Hepatitis C Elimination: Screening, Linkage and Treatment

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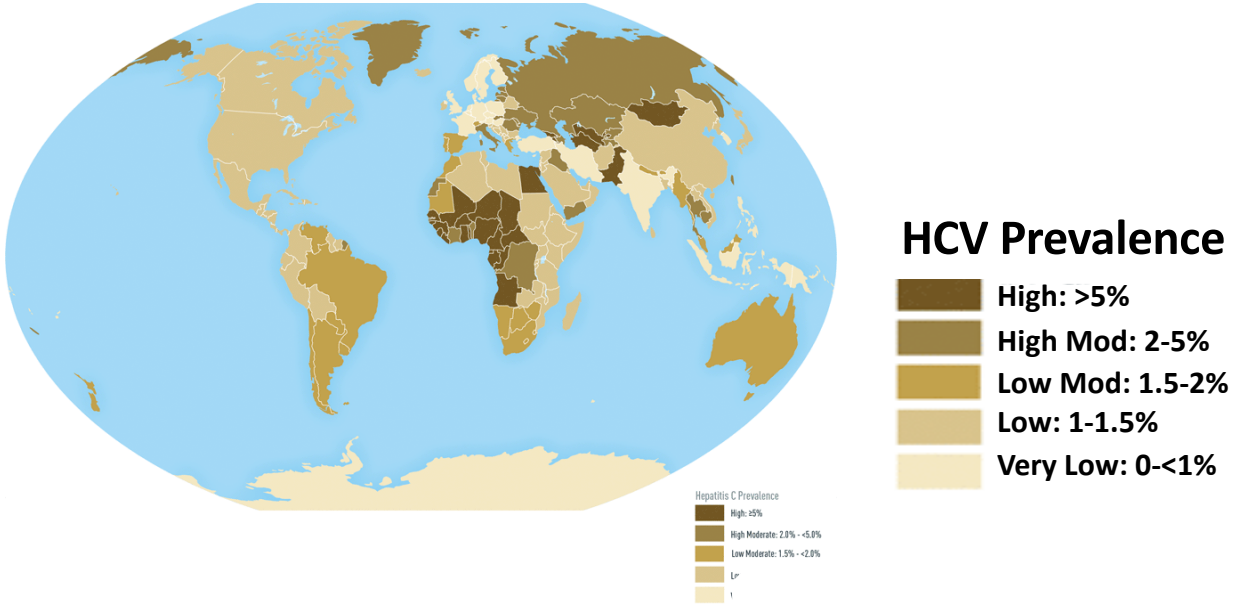
Hepatitis C: Worldwide Presence

- Worldwide prevalence: 130-150 million
  - Viral hepatitis causes >50% of cirrhosis and >70% of HCC
- US prevalence: 3.5 million
  - Most common indication for liver transplantation



www.cdc.gov; Denniston MM et al. *Annals Int Med.* 2014; Holmberg SD et al. *NEJM*. 2013.

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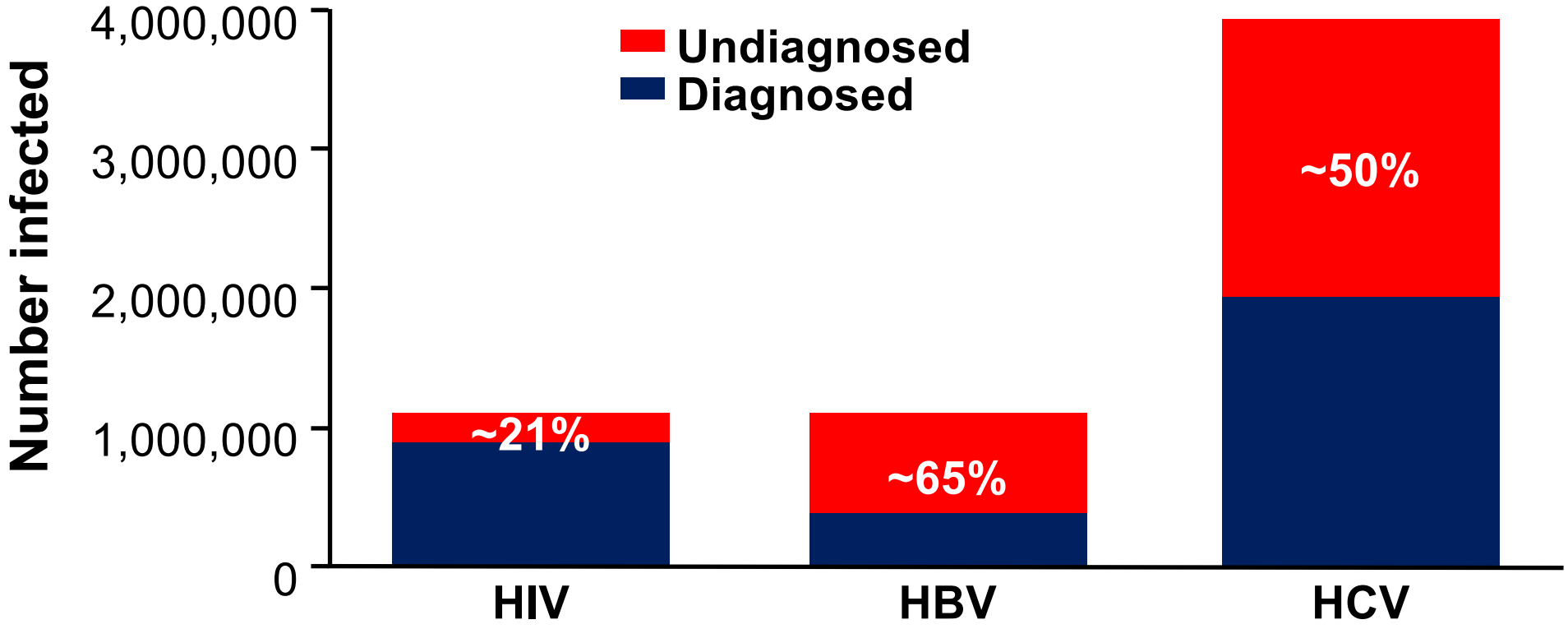
Hepatitis C Is Under Diagnosed in the United States



HCV is the most common chronic infection and the leading cause of infection related death in the US

HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus.

Smith BD et al., *MMWR Recomm Rep.* 2012; 61: 1-32; Denniston MM et al., *Hepatology*. 2012; 55: 1652-61.

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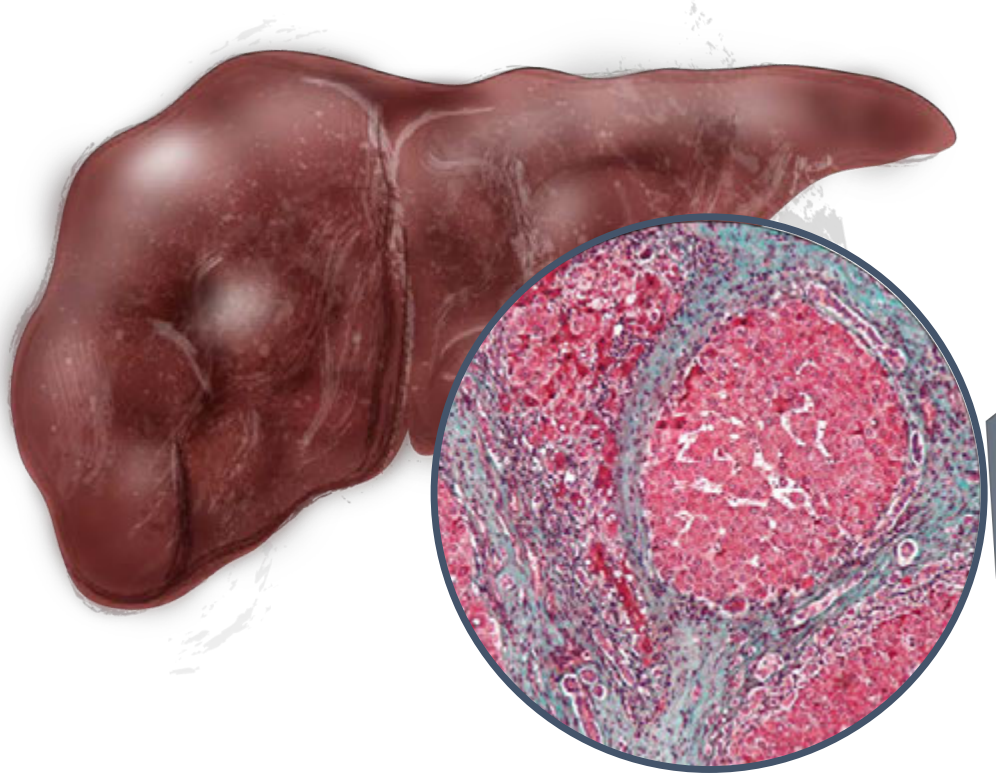
Cirrhosis Is The Final Pathway for Most Chronic Liver Diseases



Decompensation/ liver failure

Hepatocellular carcinoma

Liver transplantation

Accumulation of collagen deposition= fibrosis → cirrhosis

Histology image obtained from http://en.wikipedia.org/wiki/Cirrhosis. Accessed March 26, 2018.

Ge PS, Runyon BA. *N Engl J Med*. 2016;375:767-777.

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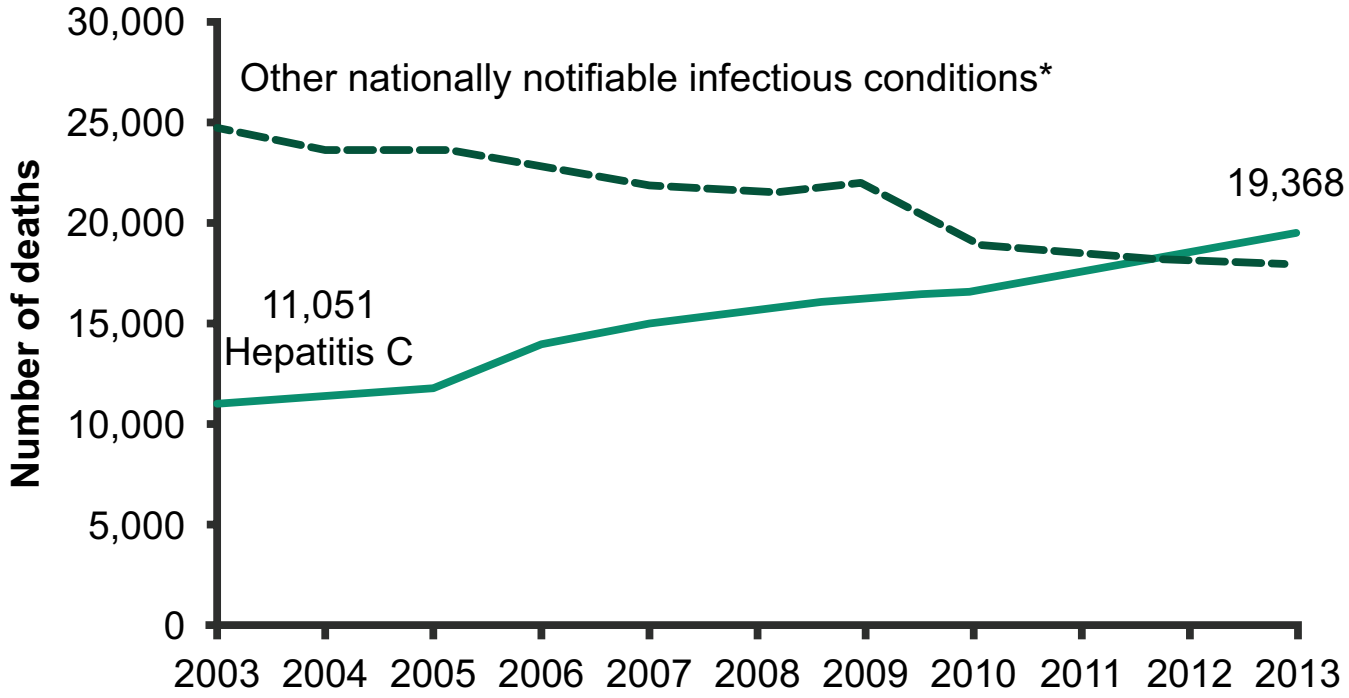
Mortality Associated with Hepatitis C Virus in the United States



