Hepatitis C: Where Are We Now?

Local Health Departments and Hepatitis C: Webcast 1.1

Presented by:
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Changing Epidemiology of HCV Transmission and Disease

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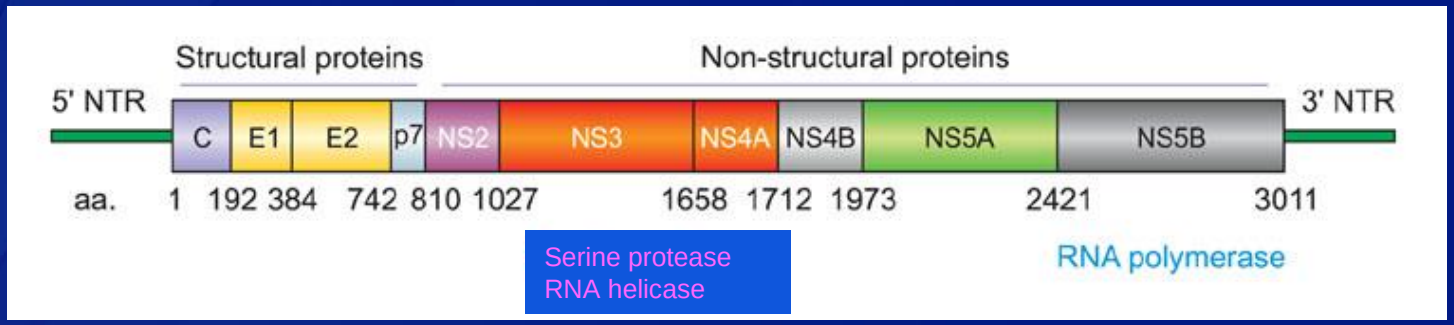
Discovery of Hepatitis C Virus (HCV)

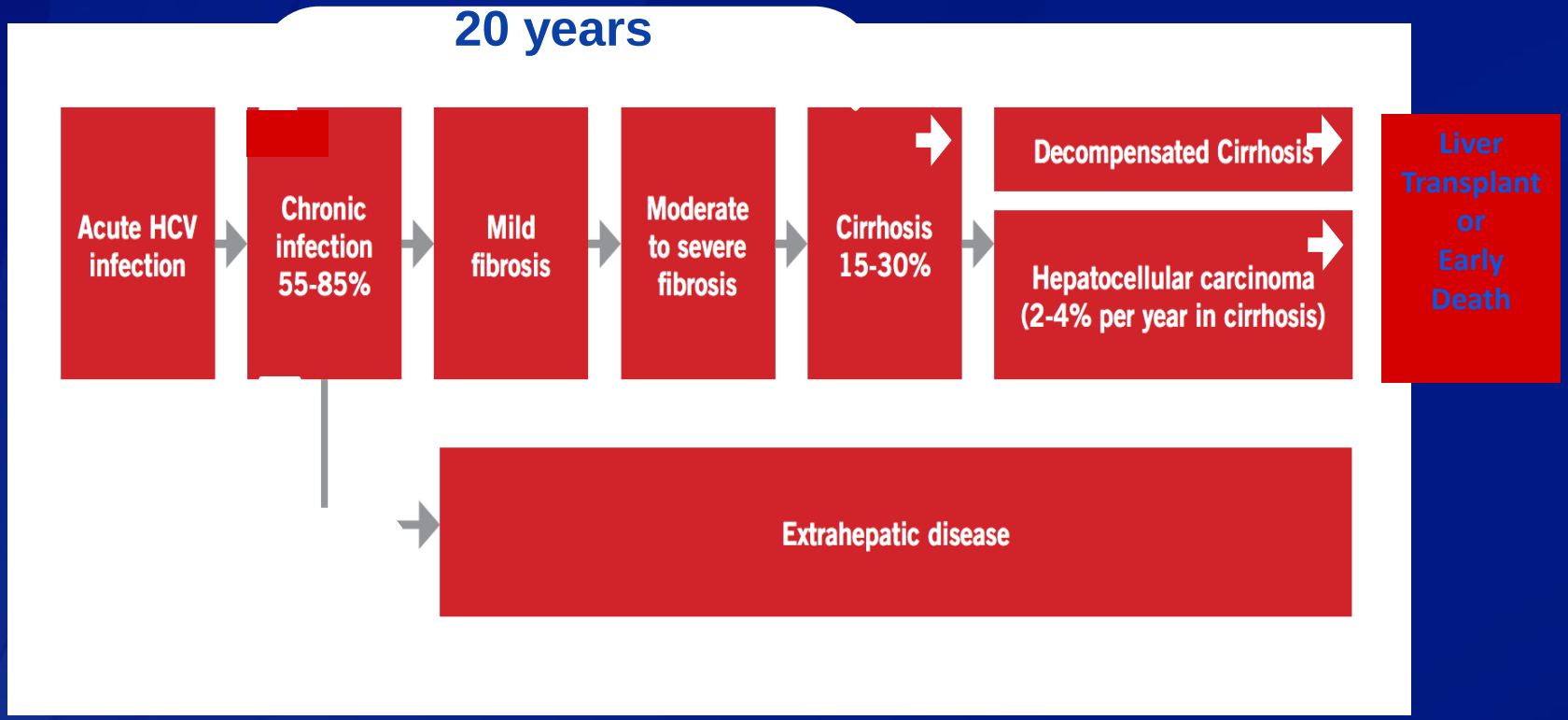
- **Discovered in 1989, RNA virus, family *Flaviviridae***
- **9,600 nucleotide genome-single polyprotein**
  - Structural proteins
  - Non-structural proteins - viral replication and targets of therapy
  - High genetic diversity leads to intra-host variants “quasispecies”
  - 7 major genotypes that predict treatment response
    - Genotype 1 accounts for ~ 70% of infections in US
  - No vaccine candidates for licensure



Lindenbach BD, Fields Virology 2001. Simmonds P, *Hepatology* 1995. Irshad M, *Hepatogastroenterology* 2010. Manos MM, *J Med Virol* 2012.

Natural History of HCV Infection

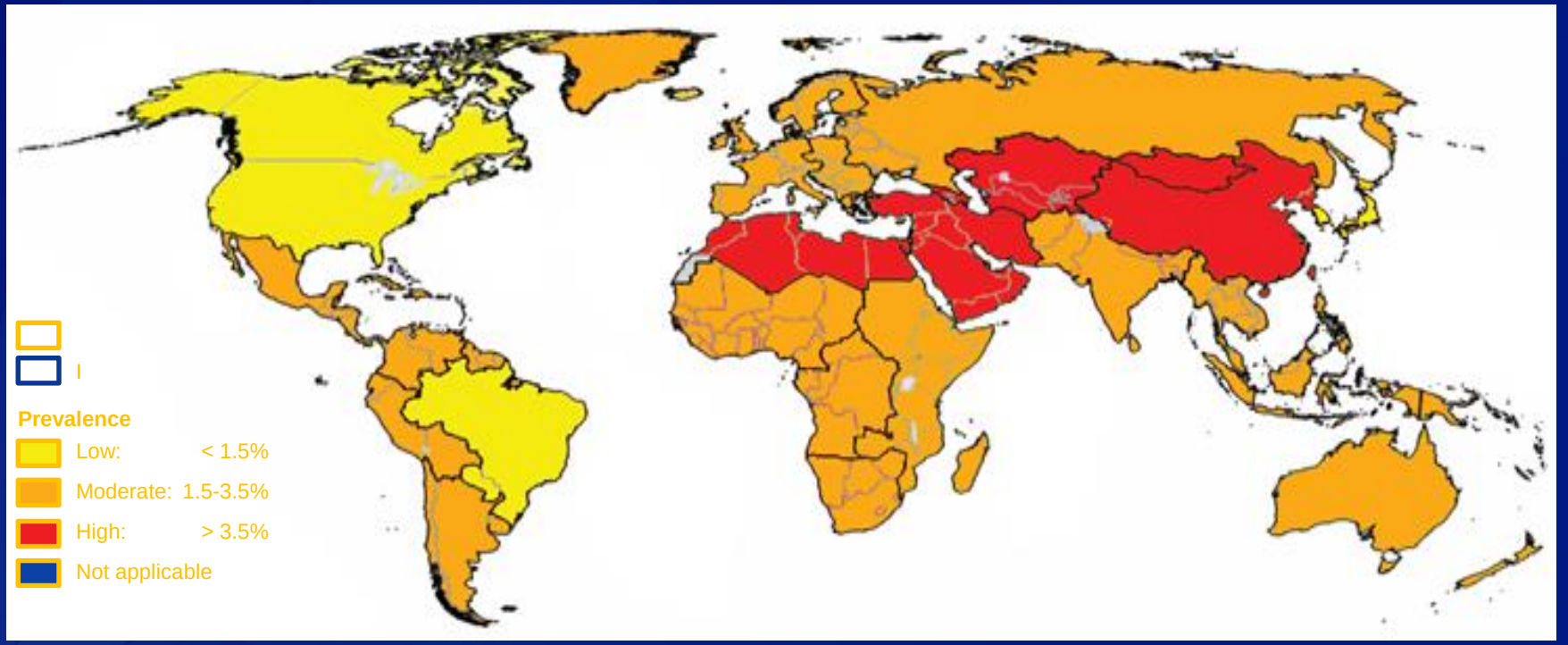
In 20 years, 15-30% progress to cirrhosis
Progression accelerated by HIV, HBV, alcohol use, and fatty liver



HIV: Human immunodeficiency virus. HBV: Hepatitis B virus.
Hepatocellular carcinoma = Liver cancer. Decompensated Cirrhosis = End stage liver disease.

