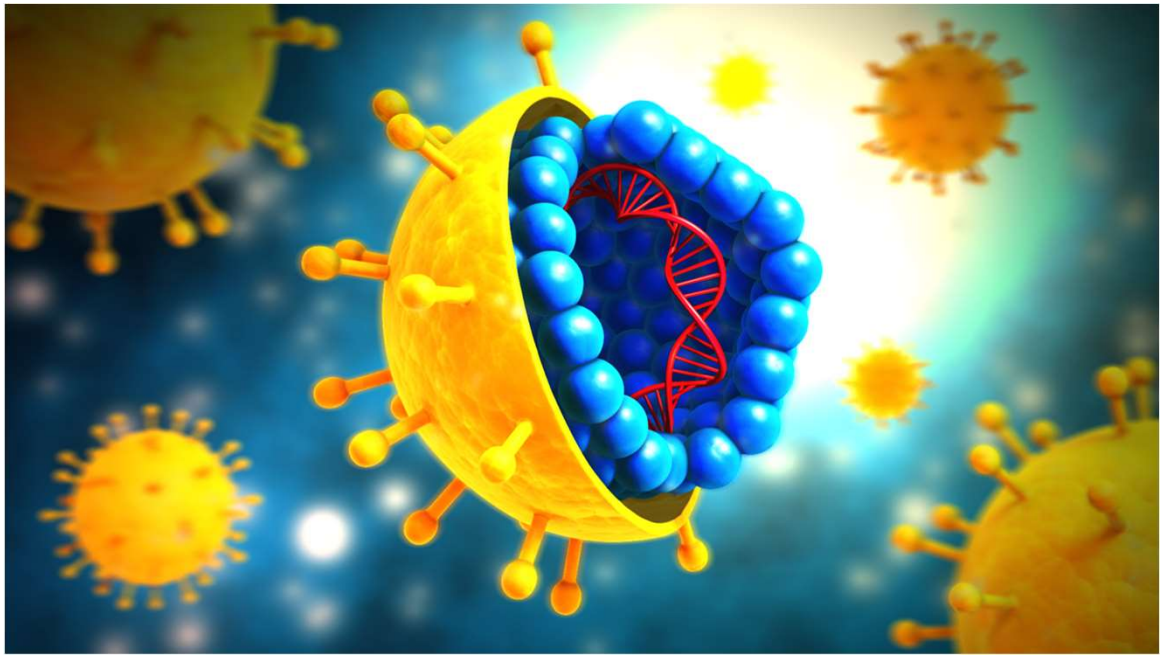
Expedited Hepatitis C Cure for the Primary Care PA



George Froehle PA-C, AAHIVS

AAPA Conference

May 21st, 2022

Disclosures:

Declaration Statement: I have relevant relationships with ineligible companies to disclose within the past 24 months.

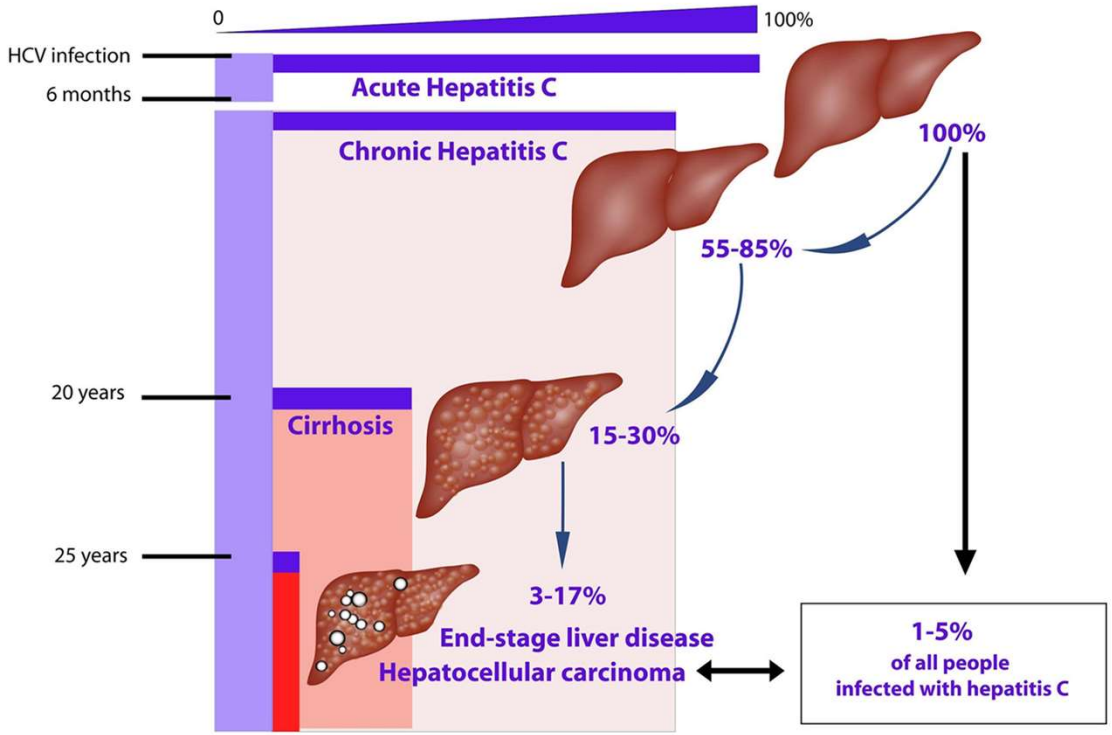
- Gilead: Attended a one-time Advisory Board Meeting on PrEP

Objectives:

- Describe the current hepatitis C epidemic and the health risks associated with chronic hepatitis C infection
- Perform screening in appropriate patient populations, confirmation of chronic hepatitis C, and staging of liver fibrosis
- Apply the American Academy of the Study of Liver Disease (AASLD) expedited guidelines to provide cure to patients with hepatitis C

