

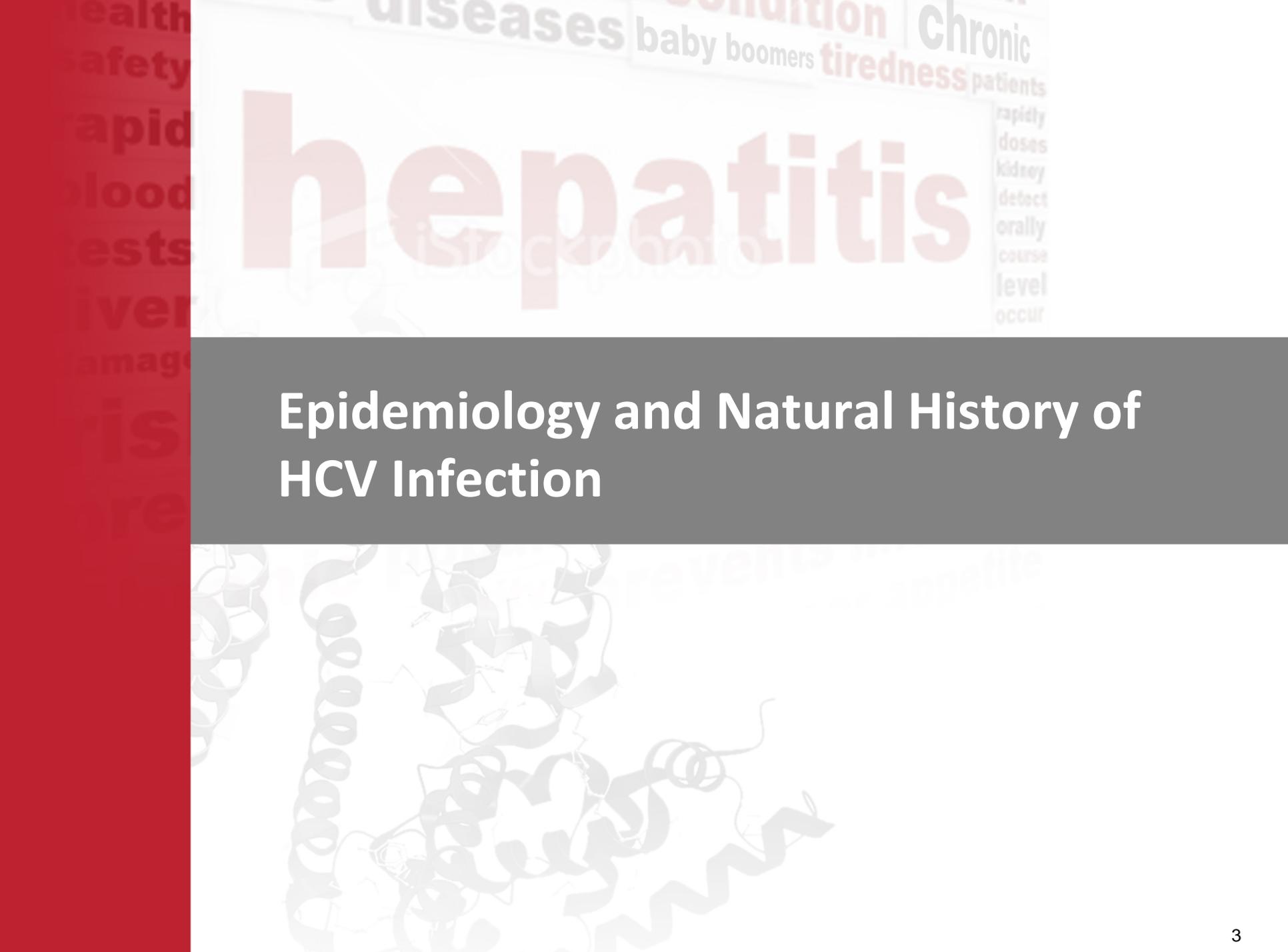
# Hepatitis C

## Prevention, Care, and Management

- **Mukul Mehra MD**
- **Gastroenterology Specialists of Birmingham**

# Objectives

- **Define the Epidemiology of Hepatitis C**
- **Discuss the Screening Recommendations for Hepatitis C**
- **Review Patient Precautions**
- **Review the Viral Life Cycle of the Hepatitis C virus**
- **Describe Fibrosis Assessment**
- **Review Current State-of-the-Art Treatments**

The background features a collage of medical-related terms in various fonts and colors, including 'diseases', 'condition', 'Chronic', 'baby boomers', 'tiredness', 'patients', 'rapidly', 'doses', 'kidney', 'detect', 'orally', 'course', 'level', and 'occur'. A large, faint 'hepatitis' is written in a bold, lowercase font across the top. A faint 'istockphoto' watermark is visible over the word. At the bottom, there is a faint, light-colored illustration of a protein structure with alpha-helices and beta-sheets.

# hepatitis

## Epidemiology and Natural History of HCV Infection

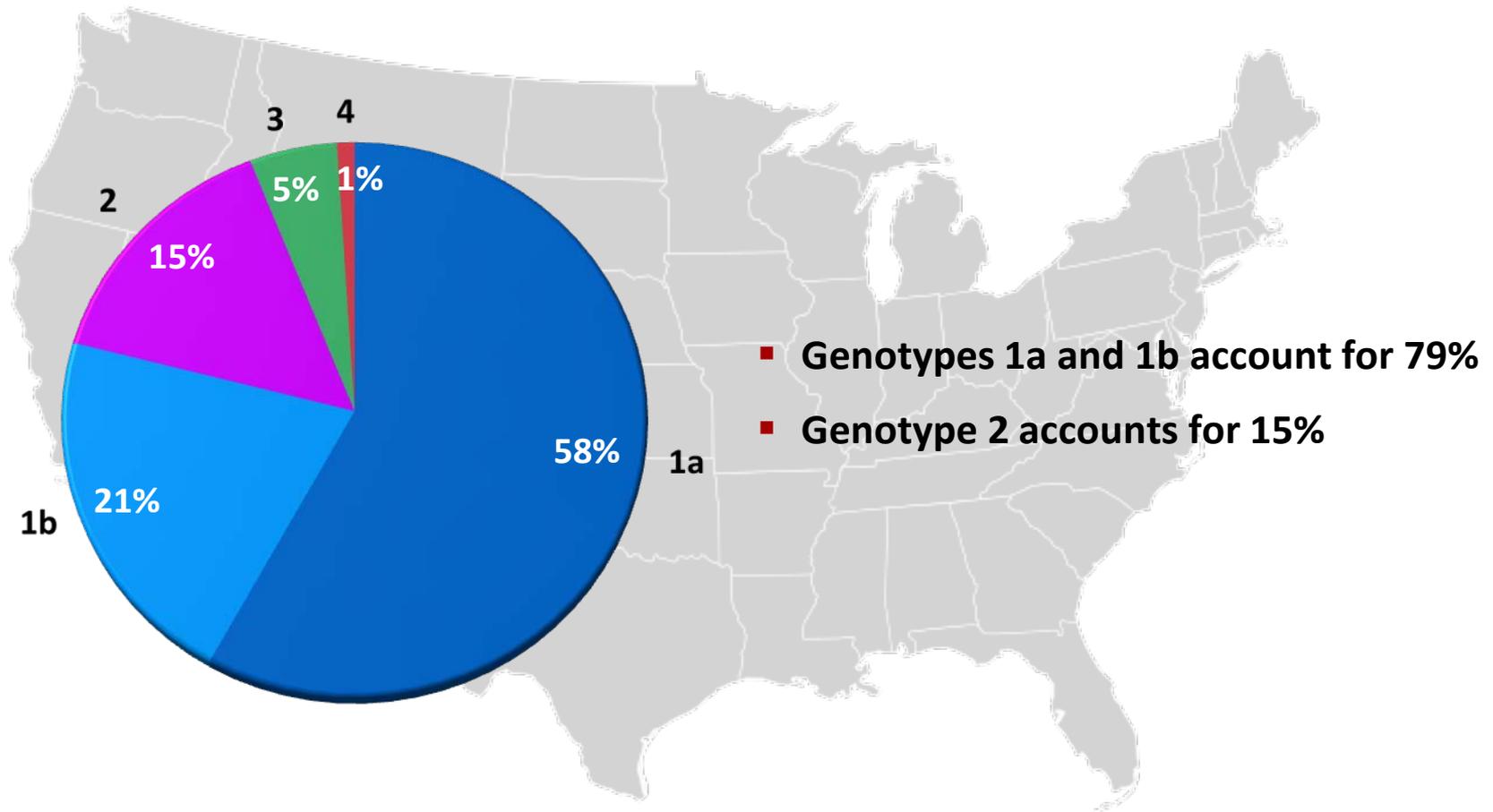
# Defining Viral Hepatitis

- **Hepatitis means inflammation of the liver**
  - Toxins, use of certain drugs, drinking alcohol heavily, “fatty liver”, bacterial and viral infections can all cause hepatitis.
  - Viral Hepatitis is also the name of a family of viral infections (A, B, C, D, and E) that affect the liver- attacking liver cells. The body’s immune response eventually causes inflammation- redness and swelling.

# Approximately 3.2 Million People in the US Have Chronic HCV Infection

- **~3.2 million people are chronically infected with HCV based on NHANES (1999-2002) population<sup>1,2</sup>**
  - ~70% born 1945-1964<sup>1</sup>
- **The number chronically infected with HCV in the US may be even higher<sup>3</sup>**
  - Accounting for populations not sampled in NHANES
    - Incarcerated
    - Homeless
    - Nursing home residents
    - Hospitalized
    - Those on active military duty

# Distribution of HCV Genotypes in the US



# Transmission of Hepatitis A, B, and C Virus

Route	Hepatitis A	Hepatitis B	Hepatitis C
IV drug use	▲	●	●
Transfusion	▲	●	●
Hemodialysis	■	●	●
Intra-institutional	●	●	●
Sexual	▲	●	▲
Household	●	▲	▲
Mother-to-newborn	▲	●	▲
Oral-oral contact	●	▲	■
Food-borne	●	■	■
Fecal (oral)	●	■	■
Water-borne	●	■	■
Raw shellfish	●	■	■

● Common

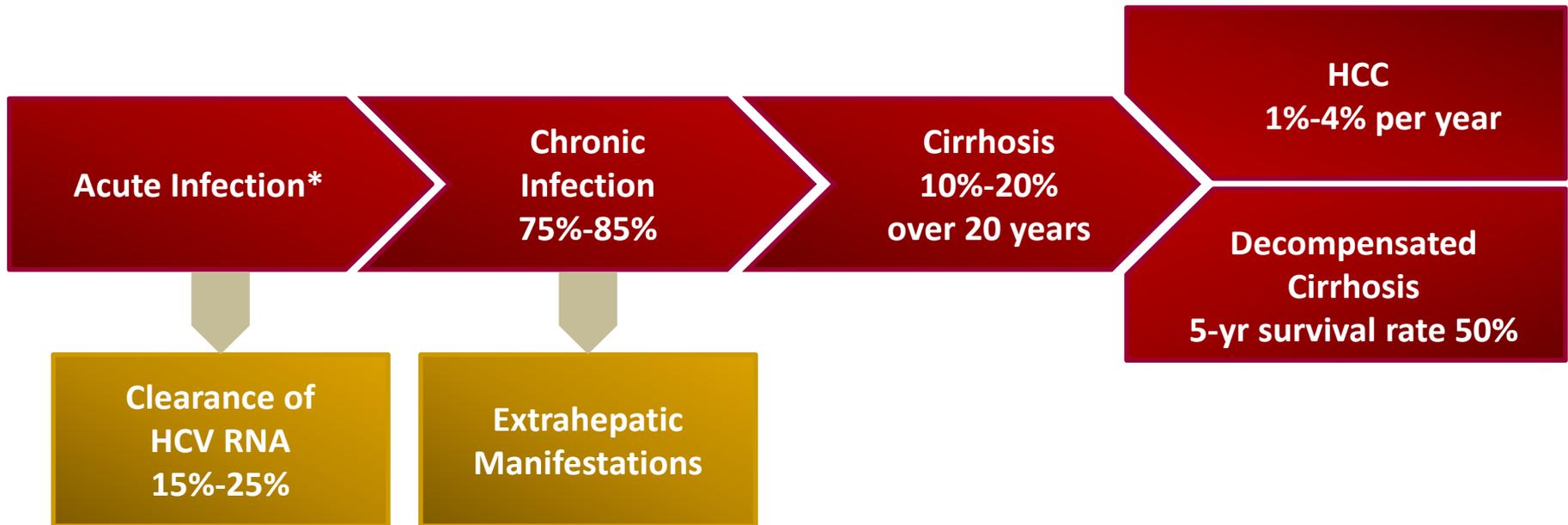
▲ Infrequent

■ Never

IV=intravenous.

Adapted from Dartmouth College. [www.epidemic.org/thefacts/hepatitisc/transmission.php](http://www.epidemic.org/thefacts/hepatitisc/transmission.php).

# Natural History of HCV Infection



\*20%-30% of individuals are symptomatic.

HCC=hepatocellular carcinoma.

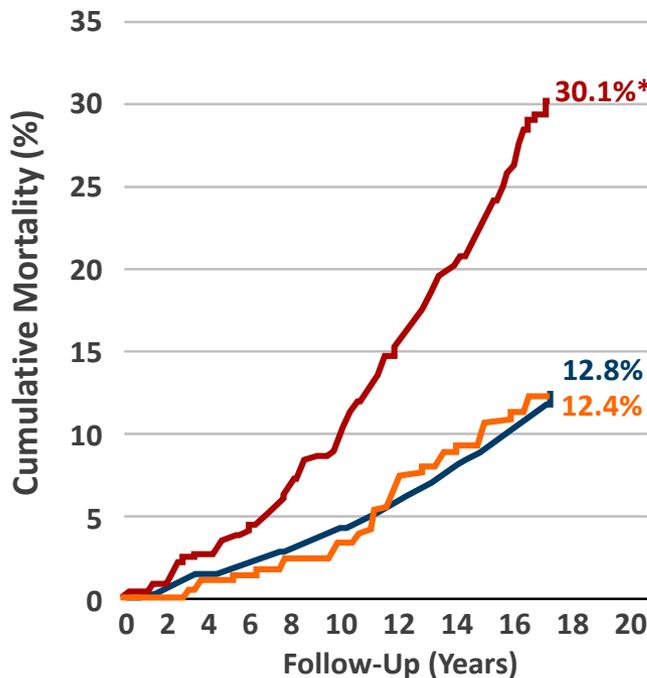
Adapted from Chen SL, Morgan TR. *Int J Med Sci.* 2006;3:47-52.