Ly KN, *Clin Infect Dis.* 2014. Mahajan R, *CID* 2014 .

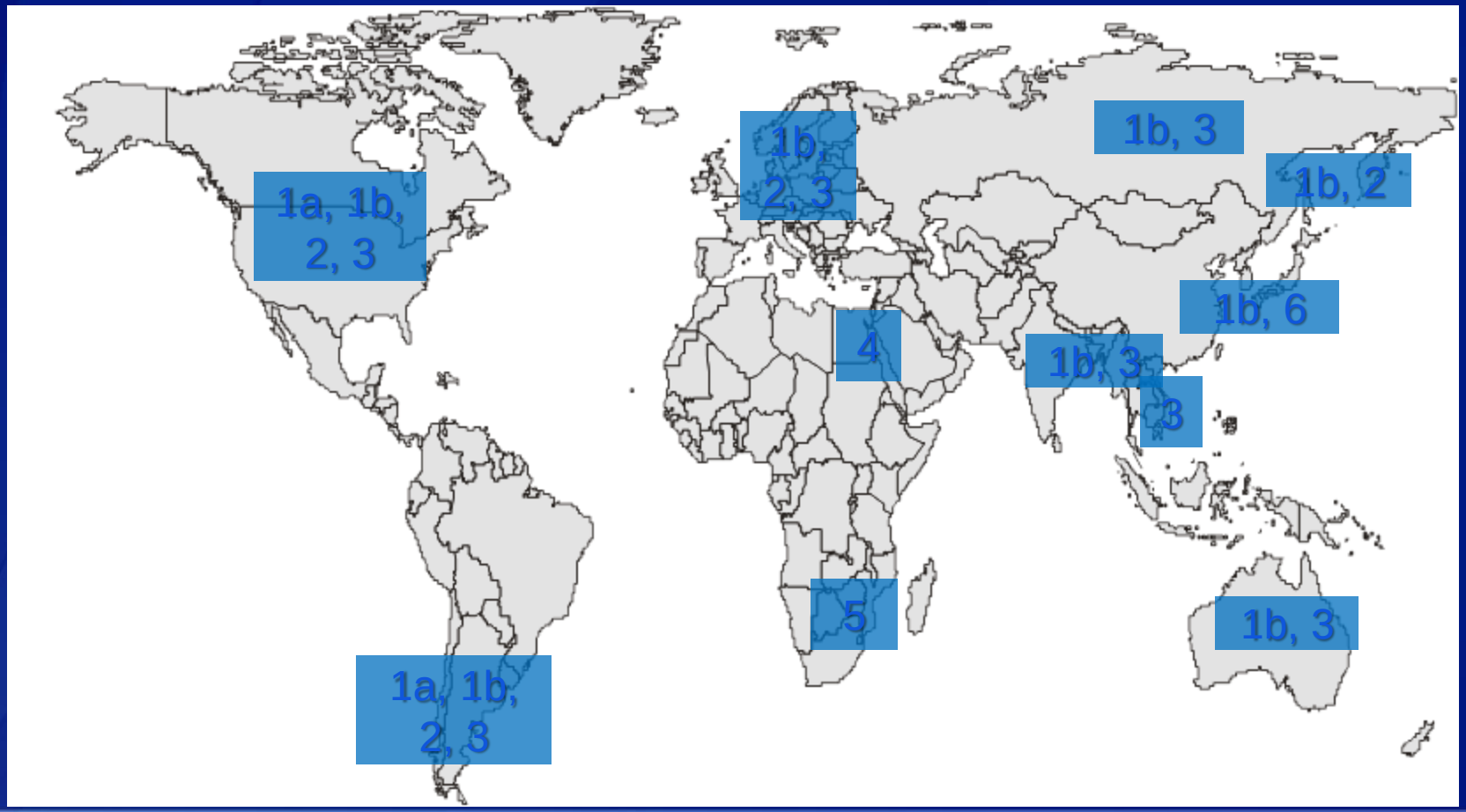
Global Hepatitis C Burden is Large and Highest in Asia and Africa



- 3-4 million new infections per year
- 130-150 million chronic infections

Liver International. WHO unpublished data; pages 1-3, June 8, 2012; Perz JF, et al. *J Hepatol*. 2006; Zhuang X, et al. *Drug Alcohol Depend.* 2012; Serano L, et al. *J Int Assoc Physicians AIDS Care (Chic)*. Jul 24, 2012; Pitt L, et al. *Eur J Public Health.* 2009;76P. http://www.who.int/mediacentre/factsheets/fs164/en/

Six HCV Genotypes and Subgenotypes Vary by Region: Important Predictor of Treatment Response



WHO.org.

Hepatitis C is a Leading Cause of Infectious Disease Deaths Worldwide, 2010

Disease	Estimated Deaths per Year
Lower respiratory tract infections	~2.65 million
HIV/AIDS	~1.34 million
Diarrheal diseases	~1.26 million
Tuberculosis	~1.29 million
Malaria	~855 million
Hepatitis C Virus	~704,000
Hepatitis B Virus	**~602,000**
Meningitis	~304,000
Measles	~96,000
Hepatitis E Virus	~50,000

Lancet. 2015 Jan 10;385(9963):117-71
2012;380.

A Large Number of Persons Are Living with Hepatitis C in the United States; Many Are Unaware of Their Infection

Virus	Prevalence	% Unaware of Infection
HCV	2.7 million (2.2 – 3.2 million)	45%-60%

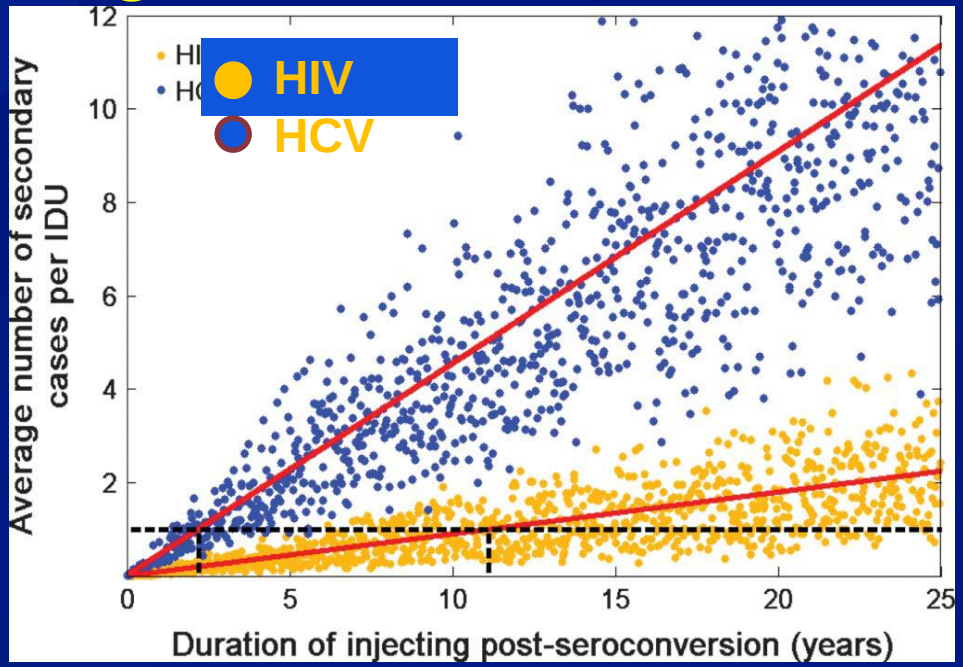
Estimated HCV Infection Among Homeless and Incarcerated Persons (Not Included in NHANES)	360,000-840,000 22%-52%

National Vital Statistics System; CDC. Denniston, Ann. Int. Med. 2014; *MMWR*. Aug 2012. Denniston M, Ann Int Med 2014. Chak E, Liver Int 2011.

HCV Transmission Risks Globally

HCV Transmission Among People Who Inject Drugs

- Transmission risks
  - Injection duration
  - Frequency of injecting
  - Equipment sharing, not just sharing needles



- Incidence declined in response to harm reduction for HIV (e.g., syringe access programs)

Hagan, et al, Int J Drug Policy 2007; Hagan et al, Amer J Public Health 2001.; Lucidarme, et al, Epid and Infect 2004; Burt et al, J Urban Health 2007; Garfein R, J Urban health 2013; Keen L Addict Behav. 2014; Amon JJ, Clin Infect Dis 2008
Kwon et al., *JAIDS* 2009

HCV Infections among Persons Who Inject Drugs

- Anti-HCV antibody + among PWID between 30% and 70%
- Anti-HCV prevalence among younger injectors (18—29 yo) between 10% and 36%
- Anti-HCV incidence among PWID between 5-42/100 person years
- HCV prevalence ~ 1.5 million HCV + PWID in United States

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Nelson PK, Lancet 2011, Hagan et al. 2010; Garfein et al. 1998; [2]Armstrong et al. 2006, Amon et al. 2008; [3] Klevens et al. 2013; Daniels et al. 2007; Amon et al. 2008 ; Weissing L, PlosOne 2014

Healthcare-associated HCV Transmission

- Larger contributor to transmission before viral discovery
- Prevention measures have reduced not eliminated transmission risk
- Total 18 outbreaks reported to CDC 2008-2013
  - 223 outbreak-associated cases
  - >90,550 at-risk persons notified for screening
  - Settings
    - Outpatient (e.g., surgical centers), dialysis
    - Hospitals
    - Long term care
  - Modes of transmission
    - Syringe reuse
    - Other poor infection control
    - Drug diversion

