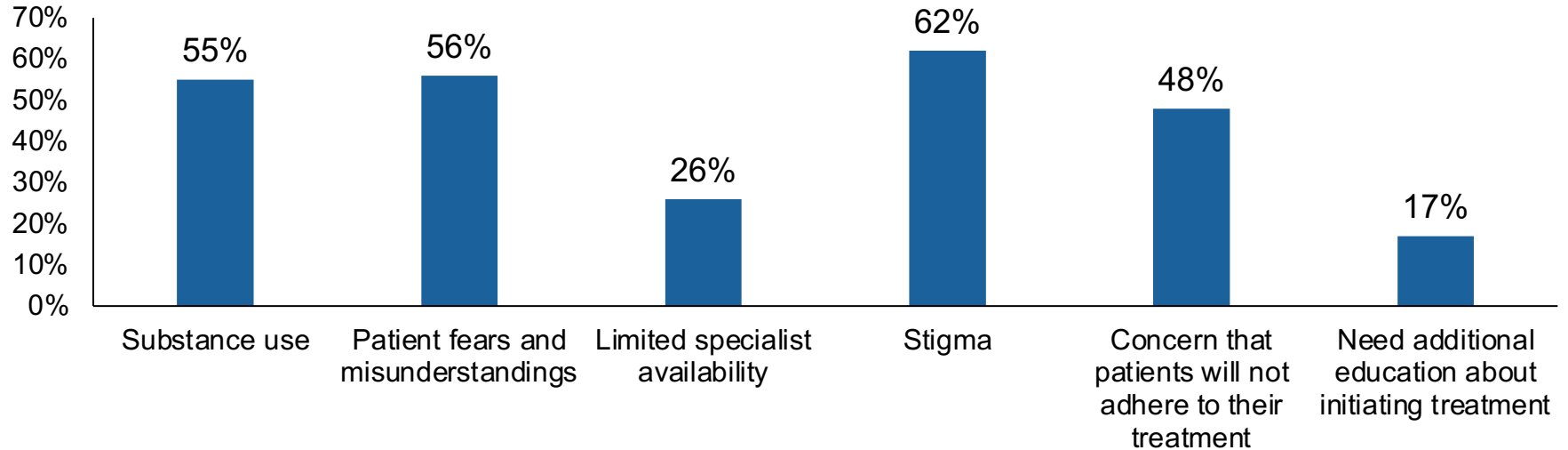


Audience Response

Identify the top 3 barriers to treating patients with HCV:

- A. Substance abuse
- B. Patient fears and misunderstanding
- C. Limited specialist availability
- D. Stigma
- E. Concern that patients will not adhere to their treatment
- F. Need additional education about initiating treatment

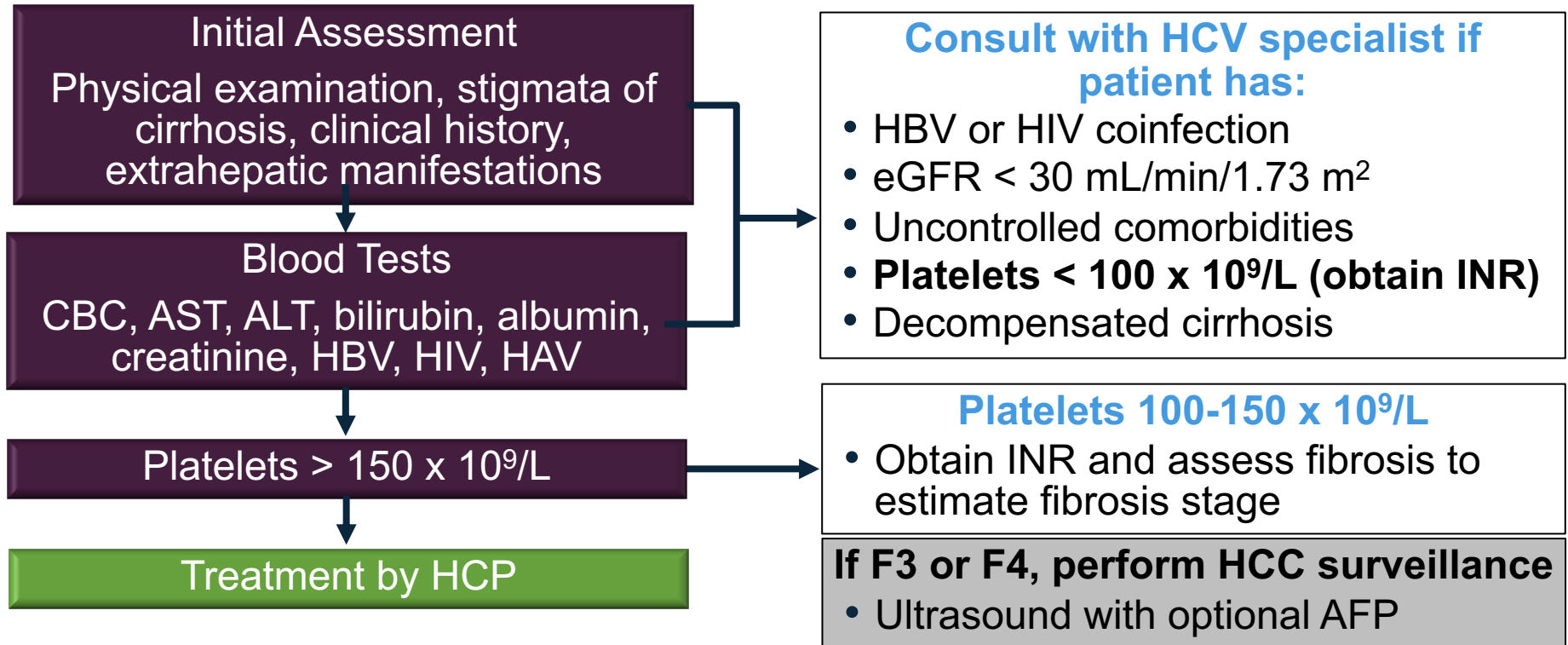
Identify the Top 3 Barriers to Treating Patients with HCV



Success with DAA Treatment

- Unlike HIV and HBV, HCV is curable
- Oral direct-acting antiviral agents (DAAs) broadly approved to treat HCV
- DAA regimens now approved for children age ≥ 3 ¹
- Achieve sustained virologic response (SVR) rates of up to 98%²
- Good results for PWID
- Good results in difficult-to-treat groups (e.g., solid organ transplant recipients, advanced liver disease)

