

Viral Hepatitis and HIV

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HIV Review

HIV Review

- HIV is the Human Immunodeficiency Virus
 - HIV is a retrovirus that attacks the body's immune system
- If left untreated, infection with HIV can lead to Acquired Immunodeficiency Syndrome (AIDS)
- There is no cure for HIV/AIDS, but medications can control the infection and prevent progression of the disease

HIV Review

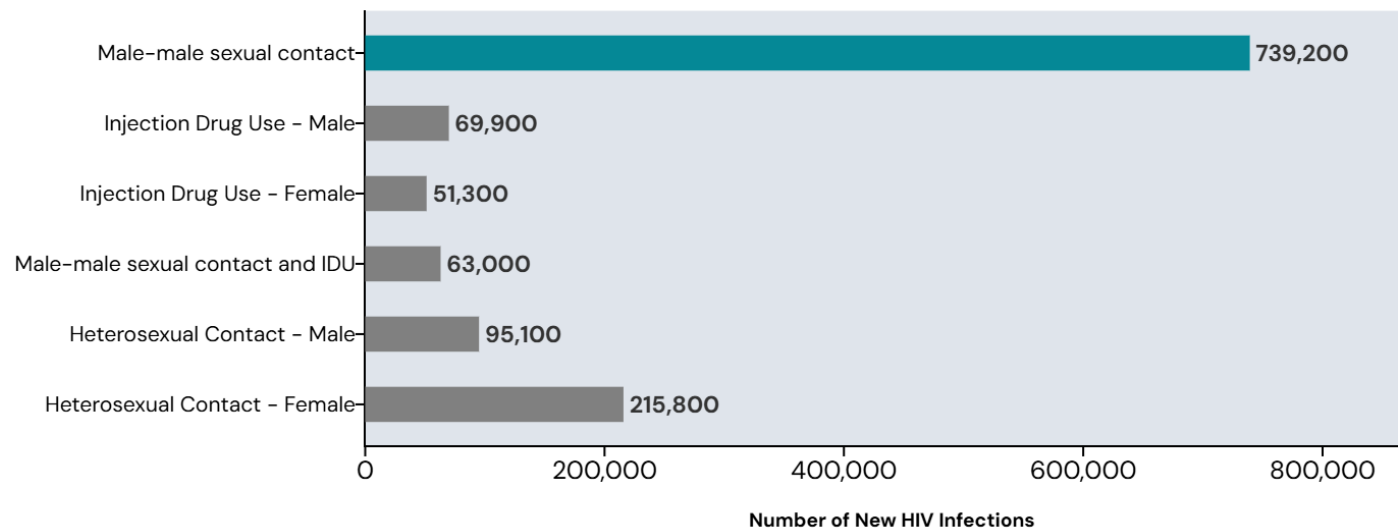
- HIV is transmitted by six main bodily fluids

