Hepatitis C Treatment in the Primary Care Setting

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Matt Chan, MD
OHSU Department of Family Medicine

Disclosures

- Site PI for clinical trial CTN XR-0102 sponsored by NIDA and UCLA

Outline

- Epidemiology and screening strategies
- Management of new Hepatitis C cases
  - Recommended primary care workup
  - Supportive care, follow-up needs
- Treatment of Hepatitis C
- Case Studies

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Epidemiology and Screening Strategies

Number of reported cases* and estimated infections† of acute hepatitis C — United States, 2015–2022

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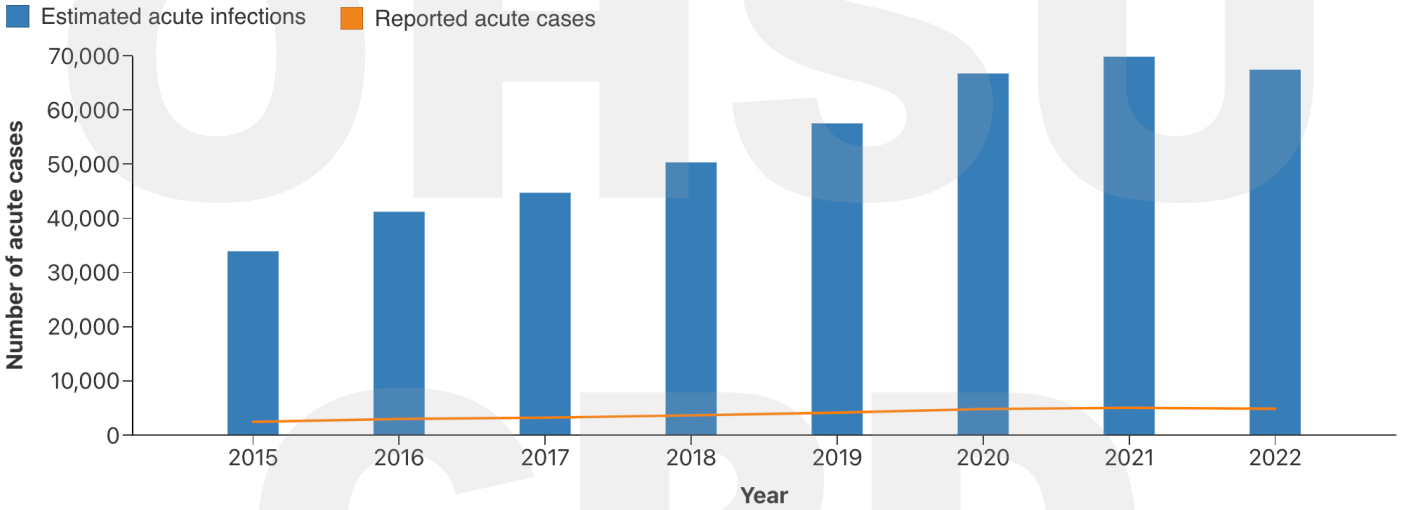
Number of reported cases* and esti...

Summary



Data Table

	2015	2016	2017	2018	2019	2020	2021	2022
Estimated acute infections	33,900	41,200	44,700	50,300	57,500	66,700	69,800	67,400
Reported acute cases	2,436	2,967	3,216	3,621	4,136	4,798	5,023	4,848

Source: CDC, National Notifiable Diseases Surveillance System.

Rates* of reported cases† of acute hepatitis C, by state or jurisdiction — United States, 2022

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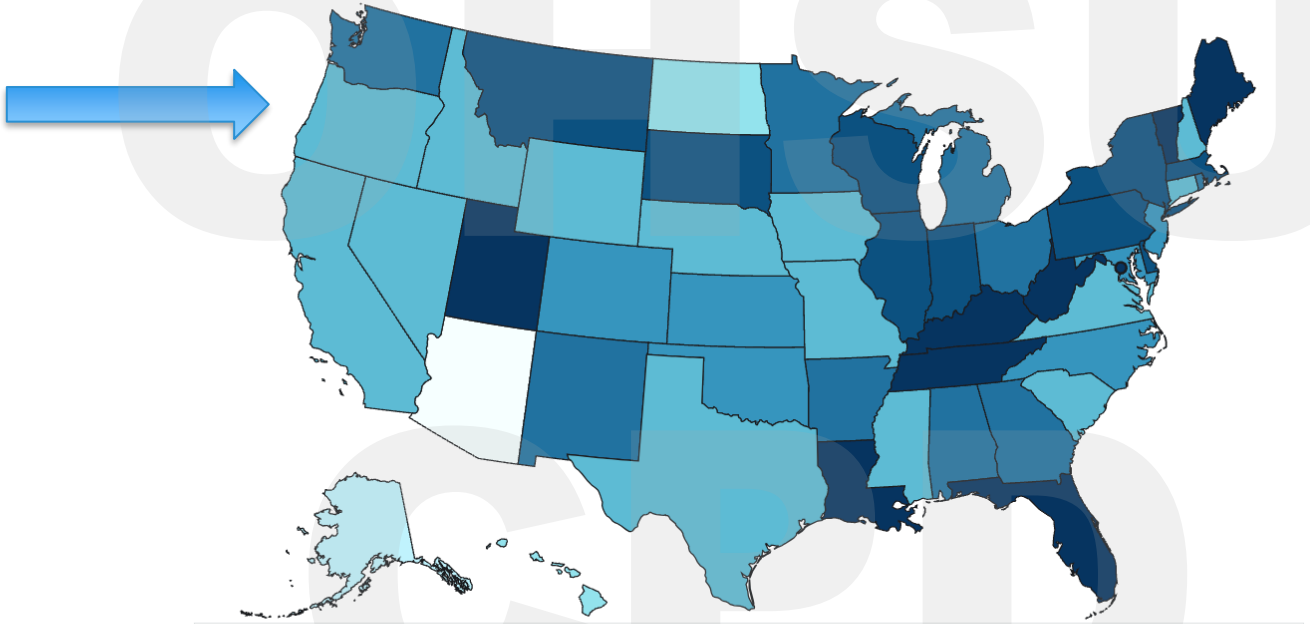

Case rates by sex

65%

During 2022, 65% of newly reported chronic hepatitis C cases occurred among men.

Highest rates of chronic hepatitis C

104.8

During 2022, the rate of newly reported chronic hepatitis C cases was highest among non-Hispanic AI/AN persons at 104.8 cases per 100,000 people.

Multiple generations are affected

Chronic hepatitis C affects multiple generations, with infections highest among two age groups: 25–45 and 55–70 years.

Number of newly reported* chronic hepatitis C cases† by sex and age — United States, 2022

