

TRIPLE E FOR HCV

**ENGAGEMENT, EDUCATION, AND ERADICATION OF HCV
AMONG PATIENTS WITH SUBSTANCE USE DISORDERS**

Stevan A. Gonzalez, MD MS

Medical Director of Liver Transplantation

Baylor Simmons Transplant Institute

Fort Worth, TX

Educational Objectives

- Review the importance of hepatitis C virus (HCV) screening, diagnosis, and linkage to care
- Describe new developments in HCV that have eliminated many of the previous barriers to the pursuit of HCV therapy in individuals with substance use disorders
- Develop strategies for the engagement of patients with substance use disorders in HCV care

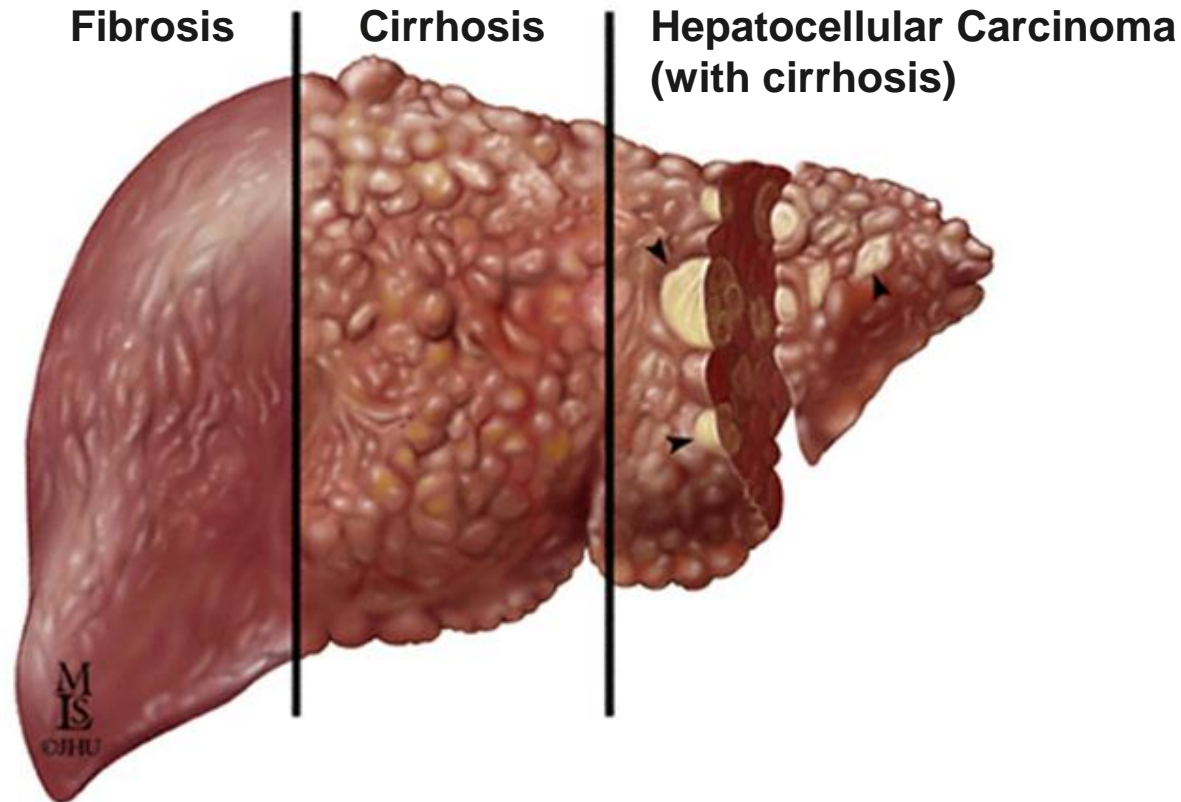
The Burden of Hepatitis C

- 150 million people worldwide; up to 5 million in the US
- Most common blood-borne infection in US
- Leading indication for liver transplantation
- Leading cause of primary liver cancer in US
- No vaccine

Transmission & Liver Disease

- Injection drug use is currently the principle risk factor for transmission
- Spontaneous resolution after exposure occurs in 15-25%
- Chronic disease leading to cirrhosis and liver cancer develops in majority
- Viral eradication (SVR) can be achieved with antiviral therapy
- Eradication = CURE

Chronic HCV Infection May Lead to Liver Disease & Liver Cancer

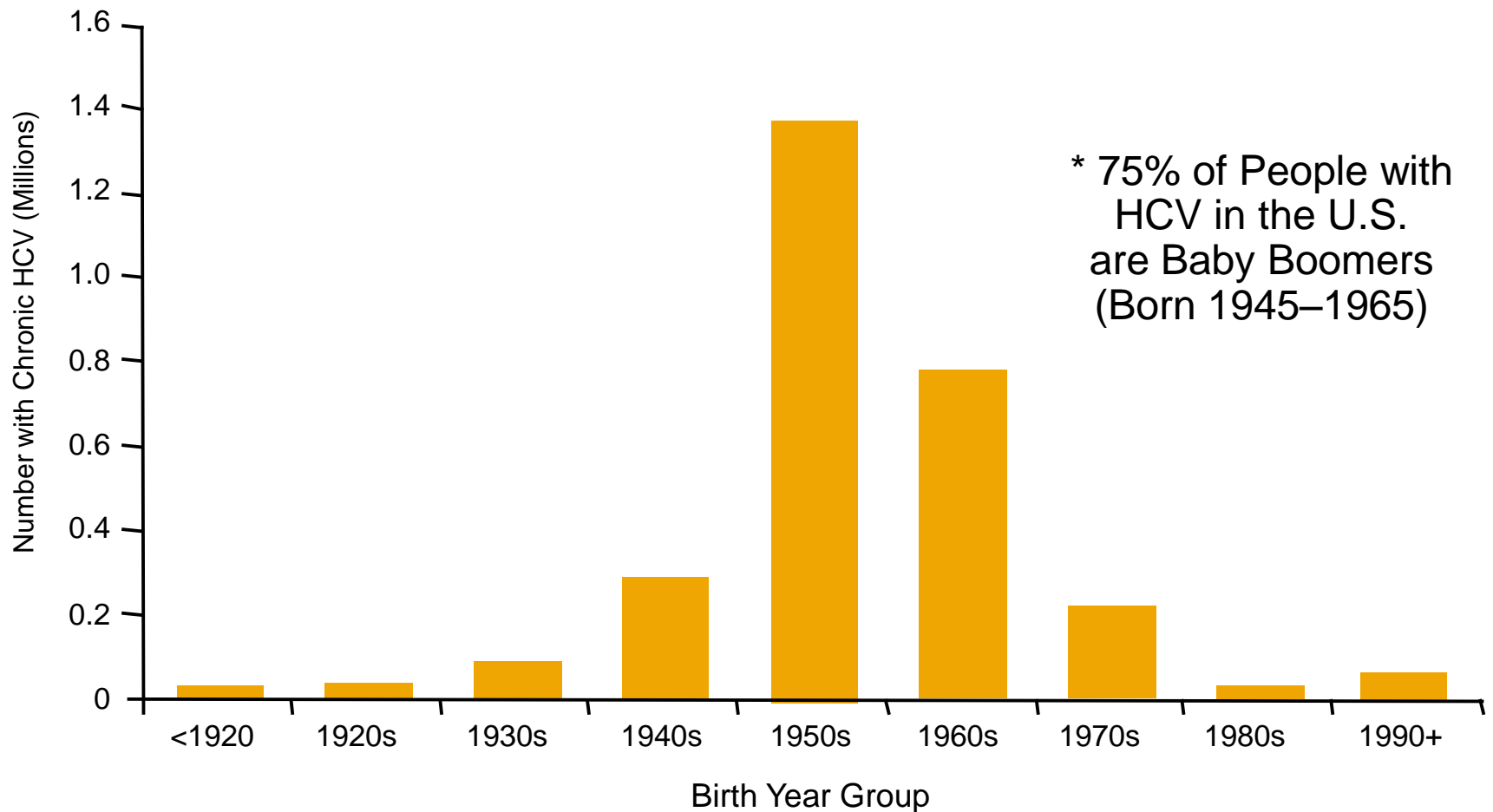


~75% of patients infected with HCV will develop a chronic infection and approximately 65% of those are expected to develop chronic liver disease

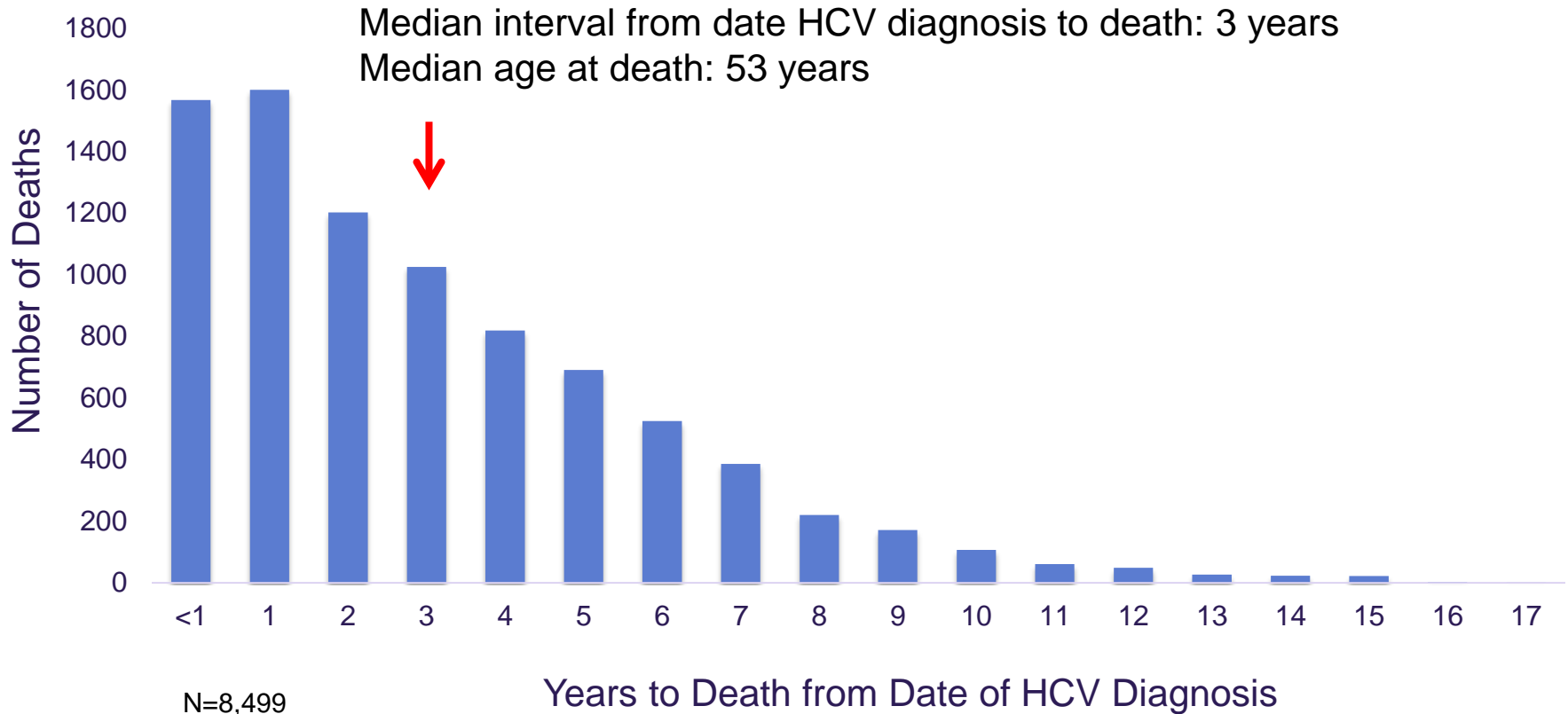
Populations at Risk

- Baby Boomers (born 1945-1965):
 - Hepatitis C virus discovered in 1989
 - Up to 300,000 cases of acute HCV per year during the 1960s
 - Risk of exposure via blood transfusion up to 33% in 1960's; ↓ risk in 1970s with volunteer donor system
 - Widespread introduction of HCV antibody testing in 1992
- People who inject drugs
 - Prevalence among people who inject drugs up to 30-70%

Prevalence of Hepatitis C by Age



Late Diagnosis for Baby Boomers



76,122 HCV diagnoses reported to the MDPH between 1992 and 2009; 8,499 of these reported HCV cases died and are represented in the figure. Data as of 1/11/2011.

