HEPATITIS C
IN THE PRIMARY CARE SETTING

Alan Williams, MD

Joshua Opperman, PA-C, MSPAS

DISCLOSURES

- This talk will include information about investigational drugs that have not yet been approved by the FDA.
- Neither speaker has any commercial or financial interests to disclose.

HEPATITIS C MANAGEMENT
IN THE PRIMARY CARE SETTING

Primary Care Provider

Screening	Diagnose	Staging	Treatment	Follow Up
HCV Ab	HVC RNA HCV Genotype Labs – Liver Fxn	Ultrasound Hep A/B IZ ETOH Drug Use	Drug Regimen Monitoring?	Cancer Surveillance? -AFP -Liver U/S

Specialist

Liver Biopsy Fibroscan IL28b, Q80K	Drug Regimen Monitoring	Cancer Surveillance

HEPATITIS C IN PRIMARY CARE

- HCV screening is recommended for all baby boomers.
- Hepatitis C is curable.
- Screening for Hepatitis C will NOT swamp your clinic with large numbers of antibody positive patients.
- Hepatitis C treatment medications are NOT too complex to prescribe at the primary care level.
- Hepatitis C treatment medications are accessible to our patients.

CONSEQUENCES OF HEPATITIS C AND LIVER CIRRHOSIS

Decreased Quality Of Life

- Fatigue
- Weight Loss
- Depression
- Muscle Wasting
- Impaired Cognition

Complications

- GI bleeding (varices, gastropathy)
- Ascites
- Bacterial Infections
- Encephalopathy
  - Overt
  - Minimal
- Hepatocellular carcinoma

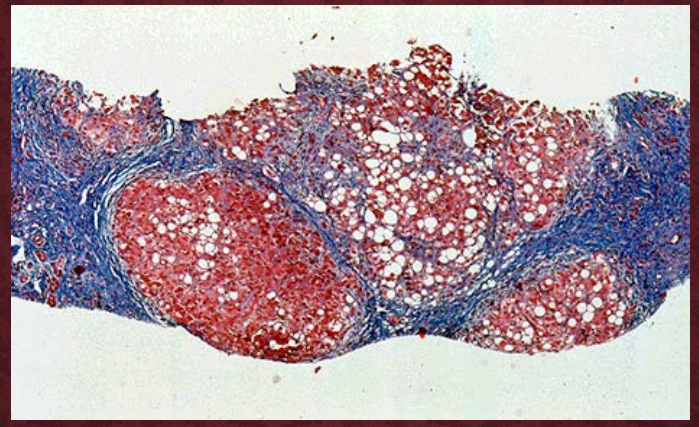
Liver Transplantation

- HCV is the most frequent indication
- 30% develop cirrhosis 5-7 yrs post-transplant

Death

- ~12,000 deaths per year (based on death certificate documentation)
- Likely an underrepresentation