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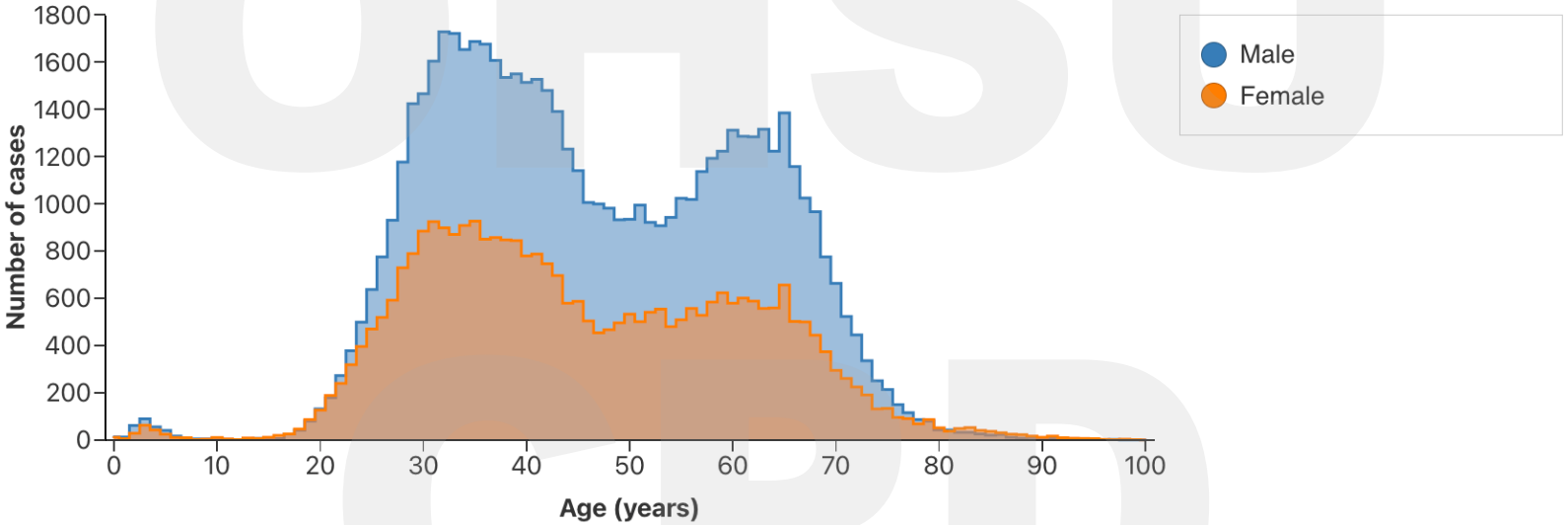
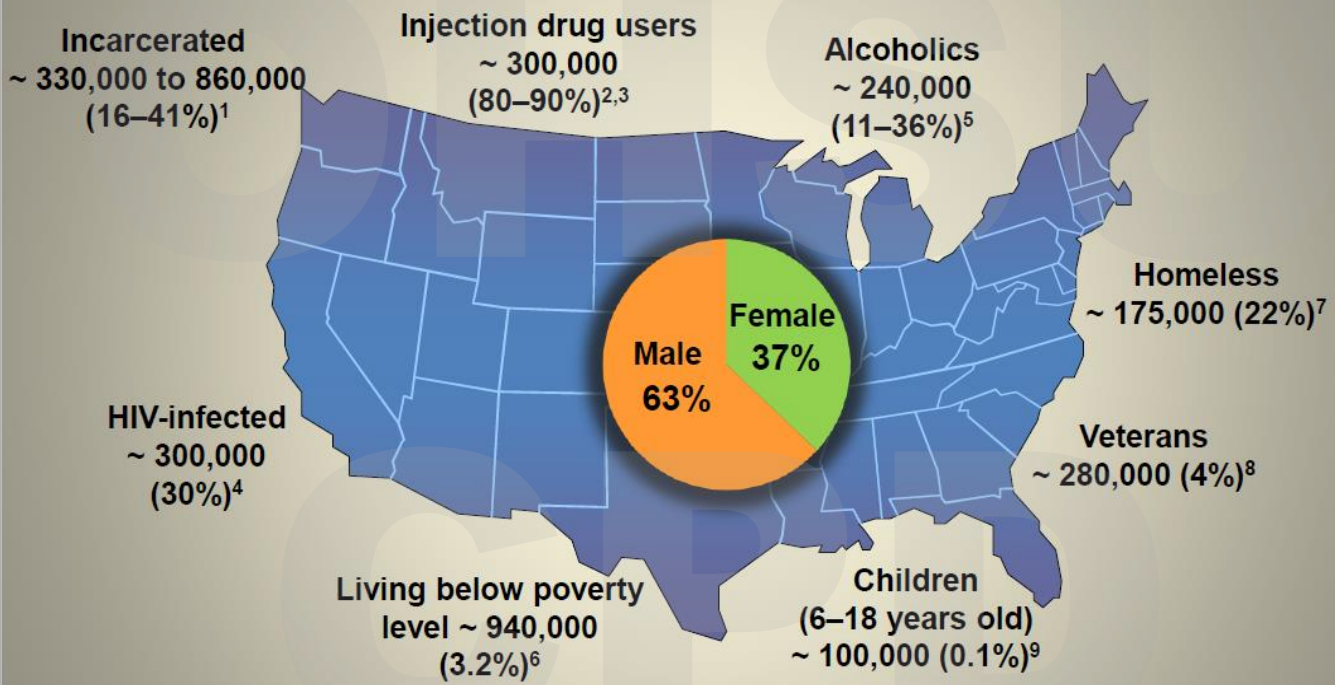


Data Table

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Male	13	12	61	89	55	40	16	3	4	4	8	2	1	2	6	5	6	25	41	80
Female	11	5	28	62	42	24	10	9	1	3	10	4	1	8	6	11	19	25	46	86

Prevalence of HCV in Select Populations



Adapted from: 1. CDC. *MMWR*. 2003;52(RR-1):1-33; 2. Edlin B. *Hepatol*. 2002;36(5 suppl 1):S210-S219; 3. NHSDA Report 2003; 4. Poles M, et al. *Clin Infect Dis*. 2000;31:154-161; 5. LaBrecque D, et al. *Hepatitis C Choices*. 2002:7-15; 6. Alter M, et al. *N Engl J Med*. 1999;341:556-562; 7. Nyamathi A, et al. *J Gen Intern Med*. 2002;17:134-143; 8. Dominitz J, et al. *Hepatology*. 2005;41:88-96; 9. Jonas M. *Hepatol*. 2002;36(5 suppl 1):S173-S178.

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Screening

- 1 in 3 people with hepatitis C are unaware of their infection status

- Approximately 80% of people with hepatitis C don’t have symptoms

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CDC, USPSTF, and AASLD/IDSA HCV Screening Recommendations

Population	Recommendation
Age	One-time screening is recommended for persons **born between 1945 and 1965, without ascertainment of HCV risk**[1-3]
Risk	**One-time screening is recommended for persons with these risk factors**[1,3]**:** ▪ History of illicit injection drug use (IDU) or intranasal illicit drug use ▪ History of long-term hemodialysis ▪ Receiving a tattoo in an unregulated facility/setting ▪ Healthcare workers upon accidental exposure ▪ Children born to anti-HCV–positive mothers ▪ History of transfusion with blood or organ transplantation ▪ Were ever in prison ▪ HIV infection ▪ Chronic liver disease/hepatitis with unknown cause, including elevated liver enzymes **Annual screening is recommended for current IDUs and HIV-infected MSM**[3]

1. Smith BD, et al. MMWR Recomm Rep. 2012;61(RR-4):1-32. 2. US Preventive Services Task Force. HCV Screening Guidelines 2013.
3. AASLD-IDSA. HCV Guidelines 2016.

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3. AASLD-IDSA. HCV Guidelines 2016.

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Screening Guideline Updates

- **USPSTF (US Preventative Services Task Force), March 2020**
  - Screen for hepatitis C virus (HCV) infection in adults aged 18 to 79 years (Grade B)
- **CDC (Centers for Disease Control and Prevention), April 2020**
  - Screen for HCV at least once in a lifetime for all adults 18 years and older (including pregnant women), except in settings where the prevalence is less than 0.1%
- **ACOG (American College of Obstetrics & Gynecology), Aug 2023**
  - Routine universal screening early in each pregnancy for hepatitis B and hepatitis C

SOURCE: https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-c-screening#tab

Screening Guideline Updates

- **American Association for the Study of Liver Diseases (AASLD), 2023**

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years or older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy.	I, B
Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP).	IIa, C

Source: AASLD. HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

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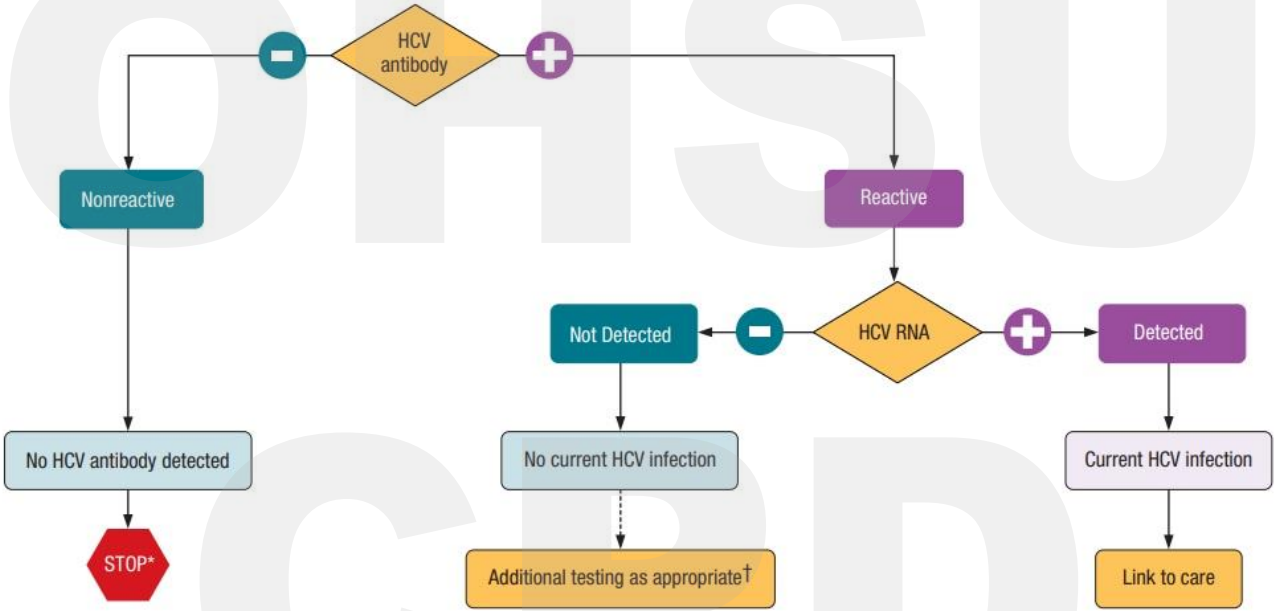
Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

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



* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Source: CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR 2013;62(18).