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Sexual Transmission

- Heterosexual
  - Attributable risk for 14 % of cases of incident HCV
  - Low risk among discordant couples- 0.07%/ 100 pyrs.
- Men Who Have Sex With Men (MSM)
  - HIV+ MSM have eight fold higher risk than HIV-MSM
    - Swiss Cohort Study- 4.1/100 pyrs.
    - U.S. cohort studies .26-.40/100 pyrs.
    - Boston clinic- 1.63/100 pyrs; 70% non IDU
  - Risks
    - Unprotected rectal intercourse
    - non injection drug use (e.g., XTC)
    - Other STIs
  - CDC recommends annual HCV testing

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Williams, I, Arch Intern Med. 2011 ; Terrault NA, et al Hepatology. 2013 Wandelar G, CID 2012; Taylor LE, CID 2011; . Garg S, Clin Infect Dis 2013

Perinatal Transmission of HCV

- **Transmission from HCV RNA + mothers**
  - Mono-infected 6.5%
  - HIV –infected- 13.6%
- **Transmission risks**
  - HCV viral load
    - < 6 log viral load- 3.9%
    - > 6 log viral load – 14.3%
  - Prolonged rupture of membranes(> 6 hours; OR 9.3)
  - Often cited but poor or no supportive data
    - Internal fetal monitoring
    - Vaginal versus cesarean delivery
- **No risk from breast feeding**
- **No recommendations for maternal testing**
- **Role of new antivirals yet to defined**

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Cottrell E, Ann Int Med 2013; Delotte J, J Matern Fetal Neonatal Med. 2014

Other Exposures Associated with HCV Transmission

- Non-injecting drug use- (e.g. cocaine); 0-17% HCV+
- Household exposures: 9% HCV+
- Unregulated tattooing: 2–3 times higher likelihood of HCV infection

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Scheinmann, et al , *Drug and Alcohol Dependence, 2006;* Gough et al. BMC Public Health 2010, Marincovich B,. *Sex Transm Infect.* Apr 2003; Yaphe S; Sex Transm Inf 2012 Aug 3; *Bottieau, et al Eurosurveillance 2010.) Ackerman Z, J Viral Hepat 2000. Waure C, et al J Epidemiol Community Health. 2010. Tohme RA, Clin Infect Dis. 2012.*

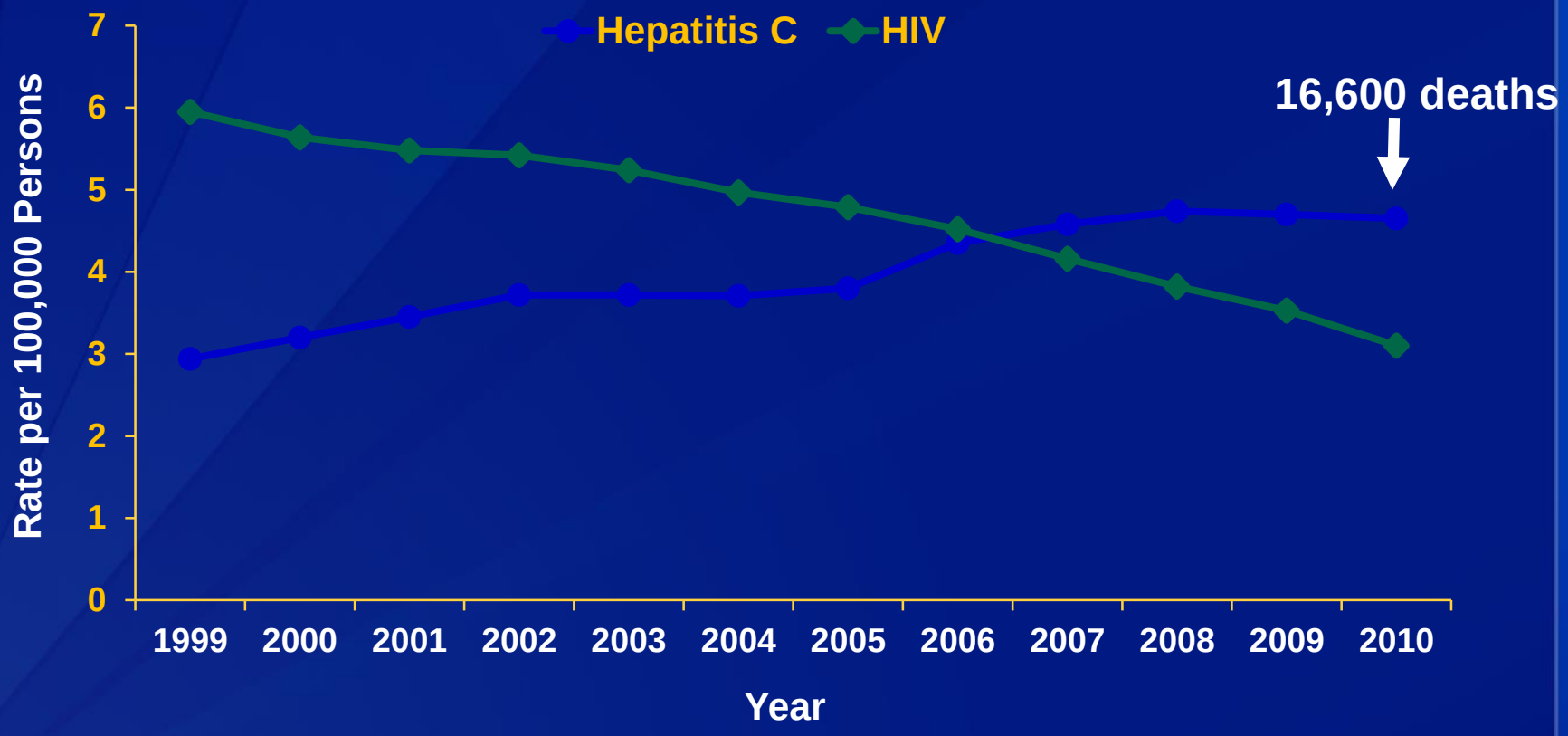
Trends in HCV- Associated Disease and Mortality in the United States

HCV is a Major Cause of Liver Disease and Associated Health Care Costs

- HCV is a major cause of liver disease
  - 40,000 (36%) of persons on liver transplant waitlist
  - 50% of persons with liver cancer; 2.5% annual increase
- Substantial HCV-related costs
  - Three-fold higher disability days (1.36 vs 0.34) than others
  - $21,000 in annual health costs vs $5,500 for others
  - From 2002 to 2010, HCV-positive patients aged 50-59 years had largest increases in hospital admissions (164%) and charges (341%)
- Successful hepatitis C treatment reduces health costs ($900 vs $1,378 per patient per month)

Kim WR, et al. *Gastroenterology*. 2009; Simard EP, et al. *Ca Cancer J Clin.* 2012; Kanwal F, et al. *Gastroenterology*. 2011; Ly K, et al. *Ann Int Med.* 2012; Rein, et al. *Dig Liver Dis.* 2010; Gordon SG, *Aliment Pharmacol Ther.* 2013.

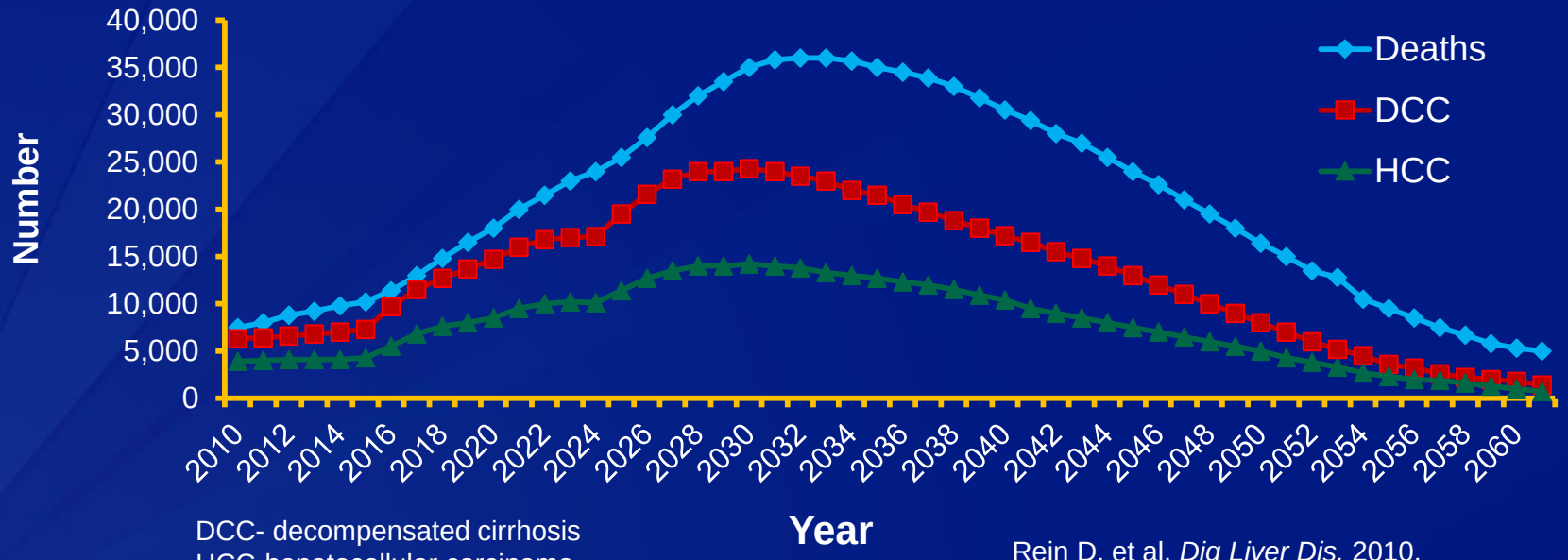
In the United States, at a Time of Declines in HIV Deaths, Mortality From HCV is Increasing



Ly KN, Xing J, Klevens RM, Jiles RB, Holmberg SD. Causes of death and characteristics of decedents with viral hepatitis, United States, 2010. *Clin Infect Dis.* 2014 Jan;58(1):40-9.