1. Semen
2. Pre-ejaculation fluid (pre-cum)
3. Vaginal/cervical fluid
4. Rectal/anal fluids
5. Blood
6. Breast milk

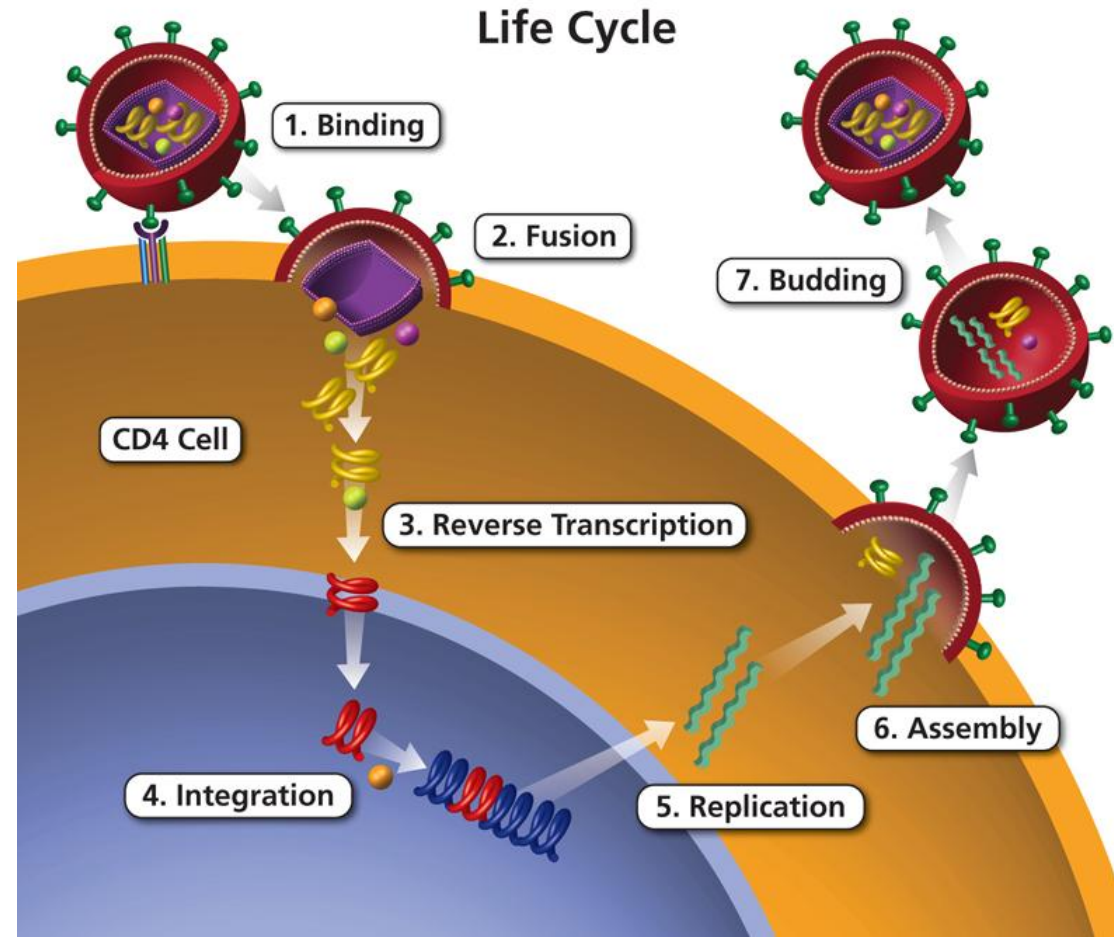


HIV Review

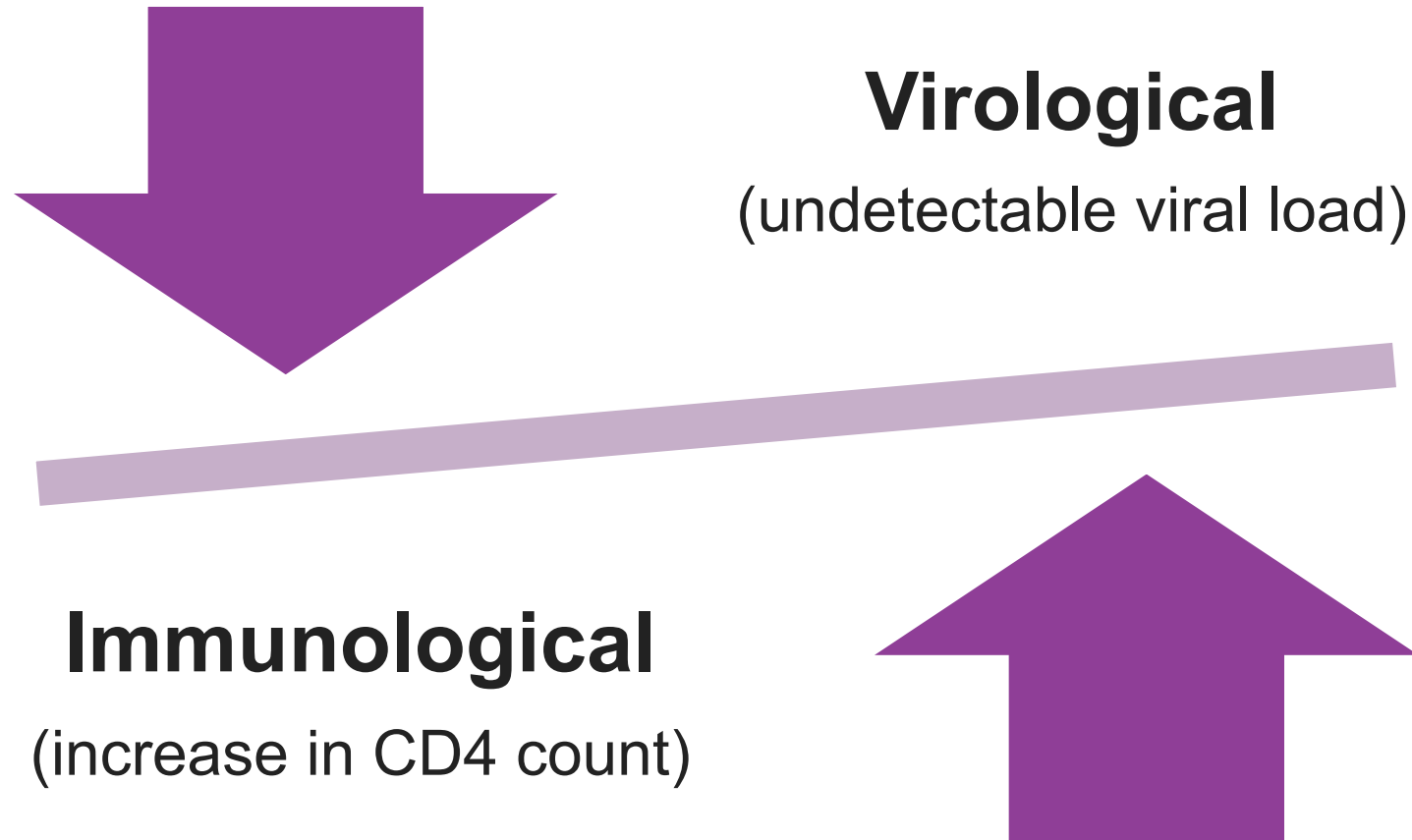
- HIV transmission can occur via:
 - Unprotected sex
 - Sharing needles or injection equipment
 - Perinatal (during pregnancy, birth, or breastfeeding)
 - Occupational exposure (i.e. needlestick injury)



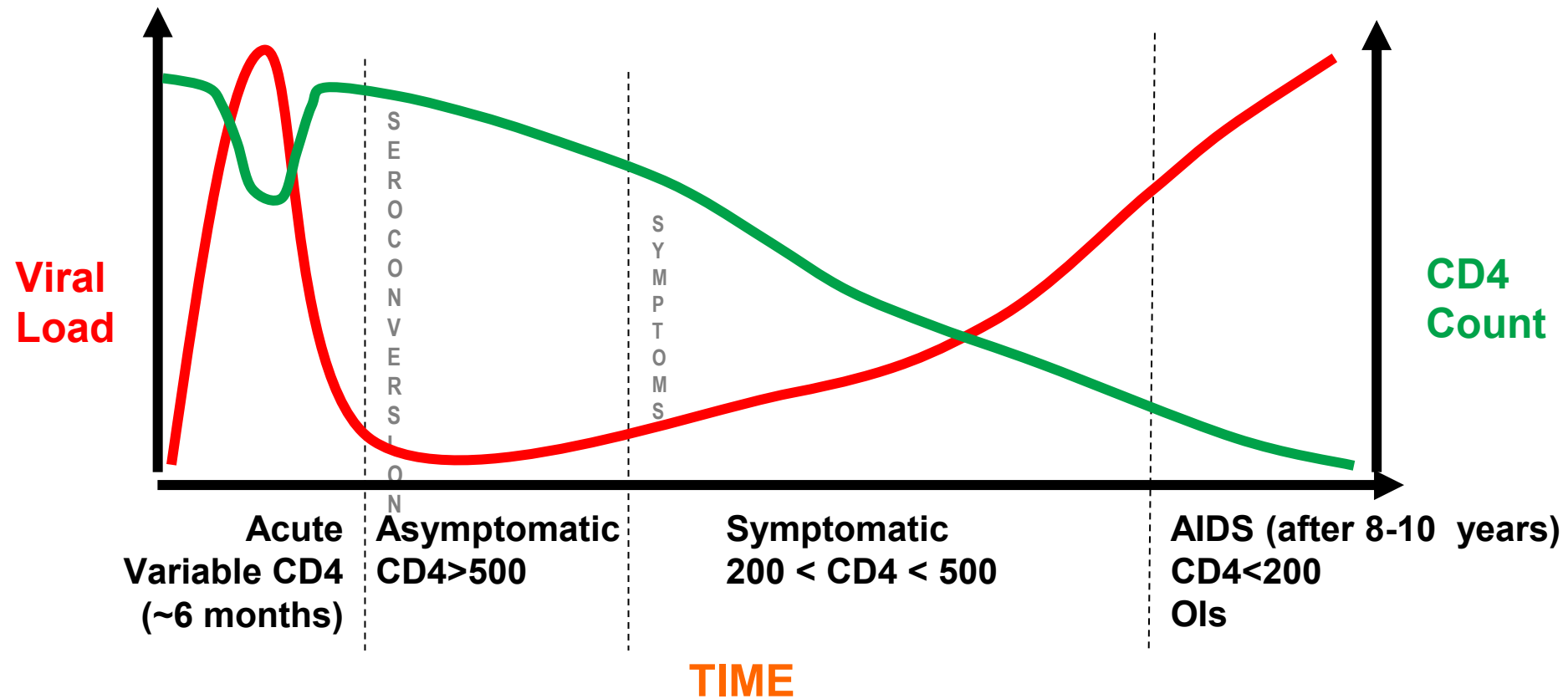
HIV Review



Goals of HIV Treatment



Progression of HIV Infection



HIV & Hepatitis

- HIV and hepatitis are both conditions caused by a virus that can lead to severe health issues if left untreated.

