Hepatitis C Infection: Updated Information for Front Line Workers in Primary Care Settings

MAMTA K. JAIN, MD, MPH

2/14/18

Overview

- Hepatitis C Virus Prevalence
- Effects of Hepatitis C
- Prevention
- Diagnosis
- Education
- Treatment
- Financial Toxicity

Objectives

Review the screening and diagnosis of hepatitis C infection

Discuss the evaluation and monitoring of chronic hepatitis C infection

Describe updated treatment options for patients with chronic HCV infection

HCV Prevalence

UNITED STATES

HCV Statistics

- HCV infection is the most common blood borne infection in the USA.

- An estimated **3.7 to 5 million** persons have HCV.

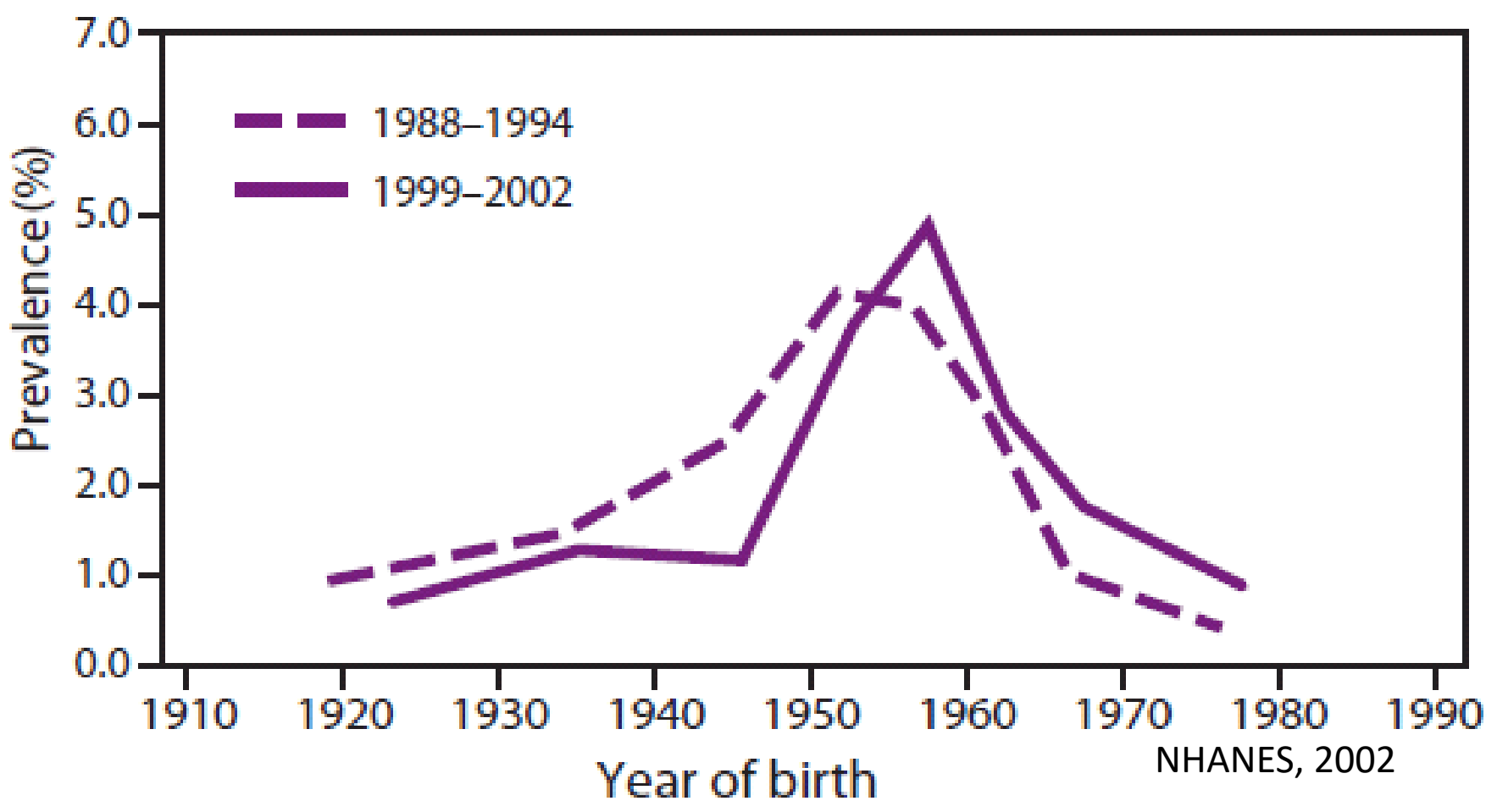
Chou R. Screening for Hepatitis C Virus Infection: Systematic Evidence Review No. 24.

HCV Statistics

- In the 1980s, yearly incidence of HCV infection was around 230,000 cases/year but by 2001 this declined to 25,000 cases/year.

Chou R. Screening for Hepatitis C Virus Infection: Systematic Evidence Review No. 24.