In Absence of New Interventions, the Burden of Hepatitis C is Projected to Continue to Grow in the United States

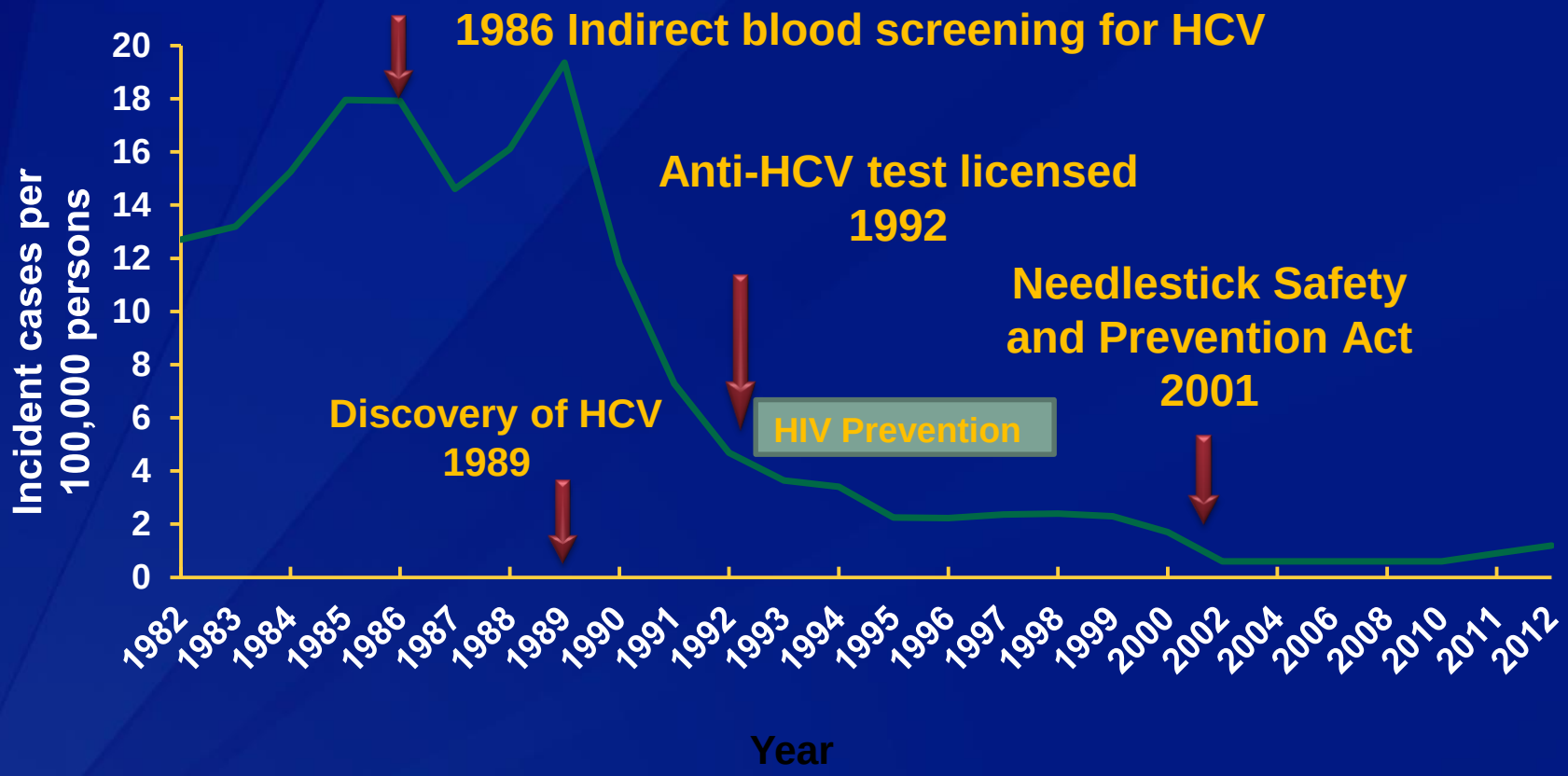
- Markov model of life-time health outcomes
  - Of 2.7 million HCV-infected persons in primary care:
    - 1.47 million will develop decompensated cirrhosis (DCC)
    - 350,000 will develop hepatocellular carcinoma (HCC)
    - 897,000 will die from HCV-related complications



DCC- decompensated cirrhosis
HCC-hepatocellular carcinoma

Rein D, et al. *Dig Liver Dis.* 2010.

Discovery of HCV and Impact on HCV Incidence in US

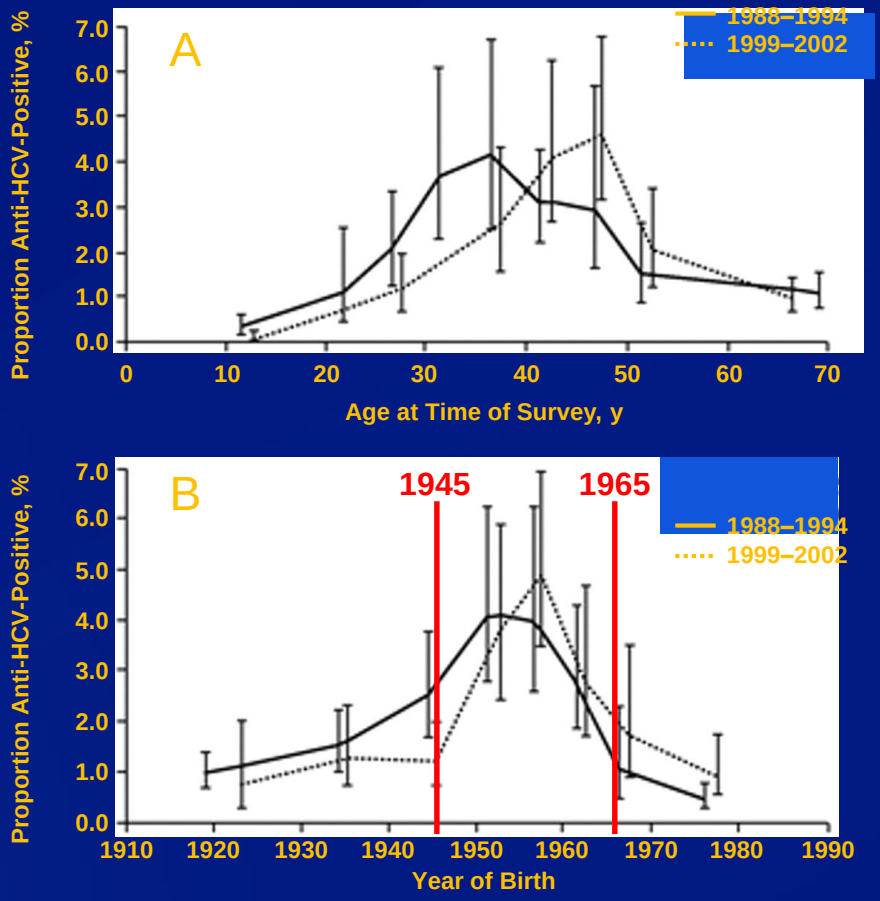


22,000 cases of incident HCV infection reported in 2012

Alter MJ JAMA 1990; Jagger J, J infect Dis Pub Health 2008;; Ward JW. *Clin Liver Dis*, 2013. CDC.gov/hepatitis;

Two of Three Americans Living with HCV Were Born During 1945-1965

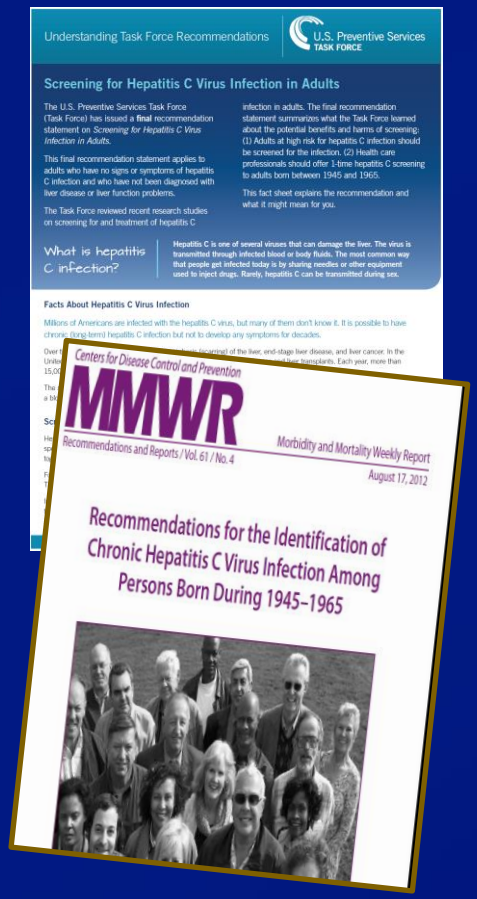
- Reflects high HCV incidence in distant past
- Five-fold higher prevalence than others (3.39% vs .55%)
- 81% of all HCV+ adults
- 73% of all HCV-related mortality