# HCV Viremia Was Associated With Increased Mortality in a Prospective Taiwanese Cohort Study

— Anti-HCV+, HCV RNA detectable    — Anti-HCV+, HCV RNA undetectable    — Anti-HCV—

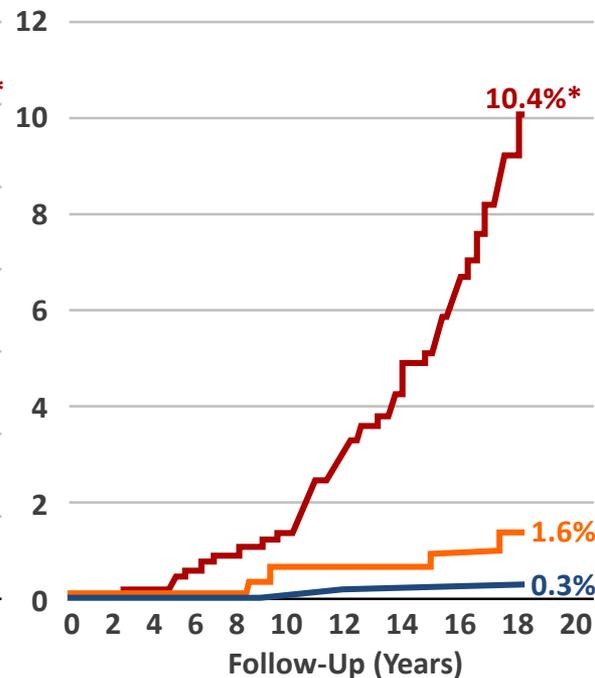
All Causes

(n=2394)



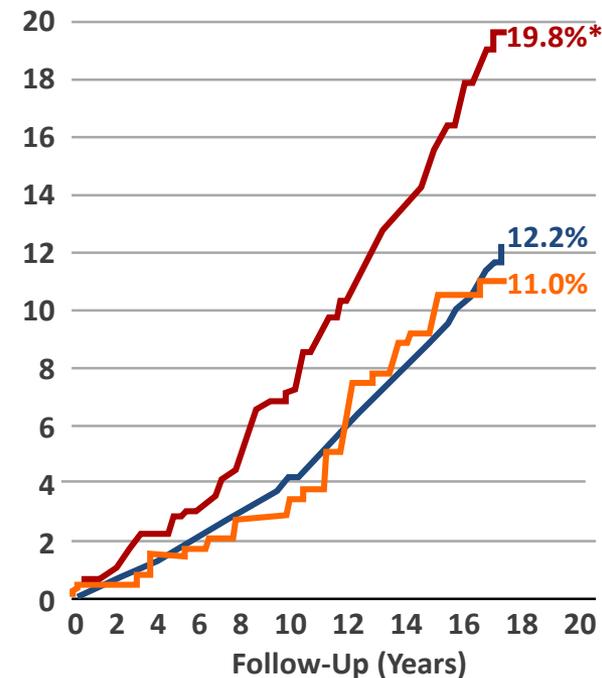
Liver Cancer

(n=115)



Extrahepatic Diseases

(n=2199)



REVEAL HCV: Risk Evaluation of Viral Load Elevation and Associated Liver Disease/Cancer (1991-2008).

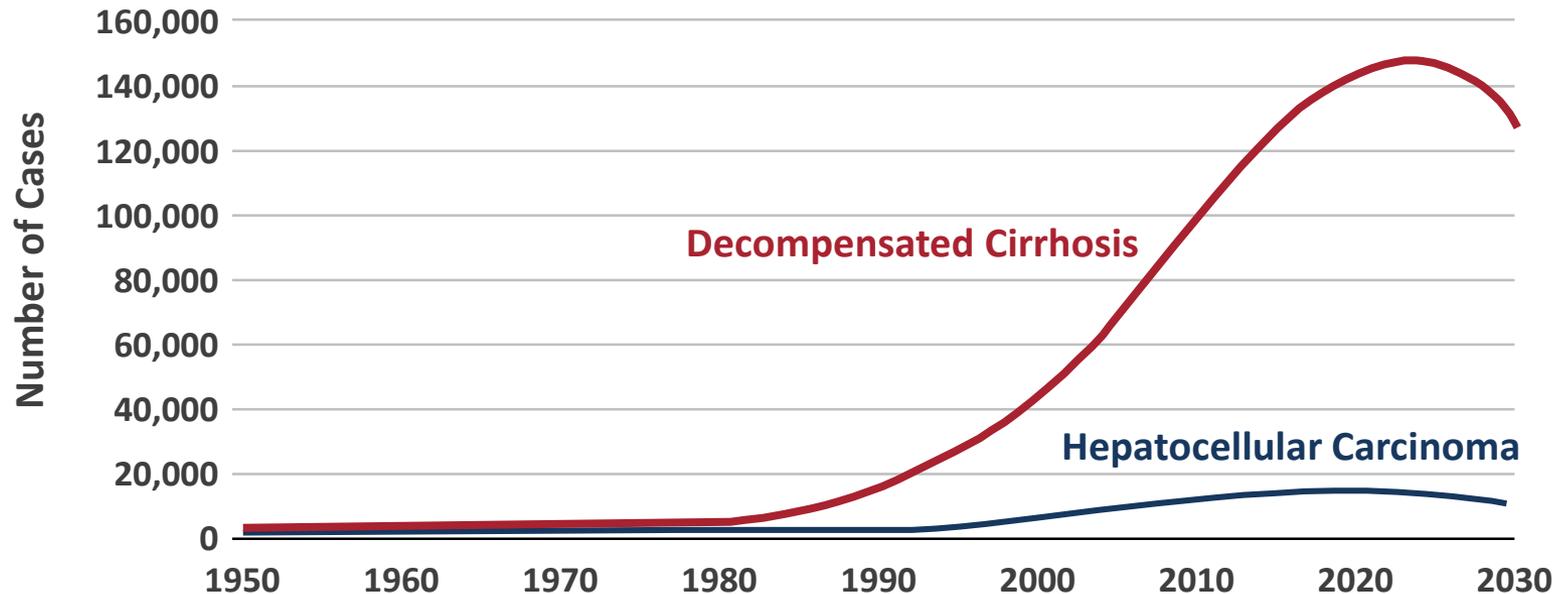
Anti-HCV seronegative (n=18,541); anti-HCV seropositive (n=1095; detectable HCV RNA: 69.4%). Average follow-up: 16.2 years.

Among extrahepatic causes of death, 68.5% and 69.3% were noncancer deaths for HCV seronegative and seropositive, respectively.

\* $P < .001$  for comparison among all 3 groups and  $P < .001$  for HCV RNA detectable vs undetectable.

Lee M-H, et al. *J Infect Dis.* 2012;206:469-477.

# HCV-Related Decompensated Cirrhosis and HCC Projected to Rise in the US



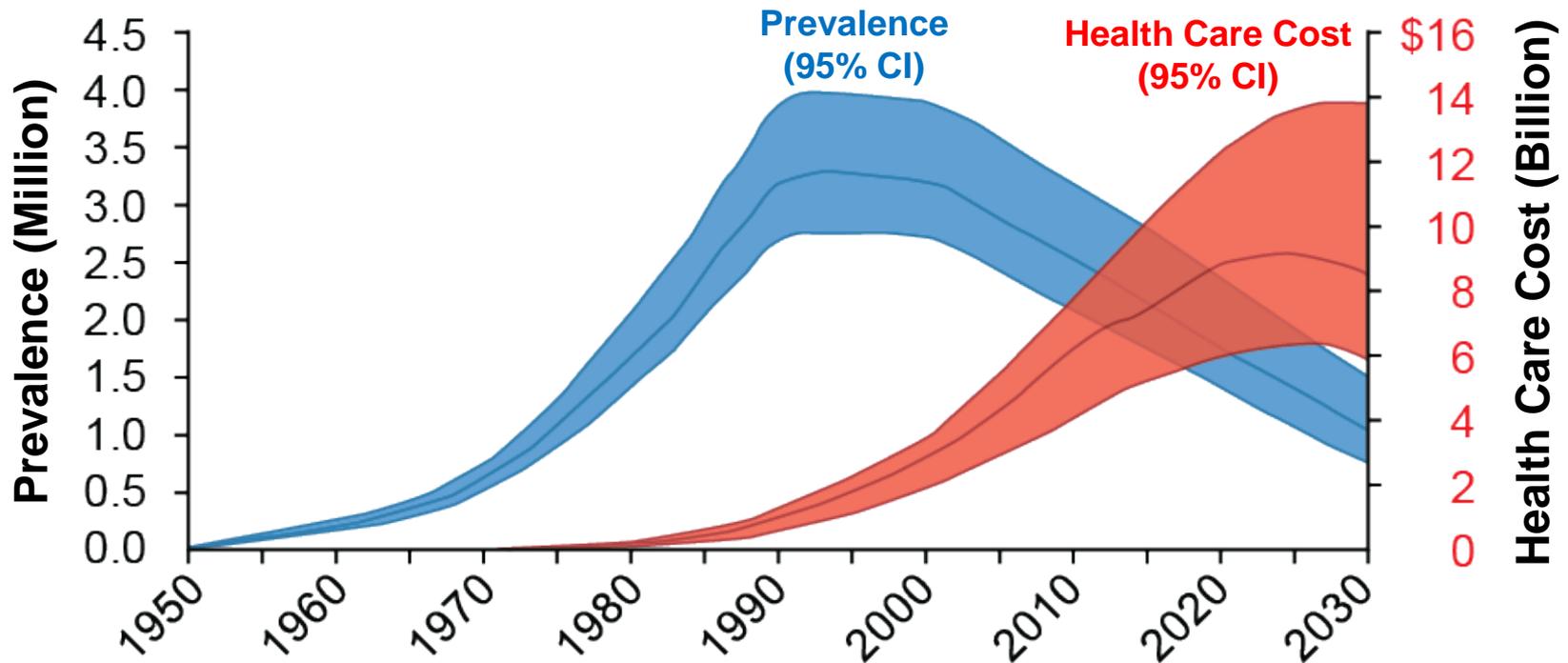
- HCV-related decompensated cirrhosis and HCC are rising as manifestations of liver disease in aging population<sup>1</sup>
- 73.4% of HCV-related deaths occurred among persons 45-64 years of age
  - Median age was 57 years; ~20 years less than the average lifespan of persons living in the US<sup>2,\*</sup>

Projection based on a dynamic, multicohort, natural history model of data from the CDC, NHANES, and a review of the medical literature, with conservative estimates of disease progression and complications. Model assumes first-year mortality of 80%-85% for HCC.

\*During the period from 1999 to 2007.

1. Davis GL, et al. *Gastroenterology*. 2010;138:513-521; 2. Smith BD, et al. *MMWR Recomm Rep*. 2012;61(RR-4):1-32.

# Increasing Health Care Costs Associated With Progressive Liver Disease in the Aging HCV-Infected Population



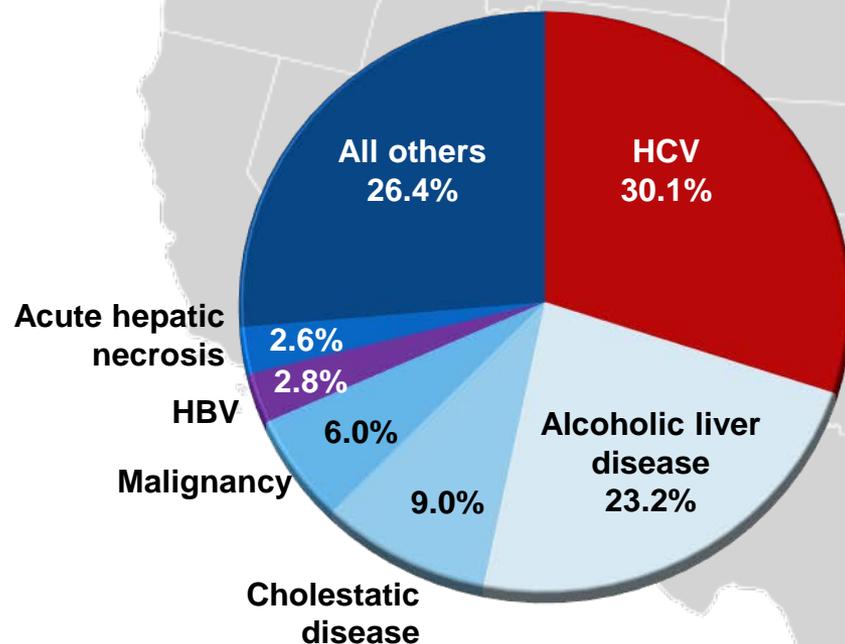
- While the prevalence of HCV infection is declining from its peak, the incidence of advanced liver disease and associated health care costs continue to rise
- Modeling does not take into account any impact of birth cohort screening

A system dynamic modeling framework was used to quantify the HCV-infected population, the disease progression, and the associated cost from 1950-2030.