Simplified Algorithm: Pretreatment Assessment and Testing



Staging of Hepatic Fibrosis

Stages of Fibrosis	
Stage 1	Some inflammation but minimal effect on function
Stage 2	Some limited accumulation of fibrosis but with liver function
Stage 3	Extensive fibrosis (cirrhosis) and scarring but with relatively normal function
Stage 4	Substantial cirrhosis damaging liver and impairing vital functions

Noninvasive Fibrosis Staging

Noninvasive Methods for Assessing Cirrhosis and Fibrosis

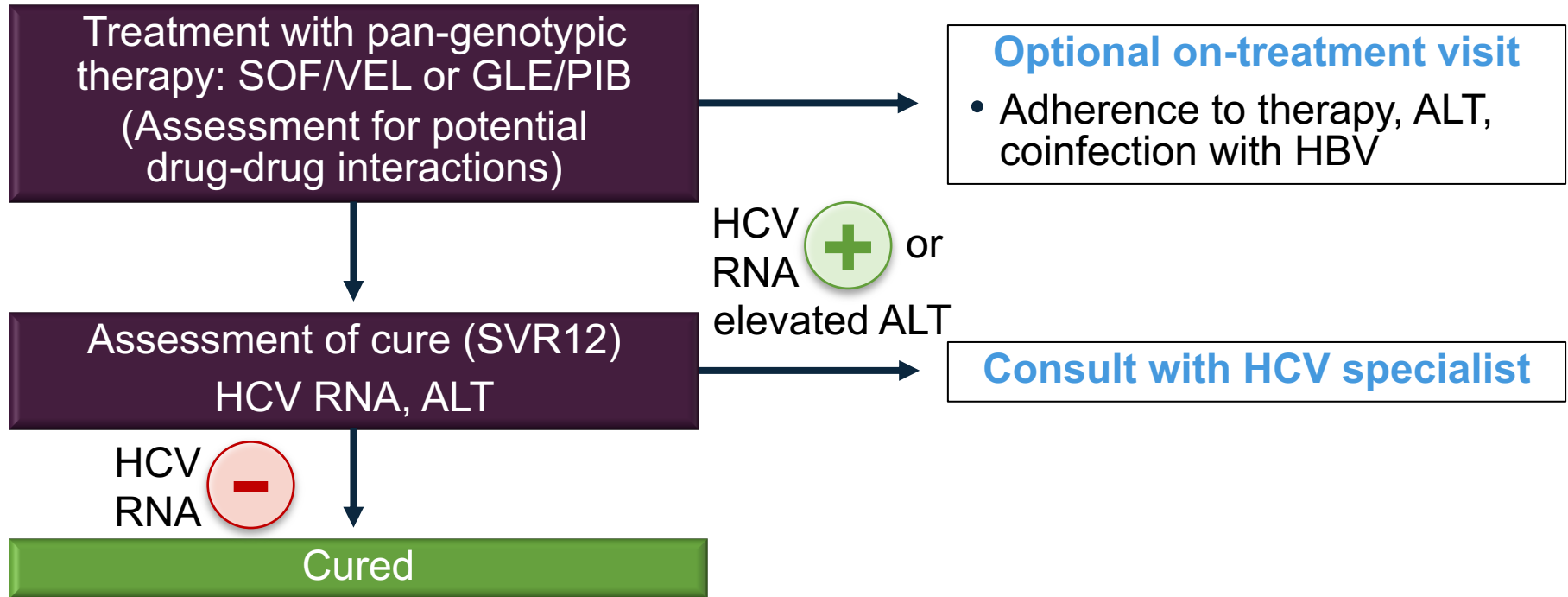
Elastography

- Transient elastography (TE)
- Magnetic resonance elastography (MRE)
- 2D shear wave elastography (SD-SWE)

Serum Biomarkers

- FIB-4
- FibroTest
- FibroSure
- Aspartate aminotransferase-platelet ratio index (APRI)

Simplified Approach to Treatment and Monitoring



Comparison of AASLD/IDSA Recommended Pan-Genotypic Regimens

	SOF/VEL	GLE/PIB
Treatment duration, weeks • No cirrhosis • Compensated cirrhosis • Decompensated cirrhosis	12 weeks 12 weeks 12 weeks	8 weeks 8 weeks Not indicated
Dosage	1 tablet (400 mg SOF = 100 mg VEL) daily with or without food	3 tablets (100 mg GLE + 40 mg PIB per tablet) once daily with food
Common side effects	Headache, fatigue, nausea, asthenia, insomnia	Headache, fatigue, nausea
Key drug-drug interactions	Amiodarone, anticonvulsants, proton pump inhibitors (high dose), rifampicin, efavirenz, St. John's wort, statins	Dabigatran, anticonvulsants, rifampicin, ethinyl estradiol-containing contraceptives, St. John's wort, atazanavir, darunavir, ritonavir, efavirenz, statins, cyclosporine
Common drugs without interactions	Angiotensin receptor blockers, methadone, buprenorphine, calcium channel blockers, lamotrigine, omeprazole, progestin-only contraceptives	

Simplified Approach to Post-Cure Management

Measures to avoid reinfection and further liver damage: patient education; harm reduction measures; alcohol, diabetes, and weight counseling



Annual screening for HCV RNA by PCR for persons still at risk

If F3 or F4 (APRI, FIB-4, FibroTest/FibroSure, FibroMeter, FibroScan) before HCV treatment, perform HCC surveillance every 6 months

Safety of DAAs in Renal Impairment

- **No dose adjustment** in DAAs is required when using recommended regimens¹
- Treatment with sofosbuvir-containing regimens is shown to be **efficacious and safe** in patients with an eGFR < 30²⁻⁴ and in those with ESRD (eGFR < 15 mL/min)⁵
- Glecaprevir/pibrentasvir efficacy and safety also confirmed in **patients with CKD and ESRD**⁶

CKD = chronic kidney disease; ESRD = end-stage renal disease


1. American Association for the Study of Liver Diseases [AASLD] – Infectious Diseases Society of America [IDSA] Website. 2020.


<http://www.hcvguidelines.org>. 2. Desnoyer A, et al. *J Hepatol*. 2019;pii: S0168-8278(19):30343-30345. 3. Nazario HE, et al. *Liver Int*. 2016;36(6):798-801.

