Hepatitis C Management for The Primary Care Provider

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Objective

Understand	Understand the epidemiology of HCV in the United States
Describe	Describe the different steps in HCV evaluation
Describe	Describe treatment options for HCV

Outline

- **Case presentation**
- HCV epidemiology overview
- HCV evaluation and treatment
- Conclusions

Mr. S: HPI

- **Mr. S** is a 24 yo AI/AN male who suffered a right femur fracture (MVA) **6 years ago** and was placed on OxyContin for pain control.
- **Two years ago** his new medical provider refused to refill the OxyContin, he then turned to his friends who gave him some, but later had to purchase them in the streets and started injecting it.
- **One year ago he started injecting heroin** since it was cheaper. He has been sharing needles and syringes since the pharmacy will not sell them to him.
- **Three days ago** he presented to the ED with opioid withdrawal symptoms (Nausea, vomiting, diarrhea, restlessness, abdominal pain). The ED medical provider induced him with Buprenorphine/Naloxone and gave him a 4-day prescription, enough until he could be evaluated and placed on MAT. During the ED visit an HCV test was positive, his HIV was negative.

MAT: Medication Assisted Treatment, ED: Emergency Department, Bup/Nal: Buprenorphine/Naltrexone, AI/AN: American Indian/Alaskan Native

Mr. S “continued”

- **PE:**
  - Vital signs are normal, BMI 26. Except for track marks in his arms the physical exam is unremarkable.

- **Labs**
  - RNA Viral load positive, 7.8 million copies /mL, Genotype pending.
  - **ALT 72 IU/L, AST 65 IU/L**, Creatinine 0.9 mg/dL, GFR 69 ml/min, Hg 13.4 g/dL,   **Platelets 288 x 10^3/mcL**, Albumin 4.5 g/dL, Total Bilirubin 0.7 mg/dL, INR 1.0.
  - **HepA Ab (-), HBsAg (-), HBsAb (-), HBcAb (-)**

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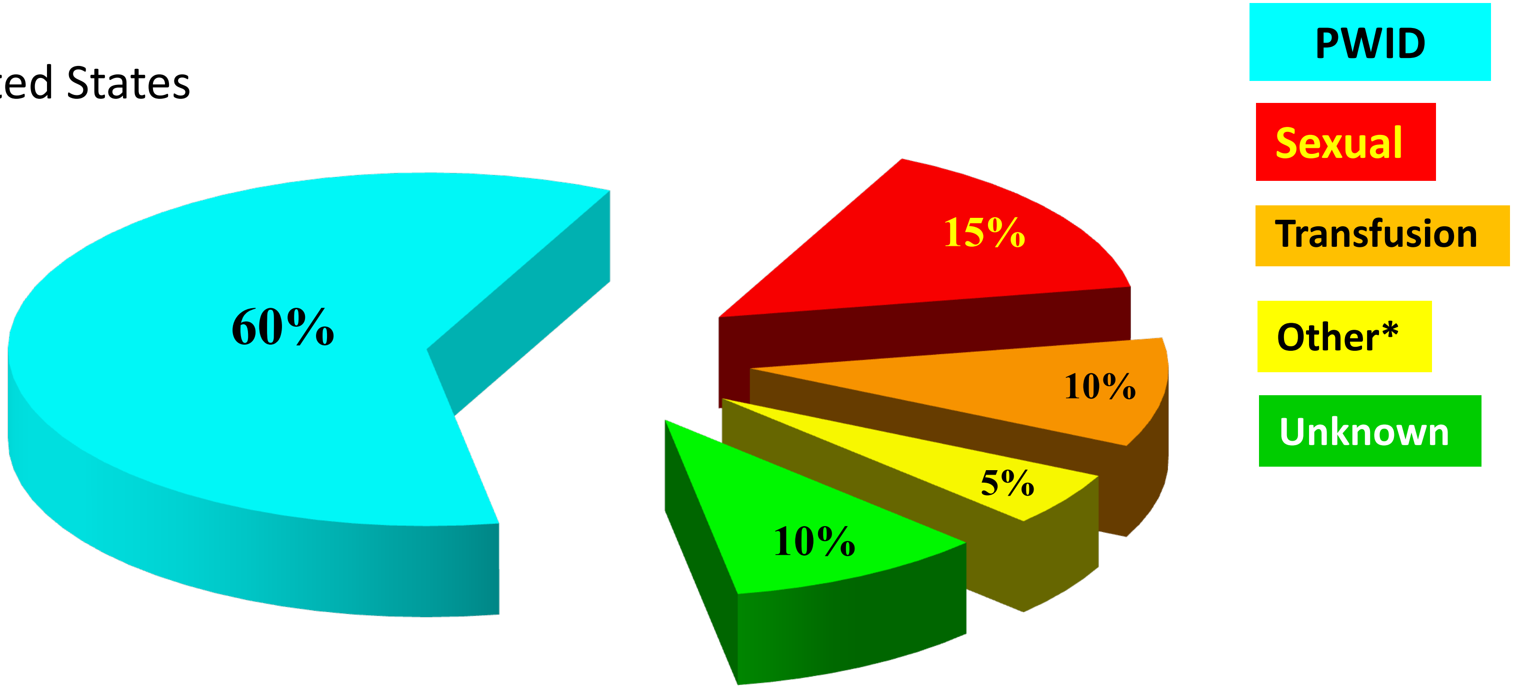
HCV: Transmission

- **Blood**
  - IVDU is the leading cause in the United States
    - Snorting
  - Percutaneous injuries
  - Dental
  - Tattooing
  - Blood transfusion (Before 1992)
- **Sexual contact**
  - Rare in heterosexual
  - More frequent in HIV + MSM
- **Mother-to-child**
  - The rate is 1.7% - 4.3 %
  - *Increased in IVDU, HIV co-infection, VL (?)*



*Nosocomial; Health-care work; Perinatal

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance—United States, 2016. Atlanta: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2018. Available at: https://www.cdc.gov/hepatitis/statistics/2016surveillance/index.htm.

HCV and Injection Drug Use

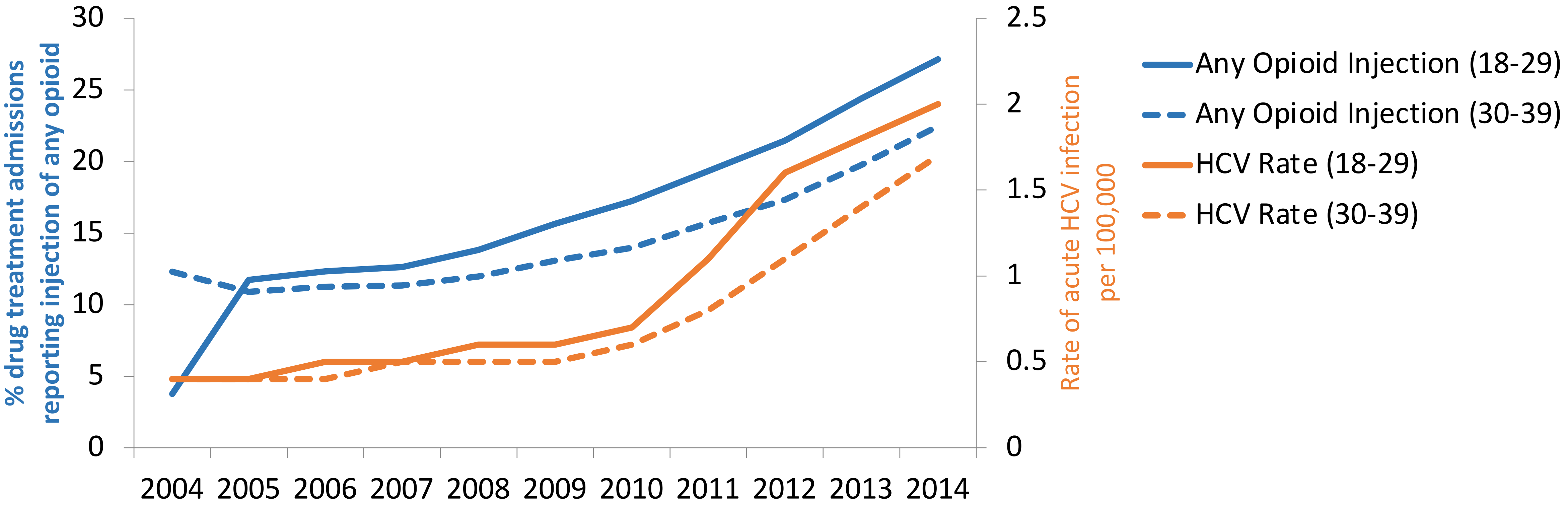
Today > 80% of HCV Transmission Occurs in PWID