Screening

HCV Antibody test

- Third-generation enzyme-linked immunosorbent assay with 99% sensitivity and specificity
- Detects exposure, but cannot distinguish between current vs past infections
- Antibodies present in 97% of people by 6 months
  - Usually detectable within 4-10 weeks after exposure, but can have false negatives if not serocoverted or immunocompromised
- Rare false positives exist, would retest or get confirmatory RNA testing

Hepatitis C Quantitative PCR

- Most institutions reflex to PCR if positive Ab detected
- Detectable 1-2 weeks after infection
- Longer turnaround time

Pawlotsky JM. Use and interpretation of virological tests for hepatitis C. Hepatology. 2002;36(5 suppl 1):S65-S73.
Lingala S, Ghany MG. Natural history of hepatitis C. Gastroenterol Clin North Am. 2015;44(4):717-734.

Clearance of Acute HCV

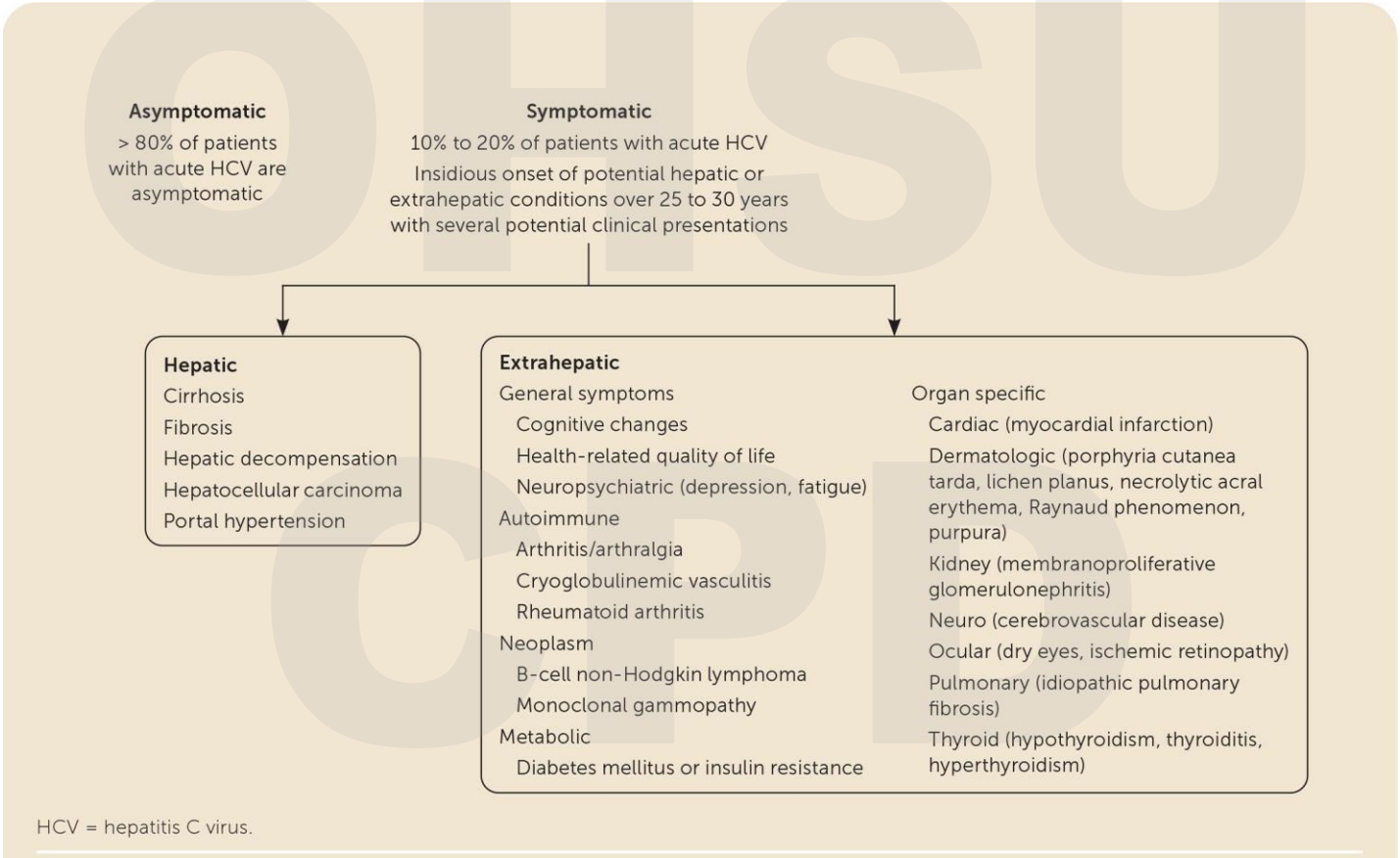
- Acute HCV (less than 6 months) may clear spontaneously
  - 15 to 45% spontaneously clear the virus
- Chronic HCV does not usually spontaneously resolve
- Allow 6 months before beginning treatment in a setting where the positive blood test could represent recent seroconversion

Presentation

- Asymptomatic (80%)

- Anorexia, malaise, jaundice, and abdominal pain occur in 10% to 20% of patients 2 to 12 weeks after exposure

Sequelae



HCV = hepatitis C virus.

AAFP. Hepatitis C: Diagnosis and Management. 2021 Dec.

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Pretreatment Assessment

- Risk Factors / Education
- Lab Testing
- Fibrosis Assessment
- Med Rec / Drug interactions

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA
Infectious Diseases Society of America

Home | Test, Evaluate, Monitor | Treatment-Naive | Treatment-Experienced | Unique & Key Populations | About

New and updated:

Updated Testing Recommendations
Review new HCV screening guidance from the AASLD and IDSA.

Search the Guidance

Enter your keywor | Search

Recent Announcements

24 Oct — What's New, Updates and Changes to the Guidance

Start Here: Choose a patient profile from the menu above.

Welcome to HCVGuidelines.org

The AASLD and IDSA in partnership with the panel have created an updated web experience to facilitate easier and faster access to this important resource. Please select a patient profile from the menu above, click on a guidance section below, or use the search box to begin.

- **Contents and Introduction** - *Select a Page*
- **Testing, Evaluation, and Monitoring of Hepatitis C** - *Browse Topics*
- **Initial Treatment of HCV Infection** - *Choose Patient Genotype*
- **Retreatment of Persons in Whom Prior Therapy Has Failed**
- **Management of Unique & Key Populations** - *Review Recommendations*

https://www.hcvguidelines.org/

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TABLE 1

Risk Factors for Hepatitis C Virus Infection

- Community exposure
  - Incarceration
  - Infants born to a person with hepatitis C virus infection
  - Injection drug use
  - Men who have sex with men (particularly people with HIV or those who have unprotected anal intercourse)
  - Percutaneous or parenteral exposure in an unregulated setting with poor infection control practices
- Hospital exposure
  - Long-term hemodialysis
  - Needlestick injuries
  - Receipt of clotting factor concentrate in the United States before 1987
  - Transfusion of blood products before 1992
- Other
  - HIV or hepatitis B infection
  - Sexually active person starting pre-exposure prophylaxis for HIV
  - Unexplained chronic hepatic disease including abnormal liver enzymes (mild, intermittent or markedly elevated)

Information from references 2, 8, and 15-18.

Maness DL, Riley E, Studebaker G. Hepatitis C: Diagnosis and Management. Am Fam Physician. 2021 Dec 1;104(6):626-635. PMID: 34913652.