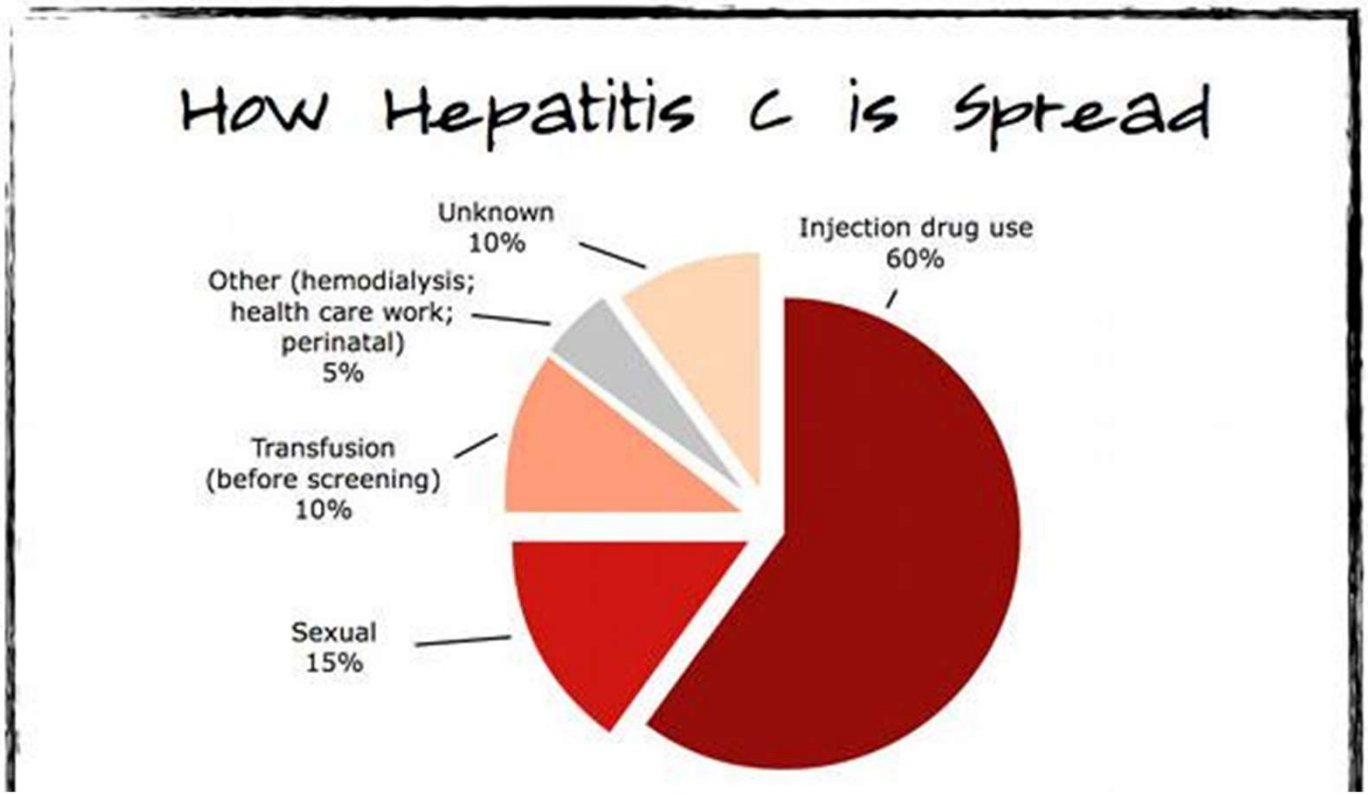
Hepatitis C: The Basics

Hepatitis C (HCV) is an RNA virus that infects and inflames the liver leading to liver fibrosis, cirrhosis, liver failure and/or liver cancer



-American Liver Foundation

Hepatitis C: Transmission



Hepatitis C: Acute Symptoms

Most people (about 70% – 80%) with an acute Hepatitis C infection **do not** experience any symptoms or show signs of the infection. If Hepatitis C symptoms do occur, they usually appear within two weeks to six months after being exposed to the hepatitis C virus (HCV). If symptoms develop they're generally mild and flu-like and may include:

- Fatigue
- Myalgias/arthralgias
- Fever
- Nausea
- Abdominal pain
- Itchy skin
- Dark urine
- Jaundice and scleral icterus

-American Liver Foundation

Hepatitis C: Chronic Symptoms

For those progressing to chronic HCV, symptoms may include:

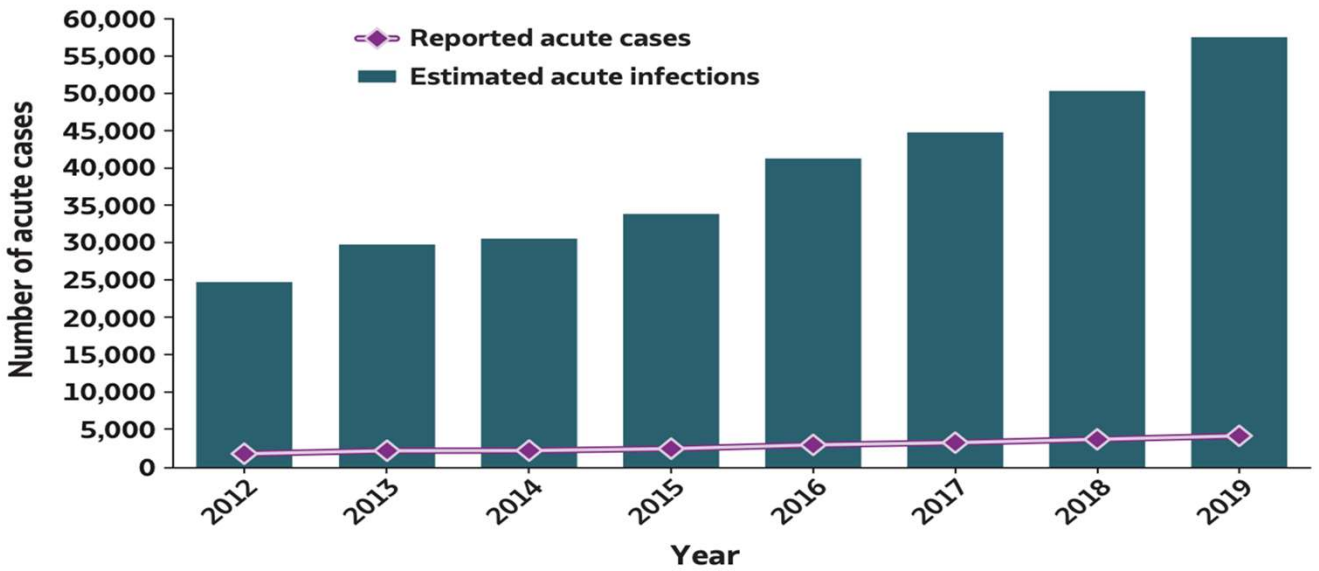
- Fatigue
- Myalgias/arthralgias
- Fever
- Nausea
- Abdominal pain
- Itchy skin
- Dark urine
- Jaundice and scleral icterus
- hepatic encephalopathy
- Ascites
- Esophageal varices
- Bruising
- Spider veins

-American Liver Foundation

Status of US Hepatitis C Epidemic: Acute Infections

2019 VIRAL HEPATITIS SURVEILLANCE REPORT

Figure 3.1. Number of reported acute hepatitis C virus infection cases and estimated infections* — United States, 2012–2019



Acute Hepatitis C	2012	2013	2014	2015	2016	2017	2018	2019
Reported acute cases	1,778	2,138	2,194	2,436	2,967	3,216	3,621	4,136
Estimated acute infections	24,700	29,700	30,500	33,900	41,200	44,700	50,300	57,500