*National multiple-cause-of-death (MCOD) data from 2003 to 2013 to evaluate trends in HCV–related mortality in the US compared to deaths associated with 60 other nationally notifiable infectious conditions reported to the CDC.

Ly KN et al. *Clin Infect Dis*. 2016.

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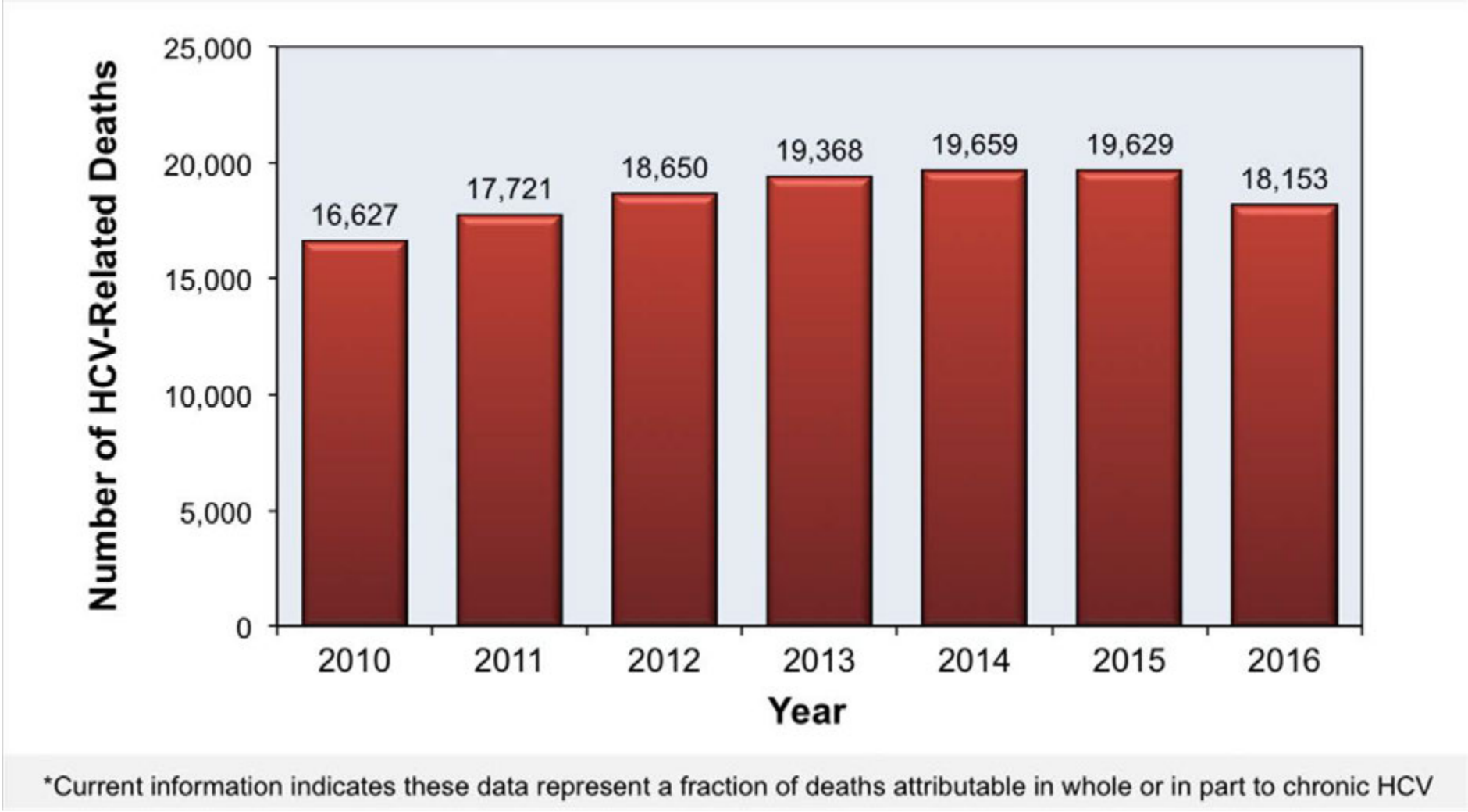
Annual Deaths Associated with CHC…Starting to Make Progress



Centers for Disease Control and Prevention. Division of Viral Hepatitis. Statistics and Surveillance.

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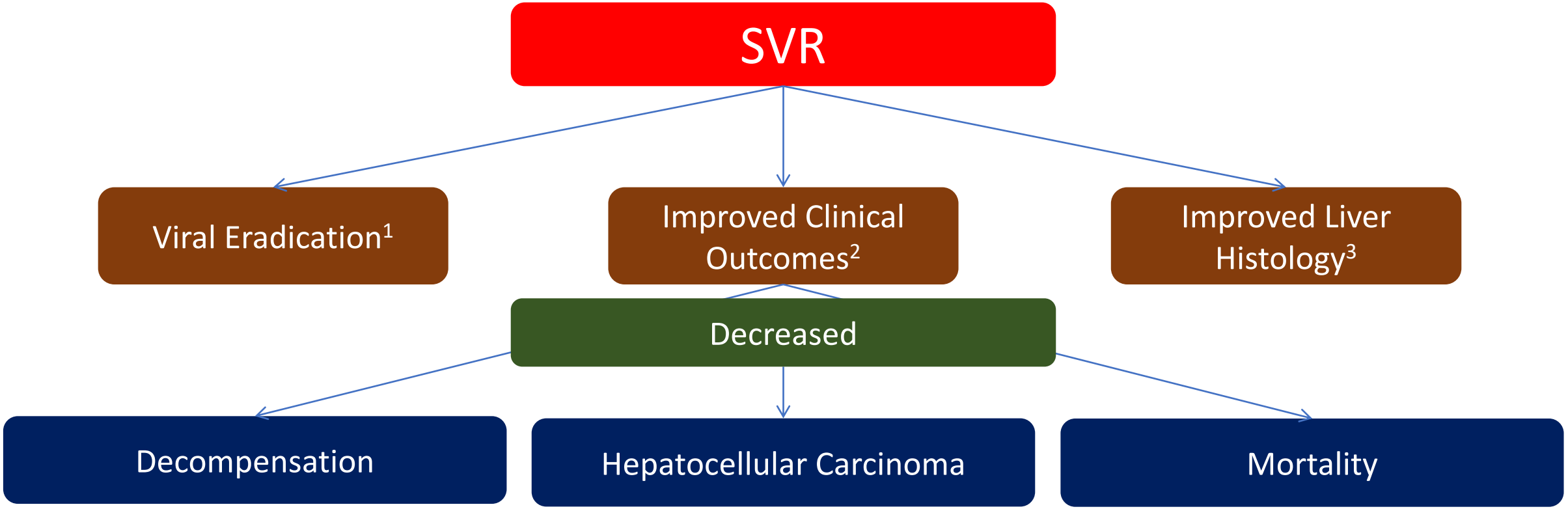
Direct-acting Antiviral Agents (DAAs) for Chronic Hepatitis C

Sustained Virologic Response (SVR) = Cure

- Unlike HIV and HBV infection, HCV infection is a curable disease
  - HCV does not archive its genome in the nucleus and does not integrate in the host DNA
- What does cure mean
  - Undetectable HCV RNA 12 weeks after completion of antiviral therapy for chronic HCV infection
  - SVR12 is almost invariably durable
- What it doesn’t mean
  - Patients who continue risk behaviors may ultimately become reinfected (no immunity from prior exposure)

Ghany MG, et al. *Hepatology*. 2009;49(4):1335-1374.

Sustained Virologic Response (SVR) Leads to Improved Outcome



1. Maylin S, et al. *Gastroenterology*. 2008;135:821-829; 2. Poynard T, et al. *Gastroenterology*. 2002;122:1303-1313;
3. Veldt BJ, et al. *Ann Intern Med*. 2007;147:677-684.

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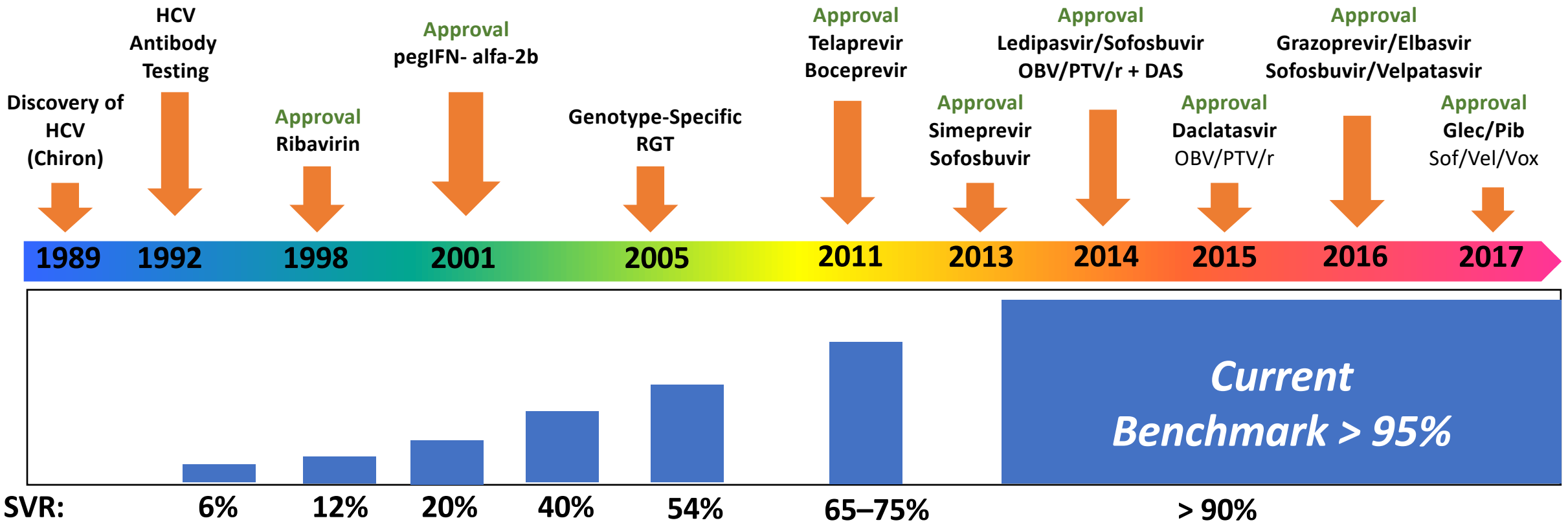
Timeline of HCV Therapy



pegIFN-alfa 2b = peg-interferon alfa-2b; RGT = response-guided therapy; OBV/PTV/r + DAS = ombitasvir/paritaprevir and ritonavir + dasabuvir (or 3D).