Paraphernalia

Needle
Syringe
Cooker
Table
Tourniquet

Palmateer N, Hutchinson S, McAllister G et al. Risk of transmission associated with sharing drug injecting paraphernalia: analysis of recent hepatitis C virus (HCV) infection using cross-sectional survey data. J Viral Hepatol 2014 Jan;21(1):25-32

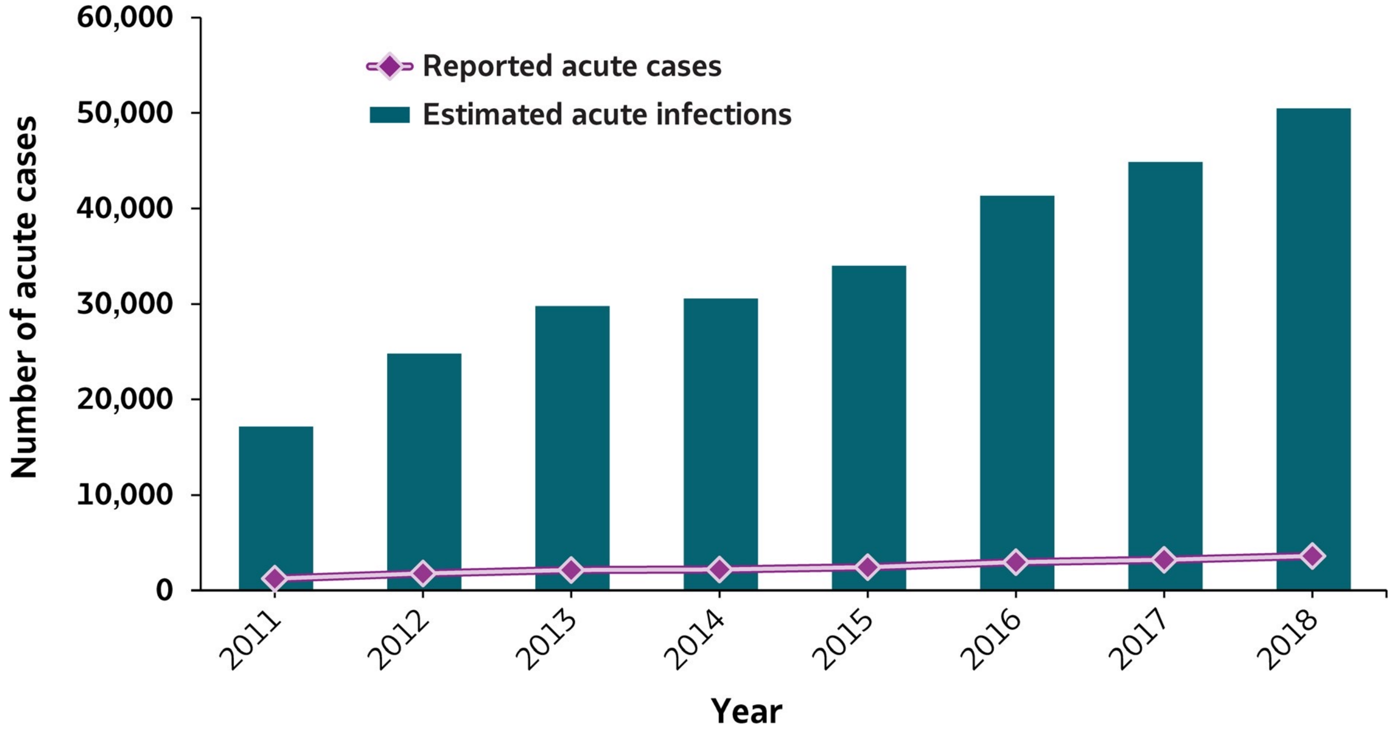
Rates of HCV Infections are Rising Among Younger PWIDs



- Among people aged 18-29, HCV increased by 400% and admission for opioid injection by 622%[1]
- Among people aged 30-39, HCV increased by 325% and admission for opioid injection by 83%[1]
- HCV seroprevalence among PWIDs is ~55% in North America[2]

1. Zibbell JE, et al. *Am J Public Health.* 2018 Feb;108(2):175-181;
2. Degenhardt L, et al. *Lancet Glob Health* 2017;5:e1192-e1207.

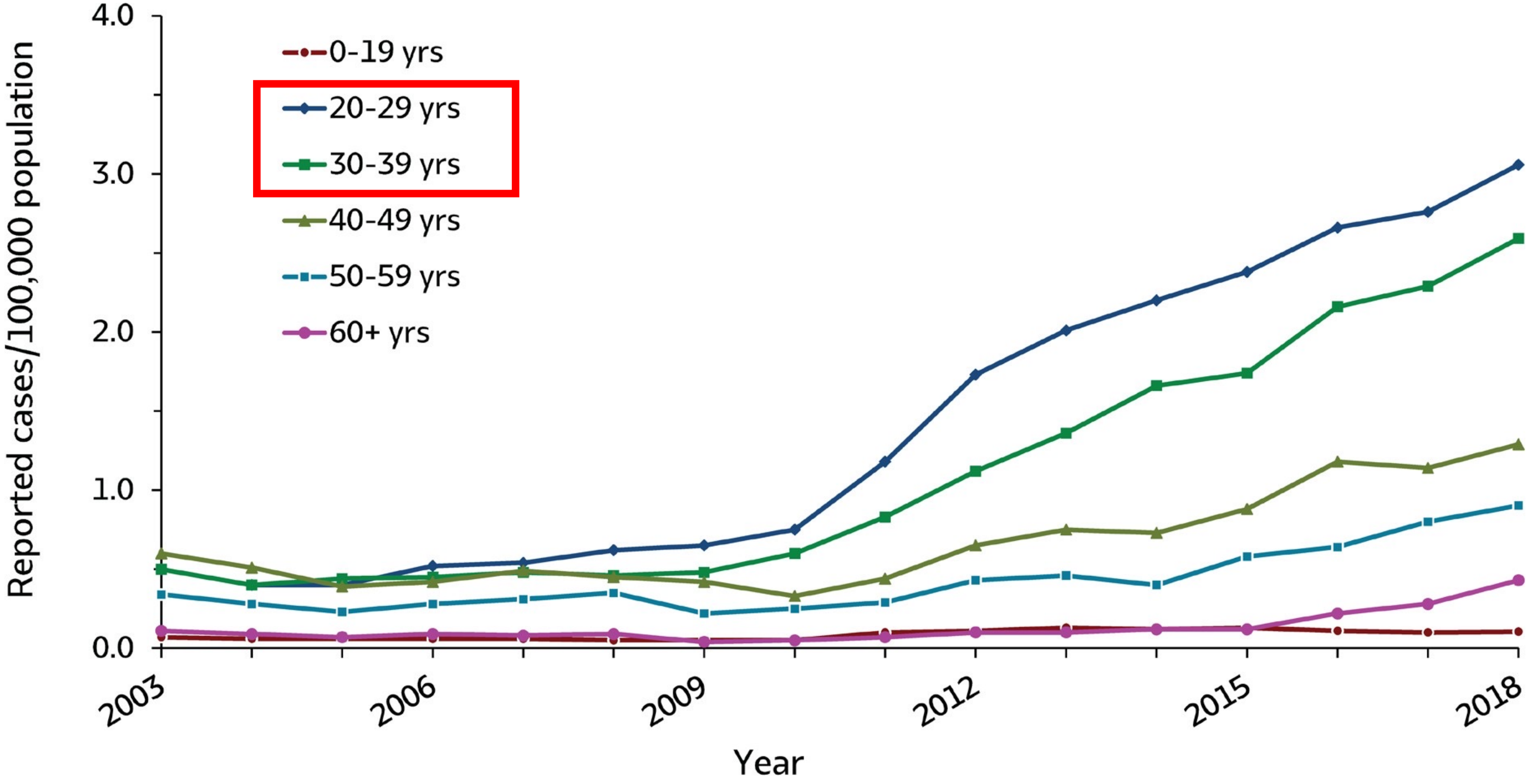
Figure 3.1. Number of reported acute hepatitis C cases and estimated infections* — United States, 2011–2018



