Management of Hepatitis C Infection: Promises and Challenges Ahead

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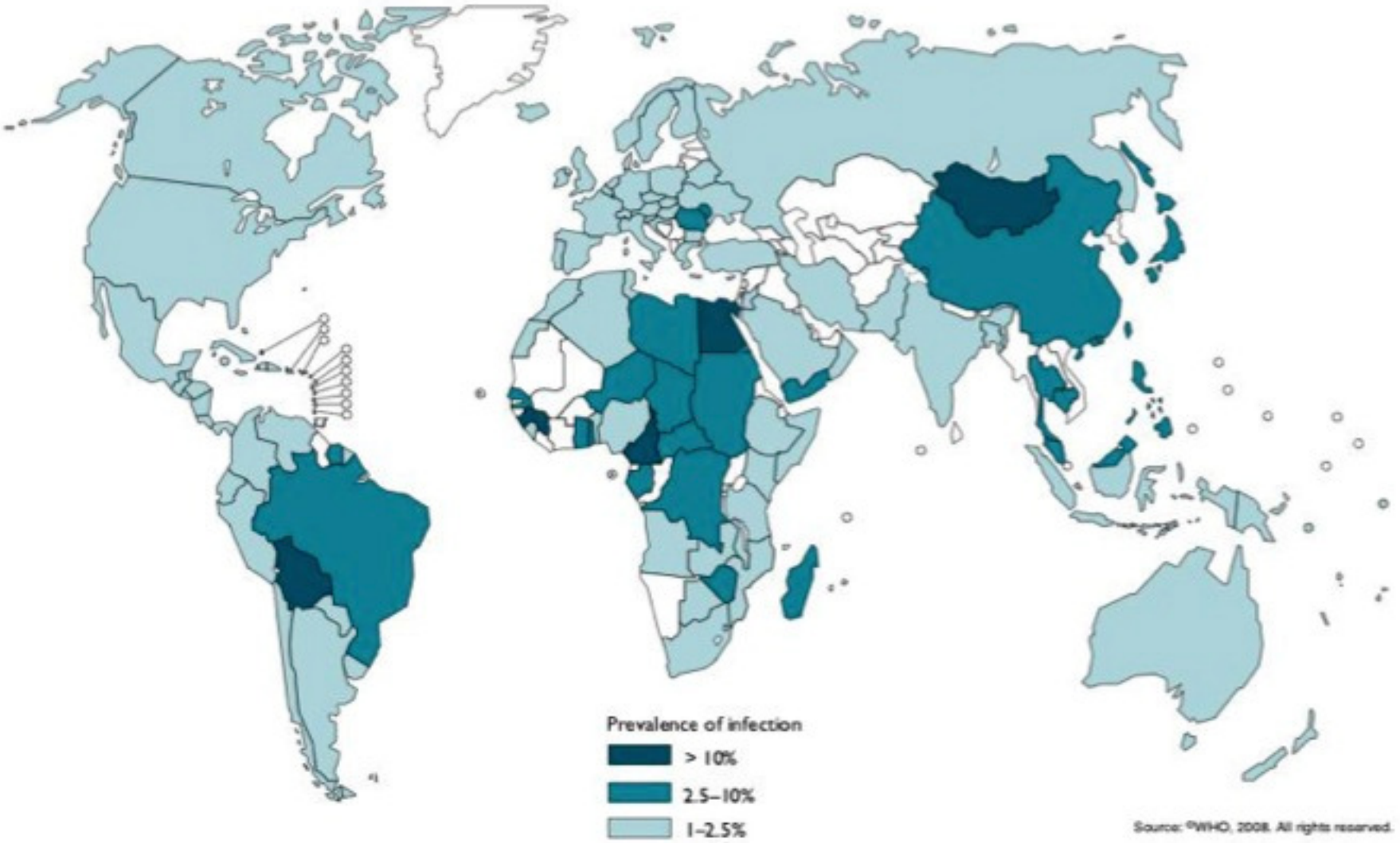
Overview

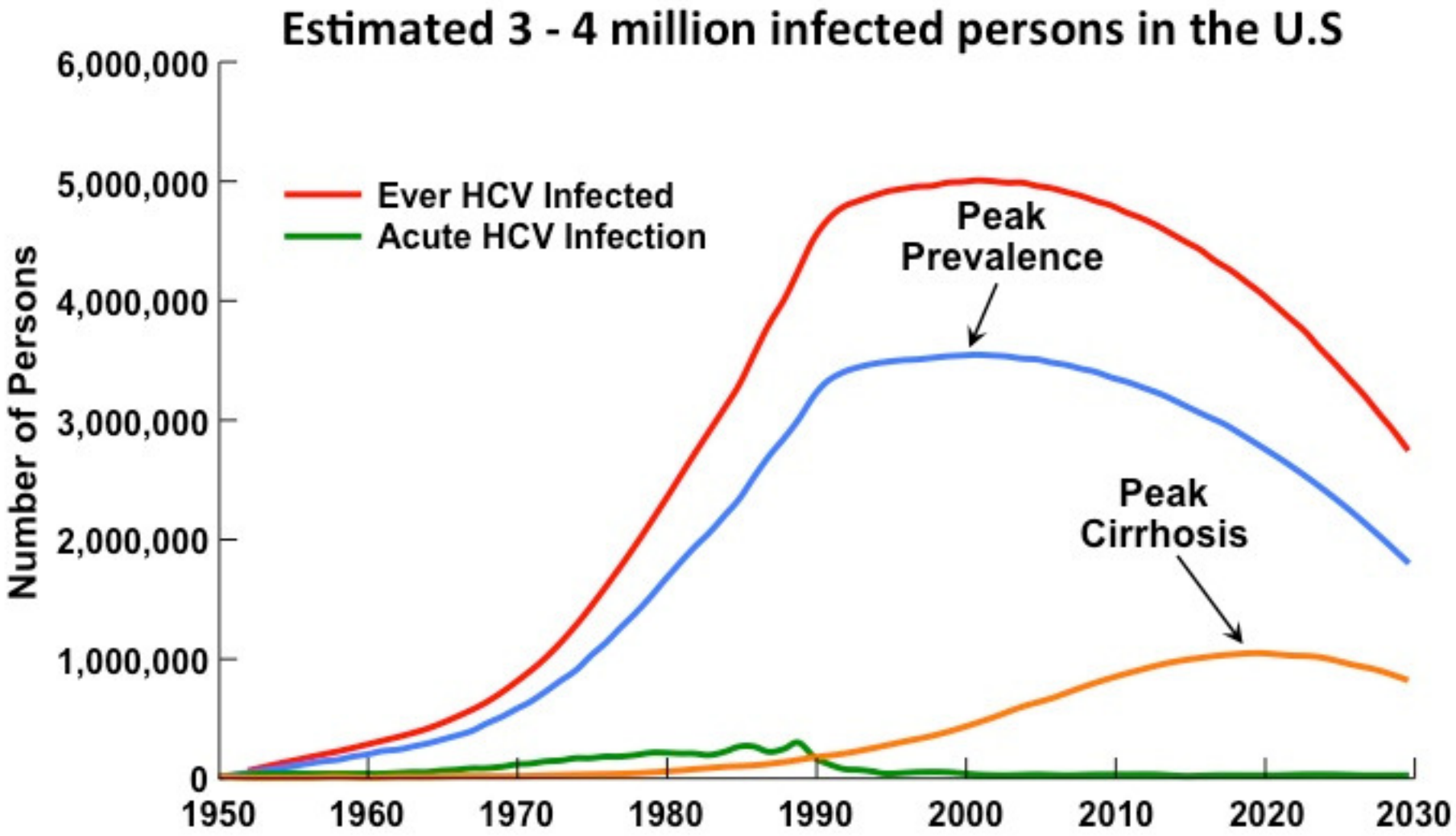
- The current landscape of hepatitis C in the United states
- Newly approved directly acting antiviral agents (DAAs) in different patient populations
- Future therapeutic options beyond 2014
- The Washington DC HCV experience (DCPFAP)

Hepatitis C : *Epidemiology*

- Estimated 170 million persons with HCV infection worldwide
- 3-4 million newly infected each year worldwide