Houghton M. *Liver Int*. 2009;29(Suppl 1):82-88; Carithers RL, et al. *Hepatology*. 1997;26(3 Suppl 1):S83-S88; Zeuzem S, et al. *N Engl J Med*. 2000; 343(23):1666-1672; Poynard T, et al. *Lancet*. 1998;352(9138):1426-1432; McHutchison JG, et al. *N Engl J Med*. 1998;339(21):1485-1492; Lindsay KL, et al. *Hepatology*. 2001;34(2):395-403; Fried MW, et al. *N Engl J Med*. 2002;347(13):975-982; Manns MP, et al. *Lancet*. 2001;58(9286):958-965; Poordad F, et al. *N Engl J Med*. 2011;364(13):1195-1206; Jacobson IM, et al. *N Engl J Med*. 2011;364(25):2405-2416; Lawitz E, et al. *N Engl J Med*. 2013; 368(20):1878-1887; Jacobson IM, et al. *Lancet*. 2014;384(9941):403-413; Afdhal N, et al. *N Engl J Med*. 2014;370(20):1889-1898; Nelson DR, et al. *Hepatology*. 2015; 61(4):1127-1135; Zeuzem S, et al. *Ann Intern Med*. 2015;163(1):1-13.

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Recommended DAA Combinations

NS3/4A Protease Inhibitor	Nucleotide NS5B Polymerase Inhibitor	Non-Nucleoside NS5B Polymerase Inhibitor	NS5A Replication Complex Inhibitor	Other
	Sofosbuvir			RBV
Simeprevir	Sofosbuvir			± RBV
	Sofosbuvir		Ledipasvir	± RBV
	Sofosbuvir		Daclatasvir	± RBV
Paritaprevir		Dasabuvir	Ombitasvir	± RBV
Grazoprevir			Elbasvir	± RBV
	Sofosbuvir		Velpatasvir	± RBV
Voxilaprevir	Sofosbuvir		Velpatasvir	
Glecaprevir			Pibrentasvir	

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Voxilaprevir	Sofosbuvir		Velpatasvir	
Glecaprevir			Pibrentasvir	

Treatment Indications (HCVguidelines.org)

		SOF/VEL		GLE/PIB
Genotype		1-6		1-6
Fibrosis Status		F0-F4		F0-F4
Duration (weeks)		12		8-16
Treatment experience		Naïve and experienced		Naïve and experienced

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Treatment Indications (HCVguidelines.org)

	SOF/LDV	SOF/VEL	SOF/VEL/VOX	GLE/PIB
Genotype	1, 4, 5, 6	1-6	1, 3, 4, 5, 6	1-6
Fibrosis Status	F0-F4	F0-F4	F0-F4	F0-F4
Duration (weeks)	8-24	12	12	8-16
Treatment experience	Naïve and experienced	Naïve and experienced	Treatment experienced	Naïve and experienced

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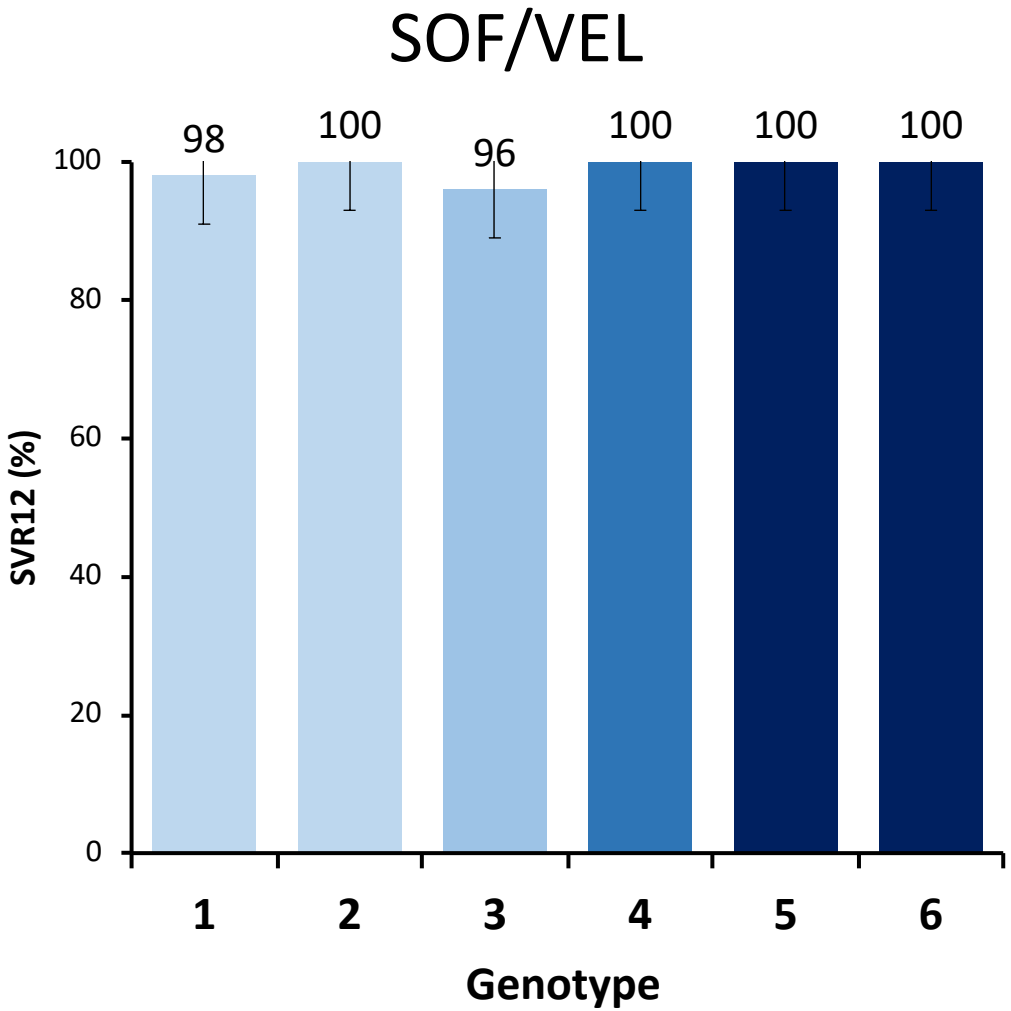
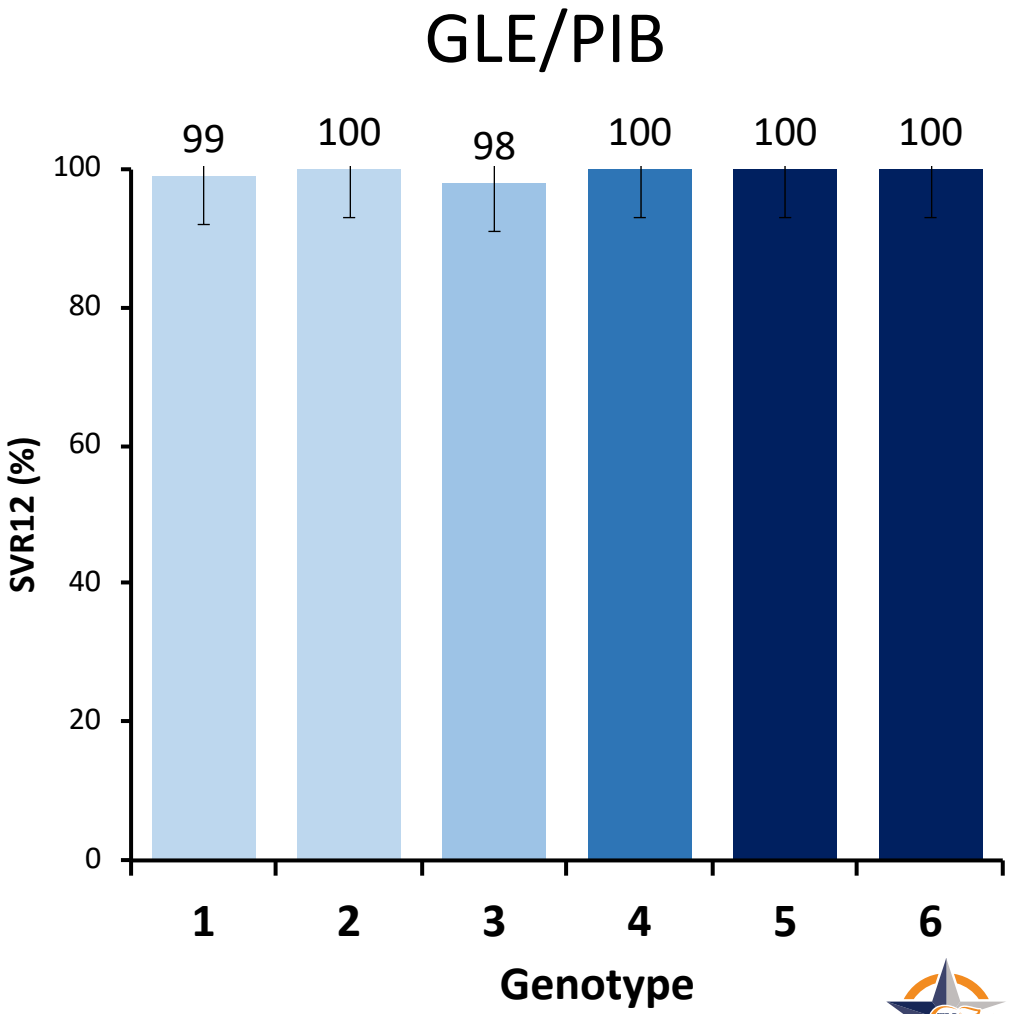
Pangenotypic Therapies in Genotype 1-6 With Compensated Cirrhosis (Not Head to Head)





Data adapted from ASTRAL, POLARIS-2, EXPEDITION-1 and SURVEYOR-4 clinical trials

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Special Populations: Cure for Everyone?

