



CLINICAL CARE OPTIONS®
HEPATITIS

HCV and COVID-19: Impact of Overlapping Pandemics

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Stacey Trooskin, MD, PhD, has disclosed that she has received consulting fees and funds for research support from Gilead Sciences.

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Ricardo Franco, MD, has disclosed that he has received funds for research support from Gilead Sciences and Merck, and has received other financial or material support from AbbVie, Gilead Sciences, and Pfizer.

Program Overview

- Focus: Improve Knowledge and Competence in the Care of HCV Infection
 - Clinical Interplay of COVID-19 and HCV Coinfection
 - Access to HCV Care and Treatment and the Impact of the COVID-19 Pandemic
- Question and Answer Session

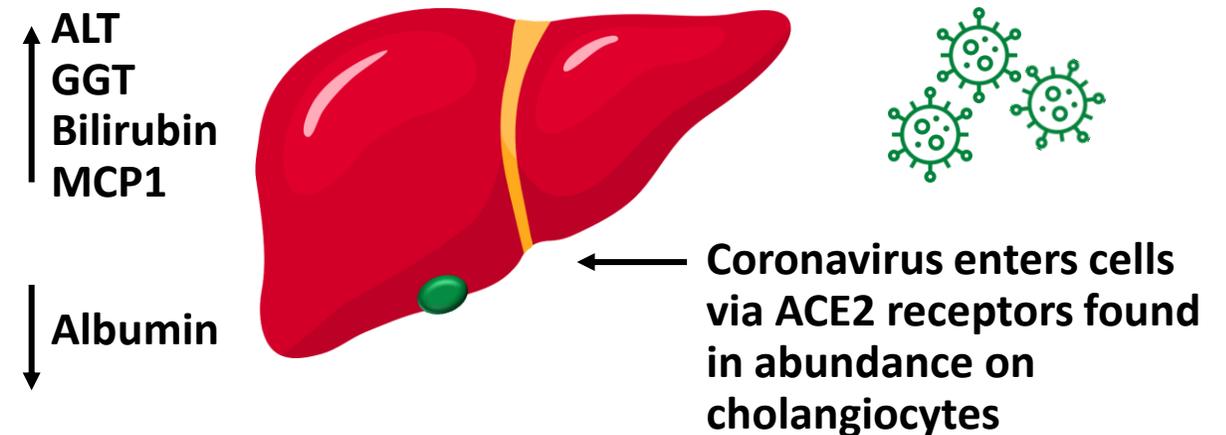
Clinical Interplay of COVID-19 and HCV Coinfection



SARS-CoV-2 Infection and the Liver

- Possible causes of liver injury in SARS-CoV-2 infection:
 - Severe inflammatory response/sepsis
 - Hypoxic injury
 - Drug-induced liver injury
 - Microthromboses of hepatic sinusoids
 - SARS-CoV-2–direct damage
 - Multifactorial?

Liver Injury in SARS-CoV-2–Infected Patients



Liver Injury Markers in COVID-19

- 14.8% to 53.0% of hospitalized patients with COVID-19 had liver injury^[1-3]
- Significant liver injury present in 58% to 78% of patients who died from COVID-19^[3]
 - Liver injury a surrogate marker for adverse outcomes^[3,4]

Covid-19–Associated Liver Abnormalities ^[5]	Albumin	Transaminases	GGT	Bilirubin	Alkaline Phosphatase
Severe liver injury from inflammatory response (cytokine storm)	↓	↑	Variable	↑	Variable
Drug-induced liver injury	Variable	↑	Variable	Variable	Variable
Direct biliary injury	Variable	Variable	↑	↑	↑
Ischemia/microthrombosis	↓	↑	Variable	↑	Variable

1. Xie. Liver Int. 2020 ;40:1321. 2. Zhang. Lancet Gastroenterol Hepatol. 2020;5:428.
3. Xu. Liver Int. 2020;40:998. 4. Huang. Lancet. 2020; 395:497. 5. Morgan. Pathogens. 2020;9:430.

COVID-19 and Preexisting Liver Disease: OpenSAFELY in Great Britain

- Retrospective analysis of factors associated with COVID-19–related deaths, using NHS England
- (N = 17,278,392; > 114,000 with chronic liver disease; total COVID-19–related deaths = 10,926)

Characteristic	aHR for COVID-19 Death (95% CI)
Age 60-69 yrs/80 yrs or older	2.40 (2.16-2.66)/20.60 (18.70-22.68)
BMI ≥ 40 kg/m ² (obese class III)	1.92 (1.72-2.13)
Black race	1.48 (1.29-1.69)
High blood pressure or HTN diagnosis	0.89 (0.85-0.93)
Chronic heart disease	1.17 (1.12-1.22)
Diabetes (A1C ≥ 58 mmol/mol)	1.95 (1.83-2.08)
eGFR < 30 mL/min	2.52 (2.33-2.72)
Cancer diagnosed < 1 yr ago	1.72 (1.50-1.96)
Hematological malignancy diagnosed < 1 yr ago	2.80 (2.08-3.78)
Liver disease	1.75 (1.51-2.03)

COVID-19 and Preexisting Liver Disease: A Multicenter Study in the United States

- In a cohort of 2780 US patients, chronic liver disease was associated with significantly higher mortality from COVID-19 (RR: 2.8; 95% CI: 1.9-4.0)
 - In patients with cirrhosis, the mortality risk was higher (RR: 4.6; 95% CI: 2.6-8.3)
 - In the liver disease group, fatty liver disease and nonalcoholic steatohepatitis were the most common causes of liver disease; **the increased mortality risk was independent of risk factors such as obesity (body mass index), hypertension, and diabetes**

SECURE-Cirrhosis and EASL COVID-HEP Registries

- Patients from 33 countries over 13 wks, with chronic liver disease and COVID-19
 - N = 904; n = 406 with cirrhosis, n = 339 without cirrhosis, n = 159 with liver transplant

Cirrhosis Characteristic, n (%)	Cirrhosis (n = 406)
Major etiologies	
▪ Alcohol	125 (31)
▪ Nonalcoholic steatohepatitis	85 (21)
▪ Hepatitis C	44 (11)
▪ Hepatitis B	28 (7)
▪ Autoimmune hepatitis	23 (6)
▪ Alcohol and HCV	22 (5)
Decompensation, any	185 (46)
▪ New or worse ascites	110 (27)
▪ New or worse encephalopathy	107 (26)
▪ Variceal hemorrhage	15 (4)

Major Clinical Outcome, n (%)	Cirrhosis (n = 406)	No Cirrhosis (n = 339)	Liver Transplant (n = 159)
Hospitalized	364 (90)	302 (89)	129 (81)
Intensive care admission	111 (27)	66 (19)	47 (30)
Invasive ventilation	72 (18)	62 (18)	31 (20)
Death	133 (33)	27 (8)	30 (19)



Increased risk

AASLD Consensus Statement: Evaluation of Patients With COVID-19 and Elevated Liver Biochemistries

- **Low threshold for SARS-CoV-2 testing when patients with cirrhosis or HCC are symptomatic**
- When assessing patients with COVID-19 and elevated liver biochemistries, consider non-COVID-19 etiologies, such as viral hepatitis and drug-induced liver injury
 - Consider ongoing myositis (particularly when $AST > ALT$), cardiac injury, ischemia, and cytokine-release syndrome
- To limit unnecessary transport of potentially infectious patients, avoid hepatic ultrasound or other advanced imaging unless results are likely to change management
- Abnormal liver biochemistries not necessarily a contraindication for using investigational or off-label drugs (eg, remdesivir, tocilizumab), unless levels $> 5 \times$ ULN
- Regularly monitor liver biochemistries of inpatients, regardless of baseline values, particularly when using remdesivir or tocilizumab

AASLD Consensus Statement: Management of Stable Outpatients With Chronic Liver Disease and COVID-19

- Patients with COVID-19 symptoms or known exposure should not be evaluated in hepatology or liver transplant clinics
 - Consider moving the evaluation to another outpatient site dedicated for this purpose
- Continue treatment for chronic hepatitis B and chronic hepatitis C, if already on treatment
- Initiating treatment of hepatitis C in a patient with COVID-19 is not usually warranted
 - Can be deferred until recovered from COVID-19