Kramer, et al. *Hepatology.* 2011; Ly, et al. *Ann Int Med*. 2012. Smith, et al. *AASLD Liver Meeting*. San Francisco, CA. 2011; Armstrong, et al. *Ann Int Med.* 2006;

CDC and USPSTF Updated Recommendations for HCV Testing

- **One time screening test for persons born 1945-1965**
- **Major risk**
  - Past or present injection drug use
- **Other risks**
  - Received blood/organs prior to June 1992
  - Received blood products made prior to 1987
  - Ever on chronic hemodialysis
  - Infants born to HCV infected mothers
  - Intranasal drug use
  - Unregulated tattoo
  - History of incarceration
- **Medical**
  - Persistently elevated ALT
  - HIV (annual testing)



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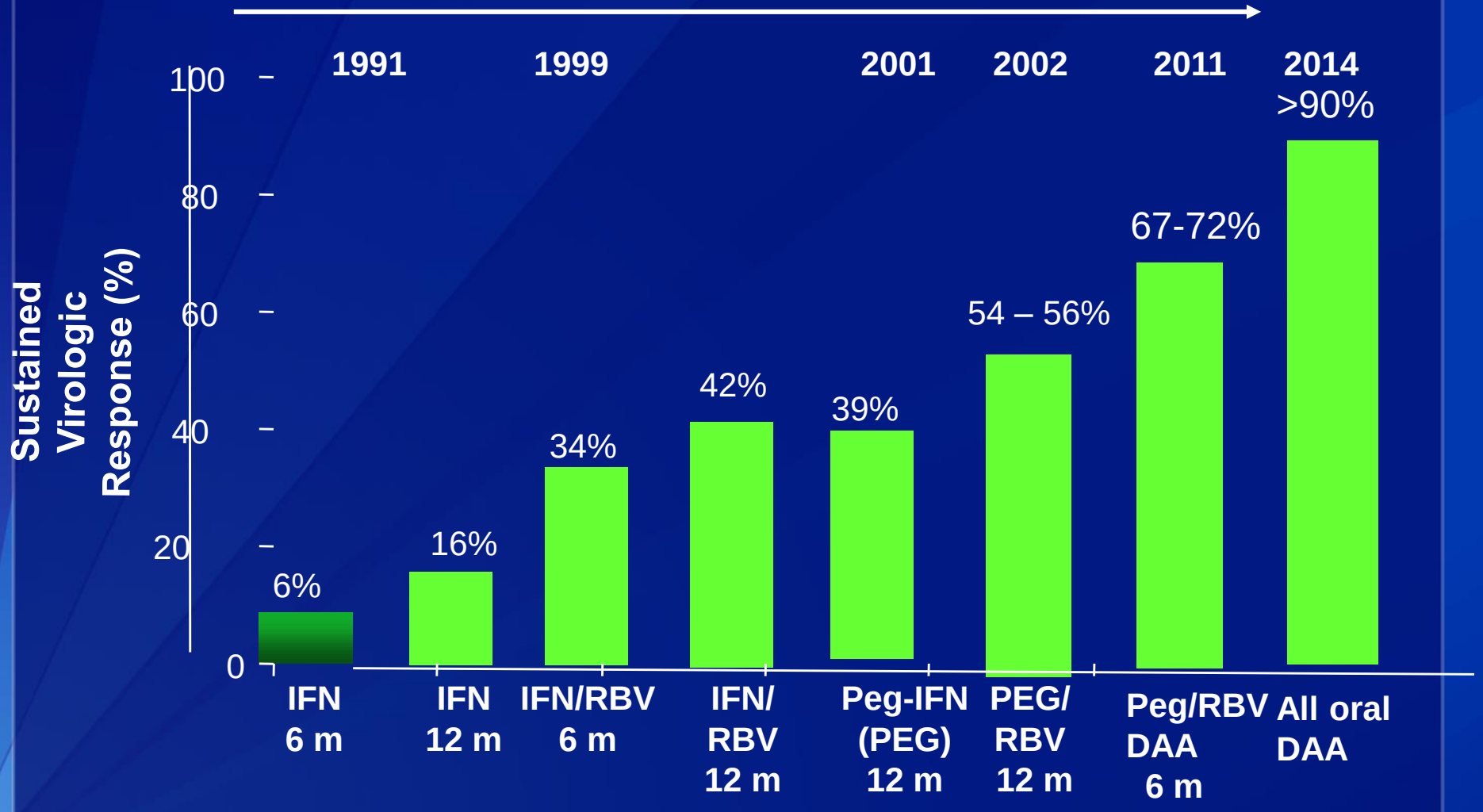
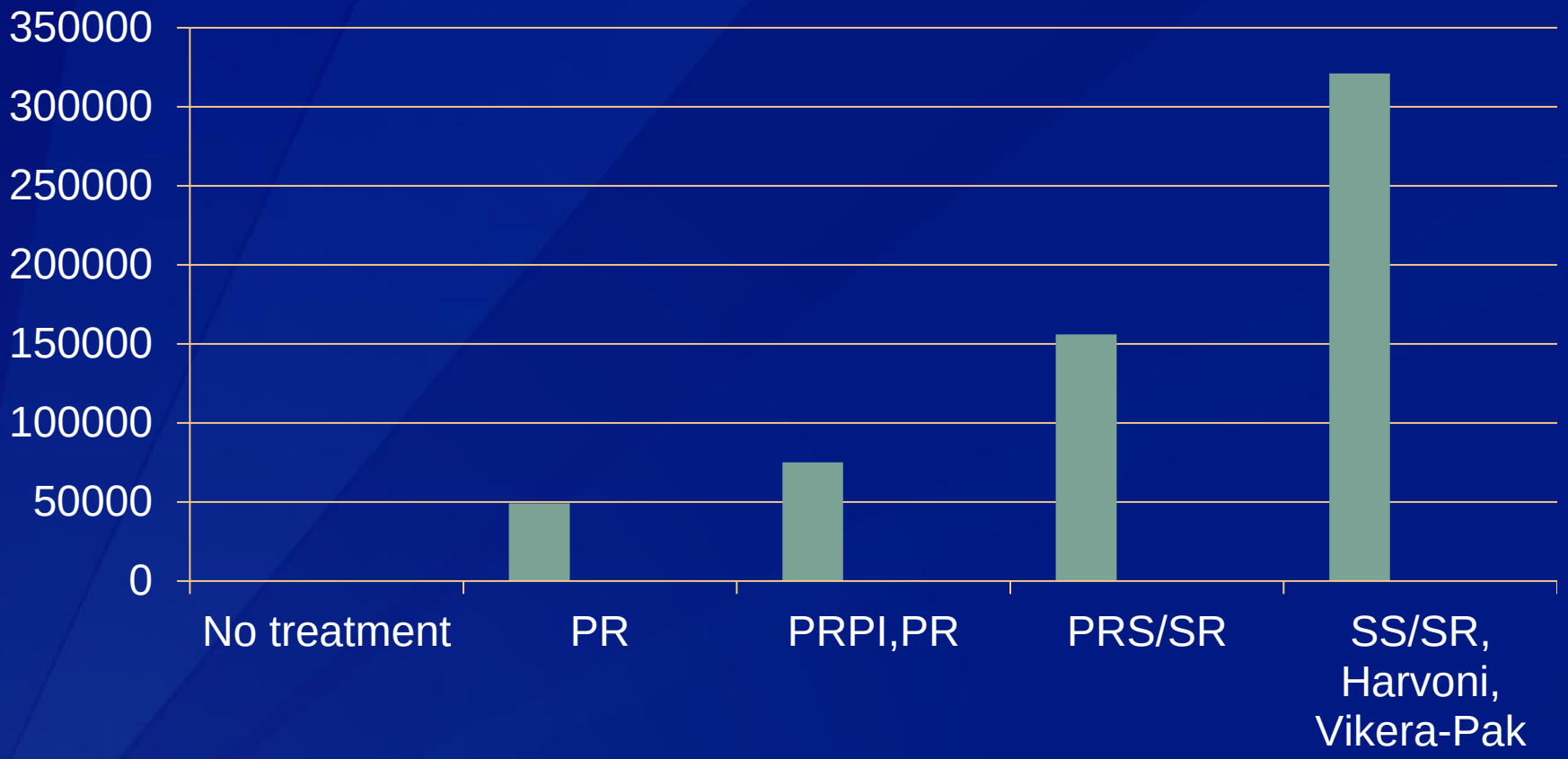
MMWR Aug 2012. Moyer VA, *Ann Int Med* 2013.
http://www.hcvguidelines.org