Source: CDC, National Notifiable Diseases Surveillance System.

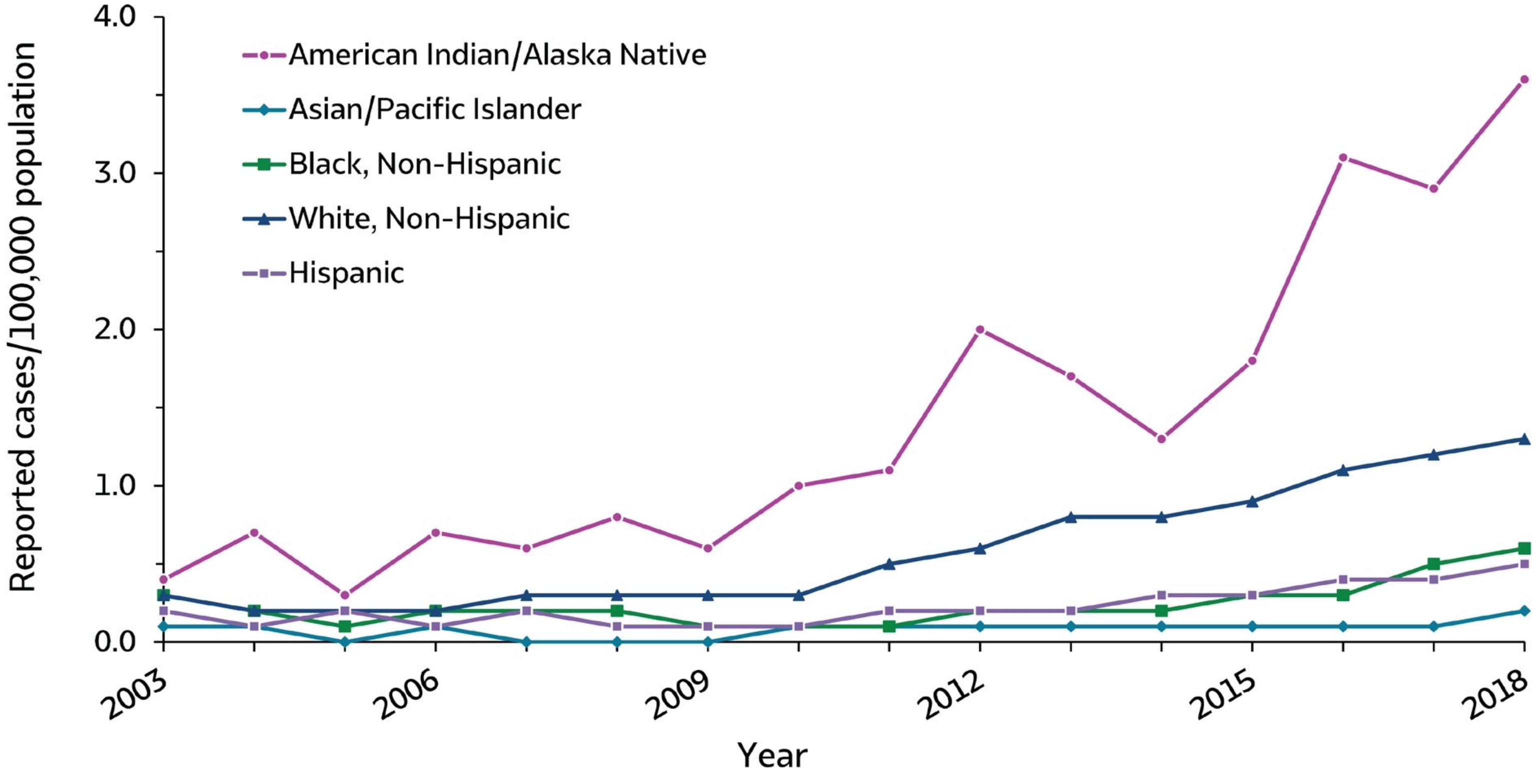
* The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases by a factor that adjusted for under-ascertainment and under-reporting[7]. The 95% bootstrap confidence intervals for the estimated number of infections are shown in the Appendix.

Figure 3.4. Rates of reported acute hepatitis C, by age group — United States, 2003–2018



Source: CDC,National Notifiable Diseases Surveillance System.

Figure 3.6. Rates of reported acute hepatitis C, by race/ethnicity — United States, 2003–2018



Source: CDC,National Notifiable Diseases Surveillance System.