Access to HCV Care and Treatment and the Impact of the COVID-19 Pandemic



Call to Action Toward HCV Elimination: Focus on Simplified Testing and Cure

■ **Simplification:**

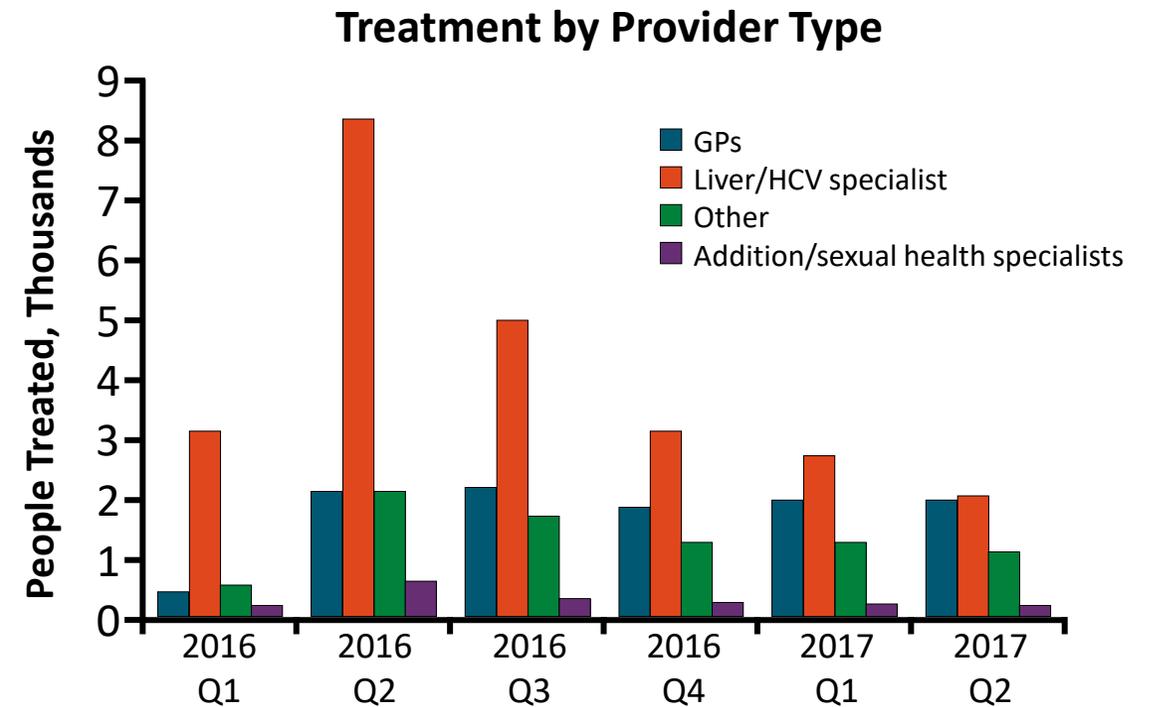
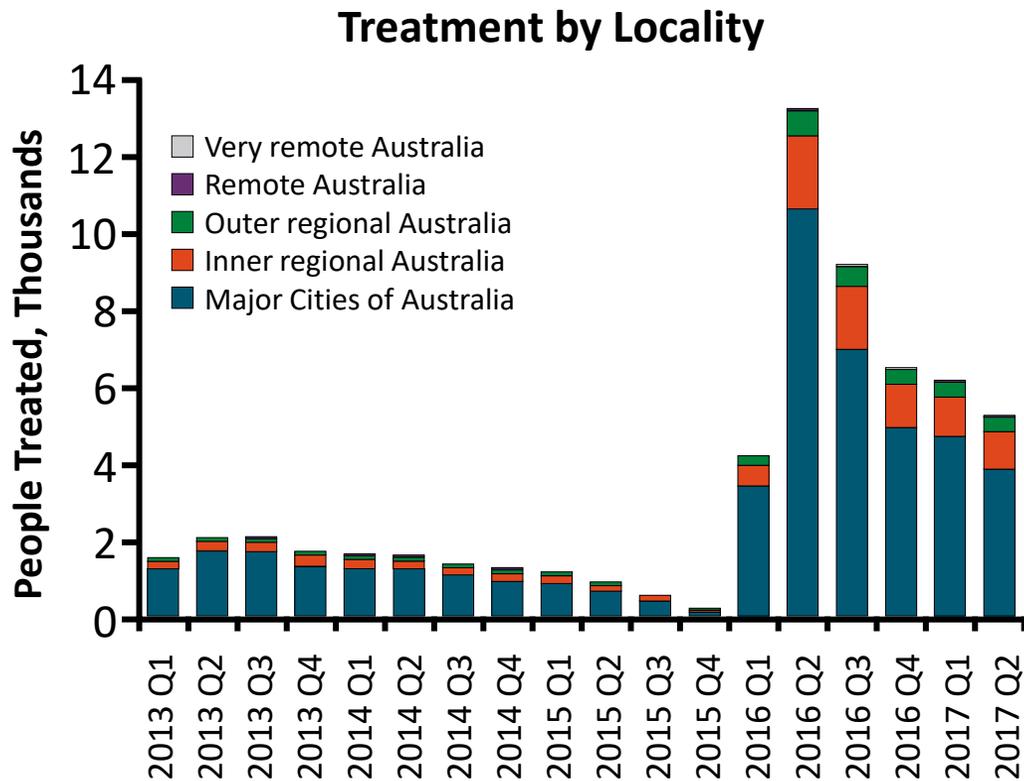
- One clinic visit with rapid antibody screening and a single reflexive viral load test
- Standardized treatment regimens with pangenotypic DAAs eliminate delay associated with genotype test
- Confirm SVR at Wk 12 with second viral load test

- **Integration** with primary care and other disease programs (eg, TB, HIV) and outreach settings (harm reduction)
- **Decentralization** of services from referral hospitals to local level care
- **Task sharing** of uncomplicated cases with primary care clinicians, medical officers, advanced practice clinicians, nurses, pharmacists, and trained community care workers

Signatories: AASLD, EASL, APASL, ALEH

Experience of Universal DAA Treatment Access in Australia: 2016 to 2017

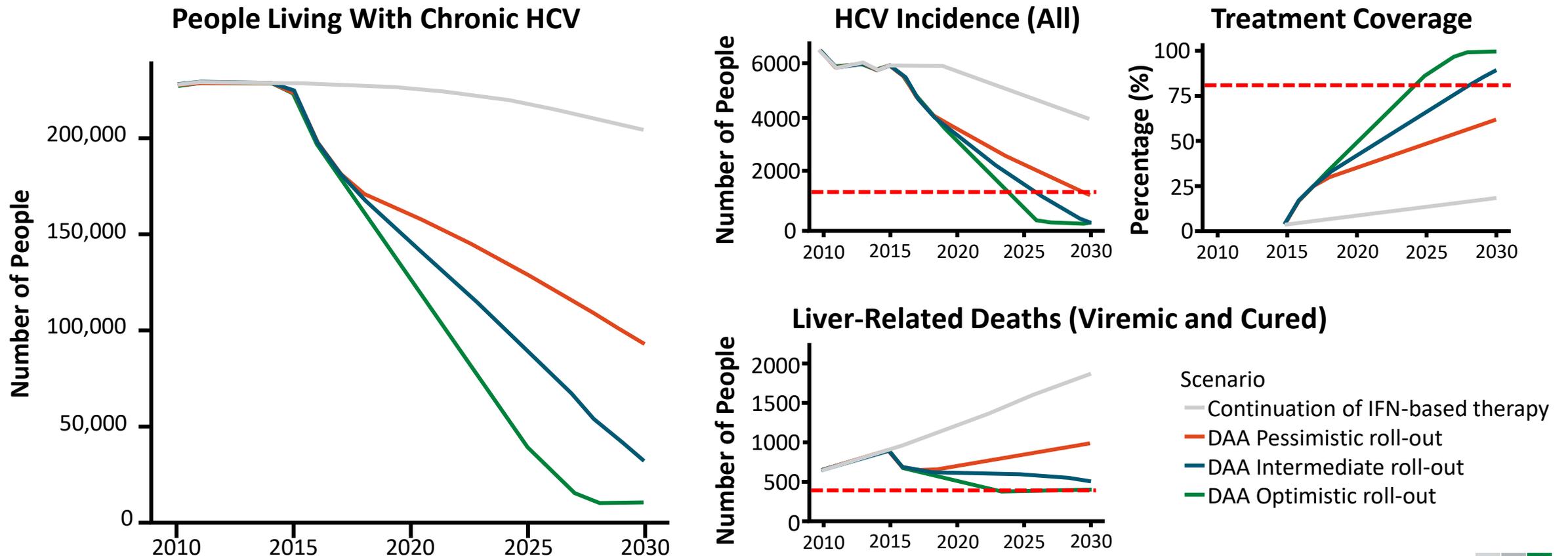
- Number of individuals treated declined from 32,600 in 2016 to 17,100 in 2018



↑ *Universal access to DAA treatment*

Australia on Track to Achieve WHO HCV Elimination Targets by 2028 After Rapid Initial DAA Uptake

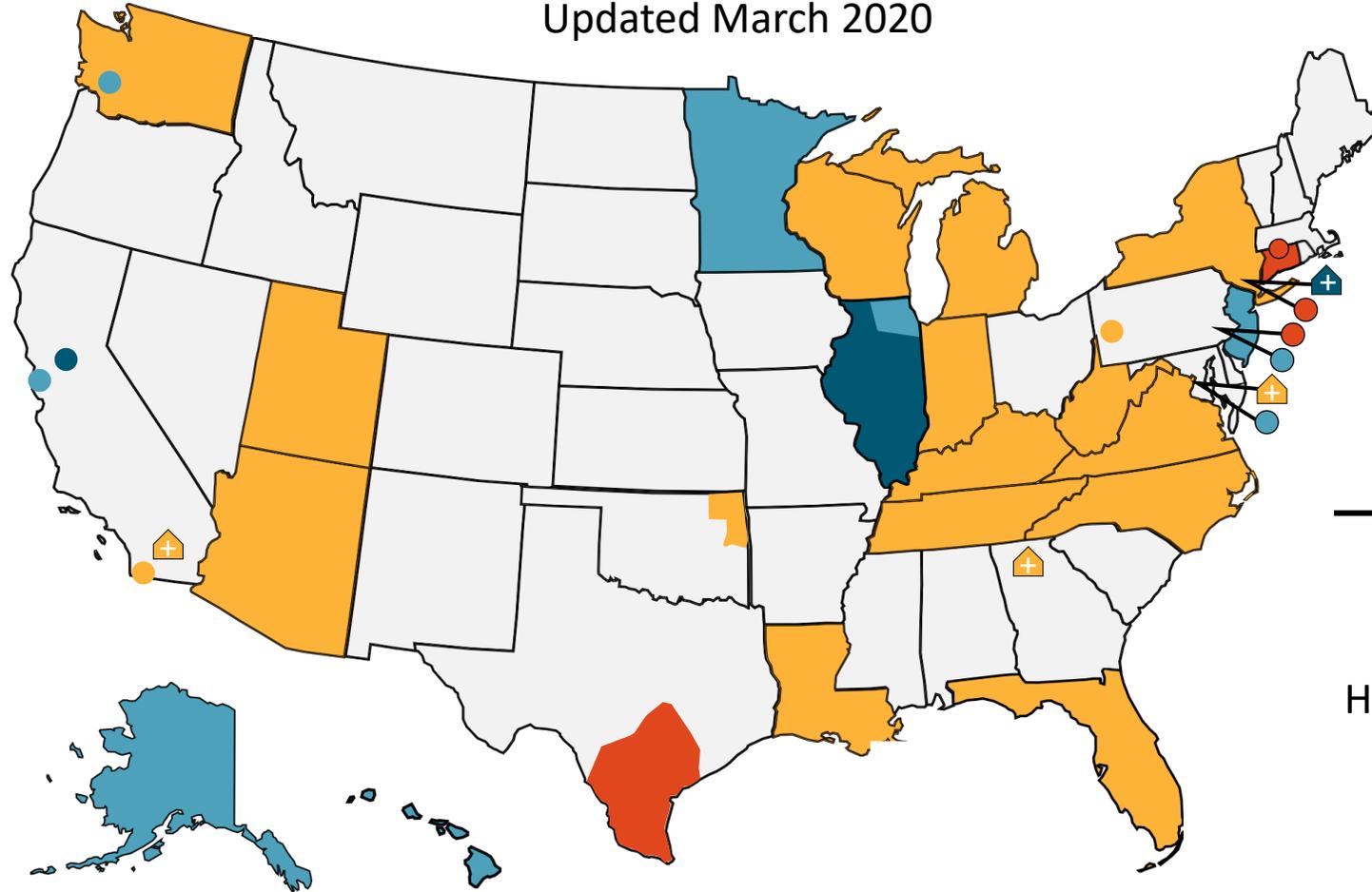
- Mathematical modeling simulation by DAA treatment scenario 2016-2030