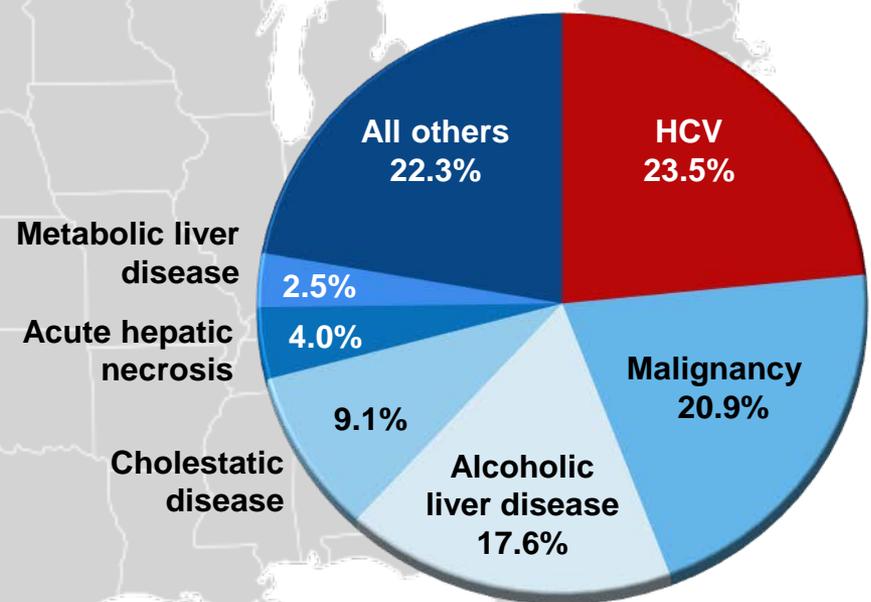
CI=confidence interval.

# HCV Is Leading Cause of Liver Transplants in the US

Primary cause of disease among adults on the liver transplant wait list, 2011



Primary cause of disease among adult liver transplant recipients, 2011



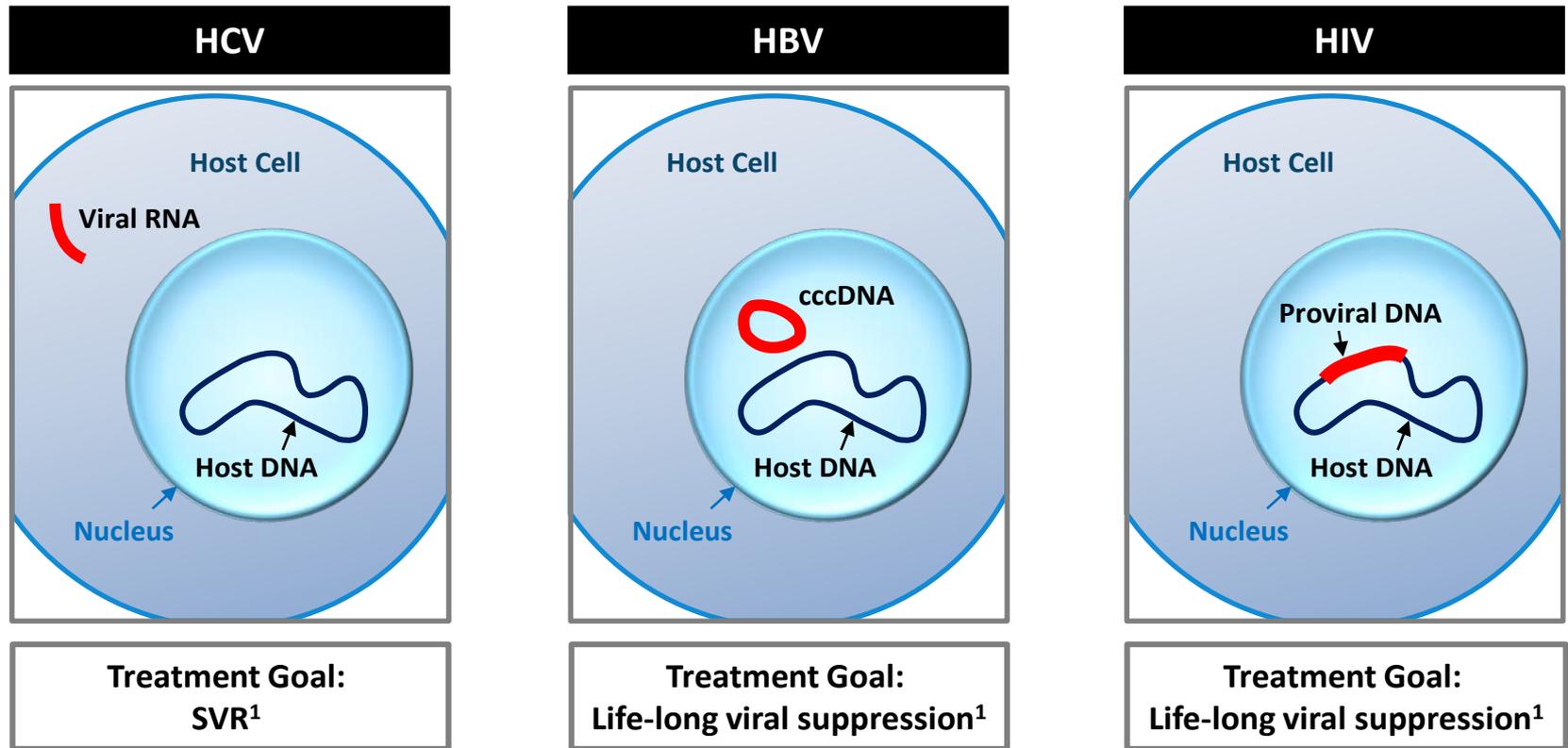
# Sustained Virologic Response (SVR) Achieved After Treatment Is Durable

- **SVR = HCV RNA negative (by a sensitive assay, <50 IU/mL) at 12 (SVR12) or 24 weeks after cessation of treatment<sup>1,2</sup>**
- **99% of patients who achieved an SVR had undetectable levels of HCV RNA in serum samples throughout the follow-up period<sup>3,\*</sup>**
  - “These data suggest that the recurrence of HCV RNA is extremely rare in patients who achieve an SVR, and it now appears likely that such patients may be considered “cured” from a virologic standpoint”<sup>3</sup>
- **For patients with cirrhosis, current guidelines recommend monitoring those who have achieved an SVR at 6- or 12-month intervals for the development of HCC<sup>1</sup>**

\*After treatment with peginterferon alfa-2a ± ribavirin; mean follow-up, 3.9 years (range, 0.8–7.1 years).

1. Ghany MG, et al. *Hepatology*. 2009;49:1335-1374; 2. Chen J, et al. *Gastroenterology*. 2013;144:1450-1455; 3. Swain MG, et al. *Gastroenterology*. 2010;139:1593–1601.

# Treatment Goal in HCV Is SVR



- Majority of patients who achieve an SVR do not experience viral recurrence<sup>2</sup>

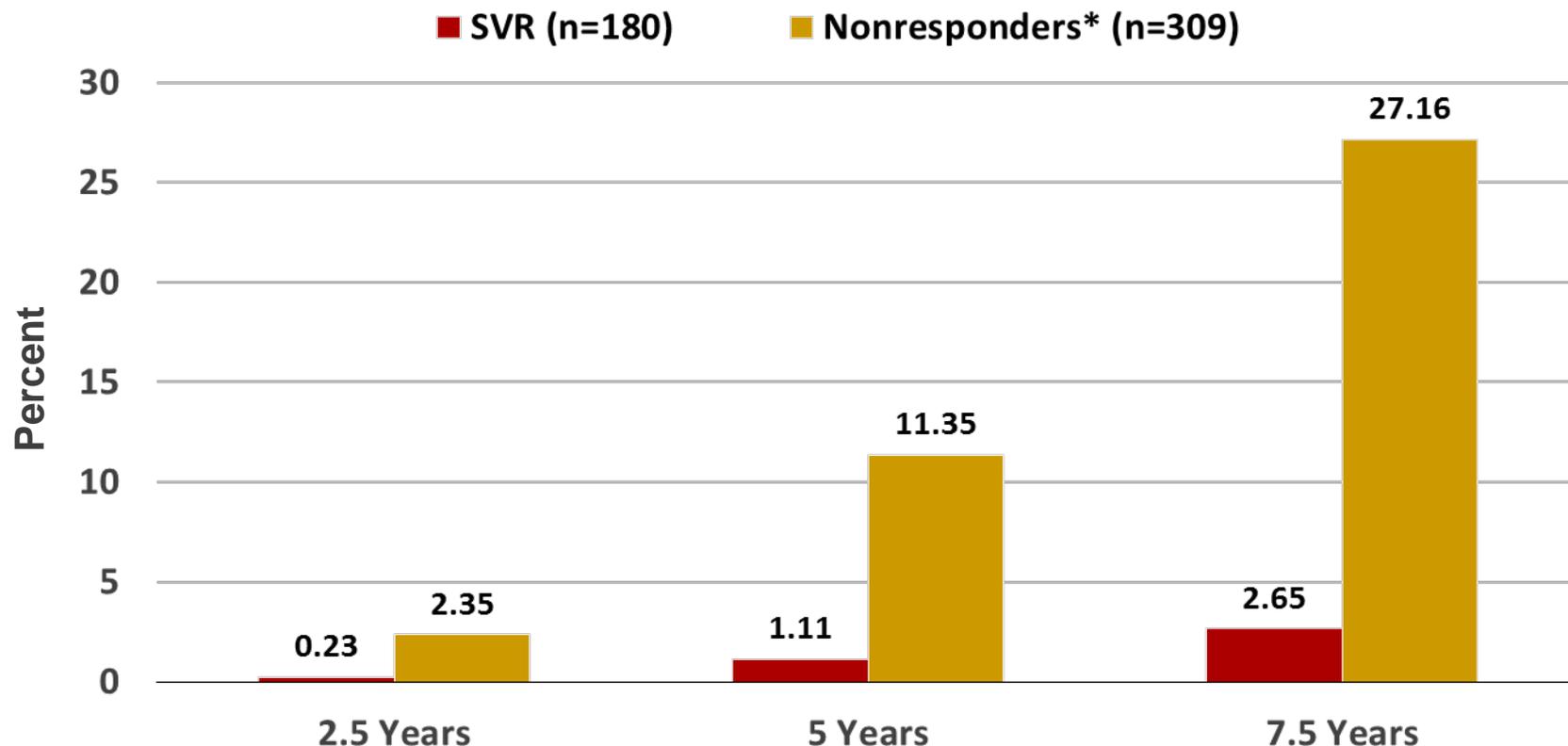
cccDNA=covalently closed circular DNA; HBV=hepatitis B virus.

Images adapted from Soriano V, et al.<sup>1</sup>

1. Soriano V, et al. *J Antimicrob Chemother.* 2008;62:1-4; 2. Swain MG, et al. *Gastroenterology.* 2010;139:1593-1601.

# SVR Was Associated With Improved Long-Term Liver-Related Outcomes in the HALT-C Trial Database

Cumulative Incidence of Any Liver-Related Outcome Among Patients With Bridging Fibrosis or Cirrhosis



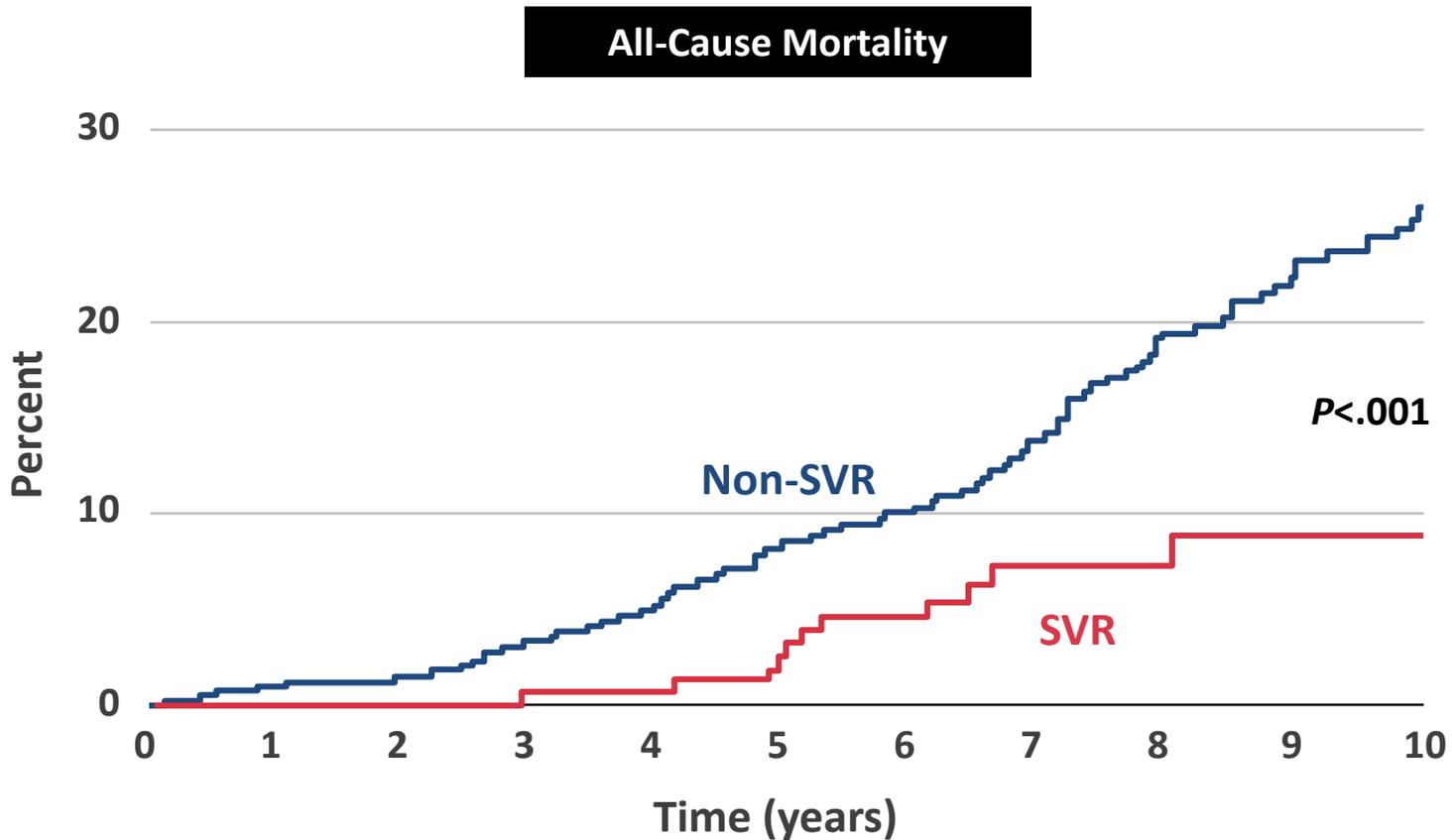
Analysis of liver outcomes (decompensation, HCC, or death) in the HALT-C trial database. All comparisons  $P < .0001$ .