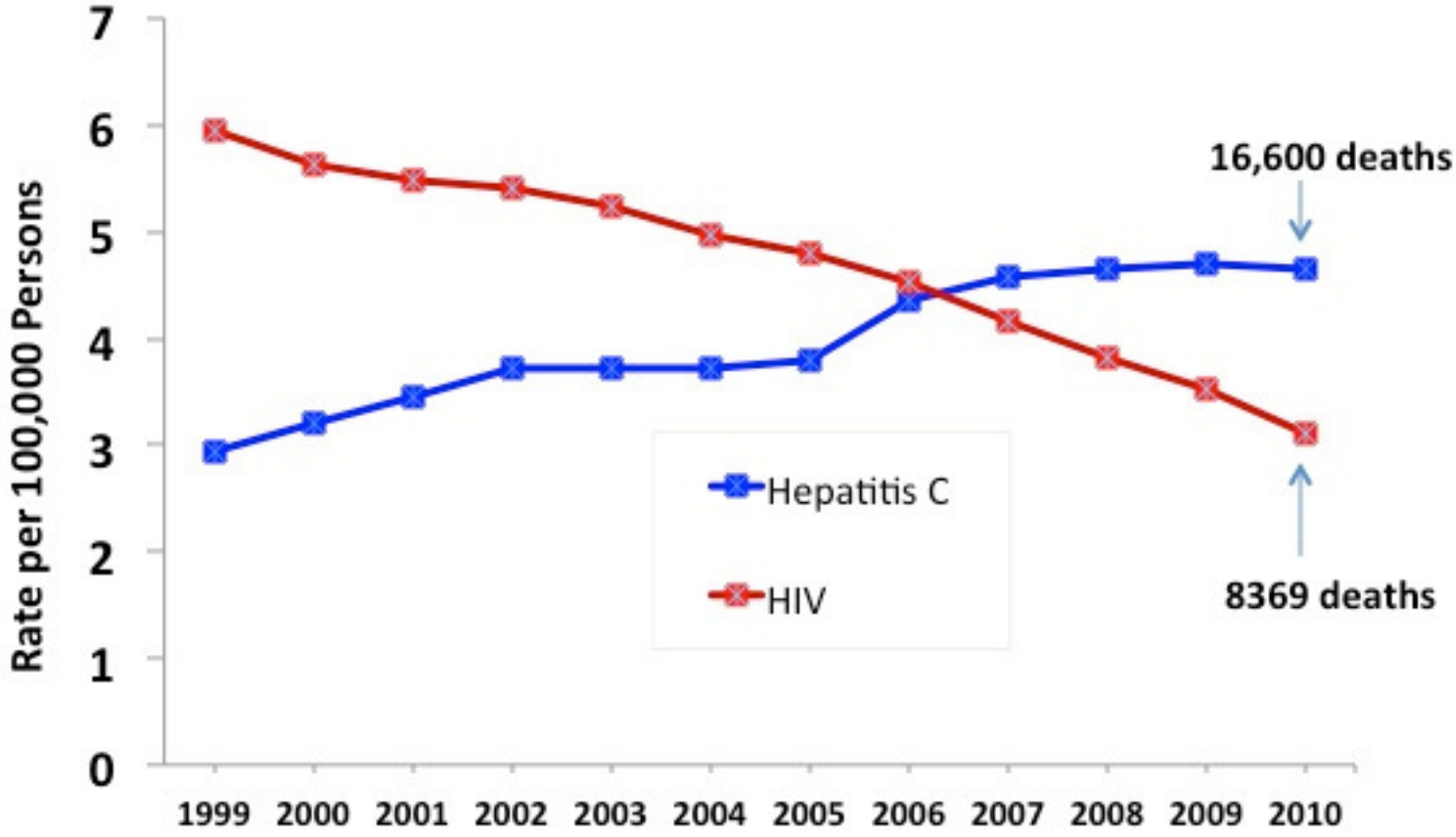
The Changing Face of HCV in US



Adapted from Davis GL et al Gastroenterol 2010;138:513-521

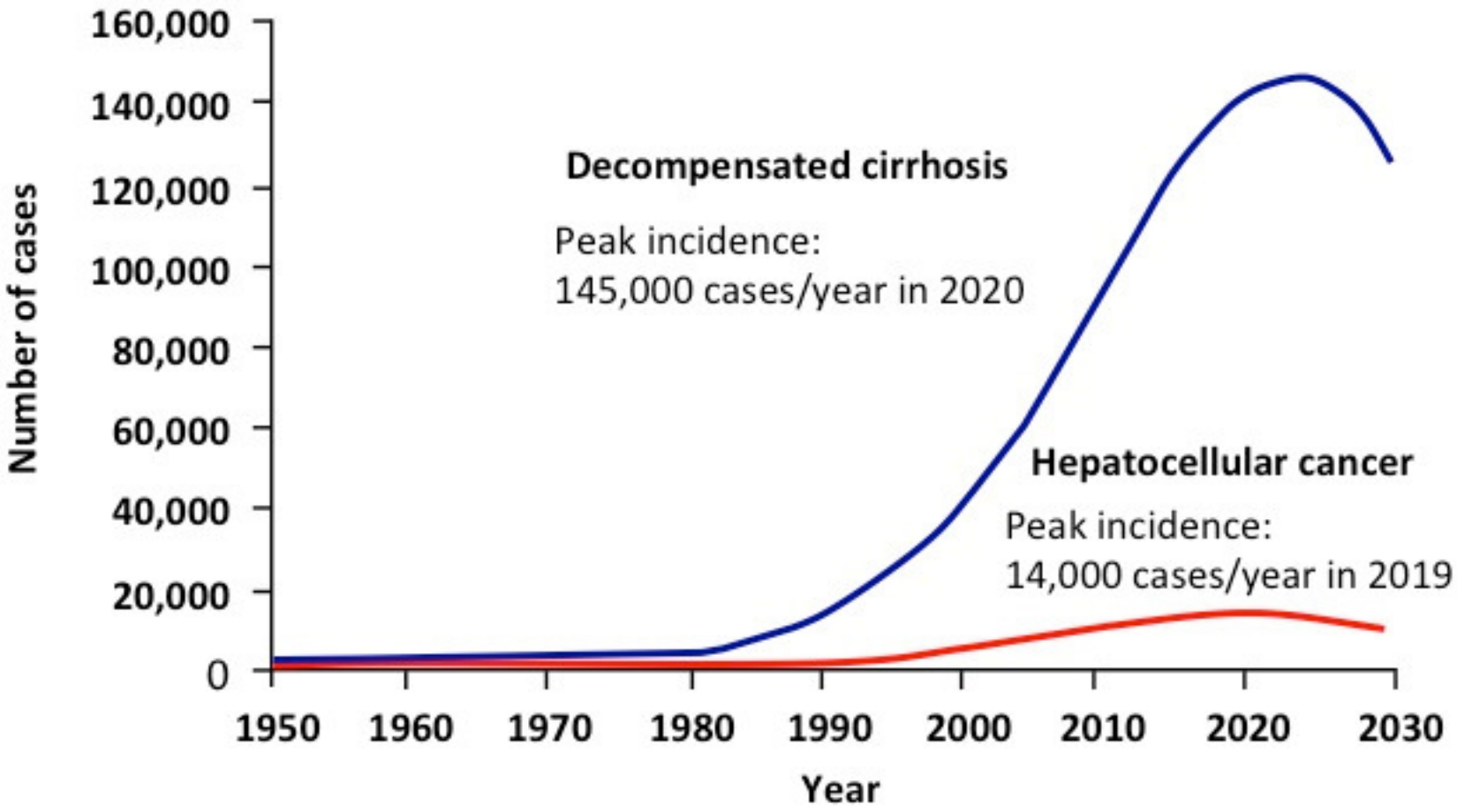
Deaths From Hepatitis C Have Surpassed Deaths From HIV Infection

Age-adjusted Mortality Rates of HIV and Hepatitis C: United States, 1999-2010



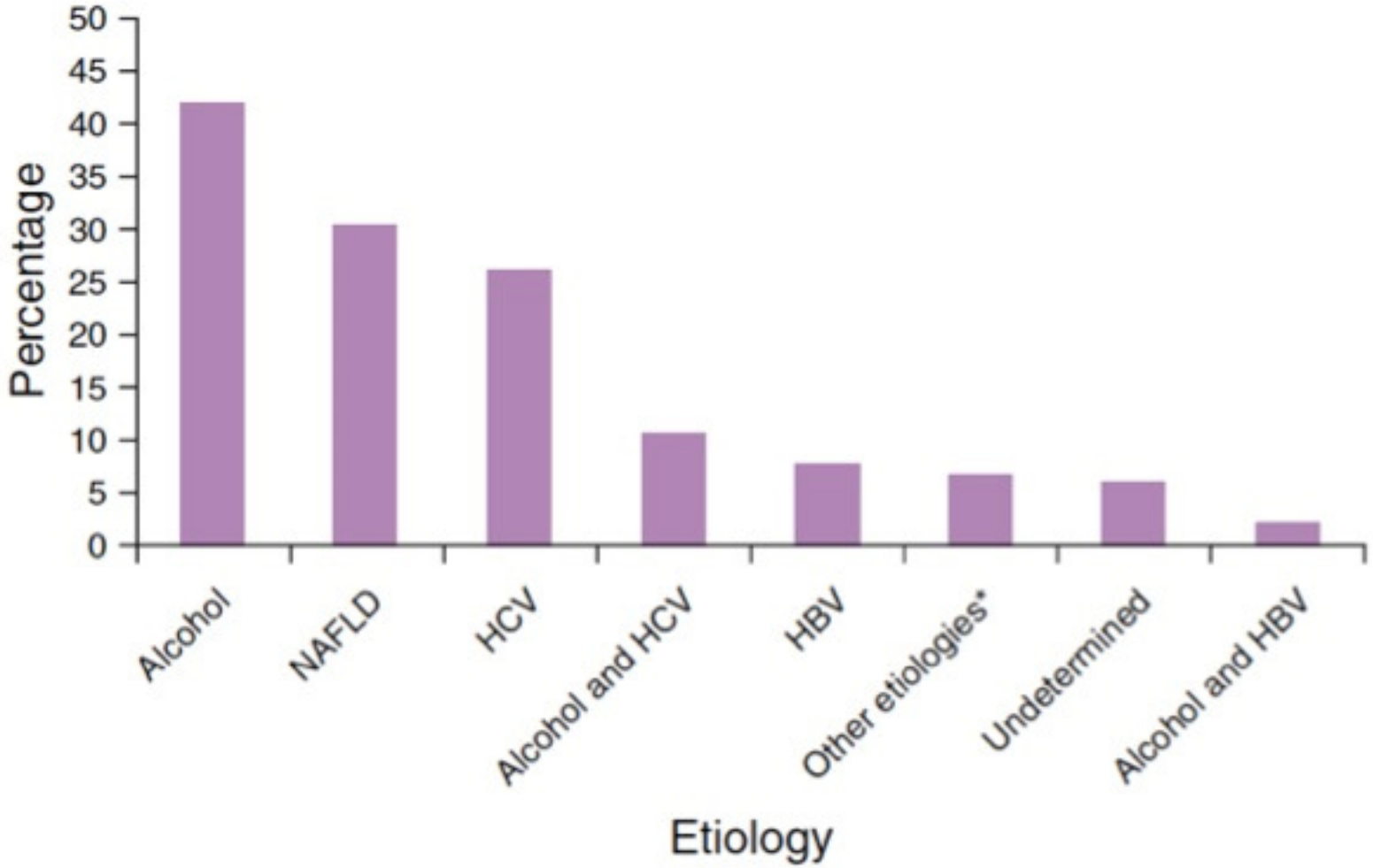
Ly K.N et al., Annals of Int. Med, 2012: 157 (9)

