Hepatitis C in the Post-DAA Era: Challenges, Innovations, and the Path Toward Elimination

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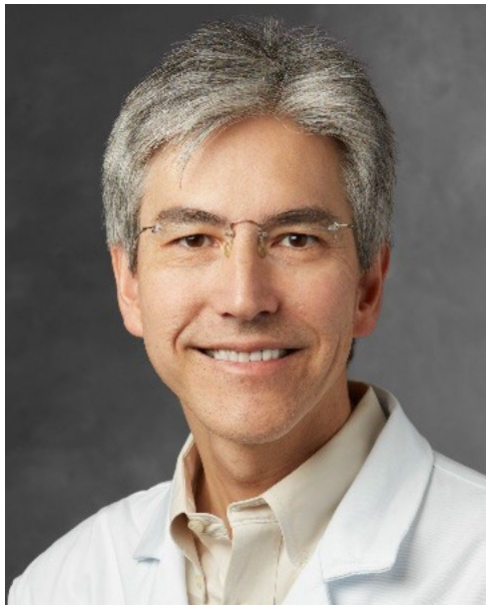


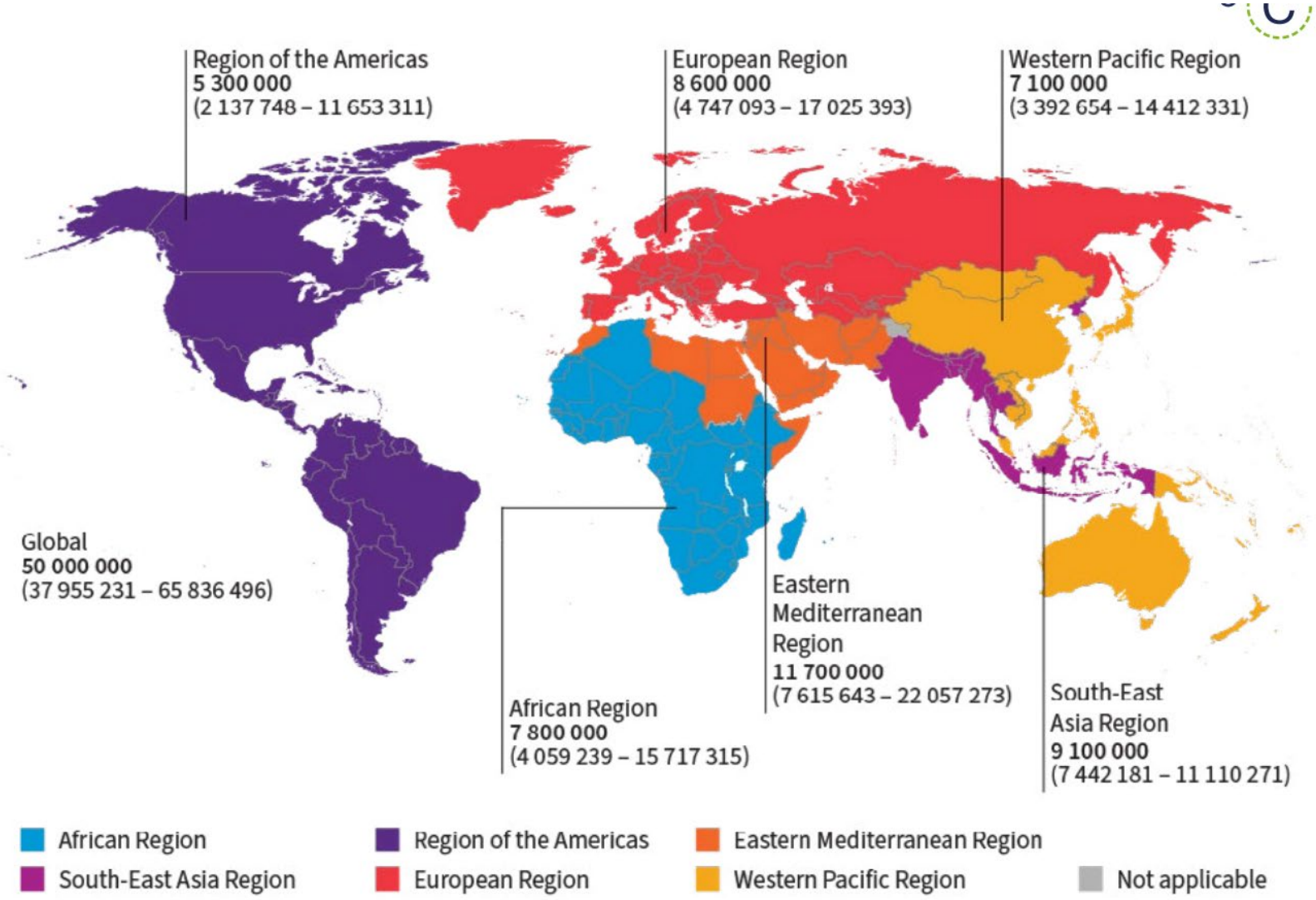
Disclosures

- *Abbvie: Consultant; Aligos: Advisory Board; Altimmune: Research Grant; Amgen: Advisory Board Arbutus: Advisory Board ; Ausper Bio: Grant Support; Durect: Consultant, Stockholder; Galapagos: Advisory Board : Genentech: Consultant; Gilead: Advisory Board, Research Grant; HepQuant: Consultant; Inventiva: Consultant, Research Grant; LyGenesis; Consultant Madrigal: Grant Support ; Mallinckrodt: Advisory Board; Mirum: Consultant; Novo Nordisk: Advisory Board, Research Grant; Ocelot: Advisory Board; PB Gene: Consultant; Salix: Grant Support; Surrozen: Advisory Board; Takeda: Grant Support; Target Registries: Research Grant; Tune Therapeutics: Consultant; Ultragenyx: Research Grant*

Case Presentation

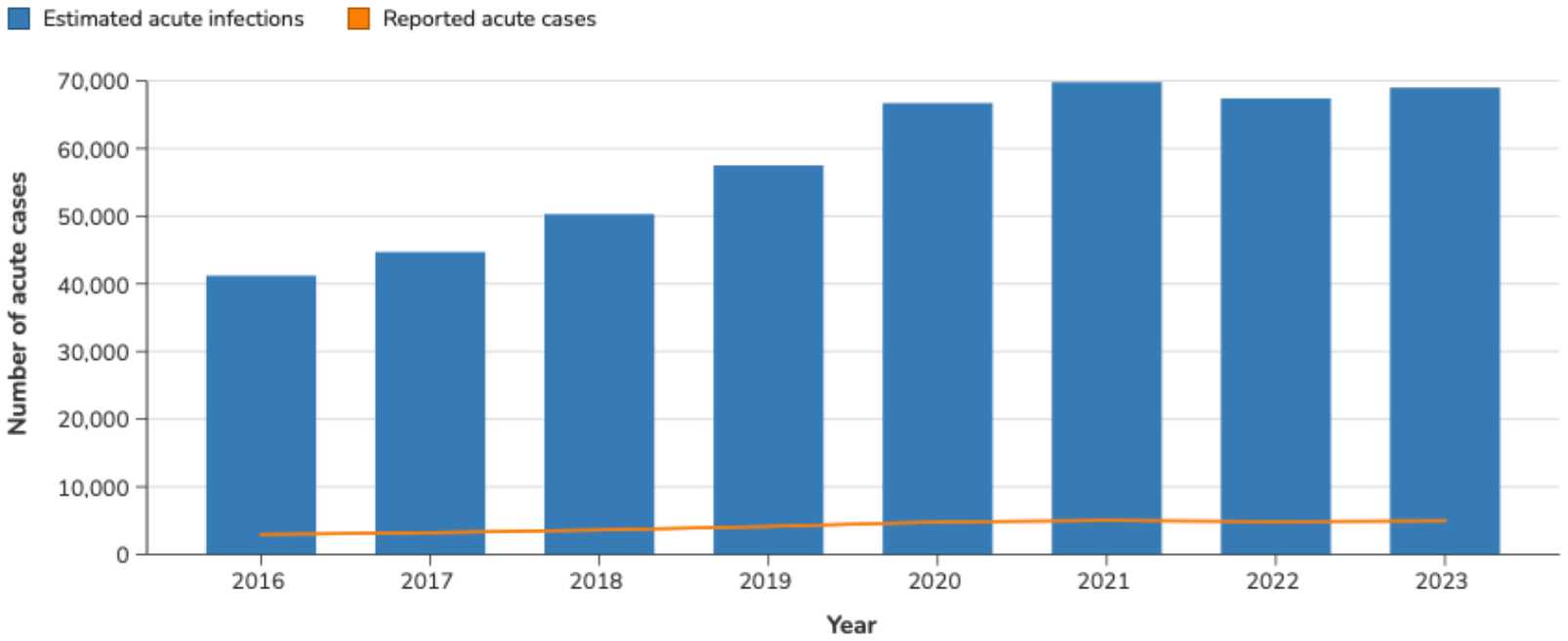
- 32 year old male with hx of injection drug use presents to your clinic for abnormal liver tests and a positive anti-HCV Ab
- Recently discharged from hospital after overdose
- Now on buprenorphine, is living with his parents
- Exam is normal
- WBC 4, Hgb 15 g/dl, Plts 280K, AST 35 IU/L, ALT 51 IU/L, INR 1, TB 0.3 mg/dl
- Anti-HCV+
- What are next steps?

Prevalent cases of chronic hepatitis C by WHO region, 2022



WHO Global hepatitis report 2024

Number of reported cases* and estimated infections† of acute hepatitis C — United States, 2016–2023

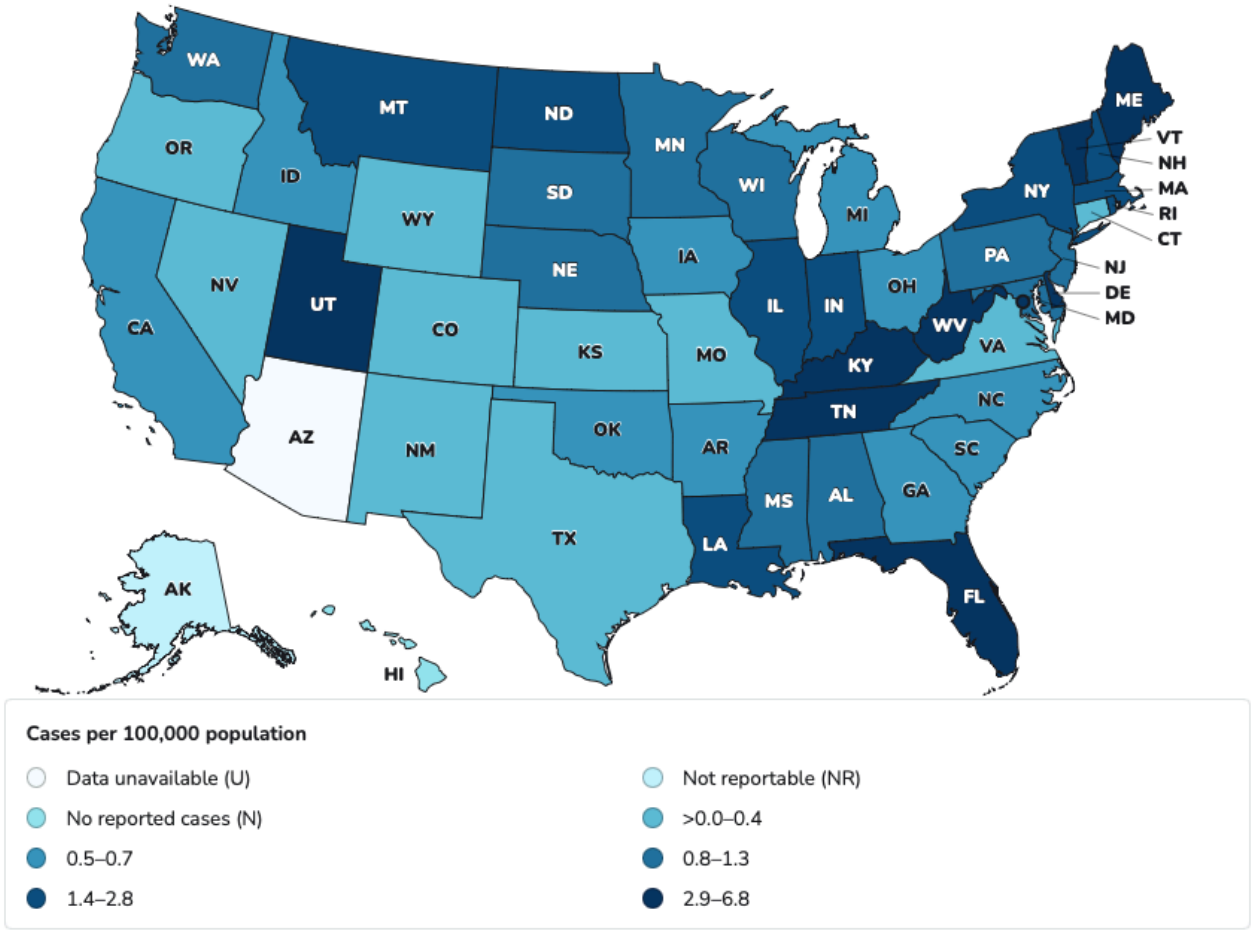


Data Table

	2016	2017	2018	2019	2020	2021	2022	2023
Estimated acute infections	41,200	44,700	50,300	57,500	66,700	69,800	67,400	69,000
Reported acute cases	2,967	3,216	3,621	4,136	4,798	5,023	4,848	4,966

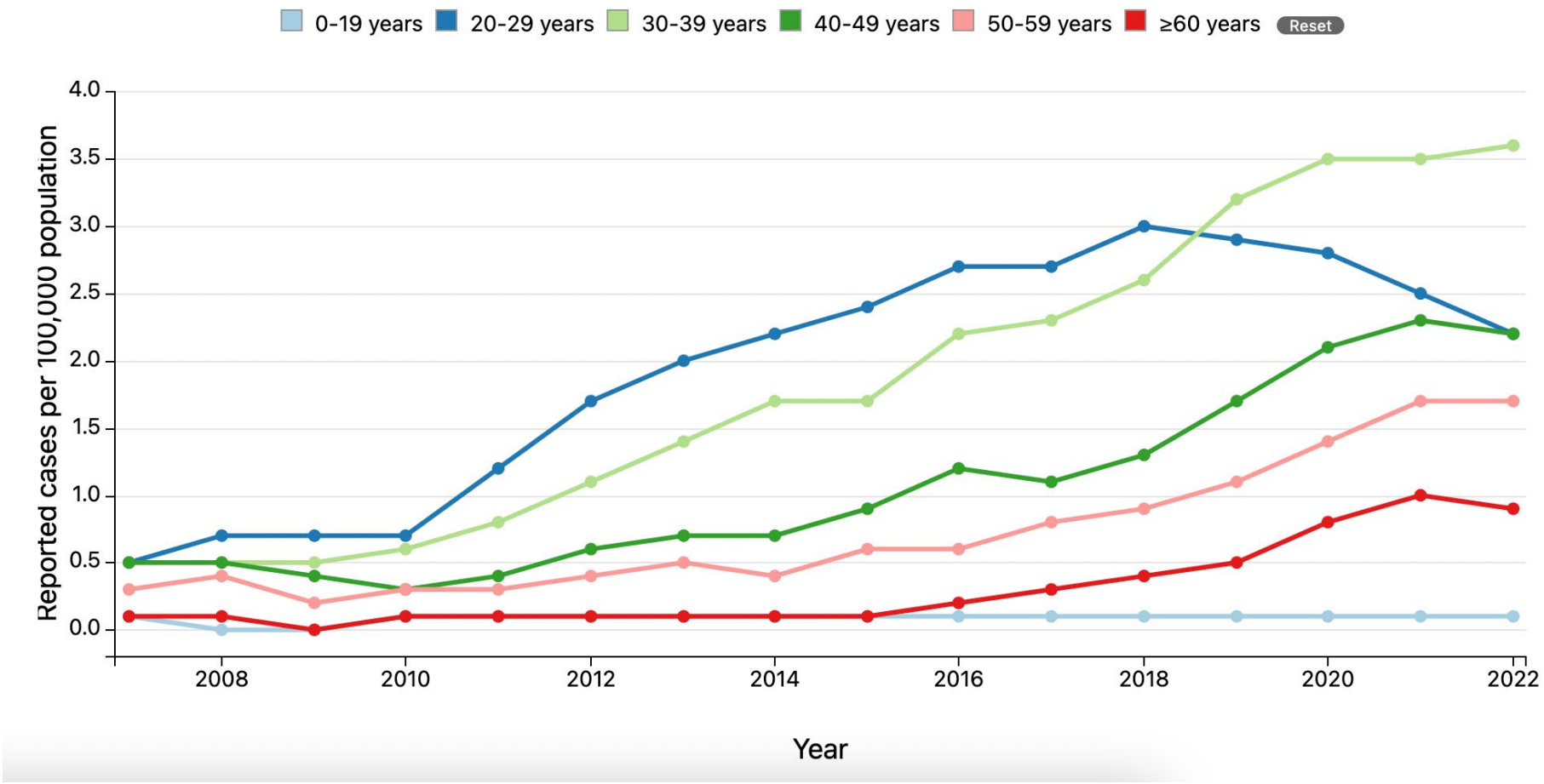
https://www.cdc.gov/hepatitis-surveillance-2023/hepatitis-c/figure-3-1.html