Hepatitis C Screening Update

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Recommendations and Reports / Vol. 61 / No. 4

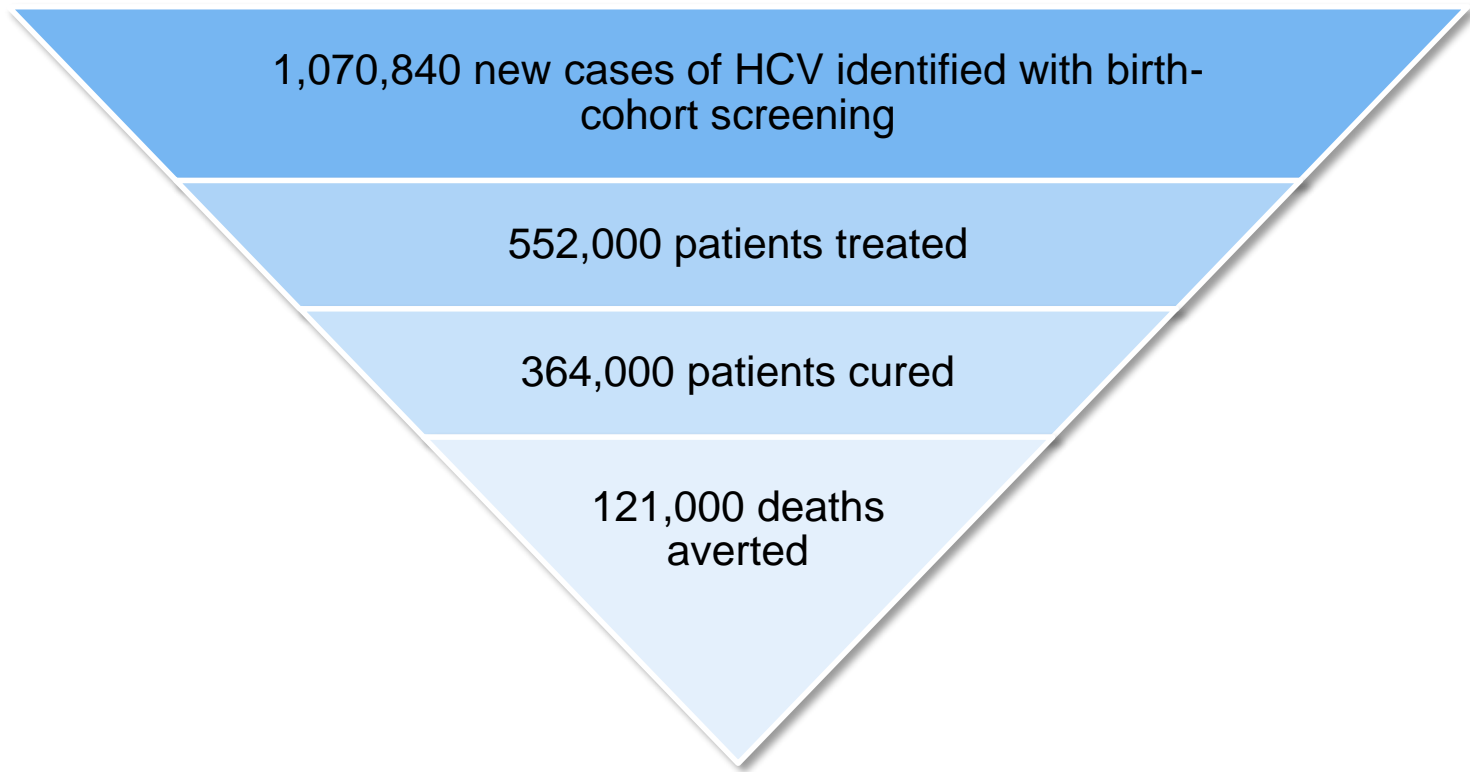
August 17, 2012

Recommendations for the Identification of Chronic Hepatitis C Virus Infection Among Persons Born During 1945–1965



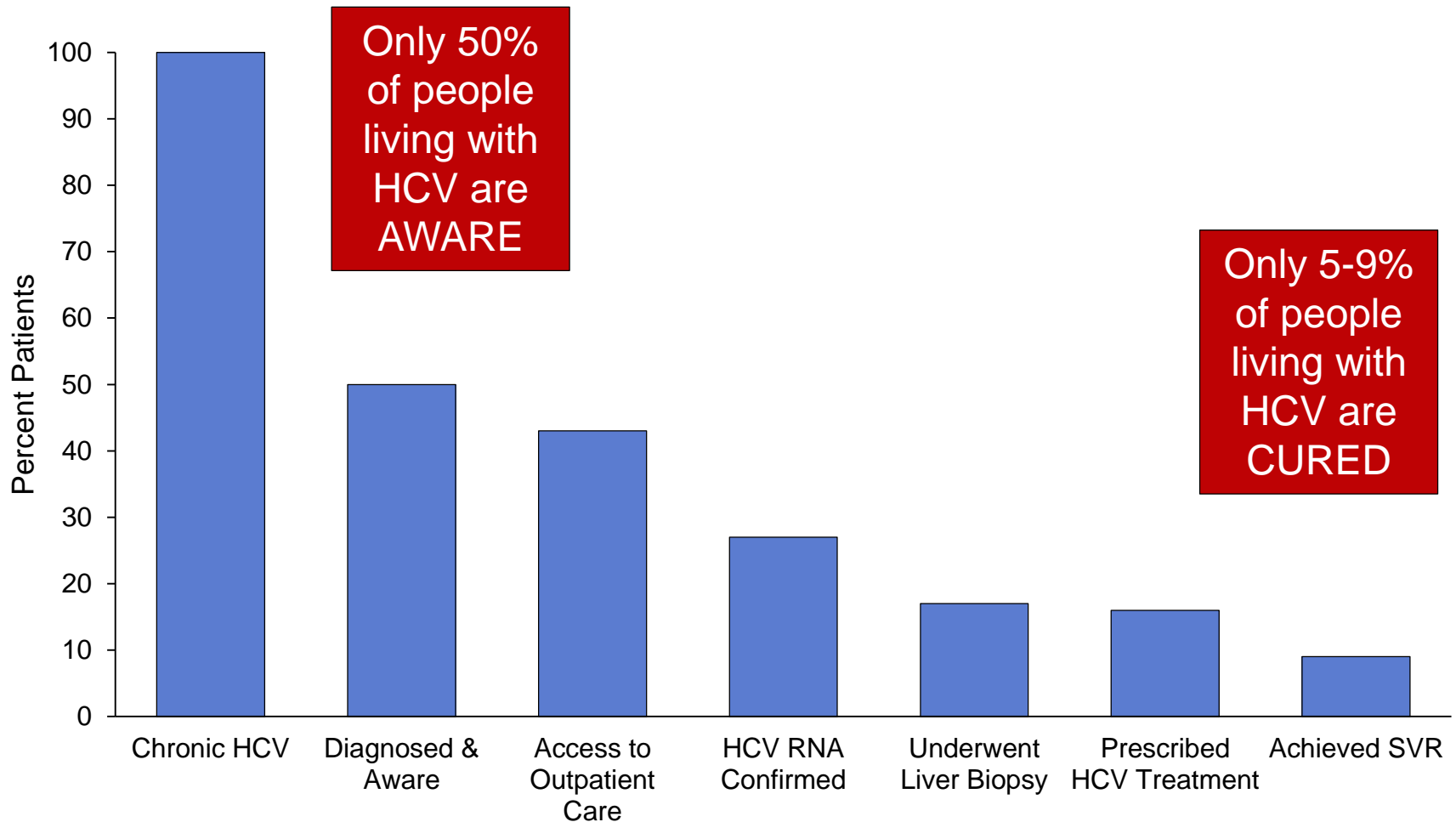
RECOMMENDATION: The USPSTF recommends screening for HCV infection in persons at high risk for infection. The USPSTF also recommends offering 1-time screening for HCV infection to adults born between 1945 and 1965. (B recommendation).

Screening Could Prevent >120,000 Deaths

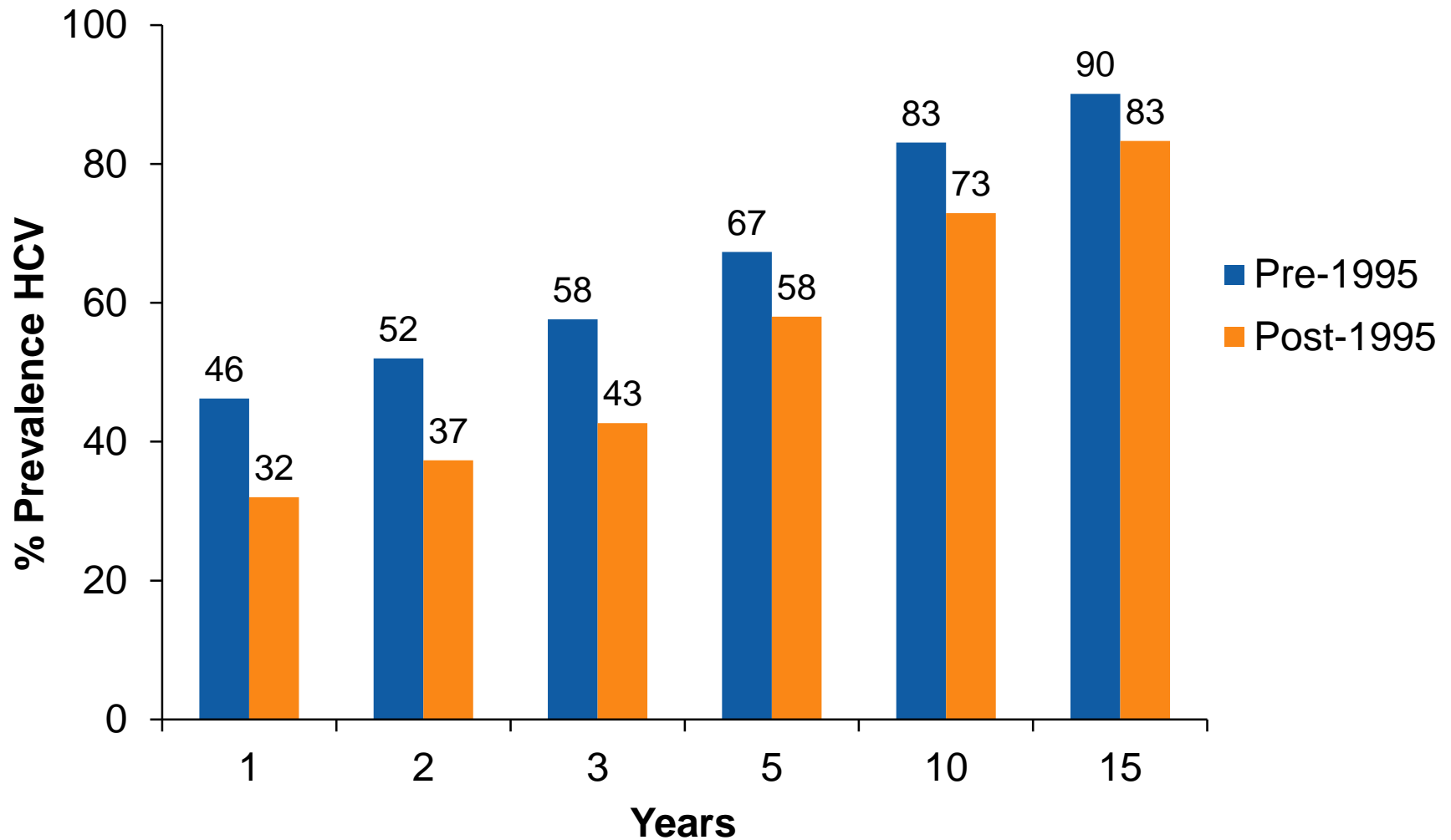


- Birth-cohort screening in primary care would identify 86% of all undiagnosed cases in the birth cohort vs. 21% using risk based screening strategy
- Cost effectiveness of HCV screening is comparable to cervical cancer or cholesterol screening

Screening & Linkage to Care Remain Low



Likelihood of HCV Infection: Duration of Injection Drug Use



What Happened Around 1995?

- Large scale HIV prevention programs, syringe exchange, pharmacy sales of injection equipment, & expanded methadone treatment began around 1995 in most high income countries
- Expansion of HIV prevention services resulted in very large reductions in HIV incidence

Why is HCV Reduction Less than HIV Reduction?

- Reduction in HCV transmission among PWID has been much less than the reduction in HIV transmission
 - HCV is much more readily transmitted than HIV
 - Less sharing is needed to transmit HCV
 - Sharing of drug preparation equipment will transmit HCV
 - The prevalence with HCV infection is much higher in PWID than is the prevalence with HIV infection

Transmission Via Contact with Contaminated Blood: Needles and Syringes



Fixed



Detachable

Transmission Via Contact with Contaminated Blood: Preparation Equipment



HCV Transmission



Bloody fingers

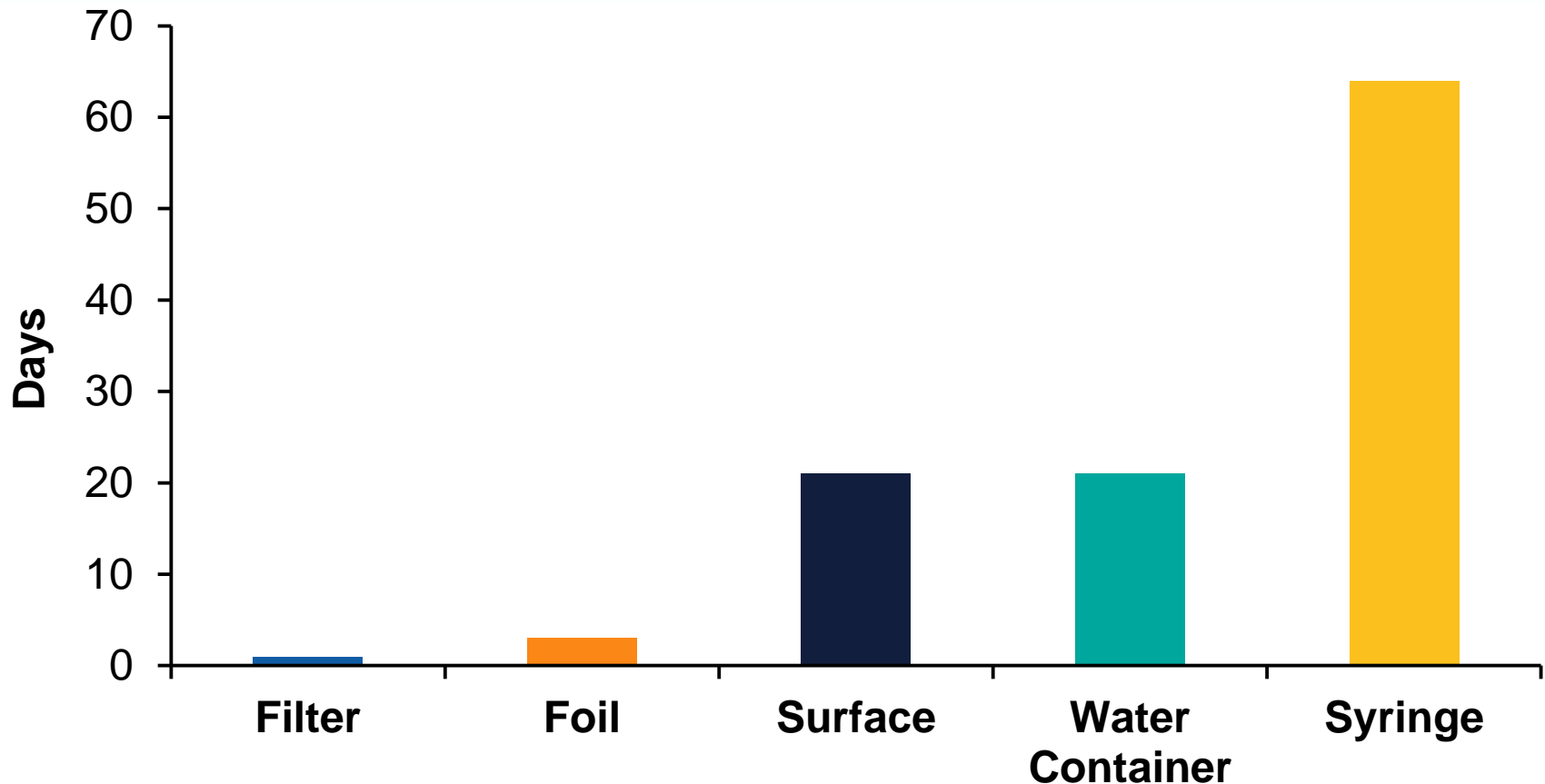


**Fingers on cooker
and in solution**

Hepatitis C & Other Drugs: More than Just Injecting

- HCV transmission from sharing of straws and/or crack or crystal meth pipes can occur
- Prevalence rates of HCV in nasal drug users ranges from 2.3% to 35.3%
- HCV has been found on the stems of crack pipes
- USPSTF and AASLD/IDSA Guidance recommend screening for persons with history of intranasal drug use
- Consider HCV in people who smoke crack or crystal meth, especially if linked to sex (“chem-sex”)