Mapping Hepatitis Elimination in Action

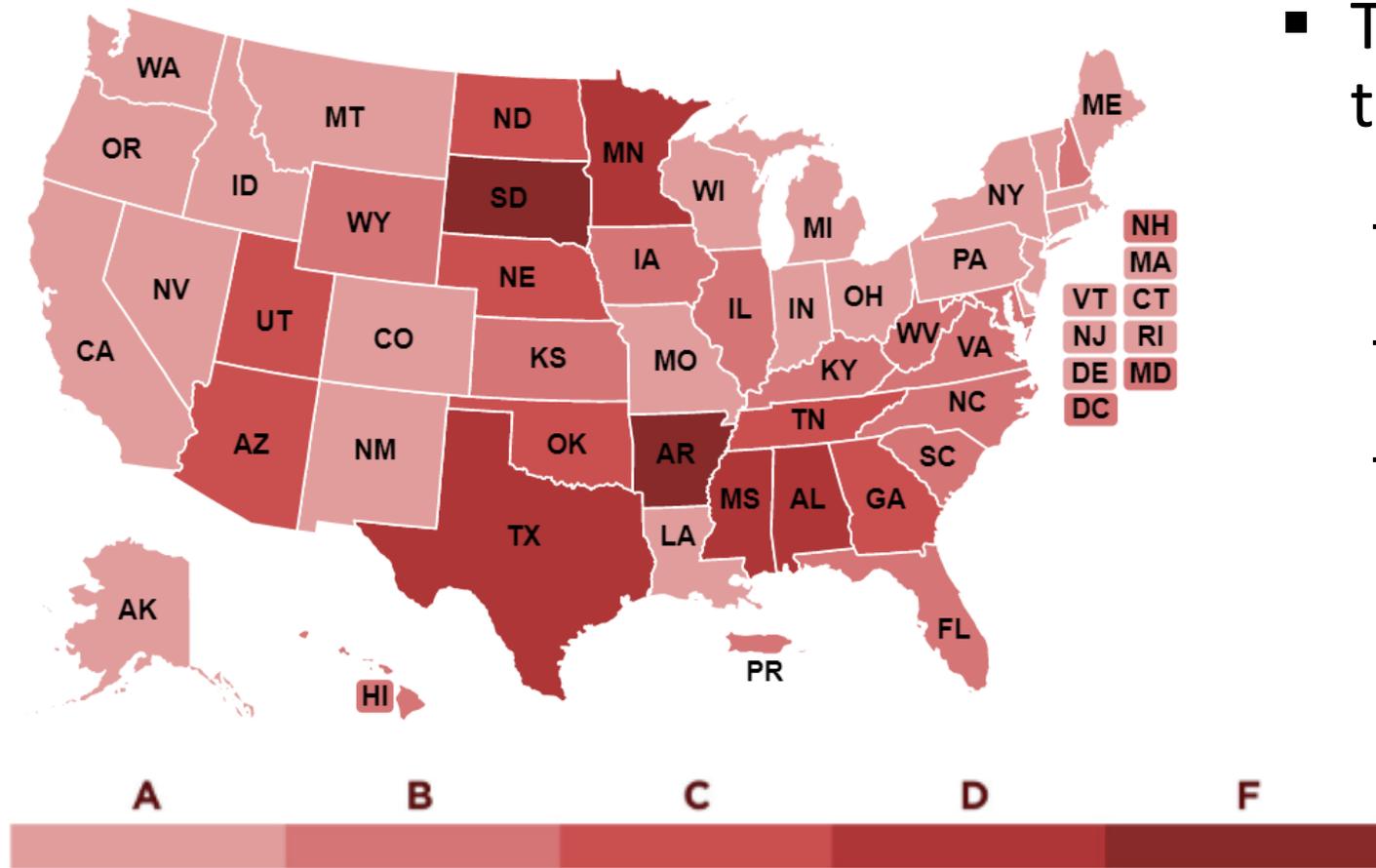
Hepatitis Elimination Projects in the United States

Updated March 2020



	State County City	Health System Clinic
Hepatitis B		
Hepatitis C		
Hepatitis B and C		
HIV/HCV Coinfection		

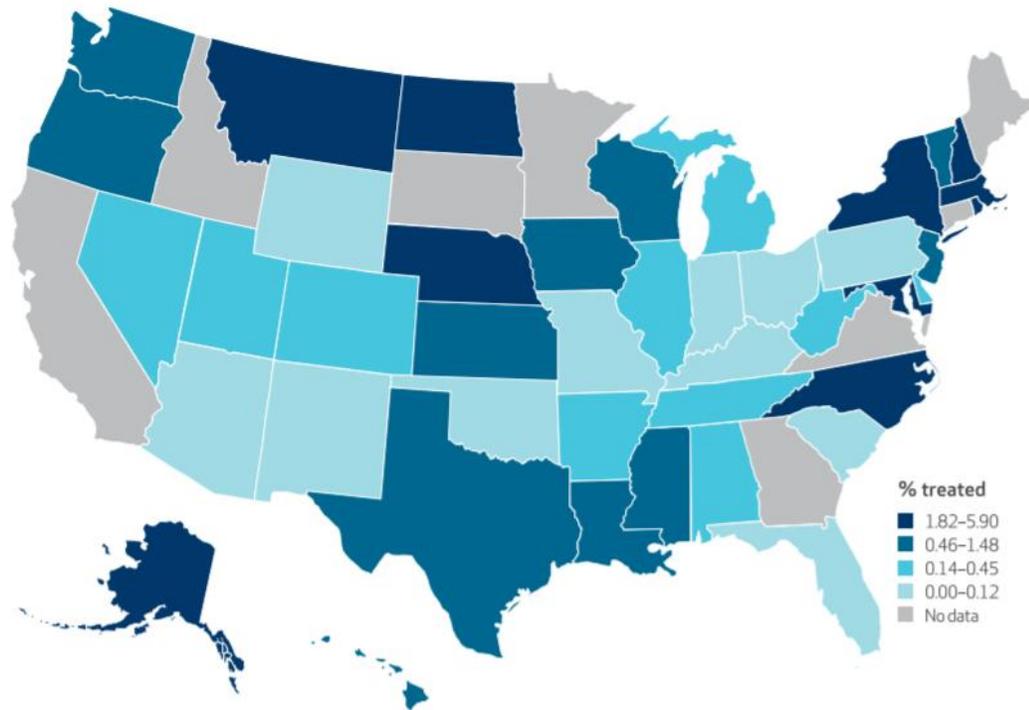
State of Medicaid Access to HCV Treatment: Letter Grades by State



- The most significant restrictions to treatment:
 - Liver damage restrictions
 - Sobriety restrictions
 - Prescriber restrictions