Rates* of reported cases† of acute hepatitis C, by state or jurisdiction — United States, 2023



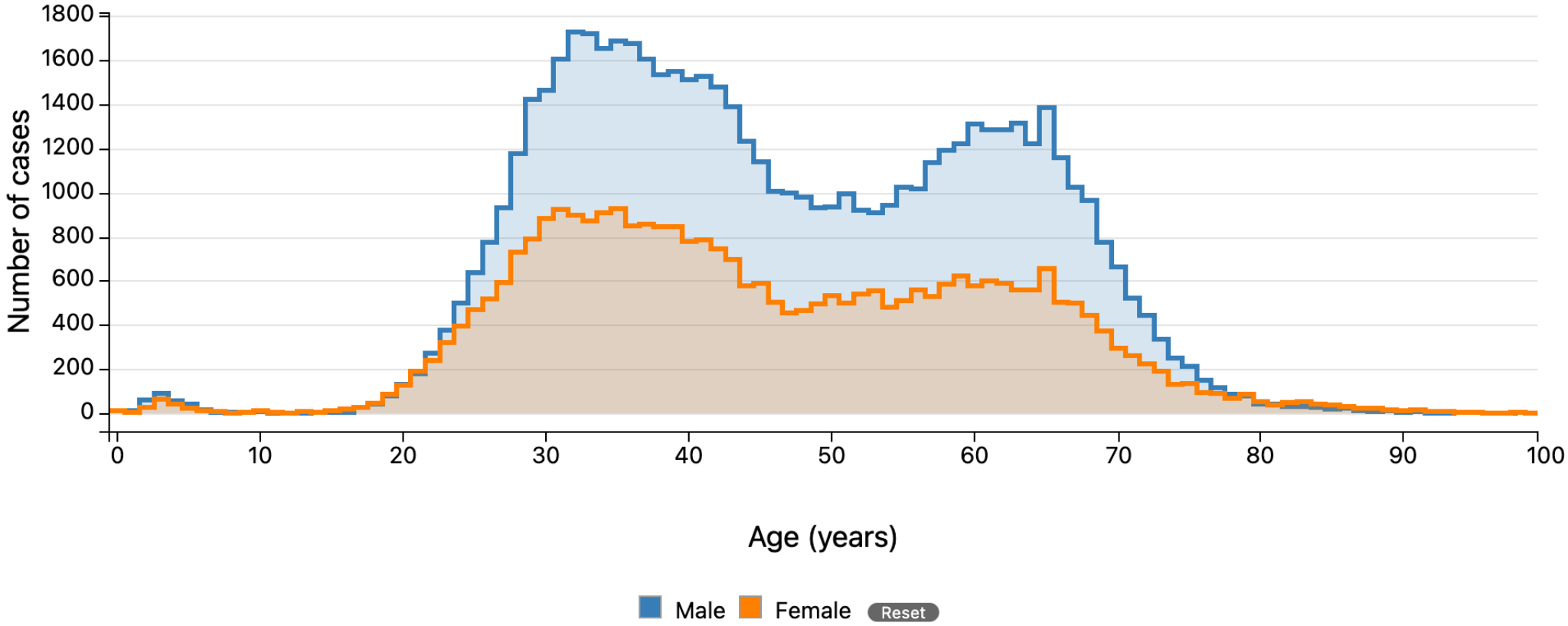
https://www.cdc.gov/hepatitis-surveillance-2023/hepatitis-c/figure-3-3.html

Rates* of reported cases† of acute hepatitis C, by age group — United States, 2007–2022



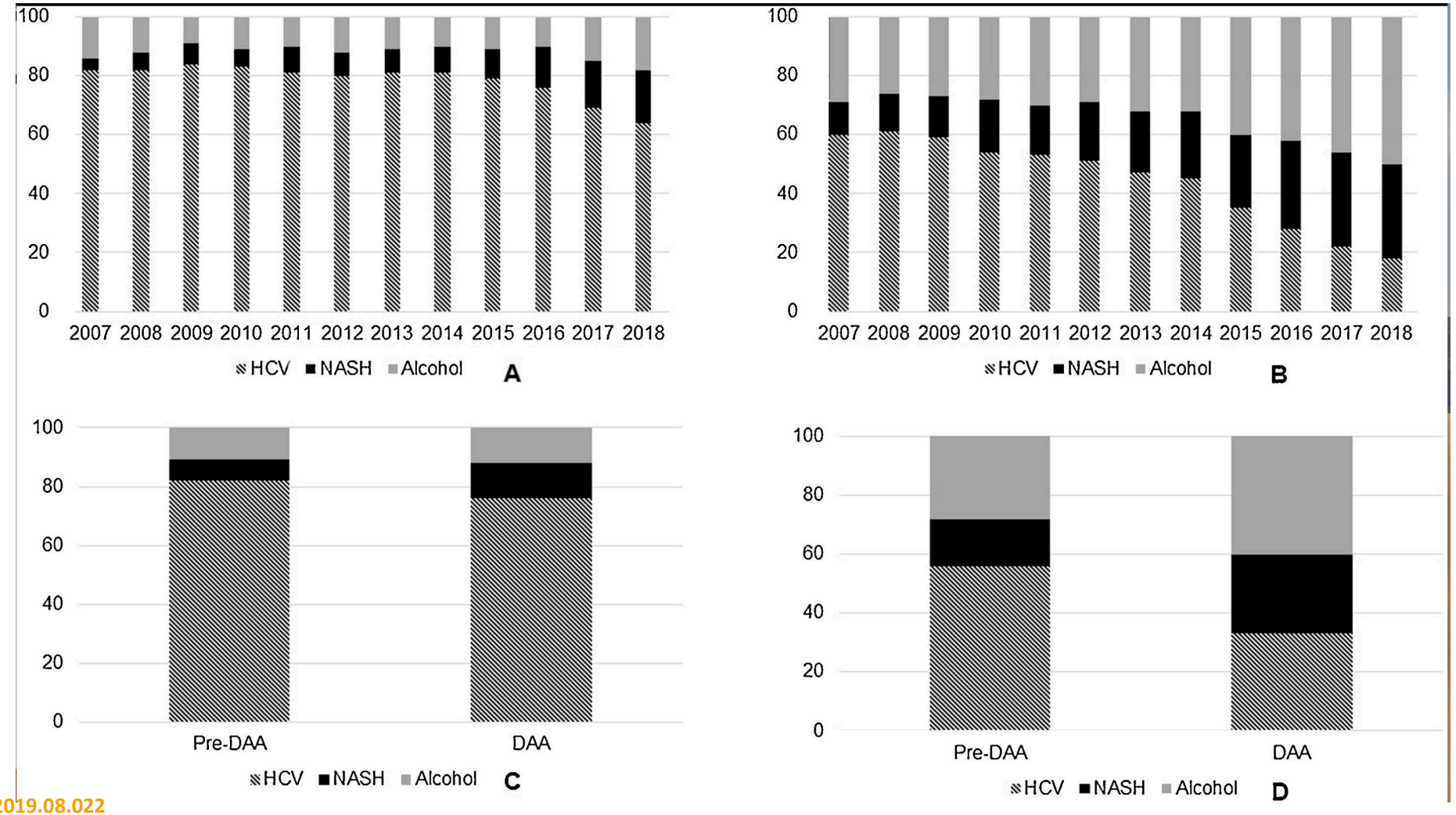
https://www.cdc.gov/hepatitis/statistics/2022surveillance/hepatitis-c/figure-3.4.htm

Number of newly reported* chronic hepatitis C cases† by sex and age — United States, 2022



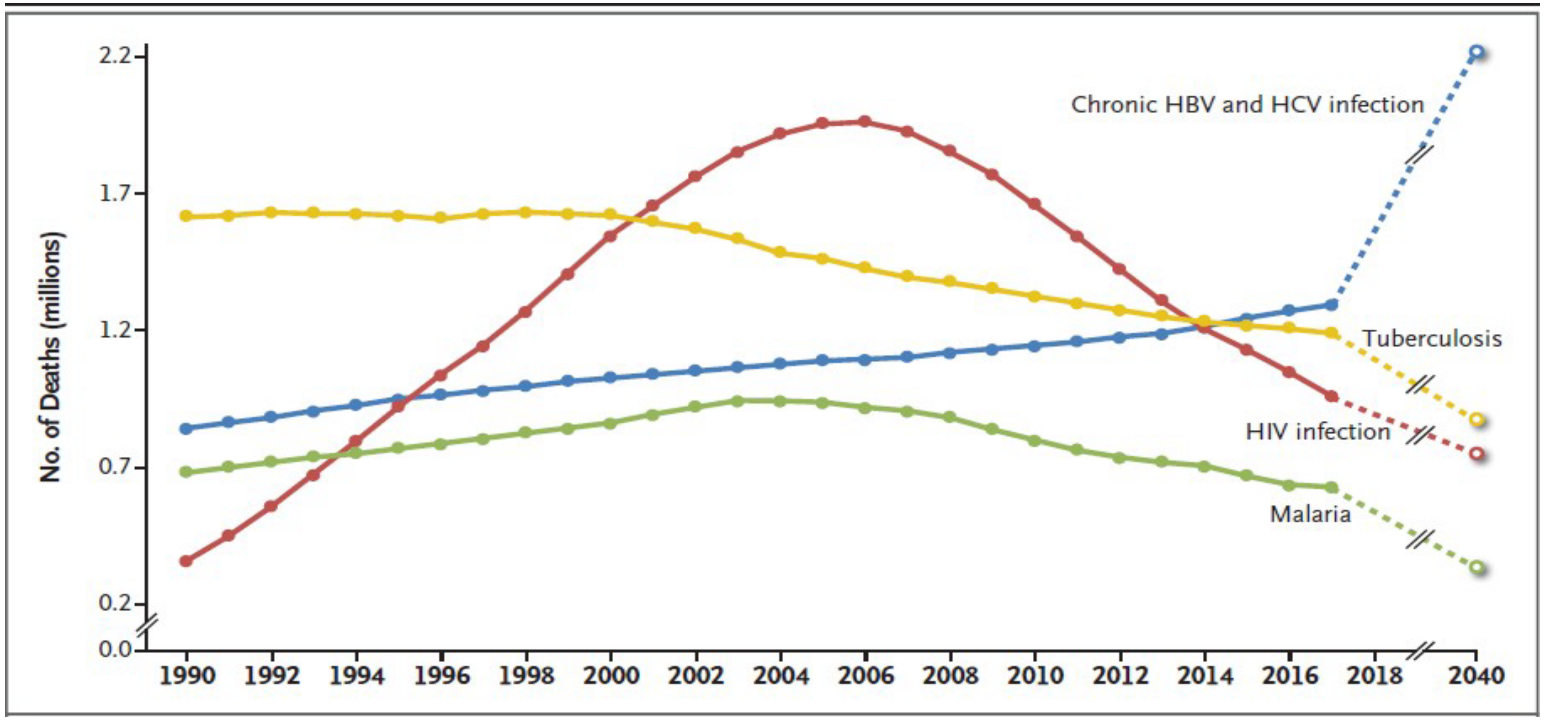
https://www.cdc.gov/hepatitis/statistics/2022surveillance/hepatitis-c/figure-3.8.htm

Transplants for HCV/HCC remain common though HCV-related cirrhosis transplant have dramatically declined



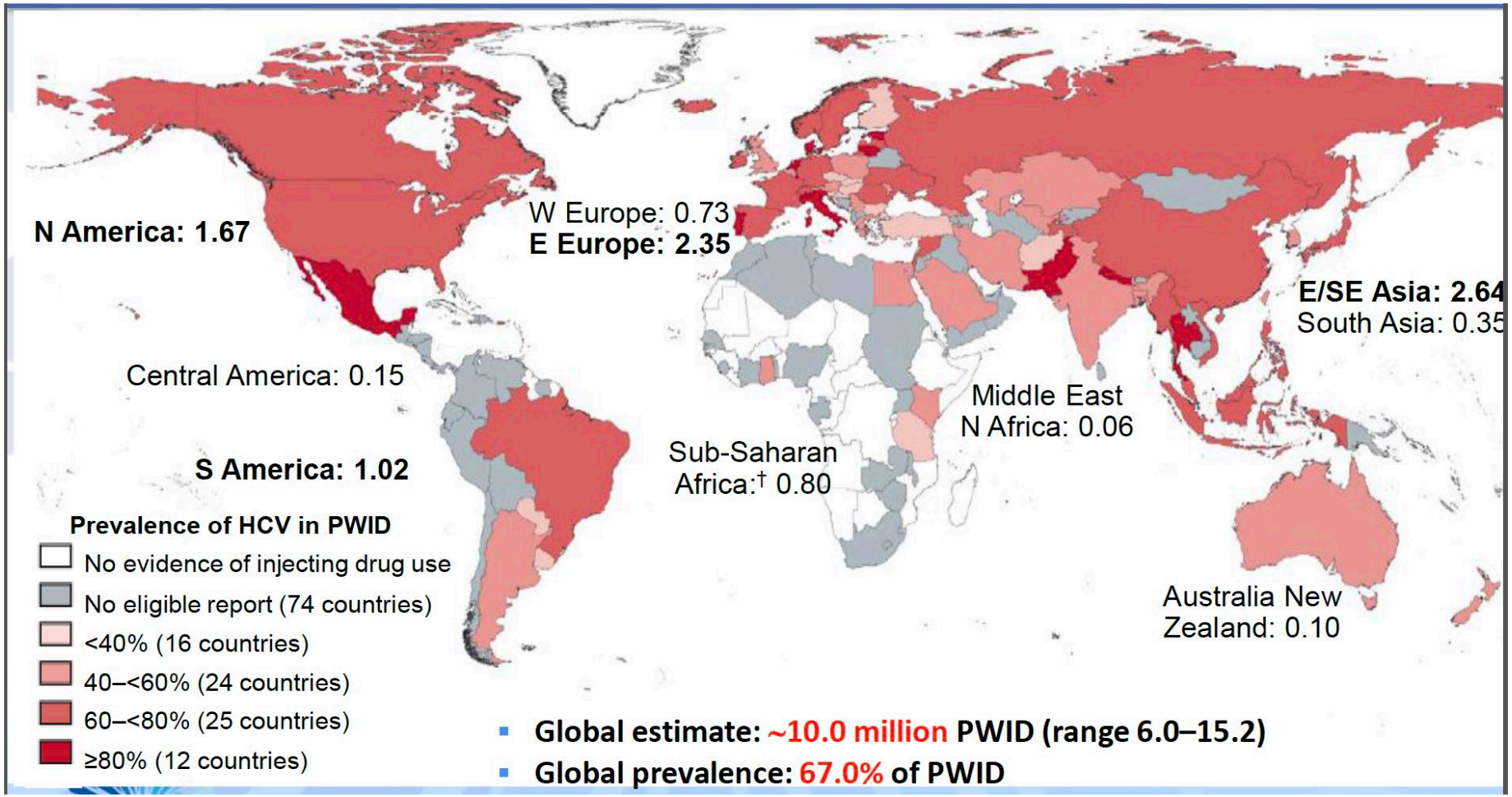
•https://doi.org/10.1016/j.dld.2019.08.022

Worldwide Deaths From Chronic Viral Hepatitis as Compared with Deaths from Tuberculosis, HIV, and Malaria



Data on deaths from 1990 to 2017 are from the Institute for Health Metrics and Evaluation as of November 14, 2018.Thomas D. *N Engl J Med*. 2019

Estimated HCV Prevalence in PWID Worldwide (millions)



Grebely J, Dore GJ. Antiviral Res 2014;104:62-72.