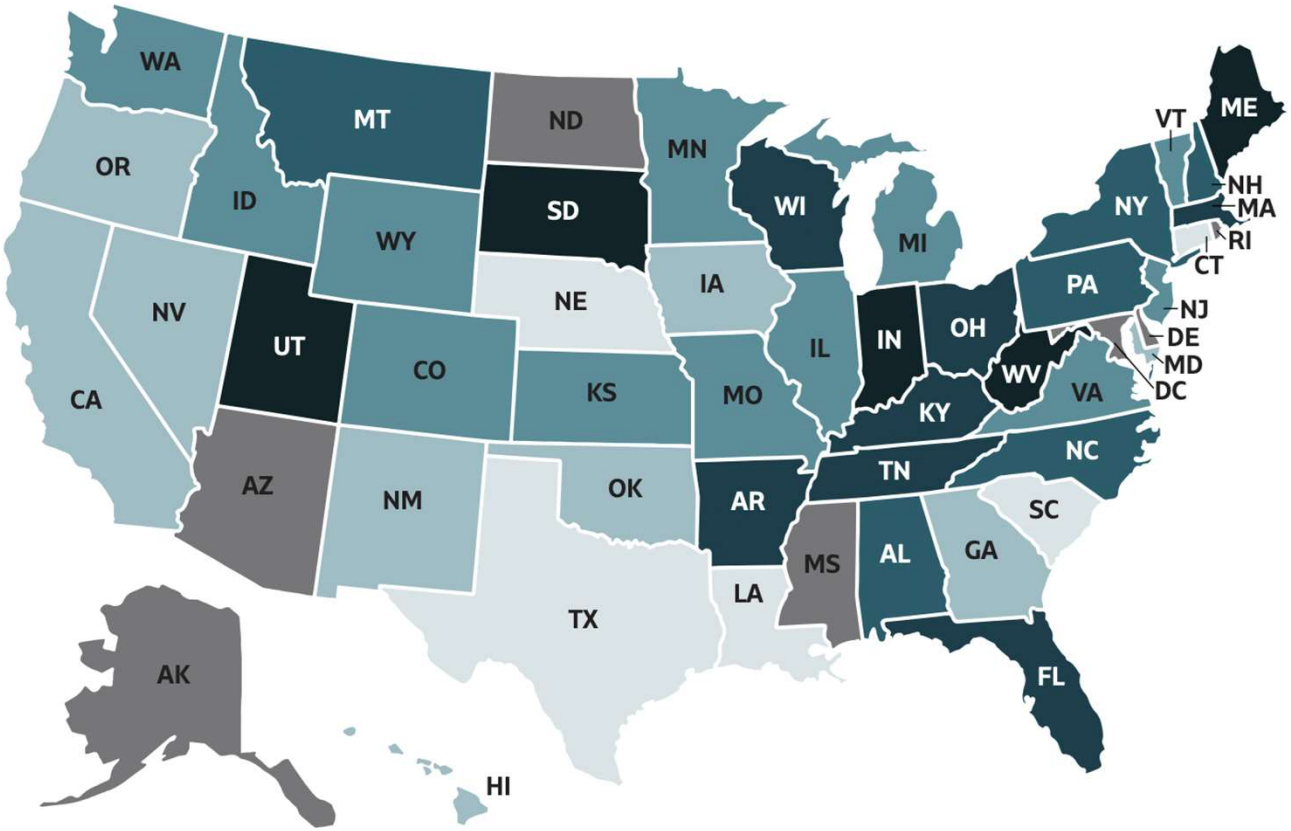
Source: CDC, National Notifiable Diseases Surveillance System.

*The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases that met the classification criteria for a confirmed case by a factor that adjusted for underascertainment and underreporting. The 95% bootstrap confidence intervals for the estimated number of infections are displayed in the Appendix.

Status of US Hepatitis C Epidemic: Acute Infections by State

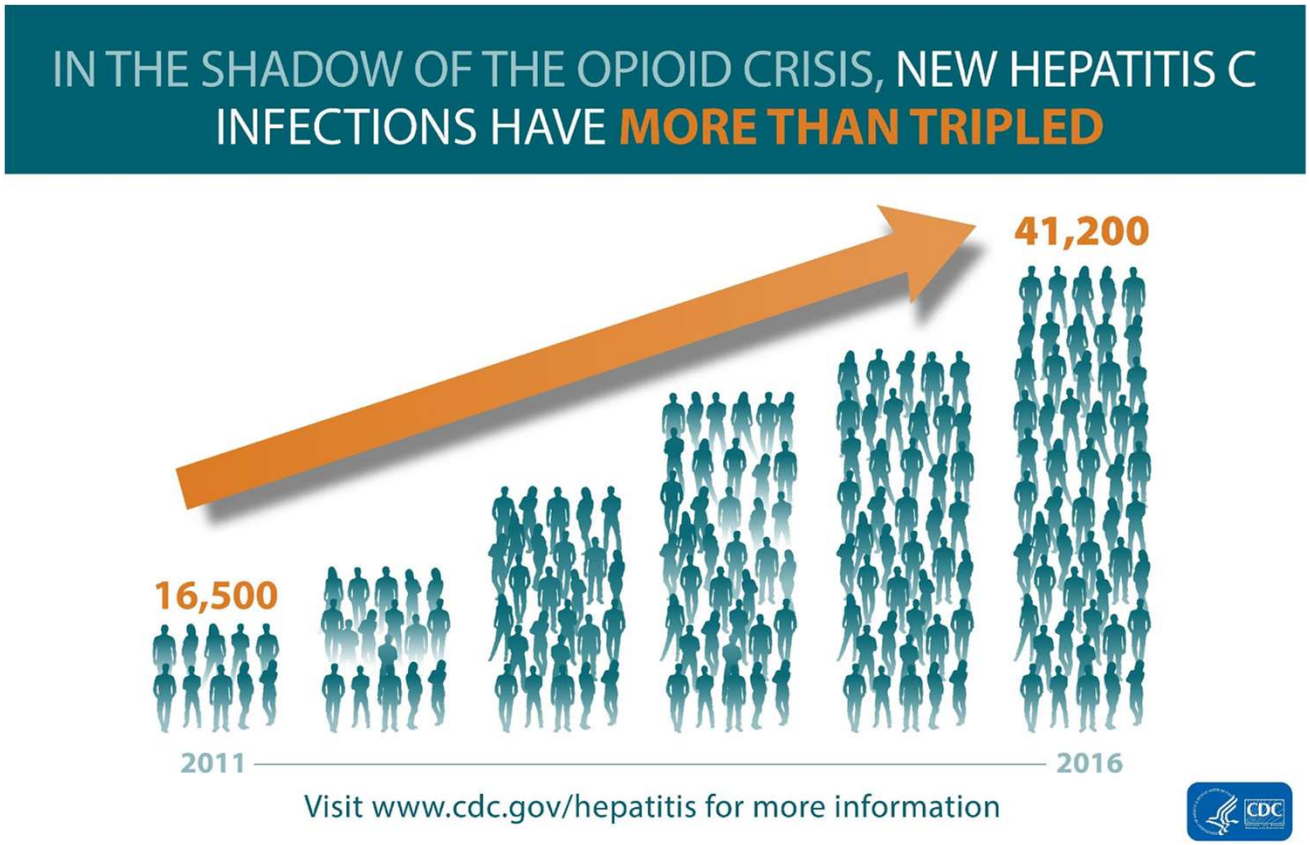
2019 VIRAL HEPATITIS SURVEILLANCE REPORT

Figure 3.3. Rates of reported acute hepatitis C virus infection, by state or jurisdiction — United States, 2019