HCV Elimination Gaps in US Correctional Facilities

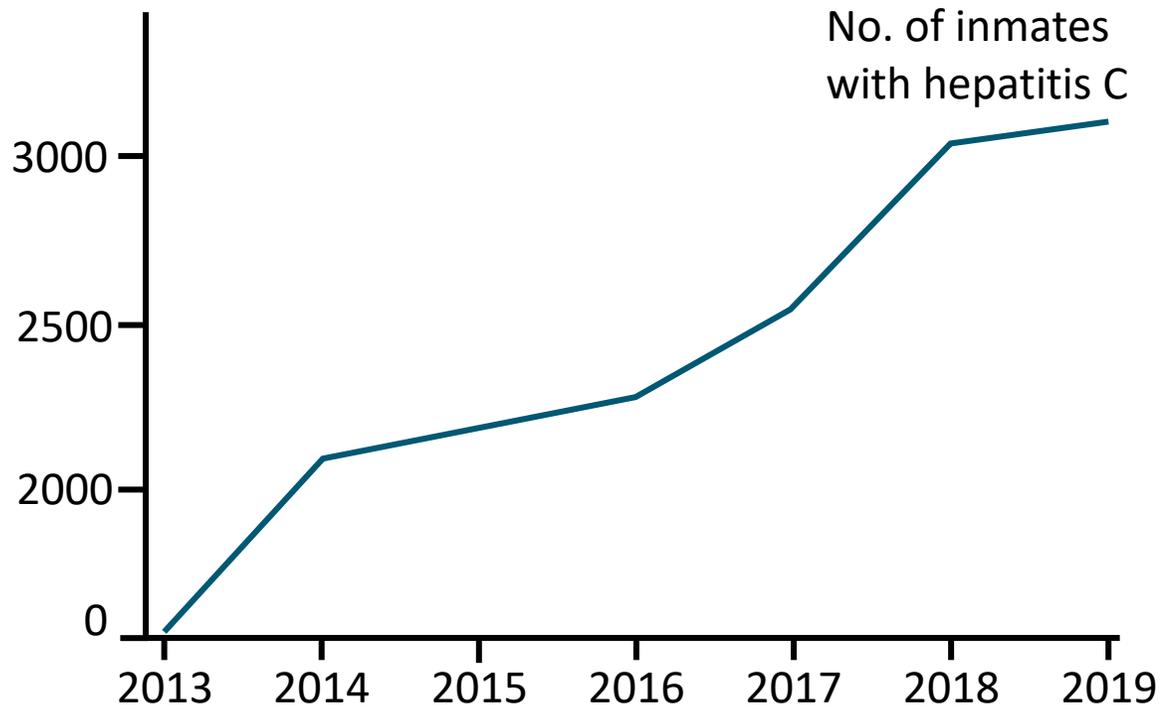
US State Prisoners Receiving Any Treatment as a Proportion of Inmates With Known HCV in January 2015^[1]



- Individual-based simulation modeling demonstrated that “test all, treat all, and linkage to care at release” model would^[2]:
 - Increase lifetime SVR rates by 23%
 - Reduce cirrhosis cases by 54%
 - Result in annual additional cost of \$1440 per prison entrant, considered cost-effective
- Targeted testing and liver fibrosis-based treatment provided worse outcomes at higher cost^[2]

Despite Progress, HCV Largely Untreated in Oklahoma Correctional Facilities

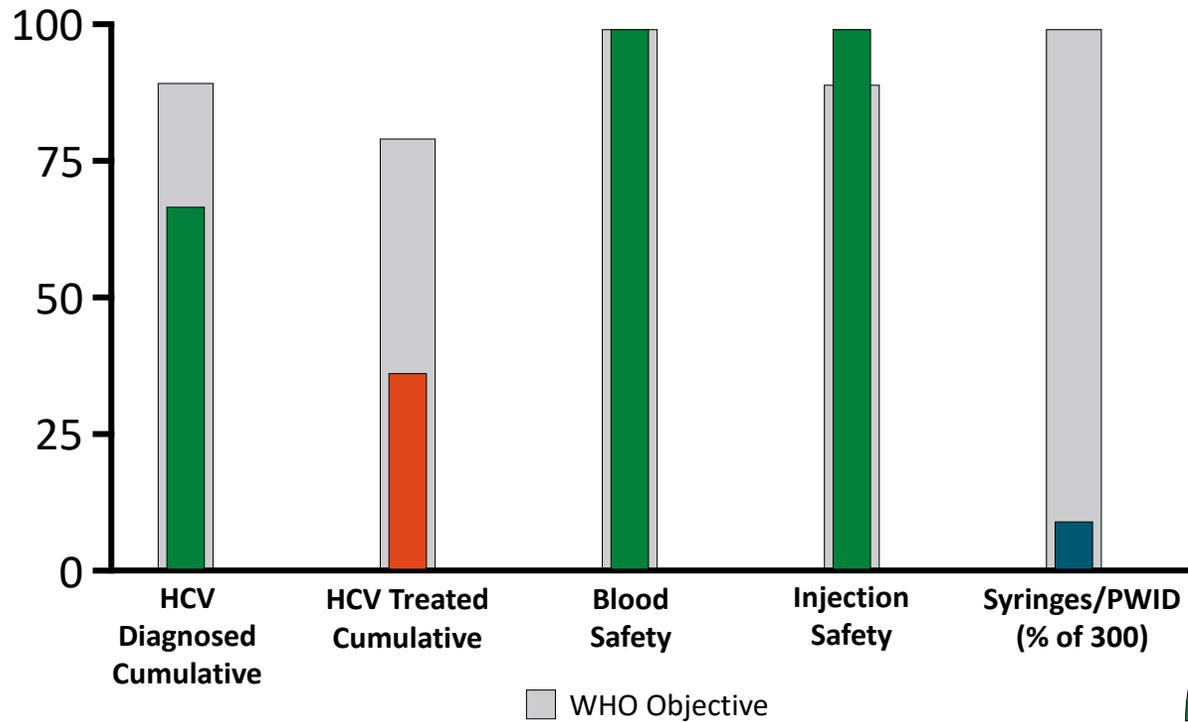
HCV Cases in Oklahoma Department of Corrections



- Estimated HCV prevalence: 1 in 12 inmates
- HCV Rx costs = \$13,200 to \$62,000 per patient; DOC drug expenditures FY 2016-2019 = \$2.5 million
- Only inmates with the most severe infections are prioritized
 - 243 (8%) of inmates with HCV received drugs from July to Oct 2019
- Oklahoma DOC requested \$91 million for HCV treatment in FY 2020 budget; state Legislature approved \$12 million, which will only cover the cost of treatment for 450 to 550 patients

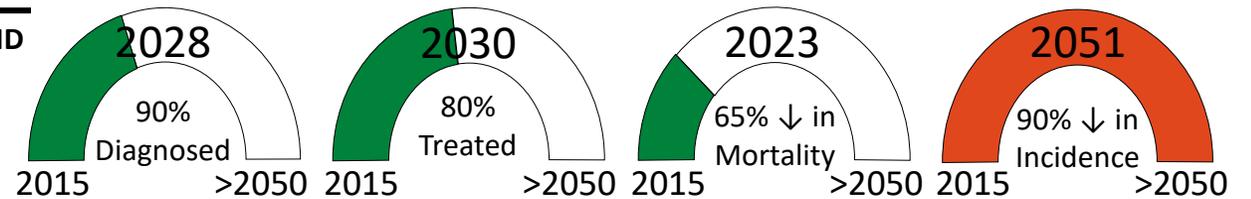
HCV Elimination by 2030: CDA Foundation Dashboard for United States

Progress Toward Elimination Targets (2019 data)

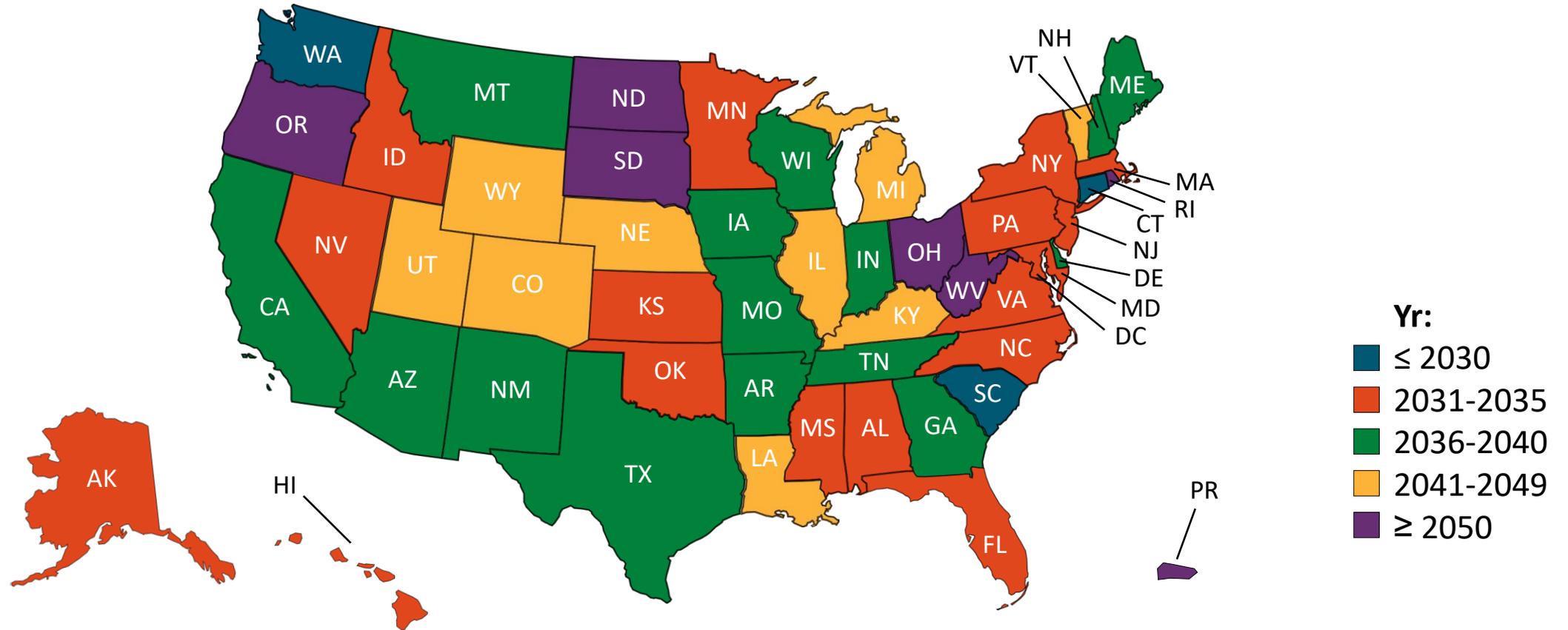


- Estimated HCV Infections in 2016: 2,936,000 (prevalence 0.9%)
 - 63% of HCV infections were diagnosed
 - 8% of HCV infections are treated annually
 - 22,300 HCV-related deaths, annually
 - 3 HCV-related deaths per hour

Year of Achieving All Goals for HCV > Year 2051



US HCV Elimination: Estimating the Yr Each State Will Hit WHO Targets



*The estimation may be less accurate owing to the small number of patients with HCV in the area.