HEPATITIS C: DISEASE PROGRESSION TO LIVER CIRRHOSIS AND CANCER



HCV infection

60%-85%

Chronic HCV

Cirrhosis

20%-50%

1-4%/yr

Liver Cancer

~ 20%

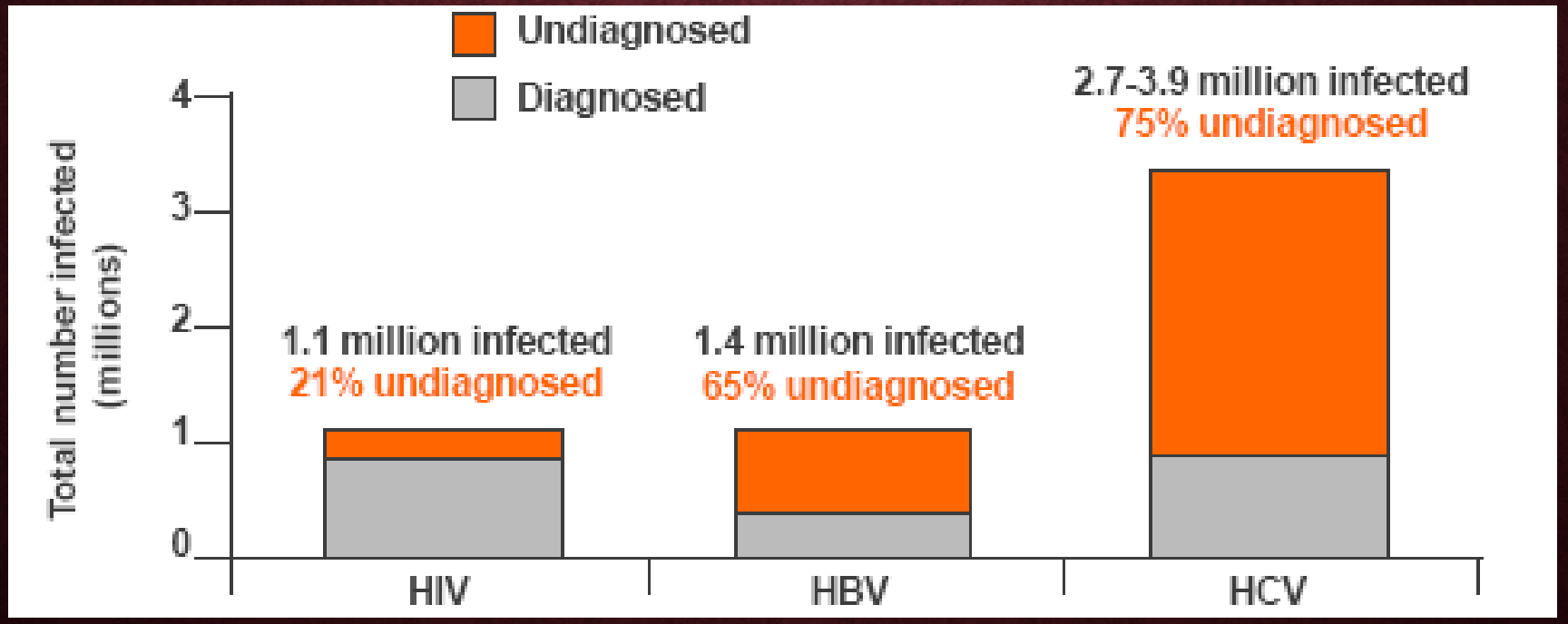
Liver Failure

Liver Transplant

Time: 20-30 years

IN THE US, PREVALENCE OF HCV HIGHER THAN HIV OR HBV

Number of infected individuals and
number aware they are infected (diagnosed)



Institute of Medicine. *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C.* Washington, DC: The National Academic Press; 2010