Projected Cases of Hepatocellular Carcinoma and Decompensated Cirrhosis Due to HCV



Davis GL, et al. *Gastroenterology*. 2010;138(2):513-521

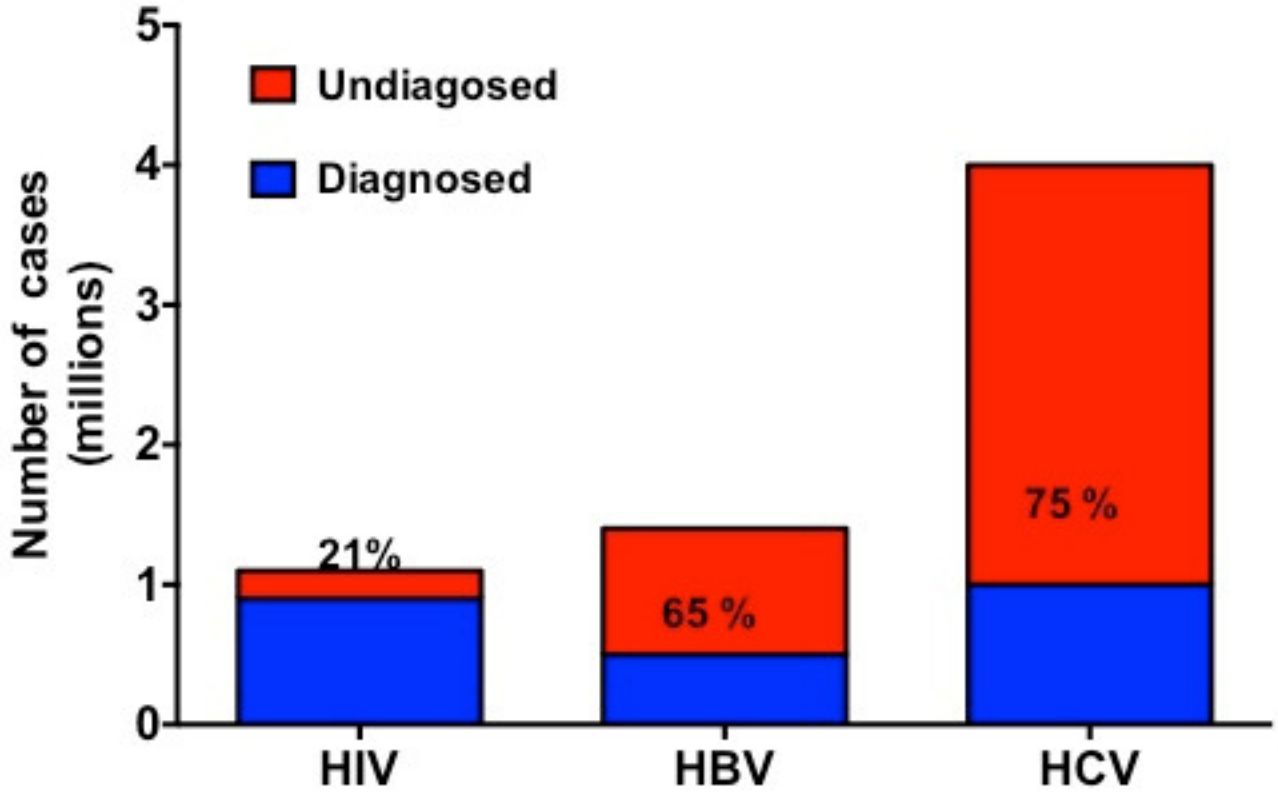
Causes of Chronic Liver Disease Among Alaskan Indian Population



Byrd KK et al .Am J Gastro, 2011, 126: 816-825

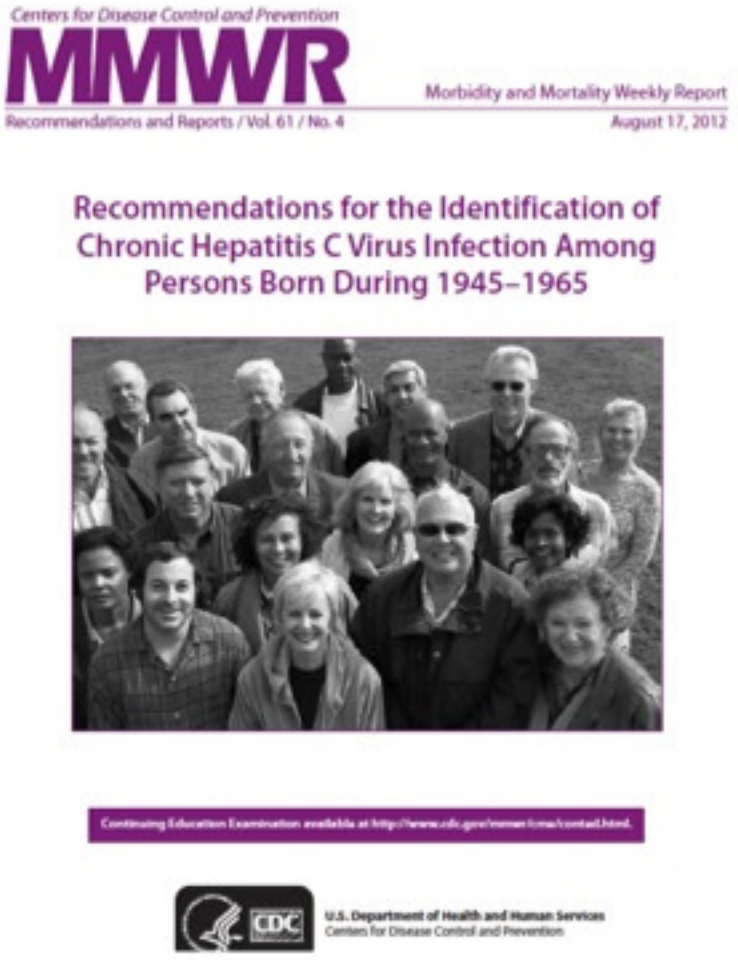
HCV Is Largely Underdiagnosed In The U.S

Number of infected persons vs number aware of their infection (diagnosed)



Institute of medicine: Hepatitis and Liver Cancer: A national strategy for prevention and control 2010

CDC HCV Screening Recommendations



CDC now recommends

- **Age based testing : All adults born during 1945 – 1965 should have a one time antibody testing without prior ascertainment of risk**
- Referral to care
- Alcohol screening and intervention

If tested and treated,

->120,000 deaths averted

- >$2.5 billion medical costs averted

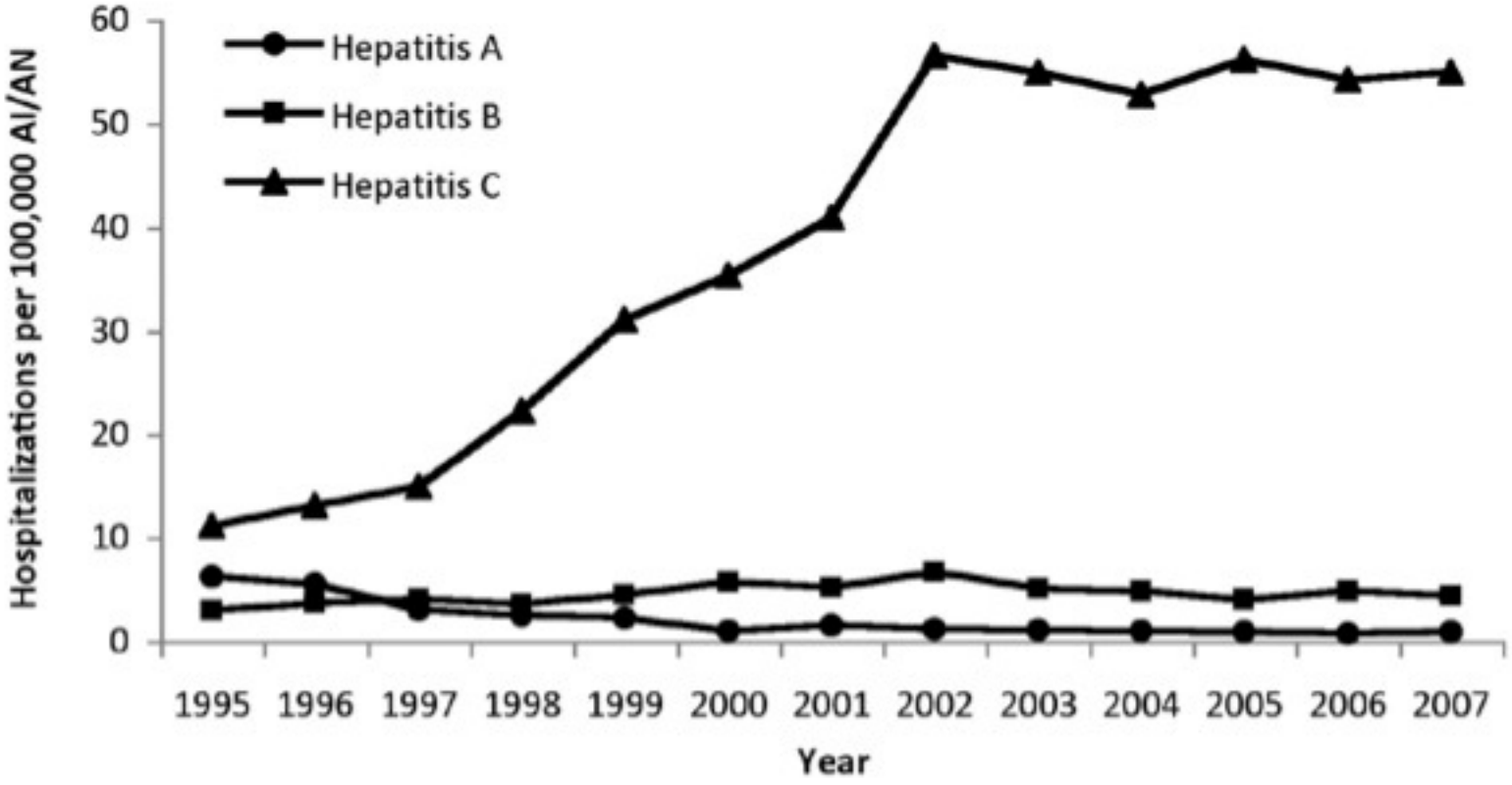
MMWR Aug 17, 2012; Rein D et al, Ann Int med 2012: 156