4. Saxena V, et al. *Liver Int*. 2016;36(6):807-816. 5. Lawitz E, et al. *Gut*. 2018;67:A99-A100. 6. Lawitz EJ, et al. *The Liver Meeting*. 2018. Abstract 0715B.

Drug-Drug Interaction Potential Between Medications for OUD and Preferred HCV DAAs

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/ Velpatasvir/ Voxilaprevir
Buprenorphine	✓	≈	≈	✓	≈
Methadone	✓	✓	✓	✓	✓
Naltrexone	✓	✓	✓	✓	✓
Naloxone	✓	✓	✓	✓	✓

 No clinically significant interaction expected

 Potential interaction may require adjustment to dosage, altered timing of administration, or additional monitoring

Why Treat HCV Infection in PWID?

- **Treating PWID priority:** high burden of infection and potential to transmit to others¹
- Several studies demonstrate that injecting risk behaviors remain **stable or decrease** during or following DAA therapy²
- Modeling of treatment in PWID highlights the need for **prevention strategies**^{1,2}
 - Syringe exchange programs with safe injecting sites
 - Harm reduction strategies
 - Opiate substitution therapy concurrent with HCV treatment
 - Education and counselling regarding HCV transmission and drug use

Barriers to HCV Treatment Uptake in PWID

Patient

- Awareness of transmission, treatment (curable)
- Stigma/fear/mistrust
- Comorbidities
- Unstable housing
- Lack of transportation
- Prior negative experiences

Provider (PCP)

- Time/experience
- Awareness of at-risk populations
- Adherence, reinfection, resistance concerns
- Knowledge of guidelines, treatment
- Comorbidities
- Unconscious biases

Systemic

- Access, navigation
- HCP availability
- Provision of services
- Outdated guidelines
- Payer restrictions/ requirements for DAA
- Health insurance
- Disparities

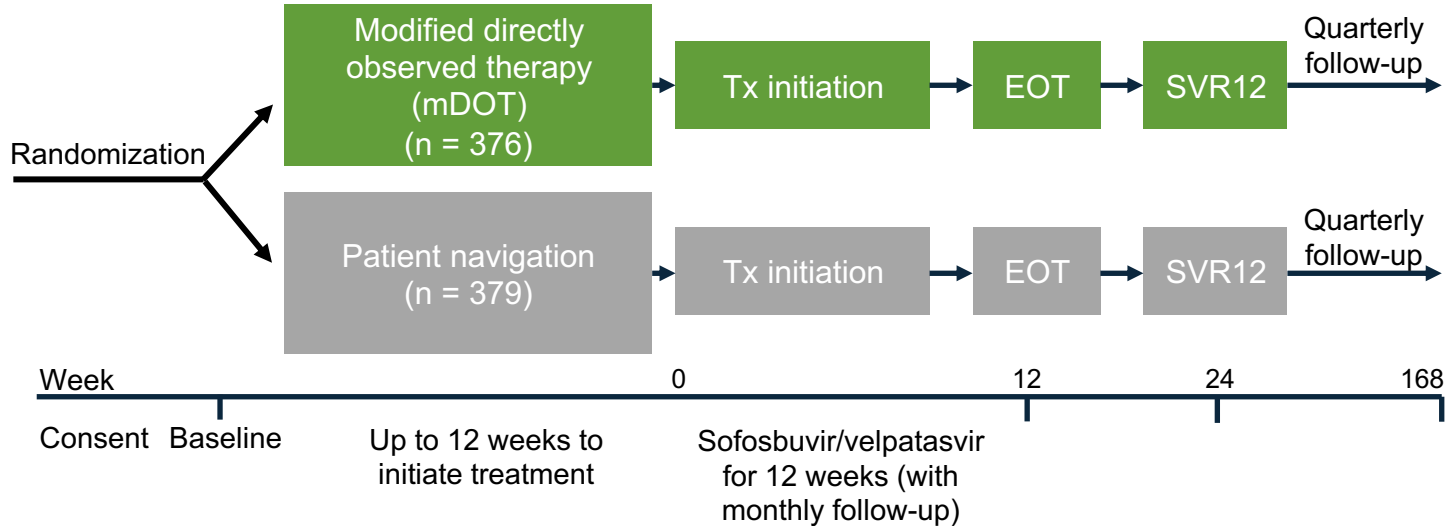
Patient-Centered Model for PWIDS

The HEpatitis C Real Option (HERO) Study

Participants (N = 755)

- HCV GT 1-6 infection
- DAA treatment initiation naïve
- With and without HIV

Participants in both treatment arms enrolled at community-based clinics and from within opioid treatment programs