Patient Population	Treatment Considerations	Response Rates
HIV Co-infection	SOC, drug-drug interactions	>95%
End-stage renal disease	Non-sofosbuvir* based regimens	>95%
Cirrhosis	SOC, extended duration, ribavirin^	>95%
Decompensated cirrhosis	Non-PI based regimens#, extended duration, ribavirin*	85-100%
Post-transplant	Drug-drug interactions	>95%
DAA failure	Resistance testing-guided, next gen and triple DAA regimens, ribavirin^	>90%
Pregnancy	No data, not recommended	--

SOC = standard of care; *Sofosbuvir not recommended for eGFR<30 ml/min; ^extended duration and/or the addition of ribavirin recommended depending on treatment history, genotype and ribavirin tolerance; #protease inhibitors contraindicated in CTP B and C

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Real-world Experience Right Here….TLI

- Prospective, observational, real-world study
- DAA choice at the discretion of the treating physician
- 875 patients included between January 2015-April 2017

Loo N. et al, *Clinical Journal of Gastroenterology*, 2019, Submitted.

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Characteristics	Patients (N=875)
Age; mean (SD)	58 (10.5)
Male; N (%)	499 (57)
Race	
White; N (%)	704 (80.5)
Black; N (%)	84 (9.6)
Other; N (%)	87 (9.9)
Ethnicity	
Hispanic; N (%)	379 (43.3)
Non-Hispanic; N (%)	496 (56.7)
Genotype	
1a; N (%)	525 (60)
1b; N (%)	192 (21.9)
2; N (%)	74 (8.5)
3; N (%)	65 (7.4)
4/5/6 multiple; N (%)	19 (2.2)
Viral load (IU/mL); mean	3,925,323
Prior HCV treatment; N (%)	219 (25)
Fibrosis Stage	
F0; N (%)	70 (8.0)
F1; N (%)	164 (18.7)
F2; N (%)	192 (21.9)
F3; N (%)	118 (13.5)
F4; N (%)	293 (33.5)
Unknown; N (%)	38 (4.3)
Diabetes; N (%)	182 (20.8)
HIV/HCV coinfected; N (%)	21 (2.4)

Loo N. et al, *Clinical Journal of Gastroenterology*, 2019, Submitted.

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98.6 % (863/875) patients were cured

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Loo N. et al, *Clinical Journal of Gastroenterology*, 2019, Submitted.

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HCV Problem Solved, Right?

Acute Hepatitis C on the Rise

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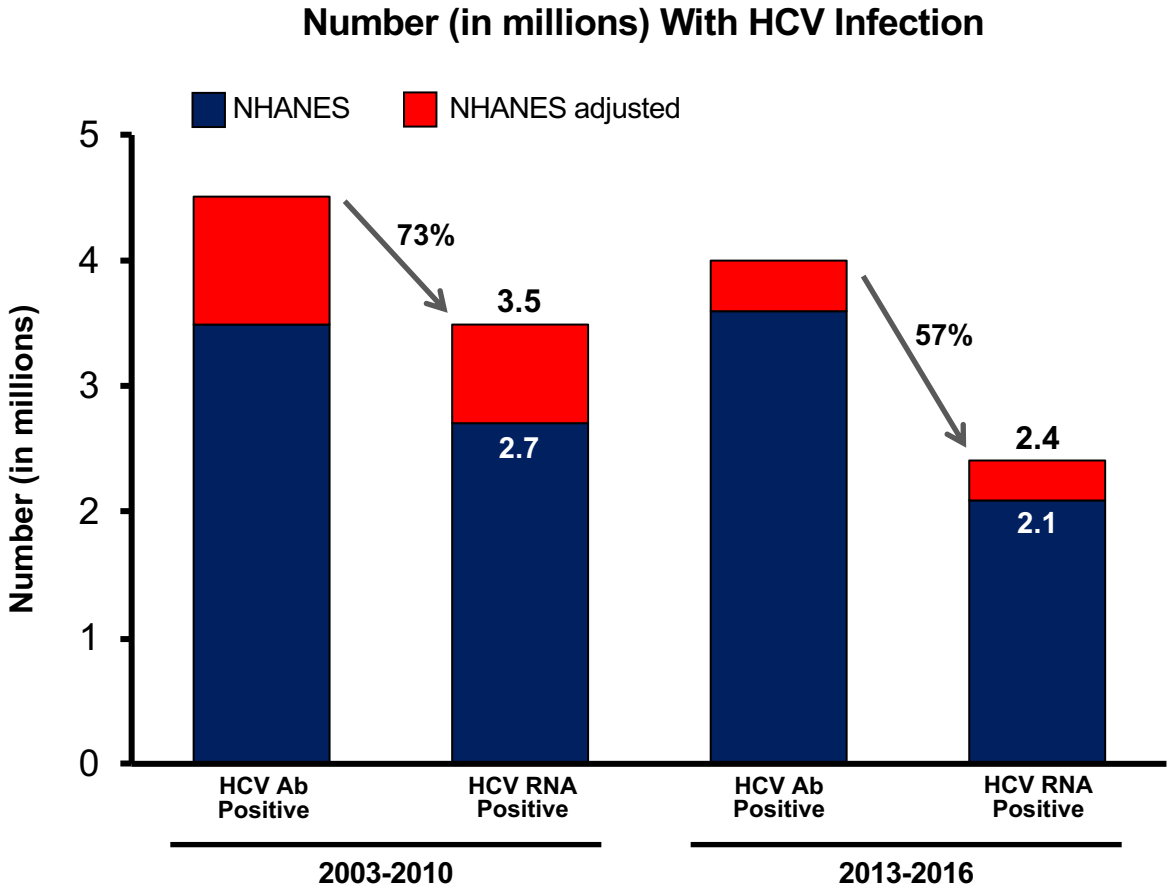
CDC (2013-2016): Estimated HCV Prevalence Among Adults in the United States

- HCV antibody positive (including past and current infection)
  - Number: 4.1 million (95% CI 3.4-4.9)
  - Prevalence: 1.7% (95% CI 1.4-2.0)
- HCV RNA positive (including current infection)
  - Number: 2.4 million (95% CI 2.0-2.8)
  - Prevalence: 1.0% (95% CI 0.8-1.1)



Estimated adult US population in 12/2016: 245 million.

Datasets analyzed:

National Health and Nutrition Examination Survey (noninstitutionalized civilian population). Combination of literature reviews and population size estimation approaches (incarcerated people, unsheltered homeless people, active-duty military personnel, and nursing home residents).

Hofmeister MG, et al. *Hepatology.* 2018;Nov 6. [Epub ahead of print].

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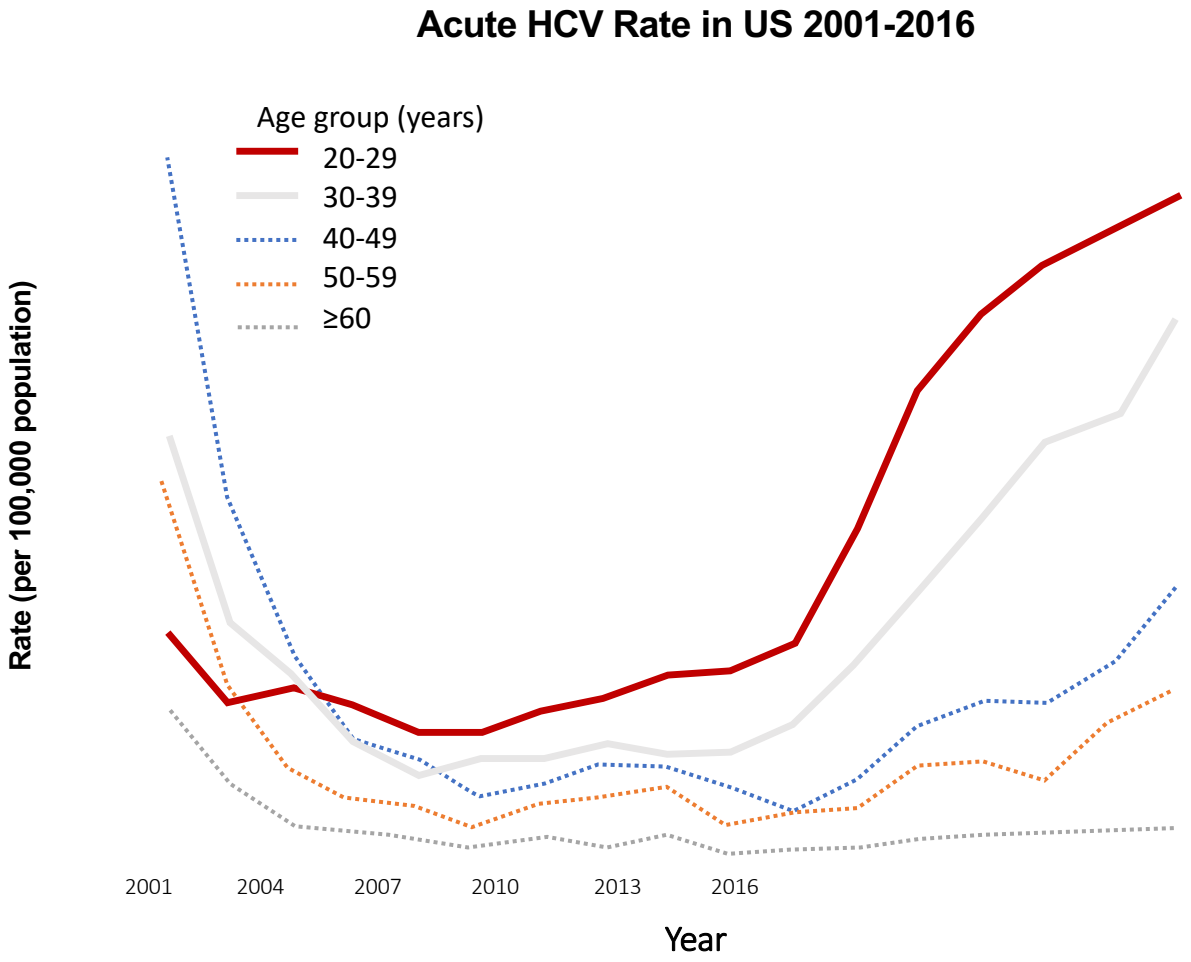
Changing Trends in Acute HCV in the US (2001-2016)

- New acute HCV infection in 2016
  - Reported cases (n=2967)
  - Estimated (n=41,200 adjusted for under-ascertainment and under-reporting)
- 3.5-fold increase in new cases since 2010
  - Reflects new infections associated with rising rates of injection-drug use



CDC. Surveillance for viral hepatitis - United States, 2016. https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm.