Primary concerns pertaining to HCV screening

Cost of treatment for hepatitis C	54.2%
Referral facilities for HCV patients	45.8%
Treatment options for HCV patients	41.7%
Cost of increasing HCV screening	39.6%
Clinical training on HCV	37.5%
Implementing HCV screening	31.3%
Rationale of CDC recommendations for age-based screening	14.6%

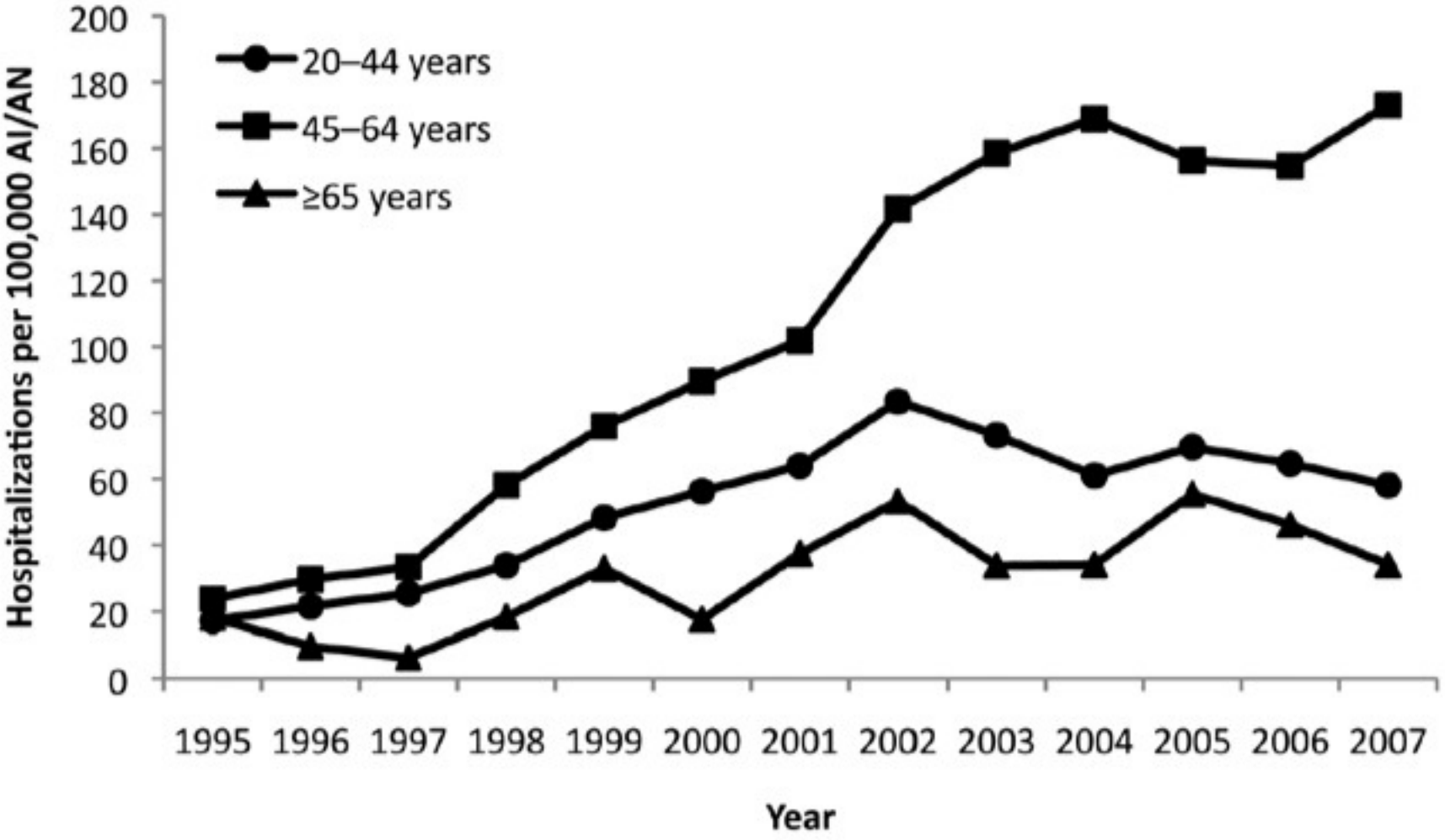
Reilley B et al. *J Public Health Manag. Pract*. 2013, 1-4

Annual Hospitalization Rates as a Result of Hepatitis



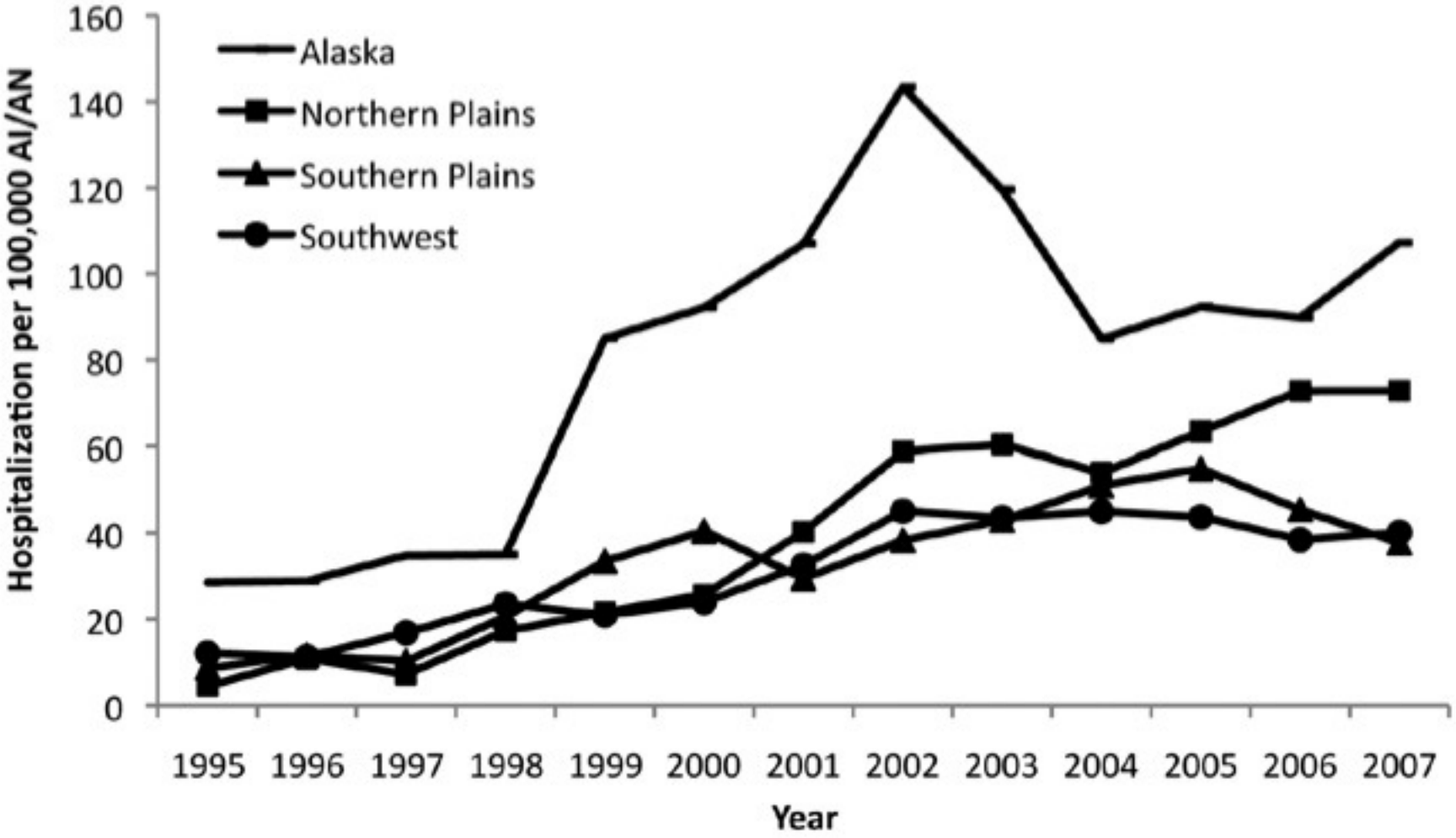
Byrd KK et al. *Public Health Reports*, 2011, 126: 816-825