	HIV	Hepatitis A	Hepatitis B	Hepatitis C
Can be transmitted through sex?	Yes	Sometimes	Yes	Sometimes
Cure available?	No	N/A. self-limiting	No, but may be self-limiting	Yes
ART effective?	Yes	No	Some	No
Cells affected?	CD4 cells	Hepatocytes	Hepatocytes	Hepatocytes
Vaccine?	No	Yes	Yes	No

HIV & Hepatitis

- Approximately 10% of people with HIV worldwide are infected with hepatitis B
- Approximately 33% of people with HIV are coinfecting with either hepatitis B or hepatitis C virus.
- HIV does not cause hepatitis but there is a link through damage to the liver
 - Hepatitis can also cause HIV to advance faster in the body
- People with HIV who have underlying liver disease are at risk for severe disease from hepatitis A virus (HAV) infection.
- Hepatitis B virus (HBV) or hepatitis C virus (HCV) infection may affect the management of HIV infection.

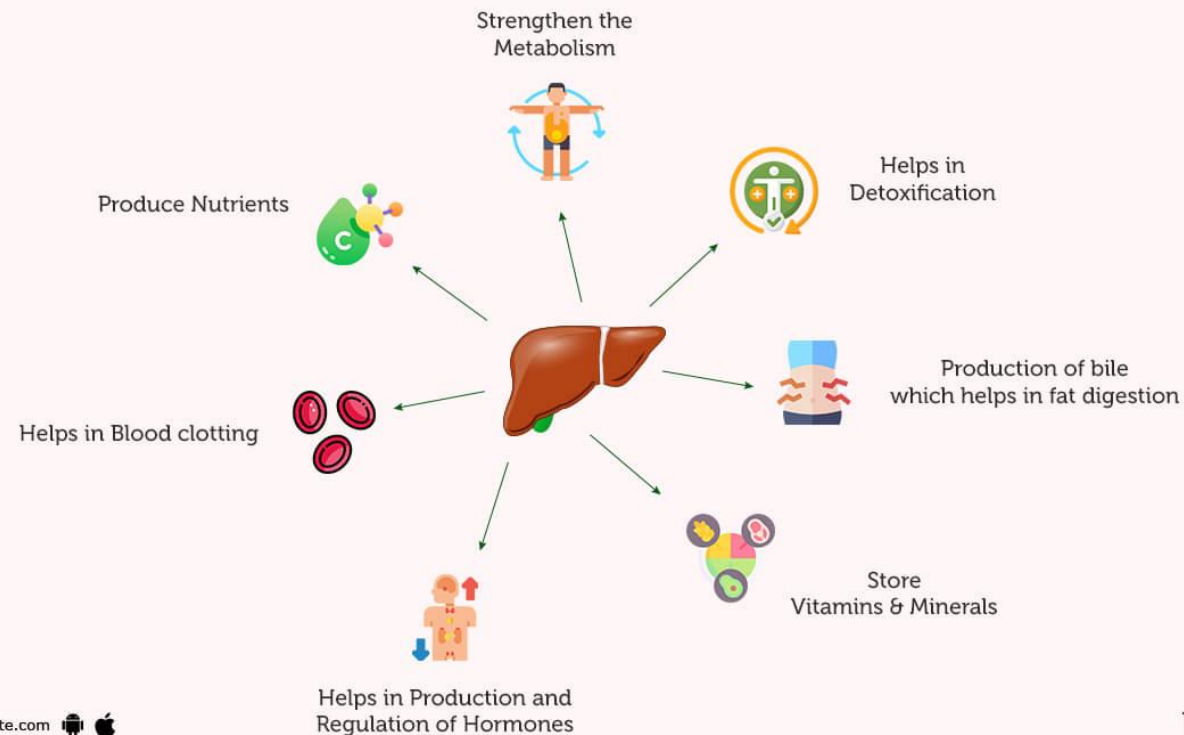
Hepatitis

Hepatitis

- Inflammation of the liver
- Necrosis of hepatocytes
- Detected clinically by elevations in serum liver transaminases (ALT > AST)
- Other liver tests may be normal or abnormal depending upon the severity of the hepatocyte necrosis.

Understanding the Liver

Function of Liver



How Hepatitis Affects the Liver

- **Accumulation of Toxins:** Inflammation can impair the liver's ability to detoxify, leading to a buildup of harmful substances in the body.
- **Digestive Problems:** Disruption in bile production can lead to digestive issues and malabsorption of nutrients.
- **Blood Clotting Issues:** Liver inflammation can affect the production of clotting factors, increasing the risk of bleeding and bruising.
- **Immune Response:** The liver's role in immune function can be compromised, potentially affecting the body's ability to fight infections.

Hepatitis: Acute Versus Chronic

- Acute hepatitis:
 - Acute elevation in serum liver transaminases
 - Resolves spontaneously within 1-3 months
 - Viral etiologies, drug, ischemia
- Chronic hepatitis:
 - Persistent elevation in serum liver transaminases for greater than 6 months
 - Viral and non-viral etiologies
 - May progress to cirrhosis

Hepatitis: Viral Etiologies

- Most common cause of acute and chronic hepatitis
- Hepatitis viruses:
 - A → E
 - Resolve spontaneously
 - Develop chronicity
- Non-hepatitis viruses:
 - Causes hepatitis as part of systemic infection
 - Can cause severe acute liver injury
 - Do not lead to chronic liver injury

Types of Viral Hepatitis

- Hepatitis A
 - Transmitted through contaminated food and water. It often causes an acute infection.
- Hepatitis B
 - Spread through contact with infectious body fluids, such as blood and semen. It can cause both acute and chronic infections.
- Hepatitis C
 - Primarily spread through blood-to-blood contact. It often leads to chronic infection and can result in liver damage over time.
- Hepatitis D
 - Occurs only in those infected with Hepatitis B. It can worsen the severity of Hepatitis B infection.
- Hepatitis E
 - Typically transmitted through contaminated water, similar to Hepatitis A. It usually causes an acute infection.

Hepatitis Transmission Methods

Viral Hepatitis Type	Fecal-oral transmission and food contamination	Blood and body fluid contact	Close personal contact	Saliva and infected droplets, such as from coughing
A	✓	✓	✓	✗
B	✗	✓	✓	✗
C	✗	✓	✗	✗
D	✗	✓	✗	✗
E	✓	rarely	rarely	✗

healthgrades.