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Populations at Risk

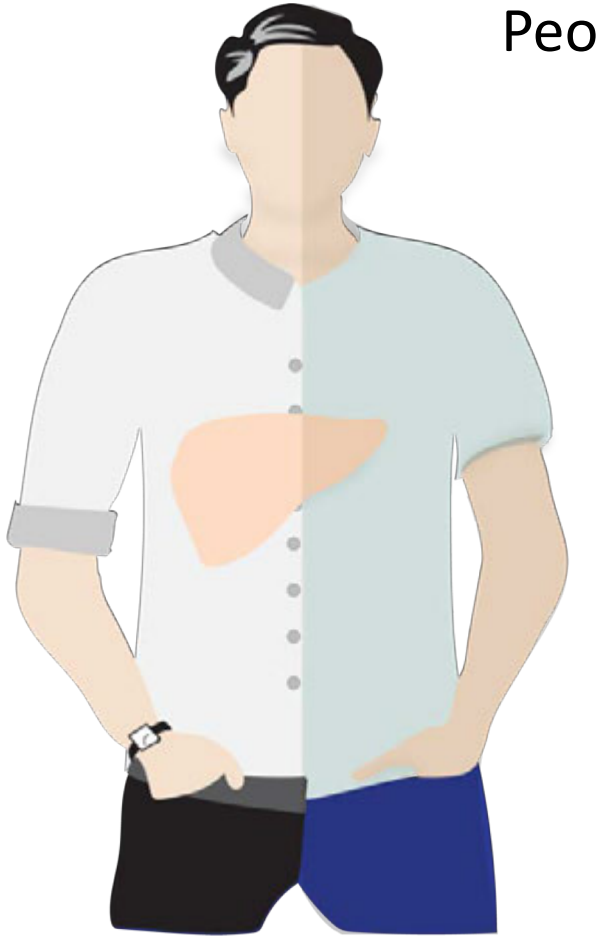
Baby Boomers (born 1945-1965)

1960s
Up to 300,000 cases of acute HCV per year; risk of exposure via blood transfusion up to 33%

1970s
Volunteer donor system reduces risk of exposure via blood transfusion

1989
HCV discovered

1992
Widespread introduction of HCV antibody testing



People Who Inject Drugs (PWID)

30-70% prevalence

Alter HJ. *Nat Med*. 2000;6:1082-1086.

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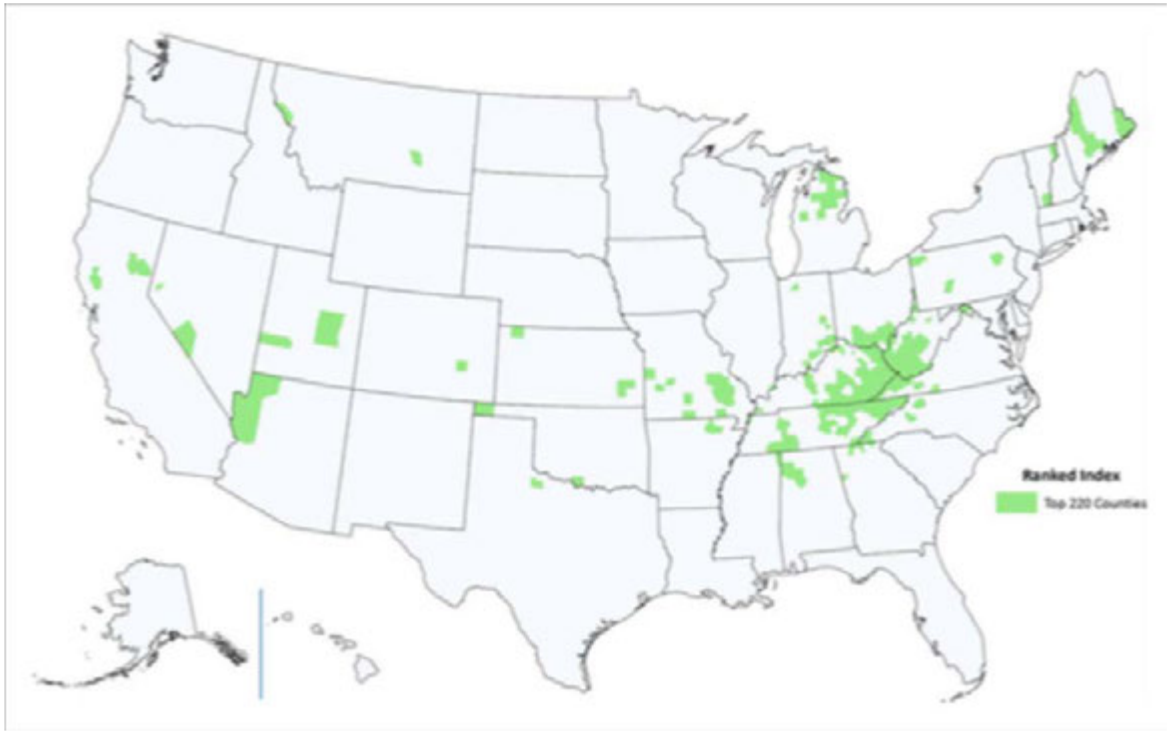
Geographic Areas Most at Risk for HCV

Counties Vulnerable to Outbreaks of HIV and Hepatitis C



CDC report identified >220 counties vulnerable to outbreaks of HIV and HCV among people who inject drugs

Risk Factors

- Unemployment rates
- Overdose deaths
- Prescription opioid sales

Van Handel MM. *J Acquir Immune Defic Syndr*. 2016;73:323.

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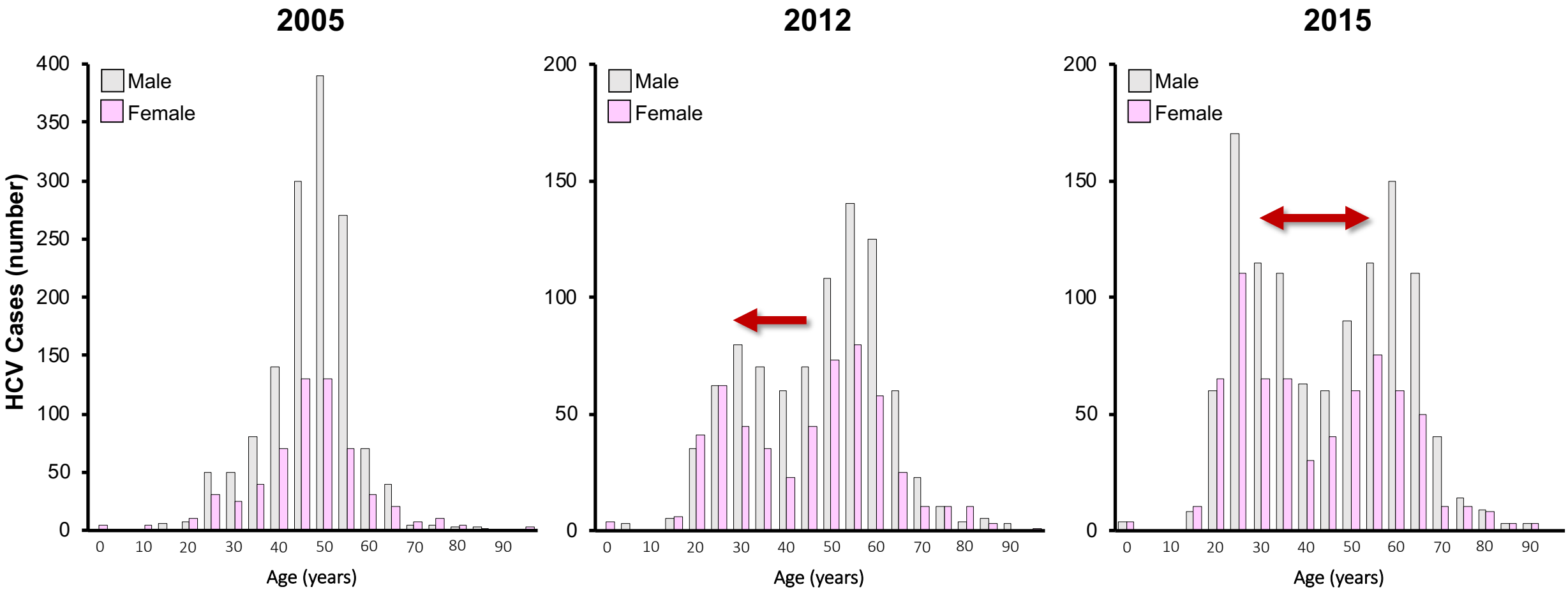
HCV No Longer a Disease Limited to Baby Boomers



Data for New York State (excluding NYC).
https://www.health.ny.gov/statistics/diseases/communicable/index.htm.

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WHO Goal: Global Elimination of Viral Hepatitis

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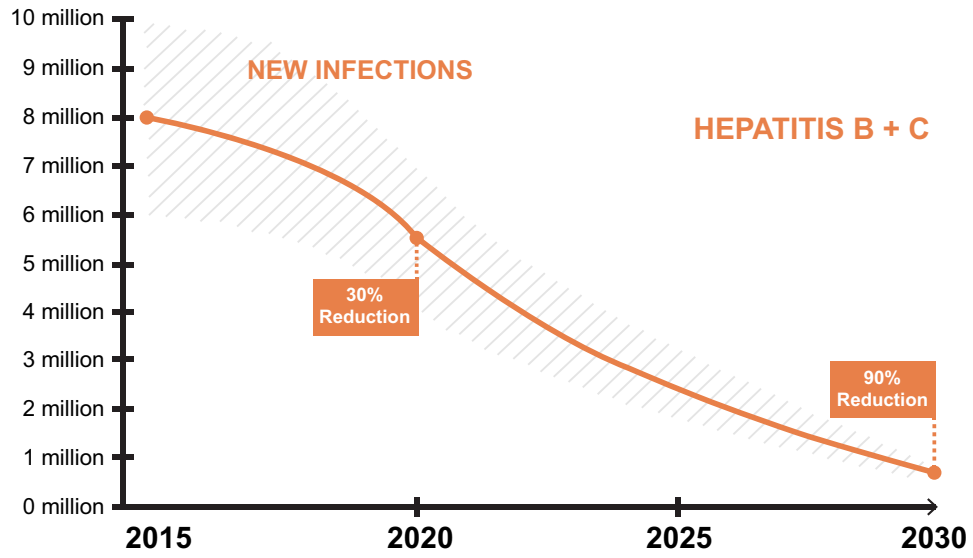
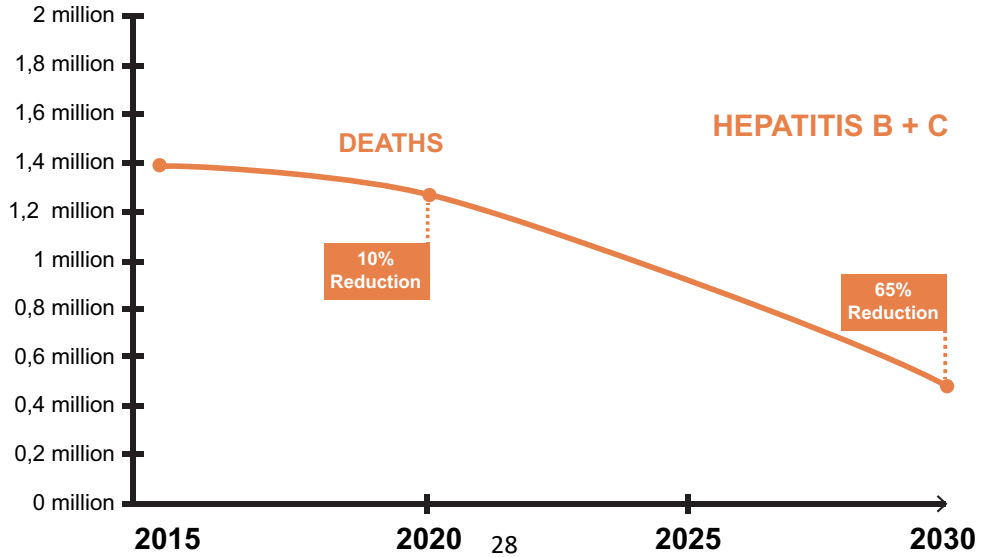
Global Health Sector Strategy:
Eliminate Viral Hepatitis as a Major Public Health Threat by 2030