Substance Use Disorders and HCV

- Alcohol use
  - Encourage abstinence or harm reduction
  - Daily consumption of >50 g (~3.6 standard drinks) of alcohol has a high likelihood of worsening fibrosis

- PWID, Opioid use d/o, Methamphetamine Use d/o
  - **Accounts for majority of new acute HCV infections**
  - Offer MOUD or other treatment if available
  - NOT a contraindication to start HCV treatment

- Tobacco and Marijuana use
  - May be pro-fibrotic

Maternal risks of HCV transmission

- HCV-positive women do not need to avoid pregnancy or breastfeeding
- Risks of 6/100 infants born to HCV-infected mothers are infected with the virus at time of birth. Risks are 2-3X greater if mother is co-infected with HIV/HCV
- Children born to HCV-positive mothers should have anti-HCV Ab no sooner than 18 months due to potential circulating maternal antibodies
- HCV-positive mothers should avoid breastfeeding if their nipples are cracked or bleeding
- Direct Acting Antiviral therapy not studied in pregnancy
- Ribavirin is CONTRAINDICATED in pregnancy

Minimizing Transmission Risks for HCV

Blood contact

- Avoid sharing tooth brushes, dental or shaving equipment
- Avoid blood donation
- Clean up any blood exposures with bleach solution (1:9 / bleach:water ratio)

Harm Reduction (for PWID)

- Avoid needle sharing
- Use new sterile syringes and filters, and disinfected cookers
- Clean injection sites with an alcohol swab
- Safe needle disposal

Sexual Health

- Recommend use of barrier precautions to prevent sexual transmission
- Sexual transmission is rare in monogamous heterosexual couples
- Risk increases in MSM, heterosexual persons with multiple partners and those with co-infection of HIV

Who gets treated?

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Baseline Labs for Chronic HCV

Baseline (usually within 3 months of initiation)

- CMP (LFTs)
- CBC, INR
- HCV Quantitative PCR (or Hep C Ab with reflex)
- HCV Genotype (most initial treatments are pan-genotypic)
- HBV serologies
- HIV Ag/Ab
- Urine HCG (if applicable)

Additional to consider:

- Hep A IgM/IgG
- Alpha-fetal protein tumor marker
- RPR or TPA-Ab (Syphilis)

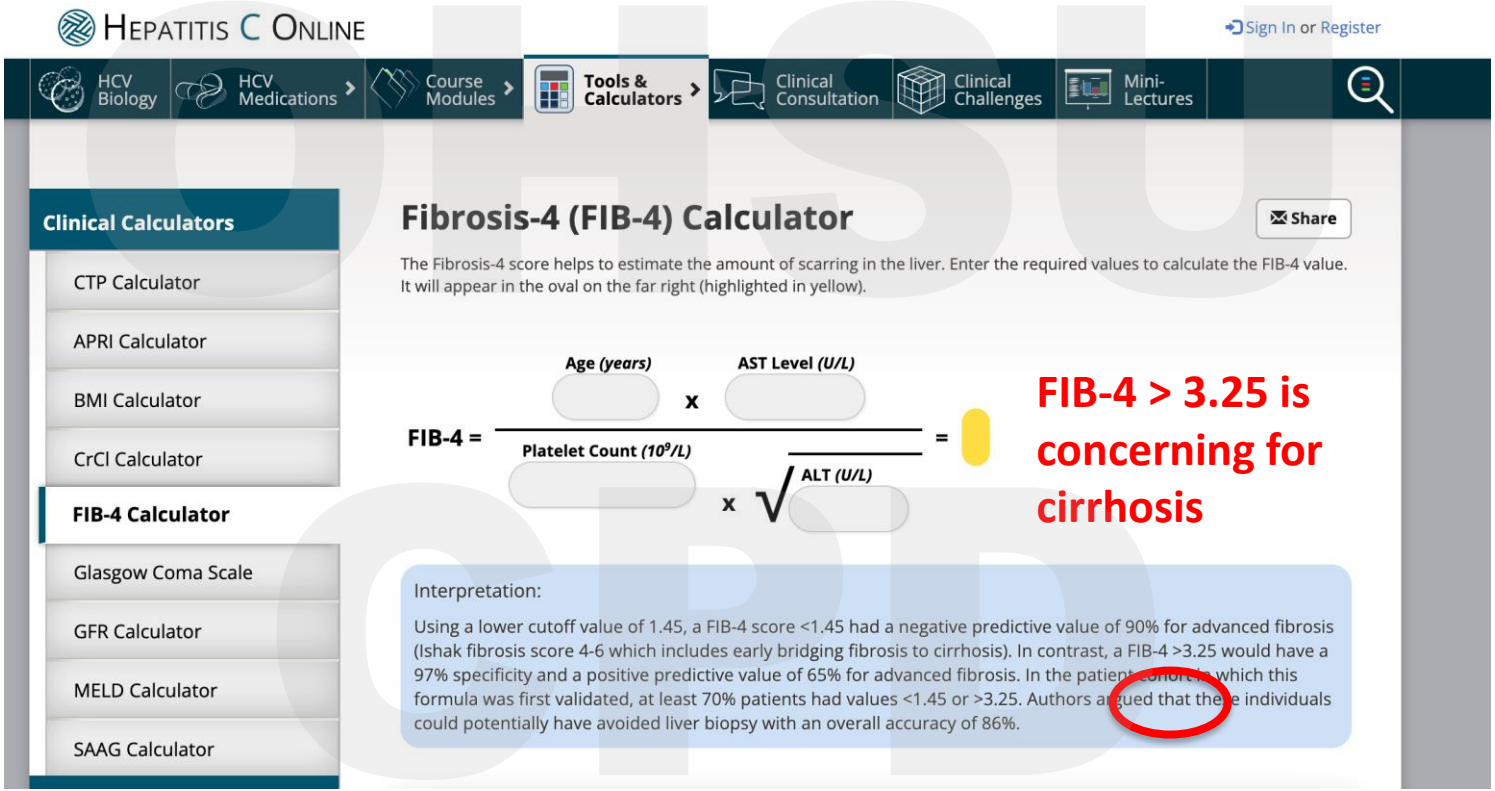
Health Maintenance

- Avoid alcohol
- Update on Hepatitis A and B vaccines (if not immune)
- Update Pneumococcal vaccine

Fibrosis Assessment

Recommendation for Pretreatment Assessment	
RECOMMENDED	RATING
Evaluation for advanced fibrosis using noninvasive markers and/or elastography, and rarely liver biopsy, is recommended for all persons with HCV infection to facilitate decision making regarding HCV treatment strategy and determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see HCV Testing and Linkage to Care).	I, A

Non invasive Fibrosis Assessment: FIB-4



https://www.hepatitisc.uw.edu/

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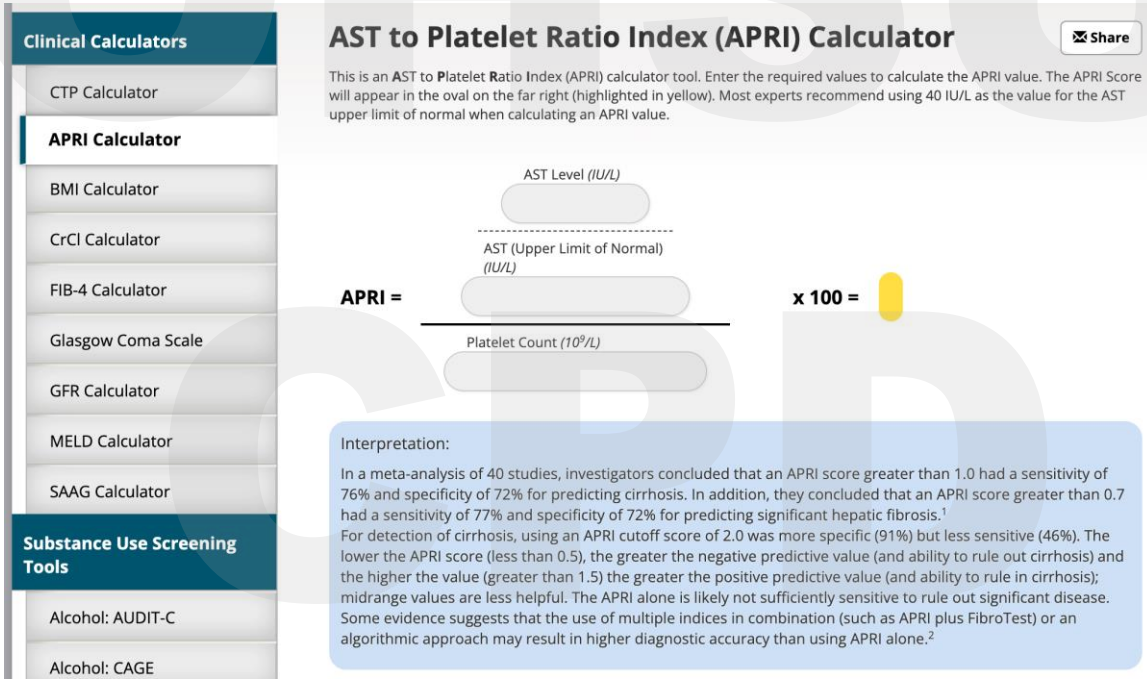
Non invasive Fibrosis Assessment: APRI