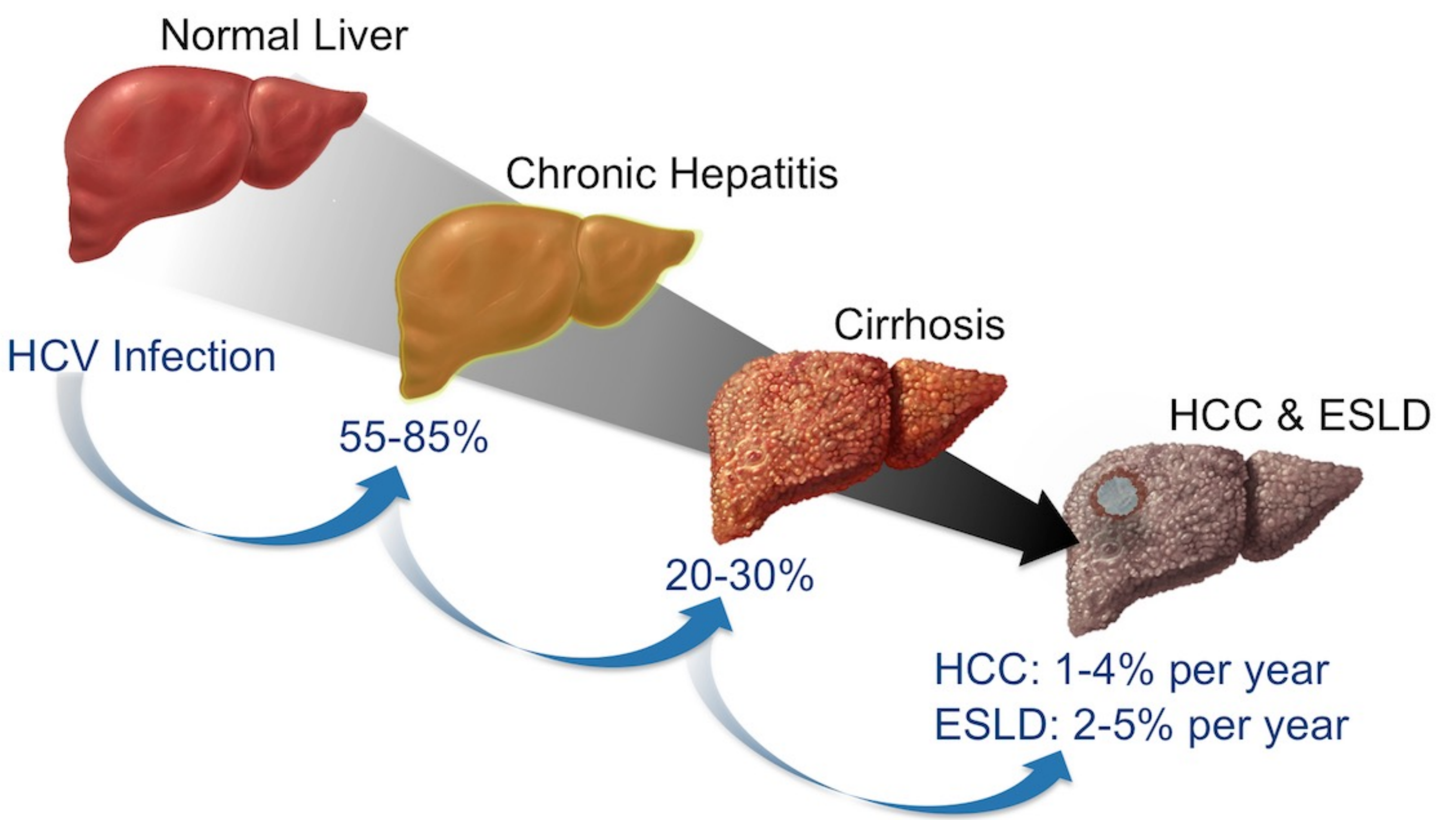
CDC is augmenting previous guidance with two new recommendations:

1) Hepatitis C screening at least once in a lifetime for all adults aged ≥18 years, except in settings where the prevalence of HCV infection is <0.1% and
2) Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection is <0.1%.
3) The recommendation for HCV testing that remains unchanged is regardless of age or setting prevalence, all persons with risk factors should be tested for hepatitis C, with periodic testing while risk factors persist.
4) Any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many persons might be reluctant to disclose stigmatizing risks.

SOURCES: CDC Recommendations for Hepatitis C Screening, MMWR, April 2020
CDC Vital Signs, April 2020

Schillie S, Wester C, Osborne M, Wesolowski L, et al. MMWR Recomm Rep 2020;69(No. RR-2):1–17.

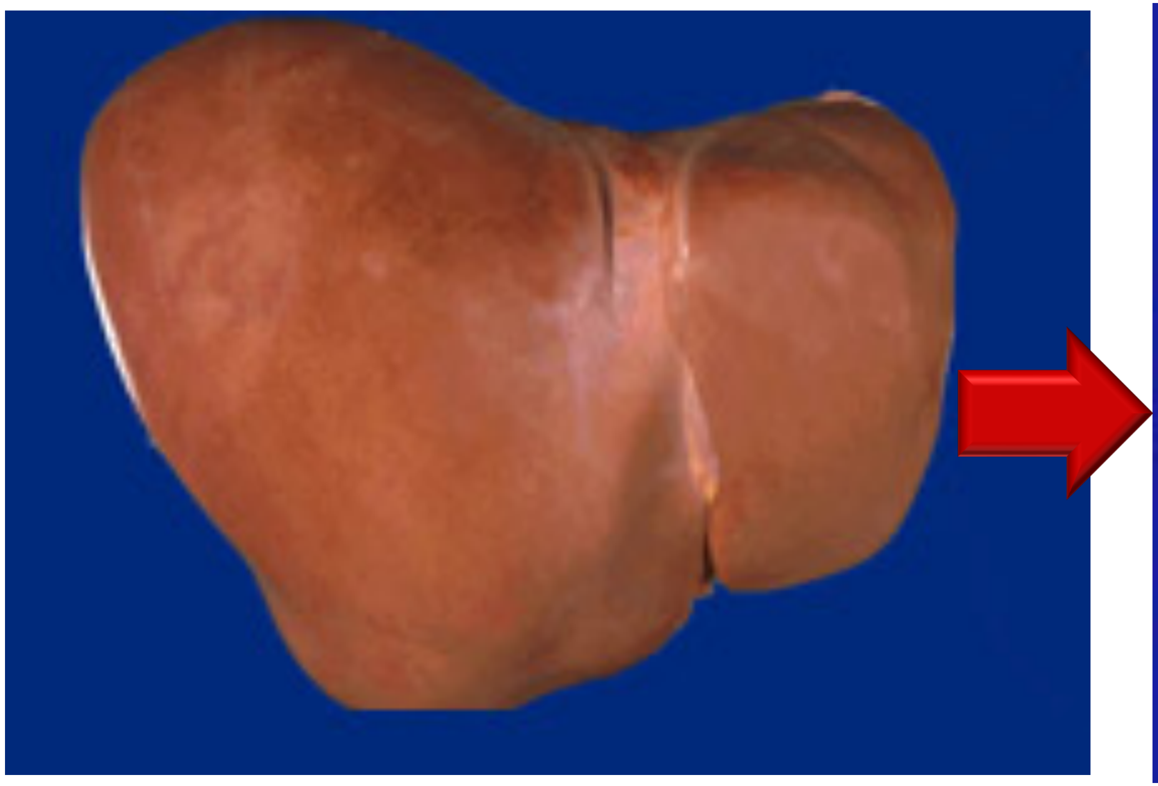
Natural History Following Initial Infection with HCV