Annual Hospitalizations due to Hepatitis C by Age Group



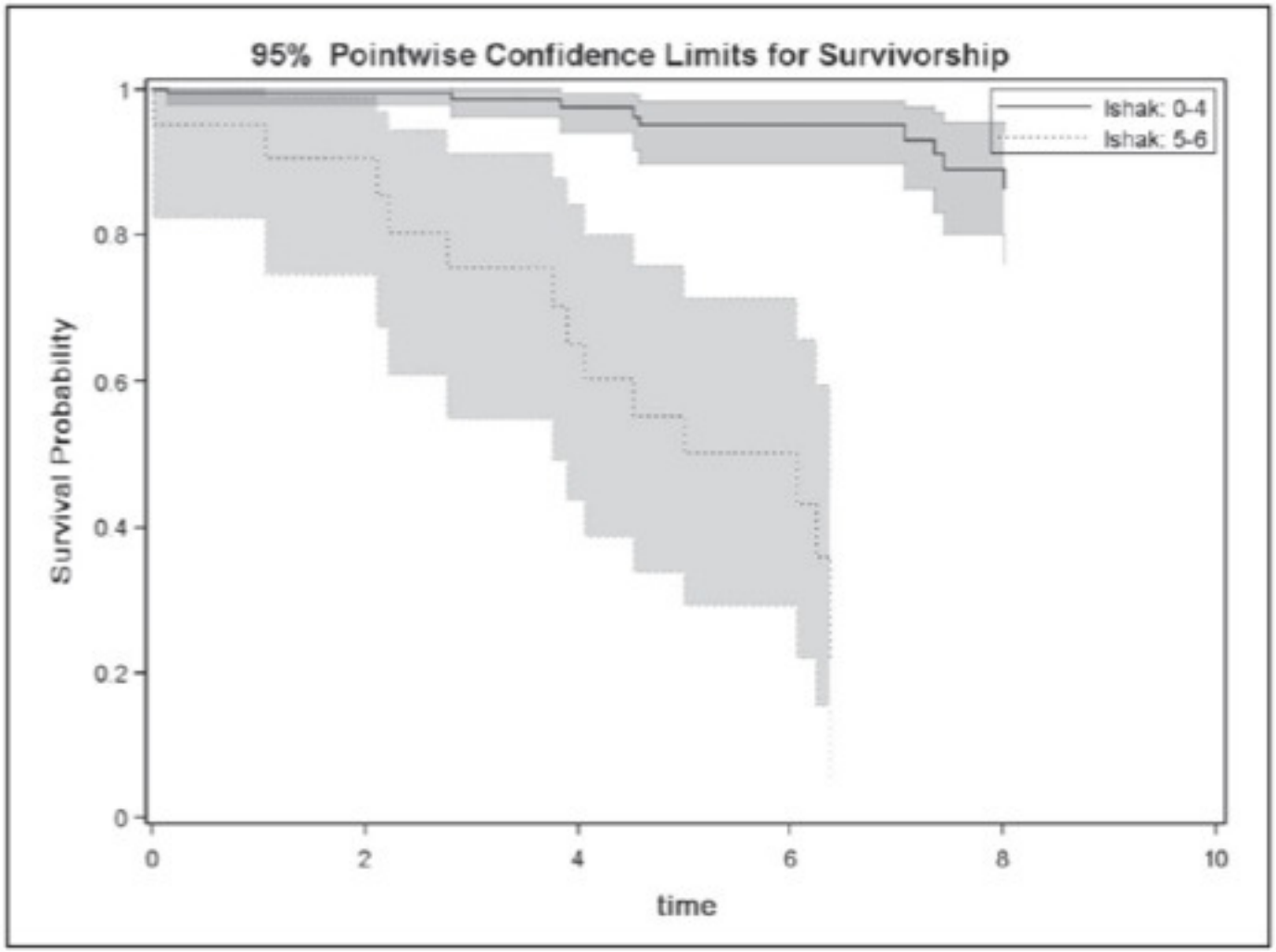
Byrd KK et al. *Public Health Reports*, 2011, 126: 816-825

Annual Hospitalizations due to Hepatitis C by Region



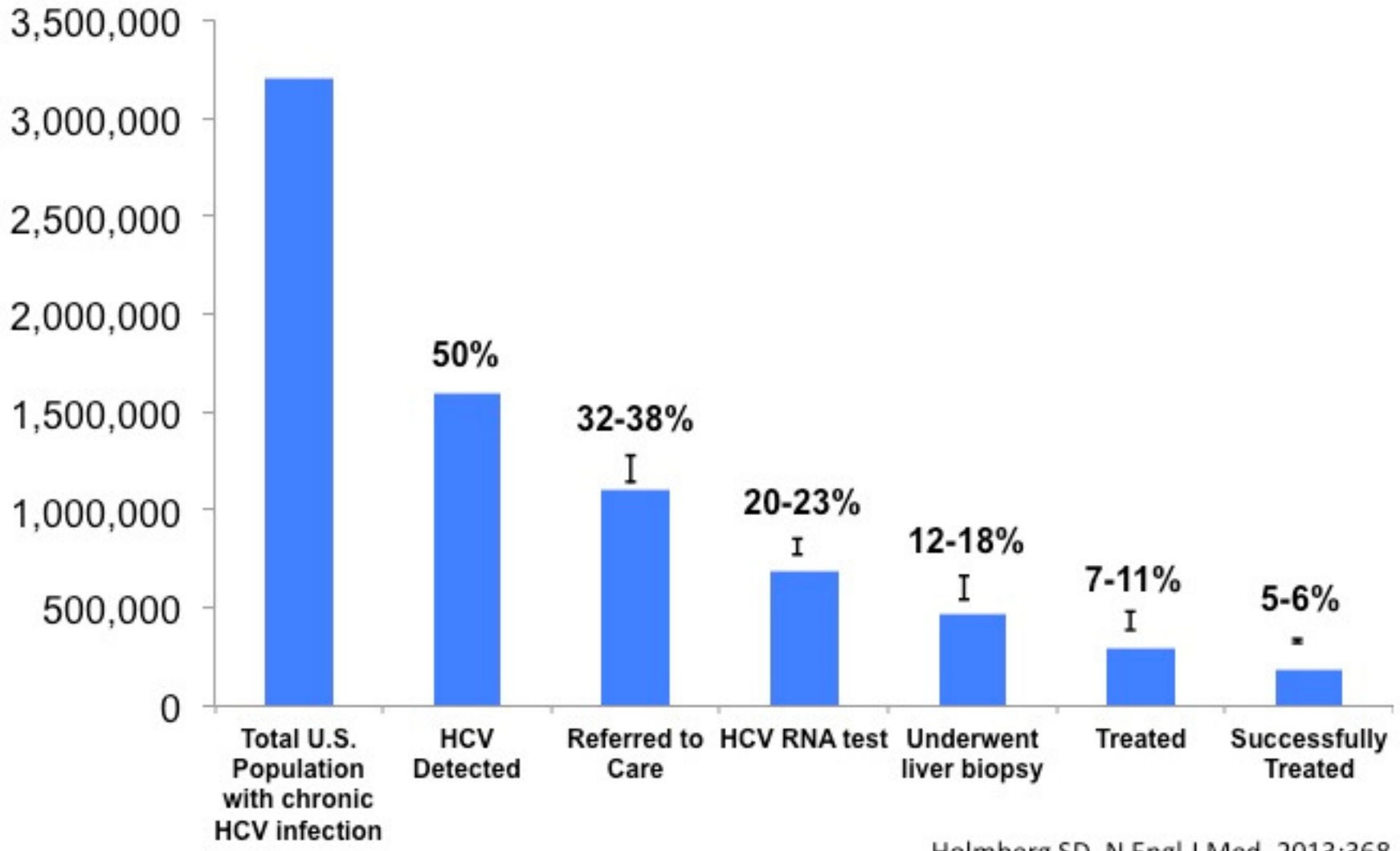
Byrd KK et al. *Public Health Reports*, 2011, 126: 816-825

Patients with Advanced Liver Disease Progress Rapidly



Livingston SE et al. *Can J Gastro*, 2010, 24: 445--451

HCV Infection in the U.S: Estimated Rates of Detection, Referral to Care, and Treatment