- APRI Score



Screening for Cirrhosis

- AST
- ALT
- Alkaline Phosphatase

Degree of LFT elevation or HCV viral load does NOT indicate fibrosis

- Albumin (true marker of liver function)
- Bilirubin (true marker of liver function)

- Platelets (thrombocytopenia might suggest portal hypertension)

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Screening for Cirrhosis

$$\frac{\text{AGE} \times \text{AST}}{\text{PLT} \times \sqrt{\text{ALT}}} = \textbf{FIB - 4}$$

> 3.25 is predicative of advanced cirrhosis

Source: Hepatitis C Provider Pocket Guide, Healthcare for the Homeless 2023

Screening for Cirrhosis

$$\frac{\text{AGE} \times \text{AST}}{\text{PLT} \times \sqrt{\text{ALT}}} = \textbf{FIB - 4}$$

> 3.25 is predicative of advanced cirrhosis

$$\frac{\dfrac{\text{AST}}{40}}{\text{PLT}} \times 100 = \textbf{APRI}$$

> 1.0 is predicative of cirrhosis

Source: Hepatitis C Provider Pocket Guide, Healthcare for the Homeless 2023

Screening for Cirrhosis

$$\frac{\text{AGE} \times \text{AST}}{\text{PLT} \times \sqrt{\text{ALT}}} = \textbf{FIB - 4}$$

> 3.25 is predicative of advanced cirrhosis

$$\frac{\frac{\text{AST}}{40}}{\text{PLT}} \times 100 = \textbf{APRI}$$

> 1.0 is predicative of cirrhosis

CTP Scoring

Points	1	2	3
Encephalopathy	NONE	Grade 1-2	Grade 3-4
Ascites	NONE	Mild-Mod	Severe
Bilirubin	<2	2-3	>3
Albumin	>3.5	2.8-3.5	<2.8
PT or INR	<4 / <1.7	4-6 / 1.7-2.3	>6 / >2.3

CTP Class

A = 5-6 points
Least Severe

B = 7-9 points
Moderately Severe

C = 10-15 points
Most Severe

Cirrhosis Severity

Source: Hepatitis C Provider Pocket Guide, Healthcare for the Homeless 2023

Screening for Cirrhosis

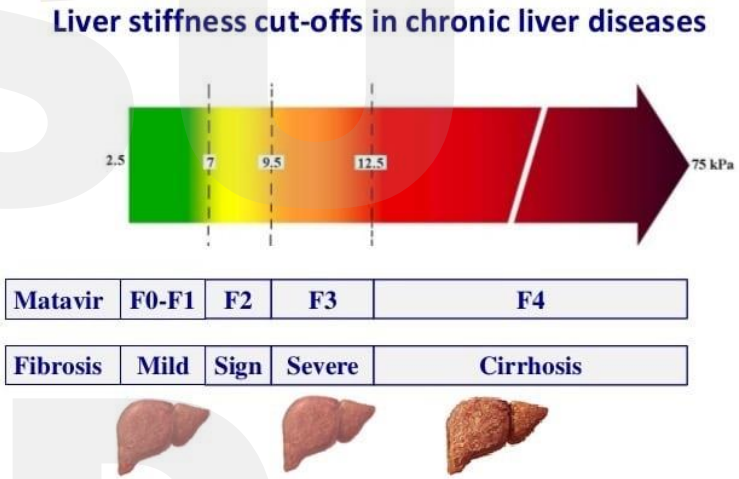
FIBROSIS EVALUATION TOOL	SUSPECTED CIRRHOSIS FINDING
Noninvasive serologic tests	FibroSure, FibroTest, etc.: F4
Transient elastography	FibroScan stiffness >12.5 kPa
Fib-4 Calculation	>3.25
Clinical Evidence	Liver nodularity, PLT <150,000

[*Prior biopsy proven cirrhosis]

Source: Hepatitis C Provider Pocket Guide, Healthcare for the Homeless 2023

Transient/Ultrasound Elastography

- Generates low amplitude shear wave to measure liver elasticity and stiffness
- Liver stiffness measurements (LSMs) are based on shear wave propagation speed and the density of the material the shear wave is traveling through
- The shear wave speed is related to the liver parenchyma stiffness, with **faster wave progression seen in stiffer tissue**
- Initial studies noted values between 2.5 to 7.0 kPa, liver fibrosis is likely absent or mild
- >12.5 kPa, cirrhosis is likely



Castera et al. J Hepatology 2008; 48, 835-41, Ziol et al, Hepatology 2005: 41,48-59, Garica-Taso Hepatology 65(1) 310-35

Table 2: Recommendation for Interpretation of Liver Stiffness Values Obtained with ARFI Techniques in Patients with Viral Hepatitis and NAFLD

Liver Stiffness Value	Recommendation
≤5 kPa (1.3 m/sec)	High probability of being normal
<9 kPa (1.7 m/sec)	In the absence of other known clinical signs, rules out cACLD. If there are known clinical signs, may need further test for confirmation
9–13 kPa (1.7–2.1 m/sec)	Suggestive of cACLD but need further test for confirmation
>13 kPa (2.1 m/sec)	Rules in cACLD
>17 kPa (2.4 m/sec)	Suggestive of CSPH

Note.—ARFI = acoustic radiation force impulse, cACLD = compensated advanced chronic liver disease, CSPH = clinically significant portal hypertension, NAFLD = non-alcoholic fatty liver disease.

Values used at OHSU with US liver elastography

Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement
Richard G. Barr, Stephanie R. Wilson, Deborah Rubens, Guadalupe Garcia-Tsao, and Giovanna Ferraioli
Radiology 2020 296:2, 263-274

Limitations of Transient Elastography

Overestimation of fibrosis

- Liver inflammation (e.g. active hepatitis)
- Cholestasis (e.g. biliary obstruction)
- Mass lesions within the liver (e.g. tumor)
- Liver congestion (e.g. heart failure)

Failure or unreliable readings

- Obesity (BMI >30–35 kg/m2)
- Older age
- Presence of ascites
- Features of the metabolic syndrome (type 2 diabetes, hypertension, increased waist circumference)

Treatment

Is treatment in primary care settings effective?