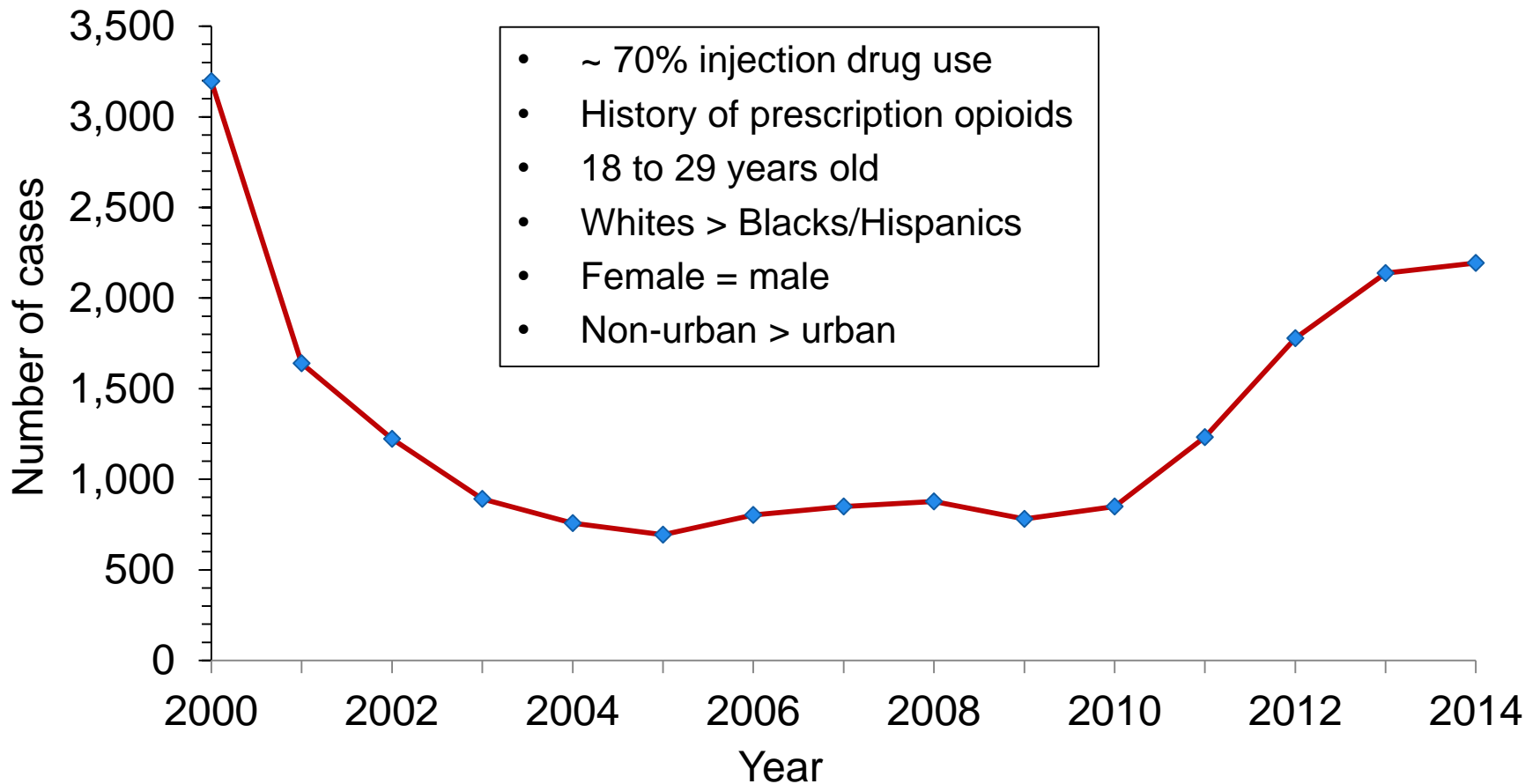
How Long Can HCV Survive on Inanimate Objects?



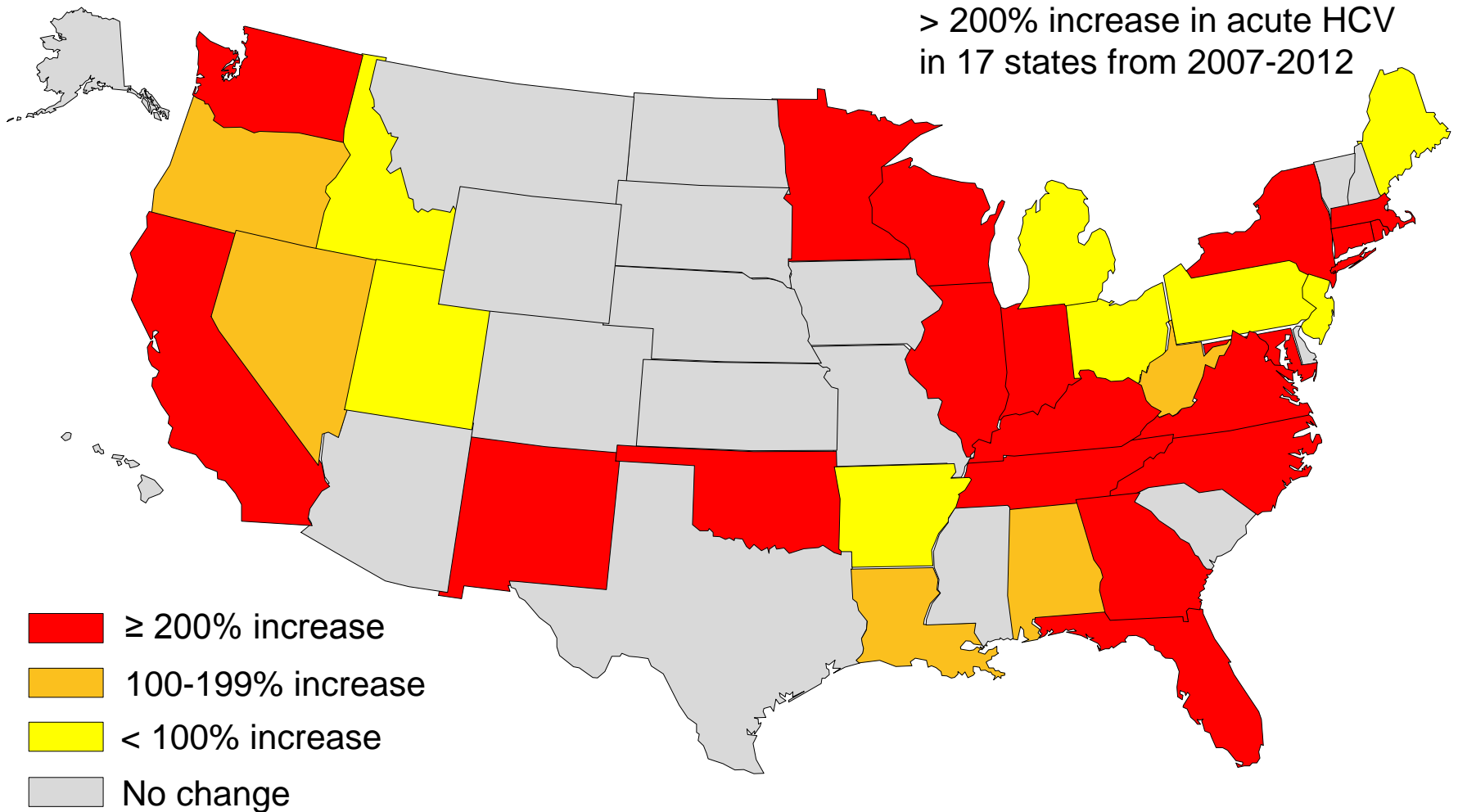
HCV-contaminated solution needs to be heated for almost **90 seconds** and reach temperatures of **144°F** for the virus to be at undetectable levels.

250% Increase in Acute HCV

Reported Number of Acute Hepatitis C Cases 2000-2014



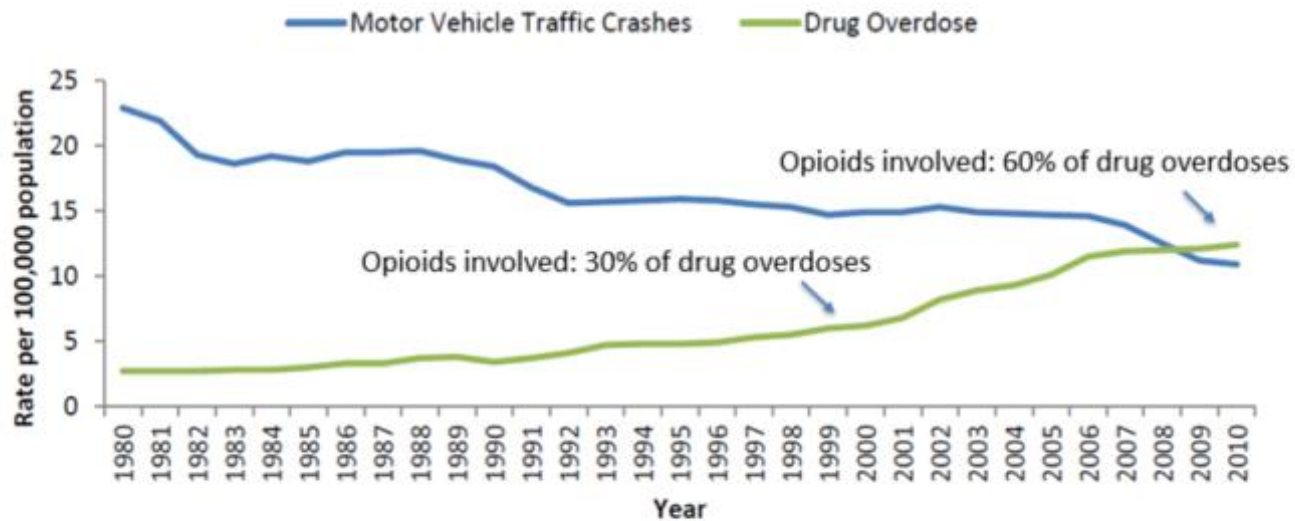
Rise of Acute Hepatitis C



Impact of the US Opioid Epidemic

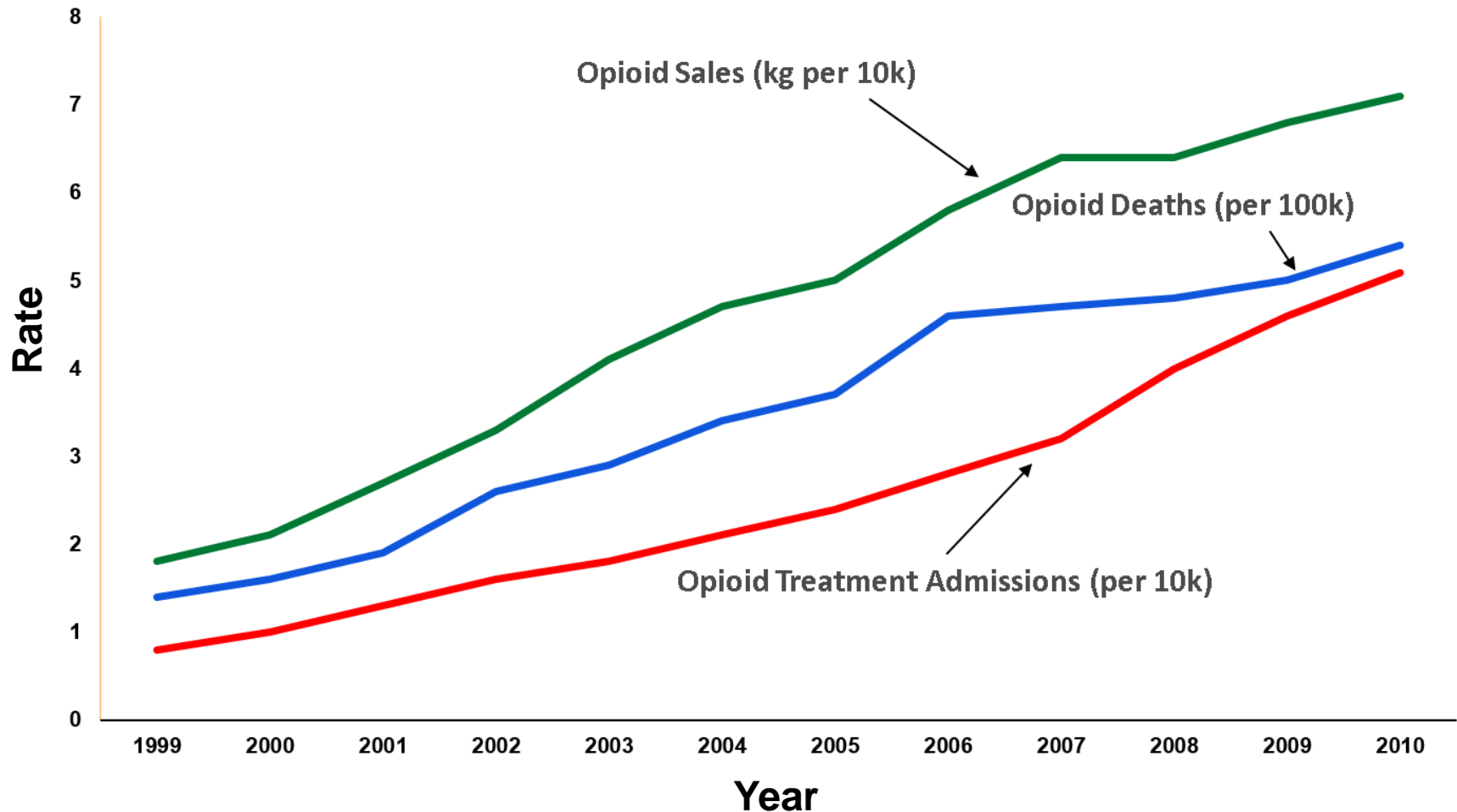
- Opioid epidemic has led to increases in drug injection, infectious disease (hepatitis C), & deaths