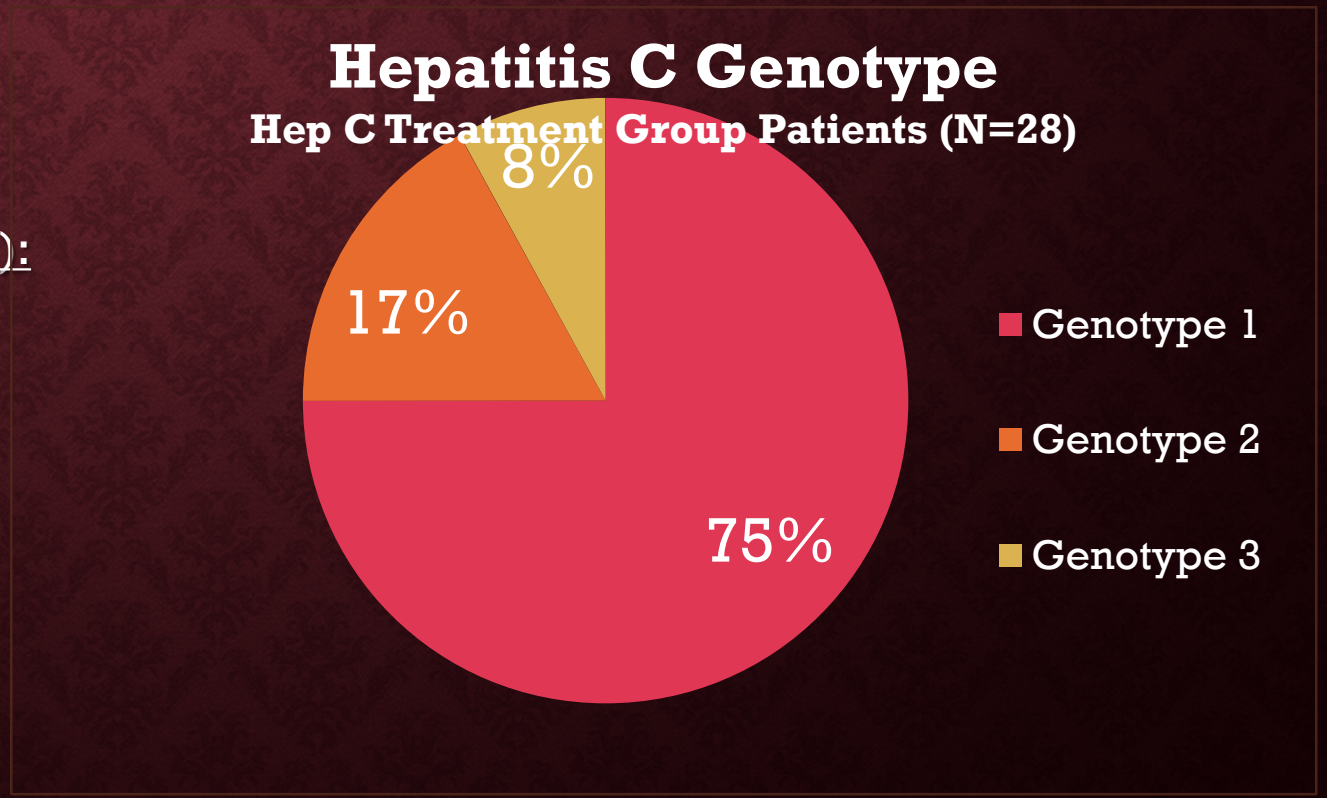
HEPATITS C IN NATIVE AMERICAN COMMUNITIES

In 2011, Sacramento Native American Health Center evaluated our Hepatitis C patient population:

- In the previous 2 years we had seen 285 patients with Hepatitis C
  - Native Patients: 86 (30.2%)
  - Non-Native Patients: 199 (69.2%)