Color Key	Cases/100,000 Population	State or Jurisdiction
	0.0-0.2	CT, LA, NE, SC, TX
	0.3-0.6	CA, GA, HI, IA, MD, NM, NV, OK, OR
	0.7-1.2	CO, ID, IL, KS, MI, MN, MO, NJ, VA, VT, WA, WY
	1.3-1.8	AL, MT, NC, NH, NY, PA
	1.9-3.0	AR, FL, KY, MA, OH, TN, WI
	3.1-4.8	IN, ME, SD, UT, WV
	Data not available	AK, AZ, DC, DE, MS, ND,RI

Source: CDC, National Notifiable Diseases Surveillance System.

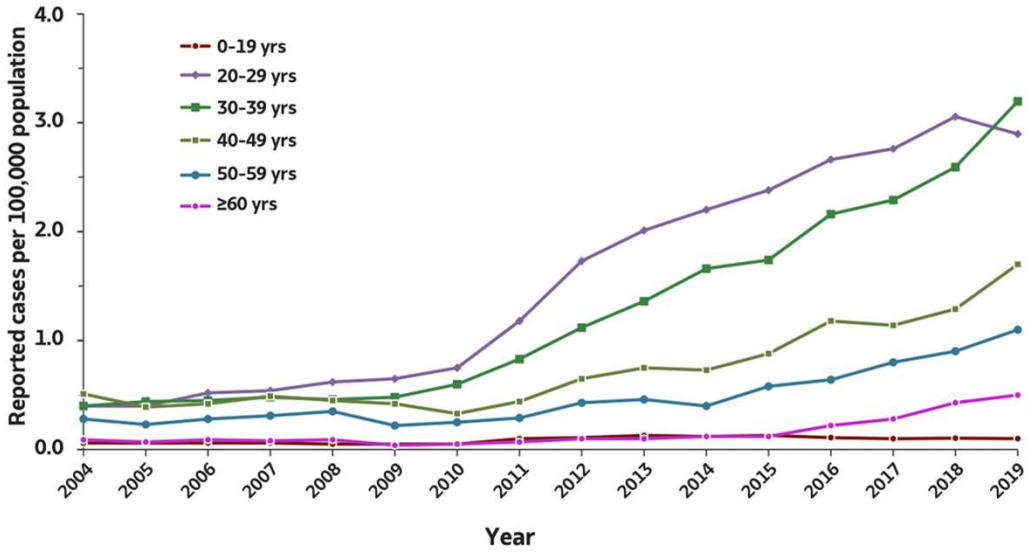


Status of US Hepatitis C & Opioid Epidemic:

- Rural areas especially impacted.

2019 VIRAL HEPATITIS SURVEILLANCE REPORT

Figure 3.4. Rates of reported acute hepatitis C virus infection, by age group — United States, 2004–2019



Age (years)	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
0–19	0.1	0.1	0.1	0.1	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
20–29	0.4	0.4	0.5	0.5	0.7	0.7	0.7	1.2	1.7	2.0	2.2	2.4	2.7	2.7	3.0	2.9
30–39	0.4	0.4	0.4	0.5	0.5	0.5	0.6	0.8	1.1	1.4	1.7	1.7	2.2	2.3	2.6	3.2
40–49	0.5	0.4	0.4	0.5	0.5	0.4	0.3	0.4	0.6	0.7	0.7	0.9	1.2	1.1	1.3	1.7
50–59	0.3	0.2	0.3	0.3	0.4	0.2	0.3	0.3	0.4	0.5	0.4	0.6	0.6	0.8	0.9	1.1
≥60	0.1	0.1	0.1	0.1	0.1	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.3	0.4	0.5

Source: CDC, National Notifiable Diseases Surveillance System.

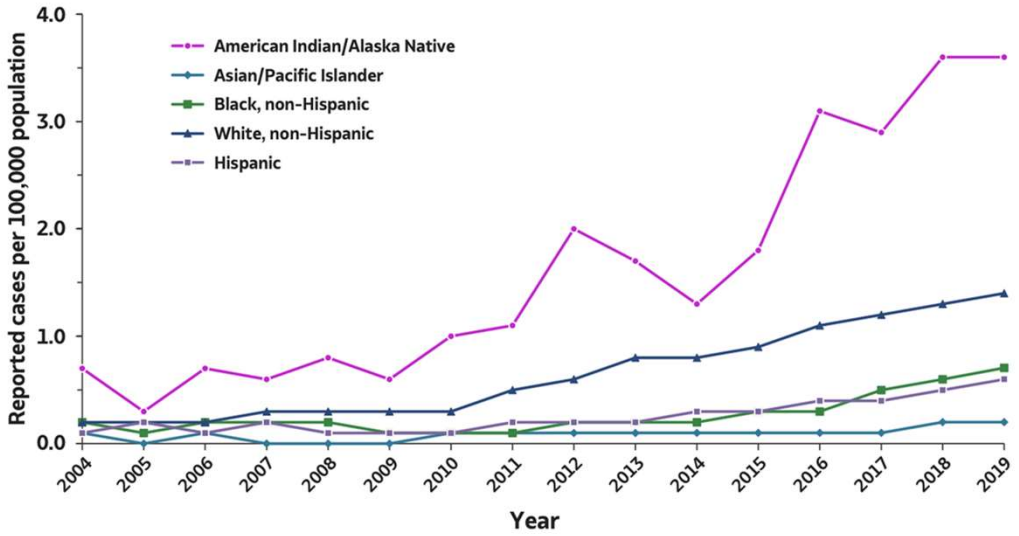
Status of US Hepatitis C epidemic: Age

- Younger ages affected

Status of US Hepatitis C epidemic: Race

2019 VIRAL HEPATITIS SURVEILLANCE REPORT

Figure 3.6. Rates of reported acute hepatitis C virus infection, by race/ethnicity — United States, 2004–2019