Hepatitis A

Management Hepatitis A

- There are no medications to treat or cure hepatitis A
- Hepatitis A is generally a self-limiting infection, meaning that most people recover without the need for specific antiviral treatment.
 - Supportive care
 - Symptom management
 - Monitoring and Follow-Up
 - Preventive measures (to prevent spread to others)

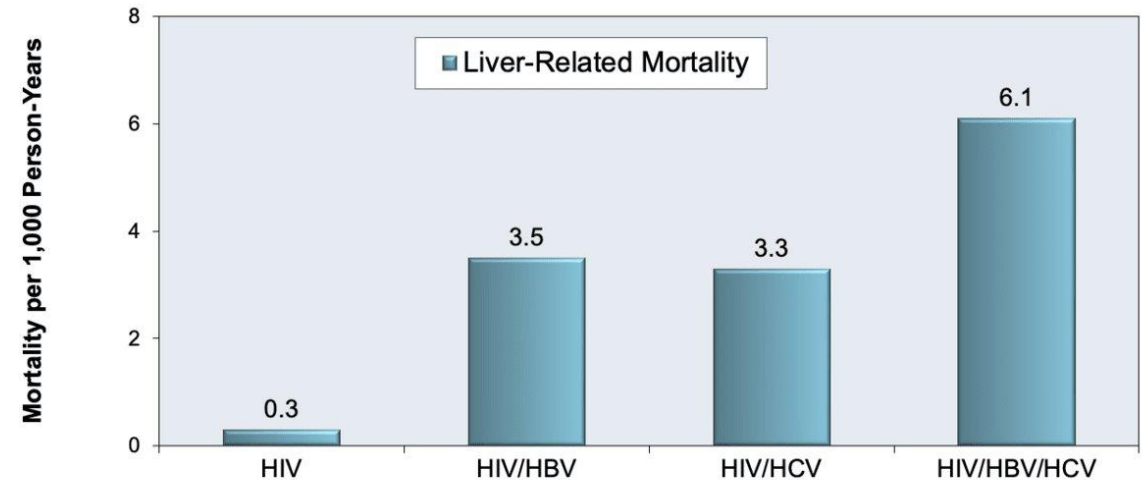
Vaccination for Hepatitis A (in PLWH)

Vaccine	Dose and Route	Schedule
Hepatitis A Vaccines		
<i>Havrix</i>	1440 ELISA Units (IM)	2 doses given at 0, 6-12 months
<i>Vaqta</i>	50 U (IM)	2 doses given at 0, 6-18 months
Combined Hepatitis A and B Vaccine		
<i>Twinrix</i>	<i>Havrix</i> 1440 ELISA Units plus <i>Engerix</i> 20 µg (IM)	Standard: 3 doses given at 0, 1, 6 months
		*Accelerated: Days 0, 7, 21-30 and 12 months
*For travelers, consider accelerated dosing		

Hepatitis B

HIV and Hepatitis B Coinfection

- About 10% of people with HIV in the United States are coinfecting with HBV
- People with HIV are at greater risk for complications and death from HBV infection.
- All people with HIV are recommended to be tested for HBV.



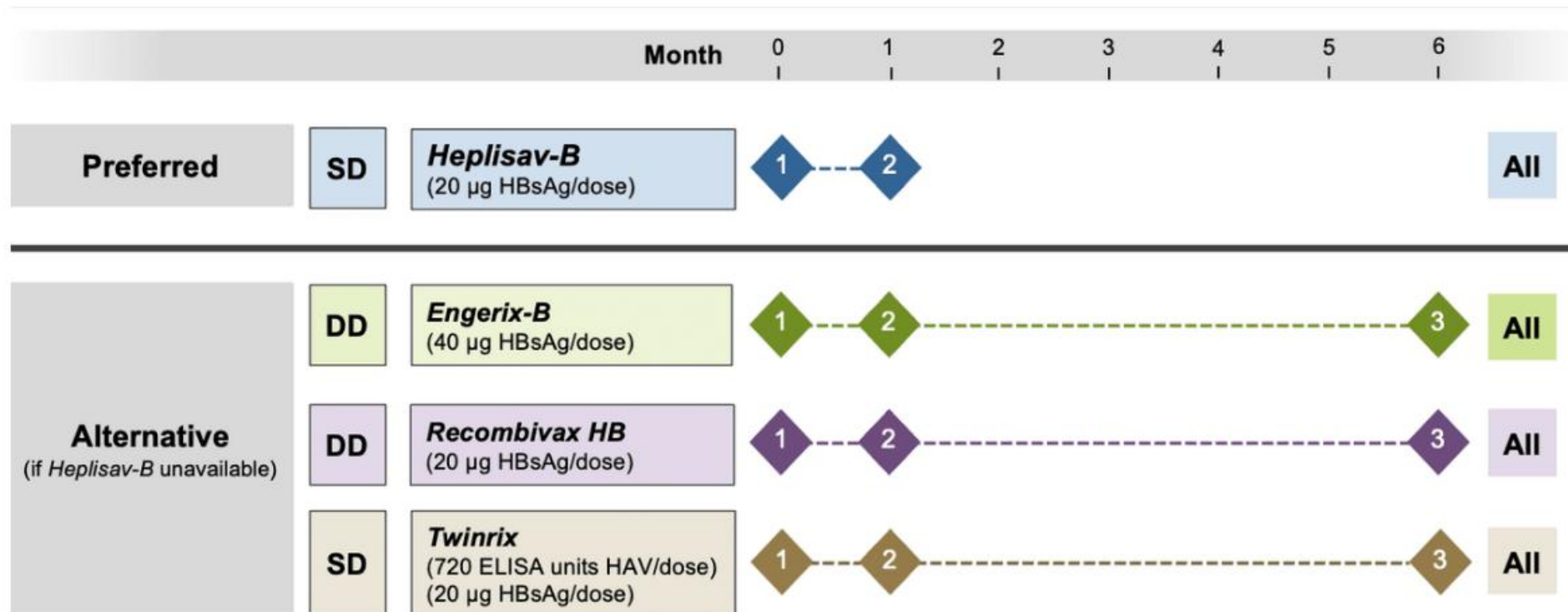
Treatment of Hep B (in PWH)

- Several HIV ART treatments also treat hepatitis B!
 - Tenofovir (TAF or TDF)
 - Emtricitabine
 - Lamivudine
- At least **two** drugs with dual coverage are recommended in co-infection
 - Dovato (DTG/3TC) or Triumeq (DTG/ABC/3TC) would **not** be appropriate
- If neither TAF nor TDF can be used (e.g. CrCl <30), then can add entecavir (Baraclude) onto another regimen containing 3TC or FTC

Monitoring Response to Treatment

- Monitoring the virologic response to HBV therapy should consist of checking HBV DNA levels every 3 to 6 months
- The HBV DNA levels accurately predict response to therapy, and regular monitoring during therapy is recommended
- Once the HBV levels become undetectable, the frequency of monitoring HBV DNA levels can extend to every 6 months

Hepatitis B Vaccination



Post-Vaccine Antibody Testing

- Post-vaccine testing for antibody to hepatitis B surface antigen (anti-HBs) should be performed 4 weeks after completing the vaccine series
 - A titer of at least 10 mIU/mL is considered protective
- Individuals who have a postvaccine anti-HB less than 10 mIU/mL are considered vaccine non-responders

Hepatitis C

Prevalence of Hepatitis C

- There were 4,966 new cases of acute hepatitis C reported in 2023
- There were a total 69,000 estimated acute HCV infections during 2023 after adjusting for underreporting.