Prevalence of HCV by birth year

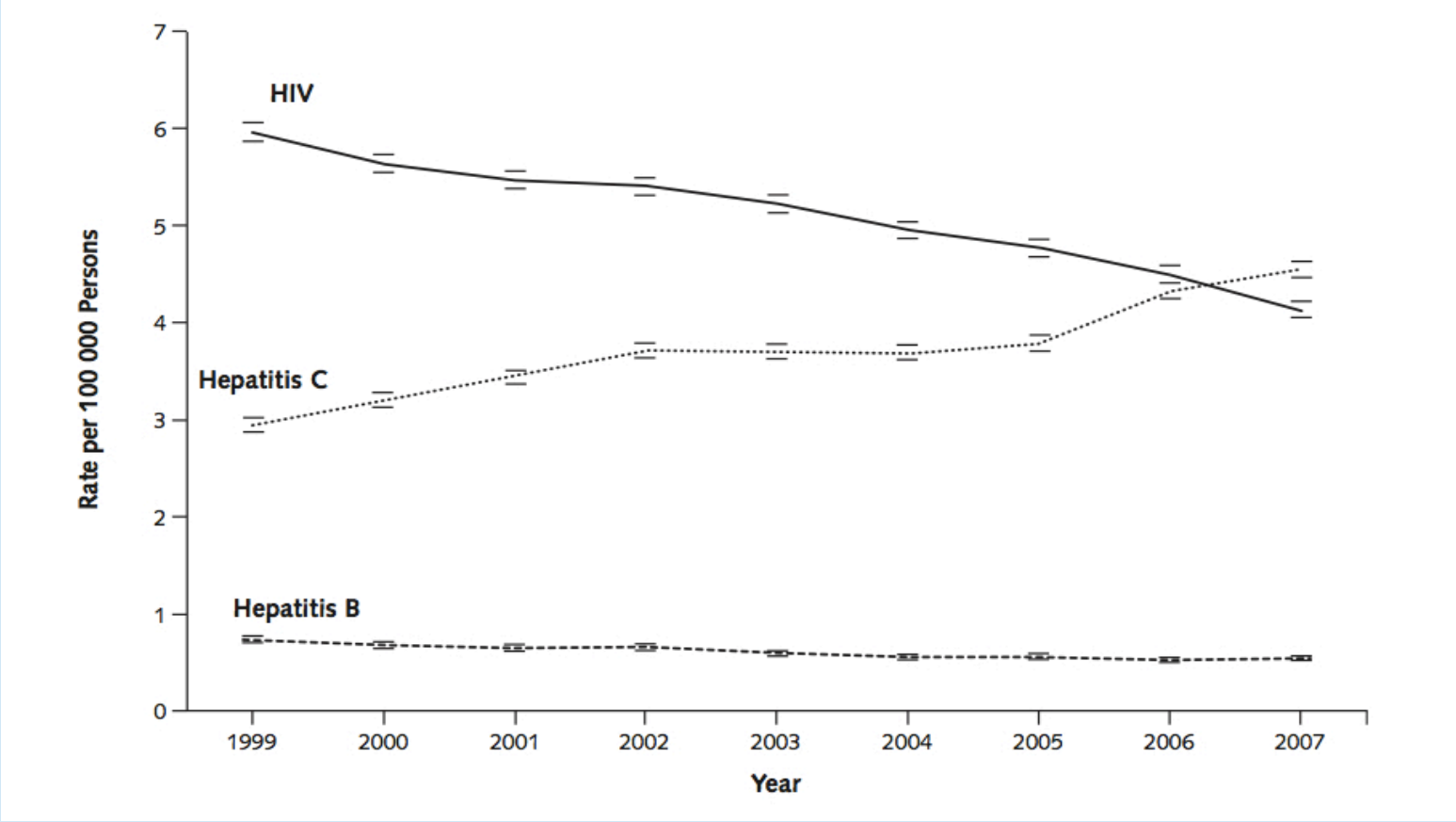


NHANES, 2002

Effects of Hepatitis C

HCV Mortality Exceeds HIV

The Increasing Burden of Mortality From Viral Hepatitis in the United States Between 1999 and 2007



Ly et al. *Ann Intern Med*. 2012;156:271-278

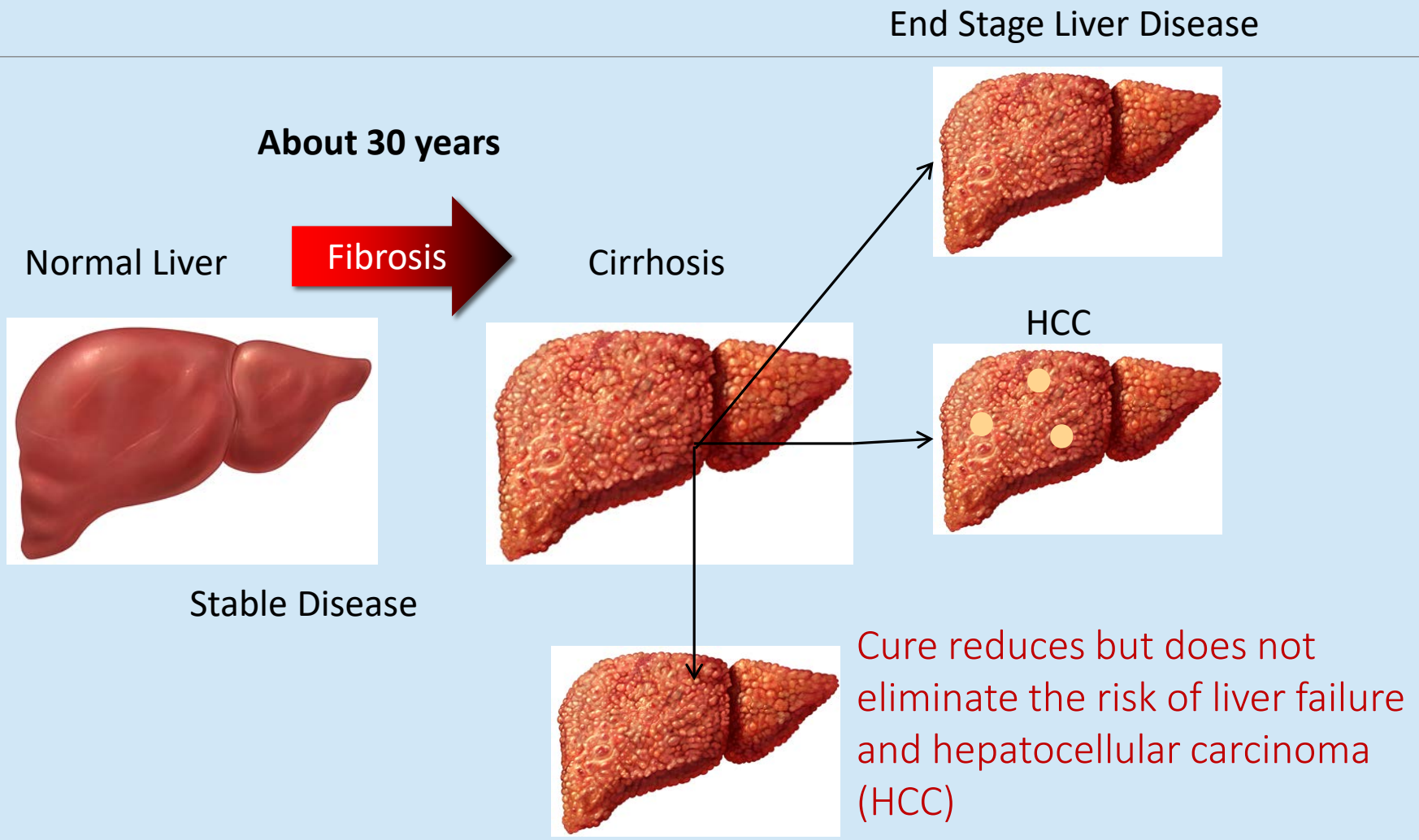
Consequence: Hepatitis C Kills

- 1999 to 2007**: HCV-associated mortality** increased 50%
- 2013: **19,368 HCV-related deaths***
  - 73% in persons aged 45-64
  - Median age of death was 57 (or about 20 years less than average life expectancy)

*These represent a fraction of deaths attributable in whole or in part to chronic hepatitis C

Ward. *Clin Liver Dis* 2013;17:1-11
http://www.cdc.gov/hepatitis/statistics/

Time from HCV infection until serious complications



Hepatocellular Carcinoma (HCC)

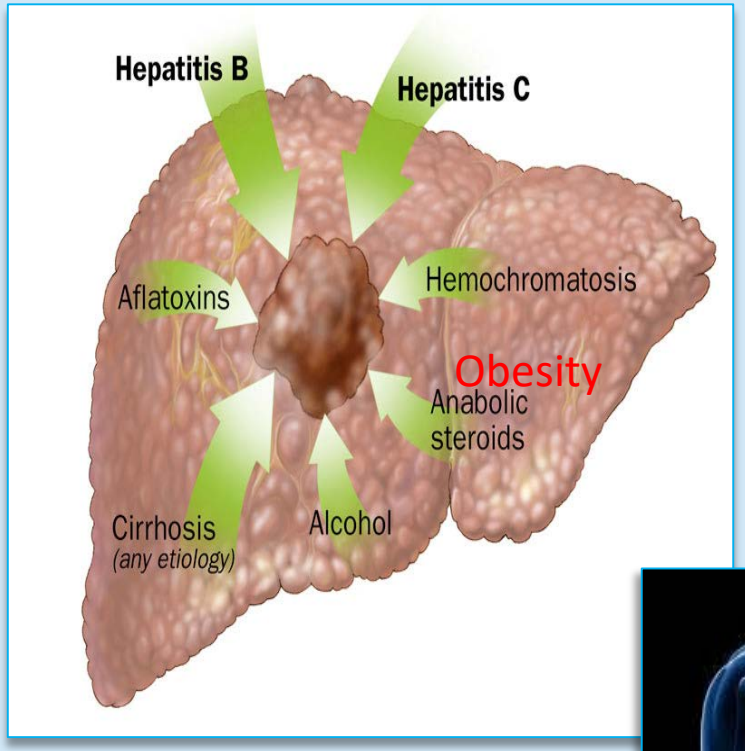
Most common type of liver cancer

Chronic HCV increases the risk

Treated with surgery, medications or liver transplant

But poor prognosis:

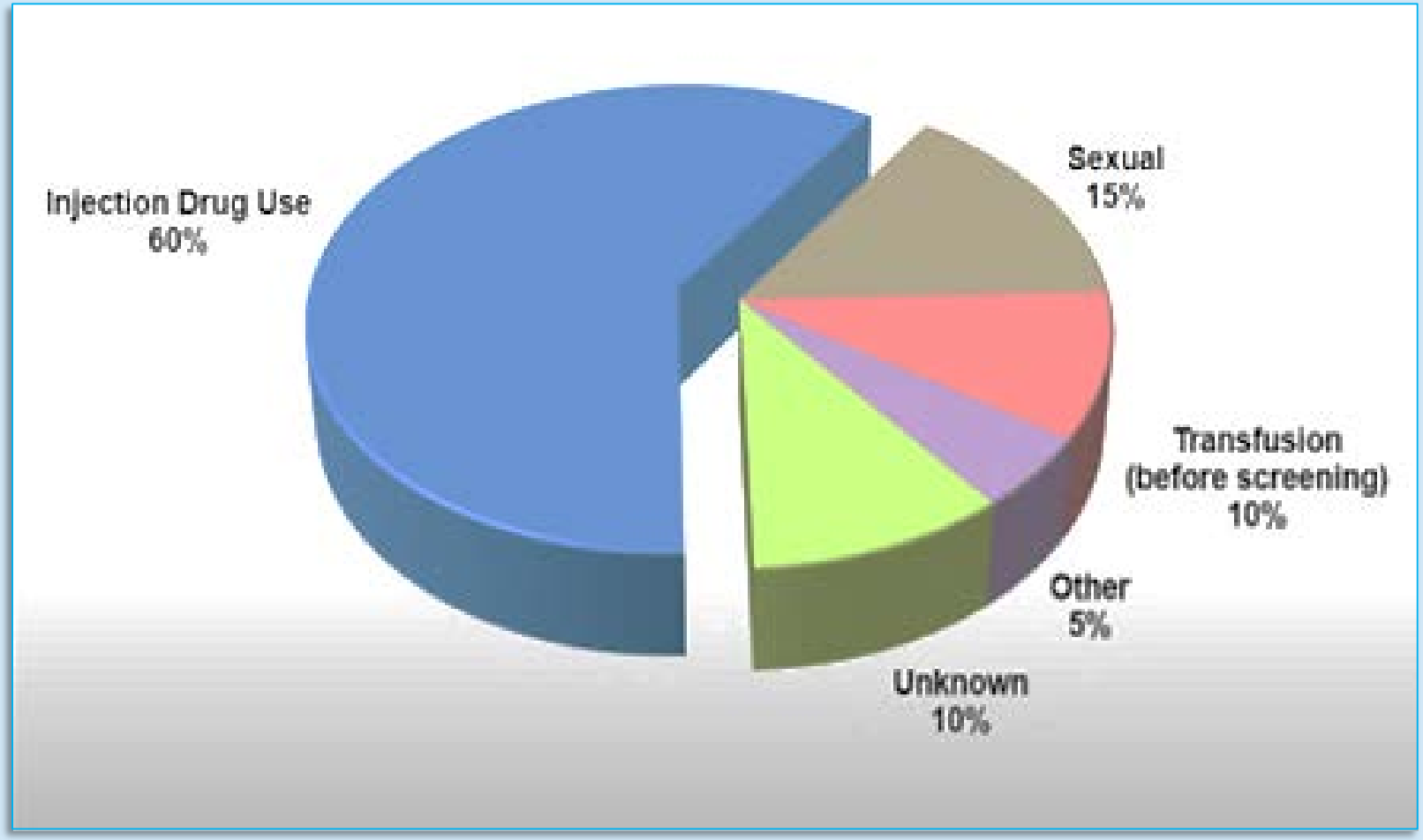
- **Solution**: prevent development



HCV Prevention

USPSTF RECOMMENDATIONS

How is HCV spread?

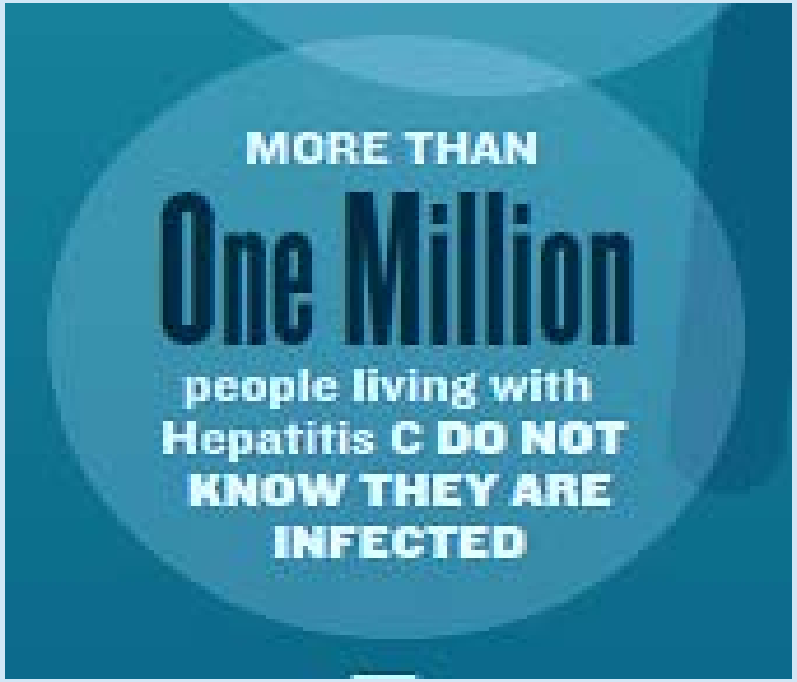


Source: CDC and Prevention

Guidelines: High Risk Groups to Screen

- Unexplained chronic liver disease or high ALT
- Injection-drug use (even once) or intranasal drug abuse
- Ever in jail
- Long-term hemodialysis (ever)
- Transfusions or organ transplants: before July 1992 or clotting factor given before 1987, HCV+ transfusion
- Tattoo in an unregulated setting
- Children born to HCV-infected women
- Healthcare/public safety workers exposed to HCV+ blood
- HIV infection
- Born in a high risk country