Hepatitis C Treatment in Louisiana: State Profile

- Estimated number of individuals living with HCV: 50,000^[1]

“Louisiana’s Big Bet” Plan to Eliminate Hepatitis C

2019^[2]: Establish Hepatitis C subscription model

2020^[2]: Treat 10,000 Louisianans in Medicaid and Corrections

2024^[3]: Treat 80% of Louisianans living with hepatitis C

Grade

Summary^[4]

A

Liver Damage (Fibrosis): Fee-For-Service (FFS) and all Managed Care Organizations (MCOs) do not impose restrictions.

Sobriety: FFS and all MCOs do not impose restrictions.

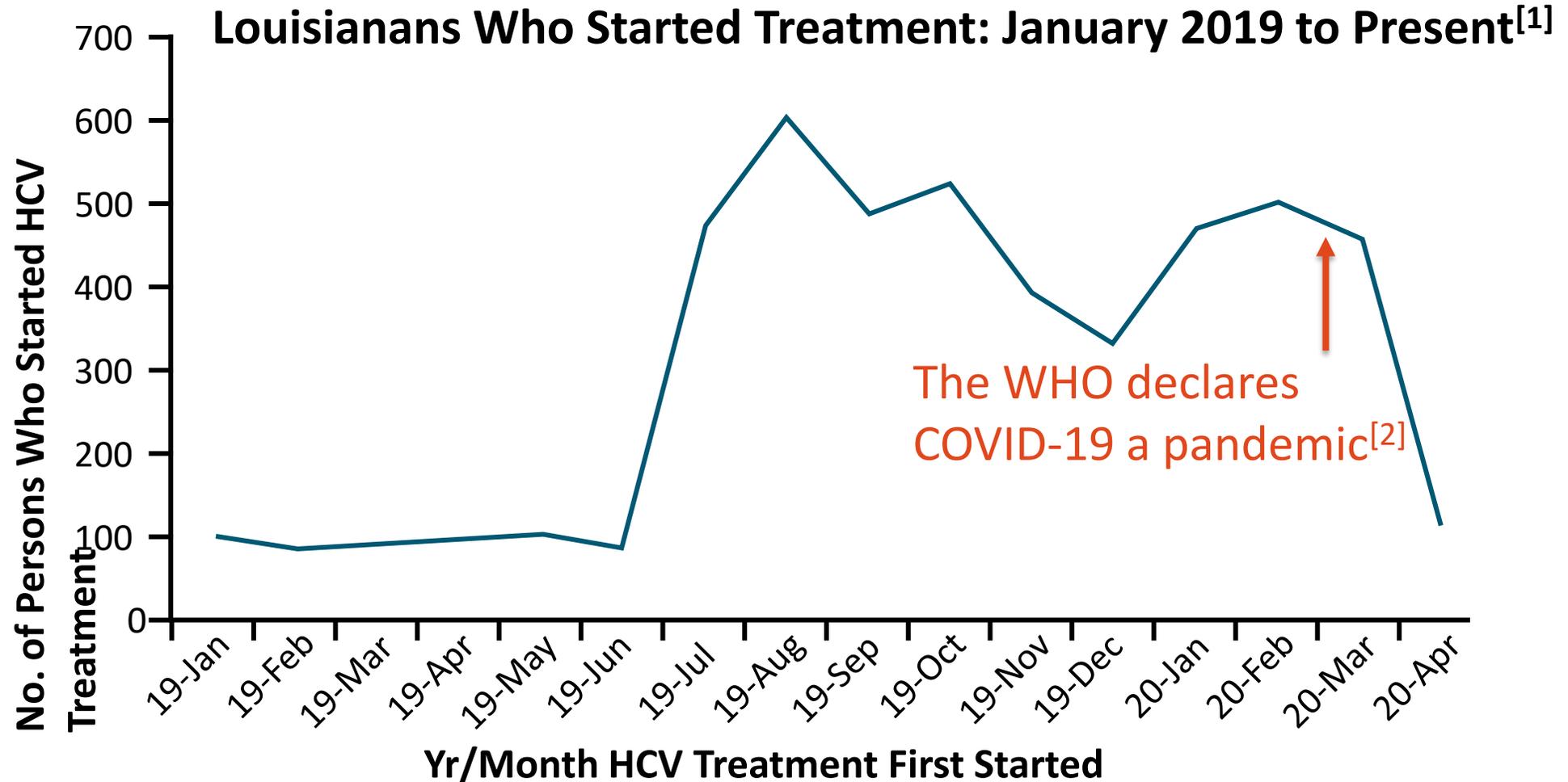
Prescriber: FFS and all MCOs do not impose restrictions.

Grade Rationale: Louisiana’s FFS and MCO programs have removed all restrictions as a result of the state’s “subscription” financing model. Additionally, Louisiana has removed the need for prior authorization for the state’s preferred agent and maintains coverage parity across FFS and MCO programs, further improving access to treatment.

1. Louisiana State Profile. Available at: HepVu: <https://hepvu.org/state/louisiana/> 2. Louisiana’s Hepatitis C Elimination Plan (2017). Available at: <https://www.nastad.org/sites/default/files/Uploads/2019/2019-am-burgess.pdf> 3. Louisiana Hepatitis C Elimination Plan: 2019-2024. Available at: <https://www.louisianahealthhub.org/wp-content/uploads/2019/08/HepCFreeLA.pdf> 4. Hepatitis C State of Medicaid Access Report Card. Available at: https://stateofhepc.org/wp-content/themes/infinite-child/reports/HCV_Report_Louisiana.pdf



COVID-19 Impact on Louisiana's HCV Treatment Through Medicaid or Corrections



1. HepVu. Available at: <https://hepvu.org/hepvu-webinar-the-impact-of-the-covid-19-pandemic-on-viral-hepatitis/>

2. AMJC. Available at: <https://www.ajmc.com/view/a-timeline-of-covid19-developments-in-2020>

COVID-19 Impact on HCV Elimination: World Hepatitis Alliance Global Survey, March 30 to May 4, 2020

N = 132 respondents from civil society organizations and hepatitis service providers in 32 countries: 123 (94%) reported hepatitis services affected

■ Lack of Testing Access

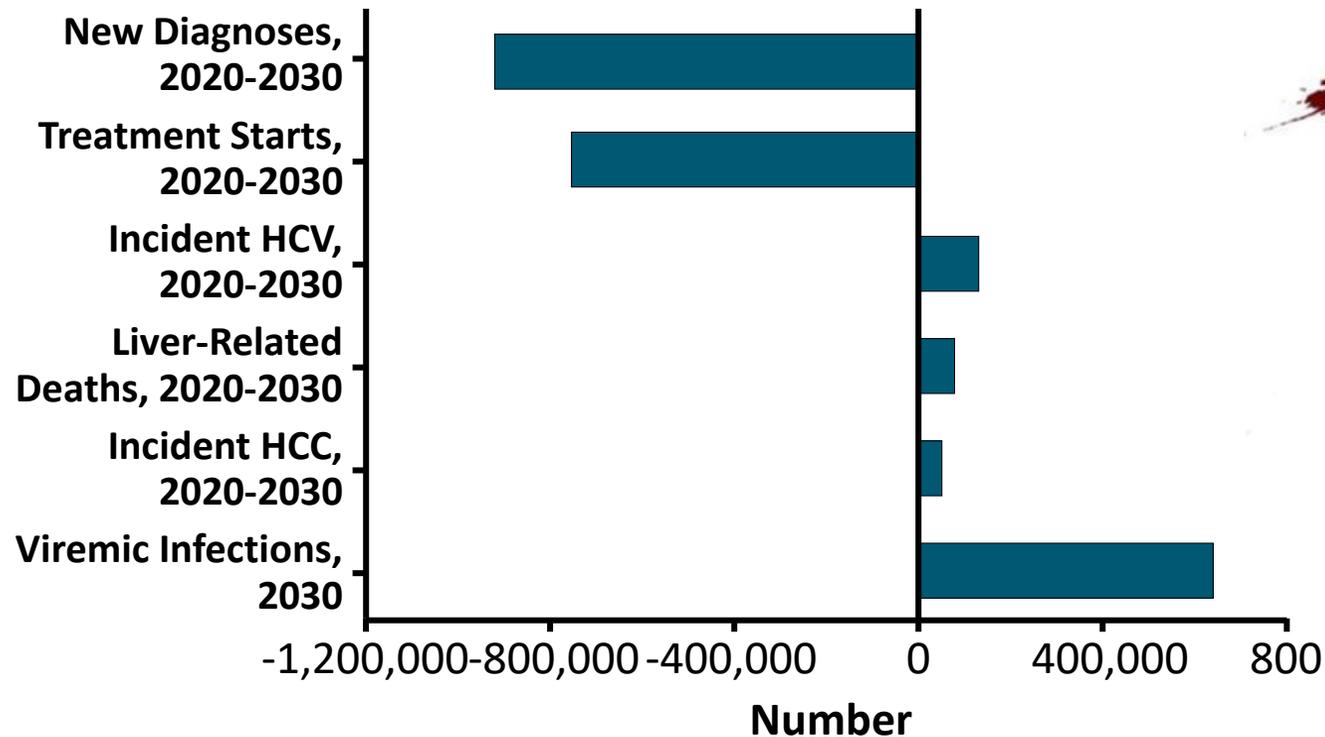
- 85/132 reported no access to viral hepatitis testing
- 46/101 reported that testing facilities had been closed
 - 16/54 respondents from outside US reported closure of facilities
- 66/101 reported that patients were avoiding testing facilities