Case rates

1.5 The rate of acute hepatitis C was **1.5** reported cases per 100,000 population, remaining relatively stable since 2021.

Total cases

1.7x The number of acute hepatitis C cases in 2023 was **1.7 times** as high as in 2016.

Case rates by age

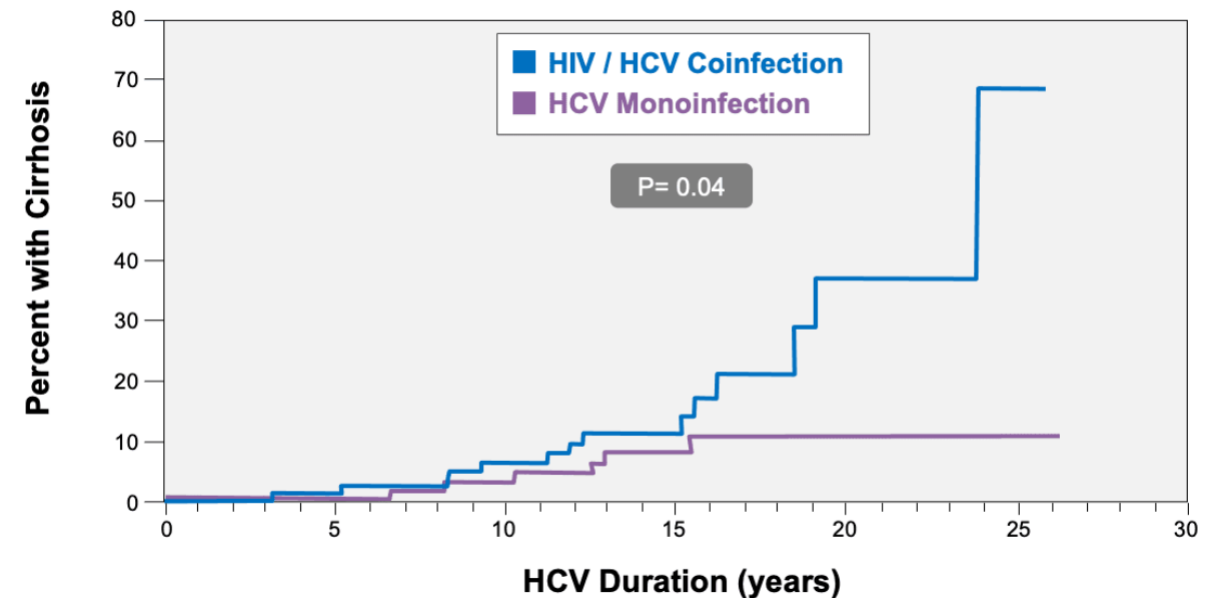
30–39 Persons aged 30–39 years had the highest rates of acute hepatitis C.

Case rates by demographics

2.3x The rate of acute hepatitis C is higher among non-Hispanic American Indian/Alaska Native persons than any other group, and is **2.3 times** as high as the rate among non-Hispanic White persons (the largest demographic in the United States).

Hepatitis C and HIV Coinfection

- In the United States, approximately 15-30% of people with HIV have HCV coinfection
- Coinfection with HIV can accelerate the progression of hepatic fibrosis and contribute to a more aggressive course of liver disease among persons with untreated HCV



Screening for Hepatitis C

- Universal Hepatitis C screening:
 - CDC recommends universal hepatitis C screening for all adults 18 and older and all pregnant people during each pregnancy.
- CDC recommends testing people in certain high-risk groups more frequently.
 - People who currently inject drugs and share needles, syringes, or other drug preparation equipment.
 - People with selected medical conditions, including people who receive maintenance hemodialysis.

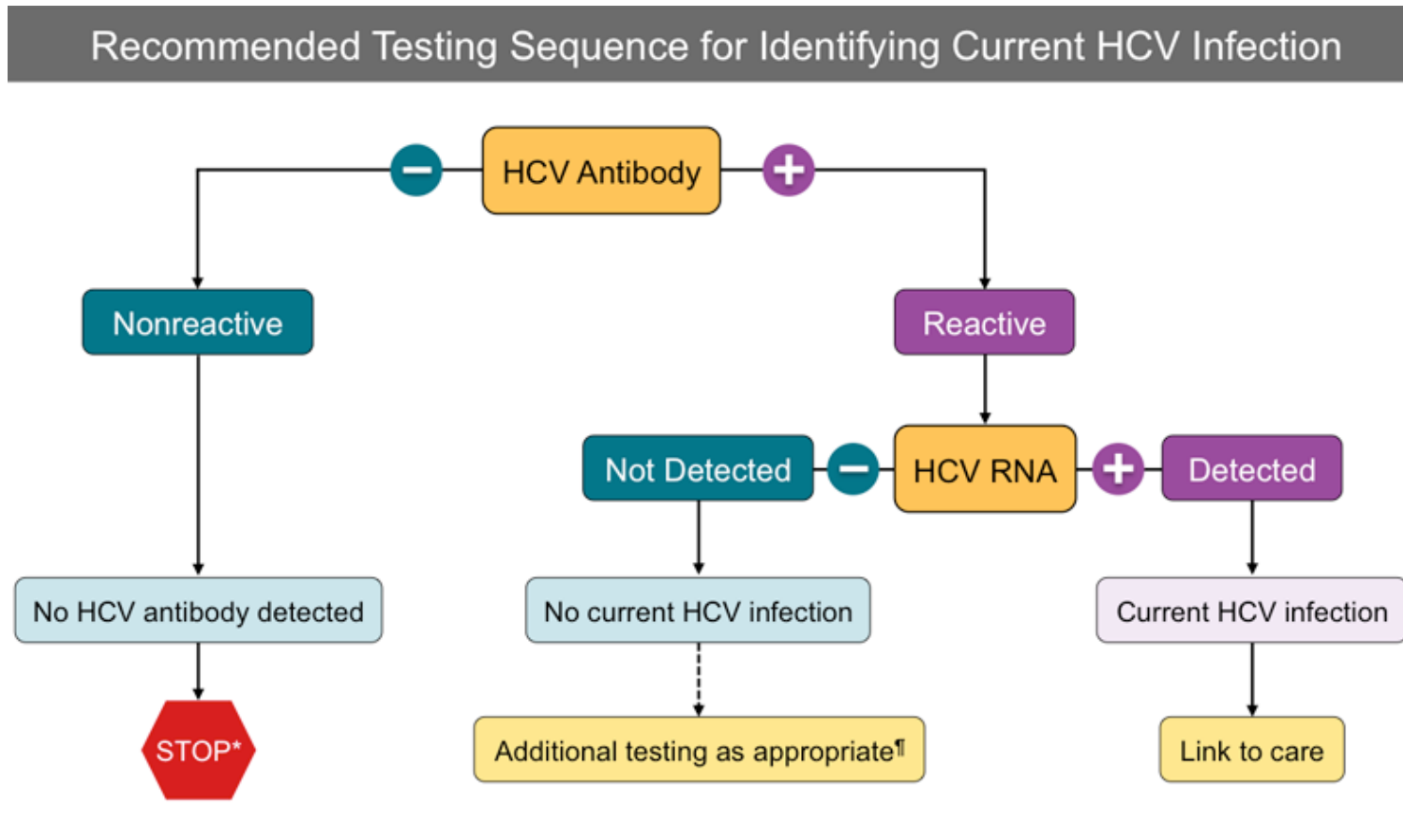
Screening for Hepatitis C in people with HIV