Risk-Based Screening is NOT Enough



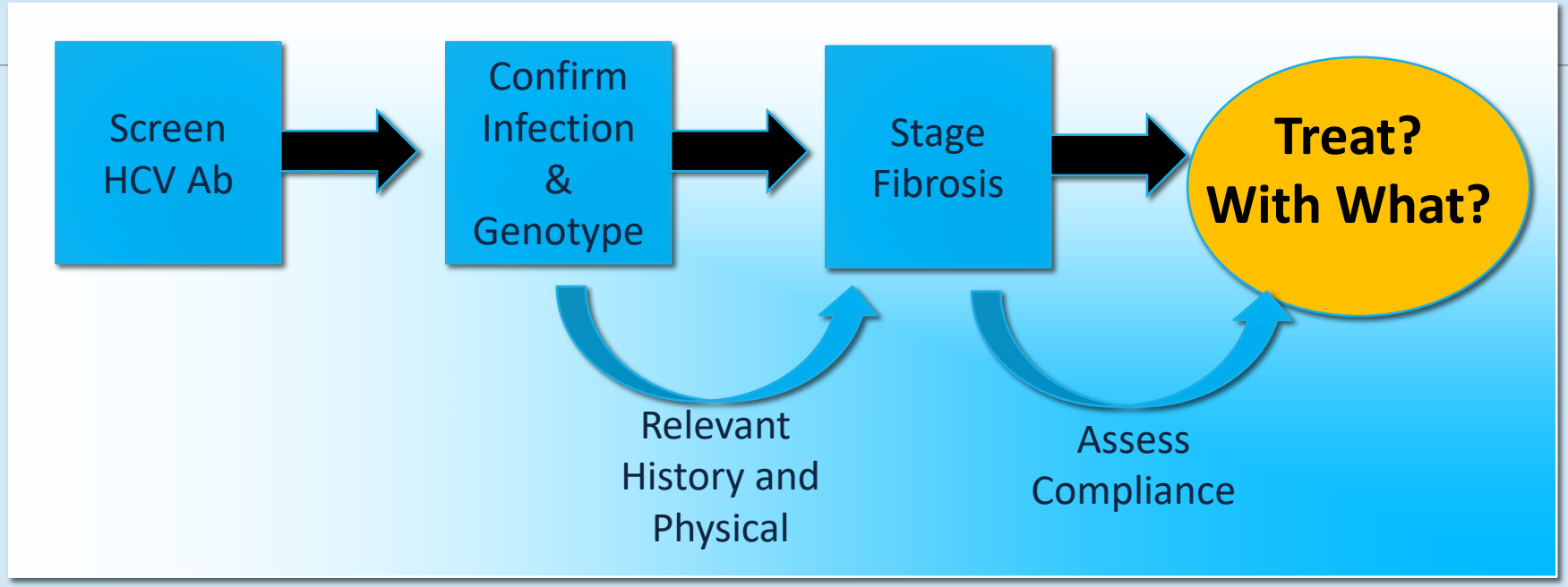
NEW US Preventive Services Task Force (USPSTF) Guidelines - 2012

- One time screening of all baby boomers (born 1945 through 1965) for HCV infection (USPSTF Rating: Class I, Level B)
- Enzyme immunoassay (EIA) is the initial screening test for anti-HCV antibodies.
- Followed by Polymerase Chain Reaction (PCR) for the virus