\*Detectable HCV RNA at treatment week 20 (combination therapy was discontinued at week 24).

HALT-C=Hepatitis C Antiviral Long-Term Treatment against Cirrhosis.

Morgan TR, et al. *Hepatology*. 2010;52:833-844.

# SVR Was Associated With Reduced Long-Term Risk of All-Cause Mortality in an International, Multicenter Study

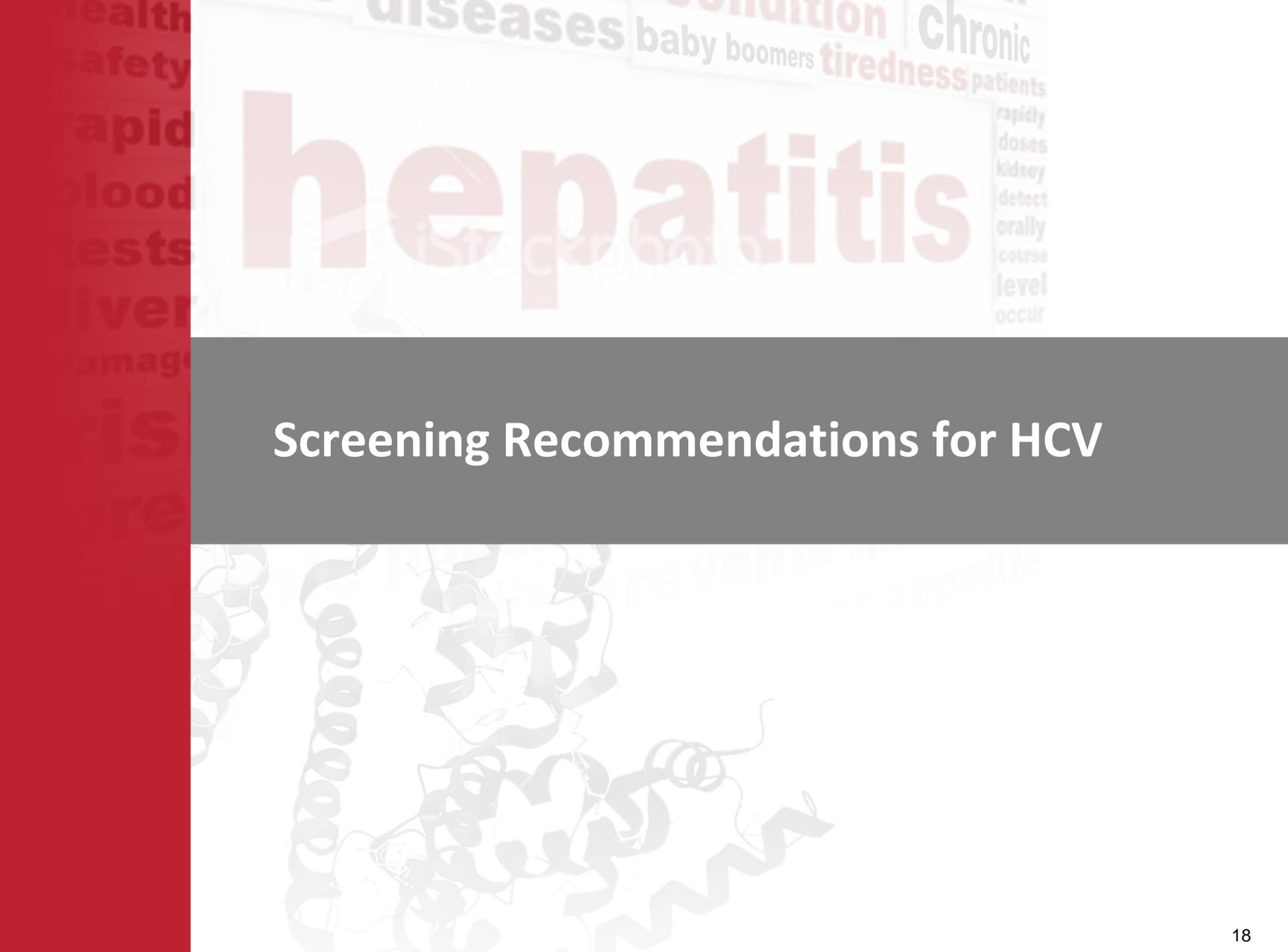


International, multicenter, long-term follow-up study from 5 large tertiary care hospitals in Europe and Canada. Patients with chronic HCV infection started an interferon-based treatment regimen between 1990 and 2003 (n=530).

van der Meer AJ, et al. *JAMA*. 2012;308:2584-2593.

# For Discussion

- **What is the most important thing a medical provider will consider when managing an aging patient with cirrhosis?**
- **What are three common medical issues that prevent a patient from reaching SVR?**

The background features a collage of medical-related terms and a protein structure. On the left, a vertical red bar contains the words 'health', 'safety', 'rapid', 'blood', 'tests', 'liver', 'damage', 'is', and 're'. The top section contains the words 'diseases', 'condition', 'Chronic', 'baby boomers', 'tiredness', and 'patients'. The word 'hepatitis' is prominently displayed in large, bold, reddish-brown letters. To the right of 'hepatitis', the words 'rapidly', 'doses', 'kidney', 'detect', 'orally', 'course', 'level', and 'occur' are listed vertically. At the bottom, there is a faint, light gray protein structure rendered as a ribbon diagram.

# hepatitis

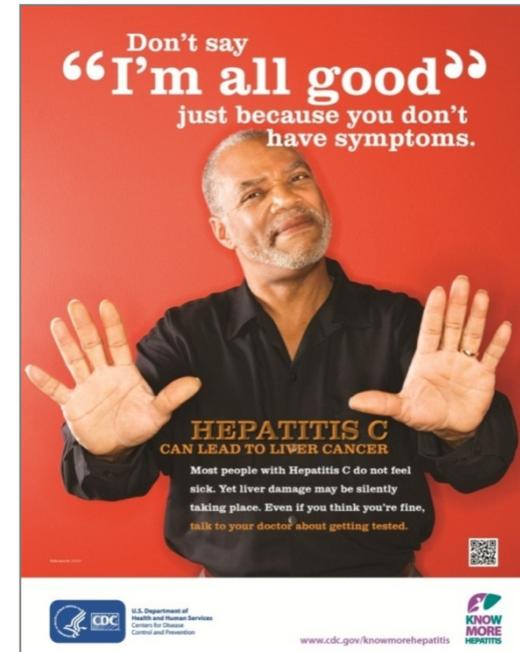
## Screening Recommendations for HCV

# Current Estimates Show a Significant Gap in HCV Care

Approximately 3.2 million in the US have chronic HCV infection<sup>1,2,\*</sup>

1.6 million (50%) diagnosed<sup>3,4</sup>

170,000 – 200,000 (5 – 6%) were successfully treated<sup>4,5</sup>



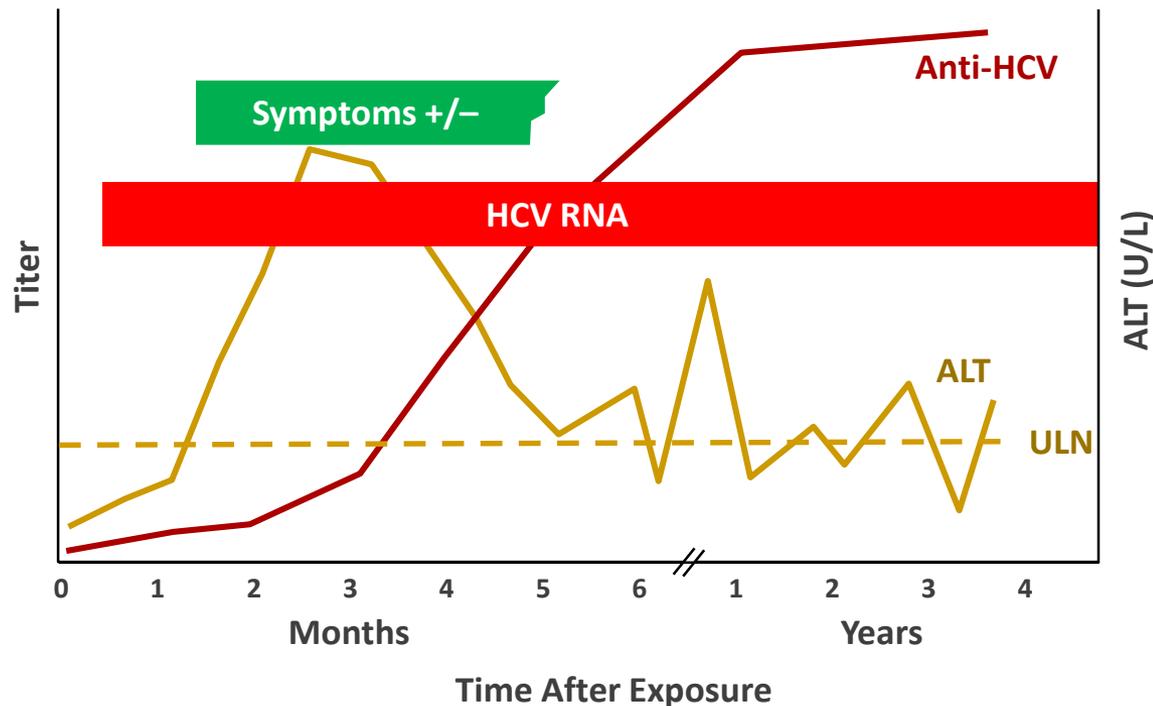
\*Prevalence estimate based on NHANES data from 1999 through 2002.<sup>1,2</sup> NHANES data underestimate the actual prevalence of HCV in the US by not accounting for incarcerated, homeless, hospitalized, nursing home and active military duty populations.<sup>6,7</sup>

1. Armstrong GL, et al. *Ann Intern Med.* 2006;144:705-714.
2. <http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm>.
3. Denniston MM, et al. *Hepatology.* 2012;55:1652-1661.
4. Holmberg SD, et al. *New Engl J Med.* 2013;1859-1861.

5. Moorman AC, et al. *Clin Infect Dis.* 2013;56:40-50.
6. Chak E, et al. *Liver Int.* 2011;31:1090-1101.
7. Smith BD, et al. *MMWR Recomm Rep.* 2012;61(RR-4):1-32.
8. [www.cdc.gov/knowmorehepatitis/](http://www.cdc.gov/knowmorehepatitis/).

# Laboratory Diagnosis of Chronic HCV Infection

- RNA testing identifies active disease in HCV-seropositive patients
- HCV antibodies appear by 6–8 weeks following infection<sup>1</sup>
  - Can be detected by EIA<sup>2</sup>
- Serum ALT is not a reliable indicator of liver damage<sup>1</sup>
- FDA-approved rapid point-of-care testing is available<sup>3</sup>
  - OraQuick® HCV Test



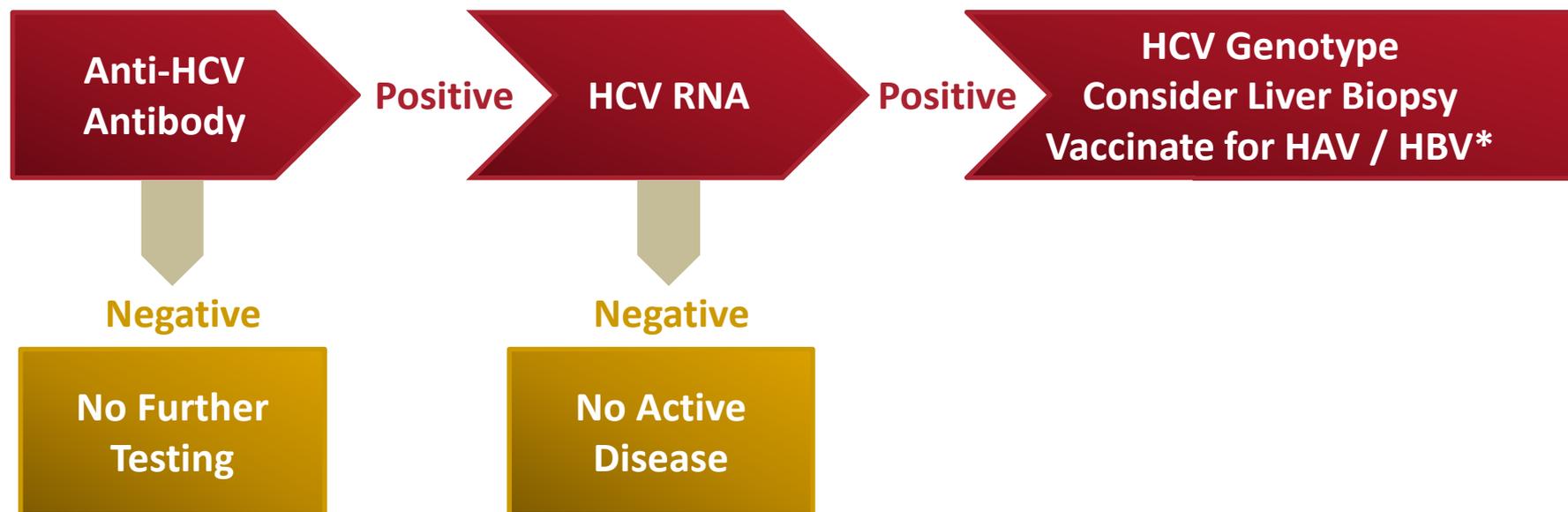
ALT=alanine aminotransferase; EIA=enzyme immunoassay; RNA=ribonucleic acid; ULN=upper limit of normal.