<u>Hepatitis C Treatment Program Participants (2011):</u>

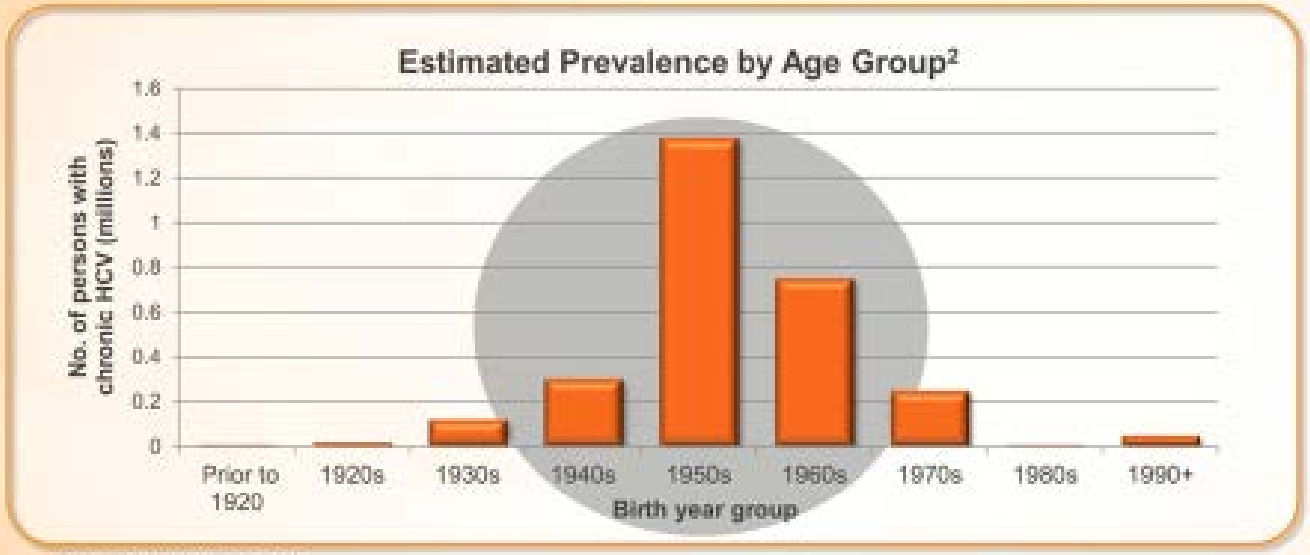
- Total Treatment Program Participants: 28
- Average age: 51.5 years
- Males: 60.7%
- Females: 39.3%
- Native Patients: 18%



WHO SHOULD BE SCREENED?

- Adults born between 1945-1965
- A history of recreational drug use
- A history of transfusion of blood or blood products prior to 1992
- Patients on hemodialysis.
- Patients with elevated aminotransferase enzymes (AST/ALT)
- Patients who are HIV positive
- Children born to an HCV positive mother (check HCV antibody after 6 months of age)
- Even for patients with none of the above risk factors, an annual anti-HCV test is recommended for all patients over the age of 18 that are being screened for other STDs or blood-borne infections.

Baby Boomers (DOB 1945-1965) are ¾ or 76% of Hepatitis C cases in US



Adapted from Pyenson et al.

- An estimated 33% of undiagnosed baby boomers with HCV currently have advanced fibrosis (F3-F4, bridging fibrosis to cirrhosis)[3,*]

*Millman report was commissioned by Vertex Pharmaceuticals.

1. Smith BD et al. Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2012;61:1-18. 2. Pyenson B et al. *Consequences of Hepatitis C Virus (HCV): Cost of a Baby Boomer Epidemic of Liver Disease.* New York, NY: Millman Inc; 2009. 3. McGarry LJ et al. *Hepatology.* 2012;55(5):1344-1355.

HEPATITIS C DIAGNOSIS AND WORKUP

Diagnosis of Hepatitis C

- Approximately 15-45% of people exposed to HCV will clear the virus and not progress to chronic infection. This population does not need treatment or further workup concerning Hepatitis C infection.
- The test of choice for diagnosis of HCV infection is HCV RNA by PCR.

HEPATITIS C DIAGNOSIS AND WORKUP

Evaluation of the HCV patient

Once active infection has been determined by PCR, the following tests are recommended to be drawn or performed:

- HCV RNA by PCR (if not previously performed)
- HCV Genotype
- Comprehensive Metabolic Panel (CMP)
- CBC with differential
- Hepatitis A & B surface antibody (to test for previous exposure to Hep A and Hep B Viruses)
- HIV screening
- Abdominal Ultrasound with specific attention to the spleen, common bile duct, and liver