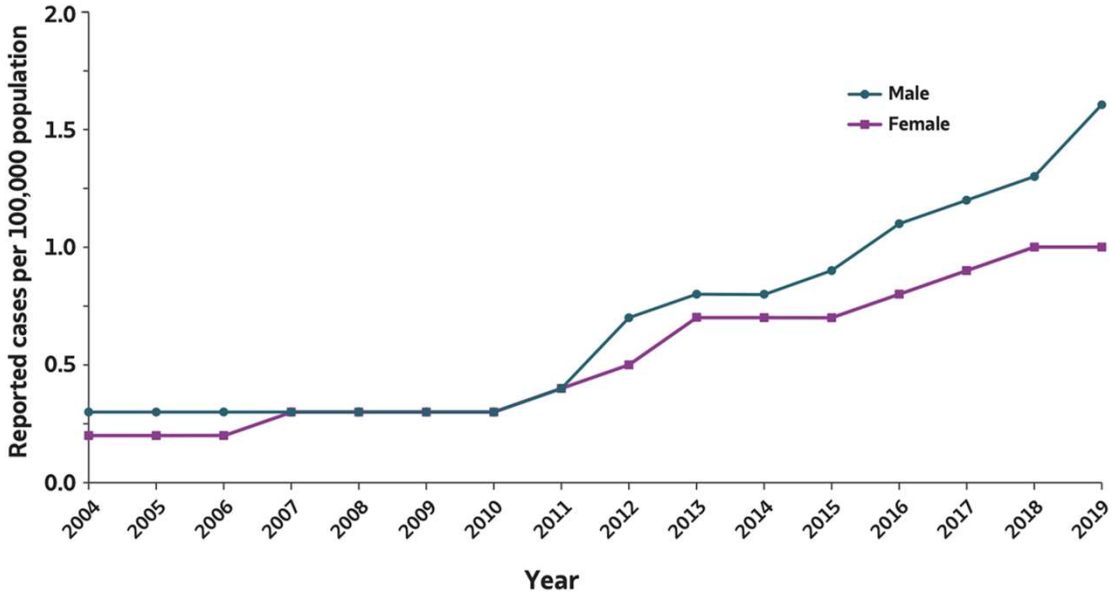
Race/Ethnicity	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
American Indian/ Alaska Native	0.7	0.3	0.7	0.6	0.8	0.6	1.0	1.1	2.0	1.7	1.3	1.8	3.1	2.9	3.6	3.6
Asian/ Pacific Islander	0.1	0.0	0.1	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2
Black, non-Hispanic	0.2	0.1	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.2	0.2	0.3	0.3	0.5	0.6	0.7
White, non-Hispanic	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.5	0.6	0.8	0.8	0.9	1.1	1.2	1.3	1.4
Hispanic	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.3	0.3	0.4	0.5	0.6

Source: CDC, National Notifiable Diseases Surveillance System.

Status of US Hepatitis C epidemic: Sex

2019 VIRAL HEPATITIS SURVEILLANCE REPORT

Figure 3.5. Rates of reported acute hepatitis C virus infection, by sex — United States, 2004–2019

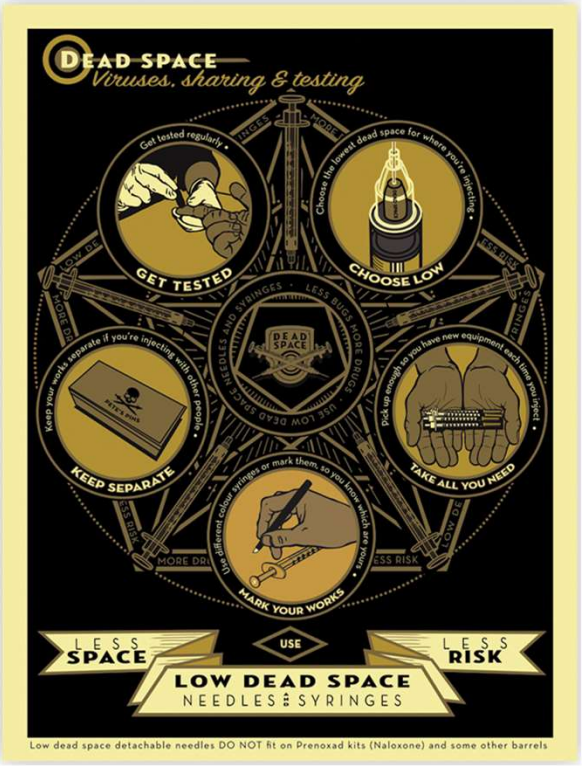


Sex	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Male	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.4	0.7	0.8	0.8	0.9	1.1	1.2	1.3	1.6
Female	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.4	0.5	0.7	0.7	0.7	0.8	0.9	1.0	1.0

Source: CDC, National Notifiable Diseases Surveillance System.

How to Prevent HCV Infection:

- Syringe exchange programs
- Suboxone
- Treatment programs
- Condoms
- Don’t share personal hygiene products: toothbrushes, razors, etc.
- Decreasing community HCV load by treating more patients



ALSO: This population is at risk for HIV infection **PrEP** - can reduce infection from needle sharing by ~70%

Why Cure HCV in a Primary Care Setting?

- Primary Care does most of the screening
- Established patient-provider relationship
- Treatment is now easier
- Low side effect profile of medications
- Decreasing barriers to care
- It can be a rewarding experience for patient and provider

Hepatitis C: Screening

Who to screen for hepatitis C:

- Anyone 18 yrs of age and up
- All pregnancies
- Current and former injection drug use
- Certain medical conditions: HIV, hemophilia, persistently abnormal ALT, anyone with a blood transfusion before 1992, children born to hep C positive mothers
- HIV positive sexually active patients should be screened annually
- No current CDC guidance on HIV negative men who have sex with men, but many major health centers have started screening annually

https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm

How to Screen for HCV:

Hepatitis C antibody test: **HCV ab**

- Positive tests will reflex to **hepatitis C RNA** = viral load.
  - If viral load is undetectable, pt does NOT have hepatitis C, but had it in the past and cleared the infection or was previously cured.
  - If viral load is detectable, pt DOES have hepatitis C. (viral load does not = level of illness)

- Acute vs. **Chronic -**

Acute - infection acquired in the past 6 months. Most acute infections lead to chronic. 15-25% of pt's can "self-cure."

Chronic - infection lasting more than 6 months. 75%-85% of pt's infected with hep C will become chronically infected.

Who should be offered HCV cure?

- **Everyone** with ***chronic*** HCV who has a reasonable life expectancy.
    - Anyone with end stage organ disease, pros vs cons of treatment should be discussed.
- A note about ***acute*** HCV:

Medical Management and Monitoring of Acute HCV Infection

Recommendations for Medical Management and Monitoring of Acute HCV Infection	
RECOMMENDED	RATING
After the initial diagnosis of acute HCV with viremia (defined as quantifiable RNA), HCV treatment should be initiated without awaiting spontaneous resolution.	I, B
Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.	I, C
Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to substance use.	I, B

Insurance coverage for Acute HCV Tx can be difficult to get.

https://www.hcvguidelines.org/evaluate/when-whom

Who should be offered HCV cure in a Primary Care Setting?