Injection Drug Use Is the Most Important Risk Factor for HCV Infection[1-7]

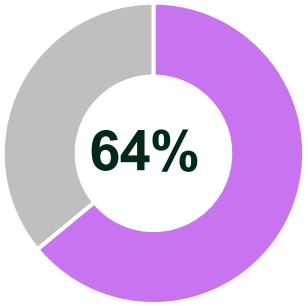
Young PWUD with propensity to share needles and preparation equipment

HCV often acquired shortly after individuals begin injecting

HCV can survive on cookers and cotton filters for days, and longer in needle barrel

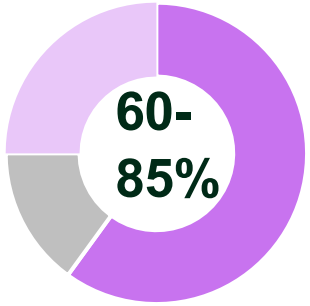
HCV is transmitted at a tenfold rate relative to HIV

HCV is prevalent in 60-80% or more in people with IDU



of PWUDs in the United States are chronically infected

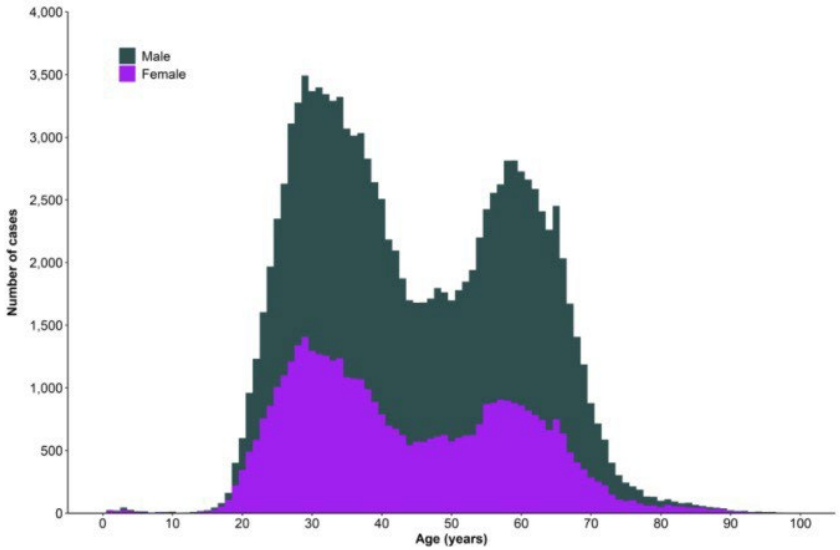
PWUD make up between 60% and 85% of all new HCV infections in USA



1. https://www.hhs.gov/sites/default/files/viral-hepatitis-action-plan.pdf; 2. https://hepfree.nyc/wp-content/uploads/2017/08/hcv-and-young-pwid-consultation-report.pdf;
3. Paintsil E, et al. *J Infect Dis.* 2010;202:984-90; 4. Doerrbecker J, et al. *J Infect Dis*. 2013;207:281-7; 5. Clausen LN, et al. *World J Gastroenterol*.2014;20:12132-43.
6. Nelson PK, et al. *Lancet*. 2011;378:571-83. 7. Lourenço L, et al. *Can Commun Dis Rep*. 2021;47(12):561-70.

HCV and Women of Child-Bearing Age (WOCBA)

•Number of newly reported chronic HCV infection cases, by sex and age — US, 2019[1]



•Changing HCV Prevalence Among Pregnant Women[2]

- During 2000–2019, prevalence of HCV diagnosed during pregnancy increased 10 fold from .05% in 2000 to .49% in 2019

Meta-analysis of 17 studies looked at HCV vertical transmission risk in women with chronic HCV: risk was 5.8% in HIV-negative women; risk doubled to 10.8% in HIV-positive women[3]

•1. https://www.cdc.gov/hepatitis/statistics/2019surveillance/Figure3.8.htm. 2. *Arditi et al* ***Deliveries Among Patients With Maternal Hepatitis C*** *OBSTETRICS & GYNECOLOGY* ***VOL. 141, NO. 4, APRIL 2023***

•3. Society for Maternal-Fetal Medicine (SMFM). *Am J Obstet Gynecol*. 2017;217(5):B2-B12.

The Effect of COVID-19 on HCV[1-3]

30% Increase in drug overdose deaths between December 2019 and December 2020; United States eclipsed 100,000 in November 2021

73% Reduction in HCV screening/testing reported by local health departments[a]

22% Decrease in HCV treatment occurred from 2019 to 2020[b]

[a] Represents percentage of local health departments offering the service. [b] Data do not include Department of Corrections and Veterans Affairs

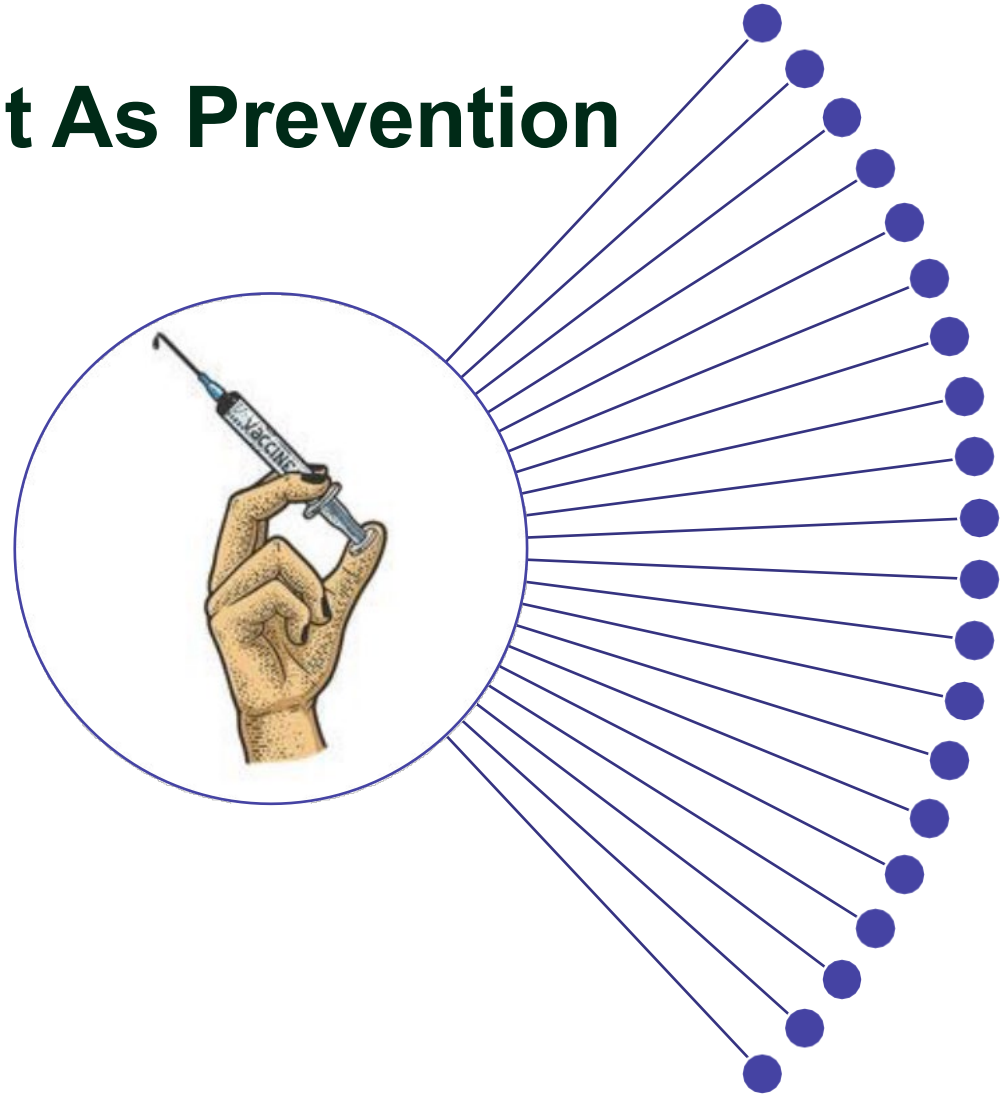
1. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. 2. https://hepvu.org/state-of-viral-hepatitis-during-covid-19/.

3. IMS Monthly Data (Week of January 4, 2019 through January 1, 2021).

Treatment As Prevention

Left untreated,

one active injector potentially will infect up to 20 others with HCV within the first 3 years of diagnosis[1,2]



•1. NIH National Institute on Drug Abuse. Heroin Research Report. Updated June 2021. Accessed November 2, 2021. https://www.drugabuse.gov/download/37596/heroin-research-report.pdf 2. NIH National Institute on Drug Abuse. Viral Hepatitis—A Very Real Consequence of Substance Use. Updated August 3, 2020. Accessed November 9, 2021. https://www.drugabuse.gov/drug-topics/viral-hepatitis-very- real-consequence-substance-use

Global Call for HCV Elimination

- **WHO**
  hepat
  health

203
90%
80%
65%

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people
identify

•1. WHO. Global Health S
elimination of hepatitis B
2019;114:150.

Eradication versus elimination

- Eradication
  - Permanent reduction to zero worldwide incidence
  - Intervention measures no longer required
  - Ex: Smallpox
- Elimination
  - Reduction to zero incidence of an infection in a certain geographical area
  - Intervention measures are required
  - Ex: Poliomyelitis

•Most infections that have been eradicated/eliminated have been as a result of effective vaccines

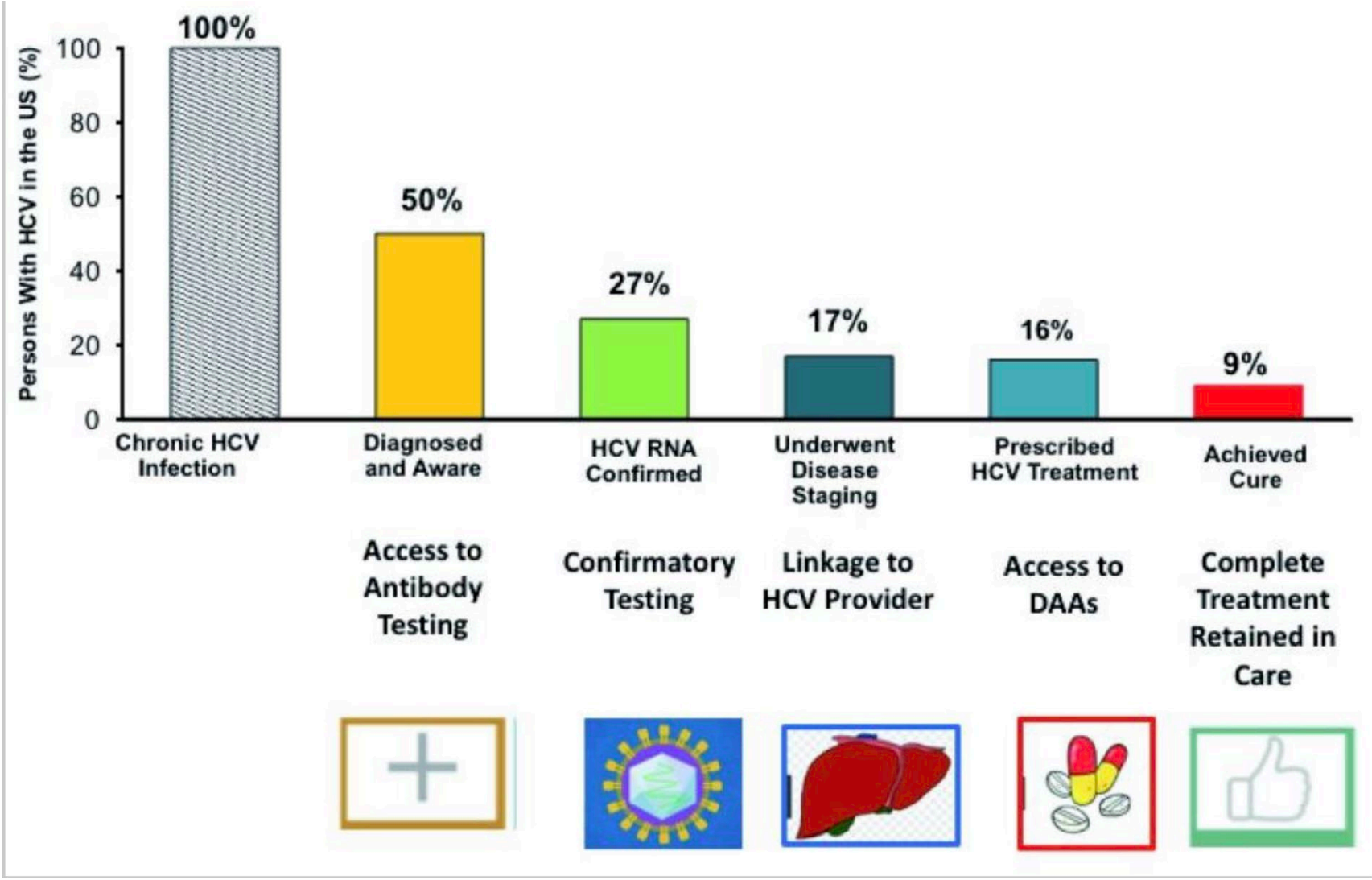
•Exception is onchocerciasis (river blindness)

•Over one hundred million individuals treated

•Eliminated in many countries with ivermectin

•Despite effective hepatitis B vaccine, we have not been able to eliminate hepatitis B

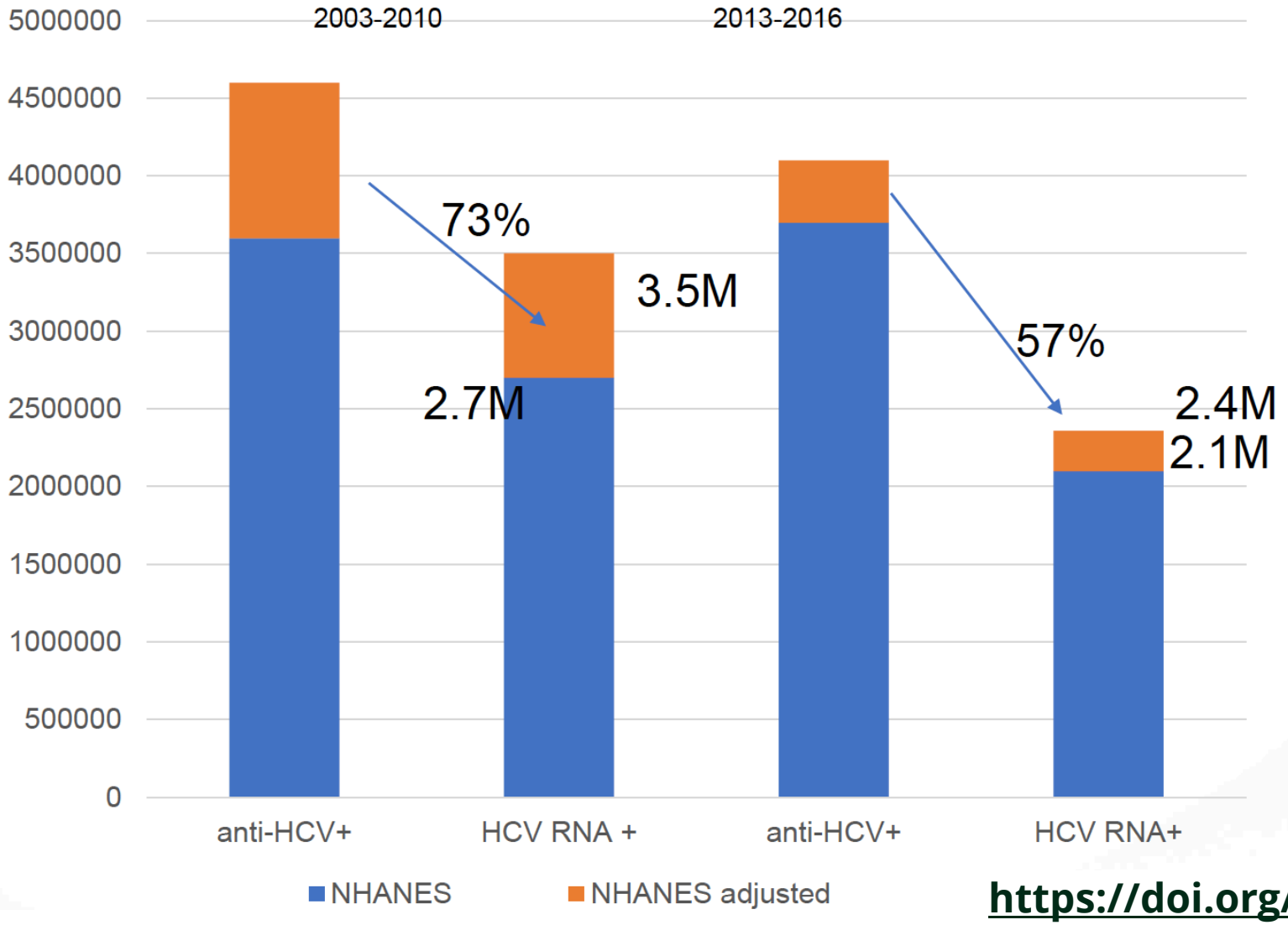
Under-diagnosis: the largest gap in the cascade of care



Terrault NA. Hepatitis C elimination: challenges with under-diagnosis and under-treatment [version 1; peer review: 2 approved]. *F1000Research* 2019, **8**(F1000 Faculty Rev):54 (https://doi.org/10.12688/f1000research.15892.1)