■ Lack of Treatment Access

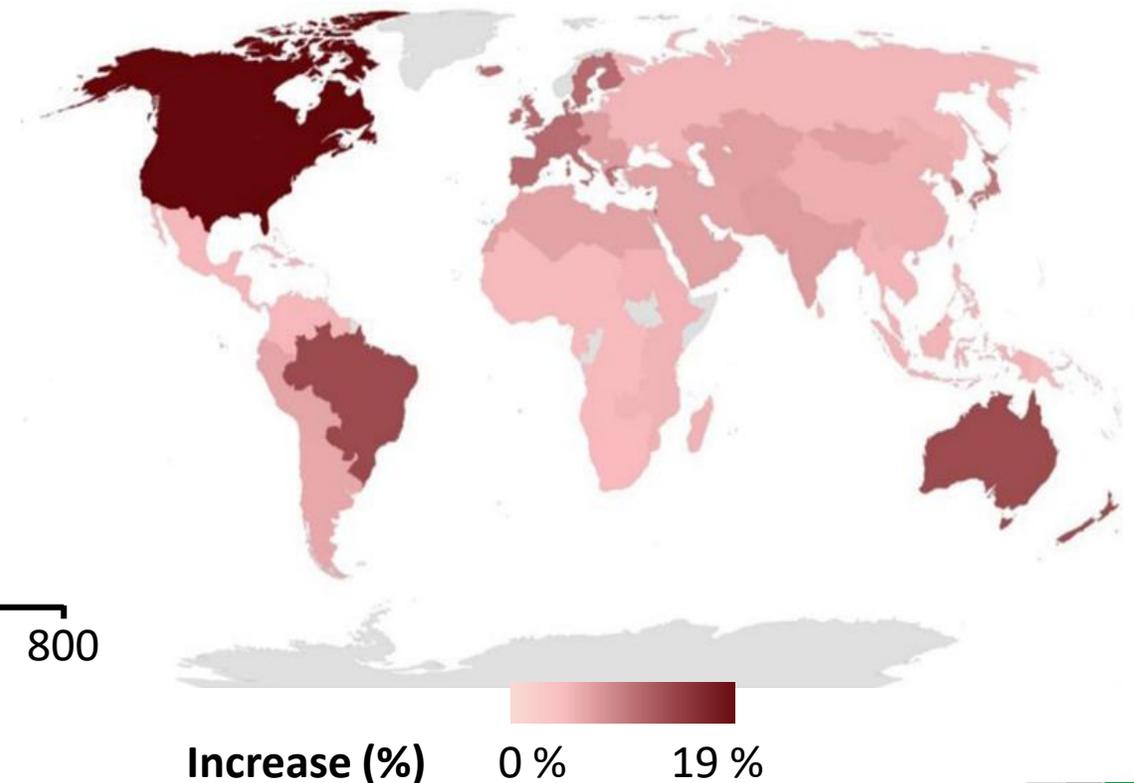
- 5/64 US respondents reported that patients were unable to access Rx
 - 23/68 respondents from outside US reported lack of access to Rx; more common in low-income countries
- 32/64 reported that patients were avoiding treatment clinics
 - 26/64 reported that COVID-19 prioritization contributed to decreased treatment access

Modelling the Global Impact of COVID-19 on Global Hepatitis C Elimination Efforts

Global Impact of 1-Yr Delay in HCV Programing
(Relative to Status Quo With No Delay)



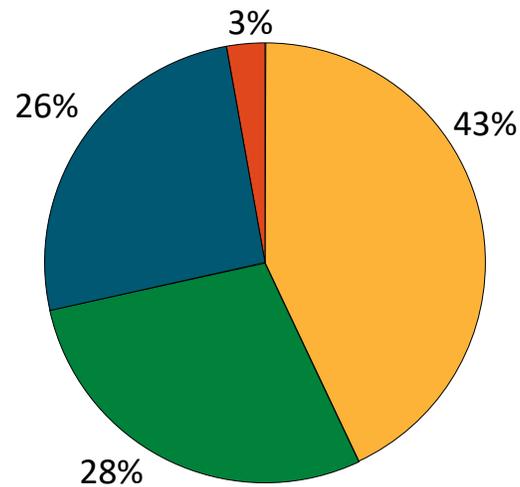
Impact of a 1-Yr Delay on Cumulative (2020-2030) Liver-Related Deaths, by Global Burden of Disease Region



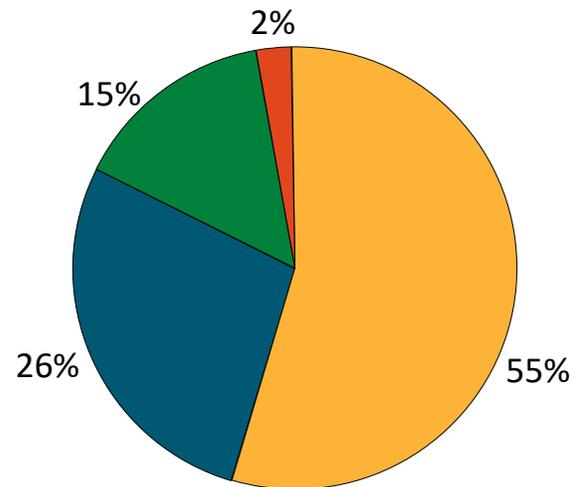
Modelling the Global Impact of COVID-19 on Global Hepatitis C Elimination Efforts

Proportion of Missed Treatments and Cumulative (2020-2030) Excess Incident HCV, HCC, and Liver-Related Deaths, by World Bank Income Group, 1-Yr Delay Scenario

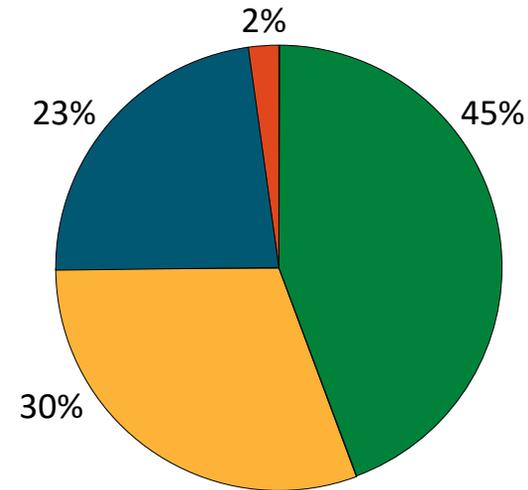
Missed Treatments, WB, 2020-2030



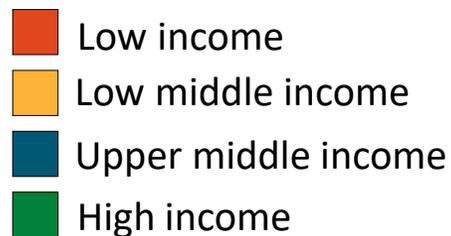
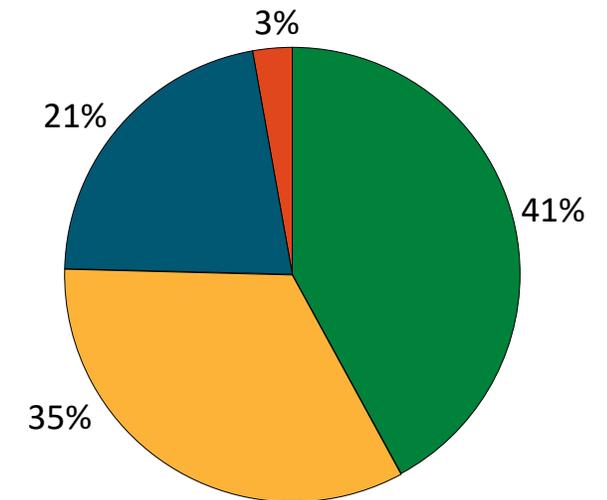
Excess Incident HCV, WB, 2020-2030