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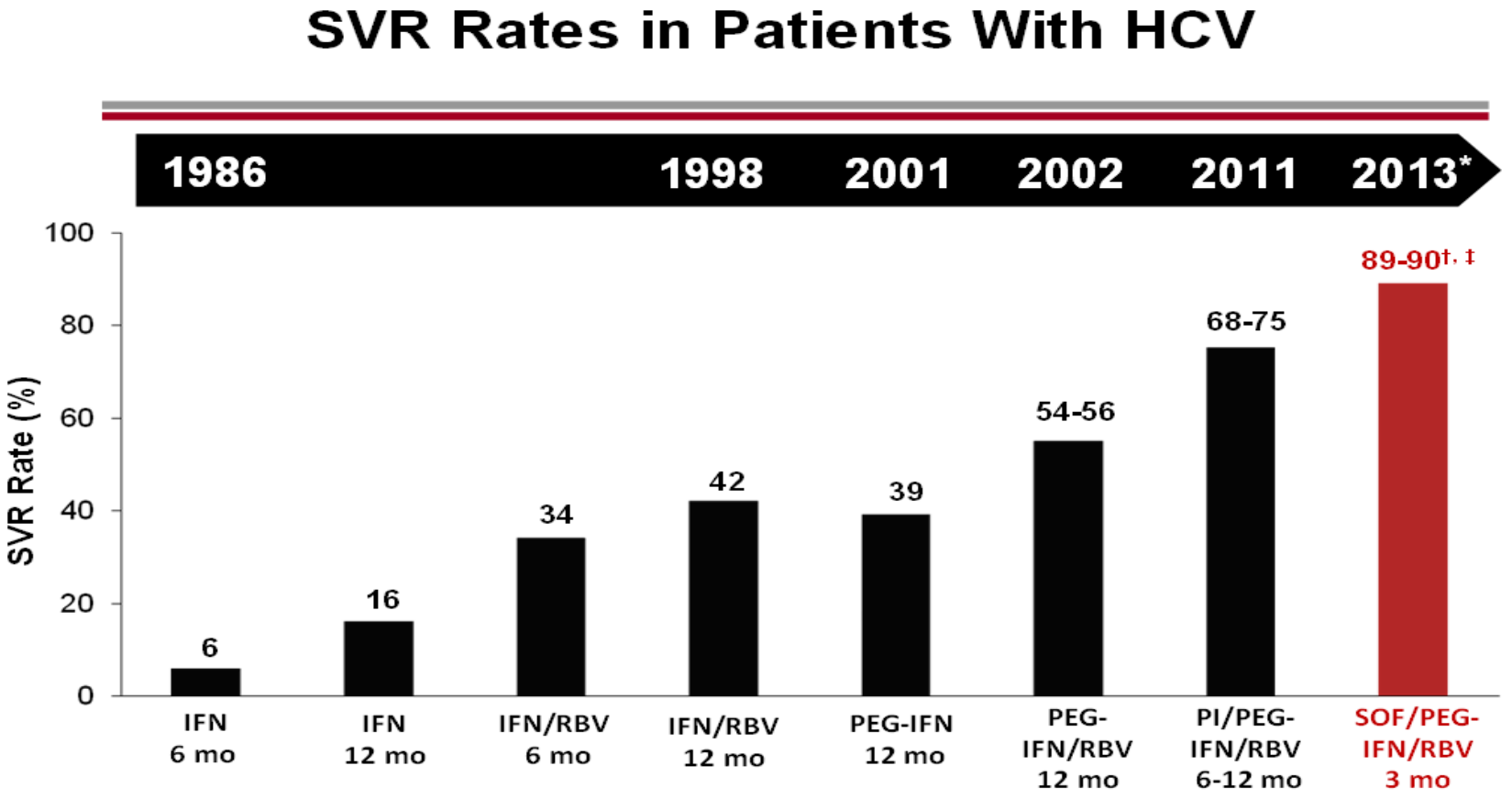
SHOULD I RECOMMEND THAT MY PATIENT PURSUE TREATMENT FOR HEPATITIS C?

- Not everyone is a good candidate for immediate treatment.
- Not everyone needs to be immediately referred to a specialist.
- Patient education is key.