Diagnosing HCV

LAB TESTS AND CALCULATIONS

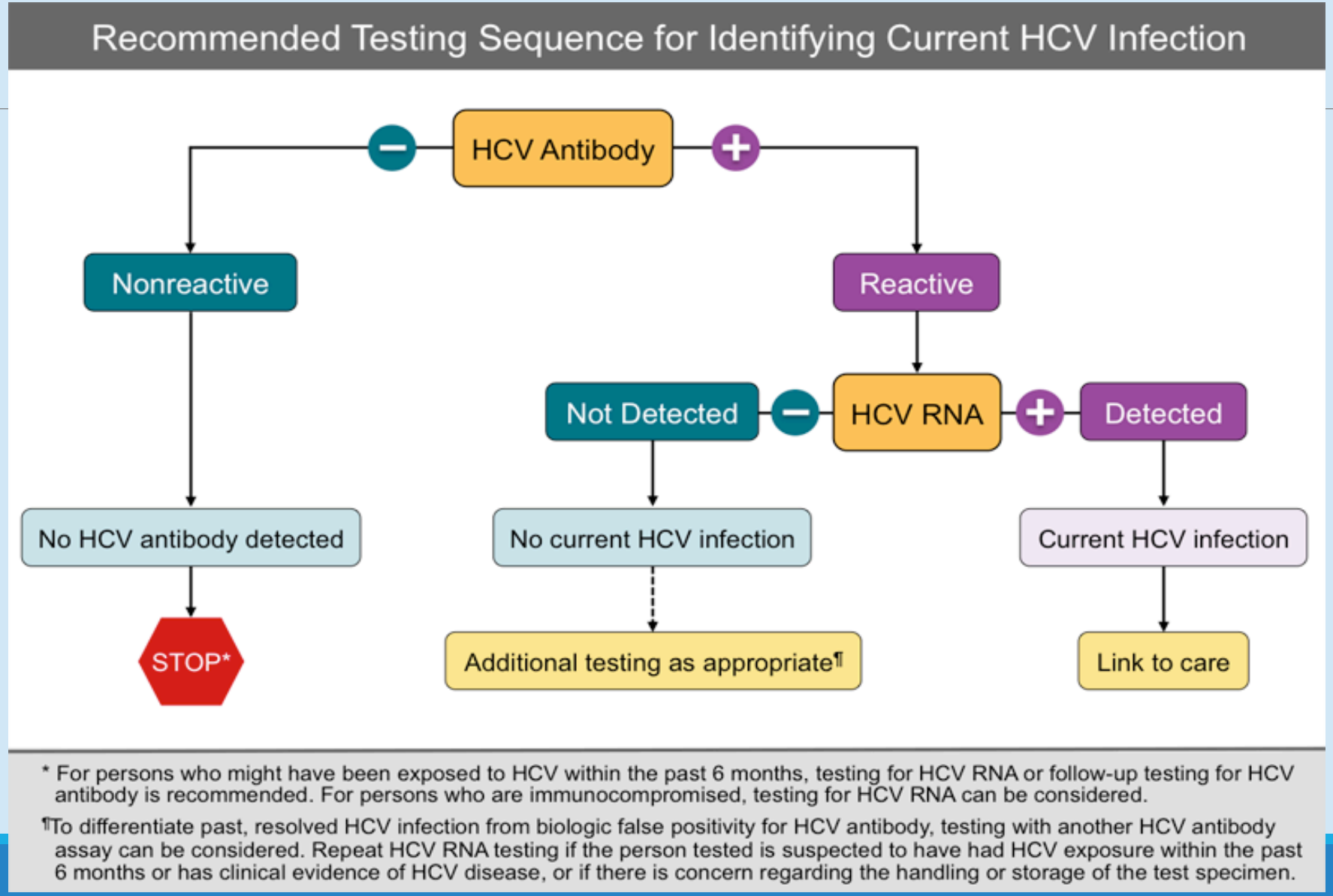
Preparing for HCV therapy



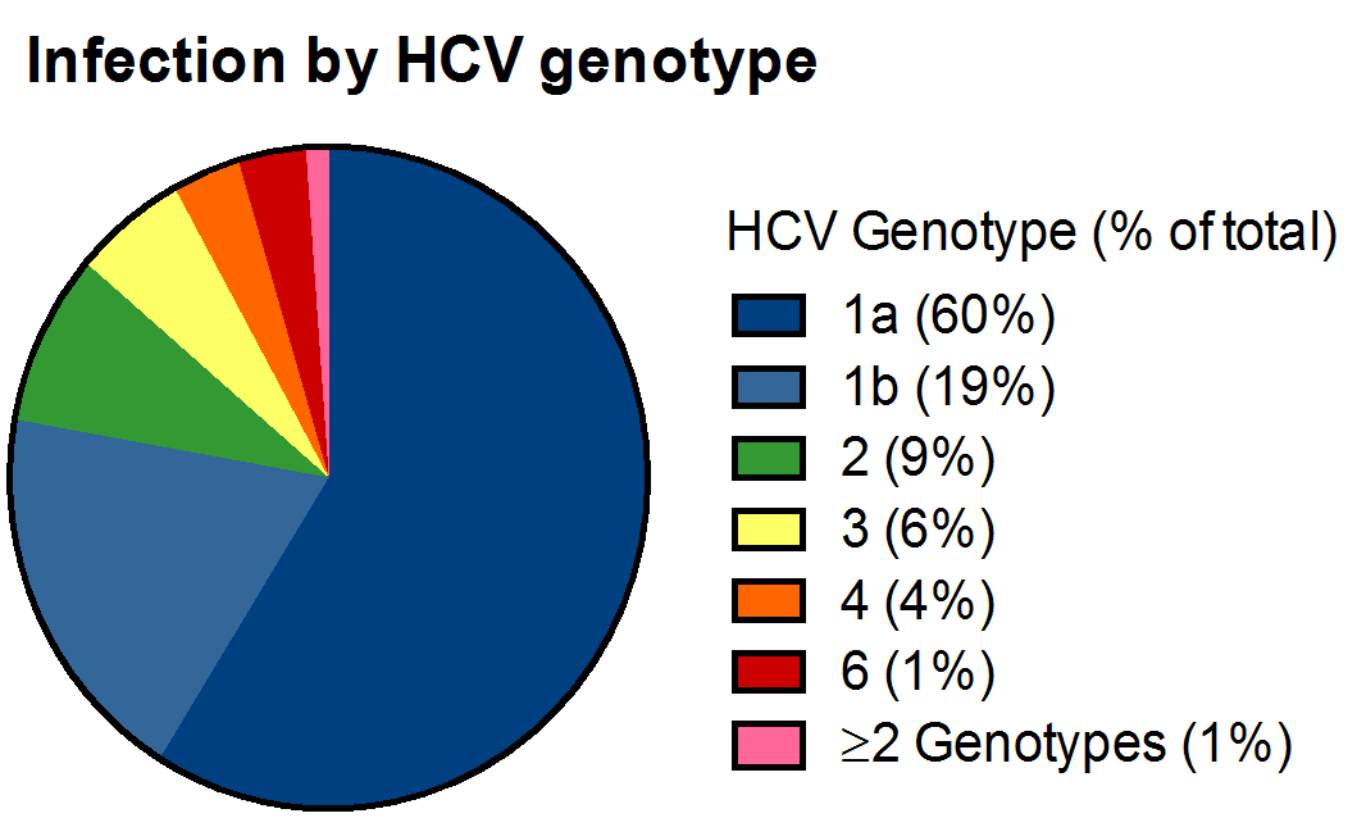
HCV Evaluation and Staging

-Treatment history (interferon therapy or DAA)
-Genotype (1, 2, 3..) and subgenotype (1a vs 1b).
-Imaging
-Viral load (copies/mL)
-Fibrosis score (i.e. Fib-4)
-Drug-drug interactions (DDIs)

Screening Tests for HCV Infection



HCV Genotype 1a: Most common in US and at Parkland



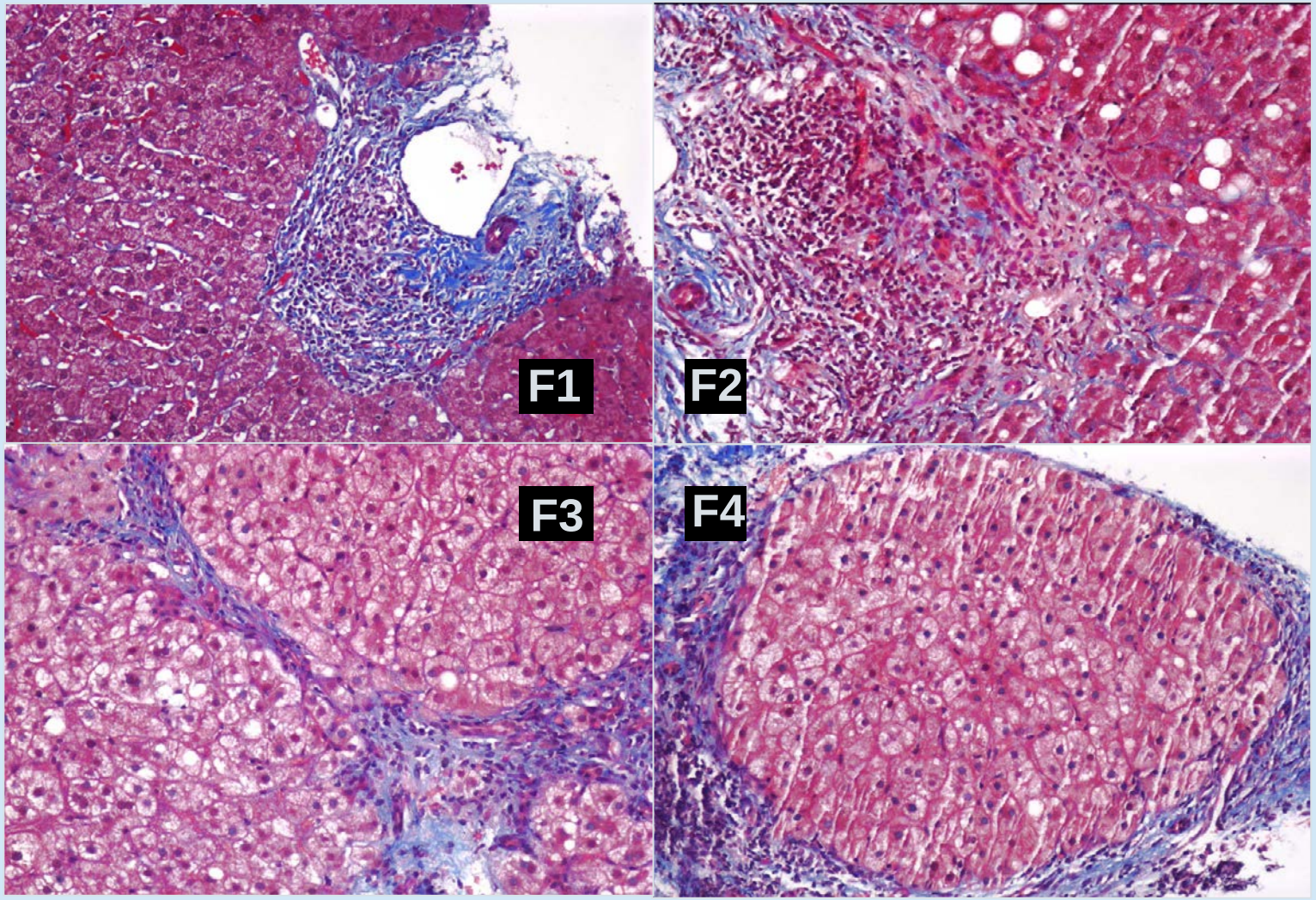
N=512

Four stages of liver fibrosis

Minimal fibrosis

Moderate fibrosis

Septal



mild fibrosis

Severe Fibrosis: Cirrhosis

Staging liver fibrosis

Liver biopsy is gold standard but excluding cirrhosis may also be possible with noninvasive estimates of liver fibrosis

- **Fib-4 or APRI score** or equivalent serum tests are widely available.
- FibroSure (# 550123 thru Labcorp)
- Imaging helpful (liver ultrasound)
- Elastography (shear wave) ultrasound
- Fibroscan® (vibration Controlled Transient Elastography) in special centers
- MRI elastography but not widely available.