Decline in HCV Prevalence

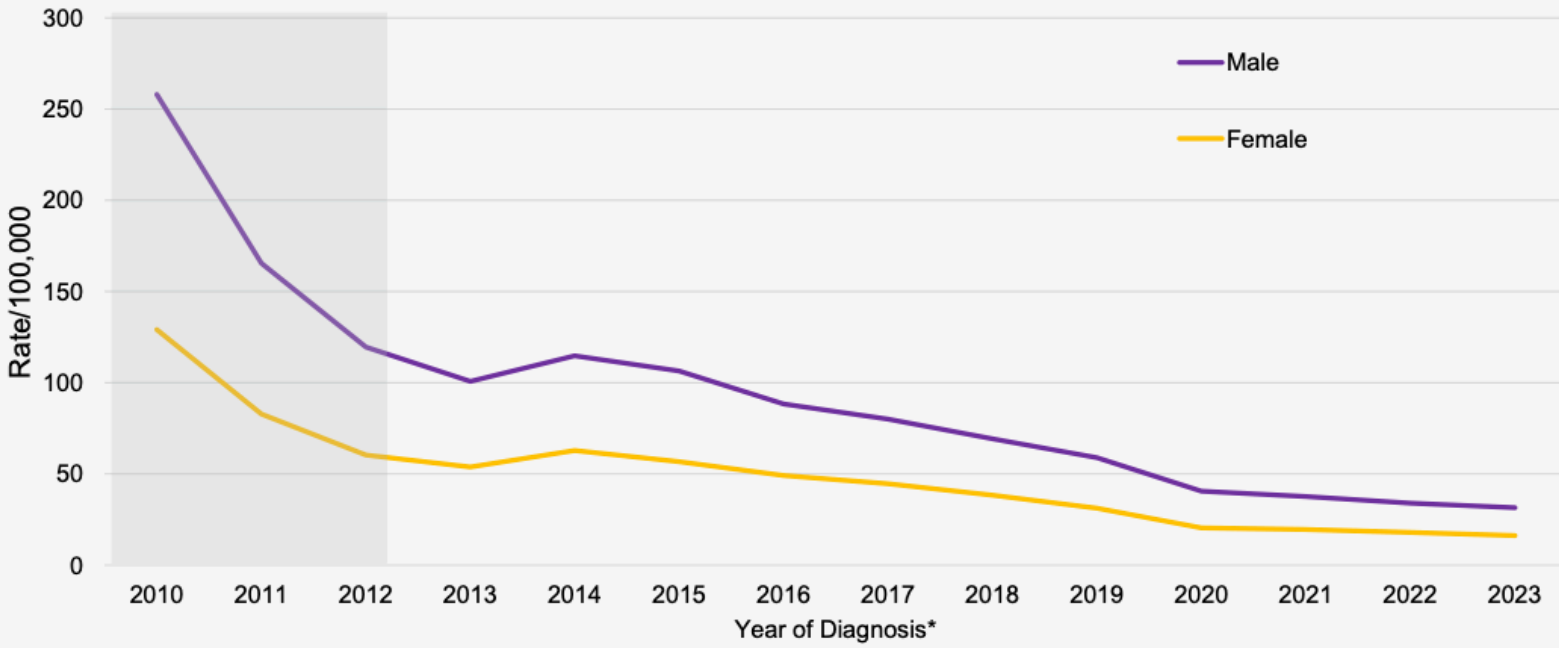
2.4 million HCV infected persons



Reduction HCV RNA+ in those who are anti-HCV+

https://doi.org/10.1002/hep.30297

Rate of Hepatitis C Diagnoses by Sex, New York State: 2010-2023



*Based on earliest positive hepatitis C RNA or genotype test reported from 2010 - 2023. Some individuals, especially those appearing here in 2010-2011, may have been first diagnosed prior to 2010, resulting in the inflation of rates for these years.

NEW YORK STATE | Department of Health

USPS Task Force: Hepatitis C Virus Infection in Adolescents and Adults: Screening

CDC has also released broadened screening recommendations

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

To read the recommendation statement in *JAMA*, select here.

To read the evidence summary in JAMA, select here.

See the Clinician Summary for a more detailed summary of the recommendation for clinicians.

https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/hepatitis-c-screening1

2020 CDC Recommendations for HCV Screening Among Adults in the United States[1]

Universal screening

Screen at least once in a lifetime for all adults ≥18 years (except in settings where HCV RNA-positivity is<0.1%)

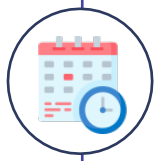
Pregnancy

Screen all pregnant women during each pregnancy (except in setting where HCV RNA-positivity is <0.1%)

Exposure

One-time testing among people with recognized conditions or exposures, regardless of age or setting prevalence)

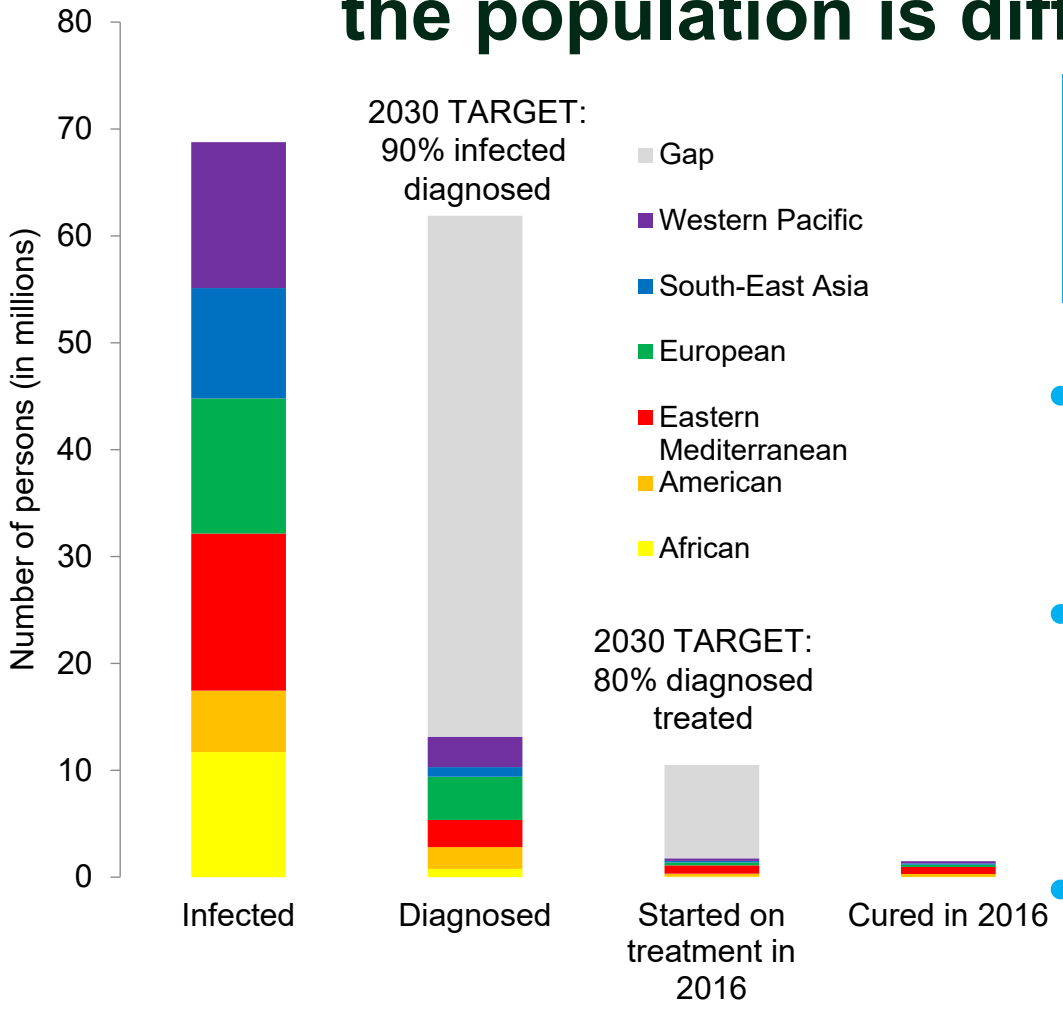
Periodic testing



Routine periodic testing for people with ongoing risk factors

1. Schillie S, et al. *MMWR Recomm Rep*. 2020;69:1-17.

Access to DAAs has increased but a large gap persists: Curing the individual is easy, curing the population is difficult



Cascade of care for HCV infection, by WHO region, 2016

- 1.76 million persons started HCV treatment in 2016 (1.1 million in 2015)
- The proportion of persons starting a new treatment increased from 7% in 2015 to 13% in 2016
- Many infected persons (80%) remain undiagnosed

•**Source: WHO on the basis of Center for Disease Analysis / Polaris**

All First Line Treatment Options Lead to Sustained response rates ≥ 95%

HCV genotype	No Cirrhosis		Compensated Cirrhosis	
1	SOF/VEL GLE/PIB LDV/SOF EBR/GZR*	12 W 8 W 8 or 12 W 12 W	SOF/VEL GLE/PIB LDV/SOF EBR/GZR*	12 W 8 W 12 W 12 W
2/3	GLE/PIB SOF/VEL	8 W 12 W	GLE/PIB SOF/VEL**	8 W 12 W
4	EBR/GZR GLE/PIB LDV/SOF SOF/VEL	12 W 8 W 12 W 12 W	EBR/GZR GLE/PIB LDV/SOF SOF/VE	12 W 8 W 12 W 12 W
5/6	GLE/PIB LDV/SOF SOF/VEL	8 W 12 W 12 W	GLE/PIB LDV/SOF SOF/VEL	8 W 12 W 12 W

GLE/PIB SOF/VEL are pan-genotypic options

*** Alternative therapy for GT1a No NS5a RAS, **No Y93H**

https://www.hcvguidelines.org

Recommended Regimens or Most People with HCV[1,2]

Agent	Composition	Duration	Dosing	Contraindications
Sofosbuvir/ velpatasvir (± ribavirin) **Geno 1-6**	Sofosbuvir, a HCV nucleotide analog NS5B polymerase inhibitor; velpatasvir, an HCV NS5A inhibitor	12 weeks	1 tablet daily	• Ribavirin combination regimen contraindicated in patients for whom ribavirin is contraindicated.
Glecaprevir/ pibrentasvir **Geno 1-6**	Glecaprevir, a HCV NS3/4A protease inhibitor; pibrentasvir, an HCV NS5A inhibitor	8 weeks	3 tablets dosed once daily with food	• Patients with moderate or severe hepatic impairment (Child-Pugh B or C) or those with any history of prior hepatic decompensation • Coadministration with atazanavir or rifampin

•1. https://hcp.epclusa.com/efficacy 2. https://www.mavyret.com/hcp/mavyret-efficacy

Common Drug-Drug Interactions

- **SOF/VEL**
- Avoid
- Amiodarone
- Topotecan
- Carbamazepine, phenytoin, phenobarb, oxcarbazepine
- Rifampin
- Atorvastatin
- St John’s Wort

- **G/P**
- Avoid
- Carbamazepine, phenytoin, phenobarb, oxcarbazepine
- Rifampin
- Atorvastatin, lovastatin, simvastatin
- St John’s Wort
- Oral estrogen (for now)

Drug-Interaction Potential Between Selected HIV Antiretroviral and Preferred HCV Direct-Acting Antiviral Agents

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Atazanavir + RTV or COBI	x	✓	✓	x	x
Darunavir + RTV or COBI	x	✓	✓	x	
Lopinavir/ritonavir	x		✓	x	x
Doravirine	✓	✓	✓	✓	✓
Efavirenz	x	x		x	x
Rilpivirine	✓	✓	✓	✓	✓
Raltegravir	✓	✓	✓	✓	✓
Elvitegravir/COBI/FTC/TAF	✓	✓	✓	x	✓
Dolutegravir	✓	✓	✓	✓	✓
Bictegravir/FTC/TAF		✓	✓	✓	✓
Tenofovir DF	✓			✓	
Tenofovir AF	✓	✓	✓	✓	✓
Abacavir	✓	✓	✓	✓	✓
Lamivudine	✓	✓	✓	✓	✓




•HEP Drug Interactions. https://www.hep-druginteractions.org/.

DAA interactions with medicines used in treatment of various addictions

Simplified regimens

Who Is Eligible for Simplified Treatment

Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

Who Is *NOT* Eligible for Simplified Treatment

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- End-stage renal disease (ie, eGFR <30 mL/min/m^2) (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

Who Is Eligible for Simplified Treatment

Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment

Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.

- Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
- Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
- Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
- Prior liver biopsy showing cirrhosis

- **Labs prior to treatment: Complete blood count (CBC), International normalized ratio (INR) Hepatic function panel Calculated glomerular filtration rate (eGFR), Quantitative HCV RNA (HCV viral load), HIV, HBsAg**
- **Assessment of potential drug-drug interactions**
  - **Many good resources (https://www.hep-druginteractions.org/ , http://www.hcvdruginfo.ca/tables.html are 2 examples)**
- **Assess Compliance, pregnancy testing in child-bearing aged women**
- **Treat acute hepatitis C when first encountered**

- **Cirrhosis adds CPT assessment**
- **US/HCC assessment**
- **HCV Genotype if using SOF/VEL**
  - **For GT 3 should obtain RAS assessment**
  - **If Y93 present add RBV to SOF/VEL or use SOF/VEL/VOX**

GLE/PIB 8 weeks

SOF/VEL 12 weeks GT 1,2, 4,5,6

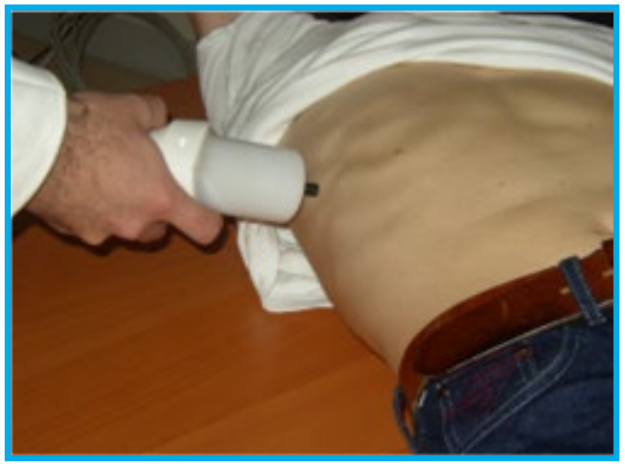
Assess SVR at week 12 post treatment

https://www.hcvguidelines.org/treatment-naive/simplified-treatment https://www.hcvguidelines.org/treatment-naive/simplified-treatment-compensated-cirrhosis

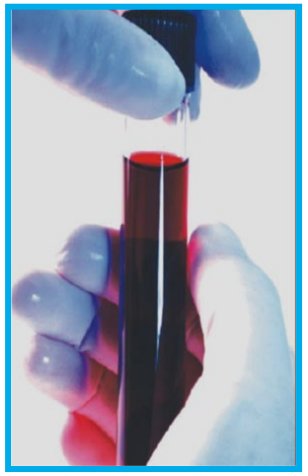
Staging of hepatic fibrosis is essential prior to HCV treatment: Do not miss cirrhosis

Liver biopsy: Gold standard

Rarely done



Elastography (> 12.5 kPa =cirrhosis

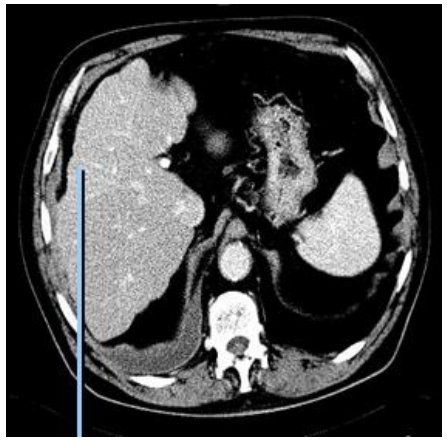


Serum Biomarkers

Serum Markers of Fibrosis: APRI, FIB-4: Very good negative predictive value

APRI<0.5, FIB-4 < 1.45 rule out cirrhosis

Commercial serum fibrosis tests also available in U.S. (FIBROSpect®, FibroSURE ®)



Axial CT/MRI, US can demonstrate cirrhotic morphology, portal hypertension

Case presentation

- HCV RNA returns 120,000 IU /ml
- Genotype 3a
- FIB-4: 0.56
- HIV/HBsAg are negative
- Next steps?