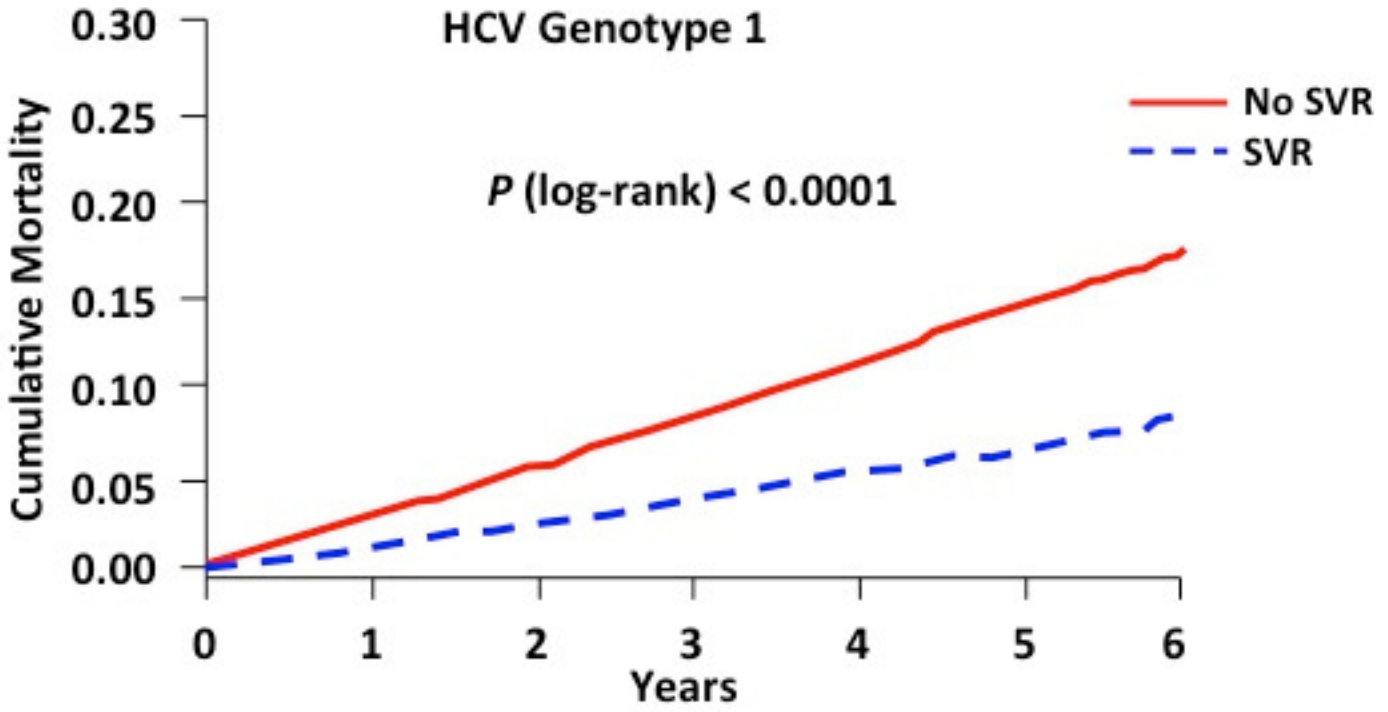
Holmberg SD. N Engl J Med. 2013:368.