Calculating FIB-4

Fibrosis-4 (FIB-4) Calculator

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)}\ 0 \times \text{AST Level (U/L)}\ 0}{\text{Platelet Count } (10^9/\text{L})\ 0 \times \sqrt{\text{ALT (U/L)}\ 1}} =$$

Non-cirrhotic

1.45

3.25

Cirrhotic

Interpretation:
Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Source: Sterling RK, Lissen E, Clumeck N, et. al. Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. Hepatology 2006;43:1317-1325.

http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

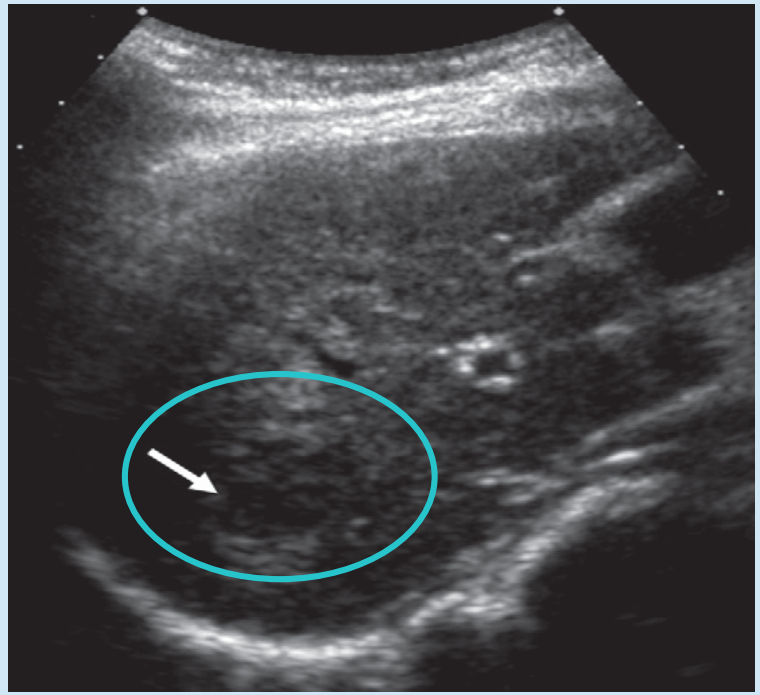
Patients with cirrhosis need to have US screening

Ultrasound is the recommended modality for HCC surveillance

Advantages: cheap, safe, readily available, supported by data

Drawbacks: operator dependent, limited sensitivity, difficult in obese patients

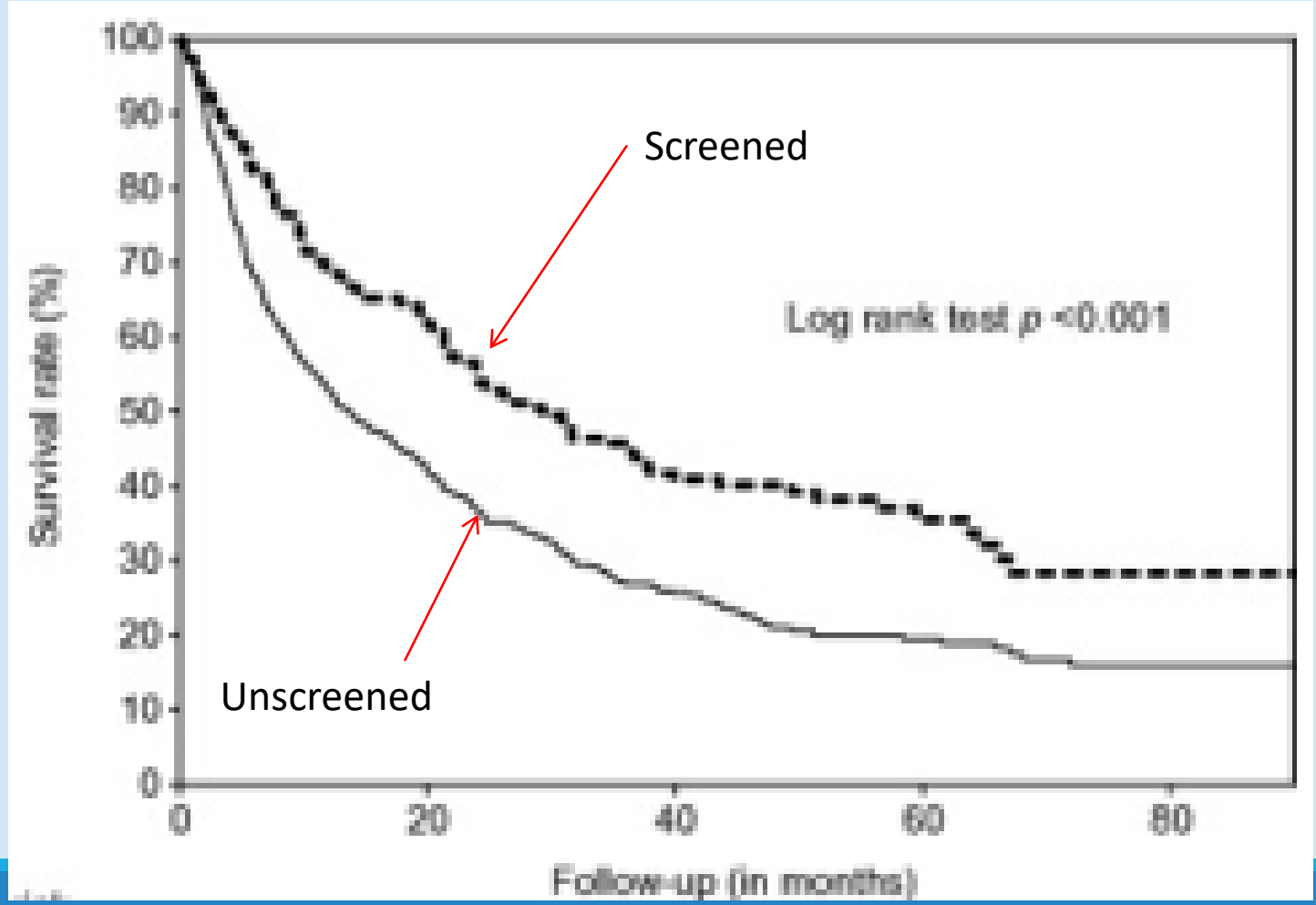
Masses detected by ultrasound require further characterization with other modalities (CT, MRI)



Sonogram shows a small hypoechoic mass

Wilson SR, et al. Radiology 2010

Screening for HCC Improves Survival in Patients with Cirrhosis



Surveillance (n=295)
vs. other (n=779)