Image adapted from MicrobiologyBytes:Virology:HCV<sup>1</sup>

1. [www.microbiologybytes.com/virology/HCV.html](http://www.microbiologybytes.com/virology/HCV.html); 2. Alter MJ, et al. *MMWR Recomm Rep.* 2003;52(RR-3):1-13, 15;

3. Shivkumar S, et al. *Ann Intern Med.* 2012;157:558-566.

# HCV Diagnostic Algorithm Based on Serologic Testing



\*If patient lacks pre-existing antibodies to HAV or HBV.

HAV=hepatitis A virus, HBV=hepatitis B virus.

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

# 2012 CDC Recommendations for Birth Cohort (1945–1965) Screening

## ■ Recommendation 1

- Adults born from 1945 to 1965 should receive one-time testing for HCV without prior ascertainment of HCV risk

**Grade: strong recommendation**

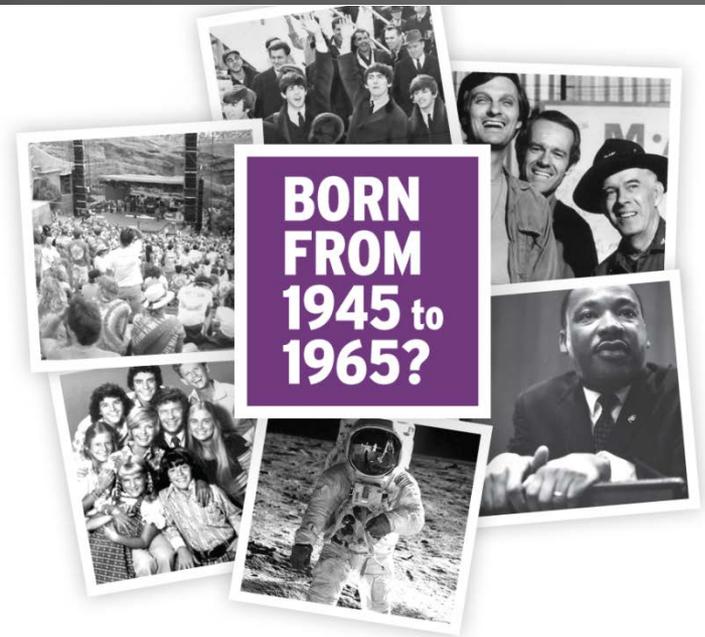
**Evidence: moderate-quality**

## ■ Recommendation 2

- All persons identified with HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment services for HCV infection and related conditions as indicated

**Grade: strong recommendation**

**Evidence: moderate-quality**



**BABY BOOMERS HAVE  
THE HIGHEST RATES OF  
HEPATITIS C.**

Talk to your doctor about getting tested.  
Early detection can save lives.



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

[www.cdc.gov/knowmorehepatitis](http://www.cdc.gov/knowmorehepatitis)



# 2013 Updated USPSTF HCV Screening Recommendations

- **In June 2013, the USPSTF issued its Grade B recommendations regarding HCV screening<sup>1</sup>:**
  - Those at high risk for HCV infection
  - Those born from 1945 to 1965 (one-time screening of “Baby Boomers,” regardless of risk)
- **For this update, the USPSTF reviewed the indirect chain of evidence showing benefits of screening through<sup>1</sup>:**
  - Improvements in SVR with current treatments
  - Reductions in all-cause and liver-related mortality, and HCC associated with SVR
- **The USPSTF gave this recommendation a Grade B<sup>1</sup>:**
  - Grade B means there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial
- **The Affordable Care Act<sup>1,2</sup>:**
  - Requires non-grandfathered private health plans to cover clinical preventive services given an A or B Grade by USPSTF without cost sharing
  - Provides incentives for Medicaid programs to cover these services

USPSTF=United States Preventive Services Task Force.

1. Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print]; 2. Ngo-Metzger, Q et al. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

# 2013 Updated USPSTF HCV Screening Recommendations

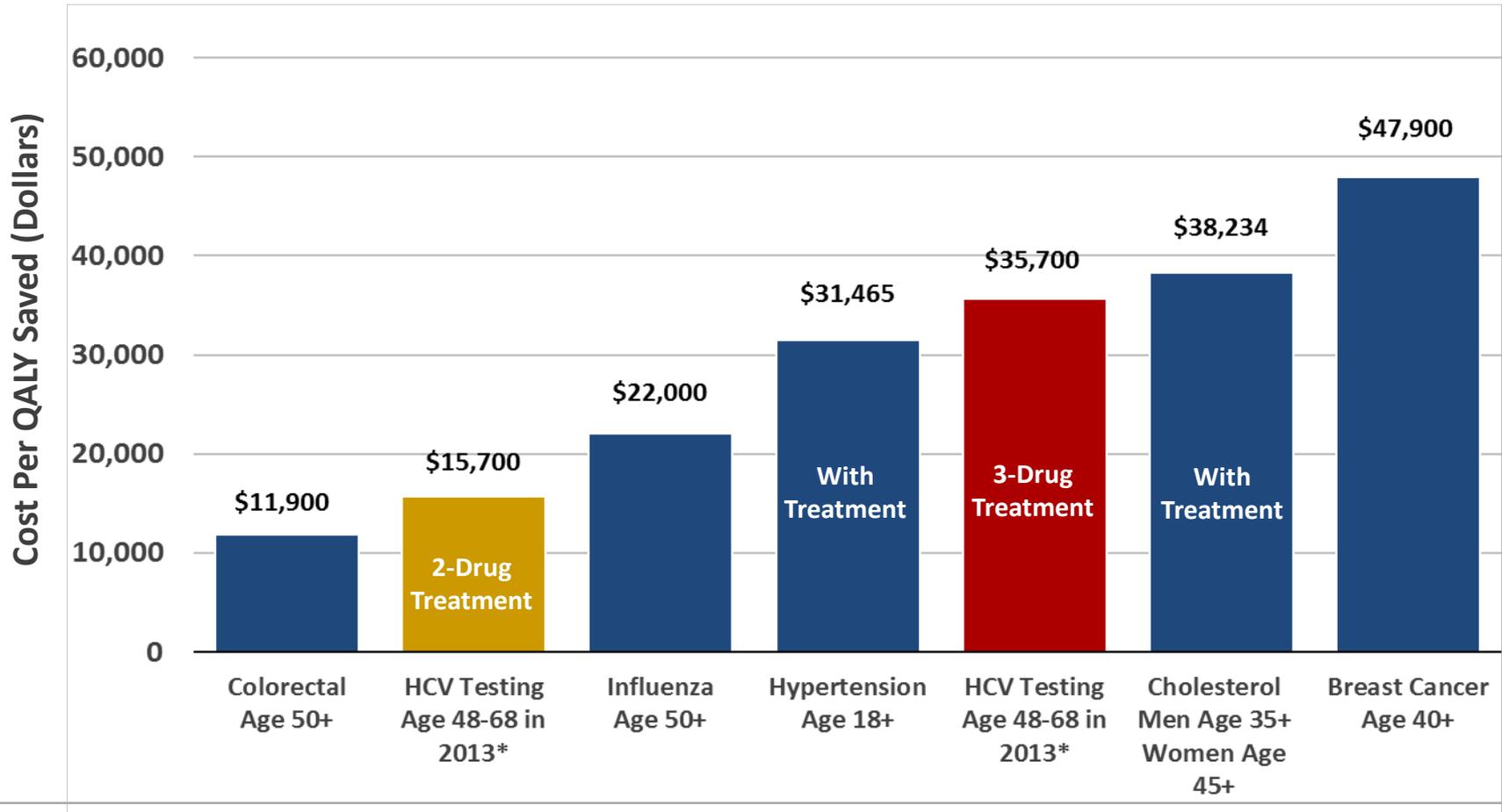
## Risk Assessment:\*

- **Those at high risk for HCV infection:**
  - Most important risk factor is past or current injection drug use
  - Additional risk factors include:
    - Receiving a blood transfusion before 1992
    - Long-term hemodialysis
    - Being born to an HCV-infected mother
    - Incarceration
    - Intranasal drug use
    - Getting an unregulated tattoo, and other percutaneous exposures
- **Adults born between 1945 and 1965 (“Baby Boomers”)**

\*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.

Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

# Cost-Effectiveness of HCV Testing vs Other Routine Preventive Services



\*Birth cohort testing, 1945-1965.

2-drug treatment=PegIFN+RBV; 3-drug treatment=PegIFN+RBV+PI.

QALY=quality-adjusted life-year.

[www.prevent.org/National-Commission-on-Prevention-Priorities/Rankings-of-Preventive-Services-for-the-US-Population.aspx](http://www.prevent.org/National-Commission-on-Prevention-Priorities/Rankings-of-Preventive-Services-for-the-US-Population.aspx).

Rein DB, et al. *Ann Intern Med.* 2012;156:263-270.

# Presentation of Patients Infected With HCV

- Patients often asymptomatic in early stages of infection<sup>1</sup>

## Symptoms may include<sup>1</sup>

- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Dark urine
- Grey-colored stools
- Jaundice
- Joint pain

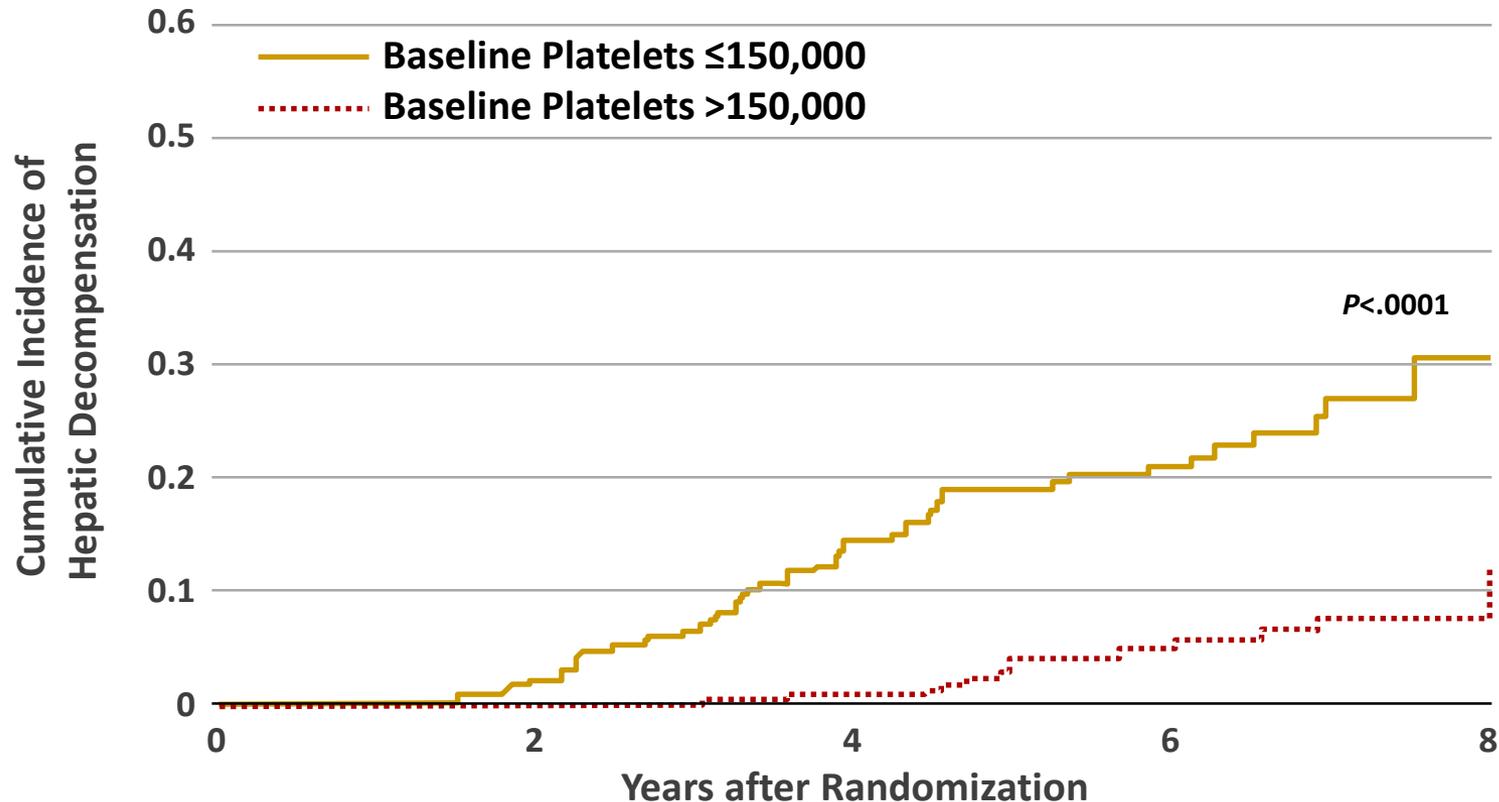
## First symptoms may be those of extrahepatic manifestations<sup>2</sup>

- Arthralgias
- Paresthesias
- Myalgias
- Pruritus
- Sicca syndrome

1. <http://www.cdc.gov/knowmorehepatitis/Media/PDFs/FactSheet-ChronicHepC-GenInfo.pdf>; 2. Ali A, Zein NN. *Cleve Clin J Med.* 2005;72:1005-1008.