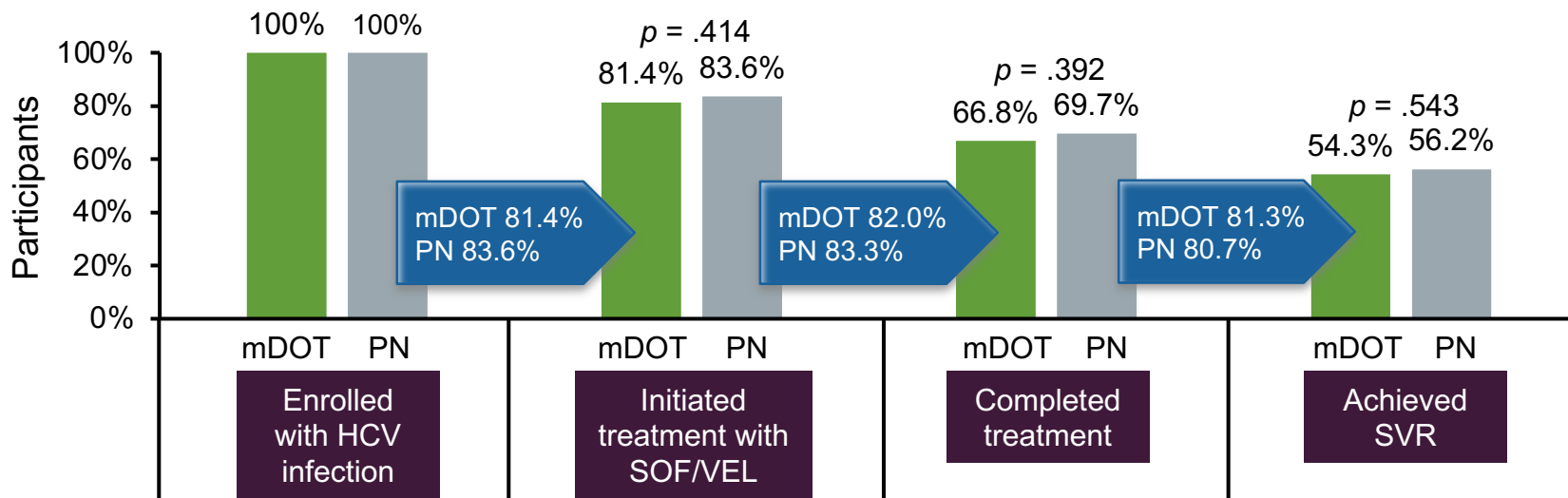


- Primary endpoint: Compare SVR12 in active PWID who initiated treatment using mDOT compared to PN at methadone programs and community-based clinics
- Secondary endpoints: Differences in and factors associated with HCV treatment initiation, adherence, HCV treatment completion (84 days)

EOT = end of treatment; GT = genotype; PN = patient navigation; Tx = treatment
Litwin A, et al. AASLD. November 11-16, 2020; virtual.

Hero Study: mDOT and PN Similar Achieve SVR Rates

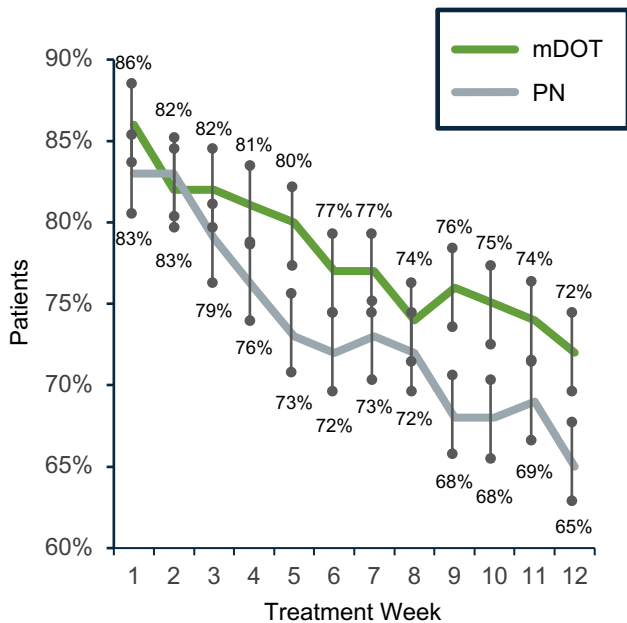
Cascade of Care



Hero Study: Adherence

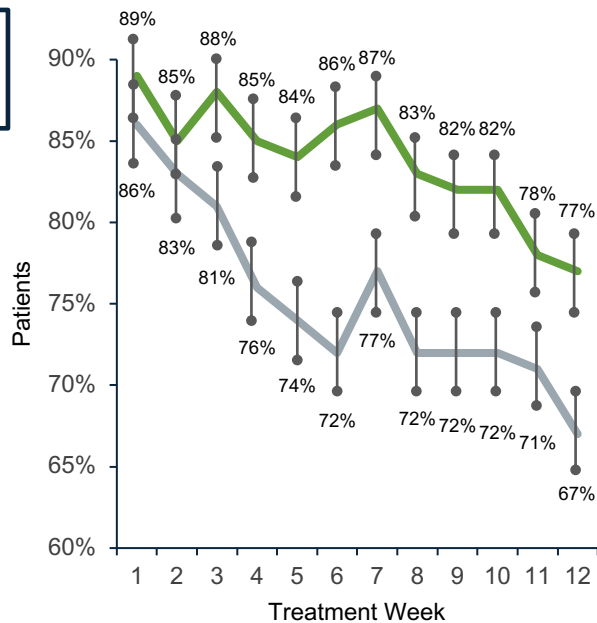
Measured Using Electronic Blister Packs

All Participants



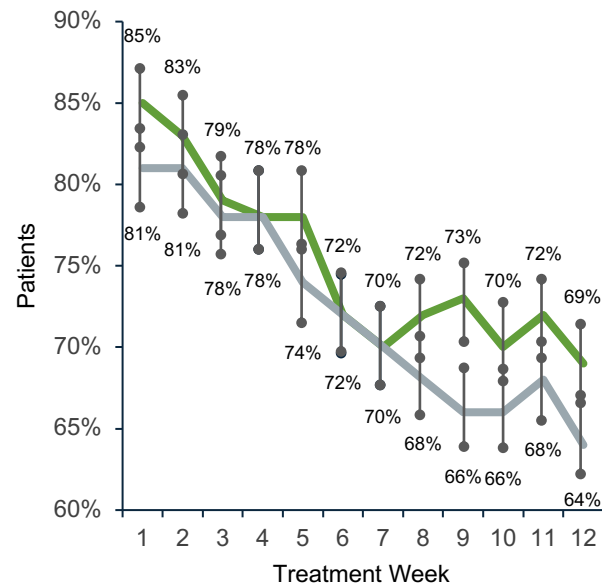
Comparison	Estimate	P Value
mDOT vs. PN	78.0 vs. 73.4	.001