Excess HCC, WB, 2020-2030

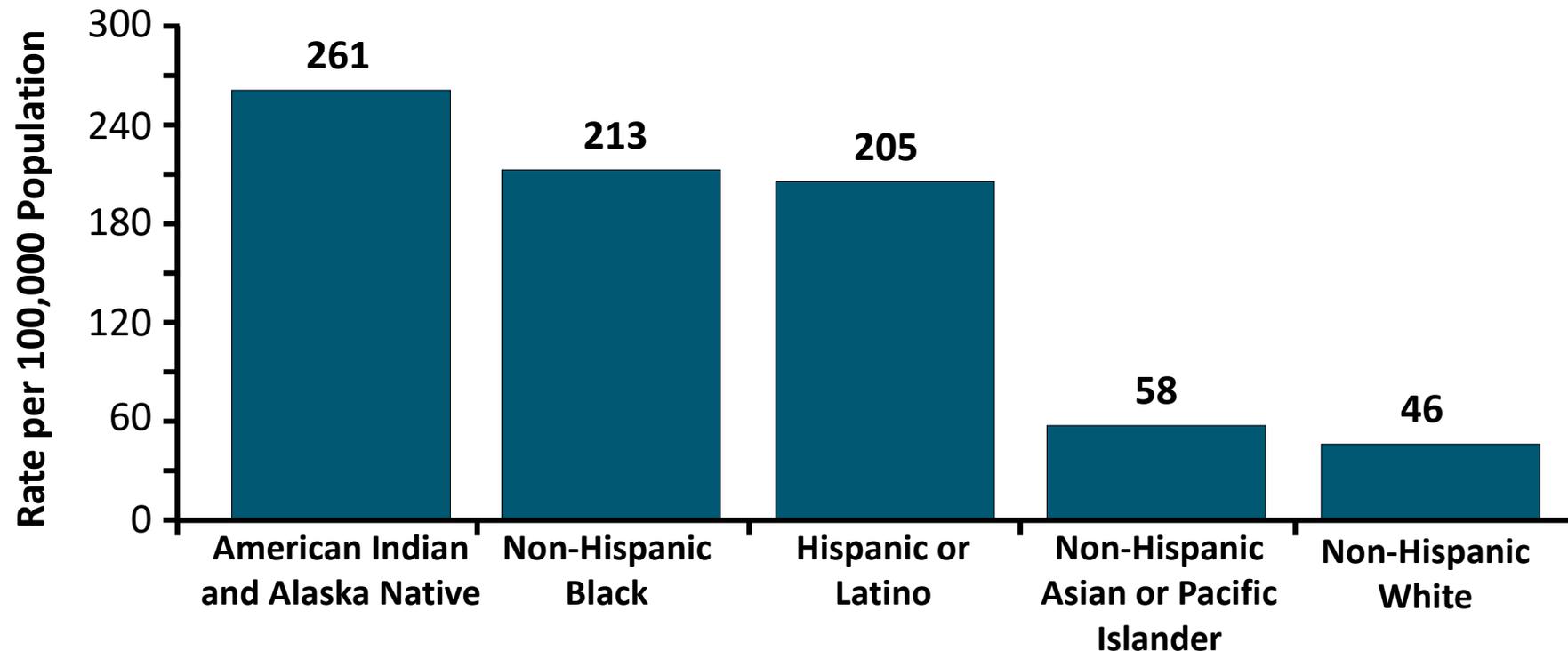


Excess LRDs, WB, 2020-2030



COVID-NET: COVID-19–Associated Hospitalization by Race and Ethnicity

Adjusted Rates of COVID-19–Associated Hospitalization*



*Data from March 1, 2020 - June 27, 2020, covers ~ 10% of US population: 99 counties in 14 states (CA, CO, CT, GA, IA, MD, MI, MN, NM, NY, OH, OR, TN, UT). Adjusted to account for differences in age distribution within race and ethnicity groups.

Racial Disparities in HCV Outcomes

Acute HCV Cases per 100,000 Population (2016)		
Non-Hispanic Black	Non-Hispanic White	Black/White Ratio
0.3	1.1	0.3
Reported HCV Cases 2013-2016, %		
Non-Hispanic Black	Non-Hispanic White	Black/White Ratio
7.7	36.4	0.2
HCV-Related Deaths (2016), Rate per 100,000		
Non-Hispanic Black	Non-Hispanic White	Non-Hispanic Black/Non-Hispanic White Ratio
7.42	3.97	1.9

COVID-19-Related Opportunities to Advance Hepatitis Elimination Goals

Testing and Contact Tracing

- Increase testing capacity in many countries
- Combine COVID-19 testing and care referral with testing for HCV and HBV
- Improve health equity: target populations with shared health risks and disparities in access
- Potentially decrease stigma and increase acceptability
- Hepatitis programs can deliver culturally competent testing and referral services for COVID-19 and HBV, HCV testing

Public Health Surveillance

- Increase awareness of importance among the public and providers
- Improved IT capacity
- Building staff with skills for data collection and analysis

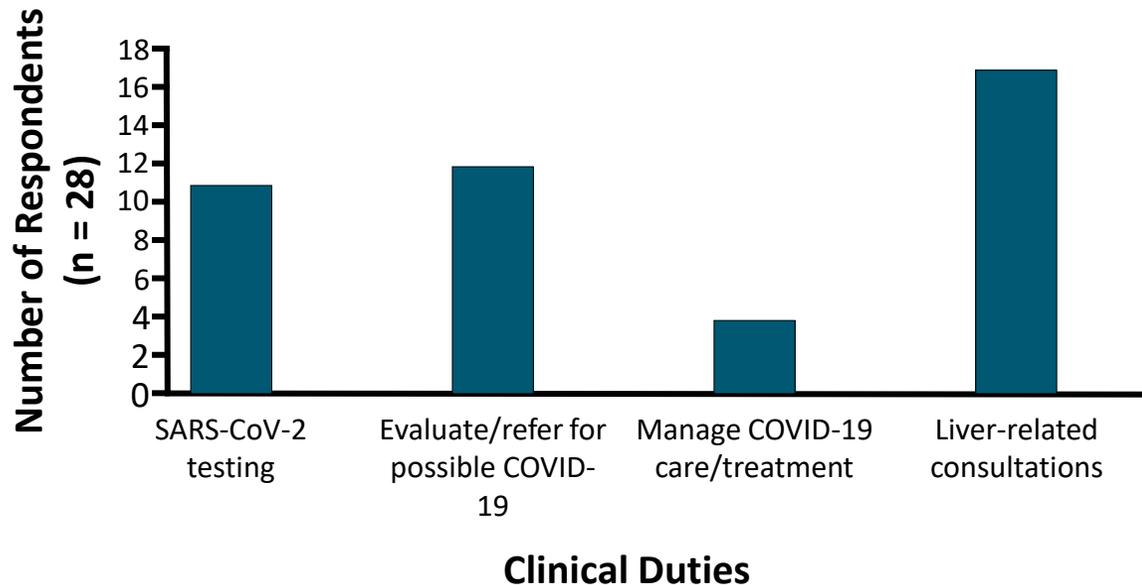
Service Delivery

- Increase awareness of benefits of infection detection and treatment; seize opportunity to eliminate an infectious disease
- Telehealth can increase access
- Diversify sources of care in clinical and community settings

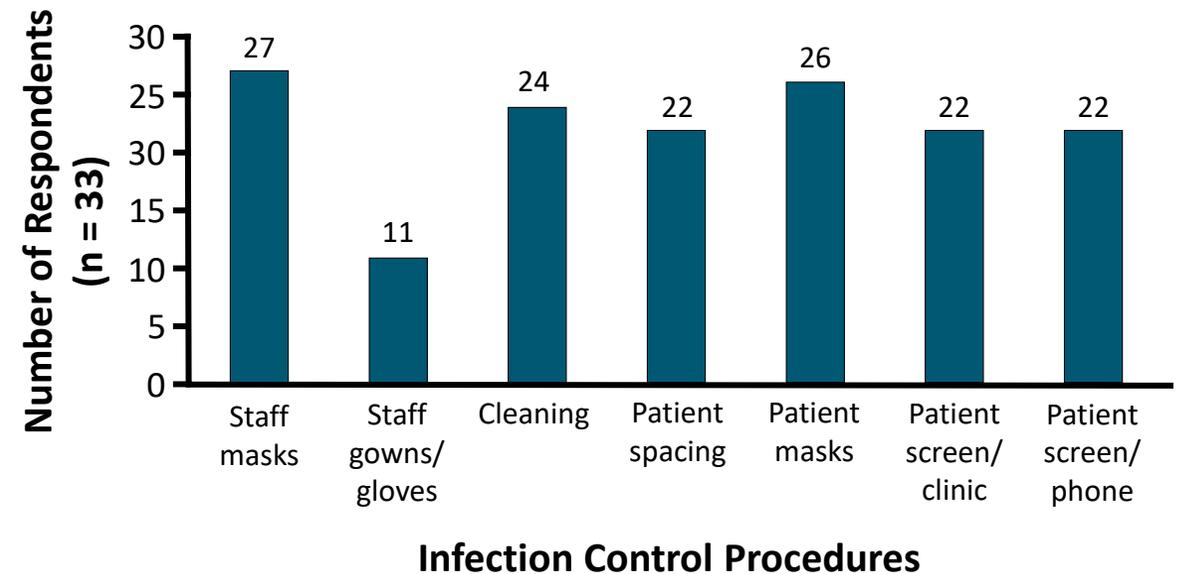
Task Force for Global Health: Global Survey of COVID-19 Impact on Hepatitis Services

- Preliminary data as of August 29, 2020: N = 33
 - 14/33 US participants; 24/33 physician specialists