Considerations

- Compensated Cirrhosis
- Patients with signs of liver decompensation such as: ascites, persistent jaundice, wasting, hepatic encephalopathy, or variceal bleeding.
- Active alcohol use or IV drug use
- Bone marrow suppression, marked anemia, thalassemia major, or sickle cell anemia
- Autoimmune Hepatitis
- Comorbid conditions that markedly limit life expectancy
- Patients with prior treatment failure or relapse
- Co-infection with HIV

HEPATITIS C TREATMENT IS RAPIDLY EVOLVING AND IMPROVING



*Year of publication of Phase 2 ATOMIC and Phase 3 NEUTRINO: Kowdley KV, et al. *Lancet*. 2013 Mar 14 [Epub ahead print]. Lawitz E, et al. *N Engl J Med*. 2013 Apr 23 [Epub ahead of print].
†SVR12 rate of 90% among patients in Group A (GT 1) in the Phase 2 ATOMIC trial (12 weeks of SOF+PEG-IFN+RBV)
‡SVR12 rate of 89% among GT 1 patients in the Phase 3 NEUTRINO trial (12 weeks of SOF+PEG-IFN+RBV)
Adapted from Strader DB, et al. Hepatology 2004;39:1147-71. INCIVEK [PI]. Cambridge, MA: Vertex Pharmaceuticals; 2012. VICTRELIS [PI]. Whitehouse Station, NJ: Merck & Co; 2011.

SOFOSBUVIR 2014: FDA APPROVED INDICATIONS

HCV and HCV/HIV Co-Infected	Treatment	Duration
Genotypes 1, 4	Sofosbuvir + Peginterferon + Ribavirin	12 weeks
Genotype 2	Sofosbuvir + Ribavirin	12 weeks
Genotype 3	Sofosbuvir + Ribavirin	24 weeks

CURRENT STATUS OF HCV THERAPY

- **Genotype 1**
  - New standard of care is 90% SVR
  - Shorter duration: 12 weeks (Sofo+PR)
  - Potential for single pill a day regimen
    - Sofosbuvir+Ledipasvir
    - 95% SVR
    - Filed with FDA in Feburary 2014

CURRENT STATUS OF HCV THERAPY

- **Genotype 2**
  - Short and simple
  - Sofosbuvir 400mg qd with food + Weight based Ribavirin BID
  - 12 weeks for everybody
  - Monitoring: Pregnancy, Anemia, Viral Load
    - At 4 weeks
  - Fibroscan to decide cancer screening