- All people with HIV should receive routine screening at entry to care
- People with HIV with highest risk of acquiring HCV (persons who inject drugs and men who have sex with men) should have yearly HCV testing or more frequent if indicated.

Hepatitis C Tests

- Antibody tests: A reactive results indicates infection with HCV at some point in time, but it does not differentiate resolved HCV infection from chronic (active) HCV infection.
- HCV RNA tests: A nucleic acid amplification test (NAAT) that can be used to distinguish between chronic HCV and resolved HCV.

Screening for Hepatitis C Algorithm

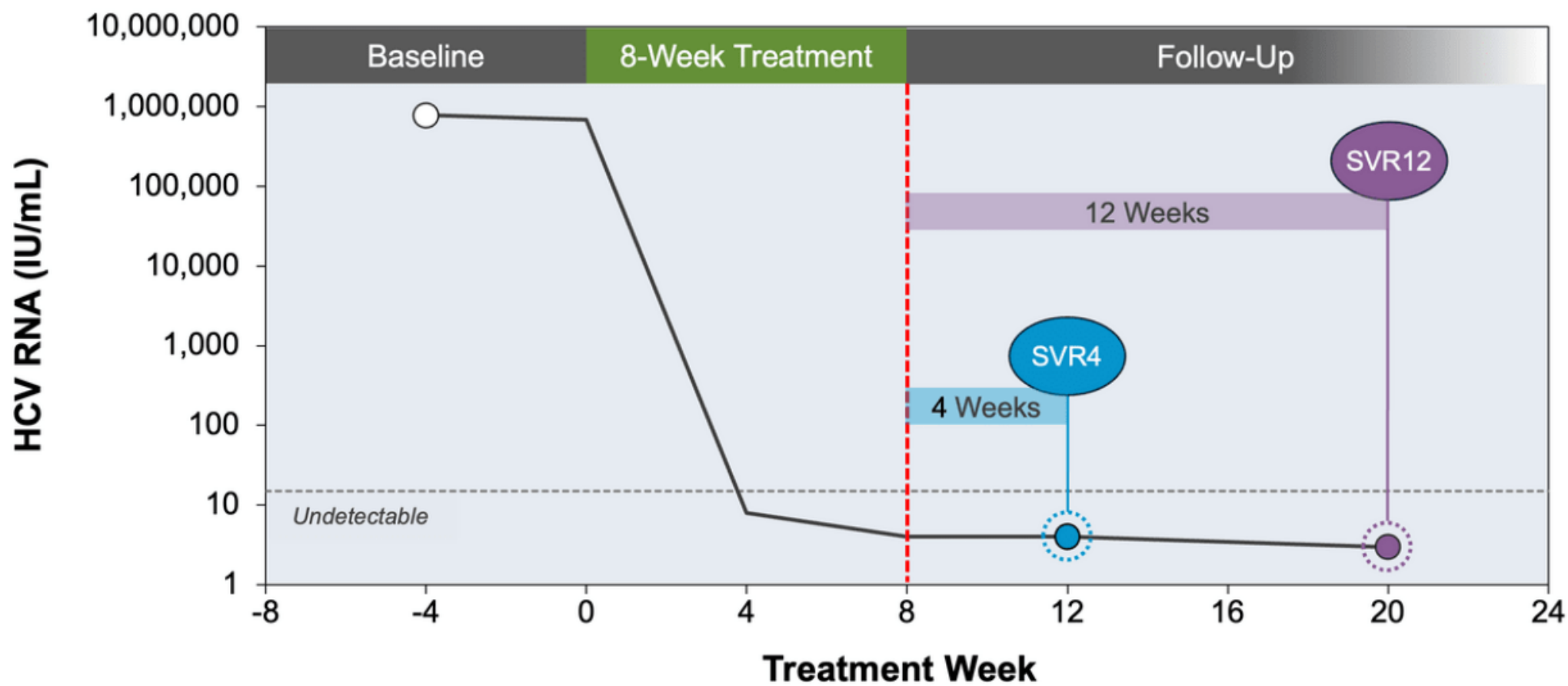


Screening for Hepatitis C Algorithm

HCV Antibody	HCV RNA	Interpretation	Further Action / Counseling
Positive	Positive	Current, active HCV infection	Provide appropriate counseling regarding active HCV infection and link the individual to treatment
Positive	Negative	- Prior exposure to HCV; no current HCV infection. - Consistent with spontaneous clearance or prior HCV treatment.	Individual remains susceptible to HCV. No linkage to care required.
Negative	Positive	- Acute HCV infection. - HCV likely acquired in the past 3 months.	Provide appropriate counseling regarding active HCV infection and link individual to treatment.
Negative	Negative	No HCV infection.	Individual remain susceptible to HCV. No linkage to care required

Treatment of HCV (in people with HIV)

- The goals for treating persons with chronic hepatitis C virus (HCV) are threefold:
 - (1) eradicate HCV
 - (2) improve HCV-related health outcomes and survival
 - (3) reduce transmission of HCV to others
- The appropriate use of current direct-acting antiviral (DAA) medications can cure chronic Hepatitis C in more than 95% of cases
 - The AASLD-IDSA HCV Guidance recommends against treating persons with a short life expectancy that cannot be improved by HCV treatment, liver transplantation, or another directed therapy.
 - Nearly every other case should be treated!