Rates of motor vehicle traffic and drug overdose deaths, United States



Source: DHHS, Addressing Prescription Drug Abuse in the United States: Current Activities and Future Opportunities, September 2013

Prescription Opioid Sales, Opioid-Related Deaths & Opioid Treatment Admissions Increased in Lock Step



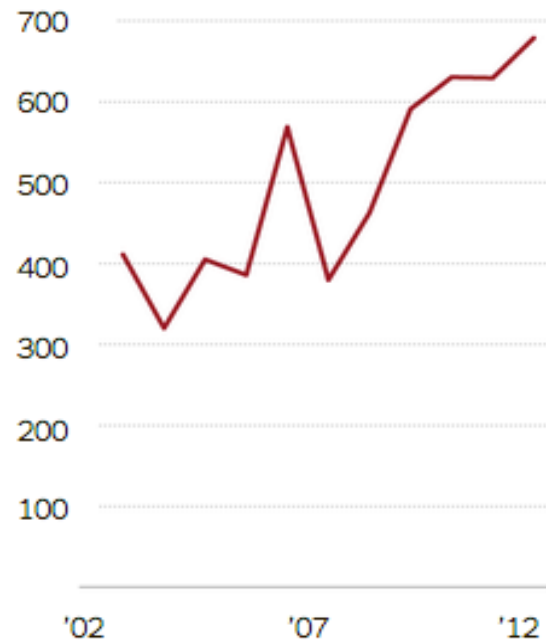
Rise of Heroin

The Resurgence of Heroin

The number of users of heroin has grown over the last decade.

Heroin users

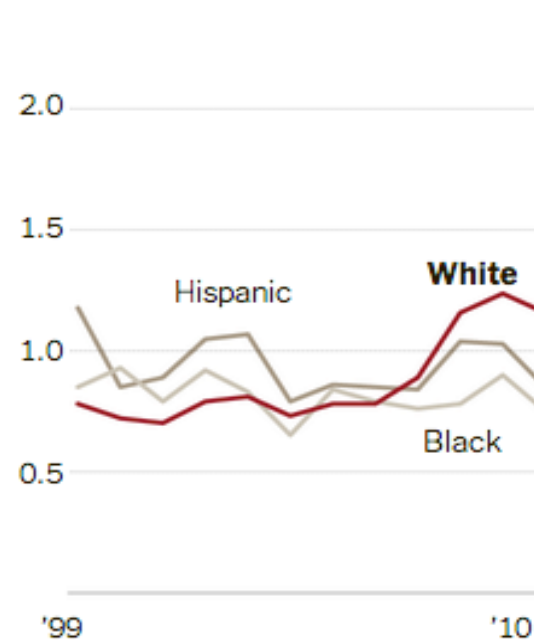
In thousands



Overdose deaths began to rise sharply in the latter half of the previous decade among young whites. Death rates since 2010 have not yet been compiled.

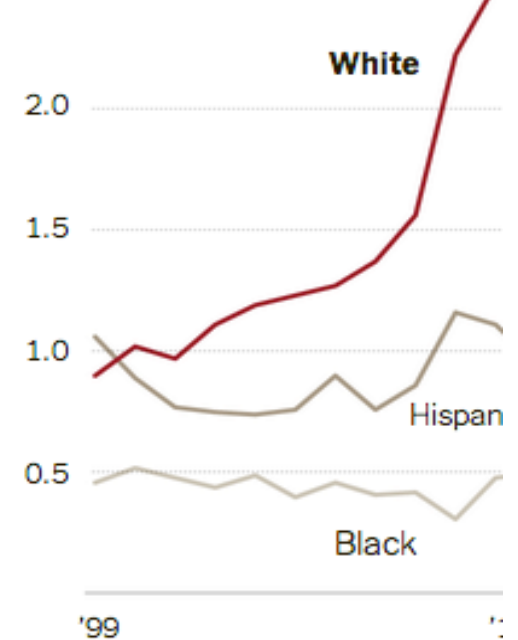
Heroin deaths by race

Per 100,000 population, age adjusted



Heroin deaths among 15- to 34-year-olds

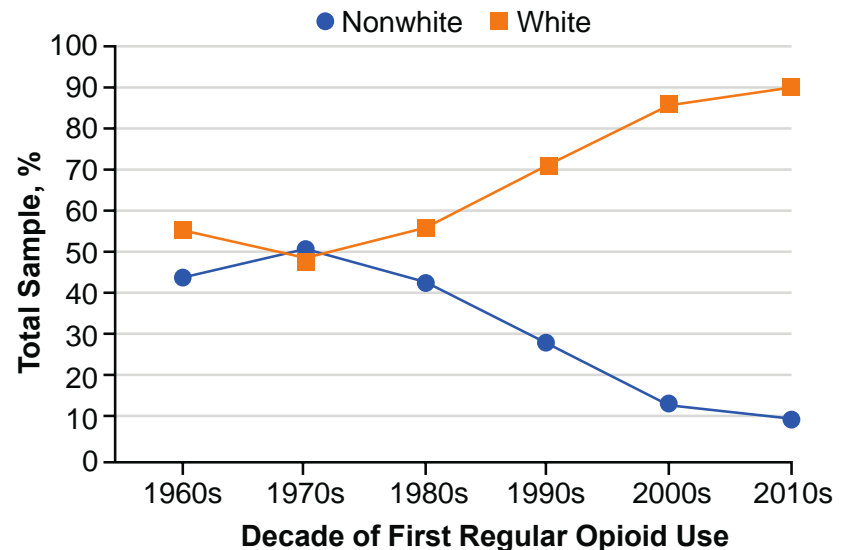
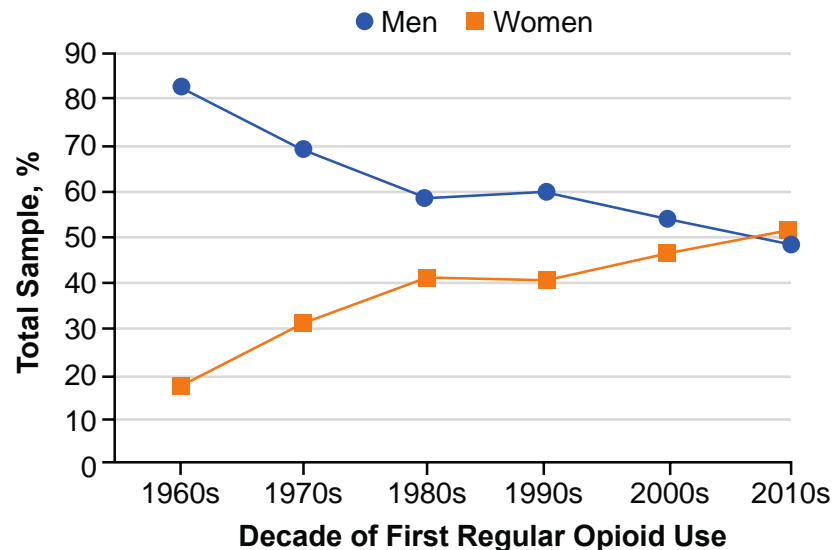
Per 100,000 population



Source: Centers for Disease Control and Prevention; Substance Abuse and Mental Health Services Administration

Heroin Use - Shifts in Demographics

- In 2012, 669,000 Americans reported heroin use in the past year, compared to 404,000 ten years earlier
- In 2011 179,000 new initiates of injecting opiates
- 4.2 million Americans ages 12 or older (1.6% of Americans) have used heroin at least once



Geographic Areas at Risk for HCV

Counties vulnerable to outbreaks of HIV and hepatitis C



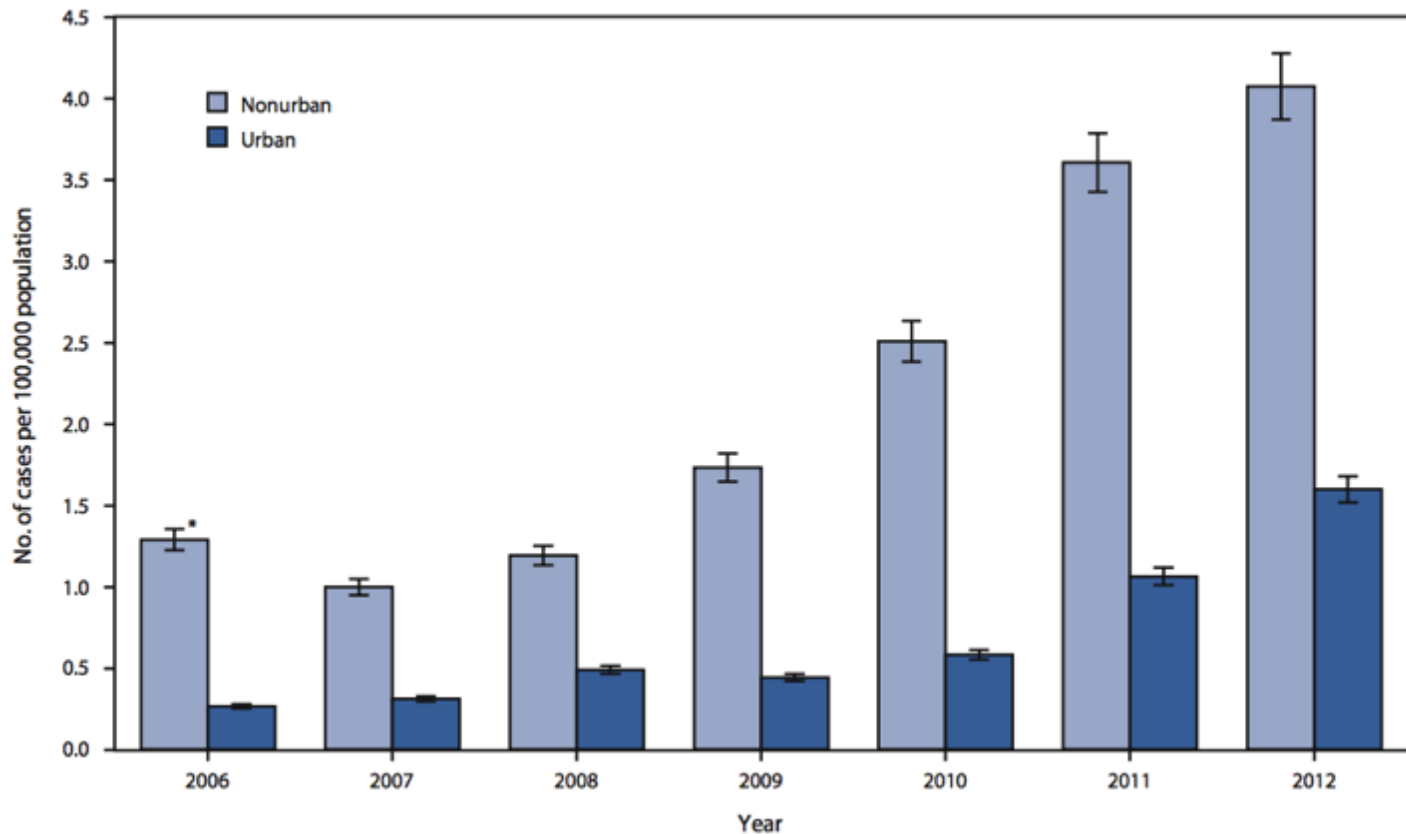
CDC report identified >220 counties vulnerable to outbreaks of HIV & HCV among people who inject drugs

Risk Factors:

- unemployment rates
- overdose deaths
- prescription opioid sales

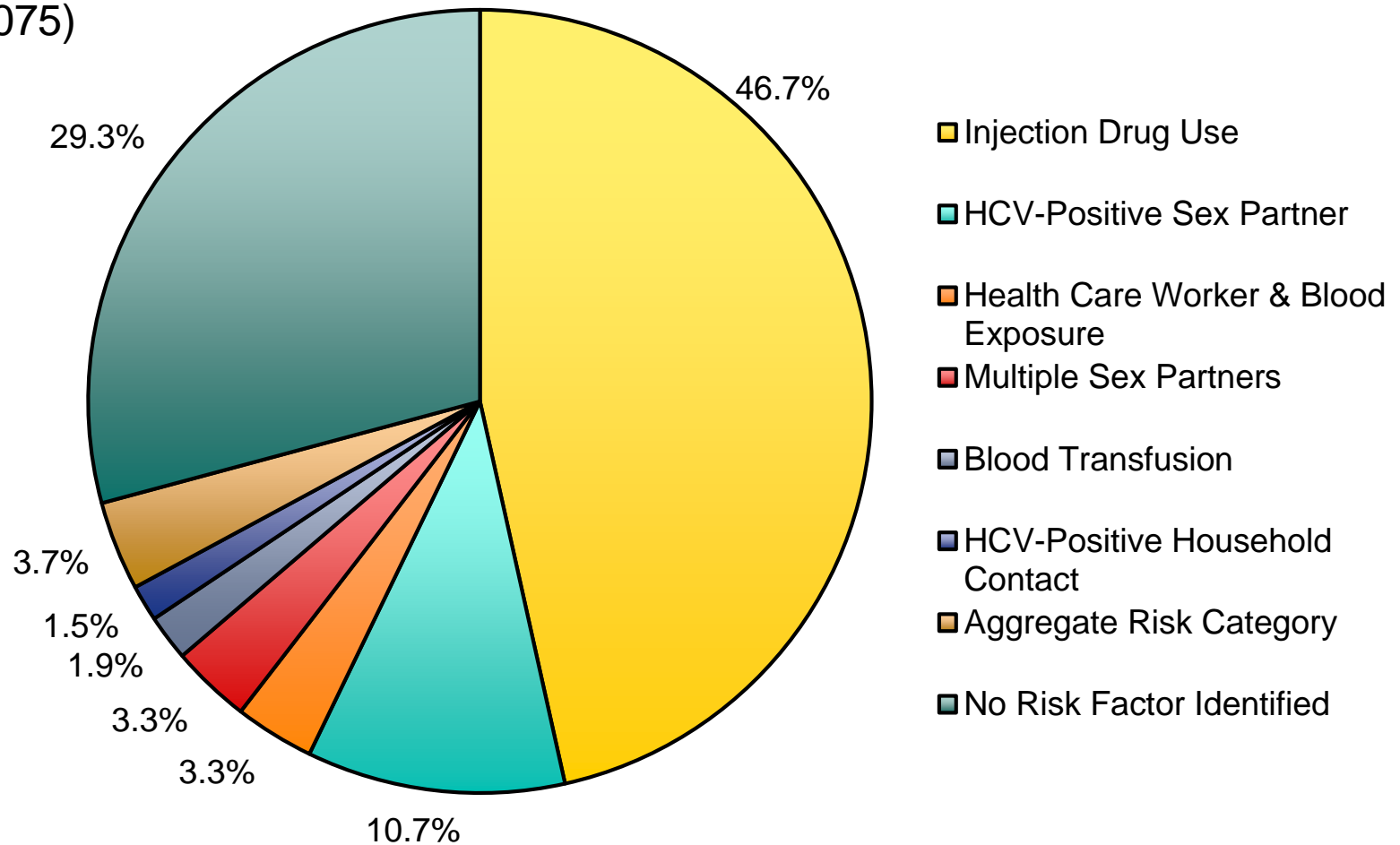
Urban vs. Non-urban

Incidence of acute HCV among persons aged ≤ 30 years —
(Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012)



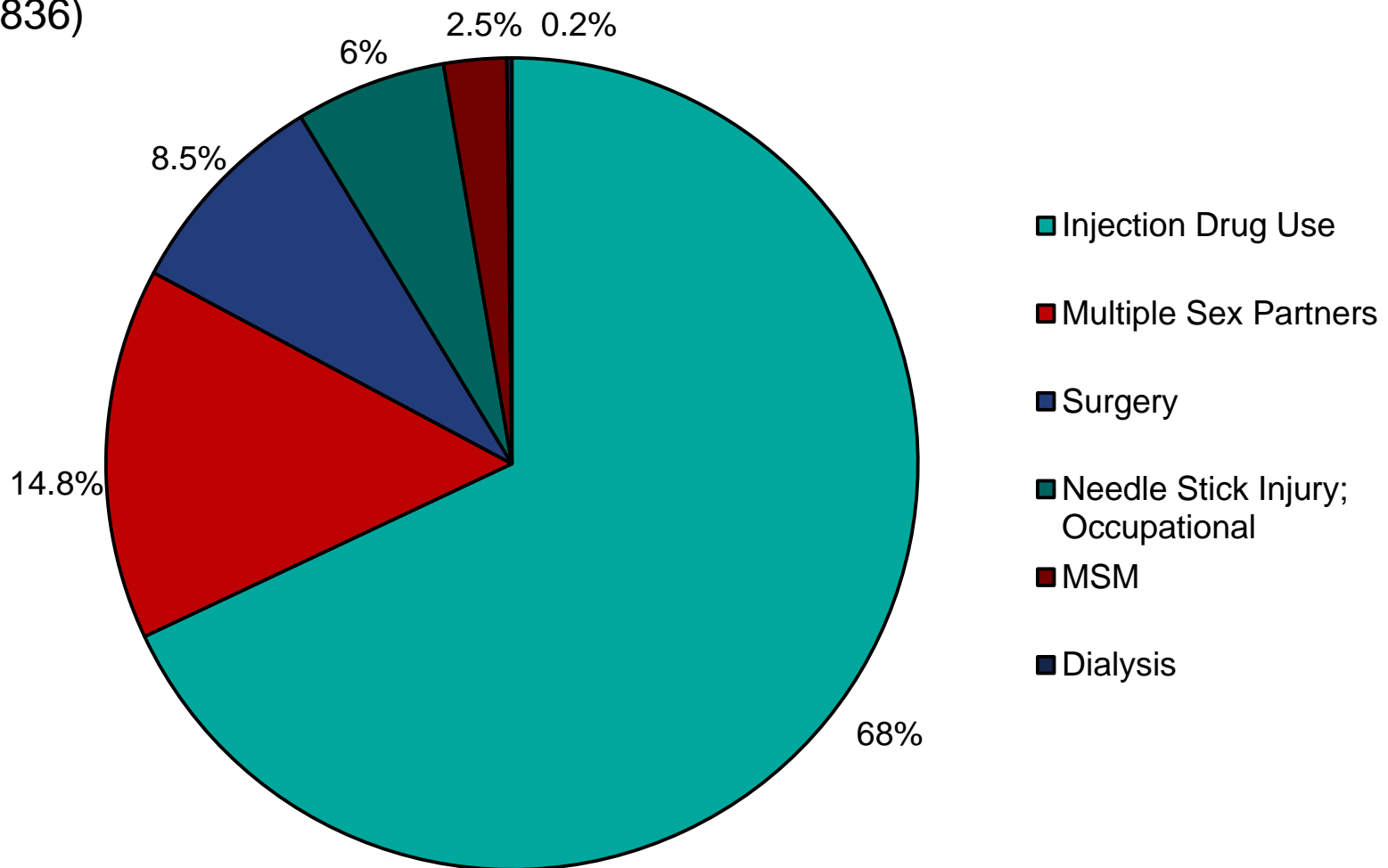
Acute Hepatitis C Exposures (1982-2006)

(n = 2,075)



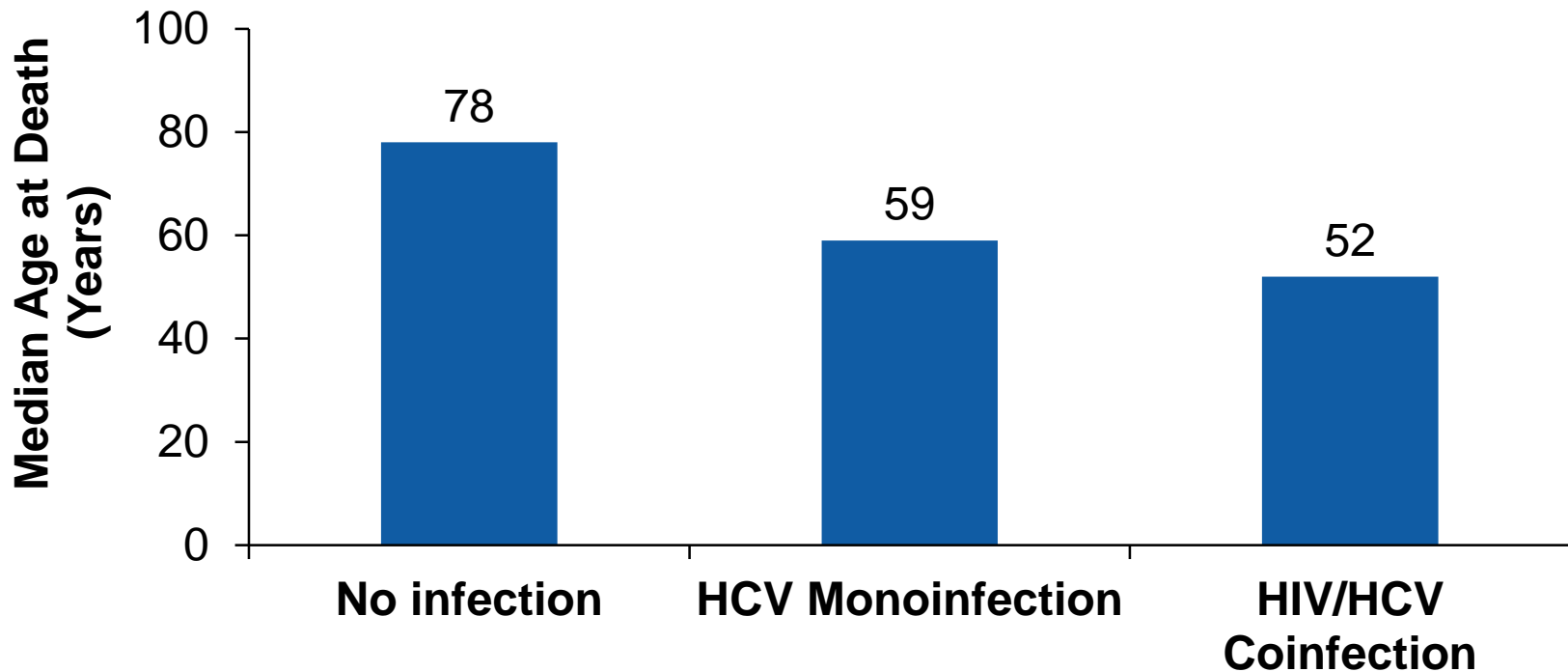
Reported Exposure Risks (2014)

(n = 836)



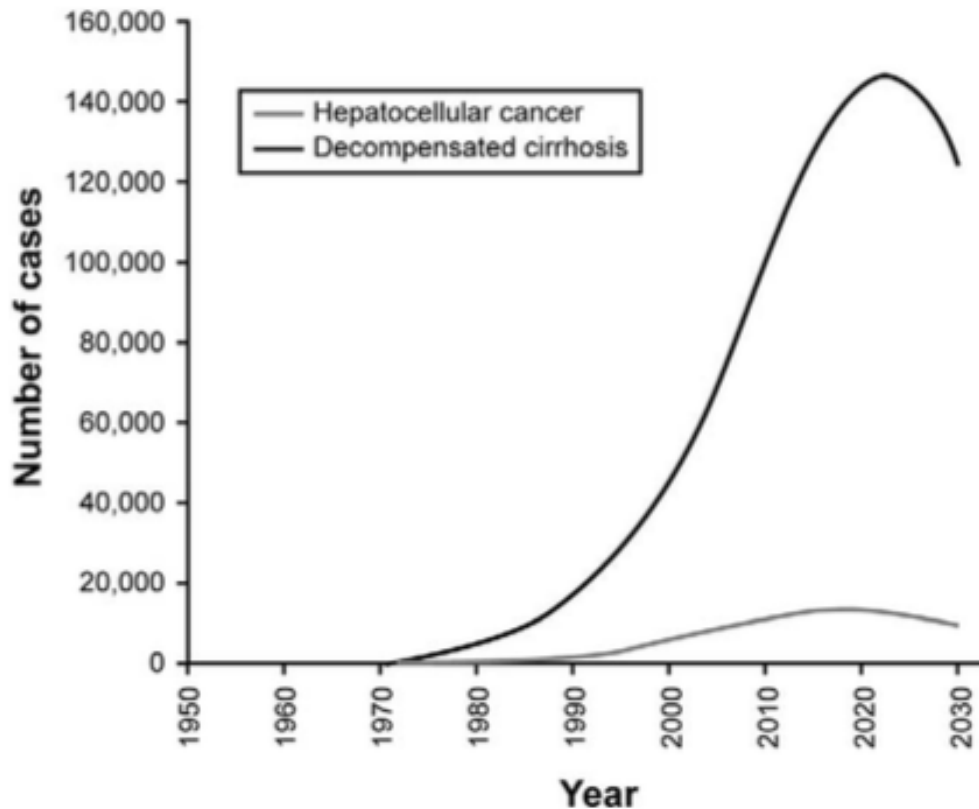
Impact of HCV on Survival

Premature Death (<65 Years Old): ~26% (No infection) vs ~67% (HCV Monoinfection) vs ~94% (HIV/HCV Coinfection)



- Among all deaths (NYC, 2000-2011)
- Time period covers ART introduction for PWID in NYC
- Many of the HCV mono and co-infected patients die from causes other than HCV and HIV

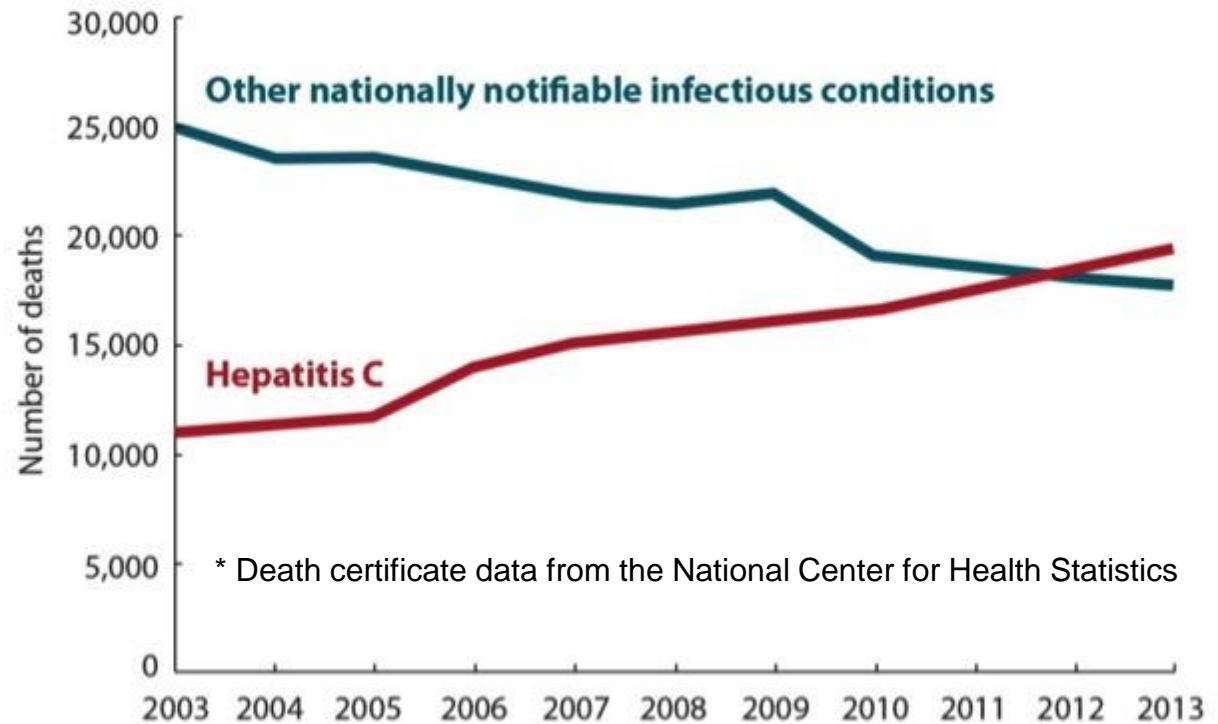
The Future of Chronic Hepatitis C



- Burden of HCV liver disease expected to triple in next 10-15 years
- Prevalence of cirrhosis 45% by 2030
- HCV deaths doubled 1999-2007 to current > 17,000 (projected peak 35,000/yr)
- Economic burden > \$10 billion per year