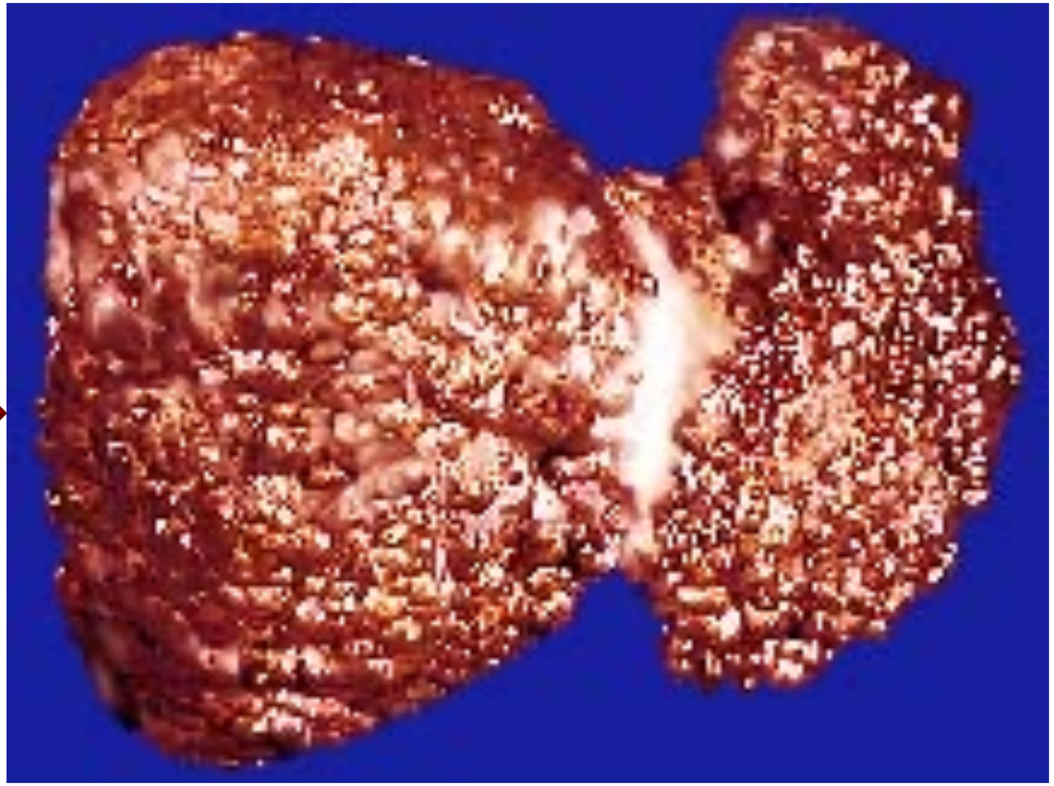


Abbreviations: ESLD = end-stage liver disease HCC = hepatocellular carcinomaSource: Lingala S, Ghany MG. Natural History of Hepatitis C. Gastroenterol Clin North Am. 2015;44:717-34.

What Does HCV Treatment Accomplish?

- SVR (cure) of HCV is associated with:
  - 70% Reduction of Liver Cancer
  - 50% Reduction in All-cause Mortality
  - 90% Reduction in Liver Failure





- Lok A. NEJM 2012; Ghany M. Hepatol 2009; Van der Meer AJ. JAMA 2012

Outline

- Case presentation
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- **HCV evaluation and treatment**
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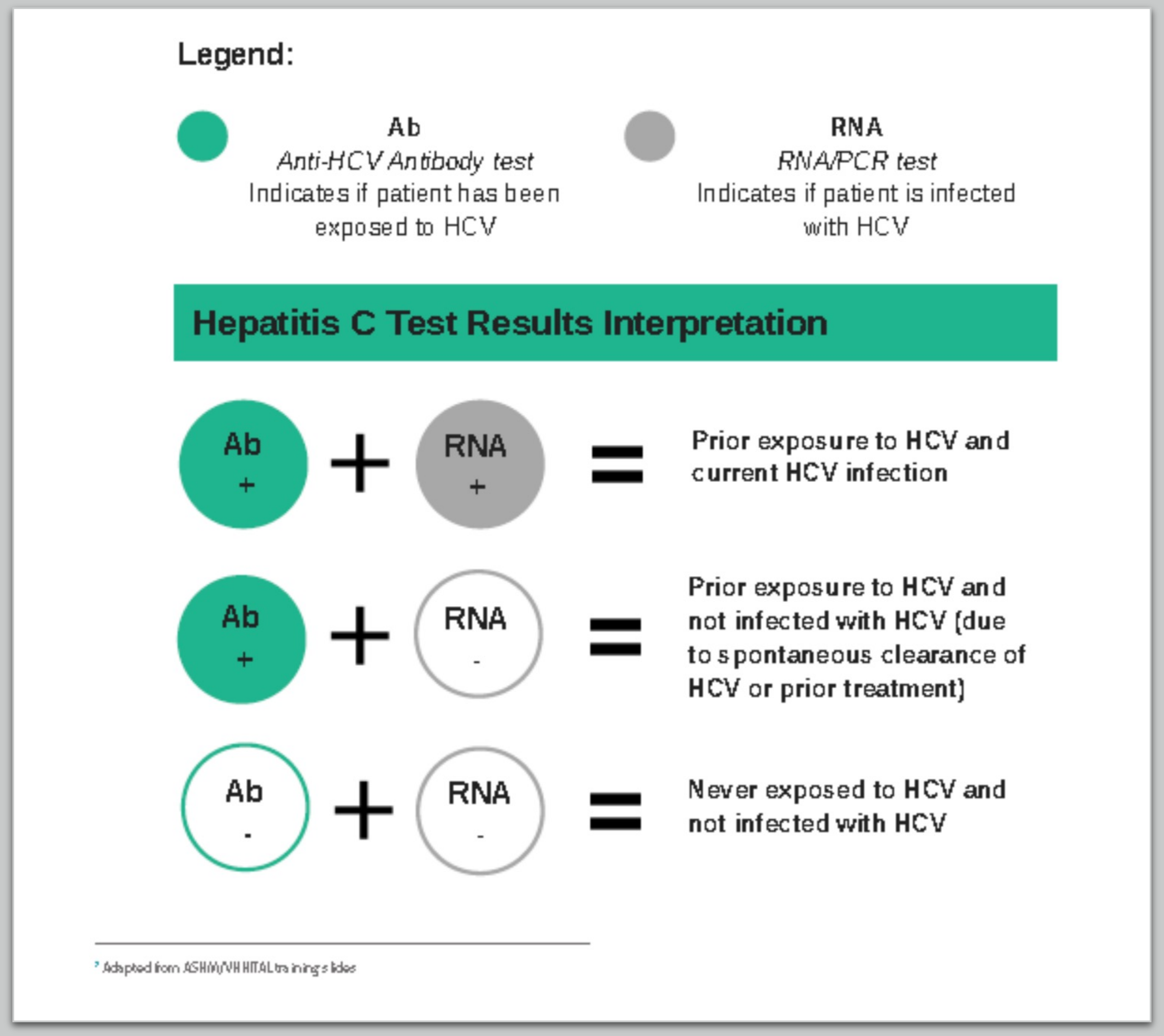
HCV Workflow

- Confirm Diagnosis
- Lab/Imaging workup
- Fibrosis Staging
- Critical Information
- Treatment
  - Cure
  - Surveillance

Confirm the Diagnosis



Laboratory Workup

- HCV Quant (Viral Load) and Genotype
- HAV IgG or total Ab
- HBsAb/HBsAg/HBcAb (not the same as a typical hepatitis panel)
- HIV screen
- CBC, Comprehensive Metabolic Panel, Urinary Drug Screen
- Alpha fetoprotein (AFP) and PT/INR (if advanced liver fibrosis)
- Fibrotest/Fibrosure if fibrosis stage is unclear