Recommended Follow-Up for Patients Who Achieved a Sustained Virologic Response (SVR)

- For patients who do not have advanced fibrosis (Metavir stage F0-F2), recommended follow-up is the same as if they were never infected with HCV
    - Verify that ALT normalizes (risk of NAFLD or alcohol related liver disease, and others may persist)
    - Assessment of other causes of liver disease is recommended for patients who develop persistently abnormal liver tests after achieving SVR
- Assessment for HCV recurrence or reinfection only if the patient has ongoing risk for HCV infection or otherwise unexplained hepatic dysfunction develops with HCV RNA testing
- Surveillance for hepatocellular carcinoma: twice-yearly ultrasound for patients with advanced fibrosis (i.e. Metavir F4 as assessed prior to Rx) who achieve SVR
- A baseline endoscopy is recommended to screen for varices if cirrhosis if indicated by AASLD guidelines for portal hypertension (or use carvedilol)

https://www.aasld.org/sites/default/files/2019-06/Garcia-Tsao_et_al-2017-Hepatology.pdf

Almost All Unique Populations Achieve High SVR rates

Population	SVR Rate	Comments
DAA failures	>95%	SOF/VEL/VOX pangenotypic option
HIV/HCV Coinfection	>95%	Must do drug-drug interactions
Post Orthotopic Liver Transplant	>95%	Must do drug-drug interactions
With Renal Impairment/Dialysis	>95%	GLE/PIB pangenotypic option
Kidney Transplant Patients	>95%	Must do drug-drug interactions
Management of Acute HCV Infection	>95% if treated for 8 weeks	20-50% of acute infections clear
HCV in Pregnancy	No treatment during pregnancy	Screen at risk women, treating before pregnancy preferred Preliminary data shows treatment feasible
HCV in Children	>95%	Treatment approved for those≥ 12 years of age

- **Drug-Drug interactions are essential to evaluate, particularly with HIV/HCV coinfection and transplant patients**
- **use available resources (https://aidsinfo.nih.gov/guidelines/htmltables/1/5536 is an example for HIV)**
- **Antiretroviral drug switches, when needed, should be done in collaboration with the HIV practitioner**

https://www.hcvguidelines.org/unique-populations

First Line Treatment Options lead to good SVR rates (>85%) in Childs B/C patients: Best left to Hepatologists

HCV genotype	Decompensated Cirrhosis, RBV tolerant		Decompensated Cirrhosis, RBV intolerant	
1,4	LDV/SOF/RBV SOF/VEL/RBV	12 W 12W	LDV/SOF SOF/VEL	24 W 24 W
2/3	SOF/VEL/RBV	12W	SOF/VEL	24 W
5, 6	LDV/SOF/RBV SOF/VEL/RBV	12 W 12 W	LDV/SOF SOF/VEL	24 W 24 W

- **Those with decompensated cirrhosis who have failed therapy remain one of the final special populations in need**
- **of additional therapies**
- **Protease inhibitors cannot be given in decompensated cirrhosis**
  - **Start RBV 600 with SOF/LDV, SOF/DAC, full dose with SOF/VEL**
  - **(600 in CPT C)**

https://www.hcvguidelines.org

Treatment of HCV in Pregnancy: Ledipasvir/sofosbuvir

- **Over the 2-year recruitment period, >170 HCV viremic pregnant women were identified,**
  - **29 women screened for the study; 20 total failed to enroll, most commonly due to having HCV genotype 2 or 3 infection, 4 due to ongoing IV drug use or use of cocaine, 3 declined to participate due to social reasons**
  - **9 participants enrolled, all have completed the study medication and delivered.**
  - **All women achieved SVR, no infant developed HCV infection**
  - **No change in pK of ledipasvir/sofosbuvir**
  - **No AEs attributed to LED/SOF in infants**
- **Recruitment was the largest challenge in this study and not because of a lack of HCV prevalence.**
- **Larger study is ongoing with sofosbuvir/velpatasvir (**NCT05140941)

•https://doi.org/10.1016/ S2666-5247(20)30062-8

Which patients with cirrhosis and decompensation due to HCV infection can you treat to achieve SVR and potentially delist?

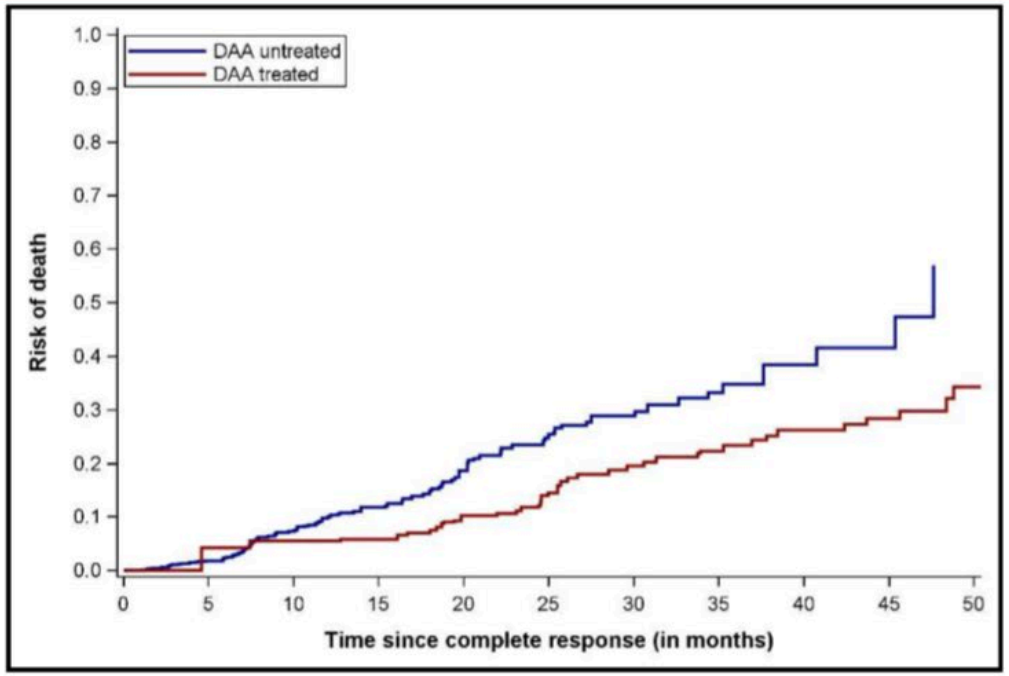
- Treatment of hepatitis C pre-transplant may reduce chance to receive HCV RNA+ graft
- Achieving SVR with DAAs will reduce inflammation in the liver
- Reversal of fibrosis is required to reduce portal hypertension, may take years
- About 20% of those with MELD <20 may improve and be delisted with DAA therapy and these individuals should be considered for treatment
  - Pay close attention to those with severe portal hypertension
- Those with MELD scores above 20 require careful assessment on individual basis

Direct-Acting Antiviral (DAA) Therapy is Associated with Improved Survival in Patients with a History of Hepatocellular Carcinoma and HCV Infection

Results:

DAA Treated:
4.6 deaths per 100 person-years follow-up

DAA Untreated:
19.6 deaths per 100 person-years follow-up



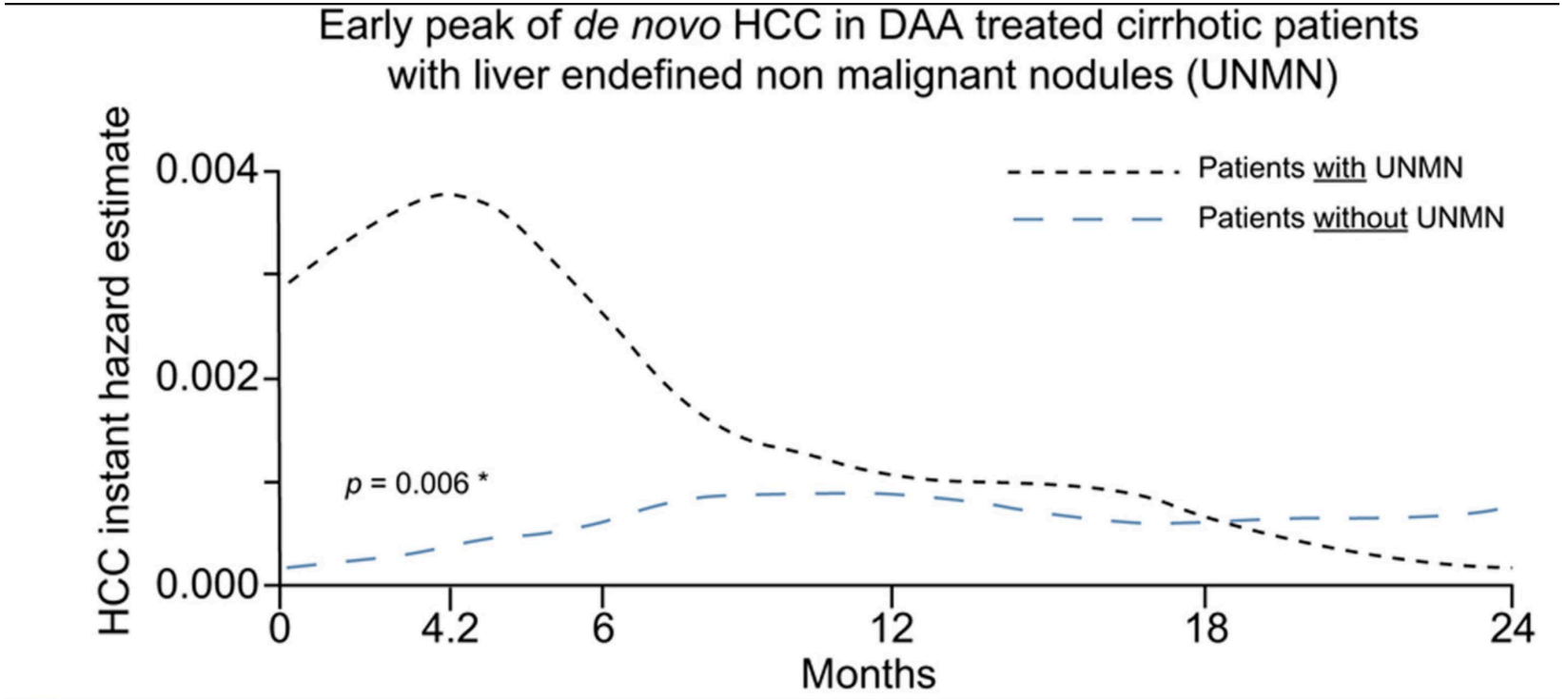
Multivariable analysis
- Adjusted for site, age, sex Child Pugh score, AFP, tumor burden and HCC treatment modality

→

DAA therapy associated with lower mortality:
HR: 0.54; 95%CI: 0.33 – 0.90

HCV/HCC risk in DAA-treated patients with cirrhosis

- Evaluate all elevated AFP and characterize indeterminate nodules prior to treatment
- Undefined non-malignant nodules, ascites and AFP were independently associated with the incidence of *de novo* HCC



N° at risk						
- - - - - - -	73	69	63	52	40	18
— — —	1,088	1,038	974	734	471	190

(*) Time dependent effect of the presence of nodules with the development of HCC in patients with vs without UNMN, proportional hazard test.

•https://doi.org/10.1016/j.jhep.2020.03.030

AASLD/IDSA Guidelines: Acute HCV infection

Pharmacologic Prophylaxis Not Recommended

NOT RECOMMENDED	RATING
Pre-exposure or post-exposure prophylaxis with antiviral therapy is not recommended.	III, C

Recommendations for Medical Management and Monitoring of Acute HCV Infection

RECOMMENDED	RATING
After the initial diagnosis of acute HCV with viremia (defined as quantifiable RNA), HCV treatment should be initiated without awaiting spontaneous resolution.	I, B
Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.	I, C
Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to substance use.	I, B

Recommended Regimens for Patients With Acute HCV Infection

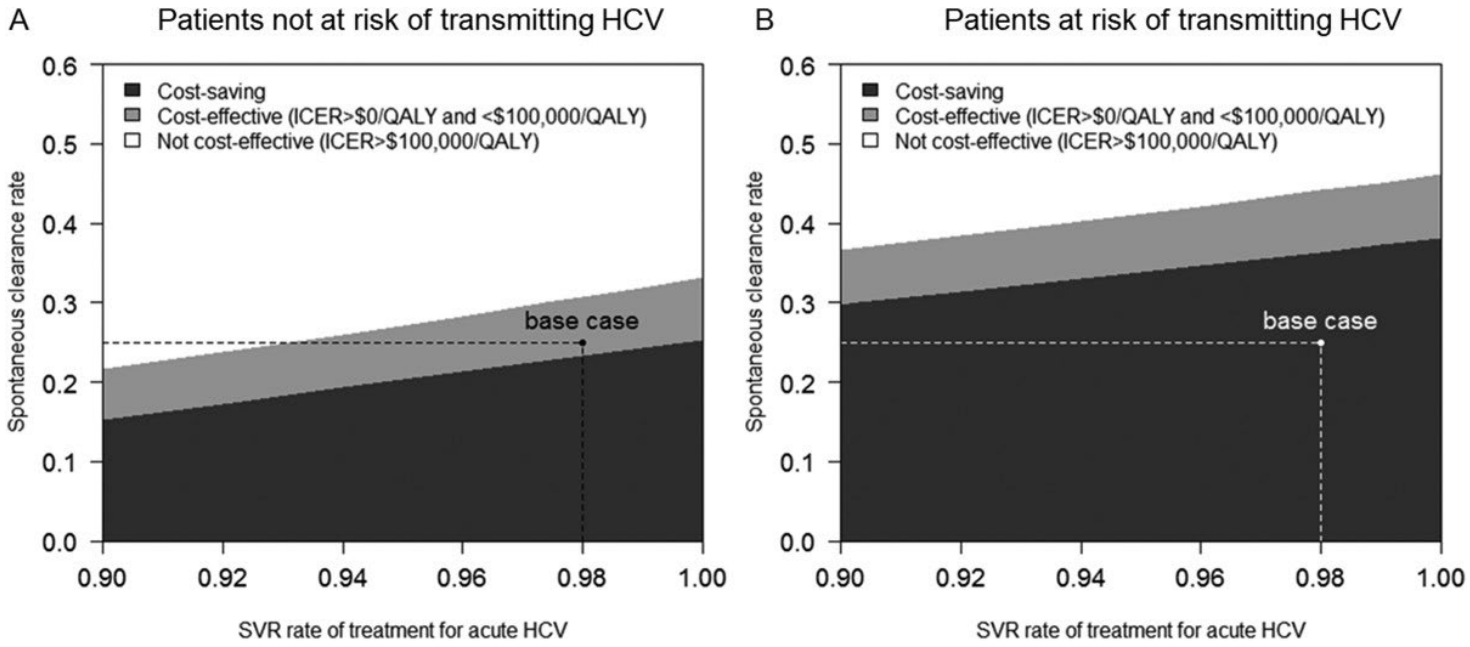
RECOMMENDED	RATING
Owing to high efficacy and safety, the same regimens that are recommended for chronic HCV infection are recommended for acute infection.	IIa, C

https://news.abbvie.com/2025-06-11-U-S-FDA-Approves-Expanded-Indication-for-AbbVies-MAVYRET-R-Glecaprevir-Pibrentasvir-as-First-and-Only-Treatment-for-People-with-Acute-Hepatitis-C-Virus

https://www.hcvguidelines.org/unique-populations/acute-infection

Cost-effectiveness: Treatment of acute HCV

- In patients at risk of transmitting HCV, treating acute HCV became cost-saving, increasing QALYs by 0.03 and decreasing costs by $3,655.



Bethea ED et al. Hepatology 2018;67:837–846

Our approach to hepatitis C must evolve to a decentralized model of care

Improved access to HCV testing

Improved education about testing

Prompts for testing

Access to HCV care providers

Improved access to care (universal access)

Co-localized testing and treatment facilities

Education about Importance of treatment

Psychological and harm reduction services for comorbid conditions

Resources for primary care to treat HCV

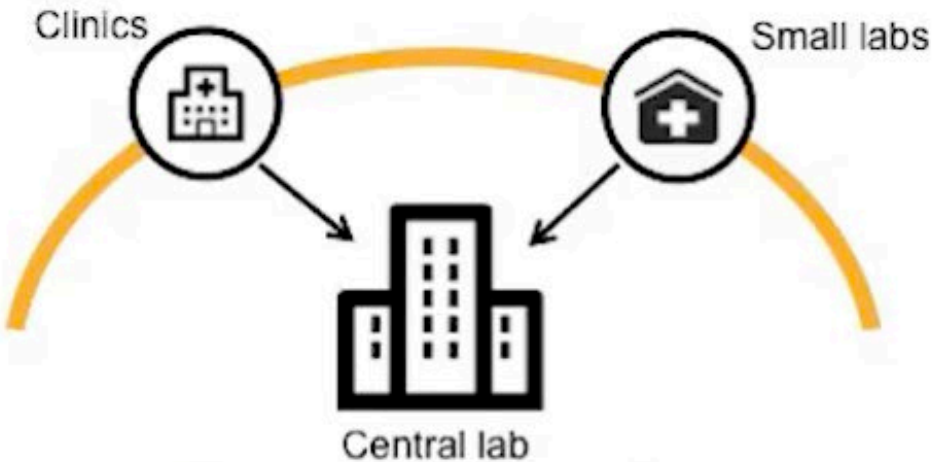
Treatment of opioid addiction

Psychological and harm reduction services for comorbid conditions

Directly observed therapy

- **Many success stories in the US: Cherokee Nation elimination program**
- **VA healthcare system has treated over 100,000 individuals, ECHO HCV projects**

Models of care: Point of care testing is optimal



Centralized

Decentralized

Components of hepatitis C elimination programs

- Data for planning and monitoring program performance
- Plan of action with time limited numerical targets
- Civic/political support for partners and target populations
- Capacity to deliver appropriate interventions to target populations
- Model for financing
- Integration of program within existing health systems
- Participation in operational research

Ward et al J Virus Erad. 2019 Jan; 5(1): 60–66.