Tumor size
2.7 vs. 6.0 cm

Early stage HCC
61% vs. 21%

Curative treatment
57% vs. 32%

Van Meer et al J Hepatology 2015

Education

PATIENTS DIAGNOSED WITH HCV

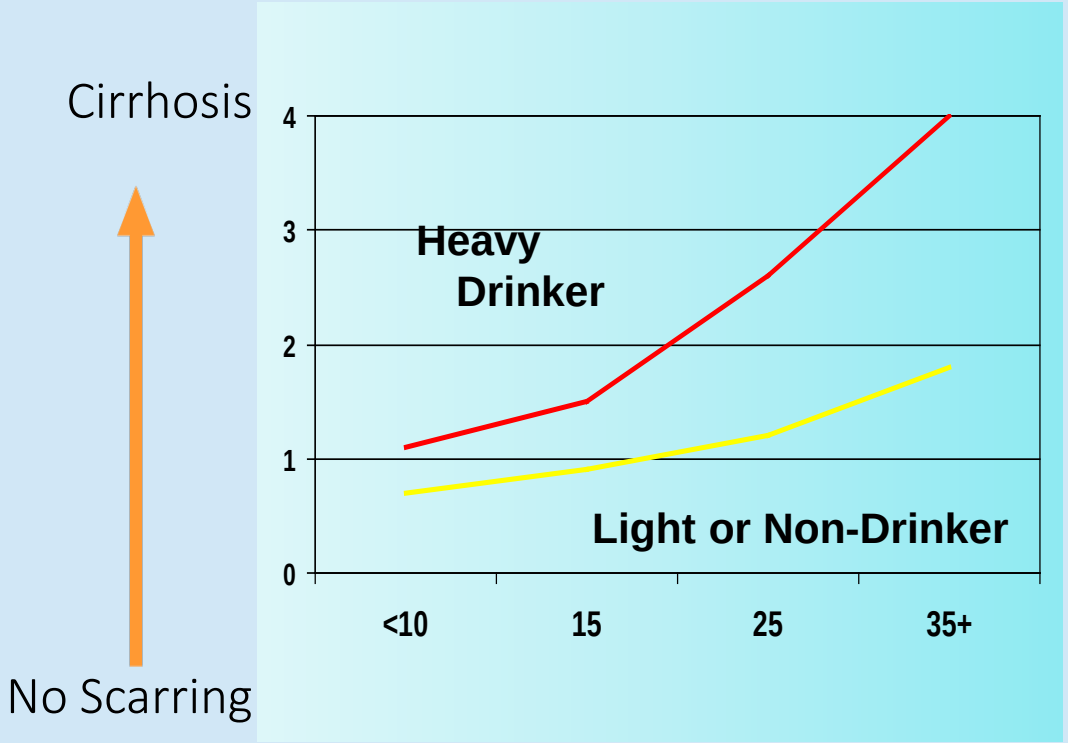
Patient Counseling

Effective patient counseling:

- **Educates patients** on:
  - HCV and how it affects the liver
  - Ways to avoid spreading to others
  - Strategies to reduce damage to the liver
-

Co-factors that worsen liver disease in person with chronic HCV infection

- Alcohol adds fuel to the fire



Treatment As Prevention

NEW HIGHLY EFFECTIVE MEDICATIONS

Goal of Treatment

CURE!

Effectiveness of HCV medications

Rate of cure for each regimen varies depending on

- Genotype
- Presence of cirrhosis
- Prior treatment for HCV

Most of these have >90% cure rate

every 10 people who get treated, 9 will be cured

All Oral HCV Treatments Available

Drug	Dosing regimen	Typical duration	genotype	Efficacy
Sofosuvir/ledipasvir (Harvoni)	1 pill once a day	12 weeks	1, 4, 5, 6	95%
Ombitasvir/paritepravir/ritonavir and dasabuvir (Viekira Pak)	2 tabs once a day+ 1 tab twice a day+- Ribavirin twice a day	12-24 weeks	1, 4	95%
Daclatasvir, sofosbuvir (Daklinza, Sovaldi)	Two pills once a day	12 weeks	1, 3	95%, 90%
Elbasvir/grazoprevir (Zepatier)	One pill once a day	12-16 weeks	1, 4	95%
Sofosbuvir/Velpatasvir (Epclusa)	One pill once a day	1 2 weeks	1, 2, 3, 4, 5, 6	95%
Glecaprevir/pibrenstavir (Mayvert)	3 pill once a day	8 or 12 weeks	1, 2, 3, 4, 5, 6	95%
Sofosbuvir/velpatasvir/voxilaprevir (Vosevi) (for prior failures)	One pill once a day	12 weeks	1,2,3,4,5,6	90-95%

Sofosbuvir/Velpatasvir:

Sofosbuvir is nucleoside NS5B inhibitor and pan-genotypic

Velpatasvir is NS5A inhibitor and pangenotypic

Can be used for all genotypes 1,2,3, 4, 5, and 6

One pill once a day

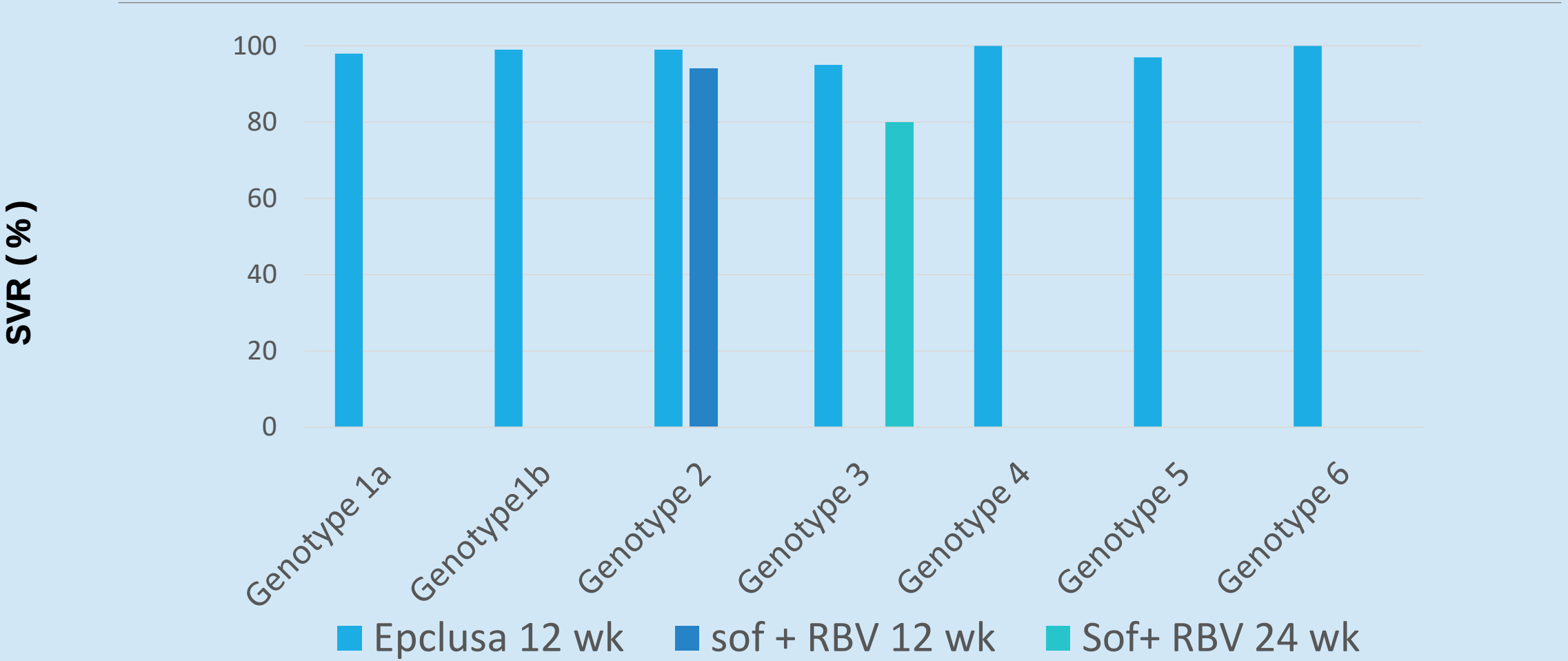
Sofosbuvir/Velpatasvir: Duration of Therapy