Impact Targets

Reduction in new infections by 90%



Reduction in deaths by 65%



Programmatic Targets

90% **of people infected are** diagnosed	**80%** **of people diagnosed are treated**	**90%** **coverage of BD and B3 doses (PAHO: 95%)**	**100%** **of blood products are safe**	**90%** **of injections in health facilities are safe**

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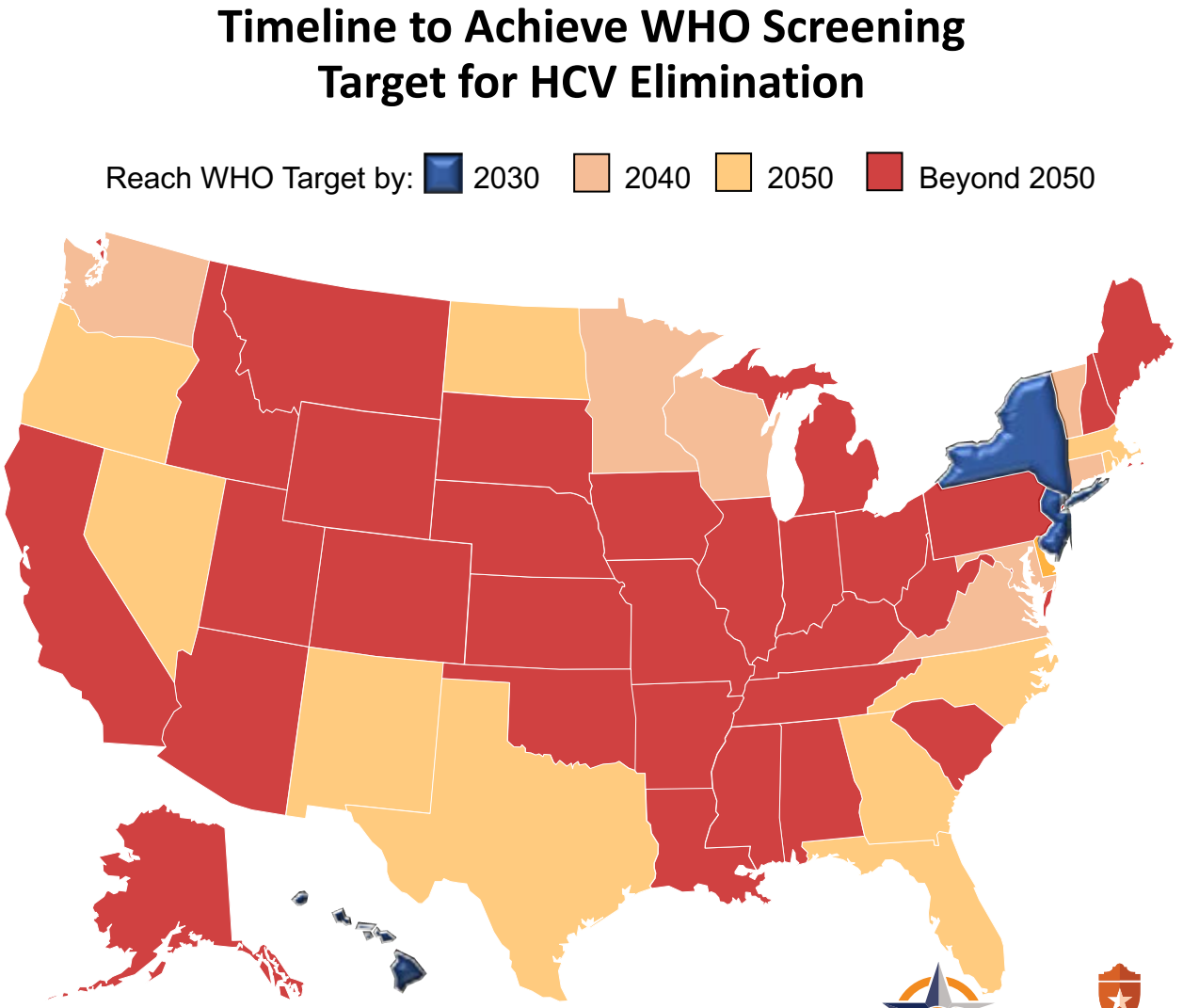
Effectiveness of HCV Screening in the US (2010-2016)

- In the US, to meet the 2030 diagnosis targets, this means diagnosing at least
  - 110,000 cases/year until 2020
  - 89,000 cases/year between 2020-2024
  - >70,000 cases/year between 2025-2030
- At the current screening rate, 92% of US states are not on target to meet WHO screening goals of HCV elimination by 2030



Claims data for HCV Ab screening from a single large commercial payer (CPT and ICD-9 codes):
Screened (n=1,056,583); not screened (n=1,243,581).
Factors that increased the odds of getting screened: female gender, Medicare, presence of comorbidities.

Mehta D, et al. *J Hepatol.* 2018;68(suppl S1):S177. Abstract THU-113.

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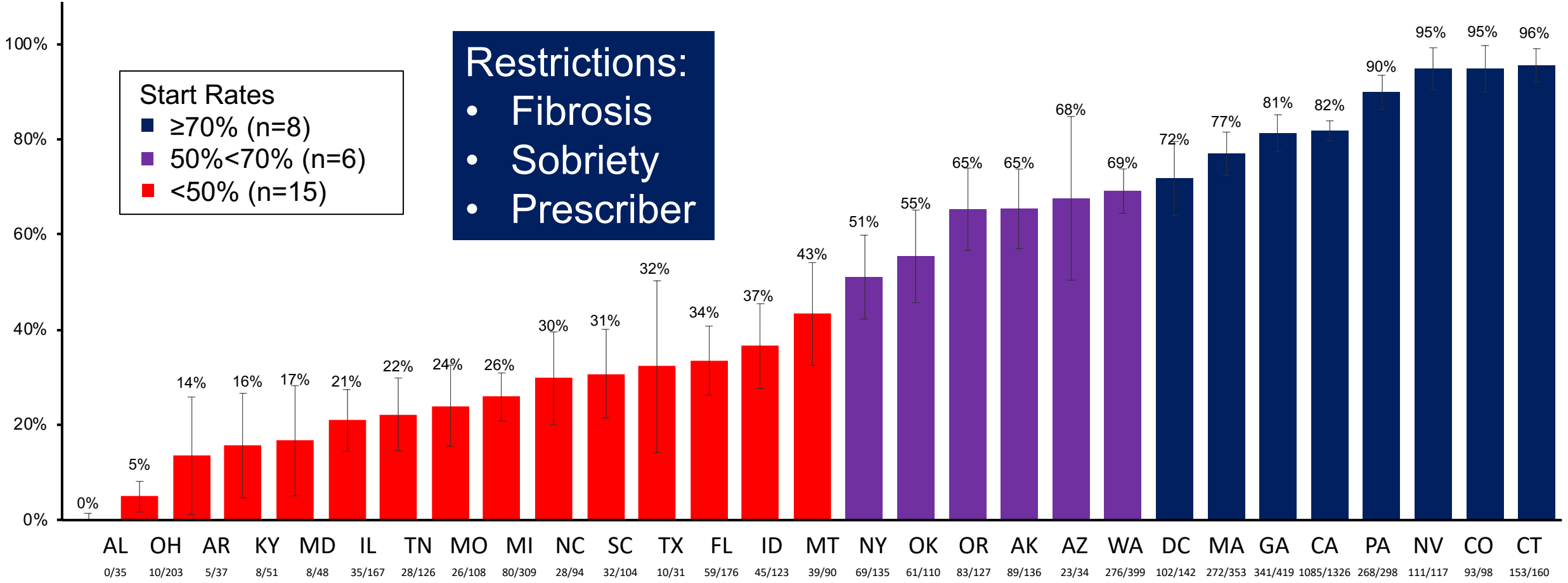
Barriers Persist – Poor Access for Medicaid Patients in the US (Varies by State)



Younossi ZM et al, AASLD 2018, Abstract 147.