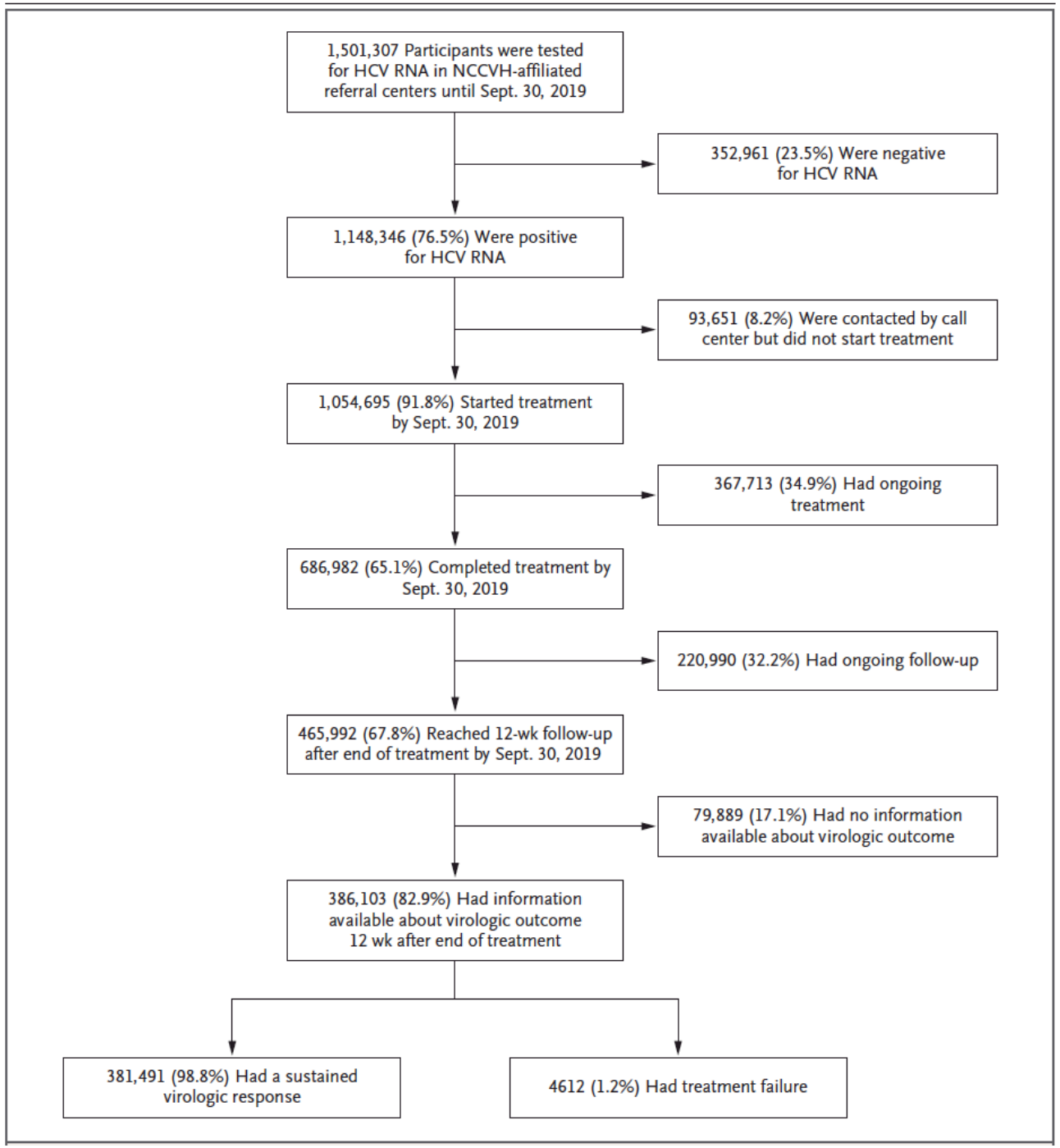
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Screening and Treatment Program to Eliminate Hepatitis C in Egypt

Imam Waked, M.D., Gamal Esmat, M.D., Aisha Elsharkawy, M.D., Magdy El-Serafy, M.D., Wael Abdel-Razek, M.D., Reham Ghalab, M.Sc., Galal Elshishiney, M.Sc., Aysam Salah, B.Sc., Soad Abdel Megid, M.Sc., Khaled Kabil, M.Sc., Manal H. El-Sayed, M.D., Hany Dabbous, M.D., Yehia El Shazly, M.D., Mohamed Abo Sliman, M.Sc., Khalid Abou Hashem, M.Sc., Sayed Abdel Gawad, M.Sc., Nevine El Nahas, B.Sc., Ahmed El Sobky, M.Sc., Sahar El Sonbaty, M.Sc., Hamdy El Tabakh, M.Sc., Ehab Emad, M.Sc., Hany Gemeah, M.Sc., Amal Hashem, M.Sc., Mohamed Hassany, M.D., Naseif Hefnawy, M.Sc., Abdel N. Hemida, M.B., B.Ch., Ayman Khadary, M.B., B.Ch., Kamal Labib, M.B., B.Ch., Faisal Mahmoud, M.B., B.Ch., Said Mamoun, M.Sc., Tamer Marei, M.Sc., Saad Mekky, M.Sc., Alsayeda Meshref, M.Sc., Alaa Othman, M.Sc., Omnia Ragab, M.Sc., Elhag Ramadan, M.Sc., Ahmed Rehan, M.Sc., Tarek Saad, Ph.D., Ramy Saeed, M.Sc., Mohamed Sharshar, M.Sc., Hesham Shawky, M.Sc., Mohamed Shawky, M.Sc., Wael Shehata, B.Sc., Hanaa Soror, M.Sc., Mohsen Taha, M.Sc., Mahmoud Talha, M.Sc., Adel Tealaab, M.Sc., Mohamed Zein, M.D., Alaa Hashish, M.P.H., Ahmed Cordie, M.D., Yasser Omar, M.D., Ehab Kamal, M.D., Islam Ammar, M.D., Mohamed AbdAlla, M.D., Wafaa El Akel, M.D., Wahid Doss, M.D., and Hala Zaid, M.Sc.

- **49,630, 319 screened, 4.61 positive**
- **Egypt will likely be amongst the first countries to eliminate hepatitis C**



Case presentation

- He calls clinic saying he took medicines for first 2 weeks , then lost his medicines and has missed 4 days
- What are next steps?

Variable Adherence

- **SOF/VEL – SIMPLIFY prospective in PWID)[1]**
  - **>90% adherence (</= 8 dosages missed) = 96% SVR (69/103)**
  - **<90% adherence (>8 doses missed) = 91% SVR (31/34)**

- **GLE/PIB- retrospective[2]**
  - **Data on 8-week regimen from 10 phase 3 clinical trials**
  - **<90% adherence = 100% SVR**
    - **(weeks 0-4 n=21/21, weeks 5-8 n=76/76**
  - **>90% adherence = 99% SVR (weeks 0-4 n=1155/1162, weeks 5-8 n=1136/1143)**

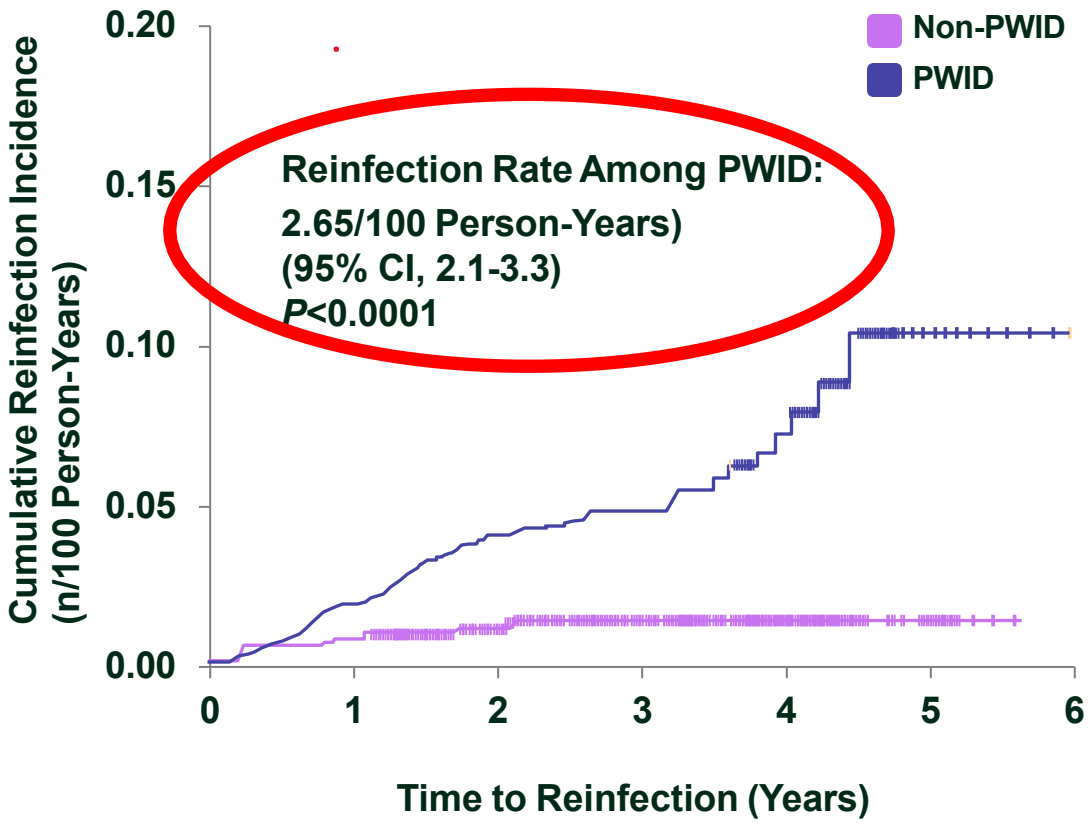
1. Cunningham EB, et al. *Int J Drug Policy*. 2018; 62:14-23; 2. Zamor PJ, et al. *Am J Gastroenterol*. 2021; 116(9):1896-904.

Recommended Management of DAA Treatment Interruptions Receiving Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir

https://www.hcvguidelines.org/evaluate/monitoring

HCV Reinfection After Successful DAA Treatment: Analysis of the British Columbia Testers Cohort

Incidence of HCV Reinfection



Factors Associated With HCV Reinfection*

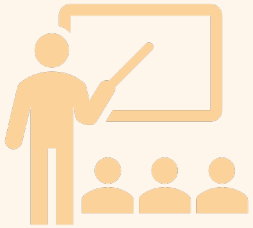
	Adjusted HR (95% CI)
Age (ref: 50-59), years	
20-29	3.4 (1.2-10.0)
30-39	2.3 (1.3-4.3)
40-49	1.1 (0.6-2.0)
≥60	0.4 (0.2-0.9)
Male (ref: female)	2.2 (1.2-3.8)
Stimulant use (ref: no)	0.8 (0.5-1.4)
Opioid use history (ref: no)	1.8 (1.0-3.1)
Antipsychotic treatment (ref: no)	0.5 (0.3-0.8)
HIV coinfection (ref: no)	1.9 (1.2-3.1)
Benzodiazepine (ref: no)	1.0 (0.4-2.3)

*Multivariate model. Covariates: age, sex, HIV coinfection, injection drug use, alcohol use disorder, and major mental illness.

Janjua N, et al. *Hepatology*. 2021;74(1 Suppl):592A-593A. Abstract 967.

Preventing Reinfection

Harm Reduction



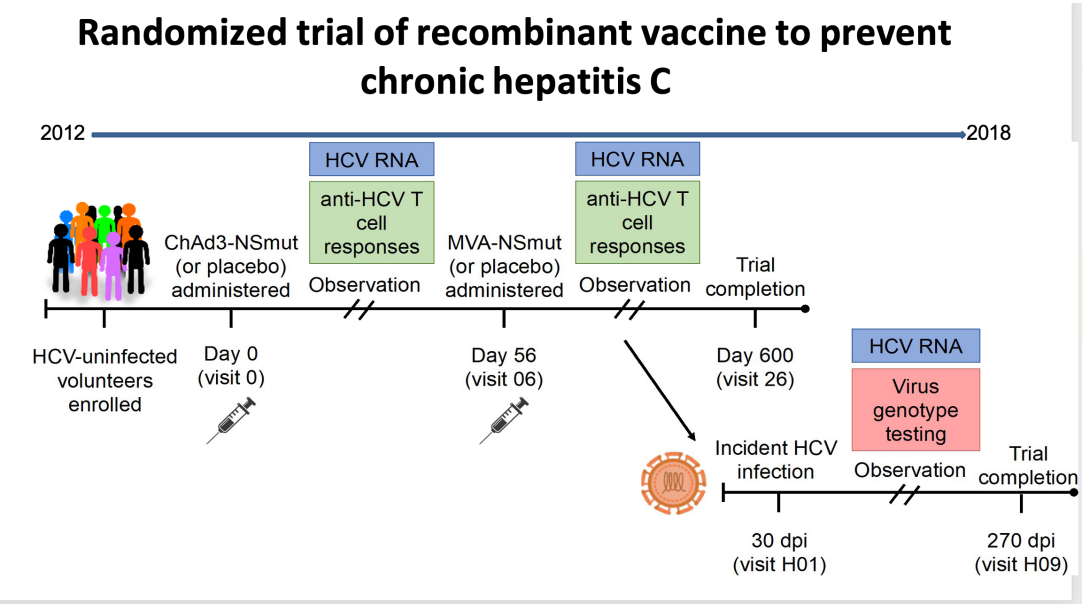
Education

Screening

Recommendation for Testing for Reinfection in PWID	
RECOMMENDED	**RATING**
At least annual HCV-RNA testing is recommended for PWID with recent injection drug use after they have spontaneously cleared HCV infection or have been successfully treated.	IIa, C

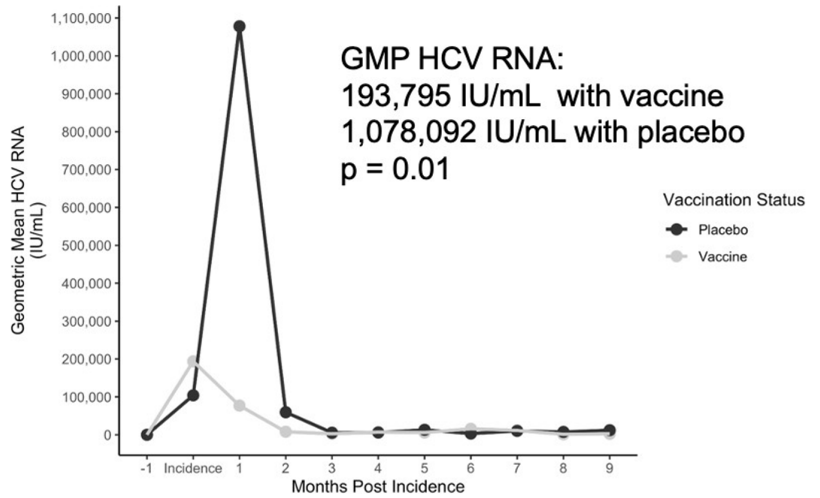
American Association for the Study of Liver Diseases–Infectious Diseases Society of America. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. Updated: January 21, 2021. Accessed August 10, 2021. www.hcvguidelines.org

Re-energize Vaccine Research:
Randomized trial of recombinant vaccine to prevent chronic hepatitis C did not achieve endpoint



Analysis and Population†	Vaccine (N = 275)		Placebo (N = 273)	
	Censored Data	Chronic Infection	Censored Data	Chronic Infection
	number of participants			
Primary efficacy analysis, per-protocol population‖	261	14	259	14
Secondary efficacy analysis, modified intention-to-treat population	256	19	257	17

- 6 years (+ planning) with 550 participants (people who inject drugs)
- Immunogenic and safe
- No effect on acute or chronic infection

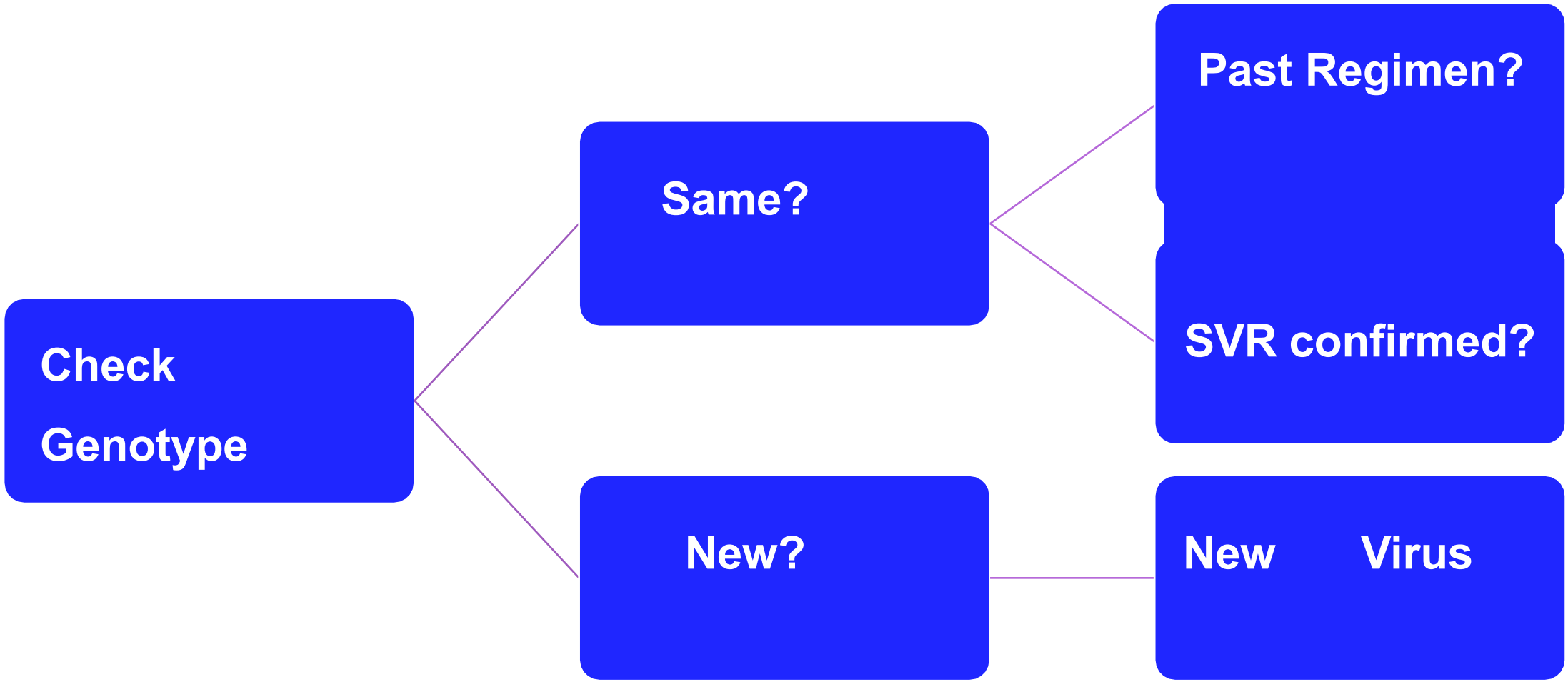


Page and Cox NEJM 2021

Case presentation

- He completes 12 weeks of sofosbuvir/velpatasvir and achieves sustained response
- You see him back in 1 year
- He has stopped buprenorphine and has unfortunately relapsed and was injecting fentanyl
- Repeat liver panel shows ALT 56 IU/L, AST 40 IU/L
- What are next steps?