Increasing Deaths Due to HCV

Annual number of hepatitis C-related deaths vs. other nationally notifiable infectious conditions in the US, 2003-2013



* Death certificate data from the National Center for Health Statistics

Source: Centers for Disease Control and Prevention

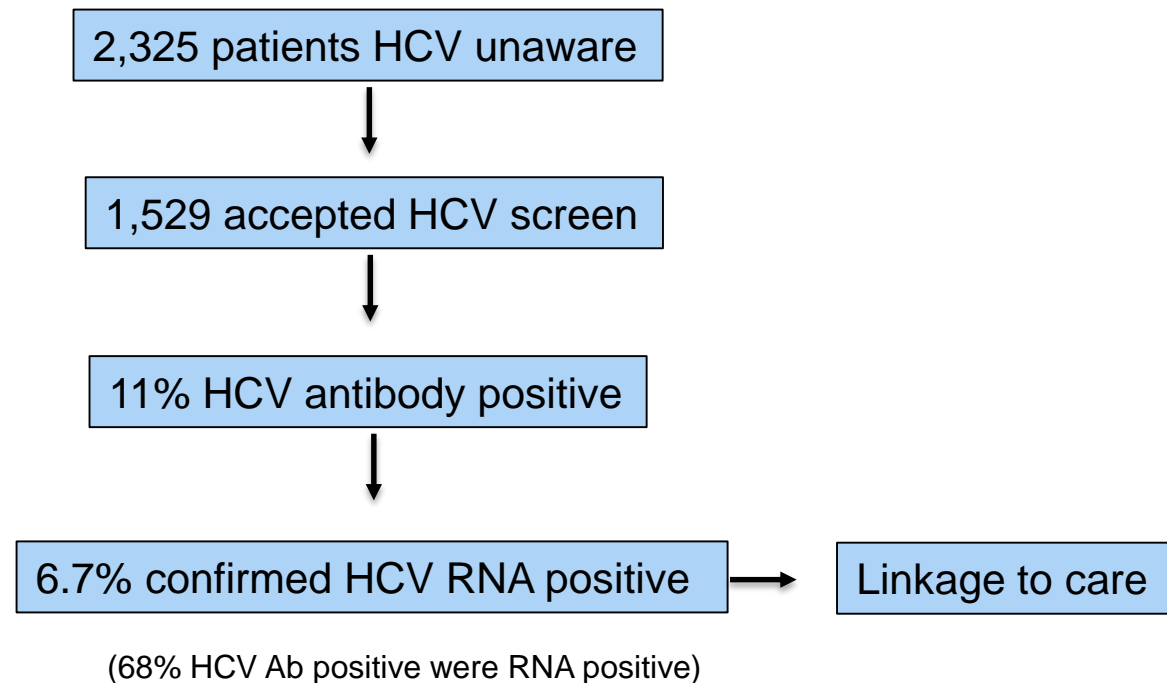
* More people are dying of HCV than all 60 other nationally notifiable infectious diseases combined

Challenges Ahead

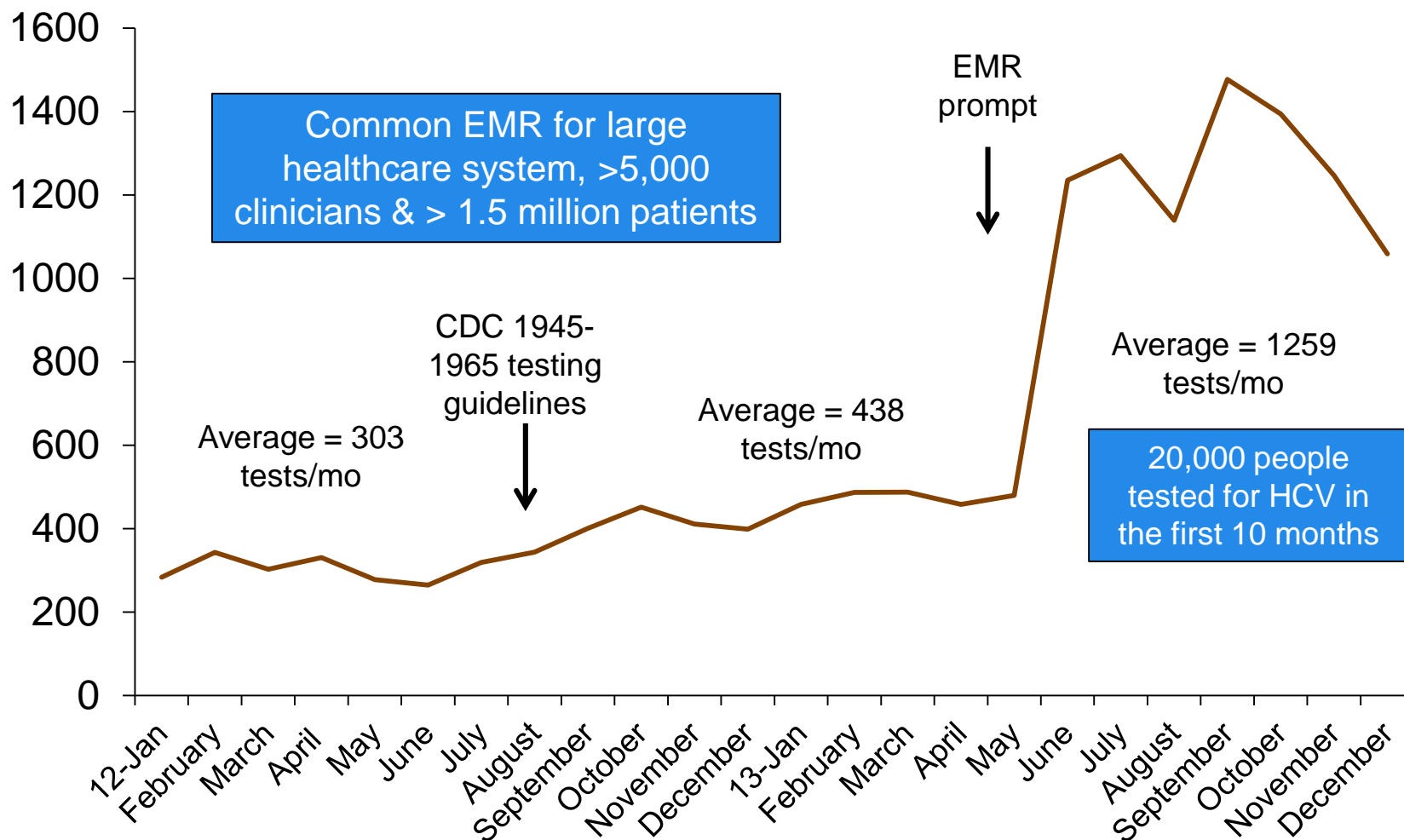
- Majority with HCV remain undiagnosed
- Projected increases in advanced disease & mortality
- Rise of acute HCV & new populations at risk of exposure
- Injection drug use & the opioid epidemic
- How can we implement screening programs?
- How can we expand access to curative therapy?

HCV Prevalence in the Community

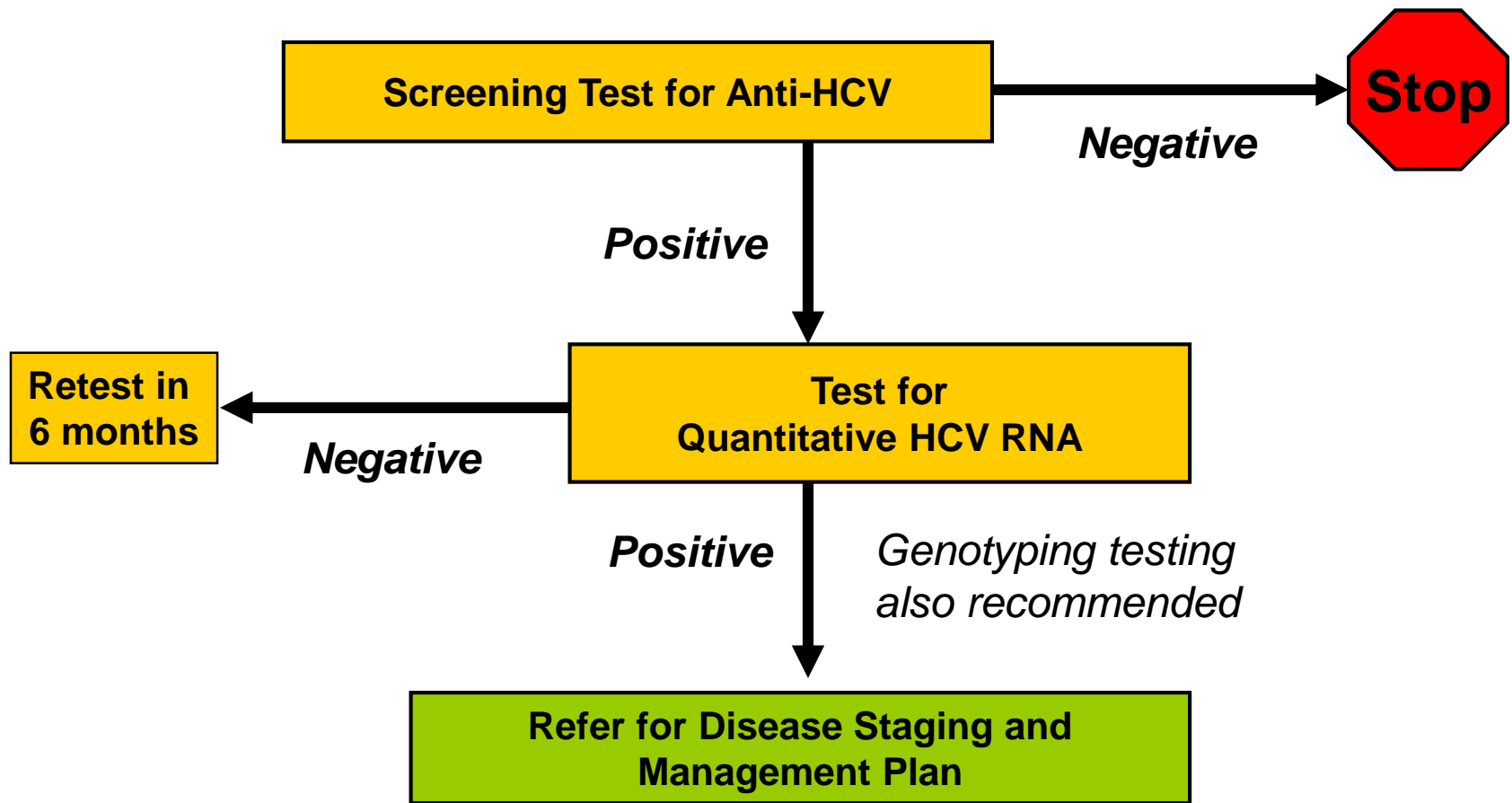
- Prospective study of consecutive ER visits in patients born 1945-1965



EMR Prompt for HCV Ab Test



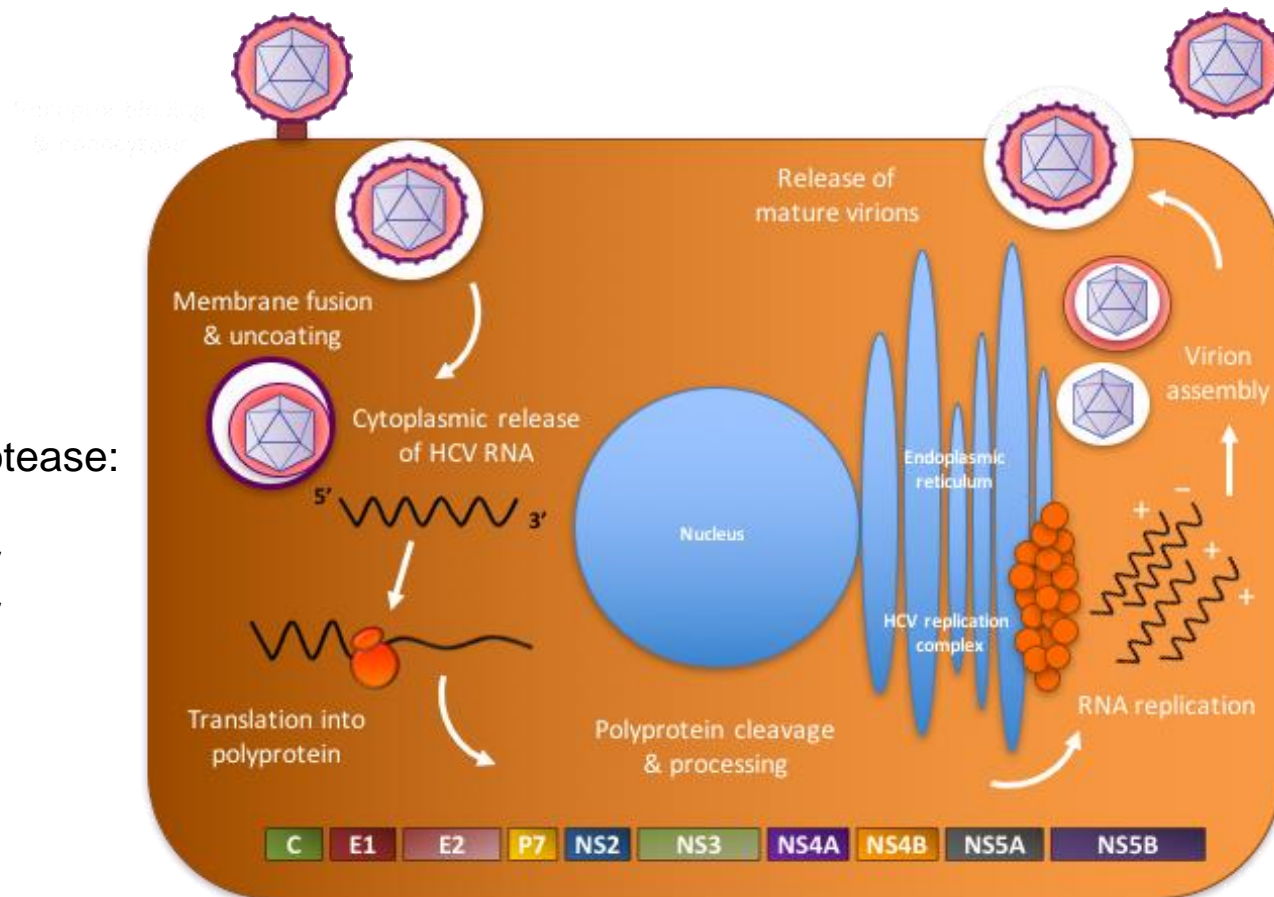
HCV Screening is Straightforward: Algorithm for Screening/Diagnosis of Asymptomatic Persons



Is Positive Anti-HCV Test Result a Diagnosis for Chronic HCV Infection?