Opioid Treatment Programs



Comparison	Estimate	P Value
mDOT vs. PN	83.7 vs. 75.3	< .001

Community-Based Clinics



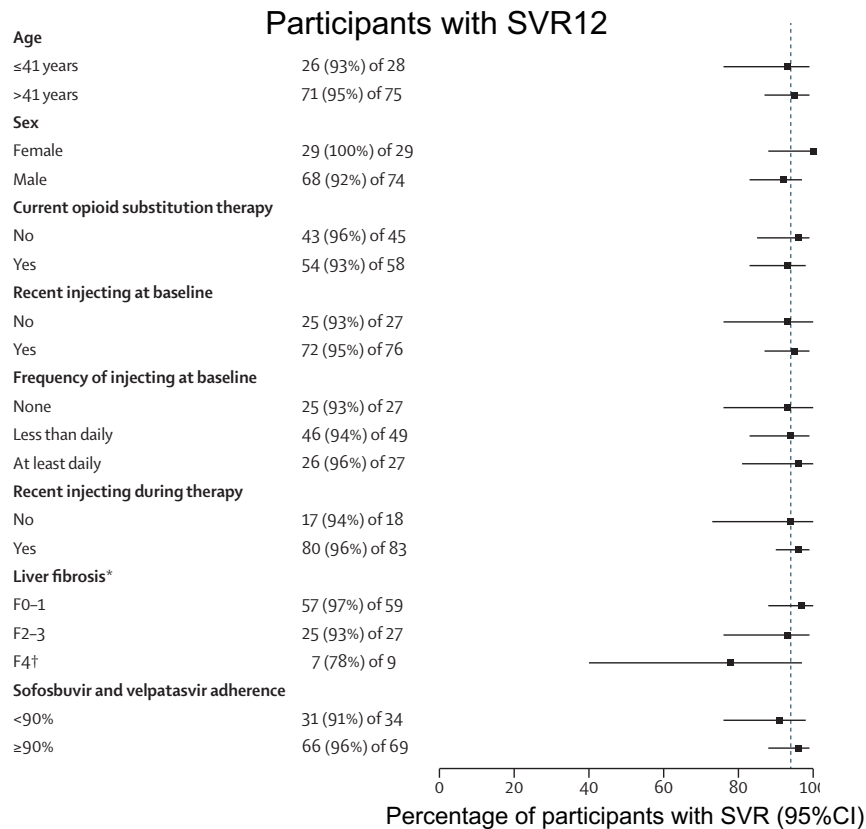
Comparison	Estimate	P Value
mDOT vs. PN	74.5 vs. 72.7	.333

mITT = modified intention to treat
 Litwin A, et al. AASLD. November 11-16, 2020; virtual.

Treatment of HCV in PWID

SIMPLIFY Trial

- 103 persons with recent injection drug use (74% in past month, 26% at least daily in last month) treated with SOF/VEL for 12 weeks
- 94% achieved HCV cure with no virologic failures
- Drug use before and during treatment did not affect SVR12
- 96% had $\geq 90\%$ adherence

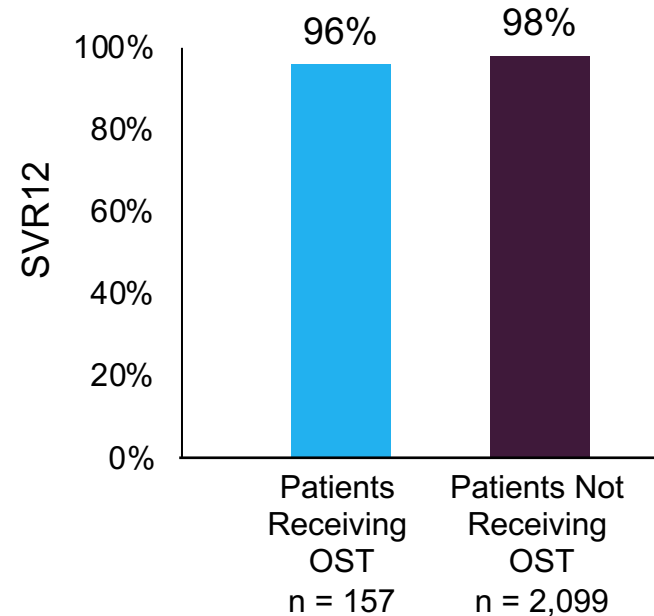


*F0-F1 < 7.1 kPa, F2-F3 7.1-12.49 kPa, F4 \geq 12.5 kPa

†Of the two participants without SVR12, neither had virological failure nor virological relapse
Grebely J, et al. *Lancet Gastroenterol Hepatol.* 2018;3(3):153-161.

Treatment of HCV in PWID

- Pooled data from eight phase II and III trials of GLE/PIB (n = 2,256) prescribed opioid substitution therapy (OST) and reported IDU in past 12 months
- Treatment adherence was 98% among OST and 99% among those not receiving OST
- Loss to follow-up was reduced when treatment was co-localized in the same medical institution



HCV Reinfection Among PWID

- Meta-analysis of 36 studies (person-years follow-up = 6,311)
 - Overall rate of HCV reinfection among people with recent drug use (injecting or non-injecting) was 5.9/100 person-years (95% CI: 4.1-8.5)
 - 6.2/100 person-years (95% CI: 4.3-9.0) among people recently injecting drugs, and 3.8/100 person-years among those receiving OST
 - 1.4/100 person-years (95% CI: 0.8-2.6) among people receiving OST with no recent drug use

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Learning
Objective **3**

Address disparities in HCV treatment initiation in underserved rural and Federally Qualified Health Centers (FQHCs).

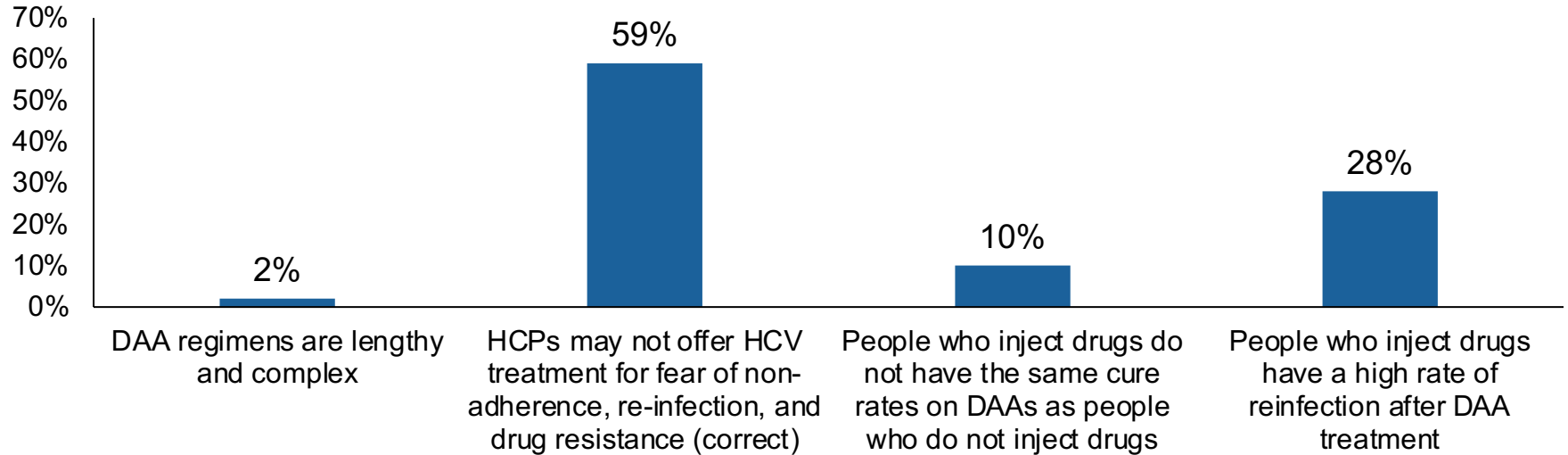


Audience Response

People who inject drugs frequently do not receive highly successful direct-acting antiviral (DAA) treatments for HCV because:

- A. DAA regimens are lengthy and complex
- B. HCPs may not offer HCV treatment for fear of non-adherence, re-infection, and drug resistance
- C. People who inject drugs do not have the same cure rates on DAAs as people who do not inject drugs
- D. People who inject drugs have a high rate of reinfection after DAA treatment

People Who Inject Drugs Frequently Do Not Receive Highly Successful DAA Treatments For HCV Because:



Changing the HCV Narrative

- Unprecedented opportunities to act
- Stop patient-blaming
- Remove restrictions to treatment
- Harm reduction; pragmatic approach
- Provider, staff training important: sensitivity to individual challenges
- Offer on-site testing
- Offer opportunities for screening
- Move toward single-visit HCV diagnosis

Simplified Reflex Testing and Treatment Linkage

Simple, effective screening, testing, and treatment:

- One clinic visit = **rapid** antibody screening and single **reflex** viral load test
- Standard treatment with **pangenotypic DAAs** eliminate genotype test delay
- HIV and HBV testing recommended
- **12 weeks after last dose:** Second viral load test to confirm SVR

Best Practices

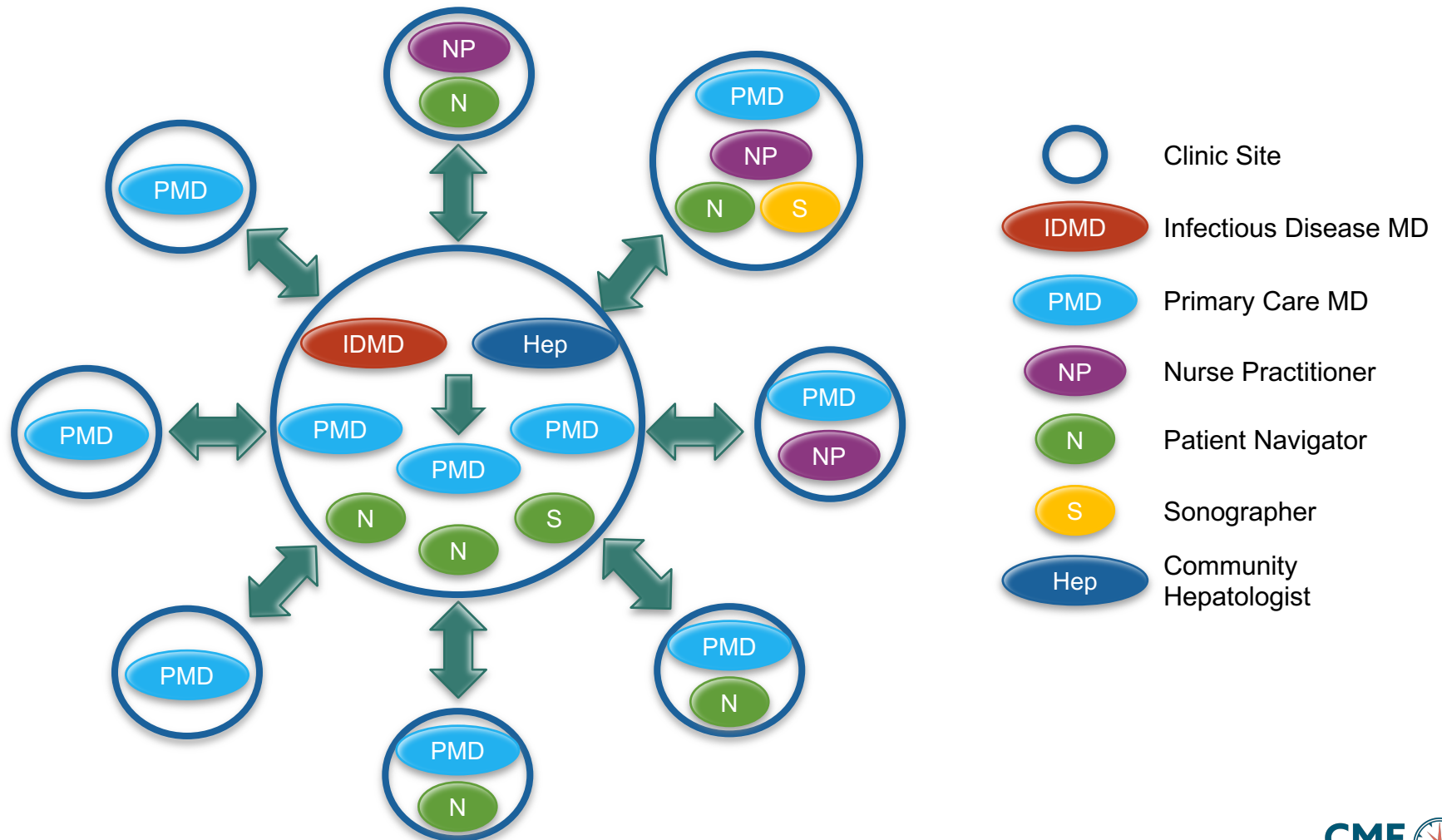
- DAA therapy available since 2013; high **cure rates**
- **Evidence-based practices** together with addiction care necessary to eliminate HCV
- Efficient methods to **identify, evaluate, implement, and monitor**
- **New model of care or stand-alone** focusing on HCV care provision that can be scaled up to decrease morbidity and mortality
- **Person-centered** and utilize innovative methods, unique sites, and creative solutions

Kentucky Hepatitis Academic Mentorship Program (KHAMP Model)

- Nationally, Kentucky is a leader in new HCV cases
- 2018: Medicaid plans ↑ treatment access by eliminating fibrosis, sobriety, and drug-testing requirements for HCV medications
 - Prescriber restrictions in place until November 2020
- Kentucky state law: Universal HCV testing and reporting required during pregnancy
- Engage PCP, addiction care, and women's health providers
- KHAMP curriculum goal: ↑ health in underserved communities in Appalachian region by training workforce to screen, diagnose, treat, and care for persons with HCV