# Platelet Counts May Serve as a Marker of Progressive Liver Disease Based on the HALT-C Trial Database

## Cumulative Incidence of Hepatic Decompensation Among Patients With Bridging Fibrosis or Cirrhosis

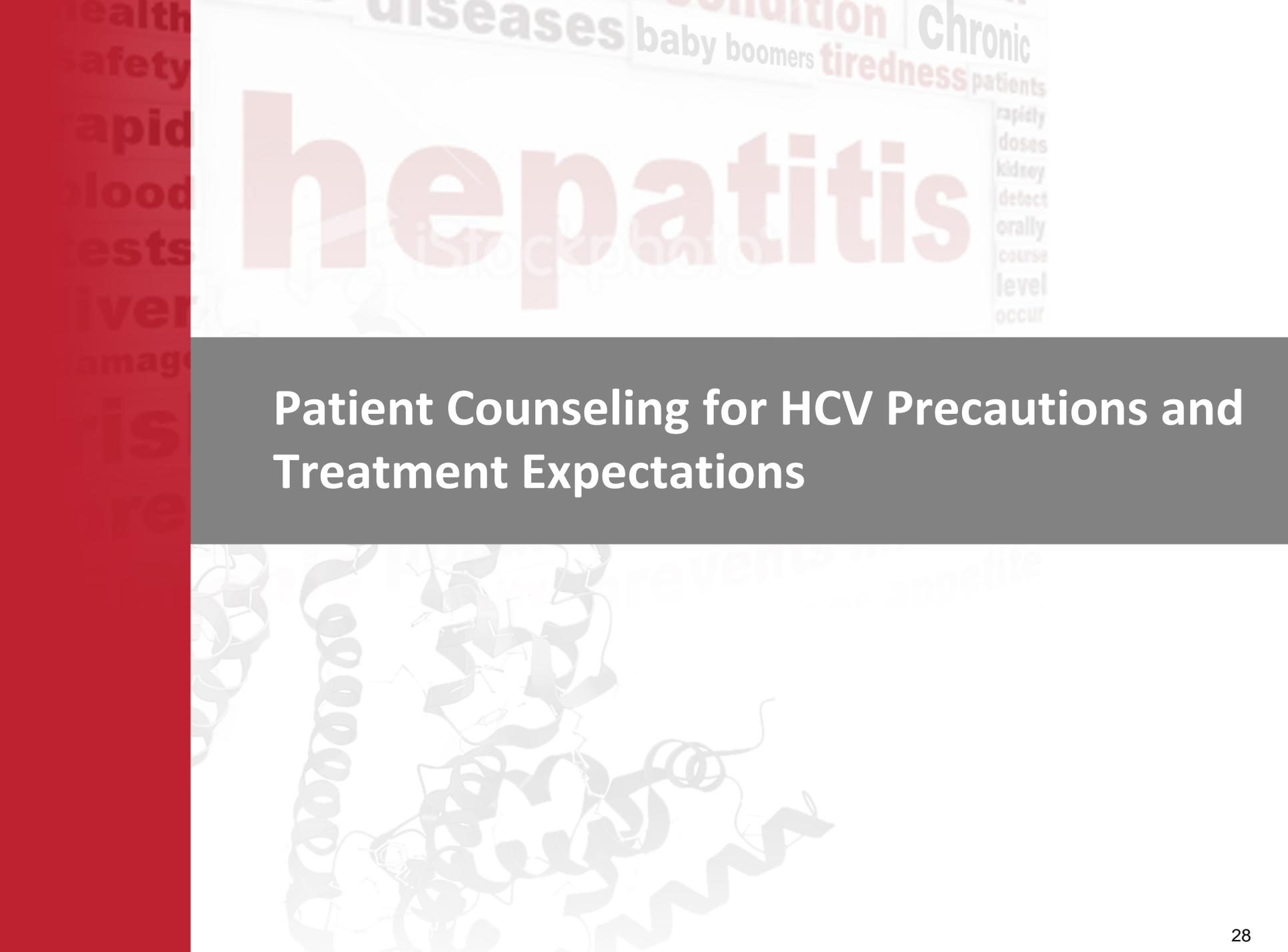


Analysis of baseline values from HALT-C trial database.

A model that included baseline platelet count and albumin as well as severe worsening of AST/ALT ratio and albumin was the best predictor of liver-related outcomes.

AST=aspartate aminotransferase.

Ghany MG, et al. *Hepatology*. 2011;54:1527-1537.

The background features a collage of medical-related terms in various fonts and colors, including 'diseases', 'condition', 'Chronic', 'baby boomers', 'tiredness', 'patients', 'rapidly', 'doses', 'kidney', 'detect', 'orally', 'course', 'level', and 'occur'. A large, stylized protein structure is also visible in the lower half of the image.

# hepatitis

## Patient Counseling for HCV Precautions and Treatment Expectations

# Counseling Recommendations for HCV-Infected Individuals

## To Prevent HCV Transmission

- Avoid sharing toothbrushes and dental or shaving equipment
- Prevent blood contact with others
- Stop using illicit drugs; those who continue to inject drugs should take precautions to avoid viral transmission
- Risk of sexual transmission is low, but practice “safe sex”

## Additional Recommendations

- Avoid alcohol consumption
  - Excess alcohol may lead to progressive liver disease, increased HCV RNA replication, and reduced response to treatment
- Consider treatment for hepatitis C\*
- Vaccinate for hepatitis A and B
- Get tested for HIV
- Encourage family members to get screened

\*If patient meets generally accepted indications for HCV treatment.  
Adapted from Ghany MG, et al. *Hepatology*. 2009;49:1335-1374.

# Generally Accepted Indications for HCV Treatment

## AASLD Guidelines

- **Age  $\geq 18$  years**
- **HCV RNA positive and significant fibrosis\***
- **Compensated liver disease**
- **Acceptable hematologic and biochemical indices<sup>†</sup>**
- **Willingness to be treated and to adhere to treatment requirements**
- **No contraindications<sup>‡</sup>**

\*Bridging fibrosis or cirrhosis.

<sup>†</sup>Hemoglobin 13 g/dL for men and 12 g/dL for women; neutrophil count 1500/mm<sup>3</sup> and serum creatinine <1.5 mg/dL.

<sup>‡</sup>Uncontrolled depression, solid organ transplant, autoimmune hepatitis or autoimmune condition known to be exacerbated by pegIFN/RBV, untreated thyroid disease, pregnancy, severe concurrent medical disease (eg, hypertension, heart failure, coronary heart disease, poorly controlled diabetes, chronic obstructive pulmonary disease), age <2 years

AASLD=American Association for the Study of Liver Diseases.

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

# Summary

- **Approximately 3.2 million people in the US have chronic HCV infection<sup>1,2,\*</sup>**
- **If left untreated, HCV infection can lead to advanced liver disease**
  - Patients often asymptomatic in early stages of HCV infection<sup>3</sup>
  - There is an increasing burden of liver disease in aging baby boomers due to manifestations of HCV infection acquired 20-30 years ago<sup>3</sup>
- **CDC and USPSTF recommend screening all baby boomers in addition to those with other specific risk factors<sup>4,5</sup>**
- **HCV infection is curable (SVR=virologic cure)<sup>6,†</sup>**
  - SVR reduces the risk of mortality and of developing advanced liver disease<sup>7,8</sup>
  - Patients with cirrhosis who achieved an SVR should continue to be monitored at 6- or 12-month intervals for the development of HCC<sup>9</sup>

\*Prevalence estimate based on NHANES data from 1999 through 2002.<sup>1,2</sup>

†Outcomes based on 2-drug therapy with PegIFN and RBV.

1. Armstrong GL, et al. *Ann Intern Med.* 2006;144:705-714.

2. <http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm>.

3. Davis GL, et al. *Gastroenterology.* 2010;138:513-521.

4. Smith BD, et al. *Ann Intern Med.* 2012;157:822.

5. Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11.

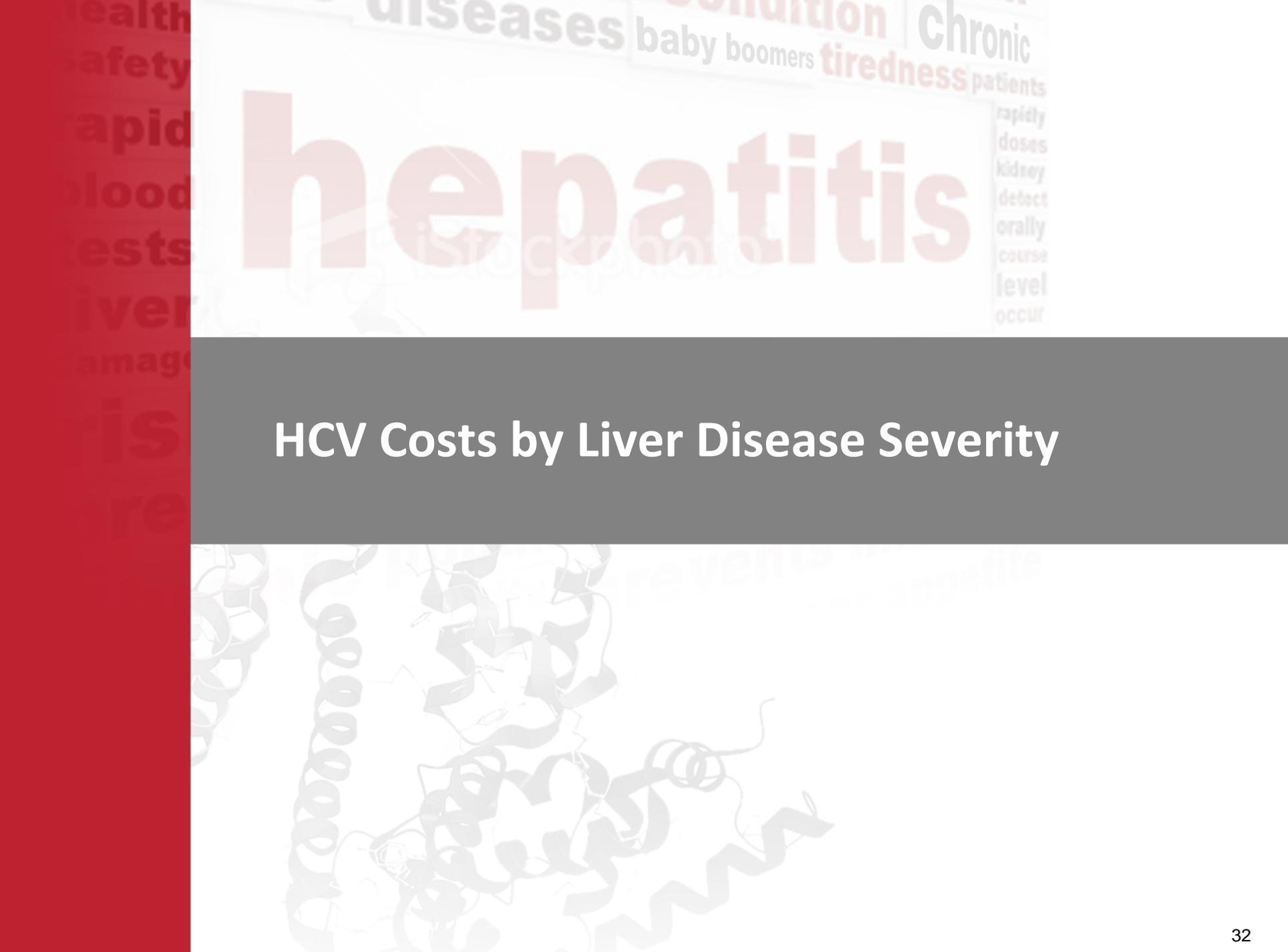
[Epub ahead of print.]

6. Swain MG, et al. *Gastroenterology.* 2010;139:1593-1601.

7. van der Meer AJ, et al. *JAMA.* 2012;308:2584-2593.

8. Morgan TR, et al. *Hepatology.* 2010;52:833-844.

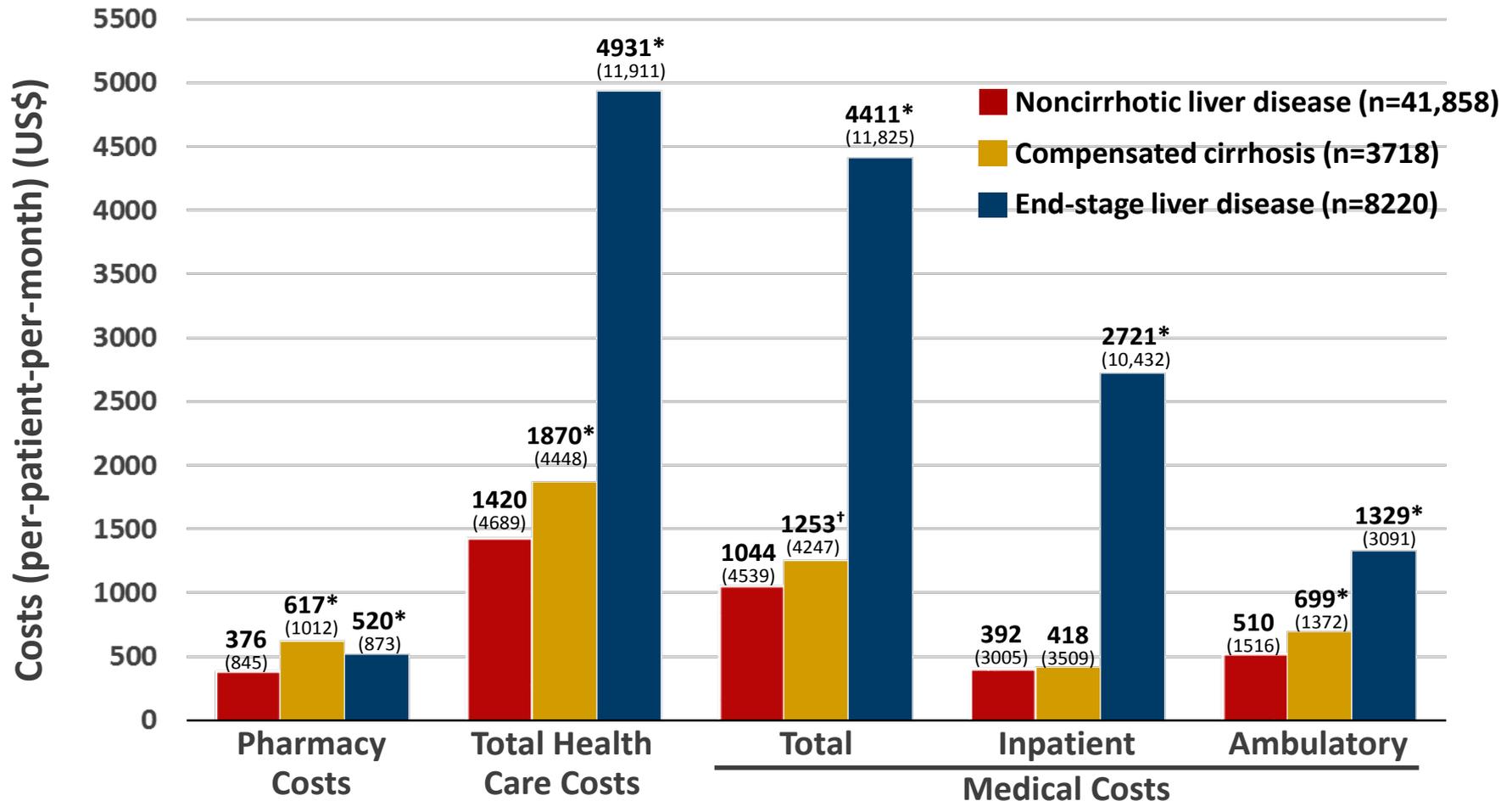
9. Ghany MG, et al. *Hepatology.* 2009;49:1335-1374.