HCV Re-Treatment



SOF Based Failure

Recommended and alternative regimens listed by evidence level and alphabetically for:

Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)[b]	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) except for NS3/4 protease inhibitor inclusive combination DAA regimen failures[c] • **Not** recommended for genotype 3 infection with sofosbuvir/NS5A inhibitor experience.	16 weeks	I, A

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Genotype 3: Add weight-based ribavirin if cirrhosis is present and there are no contraindications.
[c] This regimen is not recommended for patients with prior exposure to an NS5A inhibitor plus NS3/4 PI regimens (eg. Elbasvir/grazoprevir).

Glecaprevir pibrentasvir failures

Recommended regimens listed by evidence level and alphabetically for:

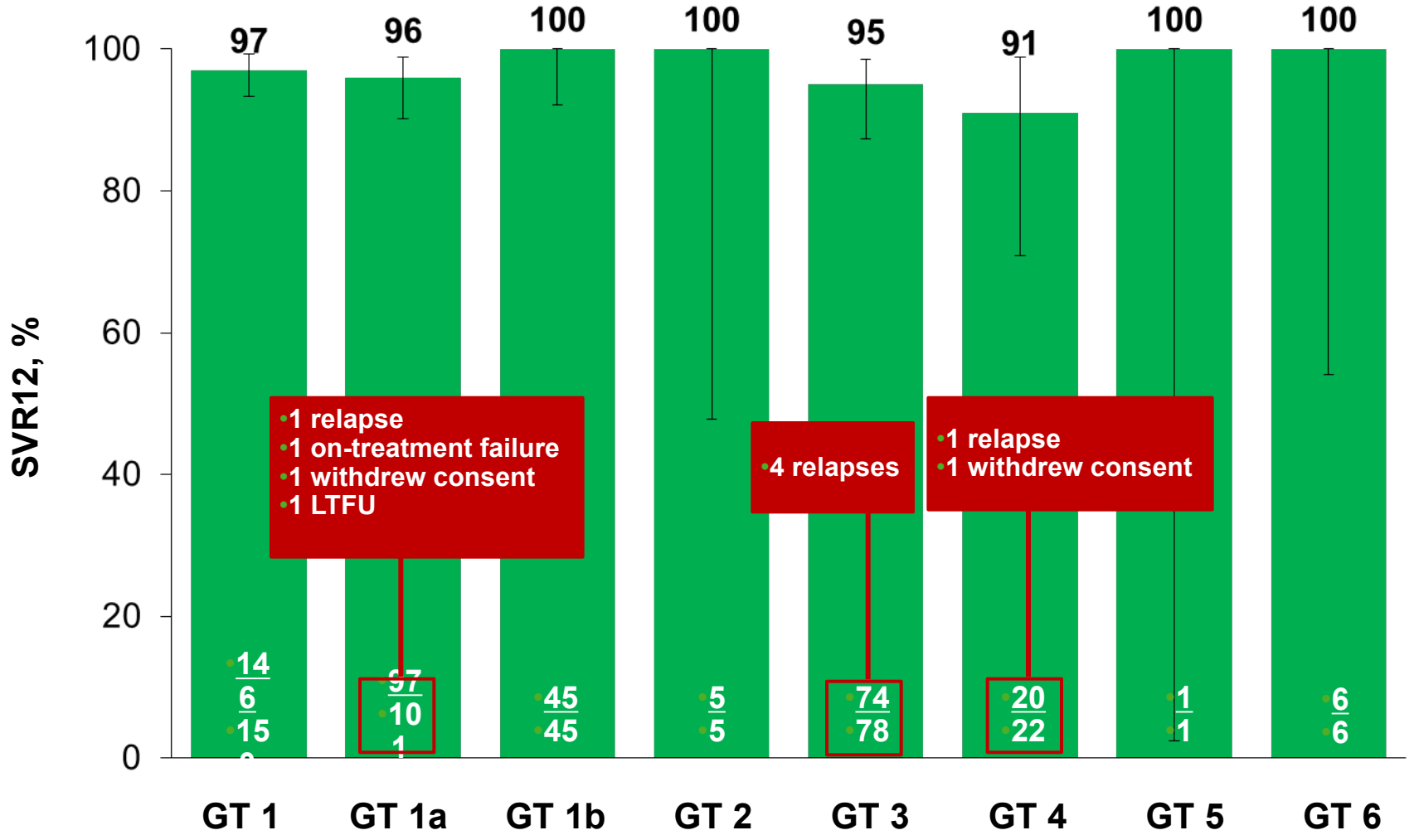
Glecaprevir/Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) plus daily sofosbuvir (400 mg) and weight-based ribavirin	16 weeks	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	IIa, B
For patients with compensated cirrhosis, addition of weight-based ribavirin is recommended.	12 weeks	IIa, C

[a] For decompensated cirrhosis, please refer to the appropriate section.

POLARIS-1: SOF/VEL/VOX for 12 Weeks in NS5A Inhibitor–Experienced HCV GT 1-6

One of the 6 patients who relapsed had treatment-emergent RASs



•Bourliere M. AASLD 2016. Oral 194.

Case presentation

- Genotype 1a, viral level 1,100,000 IU/ml
- Retreat SOF/VEL/VOX 12 weeks
- Re-engage harm reduction program

US National HCV Elimination Plan

March 9, 2023

A National Hepatitis C Elimination Program in the United States

A Historic Opportunity

Rachael L. Fleurence, MSc, PhD[1]; Francis S. Collins, MD, PhD[1]

Author Affiliations | Article Information

JAMA. Published online March 9, 2023. doi:10.1001/jama.2023.3692

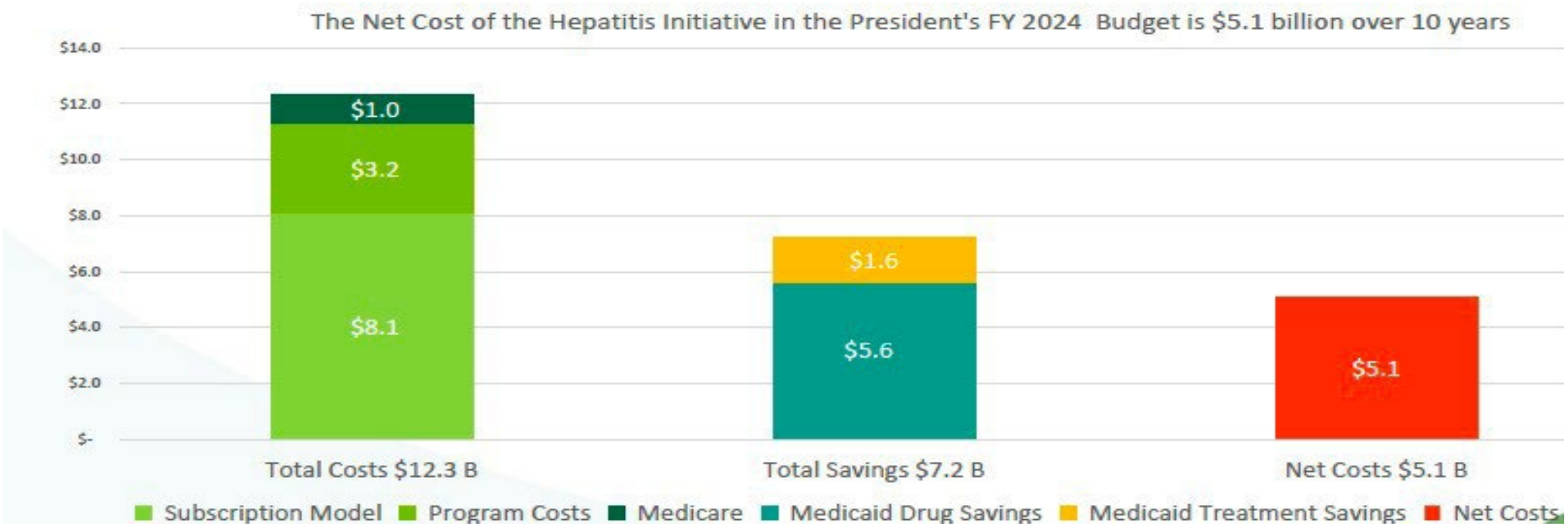
Highlights of the White House Plan

Proposed a plan to eliminate hepatitis C in five years in the United States through a mandatory authorization:

1. Supporting the development of point-of-care diagnostic tests to enable a test-to-treat model;
2. Broadening access to curative hepatitis C medications, primarily through a national subscription model; and
3. Expanding infrastructure needed to reach, test, and treat all affected individuals.

.

White House Plan Cost Estimate



Components of Federal Elimination Plan

- **Point-Of-Care (POC) diagnostic tests**
  - **Enable hepatitis C single-visit "test and treat" programs to enhance cascade of care**
  - **Obtain FDA approval of fingerstick test already in use in Australia and Europe**

- **Provide broad access to curative hepatitis C medications**
  - **National subscription "Netflix" model**
  - **Fixed sum for drug access negotiated by the US Government**
  - **Drugs then provided for free to Medicaid, uninsured, incarcerated, opioid treatment programs, Native American reservations**

- **Empower health care delivery**
  - **Expand screening settings for high-risk populations, including prisons**
  - **Employ innovative telehealth methods, mobile units**
  - **Expand number of community health workers**
  - **Re-energize vaccine research**

Test and Treat models of care

- Routine Opt-out screening
- Single visit to facilitate engagement in care, integrated treatment
  - Harm reduction settings
    - Syringe service programs
    - Safe consumption spaces
  - Shelters
  - Mobile clinics
  - Jails
- Cepheid GeneXpert: Used in Europe and Australia, now authorized by FDA
  - Fingerstick, no venipuncture required
  - Run time 60 minutes
  - 100 IU/ml-100,000,000 IU/ml
  - Factors to consider: HBV Point of Care testing, Disease staging, assay run time

•US Department of Health and Human Services. https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/data-and-trends/index.html Accessed June, 2024

Australia's DAA program: the "Netflix" model

The NEW ENGLAND JOURNAL of MEDICINE

Universal Medicine Access through Lump-Sum Remuneration — Australia's Approach to Hepatitis C

Suerie Moon, M.P.A., Ph.D., and Elise Erickson, M.A.

The New York Times

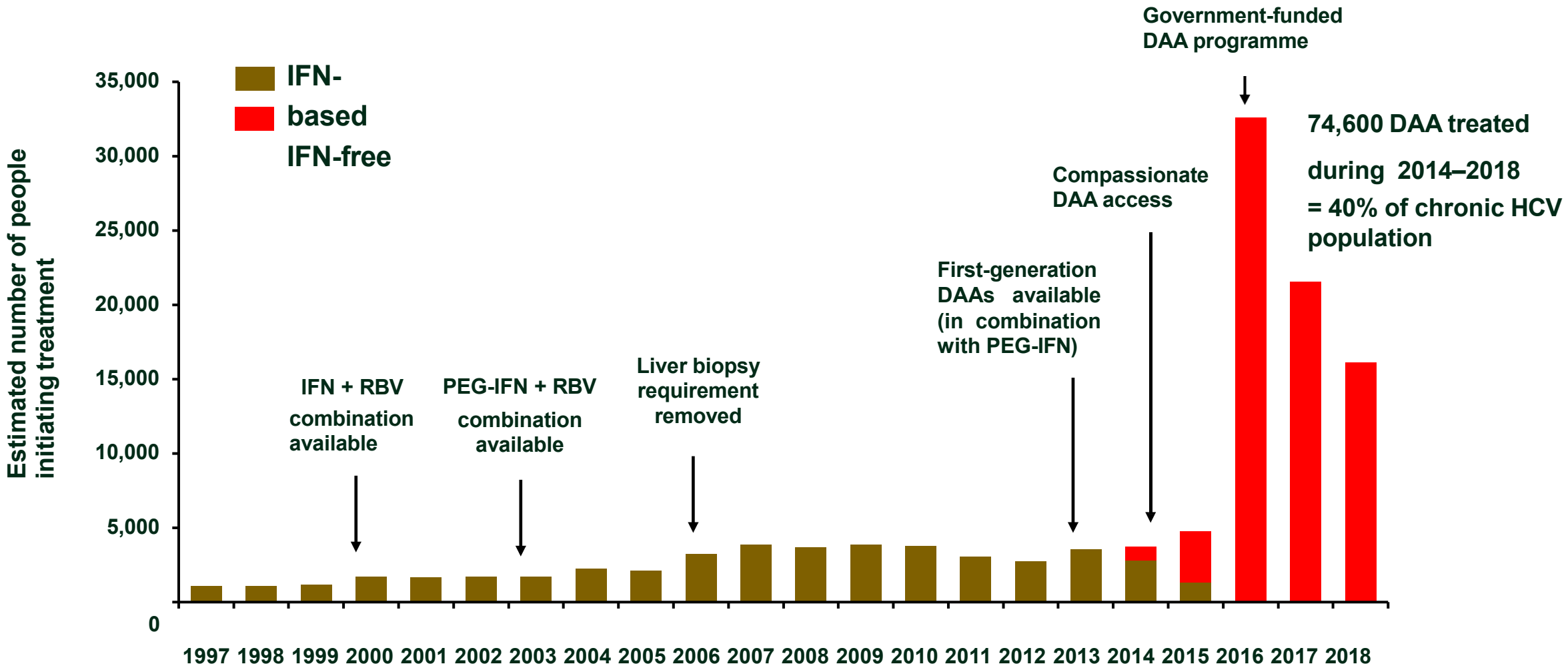
Treat Medicines Like Netflix Treats Shows

Australia seems to have found a way to entice Big Pharma into making essential new medicines affordable. Why can't the United States?

By Tina Rosenberg

Ms. Rosenberg is a co-founder of the Solutions Journalism Network, which supports rigorous reporting about responses to social problems.

HCV treatment uptake in Australia: 1997–2018



Adapted from Dore GJ, Hajarizadeh B. Infect Dis Clin N Am 2018;32:269–79

Slide courtesy of Greg Dore

News • Press Releases

JUNE 4, 2025

CASSIDY, VAN HOLLEN INTRODUCE LIFE-SAVING HEPATITIS C LEGISLATION

WASHINGTON – U.S. Senators Bill Cassidy, M.D. (R-LA) and Chris Van Hollen (D-MD) introduced life-saving legislation to cure low-income and hard-to-reach Americans with hepatitis C virus (HCV). Cassidy and Van Hollen's Cure Hepatitis C Act will establish a voluntary drug subscription model to connect HCV patients to treatment and stop the spread of the disease. Today's treatment for HCV cures more than 95% of cases with almost no side effects.

"We can virtually eliminate hepatitis C in a fiscally responsible way," **said Dr. Cassidy.** "Curing hepatitis C makes Americans healthy again while also saving the federal government billions by eliminating the need for chronic care. It's a win for patients, and it's a win for the taxpayers."