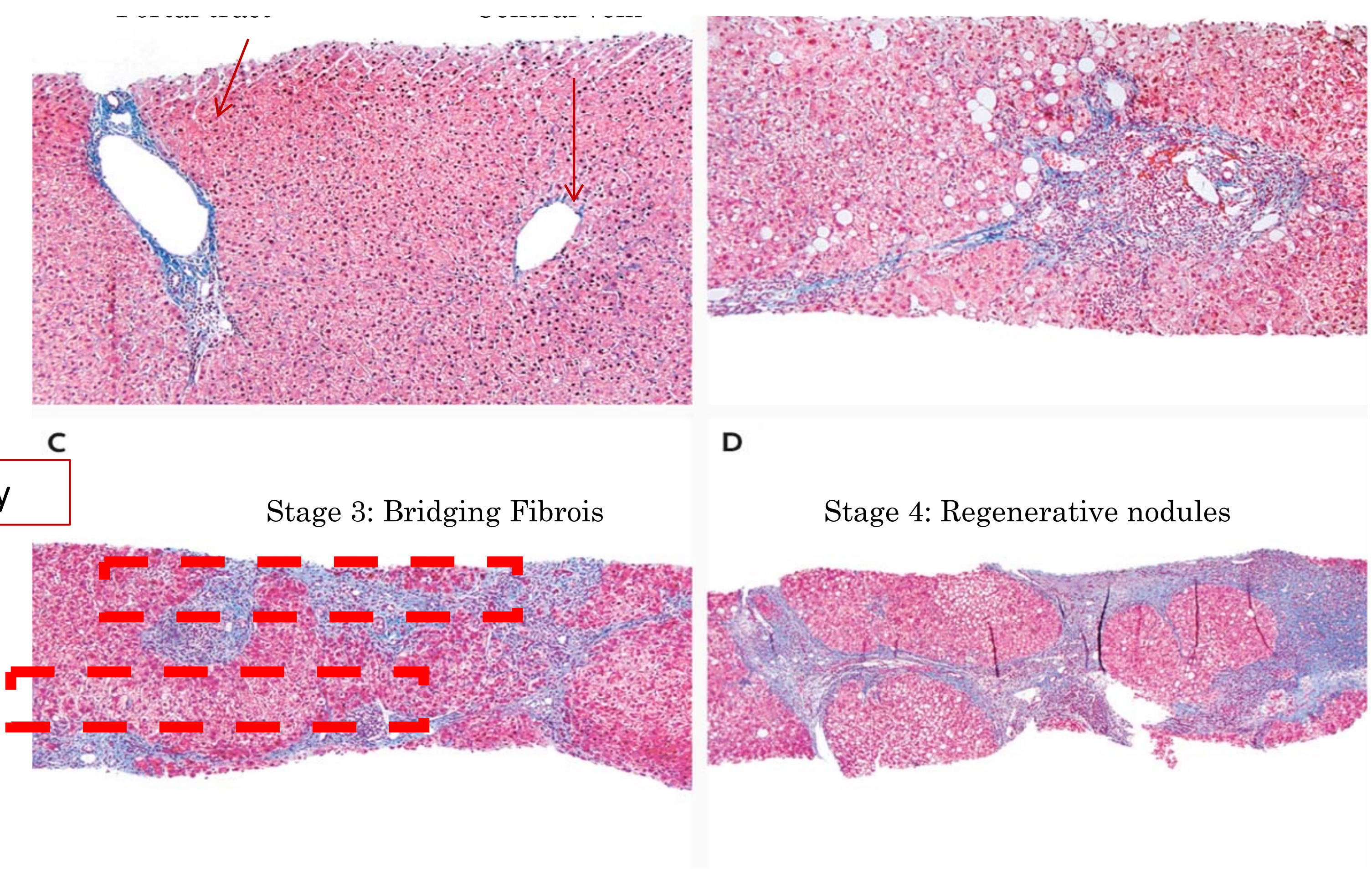
Other optional tests for completeness:
Iron profile (Fe, TIBC, Ferritin)
25 OH Vitamin D

Liver Fibrosis Staging

- F0: No fibrosis
- F1 Scattered portal fibrosis
- F2. Diffuse periportal fibrosis
- F3 Bridging fibrosis
- **F4 Cirrhosis**
    - Compensated
    - Decompensated
        - History or presence of ascites
        - Hx of esophageal bleeding due to esophageal varices
        - Hx or presence of hepatic encephalopathy
        - Jaundice

Liver Fibrosis Staging: Biopsy

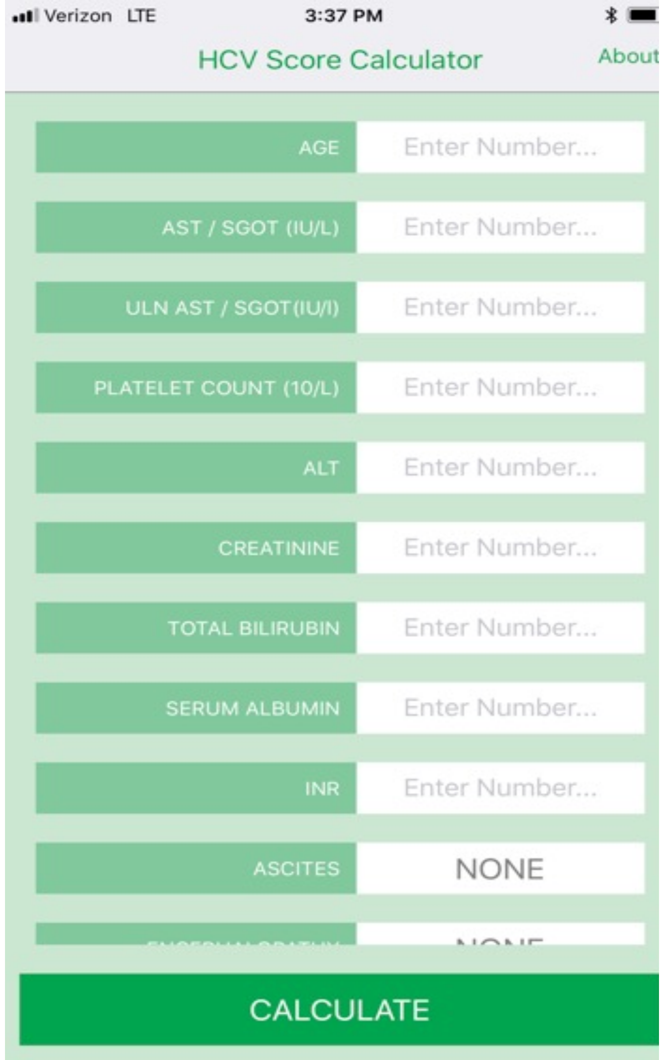
Liver Biopsy



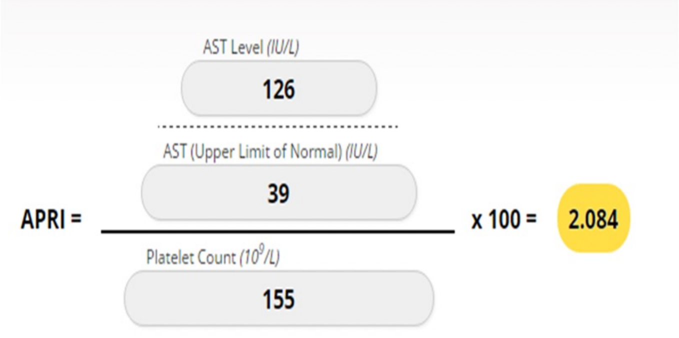
The NEW ENGLAND JOURNAL of MEDICINE

Rosen HR. N Engl J Med 2011;364:2429-2438

Non-Invasive Liver Fibrosis Staging in the Office

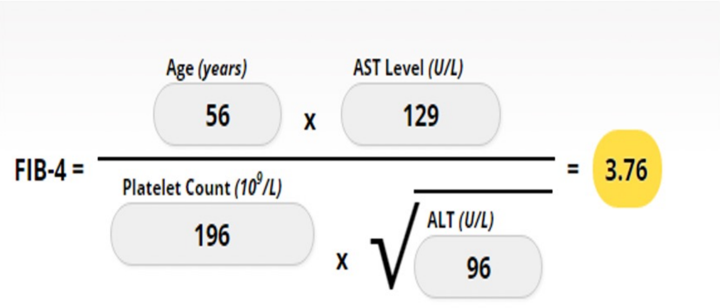


APRI: AST to Platelet Ratio Index



An APRI score greater than 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. APRI score greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