Treatment of Hep C (in people with HIV)

- Antiretroviral treatment for HIV may slow the progression of HCV-related liver disease and reduce the risk of liver-related morbidity.
- Treatment of HIV with antiretroviral therapy should be initiated for all persons with HIV and HCV coinfection, regardless of the CD4 cell count and fibrosis stage.
- If treatment for both HIV and HCV is indicated, the selection of the treatment regimens should consider potential drug interactions Treatment of HCV with DAAs should not be withheld solely based on a perceived lack of adherence or due to untreated HIV infection

Simplified Treatment of HCV (in PWH)

- The AASLD-IDSA HCV Guidance recommends using the same general approach for treating HCV in persons with HIV coinfection as with HCV monoinfection, but notes the importance of recognizing and managing potential drug interactions between HCV medications and HIV antiretroviral medications
- Persons with HIV who are treatment naïve and otherwise meet clinical criteria are also eligible for the simplified treatment approach

Simplified HCV Treatment Approach

- The simplified HCV treatment approach includes recommendations for people without cirrhosis and those with compensated cirrhosis
- PLWH are not excluded from this approach
- There are four main components of simplified HCV treatment
 - Initial criteria
 - Baseline evaluation
 - Pangenotypic regimen options
 - Treatment related monitoring

Criteria for Simplified Treatment

- Characteristics of people with HIV for whom simplified HCV treatment is **NOT** recommended:
 - Prior HCV treatment
 - Decompensated cirrhosis
 - TDF containing regimens with GFR < 60 mL/min
 - On efavirenz, etravirine, nevirapine, or boosted HIV-1 protease inhibitors
 - Untreated Chronic HBV infection
 - Pregnancy

HBV/HCV

- Because HBV reactivation can occur during treatment for HCV with direct-acting antivirals in the absence of anti-HBV therapy, all people with HIV/HBV coinfection who will be treated for HCV infection should be on HBV-active antiretroviral therapy at the time of HCV treatment initiation

Baseline Evaluation

- Routine labs: CBC, CMP (SCr, GFR, ALT, AST, total bilirubin, direct bilirubin, albumin), HCV RNA
- Hepatitis B surface antigen
- Initial fibrosis staging with FIB-4
- Medication and drug interaction review
- HCV genotype required if cirrhosis present

FIB-4 Score

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

- <1.45 has a negative predictive value of 90% for advanced fibrosis
- >3.25 has a 97% specificity and 65% predictive value for advanced fibrosis

Simplified treatment without cirrhosis

Table 1. Simplified HCV Treatment Regimens in Adults with HIV: Adult and Adolescent OI Guidelines

Treatment-Naïve Patients Without Cirrhosis

- Glecaprevir-pibrentasvir (100 mg/40 mg tablet): three tablets daily for 8 weeks (AI), or
- Sofosbuvir-velpatasvir (400 mg/100 mg tablet): one tablet daily for 12 weeks (AI)

Simplified treatment with compensated cirrhosis

Treatment-Naïve Patients with Compensated Cirrhosis	
HCV Genotypes 1, 2, 4, 5, 6	
Preferred Therapy	
- Glecaprevir-pibrentasvir (100 mg/40 mg tablet): three tablets daily for 8 weeks (AIII), or - Sofosbuvir-velpatasvir (400 mg/100 mg tablet): one tablet daily for 12 weeks (AI)	
Alternative Therapy	
Glecaprevir-pibrentasvir (100 mg/40 mg tablet): three tablets daily for 12 weeks (CI)	
HCV Genotype 3	
Preferred Therapy	
Glecaprevir-pibrentasvir (100 mg/40 mg tablet): three tablets daily for 8 weeks (AIII)	
Alternative Therapy	
- Glecaprevir-pibrentasvir (100 mg/40 mg tablet): three tablets daily for 12 weeks (CI), or - Sofosbuvir-velpatasvir tablet (400 mg/100 mg tablet): one tablet daily, with or without ribavirin for 12 weeks pending results of NS5A resistance testing (CI)	

Simplified Treatment Medications

Medication	Duration	Additional Information
Glecaprevir (300 mg) / pibrentasvir (120 mg) once daily (Mavyret)	8 weeks	• ADEs: Nausea/diarrhea, fatigue, rash • Risk of increased ALT/AST and other LFTs • Hepatitis B reactivation • Avoid in patients with history of hepatic decompensation (CI in child-pugh class B/C)
Sofosbuvir (400 mg) / velpatasvir (100 mg) once daily (Epclusa)	12 weeks	• ADEs: fatigue, headache, increased CK, skin rash, increased serum lipase • If compensated cirrhosis will require genotyping prior to starting, if genotype 3 drug resistance testing is recommended • Hepatitis B Reactivation



Epclusa

sofosbuvir/velpatasvir (SOF/VEL)
GENOTYPE 1 2 3 4 5 6

ADULT: One FDC tablet once daily, with or without food. FDA APPROVED FOR PEDIATRIC PATIENTS AGE 3 AND OLDER (WEIGHT-BASED DOSING REQUIRED): Two pellet formulas available. Ribavirin may be included in patients with decompensated cirrhosis. Generic available.



Harvoni

sofosbuvir/ledipasvir (SOF/LDV)
GENOTYPE 1 4 5 6

ADULT: One FDC tablet once daily, with or without food. FDA APPROVED FOR PEDIATRIC PATIENTS AGE 3 AND OLDER (WEIGHT-BASED DOSING REQUIRED): Smaller tablets and pellets available. Ribavirin may be added in people with decompensated cirrhosis or liver transplant recipients with cirrhosis (compensated or decompensated). Generic available.



Mavyret

glecaprevir/pibrentasvir (GLE/PIB)
GENOTYPE 1 2 3 4 5 6

ADULT: Three FDC tablets once daily, with food. FDA APPROVED FOR PEDIATRIC PATIENTS AGE 3 AND OLDER (WEIGHT-BASED DOSING REQUIRED): Pellets available. May be taken by those with compensated cirrhosis. Contraindicated in decompensated cirrhosis.



Vosevi

sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX)
GENOTYPE 1 2 3 4 5 6

One FDC tablet once daily, with food; may be taken by people with compensated cirrhosis. Contraindicated in decompensated cirrhosis. Not FDA approved for use in co-infection, but may be considered.



Zepatier

grazoprevir/elbasvir (GZR/EBR)
GENOTYPE 1 4

One FDC tablet once daily, with or without food. Ribavirin may be added in certain patient populations. Zepatier cannot be taken by people with moderate or severe liver impairment.