Advances in HCV Therapy



Adapted from Strader DB, et al. *Hepatology.* 2004;39:1147-71

HCV Deaths Averted with Birth Cohort Testing Using Different Treatments



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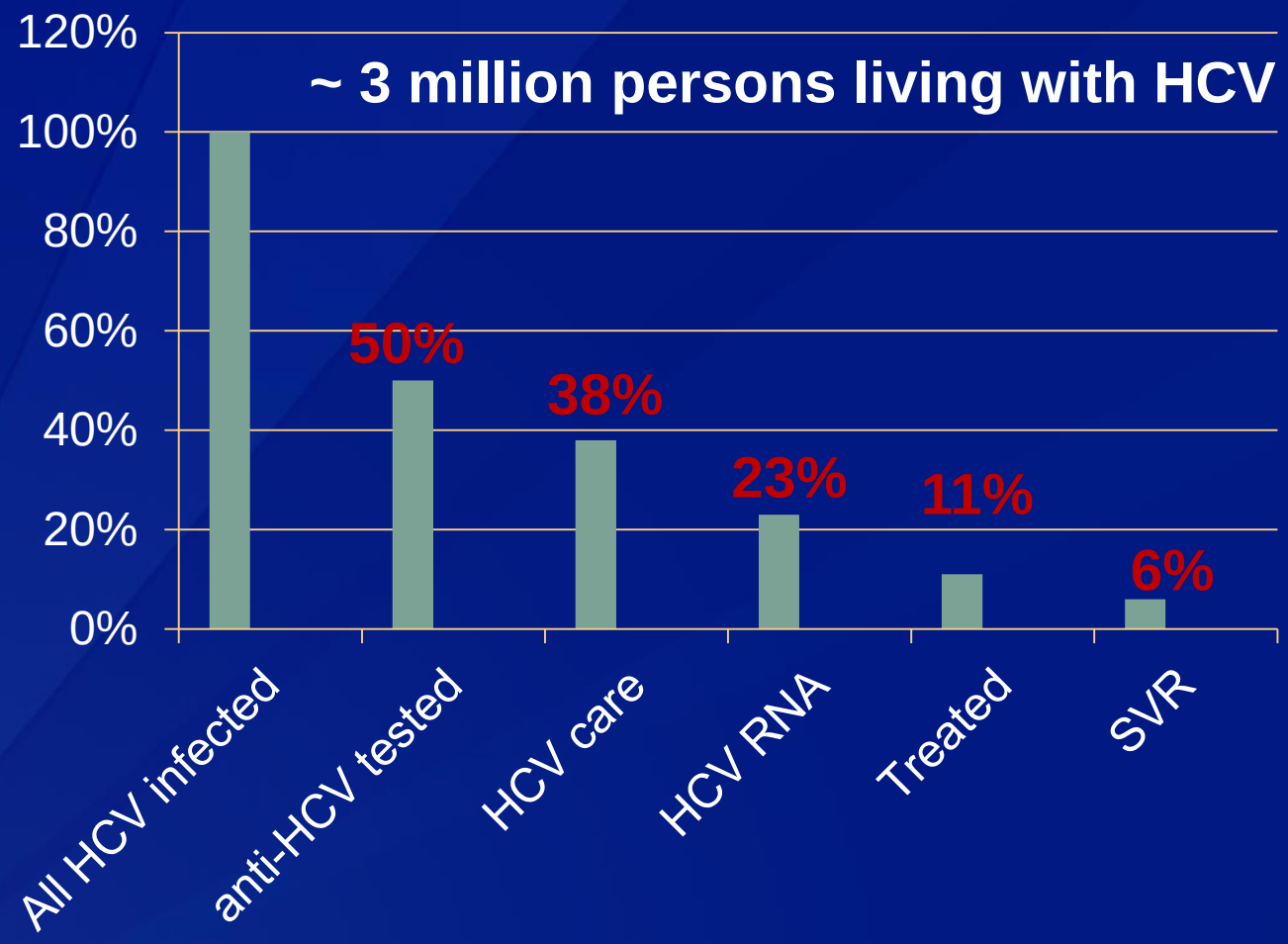
PR = Pegylated Interferon plus Ribavirin for all genotypes, PRPI; PR = PR plus a protease inhibitor for genotype 1, PR for genotypes 2/3; PRS/SR = pegylated interferon, ribaviron, and sofosbuvir for genotype 1, and sofosbuvir plus ribavirin for genotypes 2 and 3; SS/SR = Sofosbuvir and Simeprevir for genotype 1, and sofosbuvir and ribavirin for genotypes 2 and 3.

HCV Test, Care, and Cure Continuum



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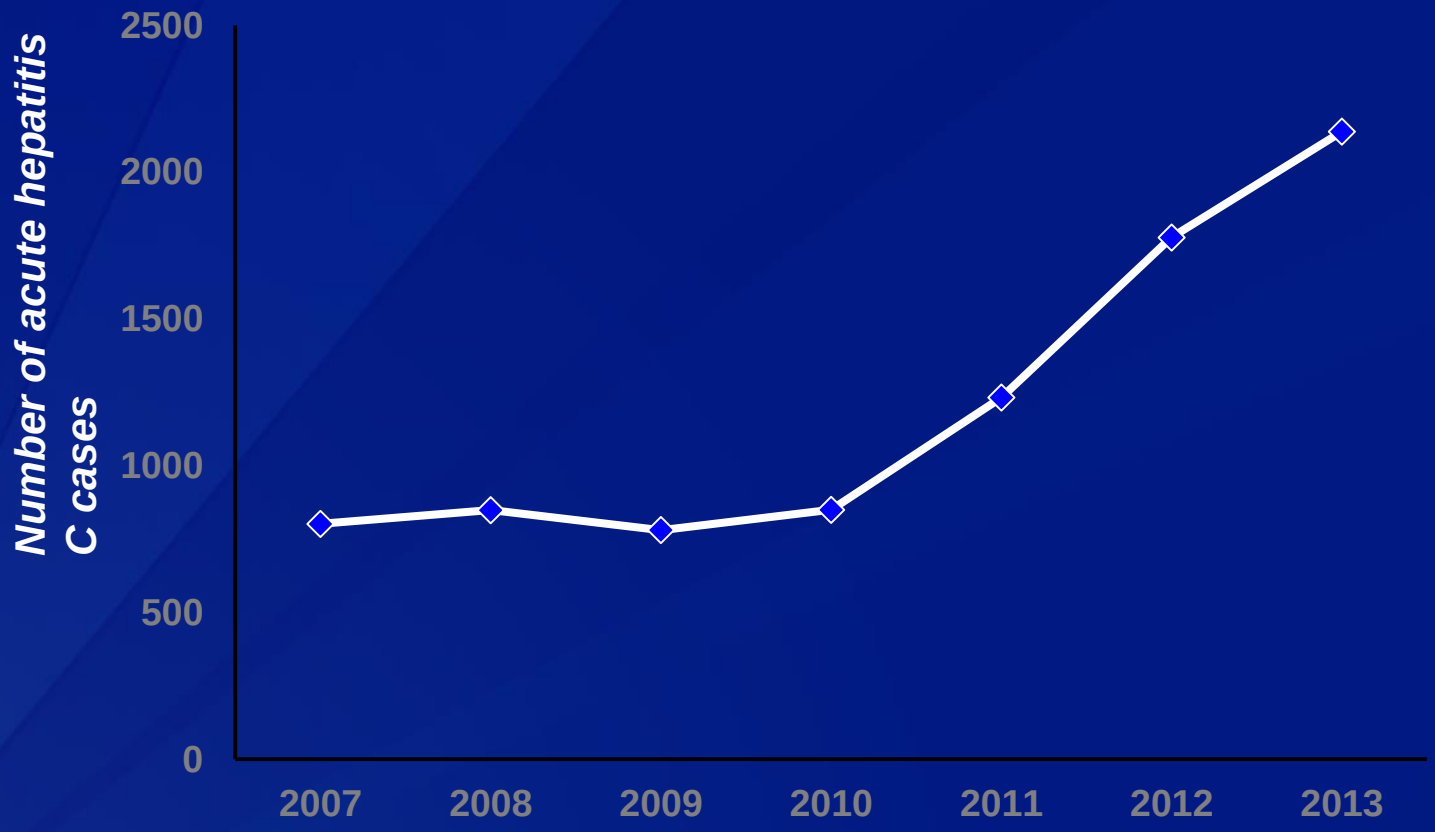
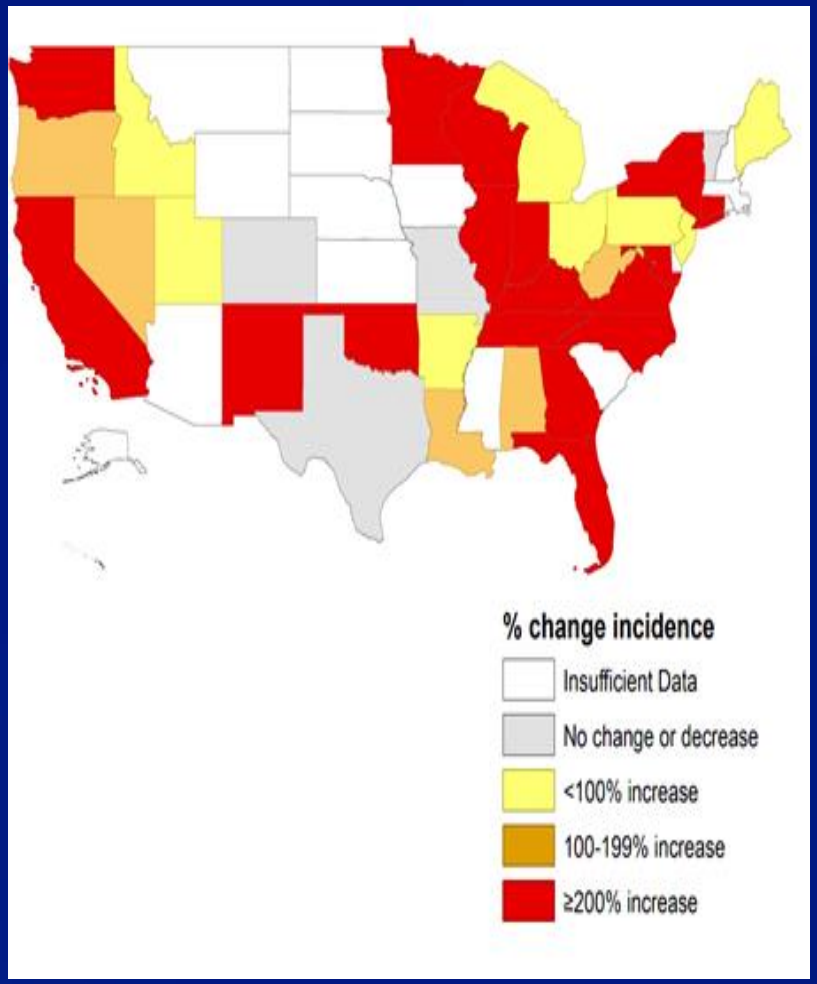
Holmberg S, et al, NEJM, 2013)