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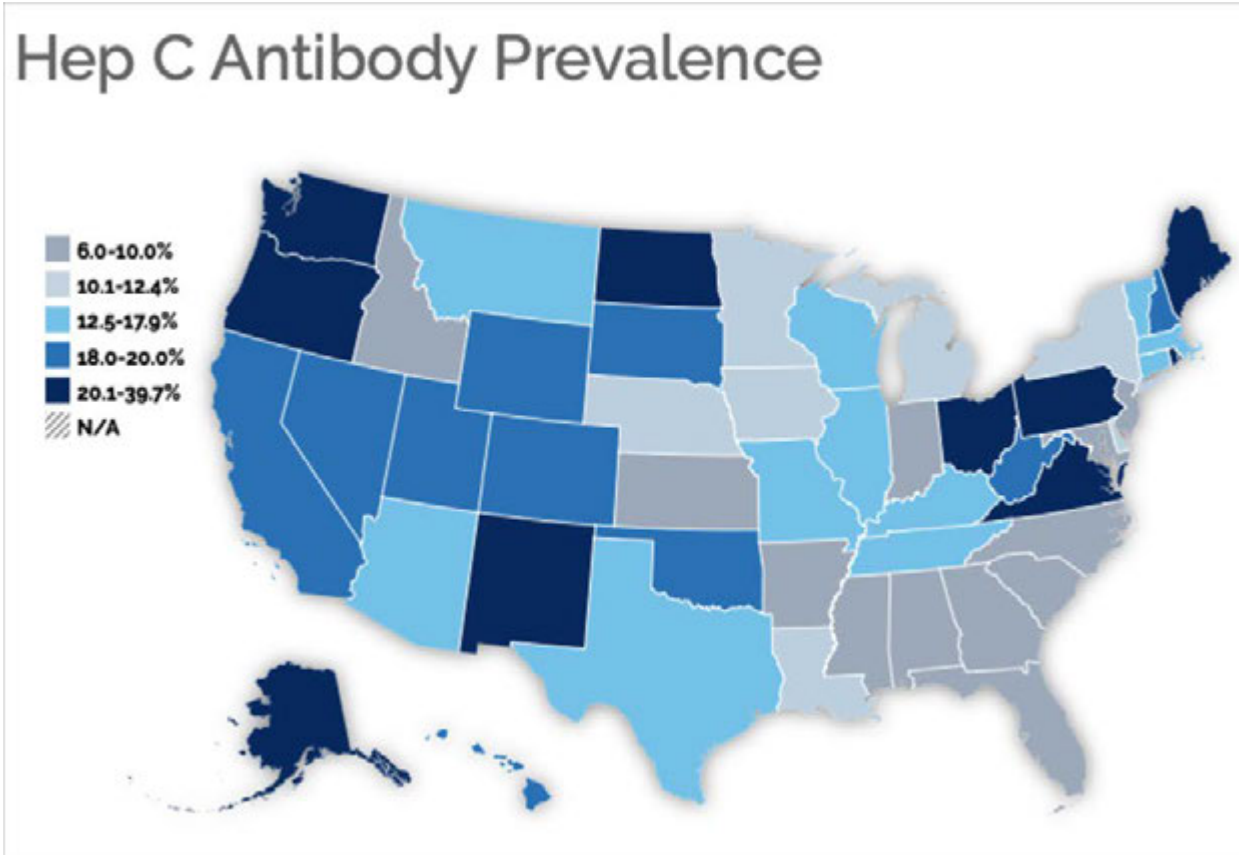
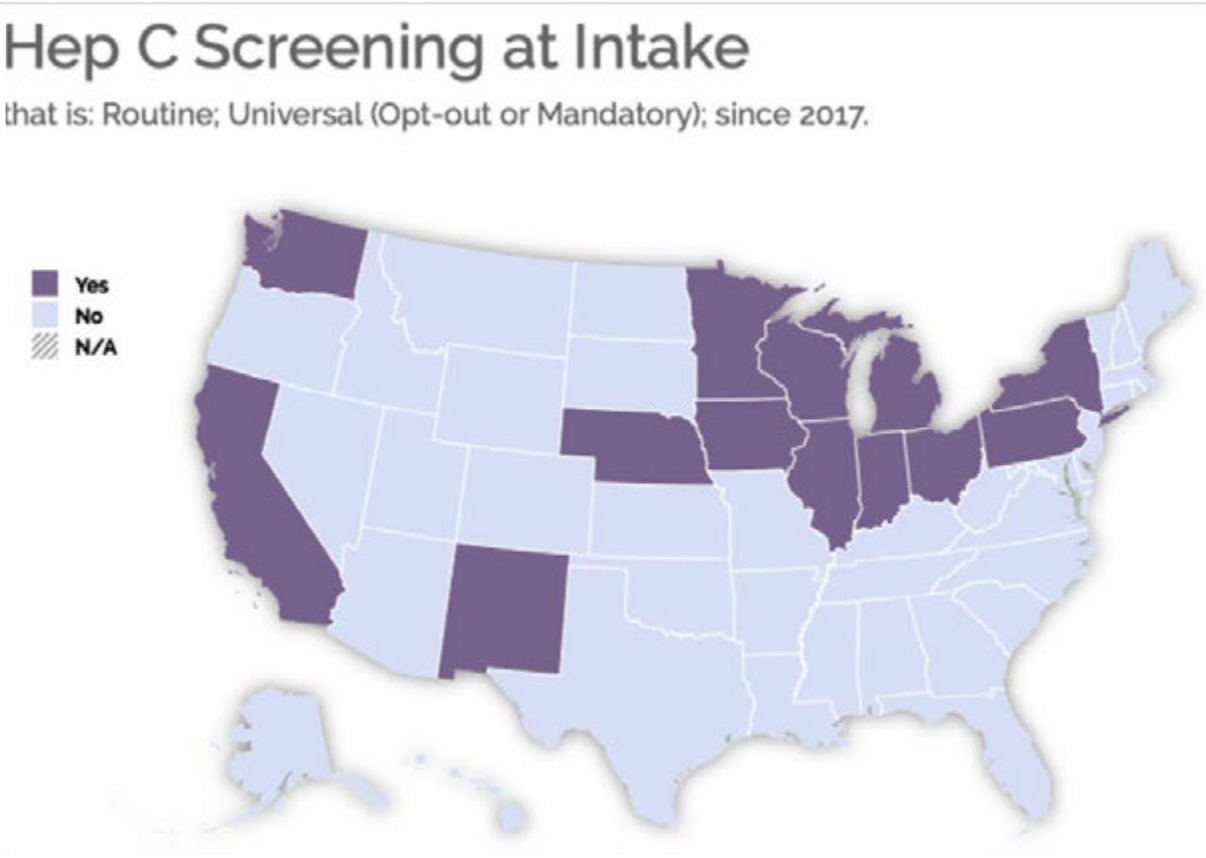
Screening in Enriched Populations: Prisons





www.hepcorrections.org

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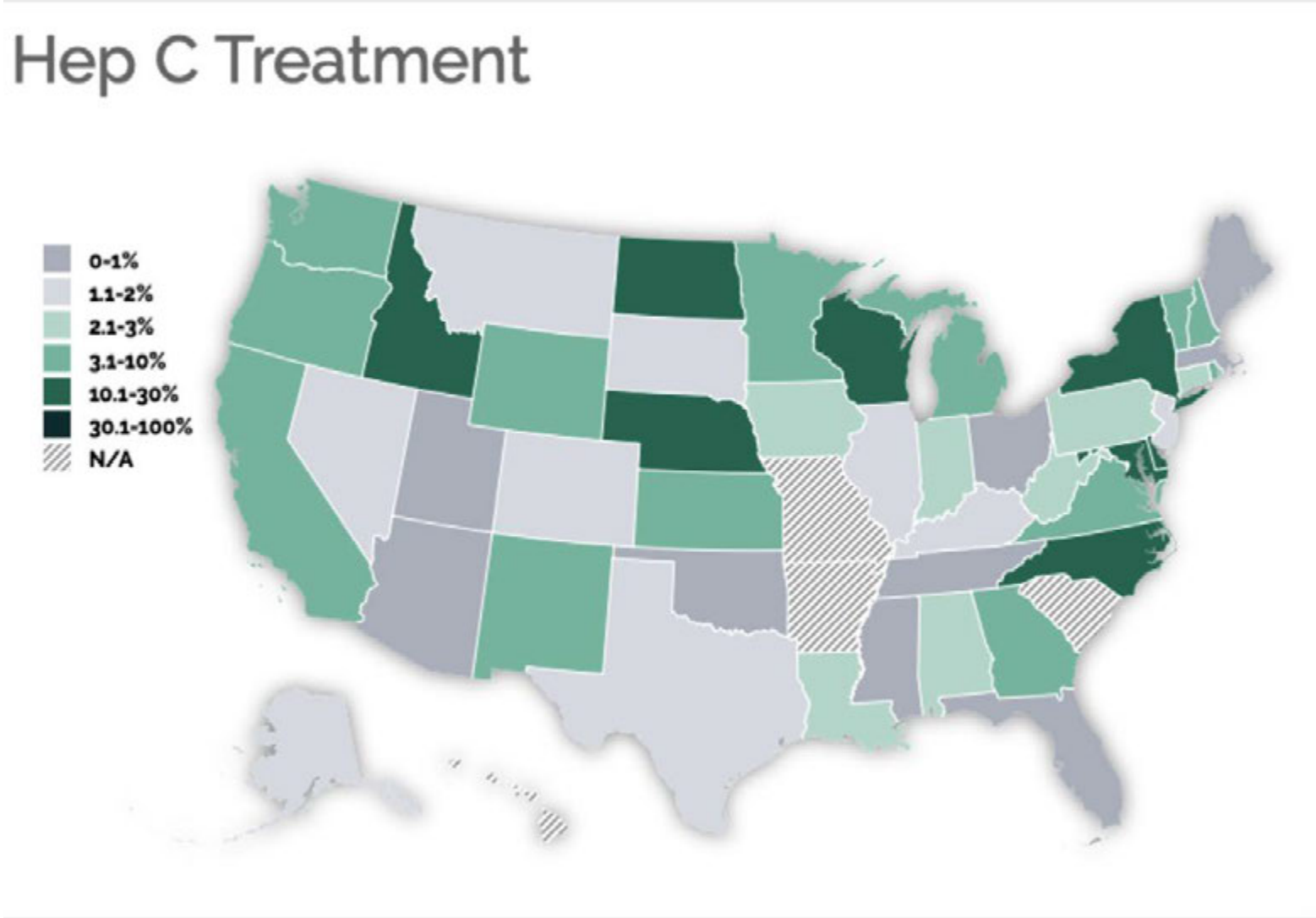
Treatment Rates in Prisons (By State)



www.hepcorrections.org

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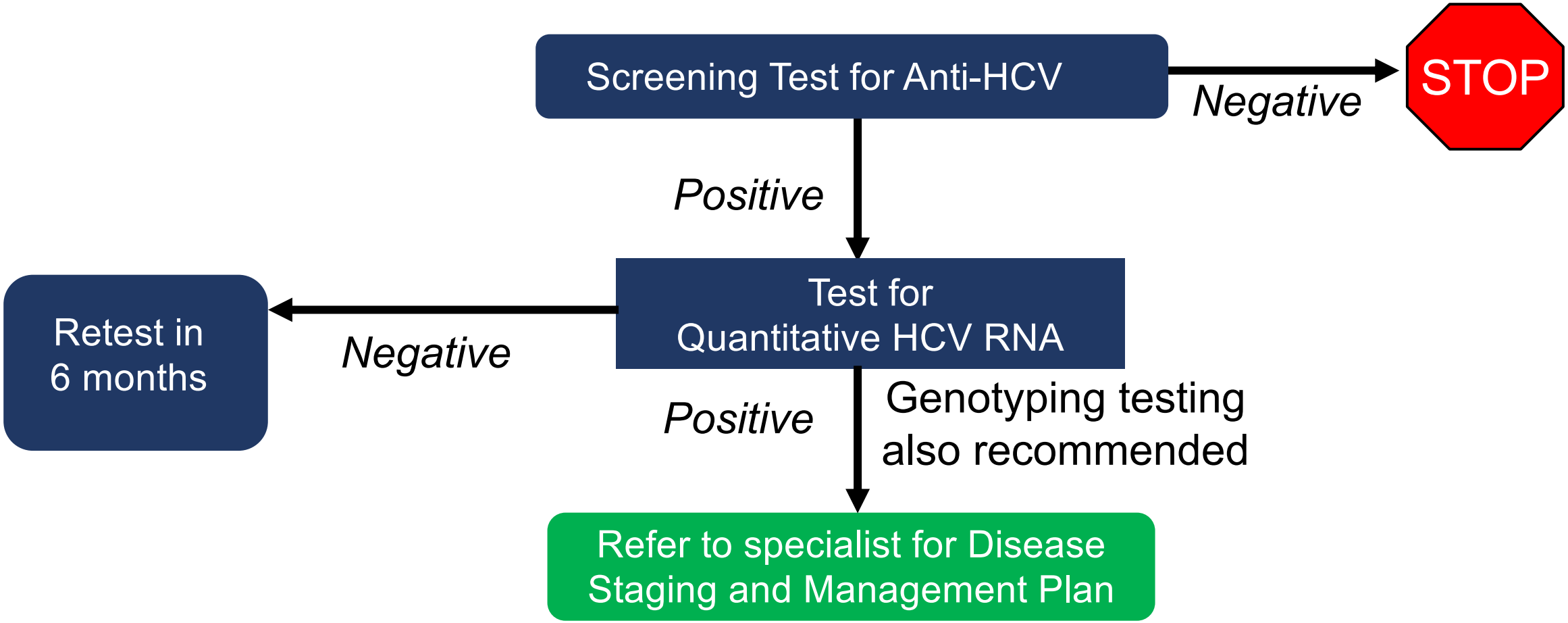
HCV Screening is Straightforward: Algorithm for Screening/Diagnosis



Modified from http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_flow.pdf.
Ghany MG, et al. *Hepatology.* 2011;54(4):1433-1444.