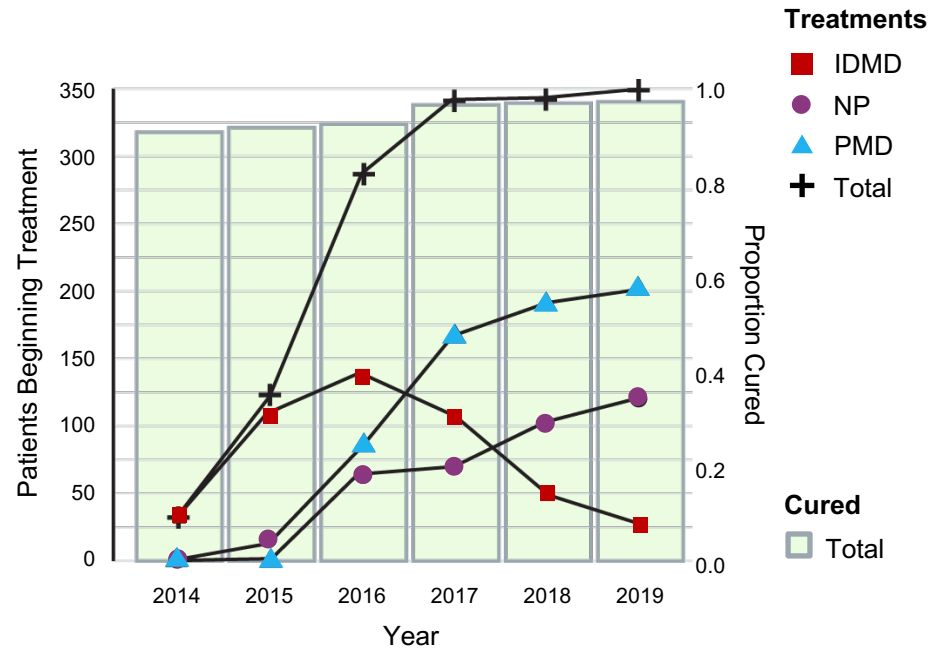
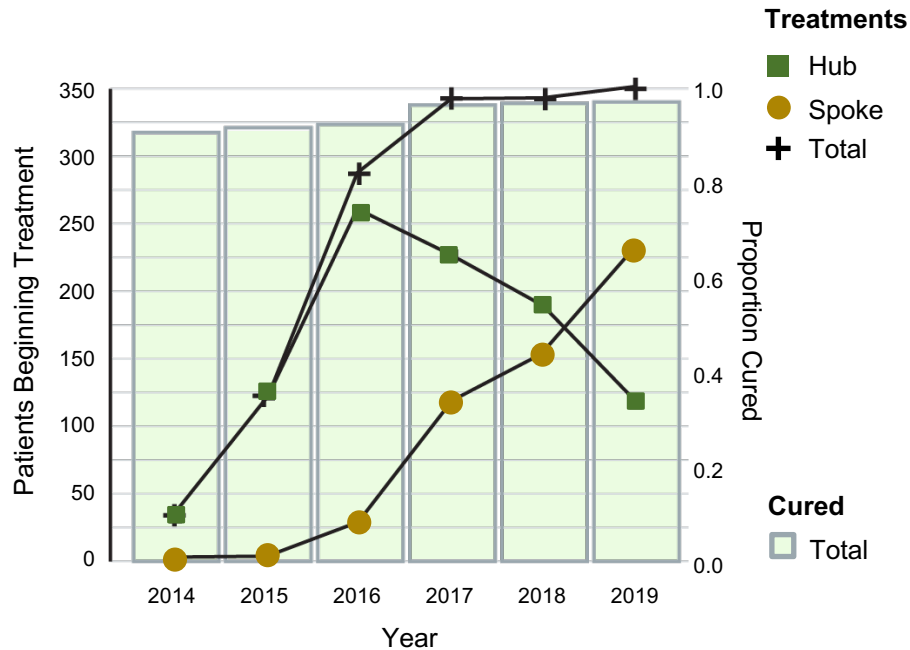
Decentralized Hub and Spoke Model for HCV Treatment in a FQHC

- Decentralized HCV treatment by NPs, primary care physicians, infectious disease physicians in FQHC (San Diego)
- 1,261 patients treated by 6 NPs, 10 primary care physicians, 1 infectious disease physician in 10 clinics; 2014-2020
- Based on Extension for Community Healthcare Outcomes (Project ECHO) model with 1 hub and 9 spokes
- HCV-positive person assigned patient navigator = linkage to care, transportation, insurance assistance, HCV provider appointments



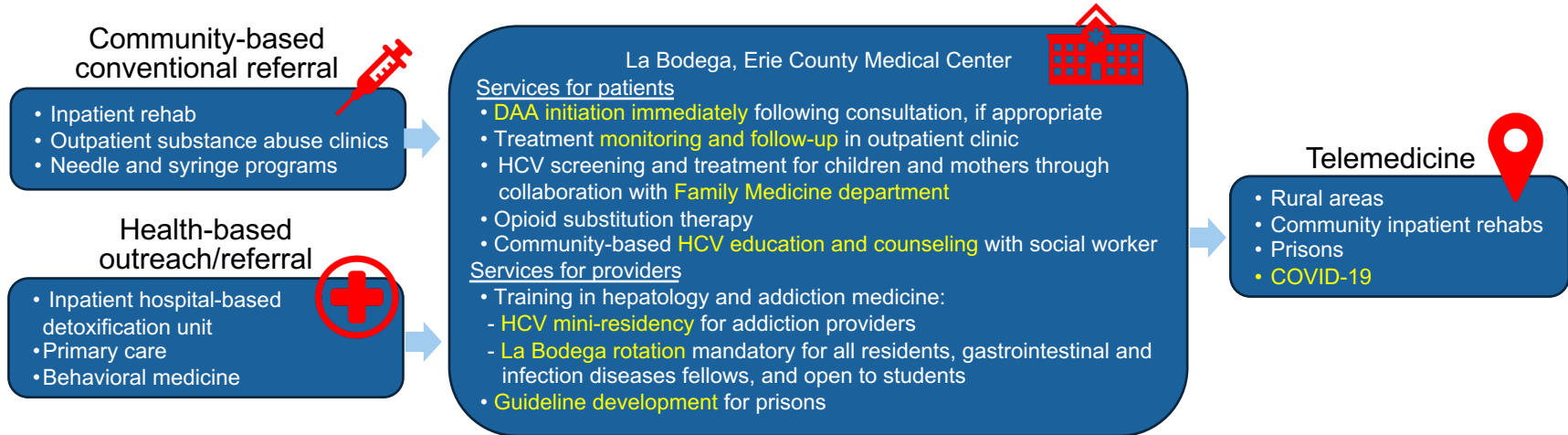
Hub and Spoke Treatment Model Results

Diverse patients treated; prevalence of cure did not differ between IDMD, PMD, or NPs
Homeless population treatment by non-specialist HCPs was not inferior: cure rate of 95%