Reports of Acute HCV infection 2007-2013



Recent Increases in New HCV Infection

- **Between 2007 and 2013**
  - Estimated 29,000 new HCV infections
  - 150% since 2010
  - 12 states report 66% of cases
  - (CA, FL, IN, KY, MA,MI,NJ, NY, NC,OH,PA,TN)



Suryprasad AG, et al. CID 2014

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Risks Among Persons 18-29 Years of Age with Acute HCV Infection

- 1202 cases of acute HCV investigated
  - 52% female
  - 85% white
  - 77% persons injected drugs
    - 57% shared needles/syringes
    - 82% shared equipment
- Percent use and mean age of drug use initiation
  - Powder cocaine: 71%,: 17.4 yrs.
  - Prescription opioids 76% : 17.9 yrs.
  - Heroin: 61%: 19.7 yrs.

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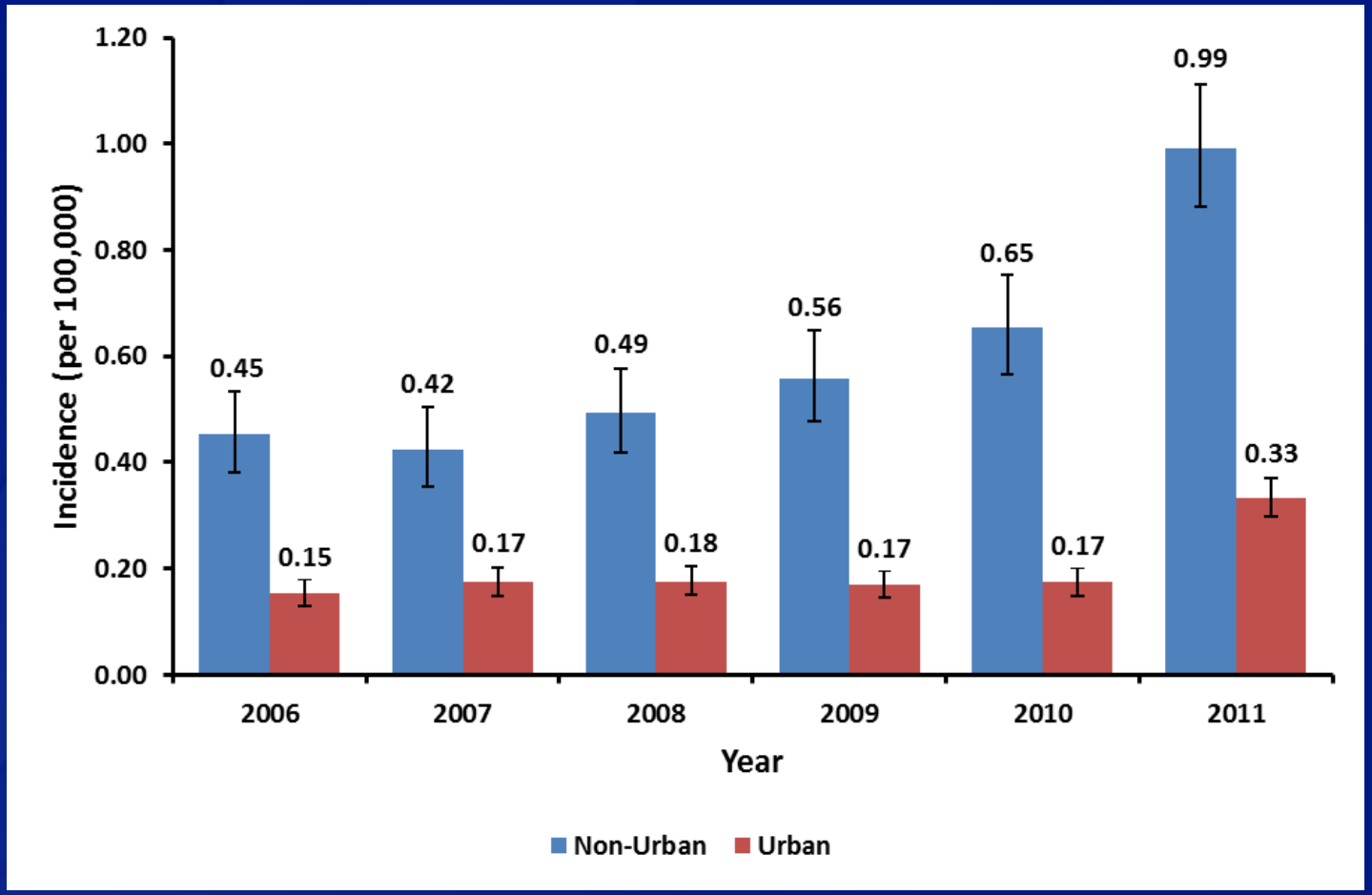
Suryaprasad A, et al CID 2014

Hepatitis C Incidence by Urbanicity and Year of Diagnosis



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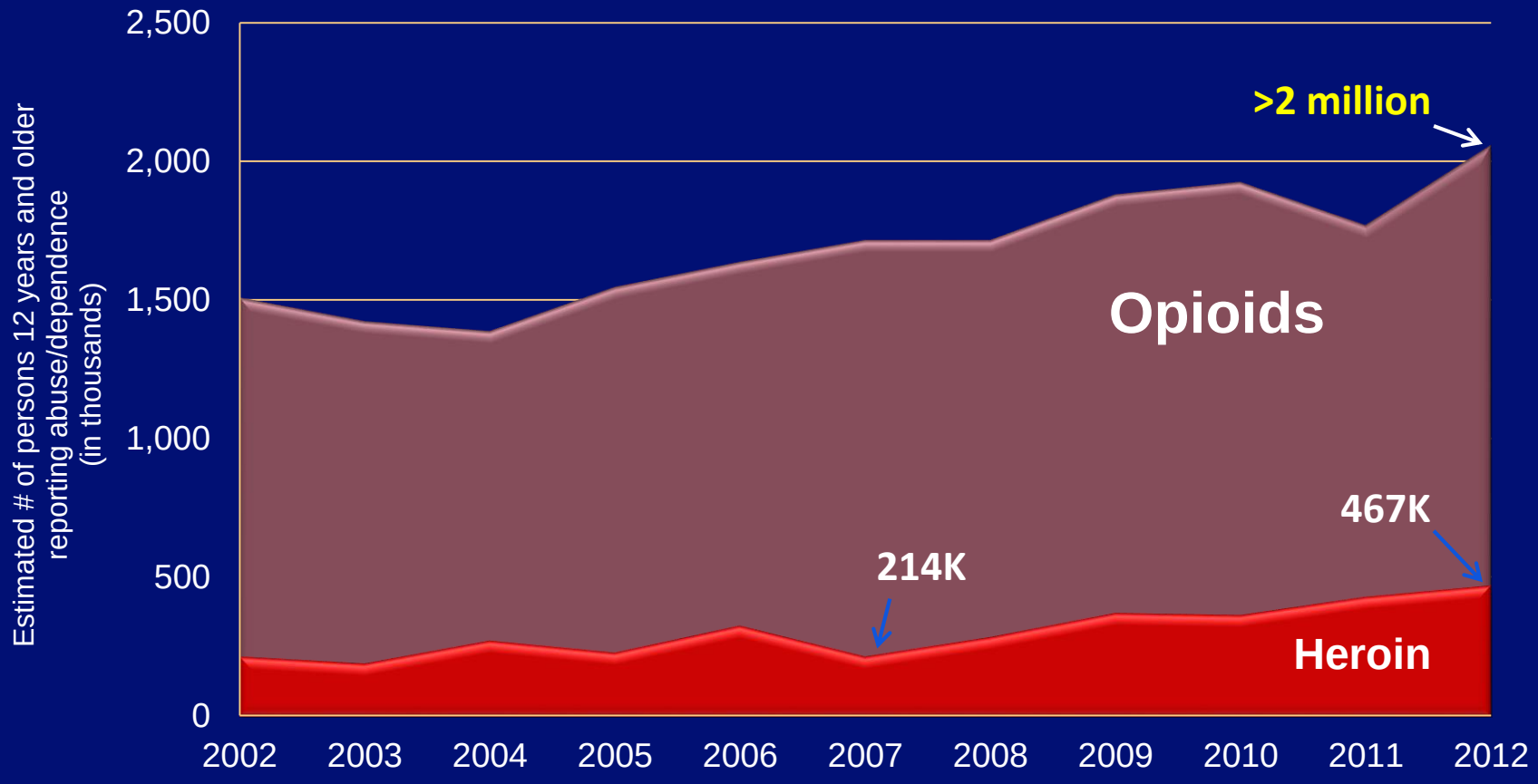
Suryprasad AG, et al. CID 2014