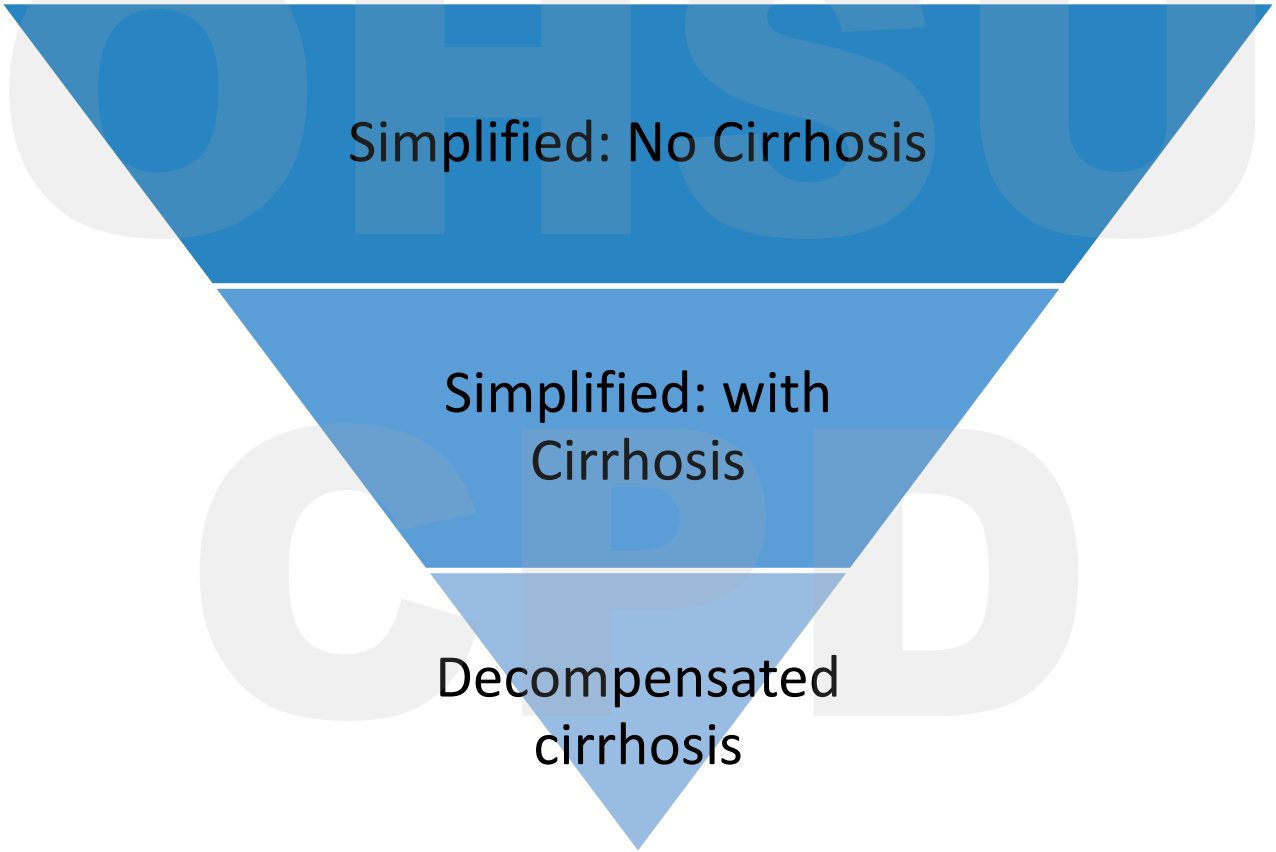
- Wade AJ, et al (2020)
  - Randomized 136 people to treatment to primary care vs. hospital-based hepatologist
  - The SVR12 rate (100%, 95% [CI] 87.7-100) of people treated in primary care was noninferior when compared to controls
  - Commencing treatment in the primary care arm (75%, 43/57) was significantly higher than in the Standard of Care (SOC) arm (34%, 18/53; P < .001; relative risk [RR] 2.48
  - Proportion of participants with SVR12 was significantly higher in the primary care arm, compared to in the SOC arm (49% [28/57] and 30% [16/53], respectively; P = .043; RR 1.63)

Wade AJ, et al. *Clin Infect Dis.* 2020 Apr 15;70(9): 1900-6.

Direct-Acting Antivirals

MEDICATION	DOSING
Mavyret Glecaprevir (300 mg) - Pibrentasvir (120 mg)	100mg / 40mg tablets 3 tablets once daily
Epclusa Sofosbuvir (400 mg) - Velpatasvir (100 mg)	400 mg / 100 mg tablets 1 tablet once daily
Harvoni Ledipasvir (90mg) - Sofosbuvir (400 mg)	90 mg / 400 mg tablets 1 tablet once daily
Zepatier Elbasvir (50 mg) - Grazoprevir (100 mg)	50 mg / 100mg tablet 1 tablet once daily
Vosevi Sofosbuvir (400 mg) - Velpatasvir (100 mg) - Voxilaprevir (100 mg)	400 mg /100mg /100 mg 1 tablet once daily

Treatment Naïve



Simplified HCV Treatment for Treatment Naïve Adults, No Cirrhosis

Who Is Eligible for Simplified Treatment
Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hepatitis C treatment

The vast majority of people you'll see in primary care!

Cure rates of >95% with DAA treatment

Simplified HCV Treatment for Treatment Naïve Adults, No Cirrhosis

Who Is *NOT* Eligible for Simplified Treatment (Without Cirrhosis)

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(see HCV guidance for treatment recommendations for these patients)

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Simplified HCV Treatment for Treatment Naïve Adults, No Cirrhosis

Recommended Regimens

- Glecaprevir 300 mg / pibrentasvir 120 mg (**Mavyret**)
  - Duration of 8 weeks

- Sofosbuvir 400 mg / velpatasvir 100 mg (**Epclusa**)
  - Duration of 12 weeks

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Simplified HCV Treatment for Treatment Naïve Adults, Compensated Cirrhosis

Who Is Eligible for Simplified Treatment

Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment

Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.

- Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
- Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
- Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
- Prior liver biopsy showing cirrhosis

Simplified HCV Treatment for Treatment Naïve Adults, Compensated Cirrhosis

Who Is *NOT* Eligible for Simplified Treatment (With Cirrhosis)

Patients who have any of the following characteristics:

- Current or prior episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m^2) (see Patients with Renal Impairment section)
- HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(see HCV guidance for treatment recommendations for these patients)

Simplified HCV Treatment for Treatment Naïve Adults, Compensated Cirrhosis

Make sure you obtain:

- Liver US (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.

OR

- POCUS exam

- HCV genotype (if treating with sofosbuvir/velpatasvir)

Simplified HCV Treatment for Treatment Naïve Adults, Compensated Cirrhosis

Recommended Regimens

- Genotype 1-6
  - Glecaprevir 300 mg / pibrentasvir 120 mg (Mavyret)
  - Duration of 8 weeks

- Genotype 1, 2, 4, 5, or 6
  - Sofosbuvir 400 mg / velpatasvir 100 mg (**Epclusa**)
  - Duration of 12 weeks

- NOTE: Patients with genotype 3 require baseline NS5A resistance-associated substitution (RAS) testing. Those without Y93H can be treated with 12 weeks of sofosbuvir/velpatasvir.

Treatment-Naive Genotype 1a Without Cirrhosis

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING

Treatment-Naive Genotype 1b Without Cirrhosis

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive Patients Genotype 1b Without Cirrhosis

Treatment-Naive Genotype 2 Without Cir

Recommended and alternative regimens listed by pangenotypic, ev

Treatment-Naive Genotype 2 Patients Without Cirrh

RECOMMENDED

Treatment-Naive Genotype 3 Without Cirrhosis

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive Genotype 3 Patients Without Cirrhosis

Treatment-Naive Genotype 4 Without Cirrh

Recommended and alternative regimens listed by pangenotypic, evide

Treatment-Naive Genotype 4 Patients Without Cirrhos

RECOMMENDED
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg)
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)[b]

[a] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily.
[b] An 8-week regimen can be considered in patients with favorable baseline characteristics (ie, n
absence of genotype 4r).

Treatment-Naive Genotype 5 or 6

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

Treatment-Naive Genotype 5 or 6 Patients With and Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, A[c]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, B
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)[d]	12 weeks	IIa, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.
[c] For compensated cirrhosis, rating is I, B.
[d] Not recommended for genotype 6e if subtype is known.

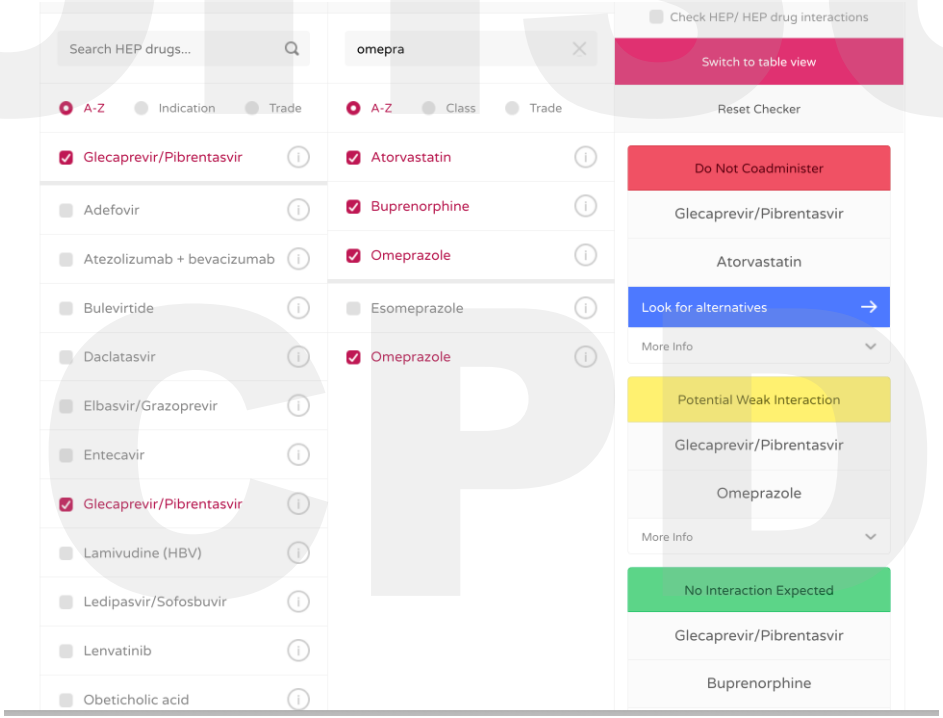
Decompensated Cirrhosis?