SVR and Reduced Risk of All-Cause Mortality - U.S Veterans Study

21,839 treated patients in VA Clinical Case registry; 16,864 with f/u

- **high rates of co-morbidities (DM, HTN, ETOH, CAD)**

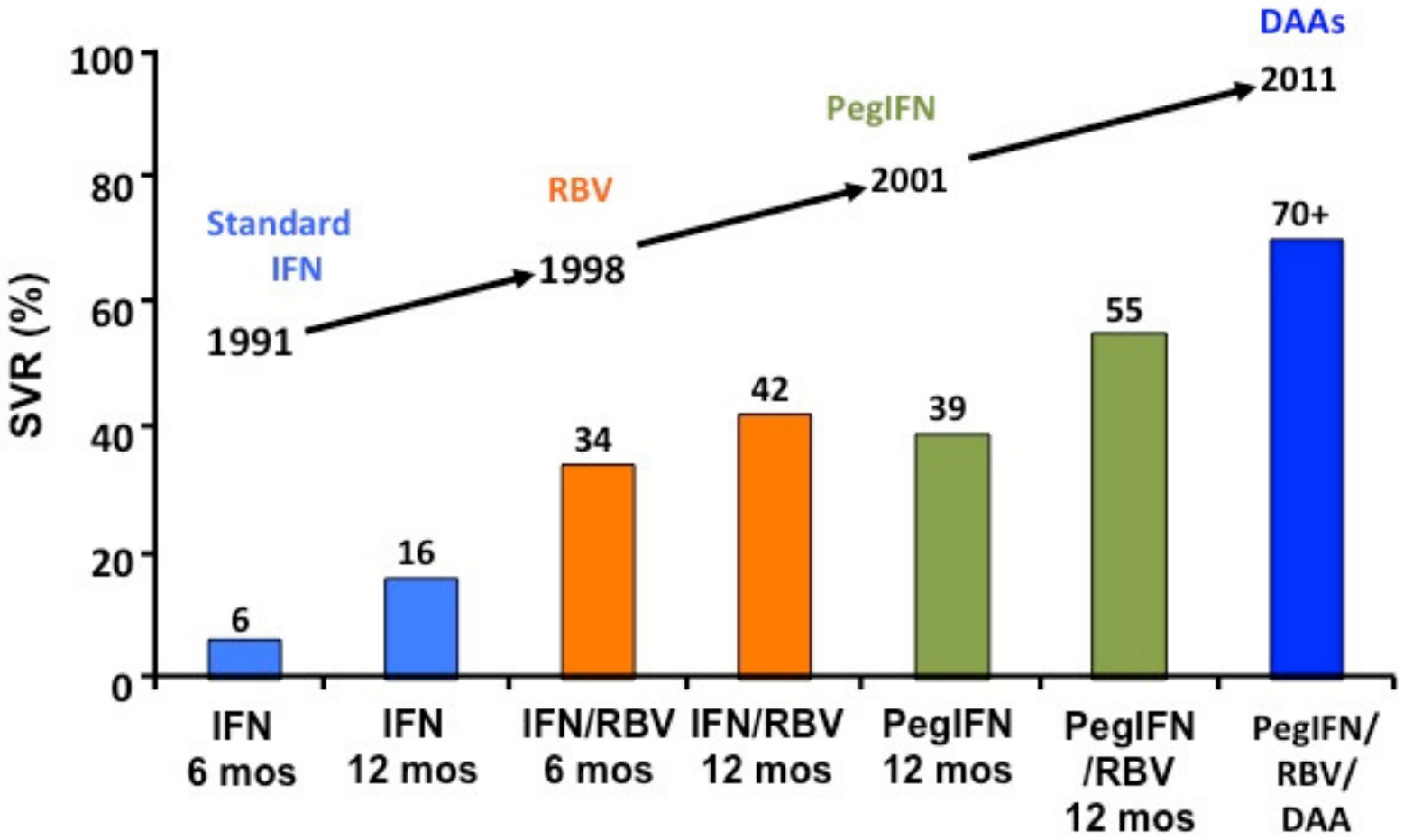
SVR: G1: 35%, G2: 72%, G3 62%



Backus L, et al. Hepatology 2010, 52: Abstract 213

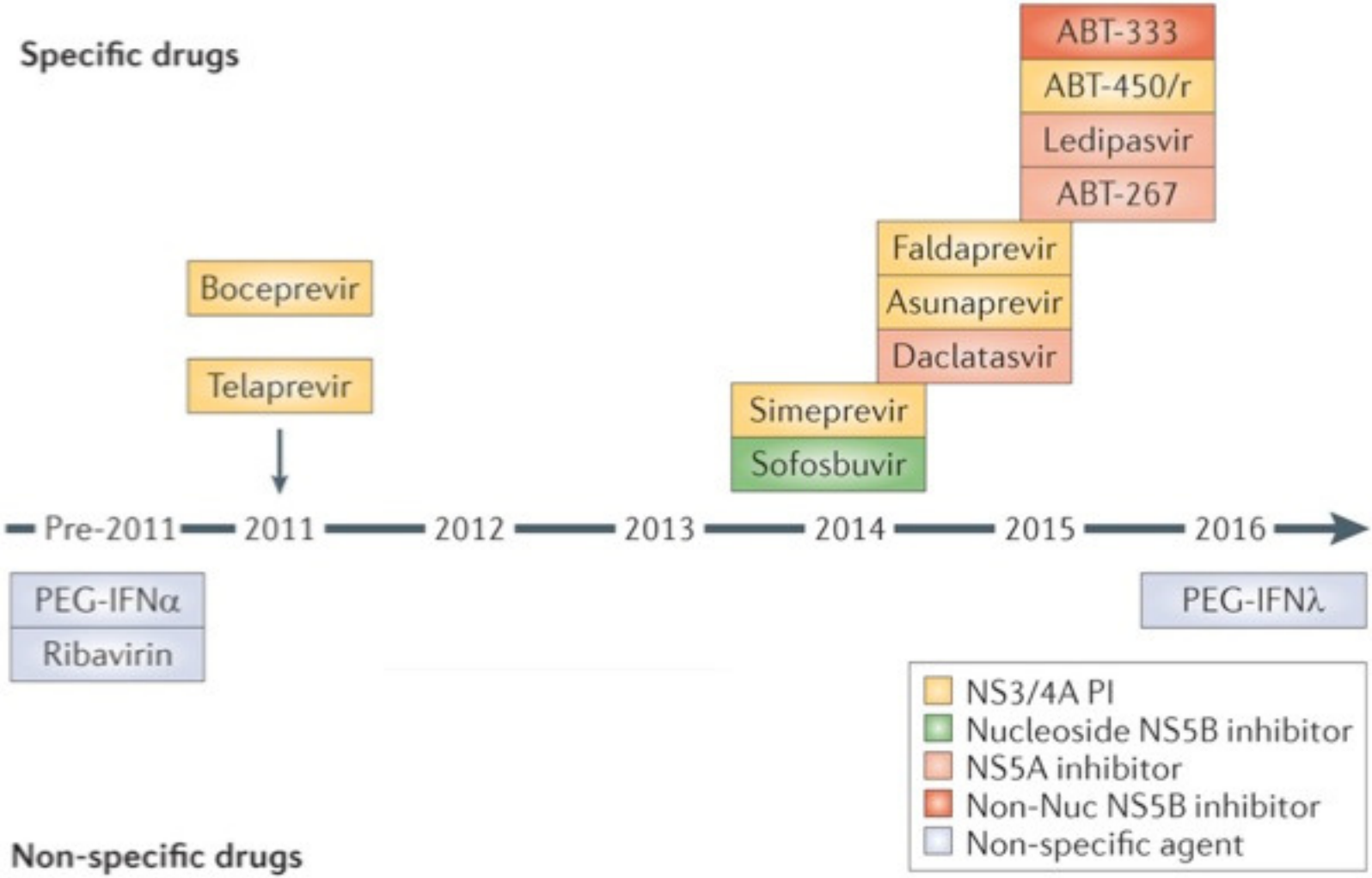
Treatment of HCV

Advances in Chronic Hepatitis C Treatment



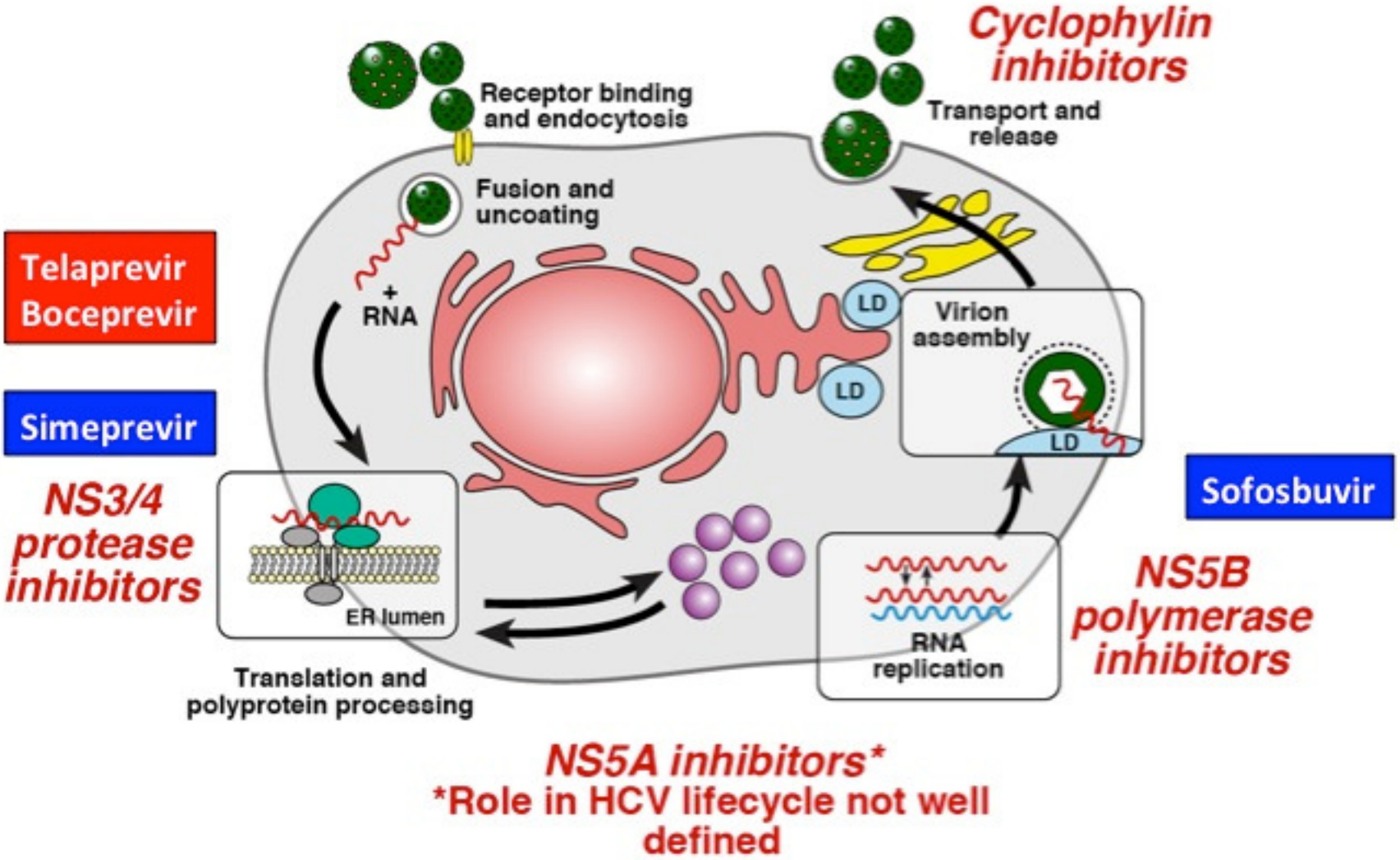
Adapted from Manns, et al. Nature Reviews Drug Discovery, 2013
Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting ,2011.

The Promise of Interferon-free DAA Therapy



Adapted from Manns, et al., Nature Reviews Drug Discovery, 2013.

HCV Life Cycle and DAA Targets



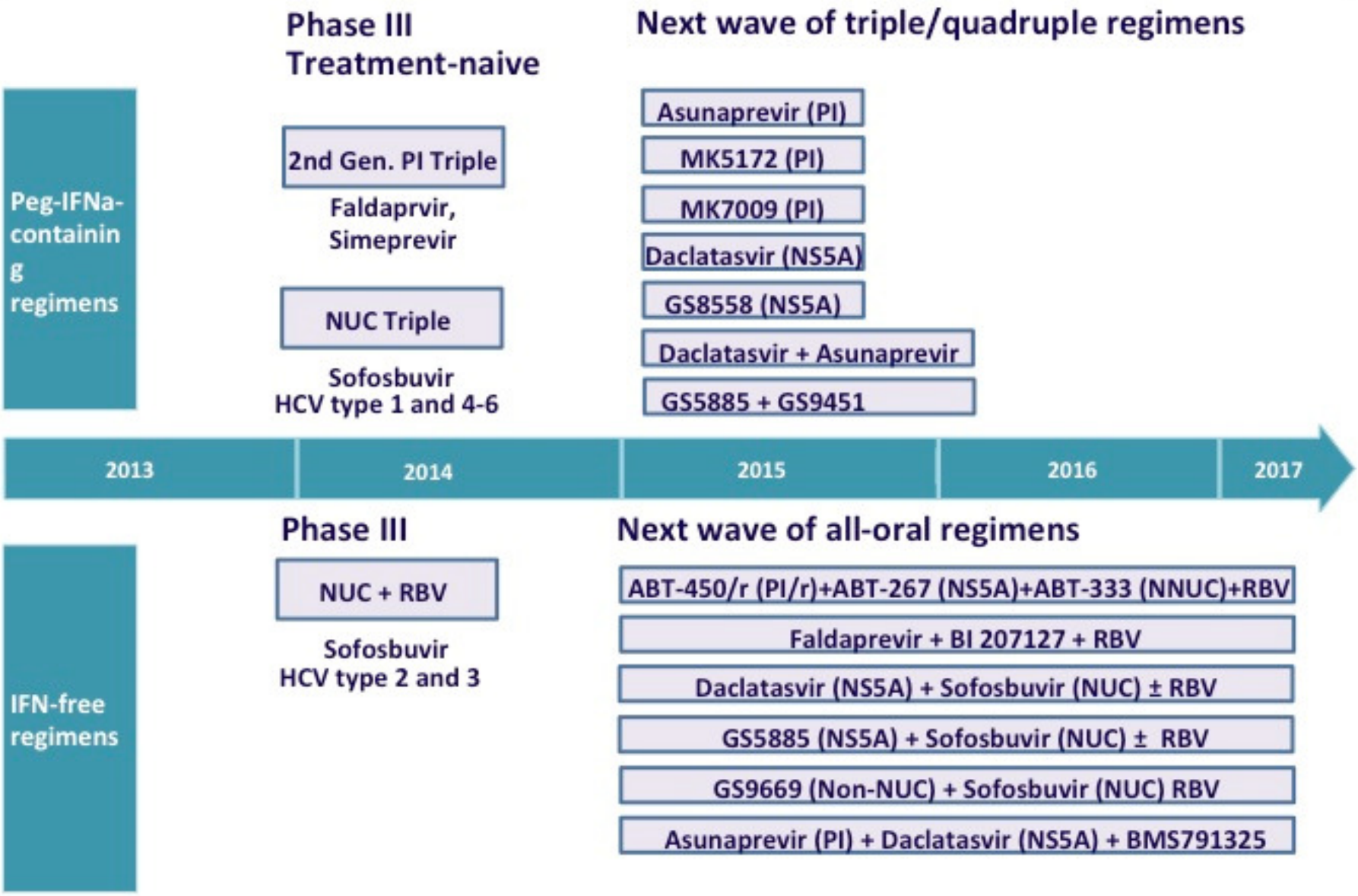
Hadigan C and Kottilil S. JAMA 2011

Primary concerns pertaining to HCV treatment

Reason	2003 (%)	2007 (%)
Inability to attend scheduled clinic appointments	32 (36%)	24 (16%)
Alcohol or drug abuse within 6 months	16 (17%)	29 (22%)
Patient decision to defer treatment	16 (17%)	36 (25%)
Liver biopsy without fibrosis or normal ALT	8 (8%)	4 (3%)
Uncontrolled psychiatric condition	7 (7%)[a]	9 (6%)[b]
Concurrent medical condition precluding treatment	6 (6%)[c]	12 (8%)[d]
Decompensated cirrhosis	3 (3%)	7 (5%)
Age >65 years	2 (2%)	2 (1%)
Considering or planning treatment	0	7 (5%)
Other	0	2 (1%)
Total	90	132