The background features a collage of medical-related terms and a protein structure. On the left, a vertical red bar contains the words 'health', 'safety', 'rapid', 'blood', 'tests', 'liver', 'damage', 'is', and 're' in white. The top section has a white background with terms like 'diseases', 'condition', 'Chronic', 'baby boomers', 'tiredness', 'patients', 'rapidly', 'doses', 'kidney', 'detect', 'orally', 'course', 'level', and 'occur'. The word 'hepatitis' is prominently displayed in large, bold, reddish-brown letters. A faint 'istockphoto' watermark is visible over the word. The bottom section shows a grey protein structure on a white background.

# hepatitis

## HCV Costs by Liver Disease Severity

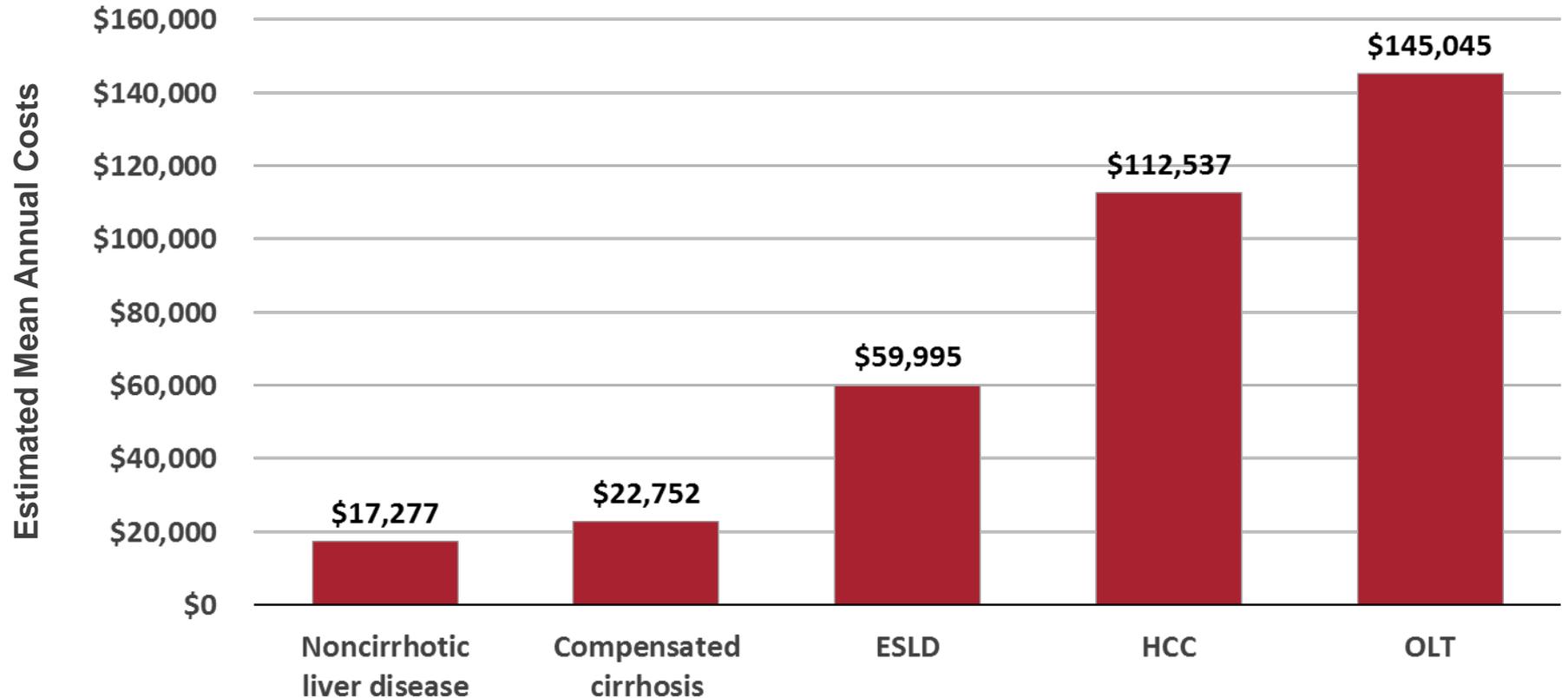
# All-Cause Health Care Costs by Liver Disease Severity (US\$, 2010)



Numbers in parentheses are  $\pm$  standard deviation. \* $P < .001$  and  $^{\dagger}P = .004$  vs noncirrhotic liver disease. Total health care costs include pharmacy and medical costs. Pharmacy costs are based on 2-drug therapy with PegIFN and RBV.

Adapted from Gordon SC, et al. *Hepatology*. 2012;56:1651-1660.

# Impact of Disease Severity on Health Care Costs in Chronic HCV Infection



\*Assumes follow-up time not associated with disease severity.  
ESLD=end-stage liver disease; OLT=orthotopic liver transplantation.  
Gordon SC, et al. *Hepatology*. 2012;56:1651-1660.

# hepatitis

## Screening



# Modeling Predicts Benefit of Birth Cohort Screening With Therapy vs Risk-Based Screening With Treatment

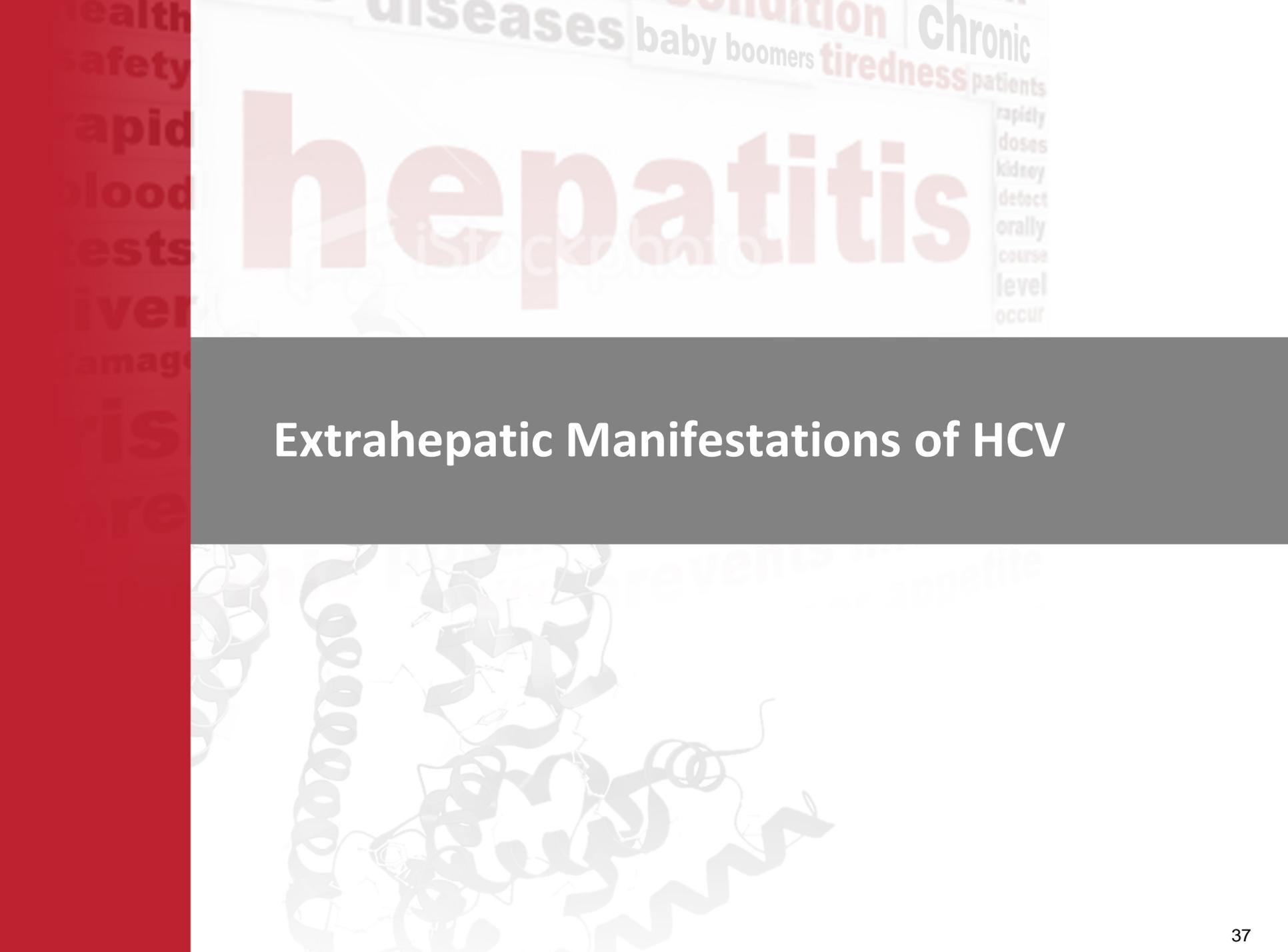
Outcome	HCV testing and treatment strategy		Difference (birth cohort – risk based)
	Risk-based testing* with 2-drug therapy	Birth cohort testing <sup>†</sup> with 3-drug therapy	
Patients treated	135,089	551,800	416,711 more patients treated
Patients who ever developed compensated cirrhosis	994,291	791,053	203,238 cirrhosis cases averted
Patients who ever developed decompensated cirrhosis (DCC)	360,388	286,699	73,689 DCC cases averted
Patients who ever developed HCC	230,784	183,595	47,189 HCC cases averted
Patients who ever received a transplant	75,752	60,268	15,484 transplants averted
HCV-related deaths	591,172	470,293	120,879 deaths averted

\*Risk-based testing applies to all persons with an identified risk regardless of year of birth and has been the standard of care for HCV screening since 1998. <sup>†</sup>Birth-cohort testing applies to all persons born during 1945-1965 regardless of risk.

Simulation was based on a Markov chain Monte Carlo model of the prevalence of HCV antibody stratified by age, sex, race/ethnicity, and history of injection-drug use and of the natural history of chronic HCV. Model for birth cohort testing assumes that all Americans born 1945-1965 who had a PCP visit in 2006 were offered screening for HCV

2-drug=PegIFN+RBV; 3-drug=PegIFN+RBV+PI; PegIFN=pegylated interferon; PI=protease inhibitor; RBV=ribavirin.

Table adapted from Smith BD, et al. *MMWR Recomm Rep.* 2012;61(RR-4):1-32; Source data from Rein DB, et al. *Ann Intern Med.* 2012;156:263-270.

The background features a collage of medical-related terms in various fonts and colors, including 'diseases', 'condition', 'Chronic', 'baby boomers', 'tiredness', 'patients', 'rapidly', 'doses', 'kidney', 'detect', 'orally', 'course', 'level', and 'occur'. A large, faint protein structure is also visible in the background.

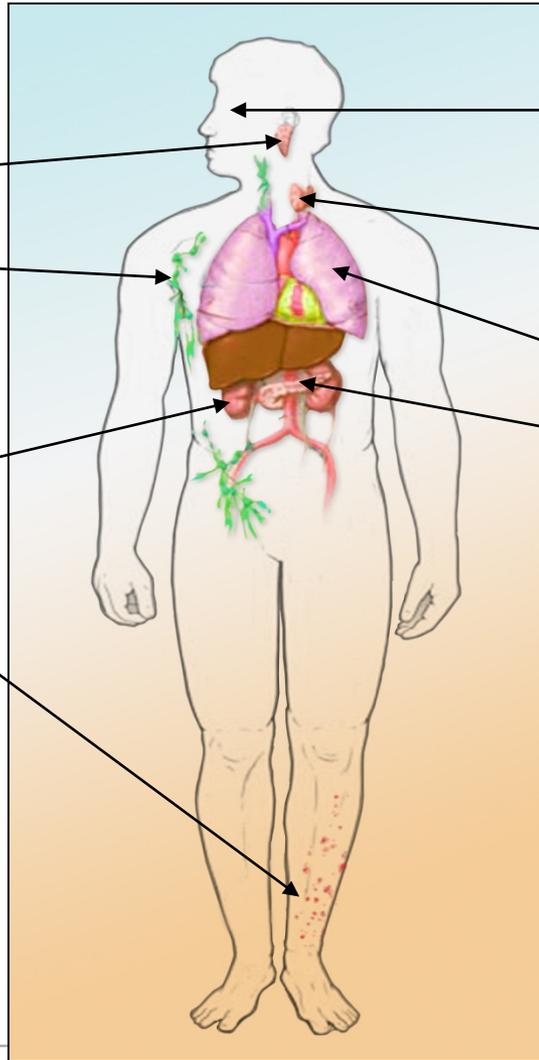
# hepatitis

## Extrahepatic Manifestations of HCV

# Extrahepatic Manifestations of HCV

## Strongly associated

- Mixed cryoglobulinemia
- Sjögren (sicca) syndrome
- Lymphoproliferative disorders
- Porphyria cutanea tarda
- Neuropathy
- Membranoproliferative glomerulonephritis
- Cryoglobulinemic vasculitis



## Possibly associated

- Corneal ulcers (Mooren ulcers)
- Thyroid disease
- Lichen planus
- Pulmonary fibrosis
- Type 2 diabetes
- Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)
- Arthralgias, myalgias, inflammatory polyarthritis
- Autoimmune thrombocytopenia

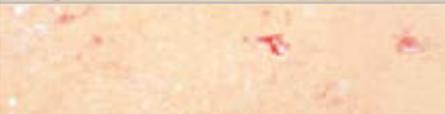


# hepatitis

## Liver Histology Scoring Systems



# Scoring Systems for Histologic Stage

Appearance	Ishak Description	Ishak Score <sup>1</sup>	METAVIR Score <sup>2</sup>
	No fibrosis	0	F0
	Fibrous expansion of some portal areas ± short fibrous septa	1	F1
	Fibrous expansion of most portal areas ± short fibrous septa	2	F2
	Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging	3	
	Fibrous expansion of most portal areas with marked bridging (P-P and portal to central [P-C])	4	F3
	Marked bridging (P-P and/or P-C) with occasional nodules (incomplete cirrhosis)	5	
	Cirrhosis	6	F4

1. Bedossa P, Poynard T. *Hepatology*. 1996;24:289-293; 2. Ishak K, et al. *J Hepatol*. 1995;22:696-699.  
Figure adapted from Standish RA, et al. *Gut*. 2006;55:569-578.