- A positive anti-HCV test result is not a diagnosis for chronic HCV infection
- Some individuals become infected with HCV and then spontaneously clear the infection
- Approximately 15%-25% of individuals clear the virus without treatment and do not develop chronic infection
- HCV RNA test is required to confirm chronic infection

Direct-Acting Antivirals (DAA)

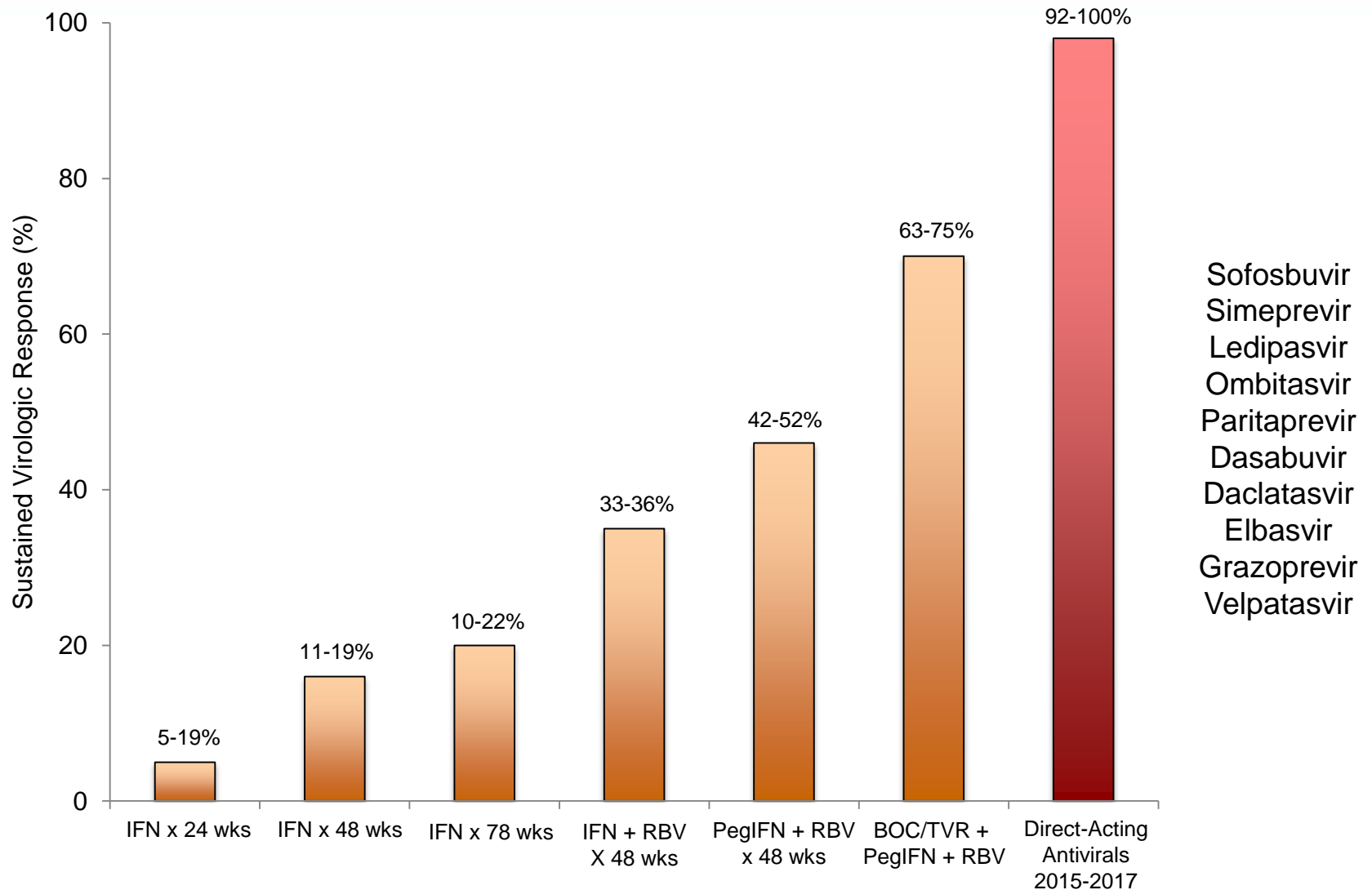


NS3/4a protease:
simeprevir
paritaprevir
grazoprevir

NS5B polymerase:
sofosbuvir
dasabuvir
elbasvir

NS5A replication complex:
ledipasvir, ombitasvir, daclatasvir, velpatasvir

Efficacy of Antiviral Therapy

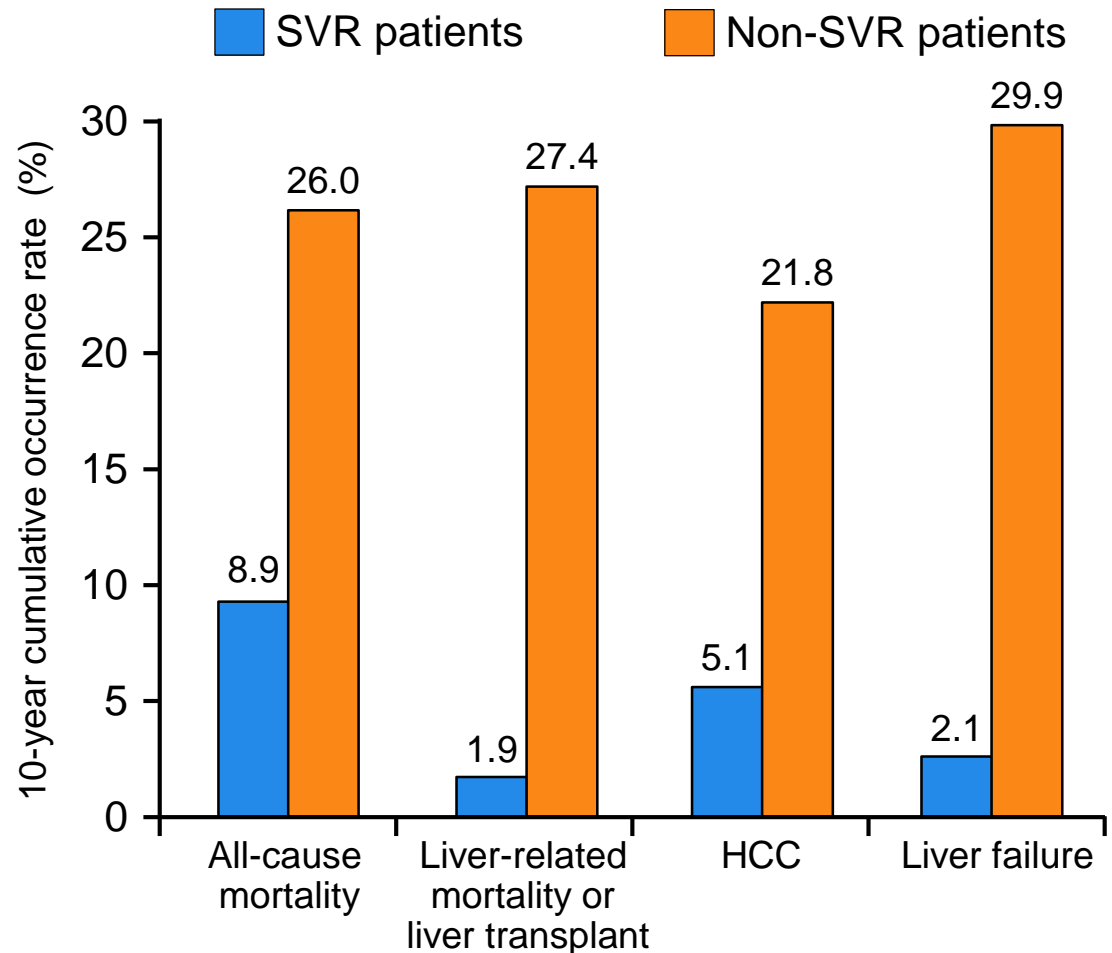


Impact of Antiviral Therapy

530 Patients with Cirrhosis Followed for a Median of 8.4 Years

Baseline factors associated with all-cause mortality:

- Older age
- GT 3 (2-fold increase in mortality and HCC)
- Higher fibrosis score
- Diabetes
- Severe alcohol use



Antiviral Therapy 2017*

Genotype	Regimen	SVR (Cure)
1a	Sofosbuvir/Ledipasvir	96-98%
	Elbasvir/Grazoprevir	92%
	Paritaprevir/Ombitasvir + Dasabuvir	95-97%
	Sofosbuvir/Velpatasvir	98%
1b	Sofosbuvir/Ledipasvir	98-100%
	Elbasvir/Grazoprevir	99%
	Paritaprevir/Ombitasvir + Dasabuvir	100%
	Sofosbuvir/Velpatasvir	99%
2	Sofosbuvir/Velpatasvir	99-100%
3	Sofosbuvir/Velpatasvir	93-98%
4	Paritaprevir/Ombitasvir + Dasabuvir	100%
	Sofosbuvir/Velpatasvir	100%
5-6	Sofosbuvir/Velpatasvir	97-100%

Direct-Acting Antiviral HCV Regimens

- Choice of regimen, treatment duration, & use of ribavirin depends on:
 - Presence of cirrhosis
 - Prior treatment experience
 - Genotype (1-6)
- All oral, virtually no side effects, no interferon
- Methadone/buprenorphine/naloxone are not associated with drug interactions and are safe to use during therapy

Effect of Opiates on the Liver

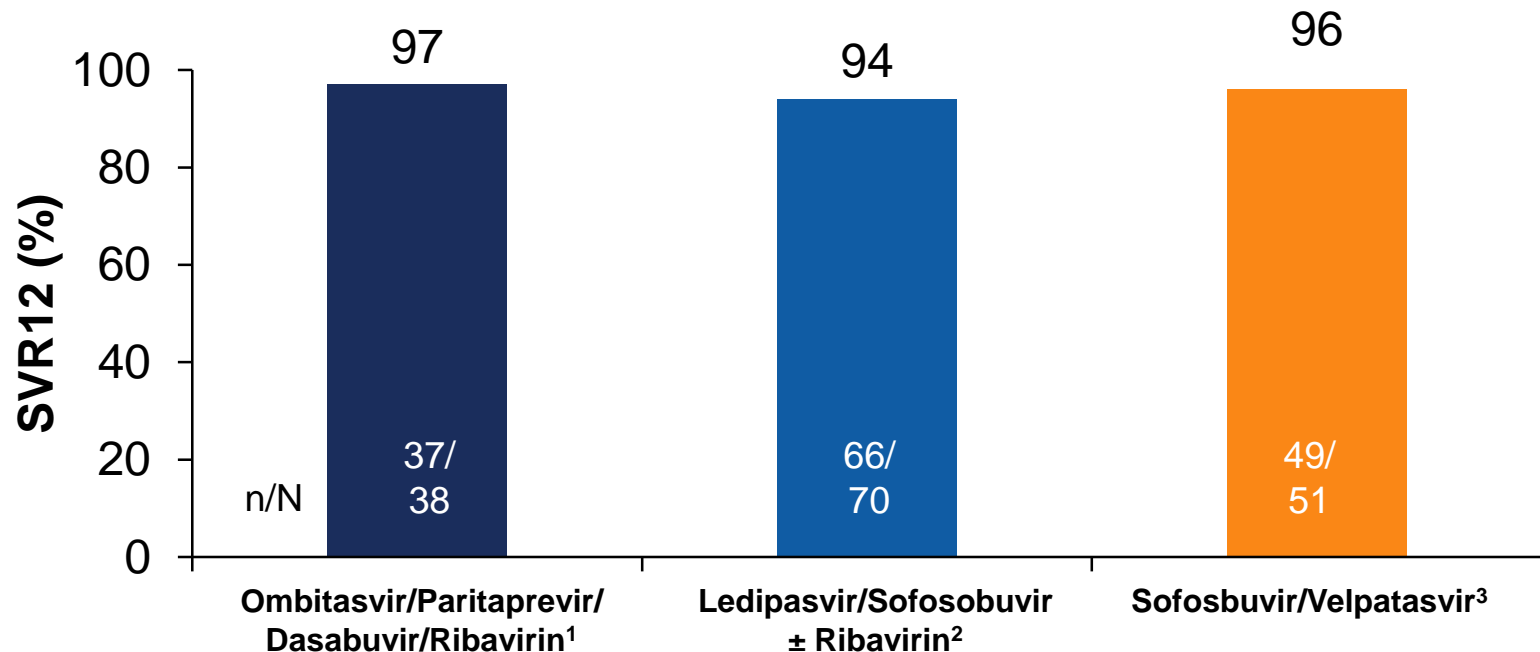
- Heroin
 - No hepatotoxicity
 - Street heroin may be contaminated with toxic substances (e.g., lead)
- Methadone
 - No hepatotoxicity
- Buprenorphine (BPN)
 - Elevated transaminases possible
 - Anecdotal case of liver failure