- Child-Pugh Turcotte B or C
- Refer to Hepatology

Check for Med interactions

University of Liverpool drug interaction checker

https://www.hep-druginteractions.org/checker



Antacids

- Increased gastric pH decreases solubility of velpatasvir and ledipasvir
- Separate antacids by 4 hours
- Administer H2RAs simultaneously with or 12 hours apart (max famotidine 40 mg BID)

- Avoid PPIs if possible. If medically necessary, omeprazole 20 mg may be administered:
  - Simultaneously with LDV/SOF (Harvoni) under fasted conditions
  - 4 hours after SOF/VEL (Epclusa) is taken with food
  - Simultaneously with SOF/VEL/VOX (Vosevi)

Statins

- Rule of thumb
  - Monitor for statin-associated adverse events and risks (i.e. myalgia, myopathy, rhabdomyolysis)
  - Coadministration not recommended
    - GCR/PBR (Mavryet): atorvastatin, lovastatin, simvastatin
    - LDV/SOF (Harvoni): rosuvastatin
    - VEL/VOX/SO (Vosevi): rosuvastatin, pitavastatin
  - Max doses
    - GCR/PBR (Mavyret): rosuvastatin 10 mg
    - SOF/VEL (Epclusa): rosuvastatin 10 mg
    - EBR/GZR (Zepetier): rosuvastatin 10 mg, atorvastatin 20 mg
    - VEL/VOX/SOF (VosevI): pravastatin 40 mg

Monitoring

Simple HCV Treatment, Non-Cirrhosis

- No monitoring

Simple HCV Treatment, Cirrhosis

- Consider checking CMP and CBC to monitor for liver injury during treatment because hepatic decompensation occurs rarely among patients with cirrhosis receiving HCV antiviral treatment.

Post Treatment Surveillance

Sustained Virologic Response (SVR12) = CURE

- 12 weeks after end of treatment course, recheck quantitative Hep C RNA (and usually CMP and CBC)
- Hep C Ab will remain positive for life

Post Treatment Surveillance

Non-Cirrhosis

- No surveillance needed unless new concerns for re-infection

Cirrhosis

- Hepatocellular Carcinoma screening with US +/- AFP every 6 months indefinitely, as well as CMP, CBC, INR
- Upper endoscopy for variceal screening

Case: “Steven”

- 49 yo with history of remote IVDU on buprenorphine, currently drinks 1-2 beers/week
- FIB-4 score normal, other labs normal, US normal
- Genotype 1a

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Simplified HCV Treatment for Treatment Naïve Adults, No Cirrhosis

Recommended Regimens

- Glecaprevir 300 mg / pibrentasvir 120 mg (**Mavyret**)
  - Duration of 8 weeks

- Sofosbuvir 400 mg / velpatasvir 100 mg (**Epclusa**)
  - Duration of 12 weeks

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Case: “Steven”

Treatment-Naive Genotype 1a Without Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[a] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[b]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) with dasabuvir (600 mg) as part of an extended-release regimen or plus twice-daily dosed dasabuvir (250 mg), with weight-based ribavirin	12 weeks	I, A
Daily simeprevir (150 mg) plus sofosbuvir (400 mg)	12 weeks	I, A
Daily daclatasvir (60 mg)[c] plus sofosbuvir (400 mg)	12 weeks	I, B
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[a] for elbasvir	16 weeks	IIa, B

[a] Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.
[b] This is a 3-tablet coformulation. Please refer to the prescribing information.
[c] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information and the section on HIV/HCV coinfection for patients on antiretroviral therapy.

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Case: “Steven”

- Start Glecaprevir 300 mg / pibrentasvir 120 mg for 8 weeks
- Counsel on alcohol cessation
- Check in ~ 4 weeks of treatment to see how things are going
- Follow-up visit 12 weeks months after completion shows undetectable viral load!

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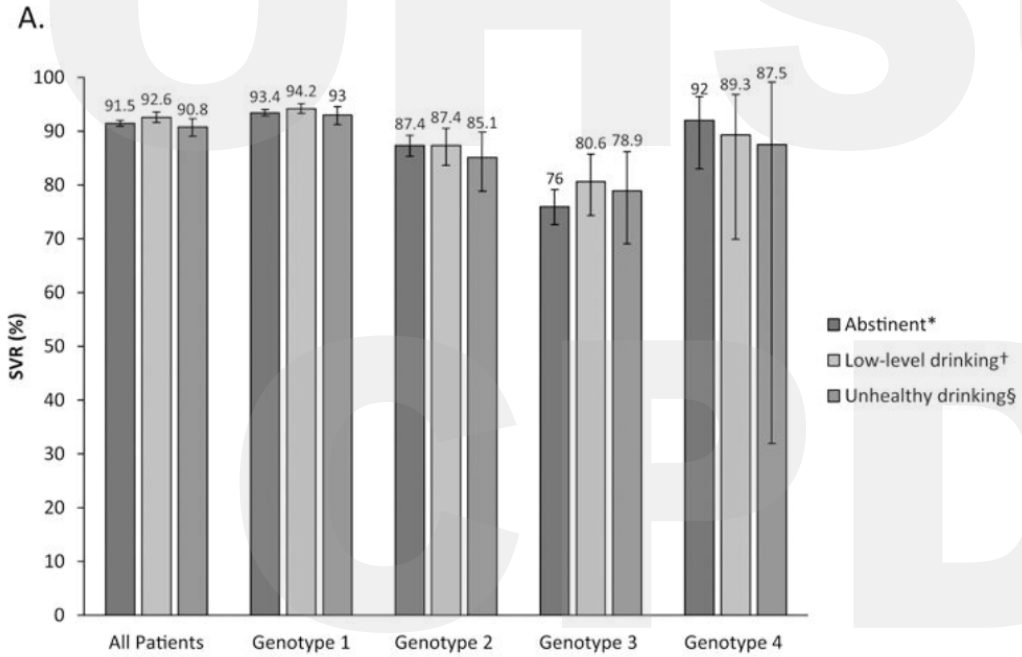
Does co-morbid alcohol use matter?

Rate of sustained virologic response (%) according to alcohol use, by genotype



*Abstinent: AUDIT-C score 0 in men and women
†Low-level drinking: AUDIT-C score 1-3 in men, 1-2 in women
§Unhealthy drinking: AUDIT-C score 4-12 in men, 3-12 in women

Tsui, et al. *Drug Alcohol Depend*. 2016 December 01; 169: 101–109

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Original Investigation | Gastroenterology and Hepatology

Alcohol Use and Sustained Virologic Response to Hepatitis C Virus Direct-Acting Antiviral Therapy

Emily J. Cartwright, MD; Chloe Pierret, MSc; Caroline Minassian, PhD; Denise A. Esserman, PhD; Janet P. Tate, ScD; Matthew B. Goetz, MD; Debika Bhattacharya, MD; David A. Fiellin, MD; Amy C. Justice, MD, PhD; Vincent Lo Re III, MD, MSCE; Christopher T. Rentsch, PhD

Key Points

Question Is alcohol use associated with achieving a sustained virologic response (SVR) when treating hepatitis C virus (HCV) infection with direct-acting antiviral (DAA) therapy?

Findings In this cohort study of 69 229 adults with HCV infection, there was no difference in SVR across alcohol use categories, even for patients with high-risk consumption or alcohol use disorder, after adjusting for potential confounding variables.

Meaning These findings suggest that restricting access to DAA therapy on the basis of alcohol use creates an unnecessary barrier for patients and challenges HCV elimination goals.