Without cirrhosis or with compensated cirrhosis (Child-Pugh A): 12 weeks (regardless of genotype)

Decompensated cirrhosis (Child-Pugh B and C) + ribavirin (weight-based) for 12 weeks

Can not use with Cr Cl <30 ml/min

Sofosbuvir/Velpatasvir: Efficacy



Sofosbuvir/Velpatasvir: Drug Interactions

- Amiodarone - symptomatic bradycardia
- Rifampin, St. John's wort, carbamazepine: may decrease concentration of drug
- Drugs decreasing velpatasvir dose
  - Antacids: take least 4 hours apart
  - H2 blockers: take 12 hours apart
  - No PPI: except take this drug with food at least 4 hours before omeprazole 20 mg
  - HIV meds: do not use with Efavirenz, Tipranavir/ritonavir

Sofosbuvir/Velpatasvir: Side Effects

SOFOSBUVIR/VELPATASVIR

- Headache (22%)
- Fatigue (15%)
- Nausea (9%)
- Asthenia (5%)
- Insomnia (5%)

WITH RIBAVIRIN

- Fatigue (32%)
- Anemia (26%)
- Nausea (15%)
- Headache (11%)
- Diarrhea (10%)

Glecaprevir/Pibrenstavir:

Glecaprevir is a NS3/4a inhibitor, pangenotypic

Pibrentasvir is a NS5A inhibitor, pangenotypic

Can use with all genotypes : 1, 2, 3, 4, 5, 6

Take 3 tablets once a day, take with food

Glecaprevir/Pibrenstavir : Duration of Therapy

Treatment naïve or experienced with no cirrhosis: 8 weeks

Treatment naïve or experienced with cirrhosis, compensated (Child Pugh A) : 12 weeks

Treatment experienced genotype 3: 16 weeks

Glecaprevir/Pibrenstavir : Duration of Therapy

Treatment experienced

- Genotype 1: NS5A inhibitor without NS3/4A– 16 weeks
- Genotype 1: NS3/4A without prior NS5A– 12 weeks
- Genotype 1, 2, 4, 5, 6 : prior interferon/ribavirin/sofosbuvir-- 8 weeks (no cirrhosis); 12 weeks (compensated cirrhosis)
- Genotype 3: prior interferon/ribavirin/sofosbuvir—16 weeks

Glecaprevir/Pibrenstavir : Adverse Event

Headache (9-17%)

Nausea (6-14%)

Diarrhea (5-7%)

Nausea (9-12%)

Glecaprevir/Pibrenstavir : Drug Interaction

Anti-convulsants

Rifamycins

Ethinyl estradiol (increased risk of ALT elevation)

St John's Wort

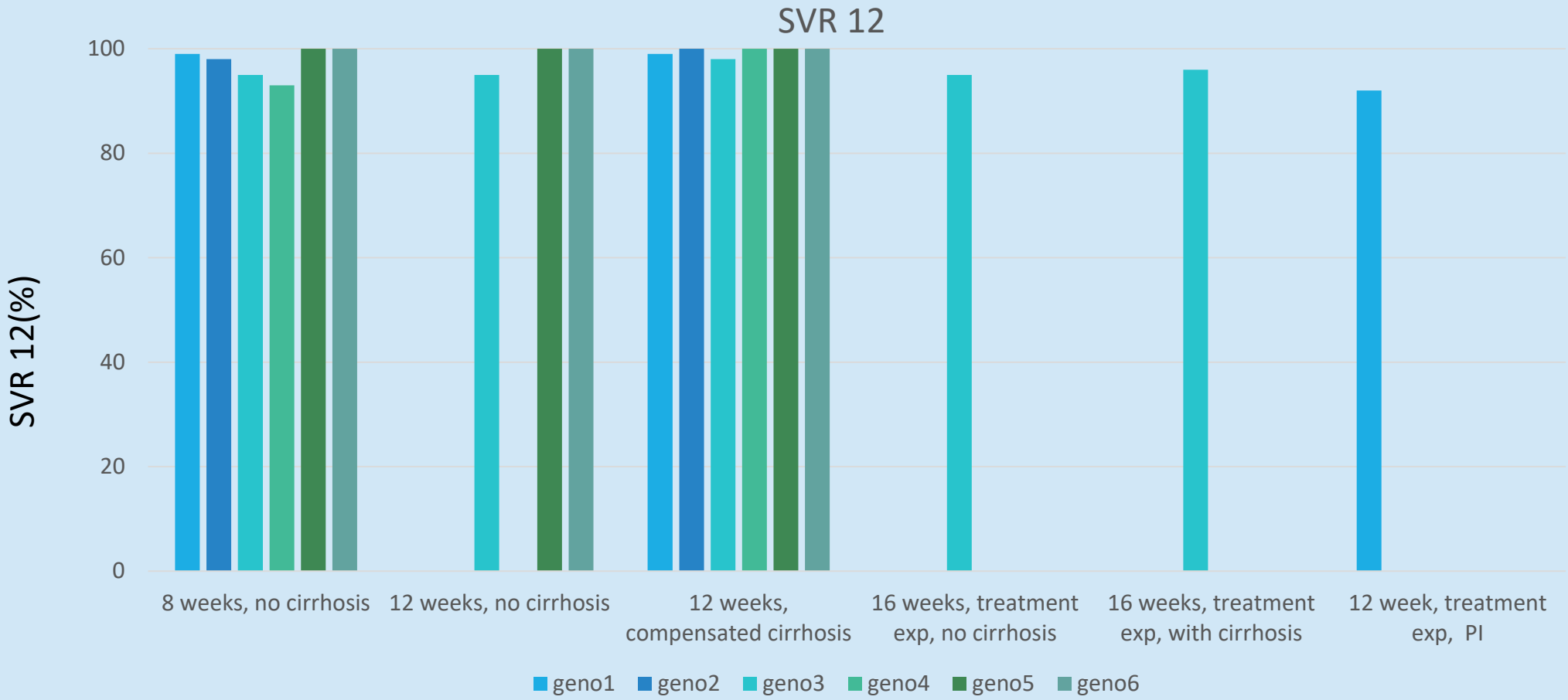
Statins (atorvastatin, lovastatin, simvastatin)

Cyclosporine

HIV Medications

- Atazanavir
- Darunavir
- Lopinavir
- Ritonavir
- Efavirenz

Glecaprevir/Pibrenstavir : Efficacy



Acknowledgement

Grant Funder:

CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Thank you for your Attention!

STOP HCC BY TREATING HCV