Antiviral Therapy Guidelines in PWID

- AASLD/IDSA:
 - Recent/active injection drug use should not be seen as contraindication to HCV therapy
- EASL:
 - Treatment should be prioritized in those at risk of transmitting HCV including active injection drug users

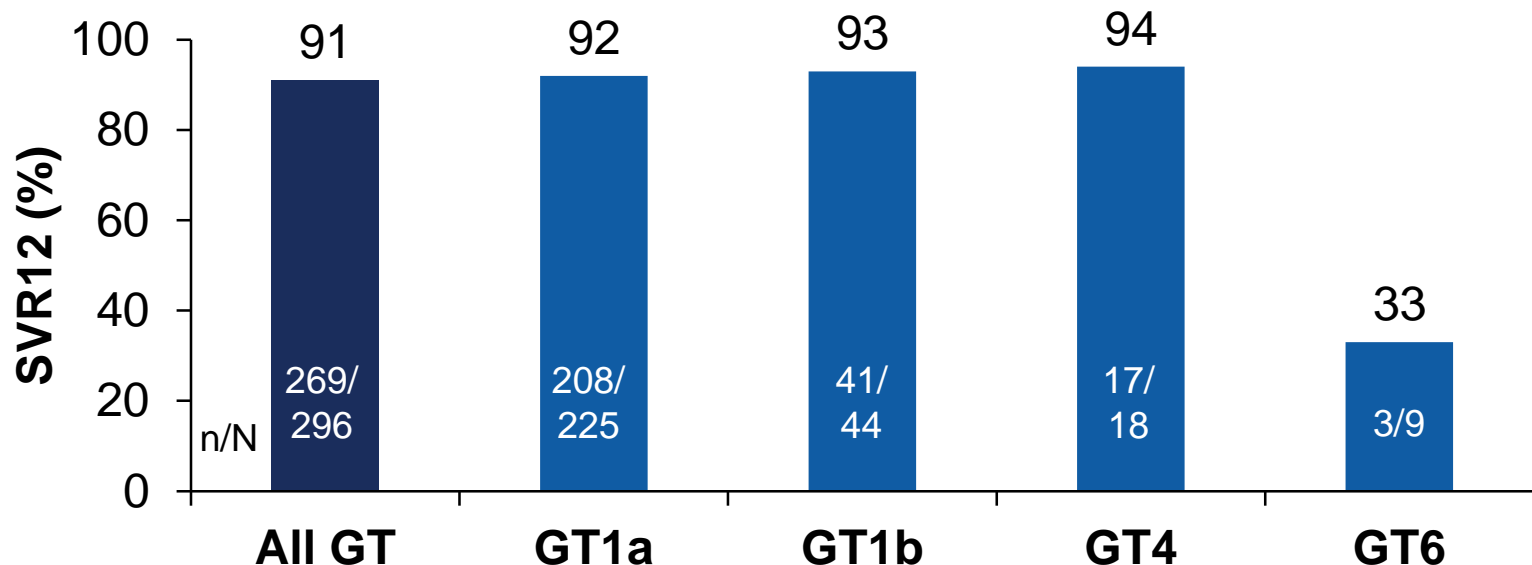
HCV Treatment & Opioid Replacement Therapy

- Patients on stable regimen of opioid replacement therapy
- Methadone vs. buprenorphine: No difference in antiviral efficacy, pharmacokinetics, no dose adjustments¹
- No difference in efficacy, adherence, adverse events vs. non-ORT^{2,3}



HCV Treatment & Drug Use

- High HCV treatment adherence, despite drug use (prospective study)
 - ~60% of patients had positive urine test for at least 1 of 8 drug classes: (amphetamines, barbituates, benzodiazepines, cannabinoids, cocaine, opiates, phencyclidine, propoxyphene)
 - 6/18 with recurrent viremia had evidence of re-infection (2% overall)



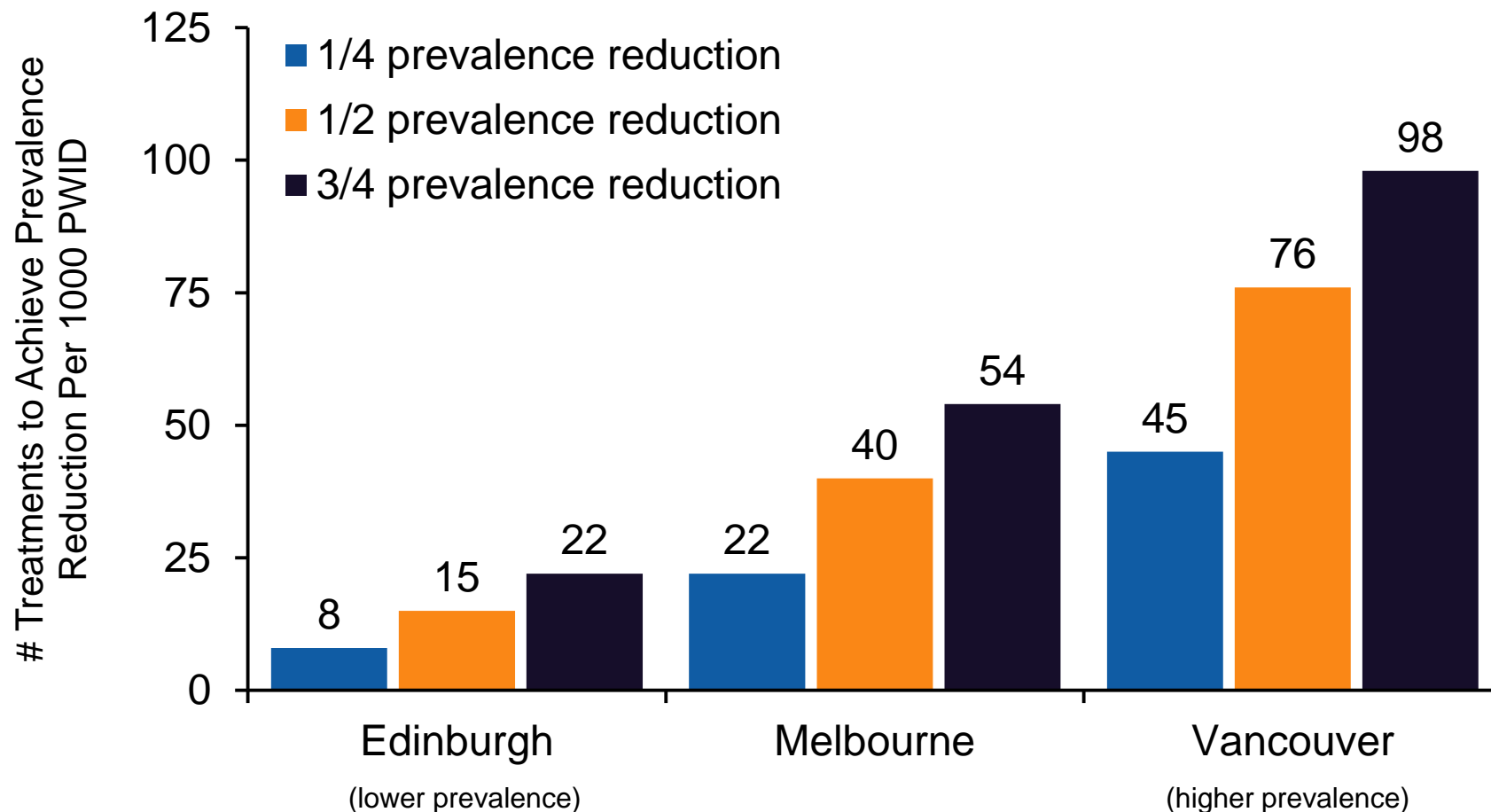
HCV Treatment in PWID

- HCV treatment does not have impact on opioid replacement therapy or increased drug use
- Drug use within 6 months of initiating HCV therapy is *not* associated with decline in response; however, more frequent use correlates with decreased efficacy
- Social functioning & attendance are better indicators of treatment outcome; independently associated with SVR after adjusting for drug use

Duration of Infection Drives Transmission Among PWID

- Those with chronic HCV infection are infectious until they are successfully treated
- To reduce viral transmission:
 - Reduce number of contacts & probability of transmission per contact
 - Safe injection equipment
 - Regular testing within networks
 - Reduce duration that patient is infectious to others via antiviral treatment

Treatment as Prevention of HCV Among PWID



Requirements for Treatment as Prevention in PWID

- Increased HCV screening, diagnosis, and linkage to care
- Infrastructure for clinical services, including antiviral therapy
- Cost-effective regimens that optimize uptake, adherence, and completion of therapy
- Educational strategies to reduce transmission and reinfection
- Treatment of addiction

Re-Infection of HCV

Patient Group	Number of Patients	5-Year Recurrence Rate	Rate per 100 person years
HCV Mono-Infected, low risk	9419	1.14%	0.23 per 100 person years
HCV Mono-Infected, high risk	819	13.22%	2.80 per 100 person years
HIV/HCV Co-Infected	833	21.72%	4.78 per 100 person years

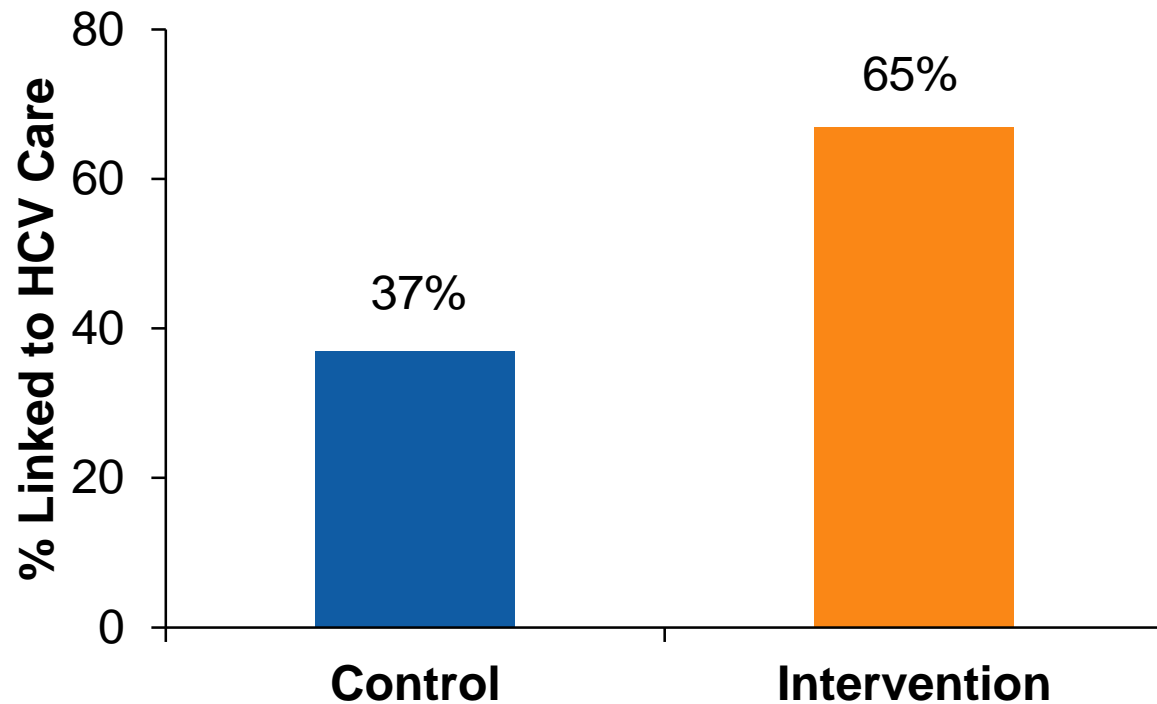
Source: CROI 2015, "Five Year Risk of Late Relapse or Reinfection with Hepatitis C after Sustained Virologic Response: Meta-analysis of 49 Studies in 8534 patients", Andrew Hill.

HCV Re-infection Awareness and Education

- Both PWID and HIV-infected MSM are at risk of HCV re-infection
- HCV antibodies do not offer protection from re-infection
- Continue prevention education in all follow-up visits
- Screen for HCV RNA at least annually; monitor for elevated LFTs to account for acute HCV infection

Impact of Care Coordination

- RCT of patients attending ORT clinics in SF and NYC (n=489)
- Intervention arm received on-site screening, education, counseling, & case management
- 59% HCV seropositive
- Intervention arm:
 - ↑ Linkage to care
 - 6 month follow up
 - OR 4.1 (2.35-7.17)



Linkage to Care: Check Hep C (NYC)

- HCV testing at 12 sites in NYC
 - Targeted outreach, community health centers and needle exchange programs
 - Rapid screening test, immediate blood draw for HCV RNA confirmation
 - Linkage to care via patient navigators



(Risk factors for HCV infection: IDU, homeless, incarceration)

Specific Challenges Faced by Substance Users

- Stigmatization regarding diagnosis of HCV
- In many states, restrictions on HCV medication provision given ongoing substance use and restrictions placed by Medicaid/Medicare
- Variations in reimbursement for HCV therapy create challenges in expanding pool of treating physicians

Summary

- HCV treatment is effective in persons with a history of IDU, receiving OMT, or have recent/active IDU
- Tolerability, adherence, and virologic response in PWID is similar to populations who do not use drugs
- HCV can be cured - impact of therapy is substantial
- Rates of screening and linkage to care remain low; care coordination is highly effective



Thank You!