Treat in PCP Clinic:

- Adults with chronic hepatitis C (any genotype) who do not have cirrhosis and have not previously received hep C treatment.

Refer to hepatitis C specialist if:

- Prior hep C treatment
- Cirrhosis
- End stage renal disease (eGFR <30)
- HIV or Hep B sA**G** positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation
- **Low platelets**

https://www.hcvguidelines.org/treatment-naive/simplified-treatment

How to assess HCV in your office:

You've confirmed your patient has ***chronic*** hep C; (i.e. they've known they have hep C for >6 months - or - you have documentation of persistent hep C viral load for >6 months) now what?

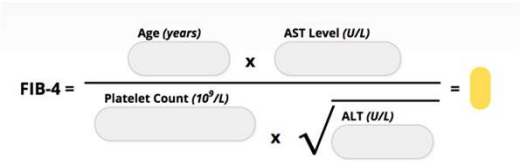
- Labs (if not previously collected. Example: known hep C positive recent transfer to your practice):
  - HCV RNA (if not collected in past year)
  - Hep C Genotype*
  - CMP (only need AST/ALT and eGFR)
  - CBC with platelets
  - Hep B serologies (consider adding hep A)
  - HIV 4th gen antibody/antigen
  - +/- pregnancy testing

    - *Caution:* Hepatic Panels (check with your lab to see if it includes the above labs)

*Genotype results are currently needed for insurance purposes

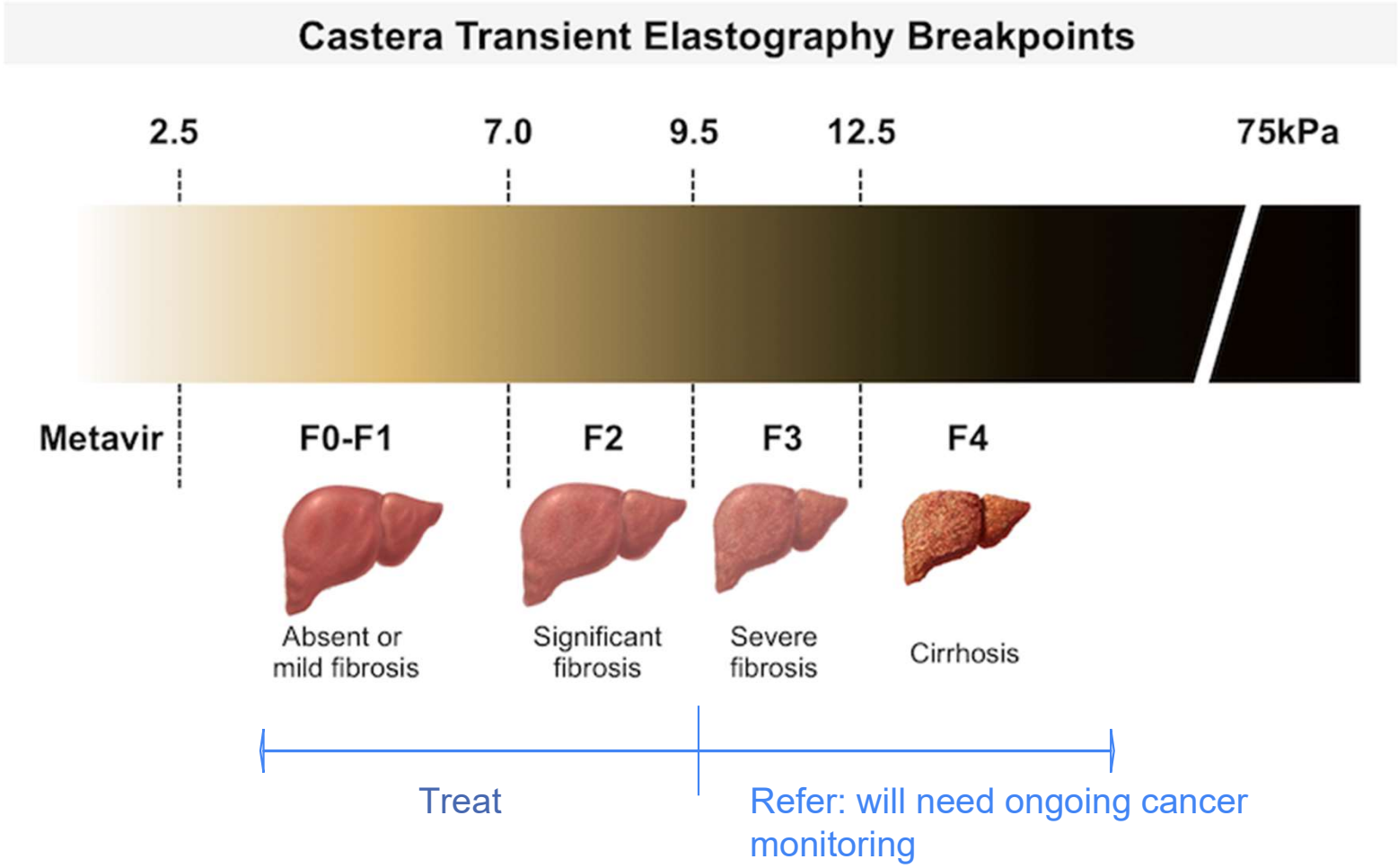
Determining Cirrhosis:

There are multiple ways to calculate this, but AASLD & IDSA recommend using the **FIB-4** score:



- No additional cost
- Patient does not need another appointment for imaging, i.e. FibroSure (biopsy no longer recommended)
- Threshold value of **<1.45** has a sensitive of 74% and a negative predictive value of 95% for excluding advanced fibrosis (F3-F4).
- If Fib4 is btw **1.45-3.25** = indeterminate and you will want to consider FibroScan (not accurate in heavy drinkers), but is not required per AASLD guidelines.
- Threshold value of **>3.25** has a positive predictive value for advanced fibrosis of 82% with a specificity of 98% in confirming cirrhosis. - We are NOT treating cirrhotic pt's in primary care, refer to specialist if >3.25.

Fibrosis: A quick detour



HCV Treatment:

	Mavyret: (glecaprevir-Pibrentasvir)	**Epclusa:** (Sofosbuvir-Valpatasvir)
Genotypes:	Pangenotypic	Pangenotypic
Dosing:	3 pills once a day (with food)	1 pill a day
Length of treatment:	8 wks	12 wks
Cure Rates:	Greater than 98%	Greater than 95%
Side Effects:	HA: 13%; Fatigue: 11%; Nausea 8%	HA: 22%; Fatigue: 15%; Nausea 9%; Asthenia 5%; Insomnia 5%
Cost	$26,000	$24,000
Interactions: Not complete list	Stop statin/Birth Control	Acid lowering agents

*I do not accept any money from pharmaceutical companies.