"Hepatitis C claims thousands of American lives every year – but we have a proven model that can make this preventable public health crisis a thing of the past. Our bipartisan legislation offers a solution towards ensuring communities most at risk have access to the highly effective treatments that are available – saving lives while also saving billions in taxpayer dollars that are currently spent on costly chronic care," **said Senator Van Hollen.**

- Cure Hepatitis C Act of 2025 is based on a successful pilot program in Louisiana
- Five-year subscription model allows the federal government to procure HCV drugs through a
- competitive bidding process between the U.S. Secretary of the HHS and DAA manufacturers

https://www.cassidy.senate.gov/wp-content/uploads/2025/06/KEN25370.pdf

SYNDEMIC APPROACH AND DECENTRALIZATION

Top 5 Priority Populations

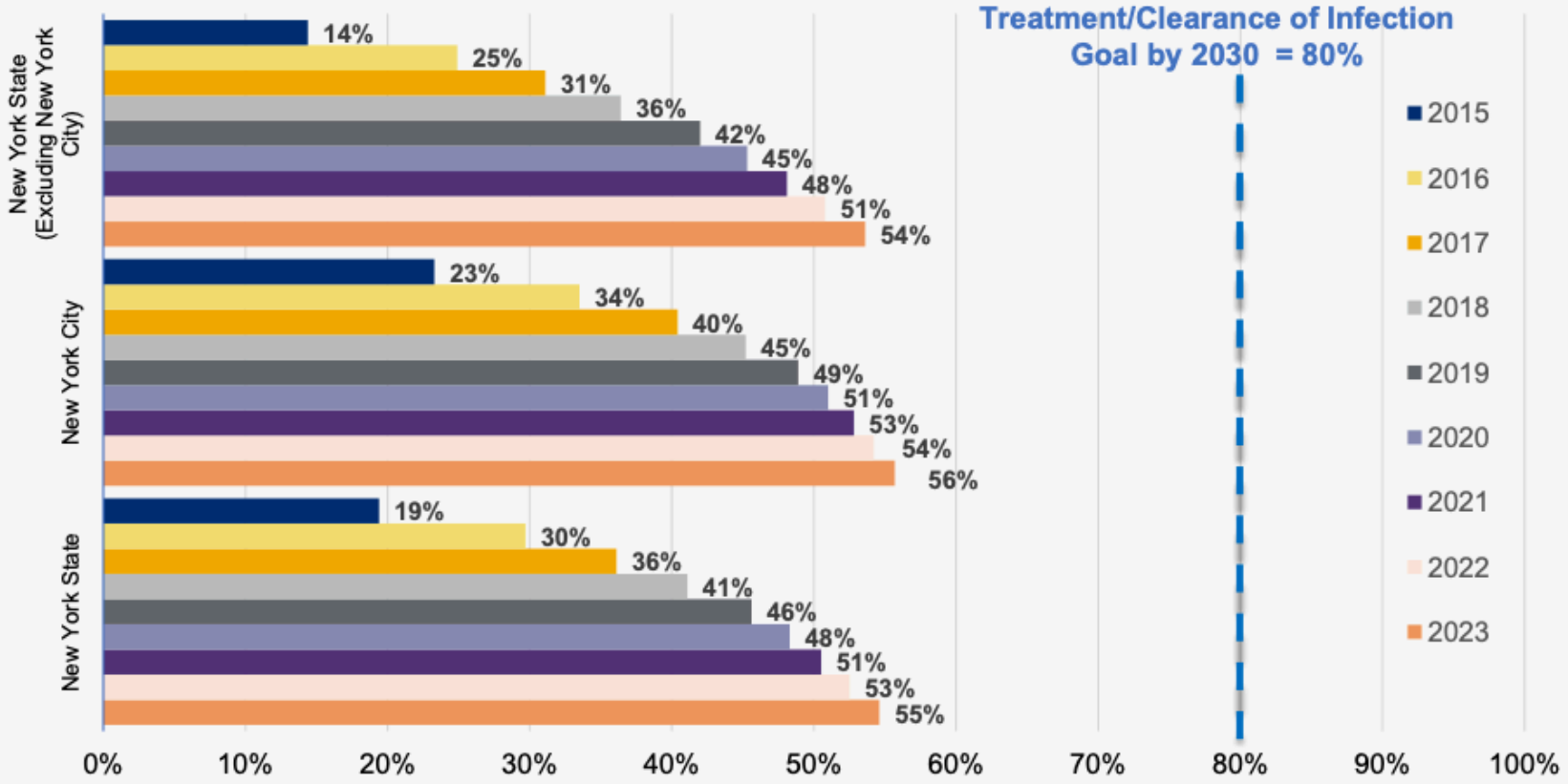
- People who use drugs
- Currently or formerly involved in the justice system
- Baby boomers (born between 1945 and 1965)
- Homeless or at risk of becoming homeless
- HIV+ individuals (including HIV/HCV coinfection)

Top 5 Priority Settings

- Correctional facilities, including jails, courthouses, prisons
- Harm reduction programs
- Drug/substance use treatment program sites
- Primary and routine health care offices, community health providers, and federally qualified health centers
- Settings serving the homeless

NEW YORK STATE | Department of Health

Cumulative Percent of Persons Diagnosed* with Hepatitis C Who Cleared** Infection by Geographic Area and Year New York State: 2015-2023



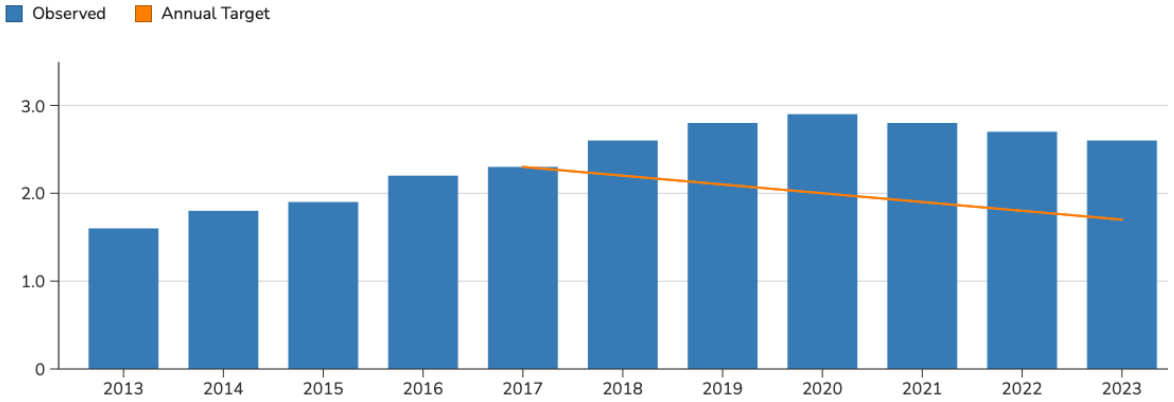
* Diagnosed as indicated by a positive hepatitis C ribonucleic acid or genotype test since 2010.

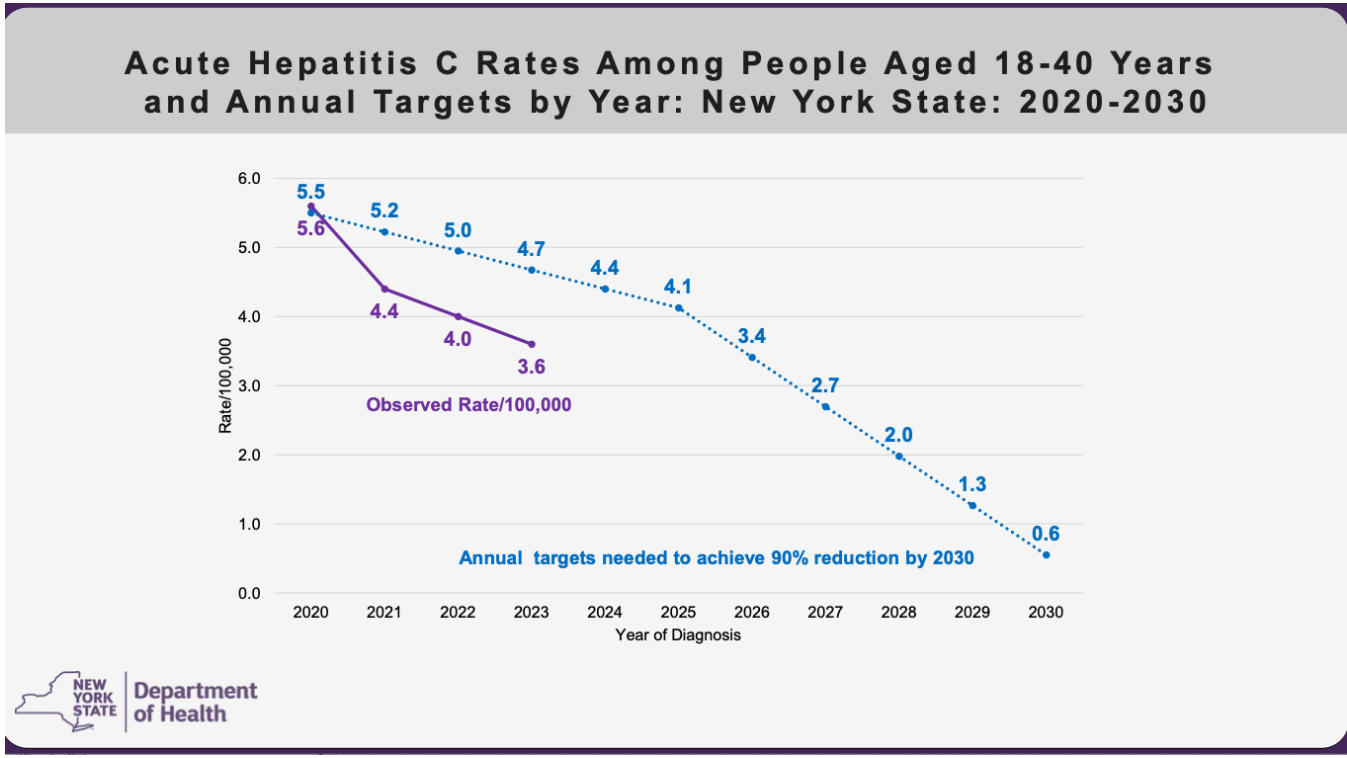
** Clearance of infection indicated if most recent hepatitis C ribonucleic acid or genotype result is negative. Clearance may occur following treatment or spontaneously, without treatment. Negative hepatitis C ribonucleic acid results reportable in New York City as of July 2014 and in New York State as of Jan. 2016.

NEW YORK STATE | Department of Health

Reported acute cases of hepatitis C in the 18-40 age group as proxy for people who inject drugs

Incidence rate* of reported new hepatitis C cases among persons aged 18–40 years† and annual targets for the United States by year





1.Centers for Disease Control and Prevention. Viral Hepatitis Surveillance – United States, 2023. Published April 2025. Accessed 6/25/25

•**https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_c/docs/2025_nyselimination_metrics.pdf**

Primary Hepatitis C Elimination Metrics: NYS

Hepatitis C Diagnoses

- Definition
  The number of persons newly diagnosed with hepatitis C.
- Data Source
  Hepatitis Elimination and Epidemiology Dataset
- Goal
  90% of people living with hepatitis C will be diagnosed

Hepatitis C Treatment

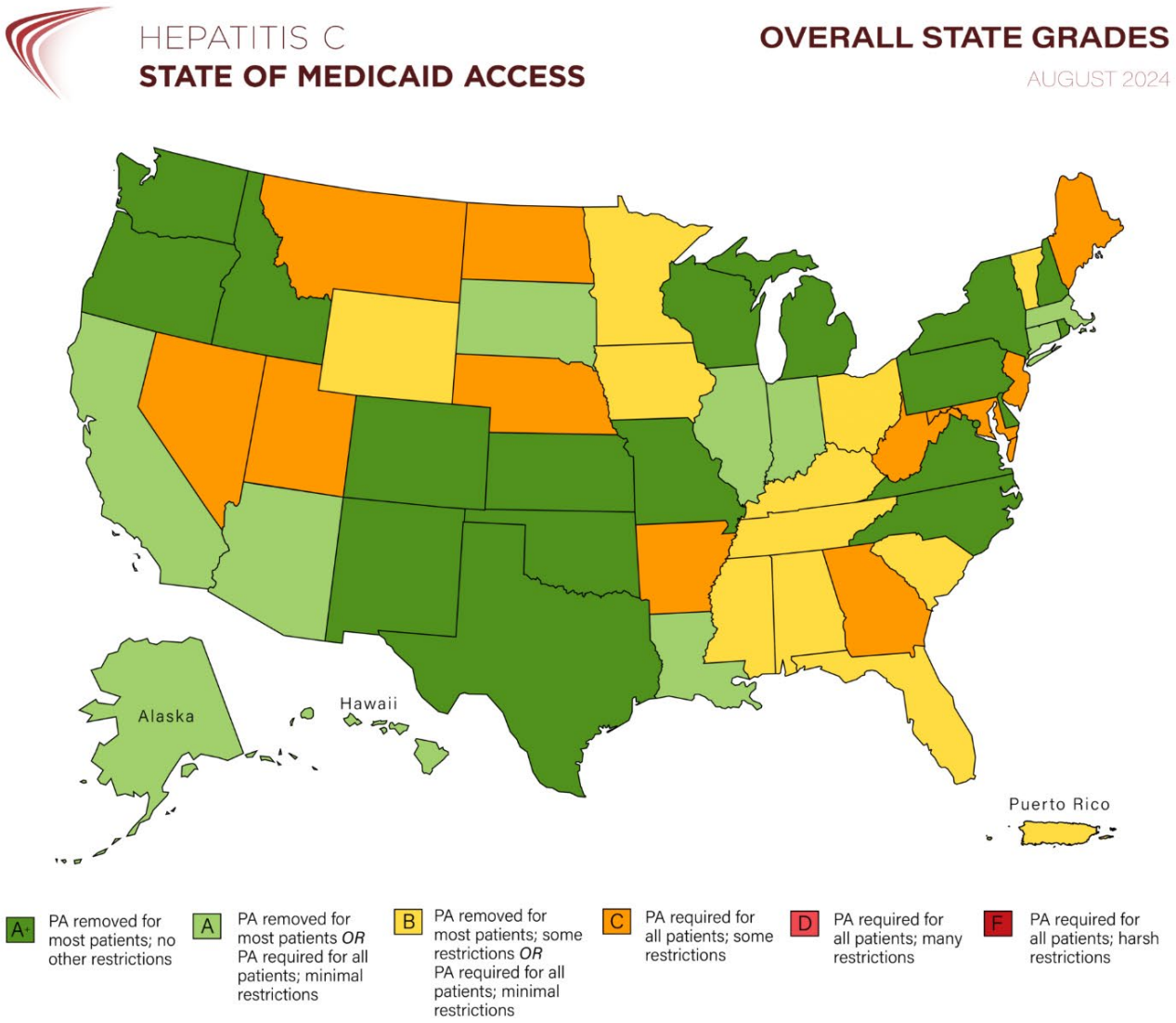
- Definition
  The number of persons diagnosed with hepatitis C with evidence of treatment for, or clearance of infection.
- Data Sources
  Hepatitis Elimination and Epidemiology Dataset
- Goal
  80% of diagnosed will be treated/clear infection

New Infections Among Persons Who Inject Drugs

- Definition
  The rate and number of reported acute hepatitis C infections in 18-40 age group.
- Data Source
  Hepatitis Elimination and Epidemiology Dataset
- Goal
  90% reduction in new hepatitis C infections

NEW YORK STATE | Department of Health

Overall State Grades: Access is improving



A+ (19): Colorado, Delaware, District of Columbia, Idaho, Kansas, Michigan, Missouri, New Hampshire, New Mexico, New York, North Carolina, Oklahoma, Oregon, Pennsylvania, Rhode Island, Texas, Virginia, Washington, Wisconsin

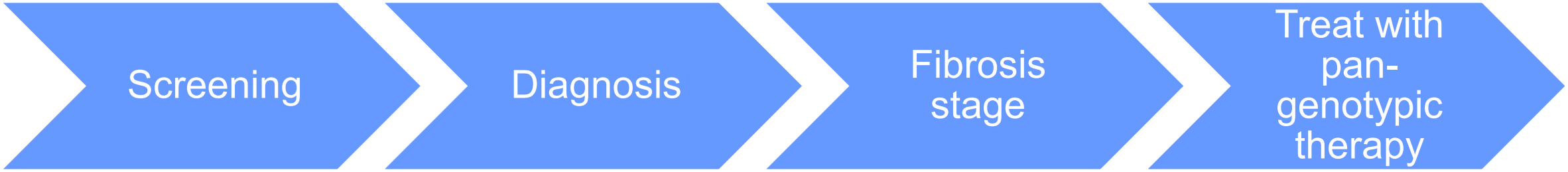
A (10): Alaska, Arizona, California, Connecticut, Hawaii, Illinois, Indiana, Louisiana, Massachusetts, South Dakota

B (13): Alabama, Florida, Iowa, Kentucky, Minnesota, Mississippi, Ohio, Puerto Rico, South Carolina, Tennessee, Vermont, Wyoming

C (11): Arkansas, Georgia, Maine, Maryland, Montana, Nebraska, Nevada, New Jersey, North Dakota, Utah, West Virginia

Citation: Center for Health Law and Policy Innovation & National Viral Hepatitis Roundtable, Hepatitis C: State of Medicaid Access (2024), www.stateofhepc.org

Universal care pathway



Rapid diagnostic test

Confirmation of active infection

Preferably POC

Remains barrier worldwide

Cirrhosis or no cirrhosis

FIB-4

Elastography

Treat

SVR-12

Dismiss from care if no cirrhosis

Take-Home Points

- Diagnosis
  - Rates remain low in US and world-wide, still the greatest gap adopt universal screening
  - A point-of-care test to diagnose viremia is now approved
- After diagnosis – many may never be treated, test and treat strategies should improve treatment rates
  - Access to providers should be decentralized, simplified models of treatment should be SOC : Syndemic Approach with decentralization
  - Access to therapy – cost, restrictions (fibrosis, sobriety) are improving
  - Competing concerns – opioid epidemic, substance use risks should be addressed, there are few reasons not to treat…SVR is expected
  - Fibrosis assessment is still important at initial evaluation
  - After SVR, screen those with cirrhosis for hepatocellular cancer
  - Periodically screen those at risk for recurrent infection; retreatment options are robust