Case 2

- 30 yo person, history of active IV fentanyl and meth use
- HCV viral count 2.2 million, genotype 2
- FIB-4 equivocal -> US Elastography F0-F1
- No meds

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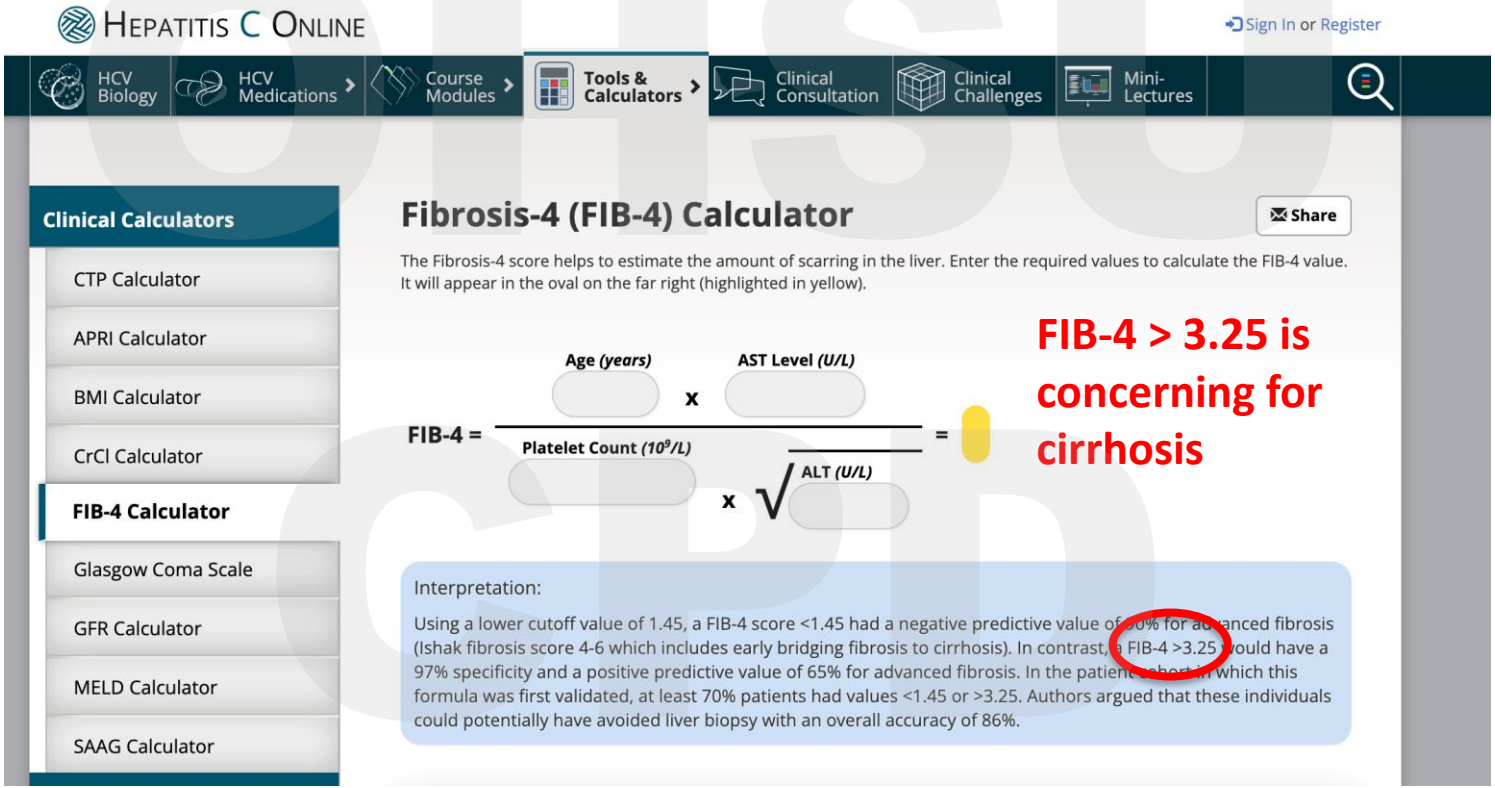
Non invasive Fibrosis Assessment: FIB-4



FIB-4 > 3.25 is concerning for cirrhosis

Does active IVDU matter?

% Participants with SVR among people with a history of injection drug use	
Receiving OST, no recent injection use	94-97% (6 studies)
Receiving OST, with and without recent IVDU	76-100% (8 studies)
History of IVDU, with and without recent use	80-96% (8 studies)
Recent injection use	93-96% (2 studies)

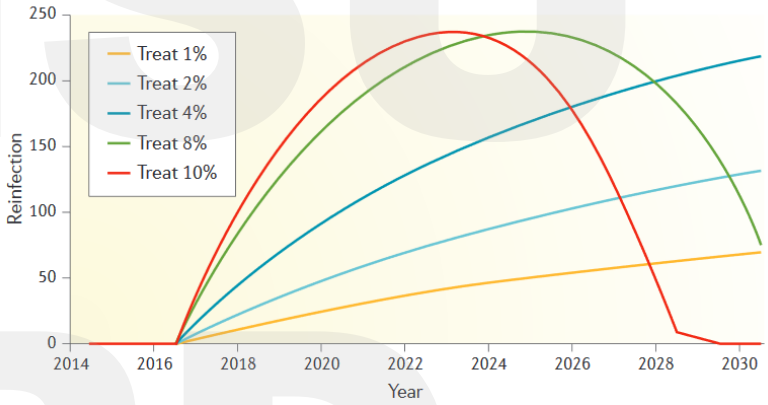


Figure 2 | **Modelling the effect of HCV treatment on reinfection in people who inject drugs.** Mathematical modelling was used to evaluate the effect of increased treatment on HCV reinfection among PWID in Australia. Each line represents the expected number of individuals with HCV reinfection (secondary infections, left axis) in each year, based on a given annual HCV treatment scenario. The coloured lines represent the annual proportion of PWID treated per year. Image and data presented[80] courtesy of H. Razavi.

Grebeley et al. *Nat Rev Gastroenterol Hepatol.* 2017 Nov;14(11):641-651.

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Case 2

- Start Mavyret for 8 weeks, however patient is lost to follow up
- They see you 3 months later, and mention that they think they took “most of the meds”
- Repeat HCV RNA with viral count of 1.2 million

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Treatment Failure

Recommended regimens listed by evidence level and alphabetically for:

Glecaprevir/Pibrentasvir Treatment Failures (All Genotypes), With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) plus daily sofosbuvir (400 mg) and weight-based ribavirin	16 weeks	IIa, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)	12 weeks	IIa, B
For patients with compensated cirrhosis, addition of weight-based ribavirin is recommended.	12 weeks	IIa, C

[a] For decompensated cirrhosis, please refer to the appropriate section.

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Case 3

- 65 yo with a history of GERD, HLD, mild depression and HCV
- Fibrosis stage 4, liver US without evidence of ascites or cirrhosis
- Mild transaminitis, INR 1.0, Cr 0.8
- No prior known history of varices or hepatic encephalopathy
- Genotype 2a

Case 3

- Child Pugh A
- Fib 4 score of 4.15
- Check for medication interactions: atorvastatin, omeprazole, sertraline
  - Shared decision to hold atorvastatin (could also switch to low dose rosuvastatin if high ASCVD risk) and switch to famotidine

- Choose Mavyret for 8 weeks
- Will continue to need variceal screening, HCC screening and labs

Sources and Resources

- Hcvguidelines.org
- www.hep-druginteractions.org
- https://www.hepatitisc.uw.edu/
- OHSU HCV Echo Program
  - https://www.ohsu.edu/xd/health/for-healthcare-professionals/telemedicine-network/for-healthcare-providers/ohsu-echo/heptitisc-and-liver-care/index.cfm

THANK YOU!

Matt Chan, MD
OHSU Family Medicine
chama@ohsu.edu

References

- Barr G et al. Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement. Radiology 2020 296:2, 263-274
- CDC, National Notifiable Diseases Surveillance System. https://www.cdc.gov/hepatitis-surveillance-2022/hepatitis-c/figure-3-1.html
- Debika Bhattacharya, Andrew Aronsohn, Jennifer Price, Vincent Lo Re, the American Association for the Study of Liver Diseases–Infectious Diseases Society of America HCV Guidance Panel , Hepatitis C Guidance 2023 Update: American Association for the Study of Liver Diseases– Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection, Clinical Infectious Diseases, 2023;, ciad319, https://doi.org/10.1093/cid/ciad319
- Melson R. Hepatitis C Provider Pocket Guide. National Healthcare for the Homeless Council. 2023. https://nhchc.org/wp-content/uploads/2023/04/NHCHC-Hep-C-Pocket-Guide-5-×-7-in.pdf
- Lingala S, Ghany MG. Natural history of hepatitis C. Gastroenterol Clin North Am. 2015;44(4):717-734.
- Pawlotsky JM. Use and interpretation of virological tests for hepatitis C. Hepatology. 2002;36(5 suppl 1):S65-S73.
- USPSTF. Hepatitis C Virus Infection in Adolescents and Adults: Screening. Published March 2, 2020. Accesseed Jan 27, 2025. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-c-screening

Thank You