Livingston SE et al. *Int J Circumpolar Health* 2012, 71: 18445

Future HCV Treatment Strategies

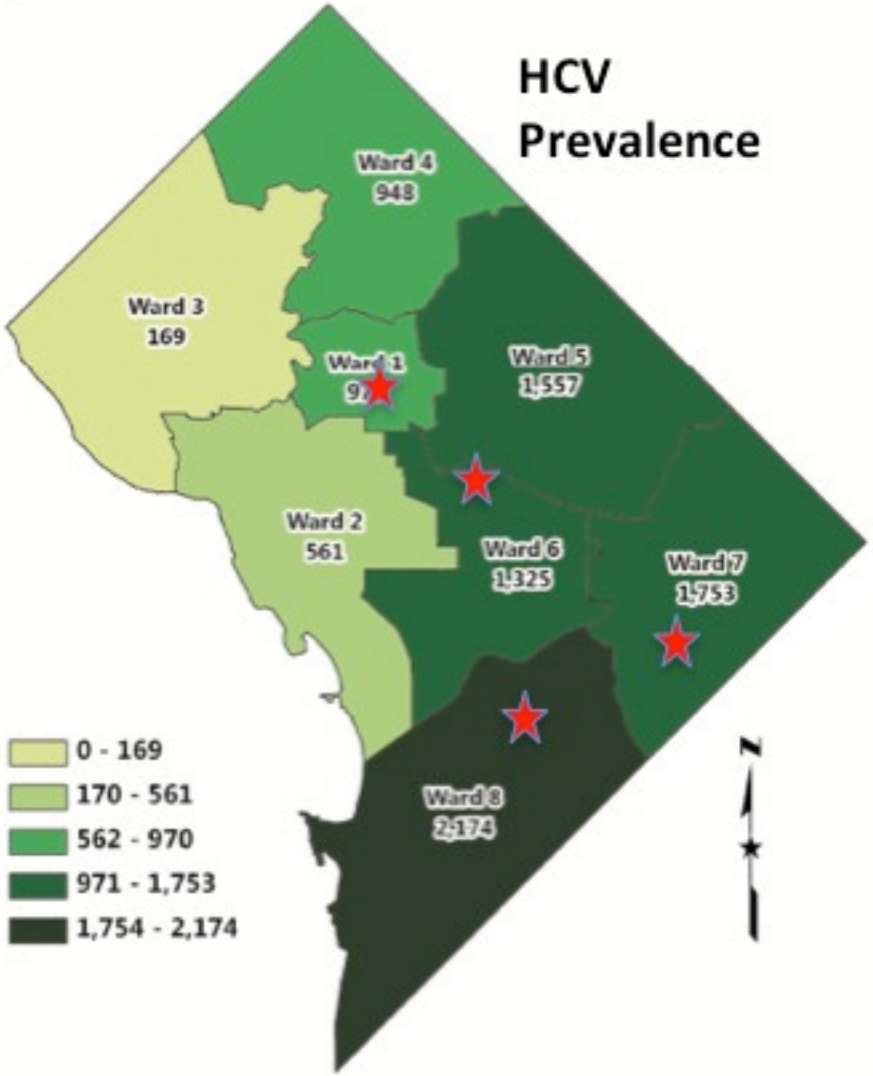


PI = Protease Inhibitor, NUC = nucleosidic polymerase (NS5B) inhibitor, NS5A = NS5A Inhibitor, PI/r ritonavir boosted PI, RBV = Ribavirin

Summary

- **New standard of care for HCV GT-1**
  - Simeprevir / PegIFN/RBV : GT-1
  - Sofosbuvir/RBV: GT-2, 3, ?1 (+ PegIFN/RBV: GT-1)
- **Future therapies likely IFN free +/- RBV**
- **Important advances for treatment in prior difficult to treat populations (cirrhosis, HIV/HCV, transplant)**
- **Identification, retention in care and delivery of new DAA therapies in the U.S and globally is the next step.**
- **Pathway going forward either:**
  - Simple, once daily, 1-2 pills, pangenotypic regimens
  - OR
  - Individualized considering genotype, comorbidities, DDI, pre-existing mutations, fibrosis etc

NIH - District Of Columbia Partnership For AIDS Progress (DCPFAP)



Federal – local partnership

Washington DC: HCV prevalence ~1.8% – Over 13,000 chronic HCV cases

Urban model for HIV and hepatitis management and translational research

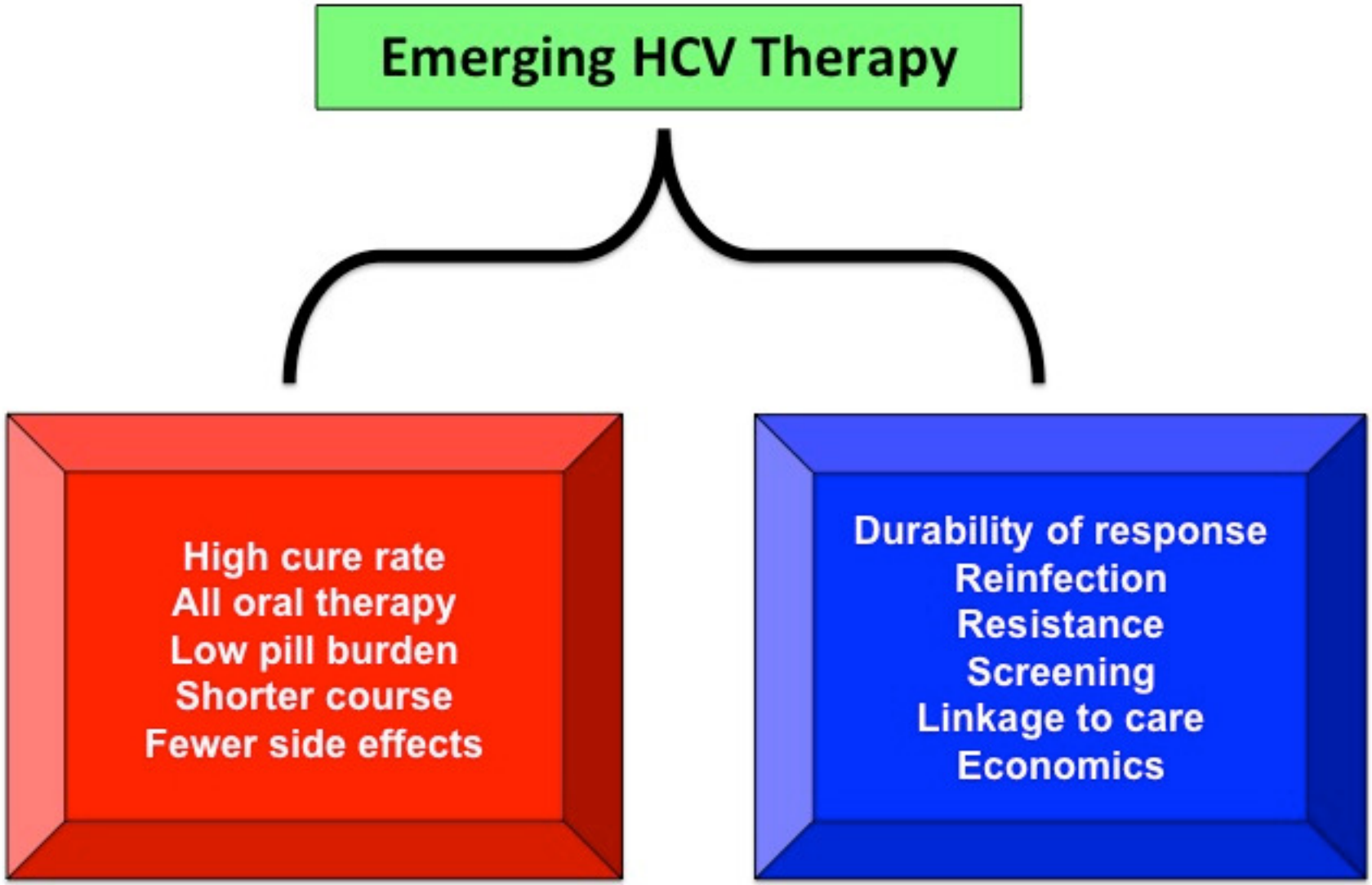
NIH Clinical Center

★ Location of NIH-supported Clinics

Key Points

- First Interferon-free regimen in the USA
- First Interferon-free regimen for difficult to treat patient population
- Established biological correlates for relapse for sofosbuvir and ribavirin
- First interferon and ribavirin free regimen for HIV/HCV coinfected subjects
- First Interferon and ribavirin free regimen for HCV genotype 4 patients
- First study to retreat previous relapsers of sofosbuvir containing regimen
- First study to demonstrate you can shorten duration of therapy by adding DAAs

Strategy for HCV Cure



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