Involvement in COVID-19 Response



Infection Control Procedures for Hepatitis Care

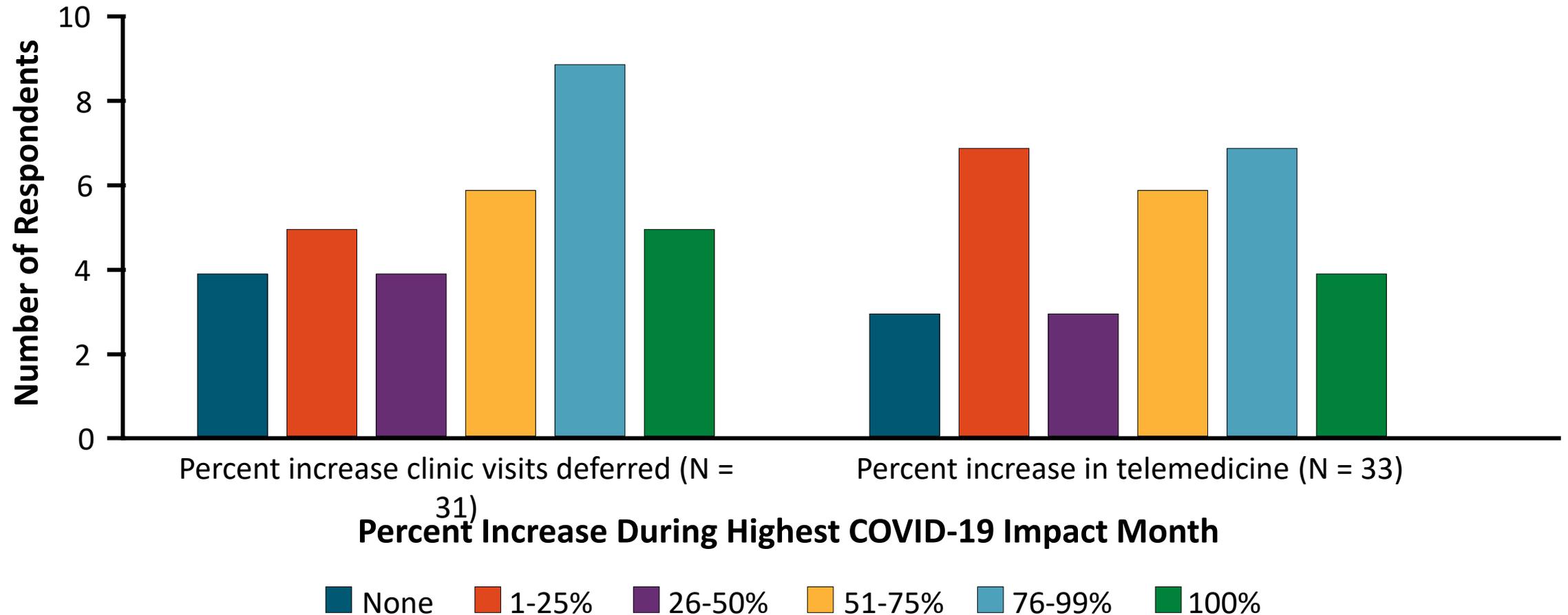


Task Force for Global Health: Global Survey of COVID-19 Impact on Hepatitis Services

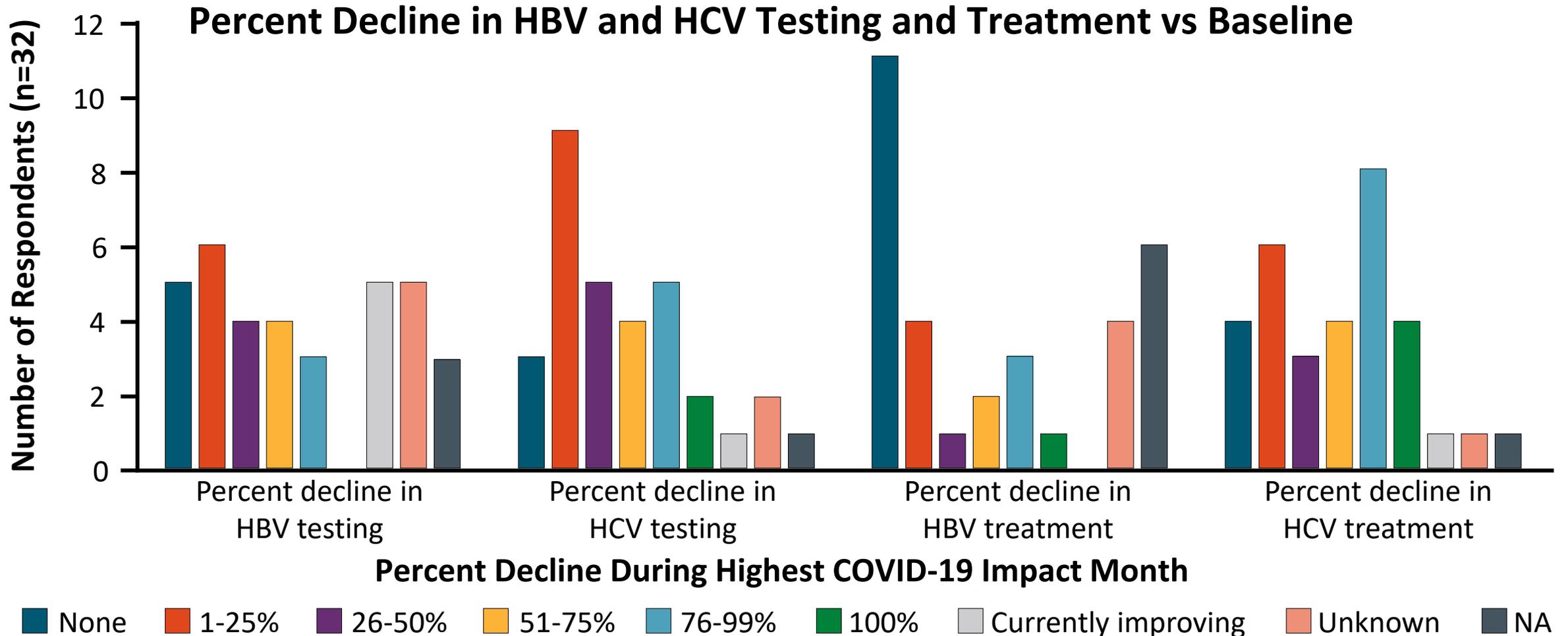
Changes in Hepatitis Clinical Services to Decrease SARS-CoV-2 Exposure, n (%)	Yes (n = 31)
Deferred laboratory testing	21 (64)
Deferred imagery	23 (70)
Increased pill count per prescription (multi-monthly refills)	22 (67)

Task Force for Global Health: Global Survey of COVID-19 Impact on Hepatitis Services

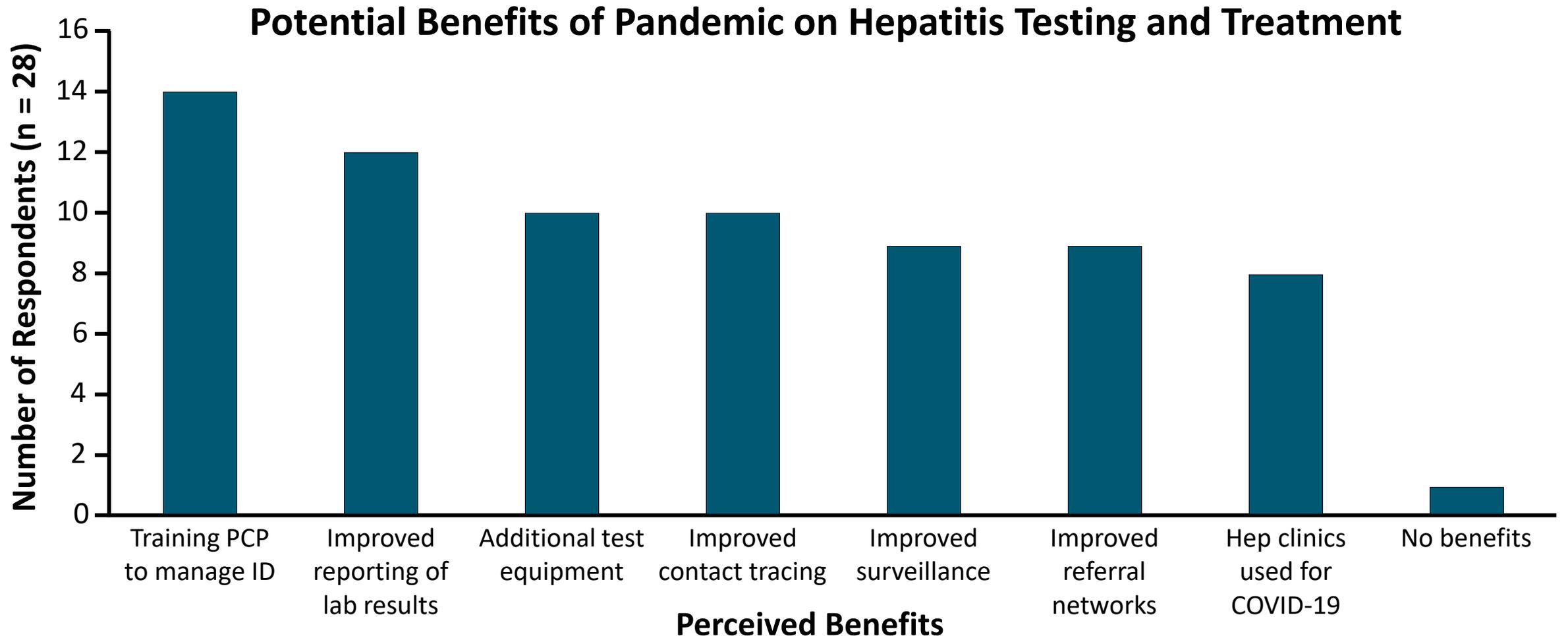
Percent Increase in Clinic Visits and Telemedicine vs Baseline



Task Force for Global Health: Global Survey of COVID-19 Impact on Hepatitis Services



Task Force for Global Health: Global Survey of COVID-19 Impact on Hepatitis Services



Global Survey Link

- Healthcare providers and hepatitis program managers who would like to participate in the CGHE Global Survey may access the survey here:
- English: <https://app.smartsheet.com/b/form/d487cee5adee40df8e5527e5a146469c>
- Spanish: <https://app.smartsheet.com/b/form/e8ba7ad661c64f6c9146cbcbe242ec16>
- French: <https://app.smartsheet.com/b/form/9fdff1e0e35949c8ba586aadd23973fa>
- To receive final survey results, follow CGHE on Twitter @globalhep



Go Online for More CCO Coverage of HCV Management!

Additional live webinars presented by expert faculty on increasing access to HCV care for key populations and simplifying the HCV care continuum

Downloadable slidesets with key data and considerations for streamlining HCV treatment and improving access to care during the COVID-19 pandemic



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