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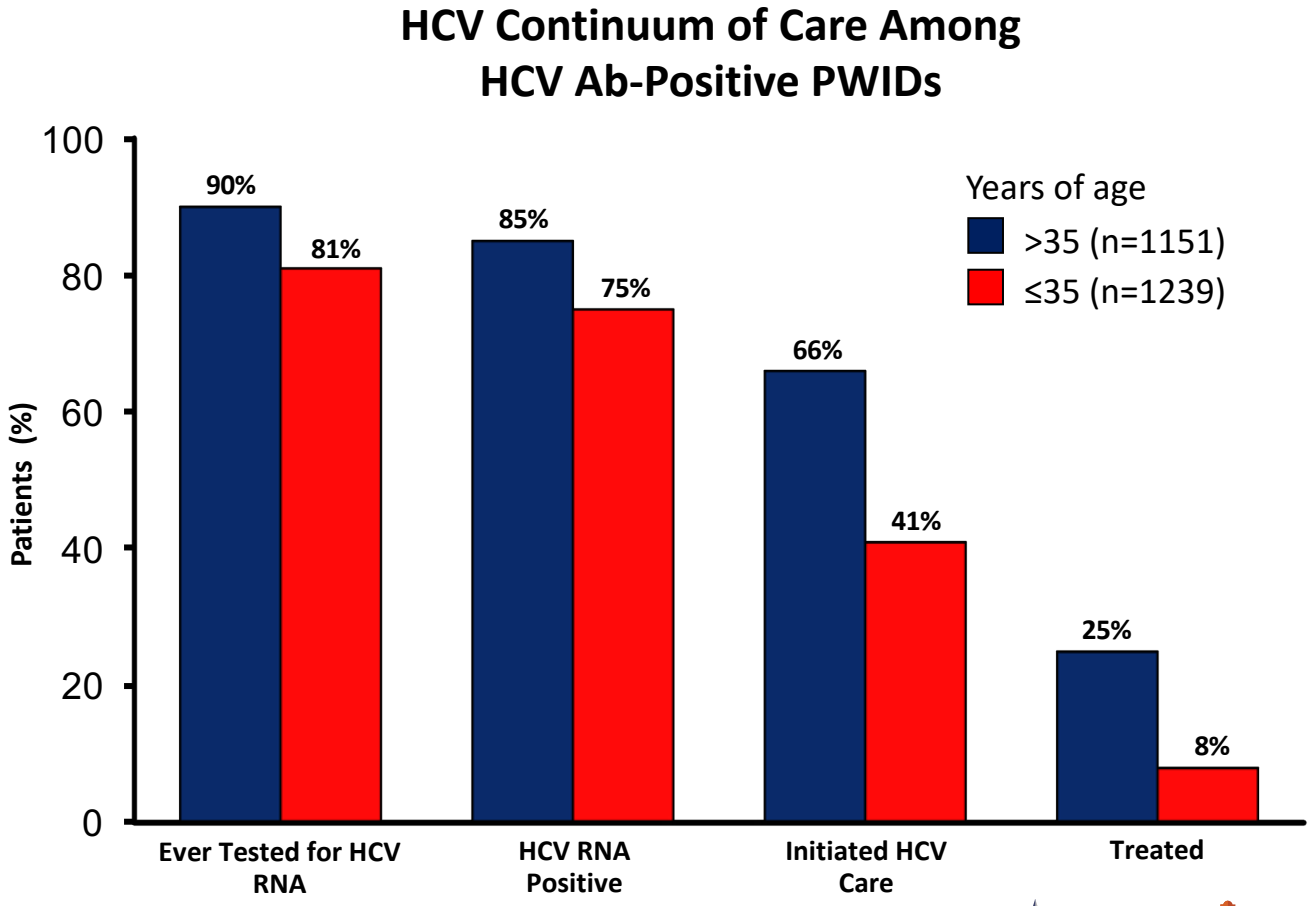
HCV Continuum of Care Among PWIDs: Philadelphia Department of Health

- Random sample of newly reported HCV antibody positive persons (n=29,820; 2013-2017)
  - Interviewed and disclosed being a PWID (n=2390)
- Measurable gaps exist in the HCV continuum of care for PWIDs, especially those ≤35 years of age
  - Among those HCV RNA positive
    - Only 29% and 10% of PWIDs >35 and ≤35 years of age, respectively, were treated
- Need for enhanced navigation to services



Addish E, et al. *Hepatology.* 2018;68:929A-930A. Abstract 1632.

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Overall Management of Your Patient With Hepatitis C

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The AASLD/IDSA Recommendations for Patients with Active HCV

- Abstinence from alcohol
- Evaluation for other conditions that may lead to fibrosis (e.g. HIV, HBV, NASH)
- Evaluation for advanced fibrosis
  - APRI, FIB4, imaging
- Vaccination against HAV, HBV and pneumococcal infection (in patients with cirrhosis)
- Education on avoidance of transmission
- HCC screening (ultrasound every 6 months) for patients with advanced liver disease

Available at: www.hcvguidelines.org. Accessed March 11, 2019.

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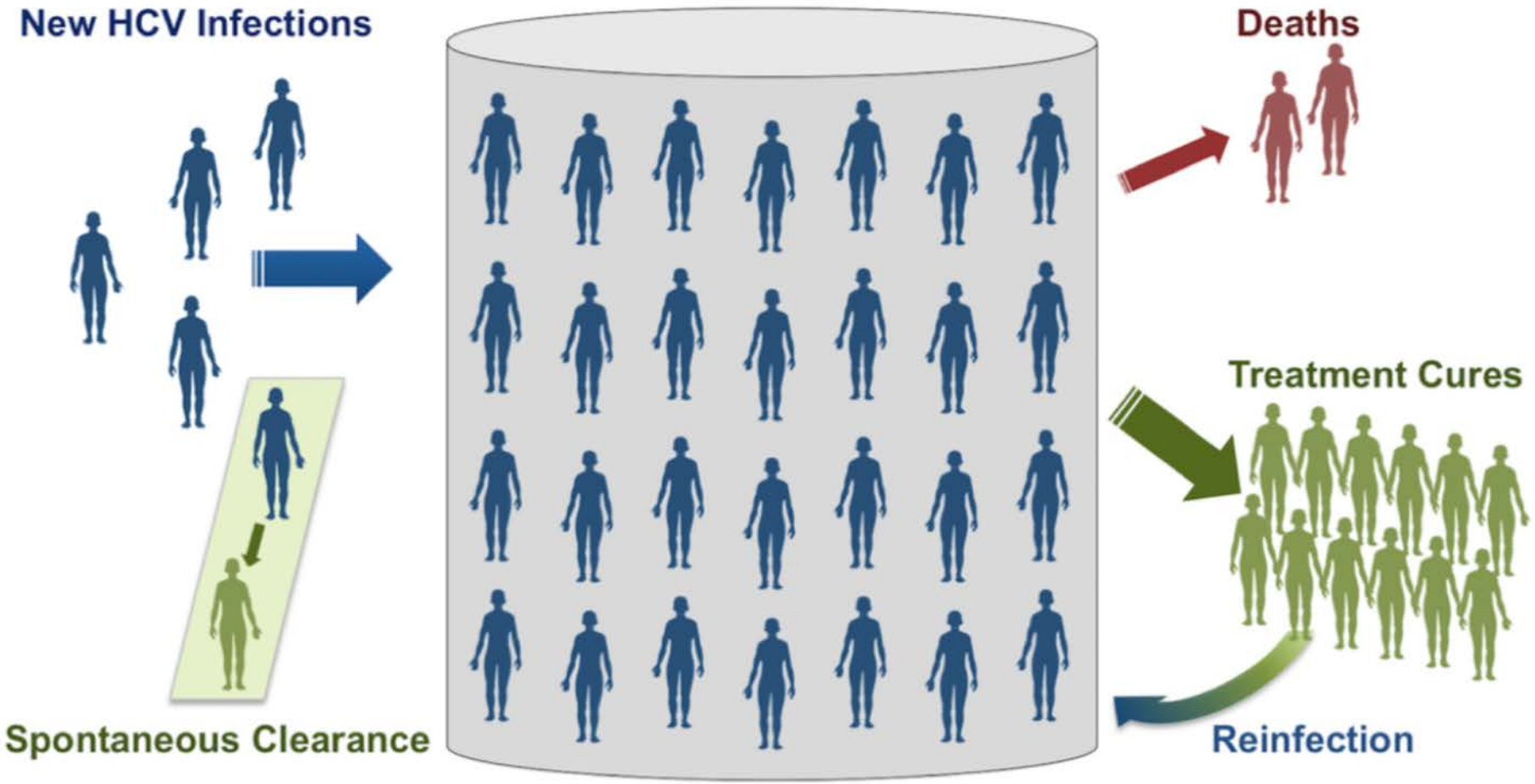
Hepatitis C Prevalence



Source: Illustration by David H. Spach, MD. Centers for Disease Control and Prevention. Division of Viral Hepatitis. Statistics and Surveillance.

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Take Away Points

- Highly safe and effective treatments available offering cure rates >95%.
- Important step now is identifying infected patients and getting them into proper care.
- Any patient of yours that has been to prison should be screened for hepatitis C antibody, regardless of age.
- Hepatitis C global eradication will not happen without aggressive screening, linkage to care and treatment.
- If your patient was cured of HCV but has advanced liver disease, they must still undergo HCC screening every 6 months.

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