FIB–4 Index

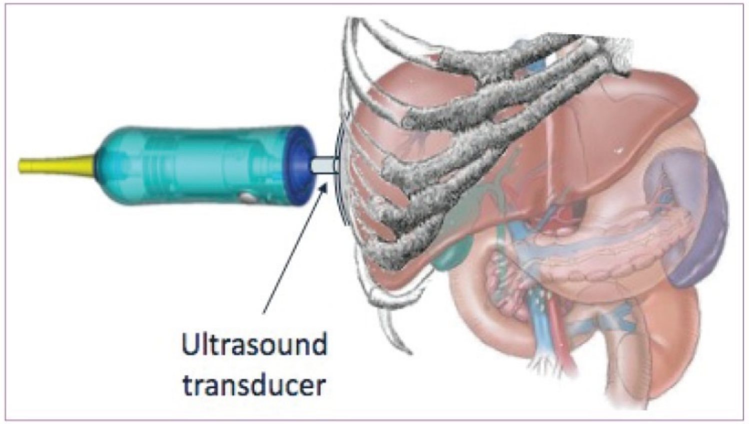


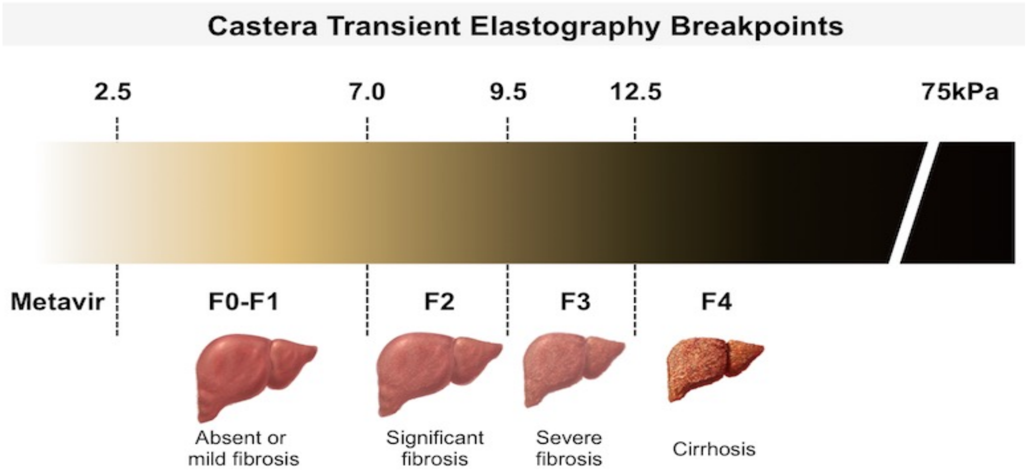
A FIB-4 score <1.45 has a negative predictive value of 90% for advanced fibrosis A FIB-4 >3.25 has a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Fibrotest/Fibrosure

Lin ZH, Xin YN, Dong QJ, et al. Hepatology. 2011;53:726-36 Sterling RK, Lissen E, Clumeck N, et. al. Hepatology 2006;43:1317-1325 University of Washington: Hepatitis C Online www.hepatitisc.uw.edu/

Liver Fibrosis Staging by Imaging: Transient Elastography





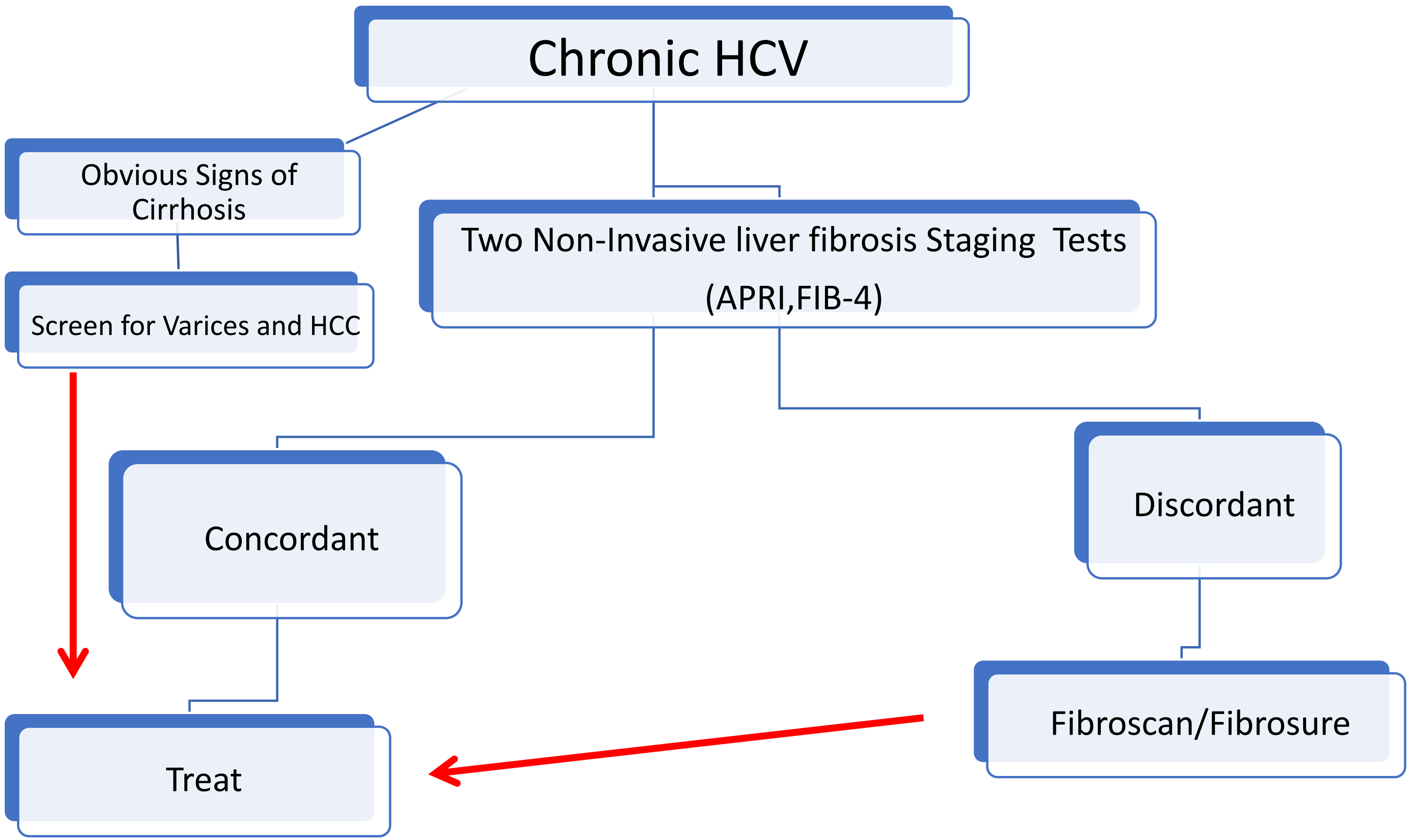
The probe of the Fibroscan device is positioned in an intercostal space near the right lobe of the liver, and a 50-MHz wave is passed into the liver from a small transducer on the end of the probe. The device then measures the velocity of the shear wave (in meters per second) as this wave passes through the liver, and this measurement is converted to a liver stiffness measurement.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3594956/

Fibrosis Staging Interpretation

<table>
<tr><th>Metavir</th><th>Biopsy</th><th>Fibroscan</th><th>Fibrosure</th><th>APRI</th><th>FIB-4</th></tr>
<tr><td>F4</td><td>F4</td><td>≥ 12.5 kPa</td><td>≥ 0.75</td><td rowspan="2">≥ 1.0</td><td rowspan="2">> 3.25</td></tr>
<tr><td>F3</td><td>F3</td><td>9.6 12.4 kPa</td><td>0.58 – 0.74</td></tr>
<tr><td>F2</td><td>F2</td><td>7.1-9.5 kPa</td><td>0.49 – 0.57</td><td rowspan="3">< 1.0</td><td>?</td></tr>
<tr><td>F1</td><td>F1</td><td rowspan="2">≤ 7.0 kPa</td><td>0.23 – 0.48</td><td rowspan="2">< 1.45</td></tr>
<tr><td>F0</td><td>F0</td><td>≤ 0.22</td></tr>
</table>

Fibrosis Staging Algorithm



HCC: Hepatocellular Carcinoma
Adapted from Boghal H, Sterling RK, Infect Dis Clin N Am 26 (2012) 839-847

Why is it Important to Stage Liver Fibrosis?