Heroin Use and Dependence is Increasing



SAMHSA NSDUH 2012

Interventions to Prevent HIV and HCV Among Persons Who Inject Drugs

Intervention	Decrease Injection Risks	Prevent HIV	Prevent HCV
Syringe exchange	++	+	±
Pharmacy access	+	±	*
Drug preparation equipment	+	*	±
Opioid substitution	++	++	+
Education	+	±	±
Supervise injection	+	±	±

++: sufficient data; ++ tentative data; ±: Inconclusive; * : no data

MacArthur GJ, Int J Drug Policy 2014

Multi-Component Interventions for HCV Prevention

A combination of *readily-available* and *low threshold* OAT (with methadone and/or buprenorphine) and SEPs have been shown to:

- **Reduce syringe sharing**
- **Lower injecting risk**
- **Reduce incidence of HIV and HCV**
  - **Up to 80% in UK**
  - **Three fold - New York**

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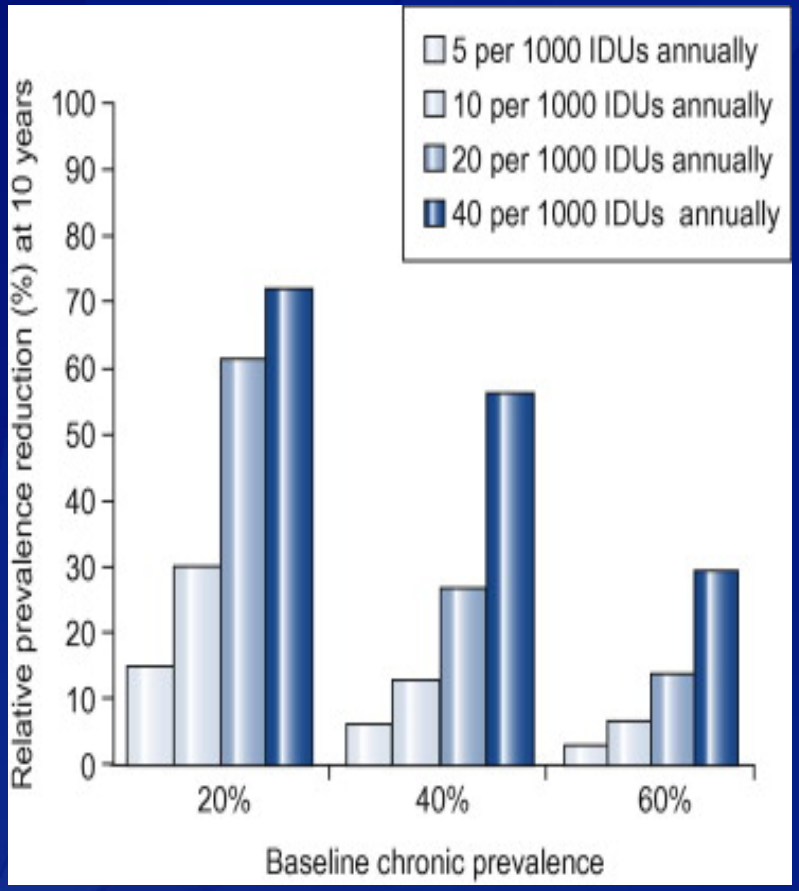
OAT: Opiod Agonist Treatment
SEP: Syringe Exchange Programs

Palmateer N, Addiction. 2010; Degenhardt L, Lancet. 2010; Kwan JA, J Acquir Immune Defic Syndr. 2009; Turner KM Addiction. 2011; DesJarlais DC, The Lancet,

Antiviral Therapy Might Be Used to Reduce HCV Prevalence Among Injecting Drug Users



- Annually treating 10 HCV infections per 1000 IDU and achieve SVR of 62.5%
- Projected to result in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% for prevalences of 20%, 40%, or 60%, respectively
- Can the HIV model of “Treatment as Prevention” be applied to HCV?

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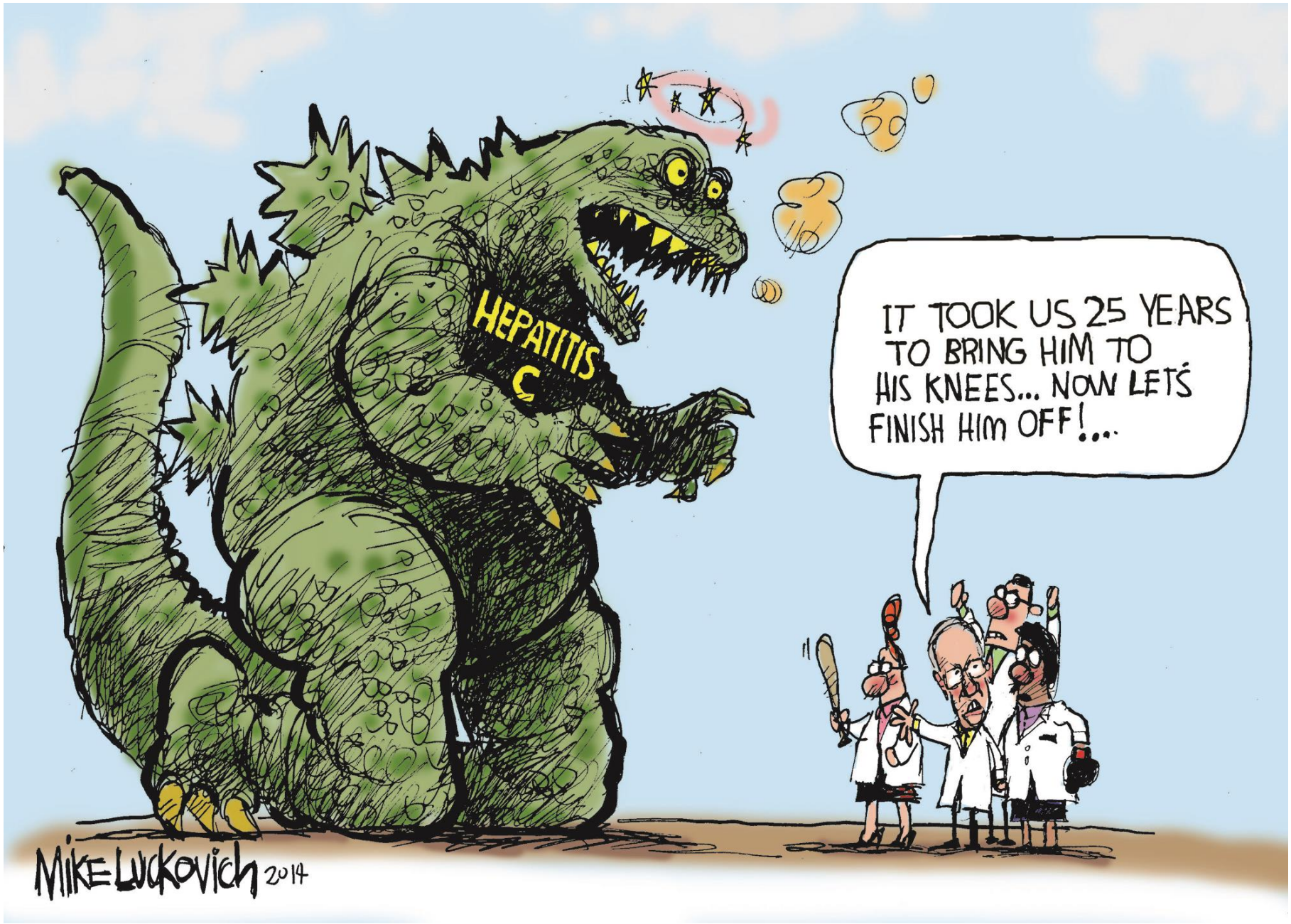
Martin et al. Journal of Hepatology 2011 vol. 54 ¡ 1137–1144

Summary

- Blood-borne exposures to HCV are major transmission risks
- The burden of HCV-related disease is large and growing
- Reports of acute HCV infection are increasing
- Many if not most persons living with HCV are undiagnosed
- CDC and USPSTF recommend HCV testing for persons born 1945-1965, past or present injection drug users, and others at risk
- Access to HCV prevention, testing, care, and treatment must improve to reduce HCV transmission and disease


HEPATITIS C
IT TOOK US 25 YEARS TO BRING HIM TO HIS KNEES... NOW LETS FINISH HIM OFF!...
MIKE LUCKOVICH 2014


OPEN YOUR WORLD.
Most don't know they're infected
SIEMENS
ends a simple blood test for Hepatitis C, a silent killer.
Worker Doubts Oly's Court Outbursts Are an Act
NEWS
to fans
ESPN
triners affiliate finishes 16-run comeback
SEPHORA

Local Health Departments and Hepatitis C

NACCHO Educational Series

Webcast 1.1 Hepatitis C: Where Are We Now?

Webcast 1.2 The National Viral Hepatitis Action Plan

Webcast 1.3 Viral Hepatitis C Testing Recommendations for Persons Born 1945-1965

Webcast 1.4 Leveraging Partnerships to Address Hepatitis C: Philadelphia's Model

All materials available at www.naccho.org/hepatitisc

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