# hepatitis

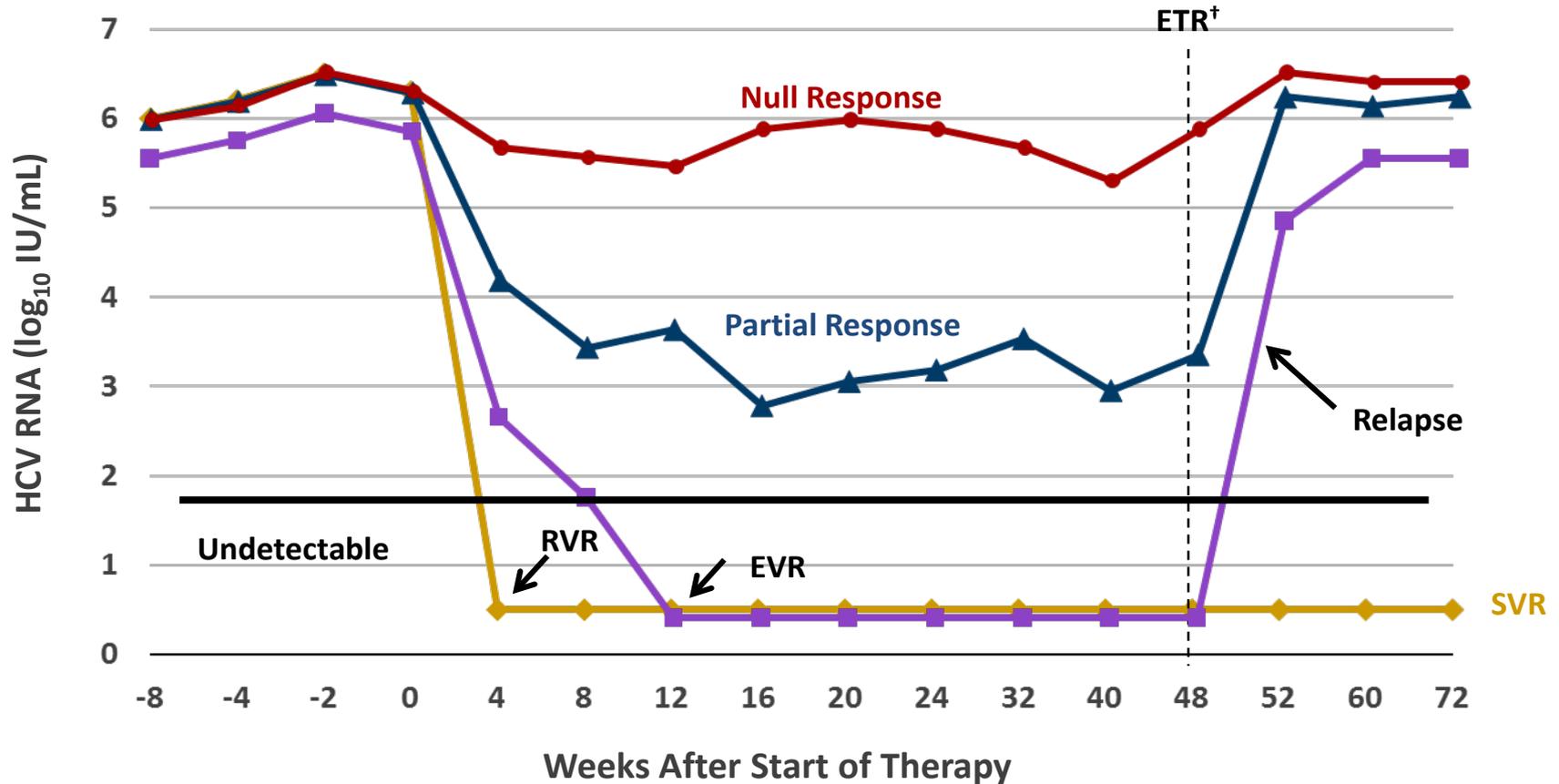
## HCV Virology



# Definitions of Virologic Response to Treatment

Response Term	Definition
Rapid virologic response (RVR)	HCV RNA negative at treatment week 4 by a sensitive PCR-based quantitative assay
Early virologic response (EVR)	≥2 log reduction in HCV RNA level compared with baseline (partial EVR) or HCV RNA negative at treatment week 12 (complete EVR). Predictive of SVR
End-of-treatment response (ETR)	HCV RNA negative by a sensitive test at the end of treatment
Sustained virologic response (SVR)	HCV RNA negative at 24 weeks (SVR24) after cessation of treatment. Best predictor of long-term outcomes
Breakthrough	Reappearance of HCV RNA in serum while on therapy
Relapse	Reappearance of HCV RNA in serum after therapy is discontinued
Nonresponder	Failure to clear HCV RNA from serum after 24 weeks of therapy
Null responder	Failure to achieve a 2 log reduction in HCV RNA after 24 weeks of therapy
Partial responder	2-log reduction in HCV RNA but still HCV RNA positive at week 24

# Virologic Response to Therapy

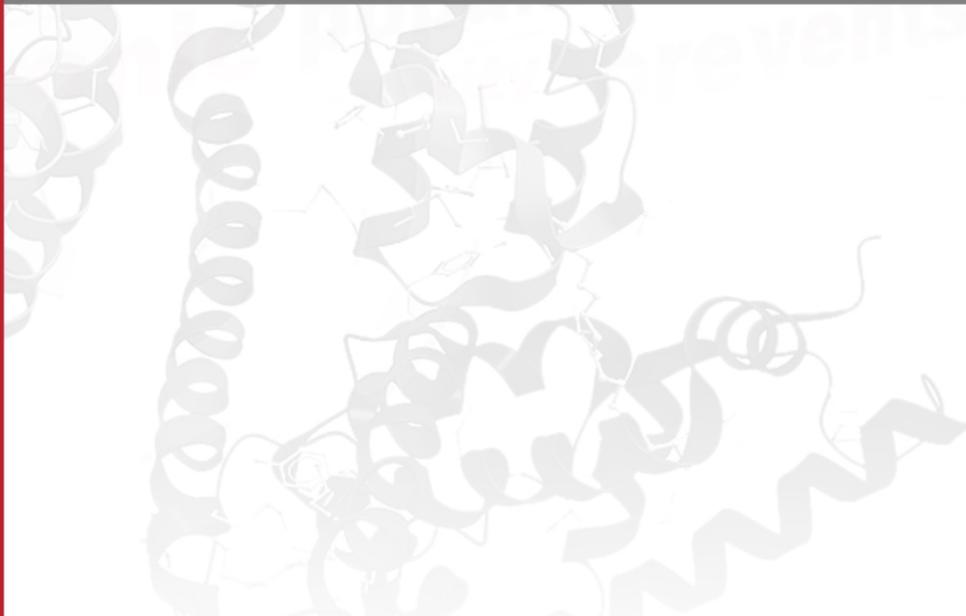


†Shown for 48-week fixed-treatment course; follow stopping rules for treatment.

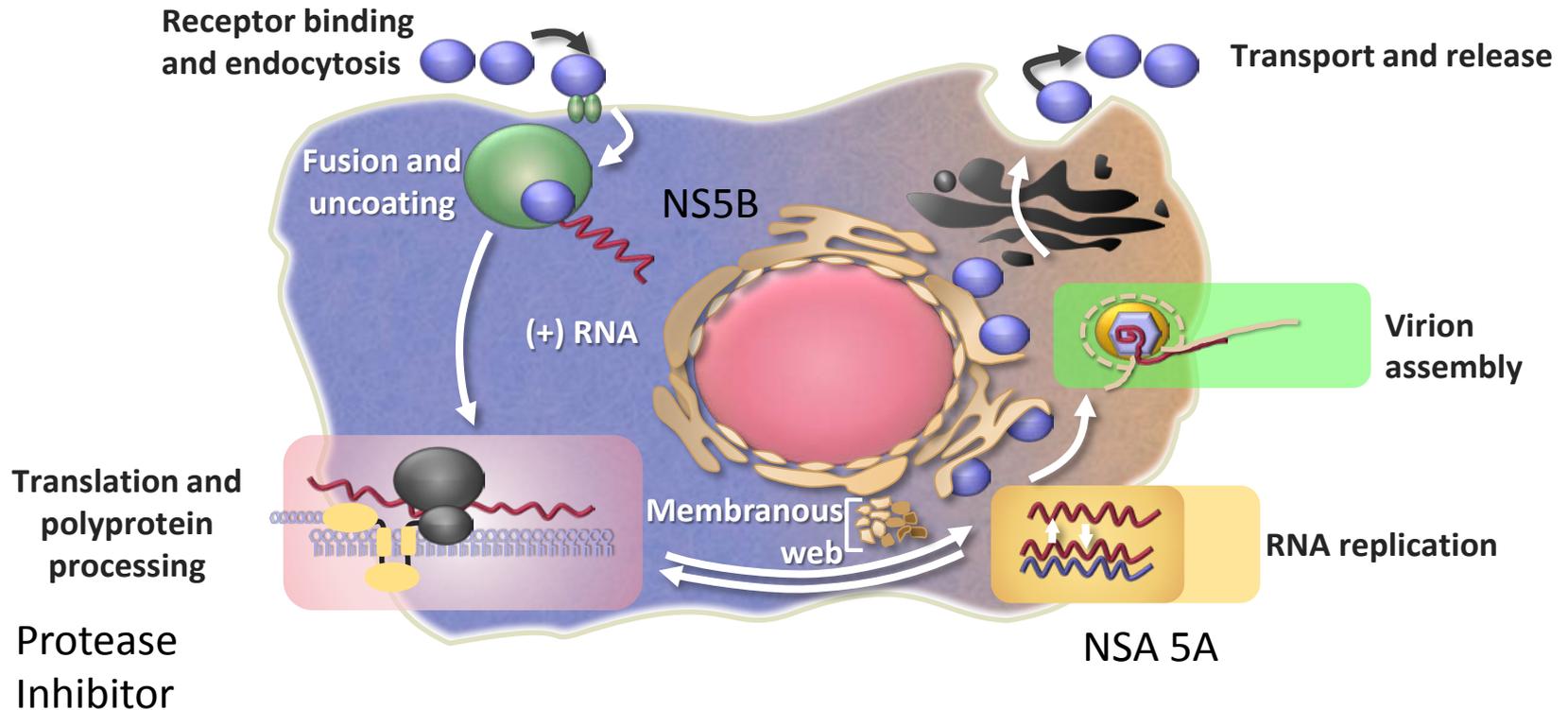
Adapted from Ghany MG, et al. *Hepatology*. 2009;49:1335-1374.

# hepatitis

## HCV Life Cycle



# Targets in All Oral Regimens



Adapted from Manns MP, et al. *Nat Rev Drug Discov.* 2007;6:991-1000 and McGovern B, et al. *Hepatology.* 2008;48:1700-1712.

# Treatment

## Genotype 1, 4, 5

- **Harvoni**
  - Ledipasvir + Sofosbuvir
  - High barrier to resistance
    - 12 -24 weeks
    - Oral regimen
    - No ribavirin
    - 96-99% cure rate
  - Avoid use with amiodarone
  - <1% discontinuation rate

\*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.

Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

# Treatment

## Genotype 1

### ▪ **Viekira**

- Ritonavir, Paritepravir, Ombitasvir, Dasabuvir
- High barrier to resistance
  - 12 -24 weeks
  - Oral regimen
  - Ribavirin for 1a
  - 97% cure rate
  - Hepatic metabolism
  - 1-2% discontinuation rate

\*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.

Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

# Treatment

## Genotype 2

- **Sofosbuvir + Ribavirin**
  - 12 week treatment
  - 96+% cure rate

\*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.  
Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

# Treatment

## Genotype 3

### Sofosbuvir + Ribavirin

- 12 week treatment
- 60-70% % cure rate
- Most difficult to treat

### IFN + Sofosbuvir + Ribavirin

- 75-80% SVR

### Harvoni + Riba

- Off label, but highest response rate

\*Grade B recommendation for persons at high risk for infection and adults born between 1945 and 1965.

Moyer VA; on behalf of the USPSTF. *Ann Intern Med.* 2013 Jun 11. [Epub ahead of print].

## For Discussion

- **What other factors add to the uncertainty around which patients will be tough to treat?**
- **What role does a specialist play in the continued monitoring of patients who reach SVR?**

health  
safety  
rapid  
blood  
tests  
liver  
damage  
is  
re

diseases  
condition  
Chronic  
baby boomers  
tiredness  
patients

# hepatitis

rapidly  
doses  
kidney  
detect  
orally  
course  
level  
occur

istockphoto

Thank You