- Treatment will be different between those patients with decompensated and NOT decompensated cirrhosis
- All patients with liver fibrosis (F3 or F4) will need HCC surveillance
- All patients with liver fibrosis F4 will need screening for
  - Esophageal varices
  - Hepatic encephalopathy
- Patients with decompensated cirrhosis need to be referred to a liver transplant center

HCV Therapies – Direct Acting Antivirals (DAAs)

Medication	NS5B Inh	NS5A Inh	NS3/4A PI	Other
Epclusa®	sofos**buvir**	velpat**asvir**		
Mavyret®		pibrent**asvir**	glecap**revir**	

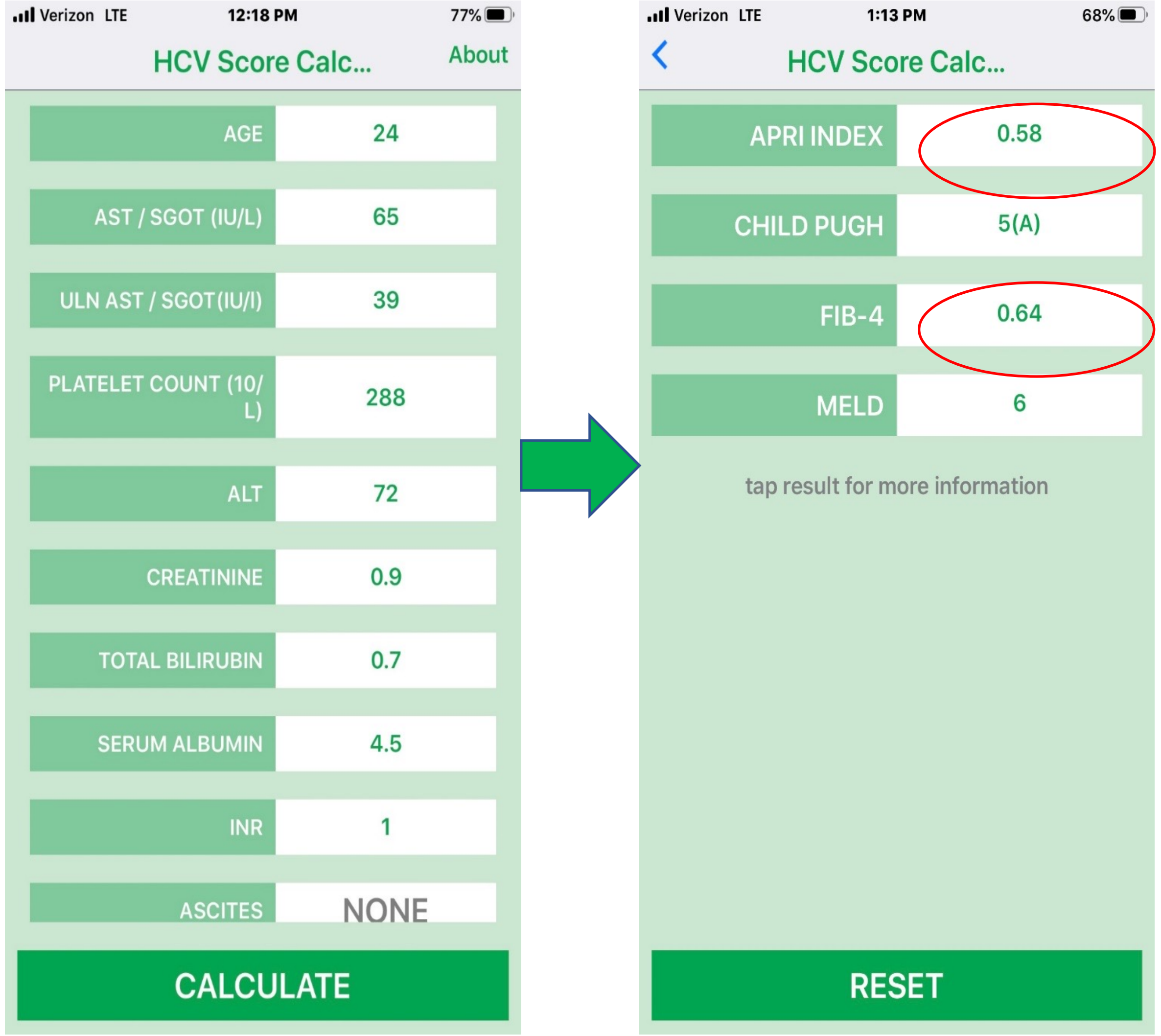
NS5B Inh – Nonstructural protein 5B Polymerase Nucleotide Analog Inhibitor
NS5A Inh – Nonstructural protein 5A Inhibitor
NS3 PI – Nonstructural protein 3/4A Protease Inhibitor

Mr. S “continued”

- **Labs**
  - RNA Viral load positive, 7.8 million copies /mL, Genotype 1a.
  - ALT 72 IU/L, AST 65 IU/, Creatinine 0.9 mg/dL, GFR 69 ml/min,
    Hg 13.4 g/dL, **Platelets 288 x 10^3/mcL**, Albumin 4.5 g/dL, Total Bilirubin 0.7 mg/dL, INR 1.0.
  - HepA Ab (-), **HBsAg (-), HBsAb (-), HBcAb (-)**

- **Questions:**
  - **As a primary care provider what can you do for this patient?**
  - **What is his liver fibrosis stage**
  - **How would you treat him**

What can you do for Mr. S?



- Vaccinate him for hepatitis A and B
- Continue buprenorphine/naltrexone
- Safe injection education
- Advocate for Syringe Service Programs
- FIB-4 is less than 1.45 and APRI is < 0.58 (concordant), low fibrosis score:
- Treatment options
  - Sofosbuvir/Velpatasvir x 12 wk
  - Glecaprevir/Pibrentasvir x 8 wk

HCV Evaluation and Treatment: Simplified Algorithm

ProjectECHO: Moving Knowledge Instead of Patients

Patient with Confirmed HCV (RNA +)

Initial Liver Fibrosis Assessment using Platelets and FIB-4

Platelets > 160K
and
FIB-4 < 1.45

↓

No Cirrhosis
Suitable for HCV Treatment in Primary Care

↓

Epclusa x12 weeks
Mavyret x 8 weeks

FIB-4 > 1.45

↓

Present in HCV ECHO or Refer to ID specialist or Hepatologist

Conclusions

- Primary care providers play a major role in:
  - Decreasing morbidity and mortality by treating HCV
  - Decreasing transmission by:
    - Having an MAT waver and prescribing buprenorphine/naloxone
    - Advocating for SSPs
- Planning and commitment can accelerate the process

Helpful Resources

http://www.npaihb.org

Text HCV 97779

http://www.hcvguidelines.org/

http://www.hepatitisc.uw.edu/

On-line curriculum on liver disease and HCV, includes clinical studies, clinical calculators, slide lectures

ECHO guidelines