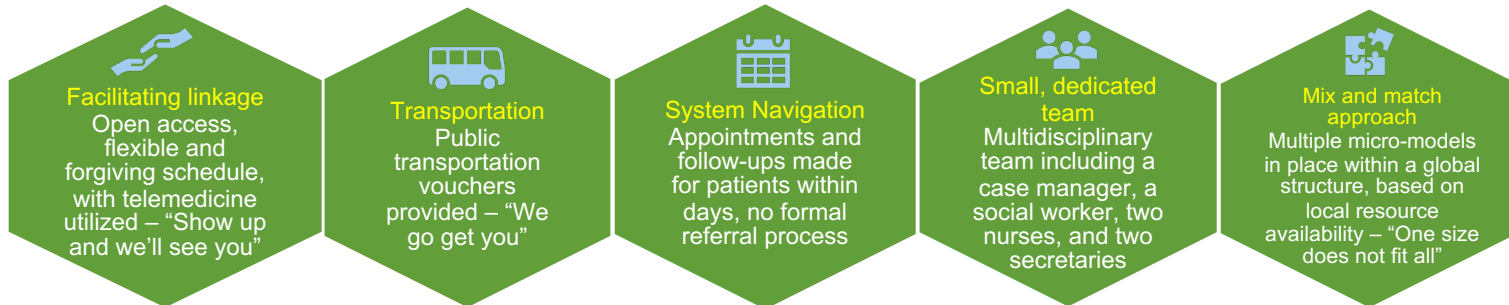


La Bodega Buffalo

A hybrid model of outreach, referral, co-localization, and telemedicine – implemented state-wide and nationally

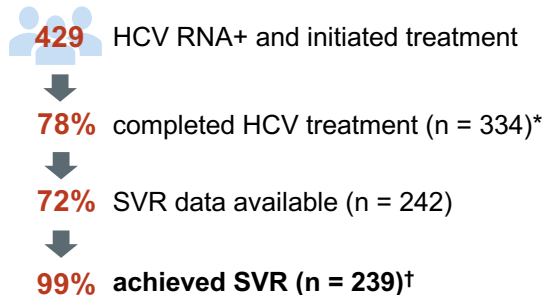


Key success factors of the model:



La Bodega Outcomes

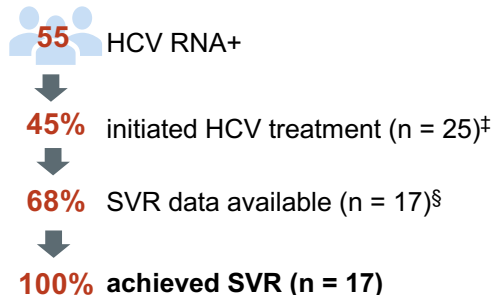
Co-localized model, 2018-2019 Opiate-dependent patients in the hepatology clinic



87% overall adherence among PWID

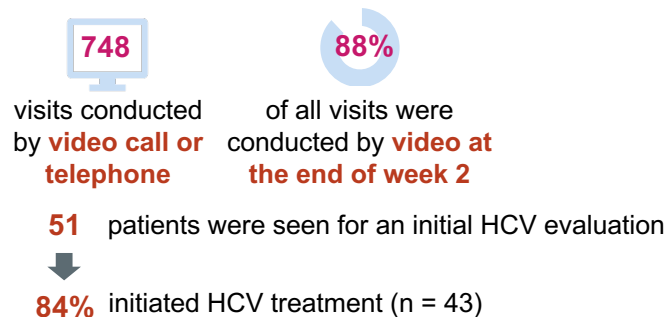
15 patients with reinfection or failed treatments were identified and retreated

Detox model, Oct 2018–Oct 2020 Patients admitted to an opiate detoxification setting



Treatment as prevention
Partnership with high-risk treatment service settings and early treatment initiation for HCV among PWID can serve as treatment as prevention and reduce rates of HCV transmission

Telemedicine, Mar-Jun 2020 HCV management among PWID in response to COVID-19



Limitations
Telemedicine can slow down the HCV management cascade from linkage to treatment initiation due to delays in obtaining lab data

A co-localized, hybrid model of care is an effective and flexible strategy, helping to increase HCV screening and treatment uptake among people with addiction disorders

*53/429 patients remain on treatment, 42/429 started but did not complete treatment or were lost to follow-up, of which 8 achieved SVR despite incomplete regimens; †The remaining 3/242 patients were pending SVR assessment at time of submission; ‡7/55 patients had spontaneous clearance of HCV; §8/25 patients were pending SVR assessment at time of submission.

1. Martinez A, et al. The Liver Meeting, 2020 (American Association for the Study of Liver Diseases [AASLD]) Abstract 0476.; 2. Martinez A, et al. Abstract 2267. International Liver Congress, European Association for The Study of Liver, London, England, 2020.; 3. Martinez A, et al. The Liver Meeting, 2019 AASLD; Boston, MA. Abstract 1608.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Align screening protocols to updated **CDC guidelines** to ensure all people are screened for HCV and linked to care when necessary
- Provide successful screening and care continuum with **PCPs and non-specialist providers**
- Initiate treatment in primary care setting to **expand access** to treatment and HCV cure
- Adopt **new health care models** to meet changing HCV landscape

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AFTER THE SHOW

Questions & Answers
Recorded on April 20, 2021



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Visit the
Liver Disease Hub

Free resources and education to educate health care providers and patients on hepatitis C

<https://www.cmeoutfitters.com/liver-hub/>