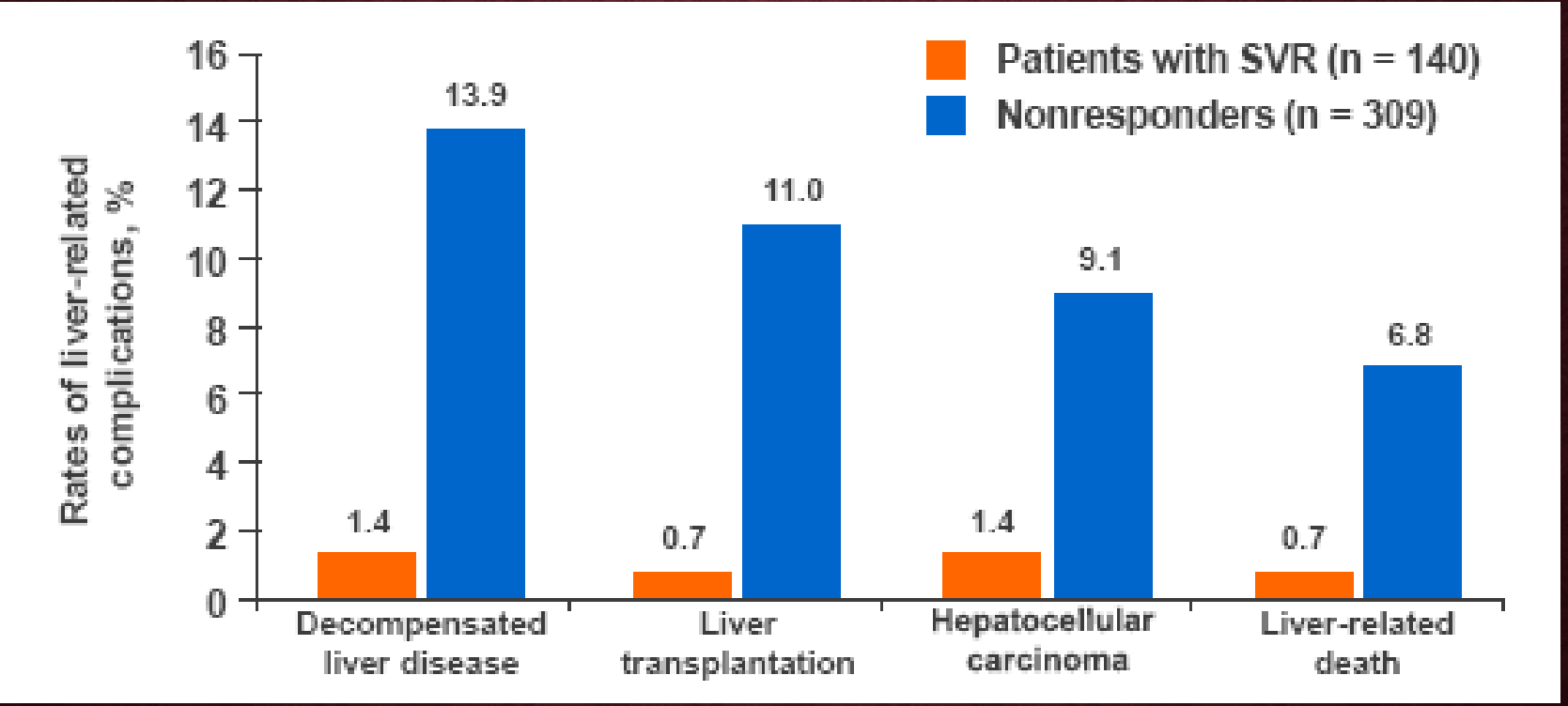
CURRENT STATUS OF HCV THERAPY

- **Genotype 3**
  - Sofosbuvir 400mg PO Daily with food + Weight Based Ribavirin BID
  - 24 weeks
  - 12 weeks with Peg+Ribavirin for Cirrhostics with previous failure on PR
  - Monitoring: Pregnancy, Anemia, Viral Load
    - At 4 weeks
  - Fibroscan to decide cancer screening

FUTURE OF HCV THERAPY

- **Genotype 1**
  - Standard of care will be >95% SVR
  - Without Interferon and without Ribavirin
  - At least 2 direct antiviral agents (DAA)

CURE IMPROVES OUTCOMES IN PATIENTS WITH HCV-ASSOCIATED ADVANCED FIBROSIS



In the HALT-C trial, achieving SVR significantly reduced HCV-associated complications and mortality

• Median follow-up 96 months for patients with SVR, 79 months for nonresponders

Morgan TR, et al. *Hepatology.* 2010;52(3):833-844.

TREATMENT EXPERIENCES AT SAC NATIVE HEALTH/CASE PRESENTATIONS

WHERE CAN I START?

- Implement screening guidelines.
- Start a Hepatitis C support group
  - find community partners to work with
  - utilize patient volunteers
- There are teleconferences/training available through IHS
  - Project ECHO
- Work with your local pharmaceutical representative
- Moving Mountains – Sacramento Area

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QUESTIONS?

- Joshua Opperman, Sacramento Native Health Center
  - joshuao@snahc.org
- Brigg Reilley – IHS National Program, HIV/AIDS
  - Brigg.reilley@ihs.gov
- AASLD/IDSA HCV guidelines:
  - http://hcvguidelines.org
- Project ECHO [medical consultation, training and no cost CME]:
  - http://echo.unm.edu/

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