Treatment monitoring:

Monitoring patients on treatment:

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.
- 2 Visit protocol with 12 week SVR lab visit only

Note: Some providers like to see patients back at 4 wks, 8 wks, and then 12 wks after treatment is completed. If not virologically suppressed - refer to specialist.

Patient Counseling:

It's important for patients to understand their role in this important treatment option:

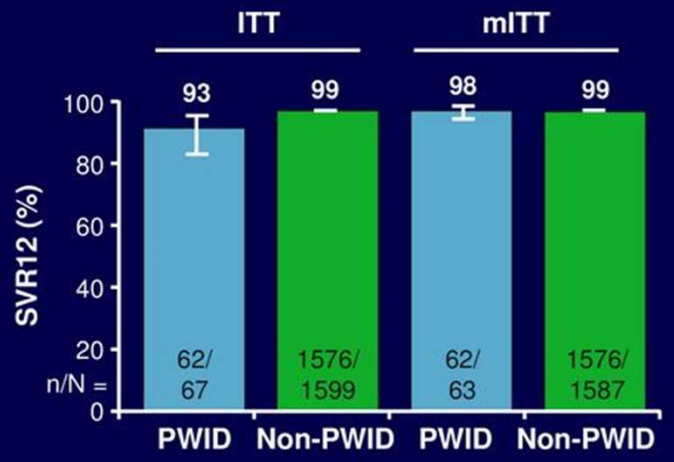
- ***Adherence**:* if not adherent pt may not cure hep C and treating in the future will be much more difficult.
- ***Hepatotoxic agents**:* encourage pt's to abstain or greatly reduce alcohol and other liver related toxins. Look for drug-to-drug interactions with pt's meds.
- ***Communication**:* reassure pt's that there are few side effects and medications are generally safe, but to reach out with any concerns before stopping treatment. Get active phone or other way of contacting patient.
- ***Follow-up**:* Pt's should be aware of when you want to see them back in office and what those visits will entail.
- ***Risk of future infection**:* unlike other infections, antibody response for hep C is not protective in the future and pt's can be re-infected.
- ***Contact testing**:* sexual partners, injection drug use partners, and close contacts should be tested.

What about HCV patients actively using drugs?

GLE/PIB in Pts With GT1-6 HCV and Recent Drug Use

- Pooled analysis from 6 phase III trials of GLE/PIB for 8 or 12 wks to evaluate outcomes in pts with recent IDU (self reported ≤ 12 mos before screening and/or positive urine drug screen)
  - Non-PWID: n = 1599; PWID: n = 67
  - ≥ 90% adherence: 98% in PWIDs

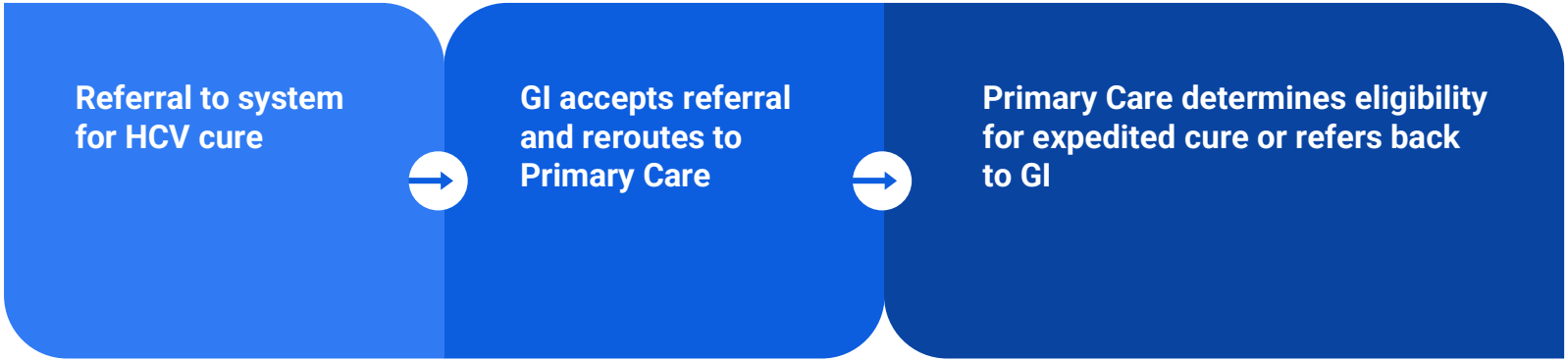
SVR12 by GT (mITT), %	PWID	Non-PWID
GT1	100	99
GT2	100	99
GT3	97	98
GT4-6	100	99



Foster GR, et al. AASLD 2017. Abstract 1182.

Slide credit: clinicaloptions.com

PA Led Expedited Cure Protocol:

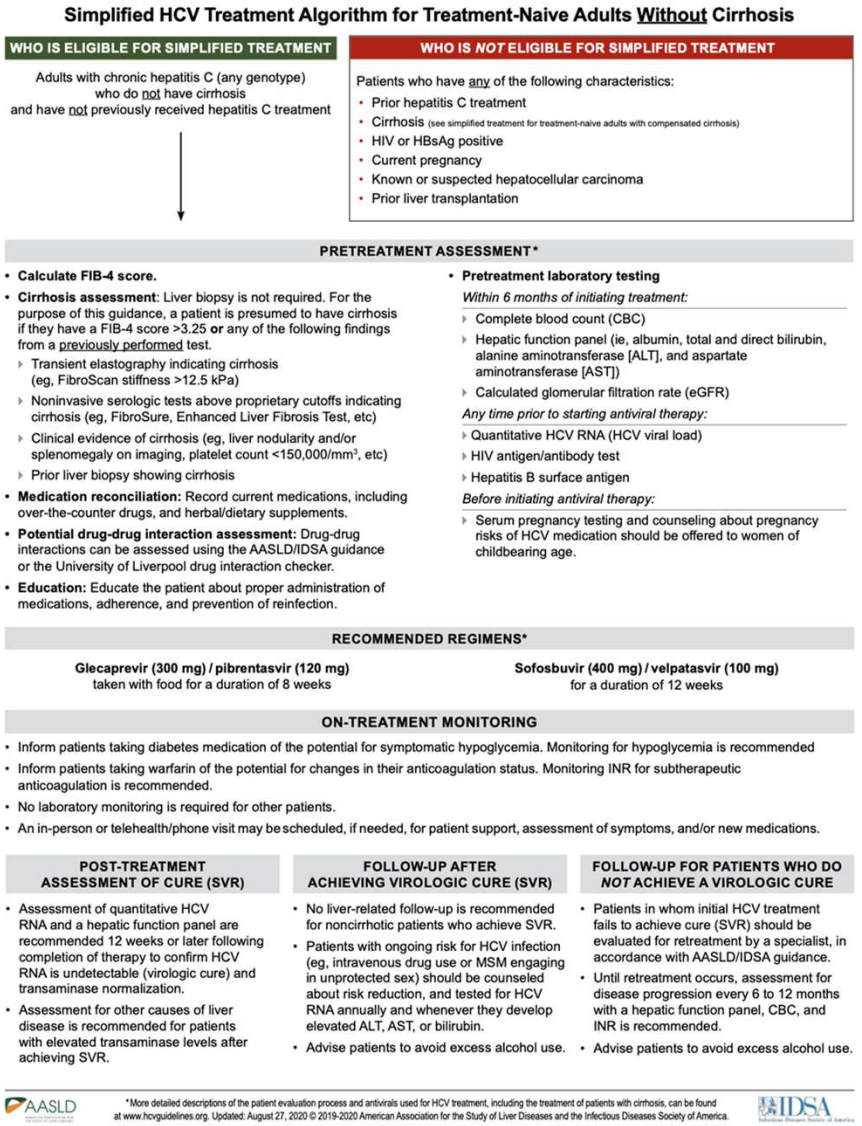


Total patients seen for HCV Cure in 2 years (Including in-office visits and telemedicine visits):

- Total Patients: **94**
  - **39 = Cured**
  - 16 = Finished treatment and waiting 3 month post treatment viral loads
  - 10 = Currently Treating
  - 10 = “Pretreatment” – needing to finish labs/imaging or not eligible due to pregnancy or acute HCV status.
  - 12 = Referred back to GI as they fell out of our expedited program
  - 1 = Referred to Oncology after detecting liver cancer
  - 6 = Lost to follow up

AASLD & IDSA Expedited HCV Treatment Guidelines for non-cirrhotic patients:

download available: https://www.hcvguidelines.org/treatment-naive/simplified-treatment



Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without 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

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

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

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: 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
- **Medication reconciliation:** Record current medications, including over-the-counter drugs, and herbal/dietary supplements.
- **Potential drug-drug interaction assessment:** Drug-drug interactions can be assessed using the AASLD/IDSA guidance or the University of Liverpool drug interaction checker.
- **Education:** Educate the patient about proper administration of medications, adherence, and prevention of reinfection.
- **Pretreatment laboratory testing**

  Within 6 months of initiating treatment:
  - Complete blood count (CBC)
  - Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
  - Calculated glomerular filtration rate (eGFR)

  Any time prior to starting antiviral therapy:
  - Quantitative HCV RNA (HCV viral load)
  - HIV antigen/antibody test
  - Hepatitis B surface antigen

  Before initiating antiviral therapy:
  - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg)
taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg)
for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth/phone visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Assessment of quantitative HCV RNA and a hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.
- Advise patients to avoid excess alcohol use.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Patients in whom initial HCV treatment fails to achieve cure (SVR) should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA guidance.
- Until retreatment occurs, assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and INR is recommended.
- Advise patients to avoid excess alcohol use.

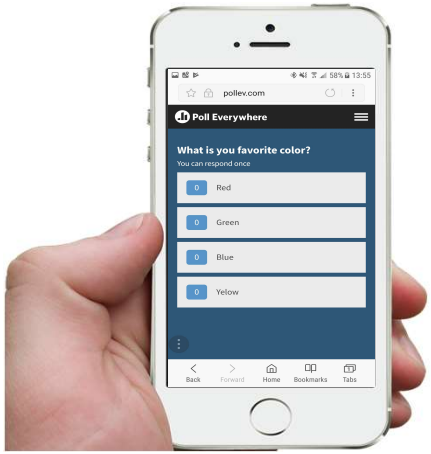
AASLD

*More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at www.hcvguidelines.org. Updated: August 27, 2020 © 2019-2020 American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.

IDSA

Answering the Poll Questions

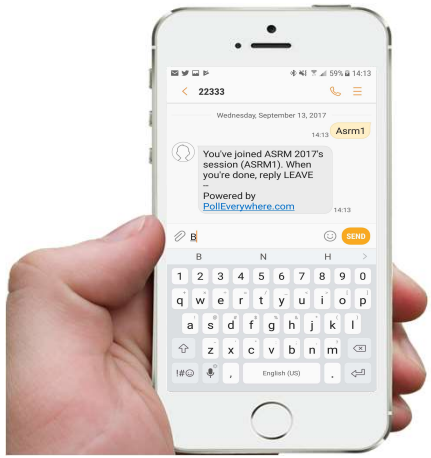
Attendees can participate by answering polling questions during the event.



Web Access

To do so, please use your own mobile device and go to **pollev.com/aapawab1**

Attendees do not need to log in to answer the questions.



Text Access

To do so, please use your own mobile device and go to the **Text: aapawab1 to the number 22333**

You will receive a confirmation message that you have joined the session. Then simply respond with the letter of your choice for each question.

If you leave and go to another room text **LEAVE** to exit the session then test the new keyword for the new room.

Questions 1:

Your patient's blood work is back showing: HCV Ab "reactive" and HCV RNA "undetectable". What is your patients hepatitis C status?

A. Active hepatitis C infection

B. Historic hepatitis C infection, but not currently infected

When poll is active, respond at **pollev.com/aapawab1**

Text **AAPAWAB1** to **22333** once to join

Question #1: Your patient's blood work is back showing: HCV Ab "reactive" and HCV RNA "undetectable". What is your patients hepatitis C status?

A. Active hepatitis C infection

B. Historic hepatitis C infection, but not currently infected

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

Answer 1:

B: Historic hepatitis C infection, but not currently infected

Questions 2:

Which patient is eligible for expedited HCV cure?

A. HIV and HCV co-infected patients
B. HCV positive pregnant patient
C. A patient who was treated unsuccessfully in the past
D. A HCV positive patient without HIV, or hep B, with normal kidney function, no cirrhosis and no HCV treatment history

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Question #2: Which patient is eligible for expedited HCV cure?

A. HIV and HCV co-infected patients

B. HCV positive pregnant patient

C. A patient who was treated unsuccessfully in the past

D. A HCV positive patient without HIV, or hep B, with normal kidney function, no cirrhosis and no HCV treatment history

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Answer 2:

D: A HCV positive patient without HIV, or hep B, with normal kidney function, no cirrhosis and no HCV treatment history

Questions 3:

Which behavior has the HIGHEST risk of HCV transmission?

A. Condomless sexual activity

B. Receiving a tattoo

C. Sharing injection drug equipment

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Question #3: Which behavior has the HIGHEST risk of HCV transmission?

A. Condomless sexual activity

B. Receiving a tattoo

C. Sharing injection drug equipment

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Answer 3:

C: Sharing injection drug equipment

Additional Training & References:

Hepatitis C:

- https://www.hepatitisc.uw.edu/ (free CME)
- https://www.hcvguidelines.org/ (expedited treatment guide)
- https://www.cdc.gov/hepatitis/hcv/index.htm
- https://liverfoundation.org/medical-professionals/

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Thank you!