FDA approved HCV medications that are no longer or rarely used:



Sofvaldi

sofosbuvir (SOF)
(Sofosbuvir is used in FDCs.)



ribavirin (RBV)
(PHOTO UNAVAILABLE)

Major Drug Interactions

HIV Antiretrovirals	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
Efavirenz, Etravirine, Nevirapine, and other strong CYP3A4 and P-gp inducers	Significant decrease in glecaprevir and pibrentasvir concentrations (avoid)	Significant decrease in velpatasvir concentrations (avoid)
Protease inhibitor/ritonavir, Protease inhibitor/cobicistat, unboosted Atazanavir	Significant increase in glecaprevir and pibrentasvir concentrations (avoid)	Boosted PIs may increase velpatasvir concentrations, but no significant adverse events in clinical trial Coadministration allowed
Tenofovir DF, Tenofovir alafenamide	Coadministration allowed	Tenofovir alafenamide preferred If Tenofovir DF is used with boosted protease inhibitors if GFR <60 mL/min, monitoring is recommended.
Rilpivirine, Doravirine, Elvitegravir-cobicistat, Raltegravir, Bictegravir, Dolutegravir, Abacavir, Emtricitabine, Lamivudine, Maraviroc	Coadministration allowed	Coadministration allowed

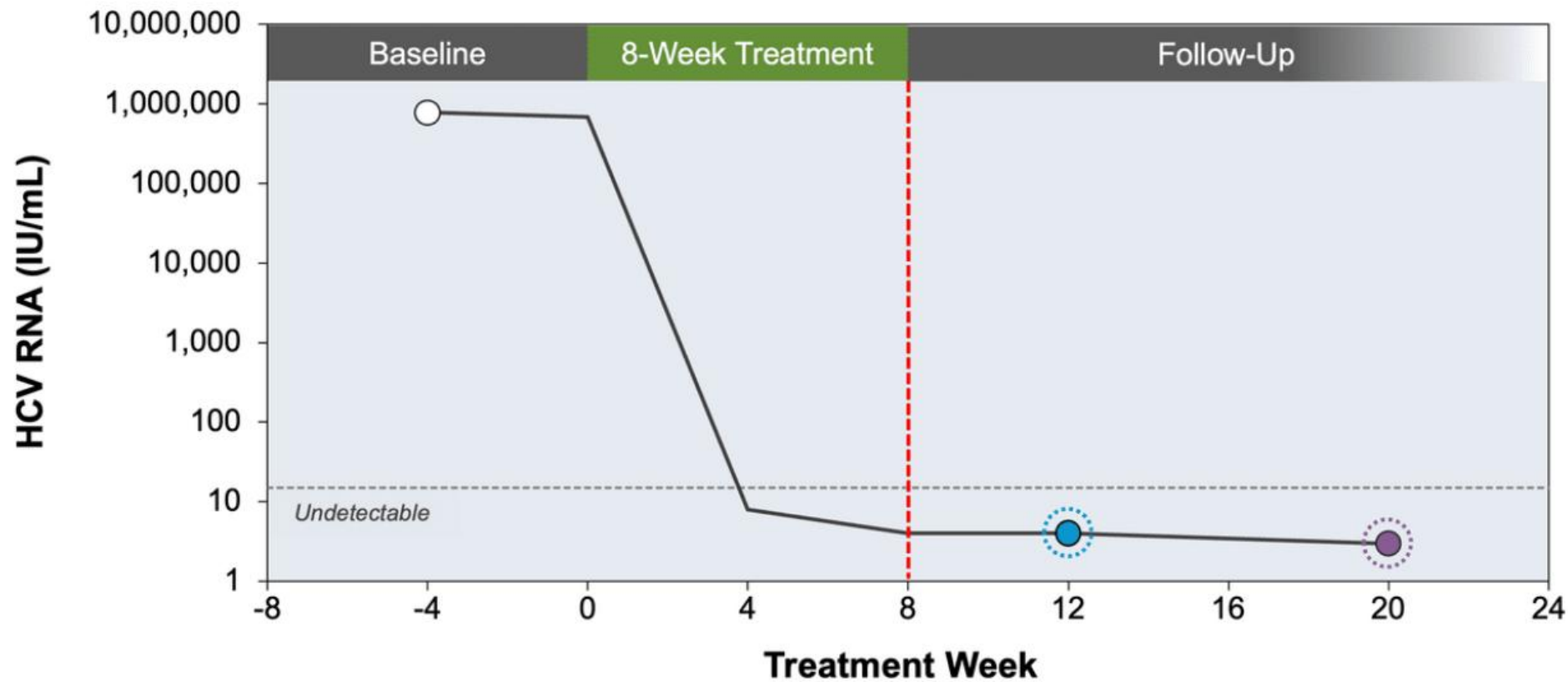
Monitoring Response to Treatment

Post-Treatment Monitoring: Assessment of Cure (SVR)

- Obtain quantitative HCV RNA and hepatic function panel 12 weeks or later following completion of HCV therapy.
- If quantitative HCV RNA is undetectable 12+ weeks following completion of HCV therapy, the patient is considered to have achieved a sustained virologic response (SVR), also known as a cure.
- Assess for other causes of liver disease if transaminase levels remain elevated after achieving an SVR.

Abbreviations: SVR = sustained virologic response

Monitoring Response to Treatment



Monitoring Response to Treatment

On-Treatment Monitoring

- Monitor for hypoglycemia in patients taking medications for diabetes.
- Monitor for sub-therapeutic INR in patients taking warfarin.
- No laboratory monitoring is required for other patients.
- In-person or remote (telehealth/phone) visits may be scheduled, as needed, for patient support and to assess tolerance of new medications.

Monitoring Response to Treatment

Post-Treatment Monitoring: Follow-up After Achieving Virologic Cure (SVR)

- No liver specific follow up is needed for patients without advanced fibrosis following SVR.
- Patients with ongoing risk factors for HCV should be counseled regarding their risk for reinfection and undergo testing for HCV RNA annually and with any elevation in ALT, AST or bilirubin.
- Patients should be advised to avoid excessive alcohol.

Abbreviations: SVR = sustained virologic response

Monitoring Response to Treatment

Post-Treatment Monitoring: Follow-up for Patients who Do *NOT* Achieve Virologic Cure

- When initial HCV treatment fails to achieve a cure (SVR), patients should be evaluated for retreatment by a specialist, in accordance with AASLD/IDSA HCV guidance.
- Assess disease progression with a CBC, hepatic function panel, and INR every 6 – 12 months until retreatment occurs.
- Patients should be advised to avoid excessive alcohol.

Abbreviations: SVR = sustained virologic response; CBC = complete blood count; INR = international ionized ratio

Hepatitis C Summary

- An estimated 15 to 30% percent of persons with HIV have HCV coinfection
- People with HIV and HCV co-infection have accelerated rates of liver fibrosis that result in a more aggressive course of liver disease and higher rates of liver-related mortality.
- All persons with HIV should be tested for HCV at entry to care
- All persons with HIV and HCV coinfection should undergo treatment for HCV with the goal of achieving sustained virologic response and cure of HCV.
- Most people with HIV can receive the simplified HCV treatment approach
- All persons with HIV and HCV coinfection who are not eligible for the simplified HCV treatment strategy can be treated using the standard approach as outlined in the AASLD/IDSA treatment guidelines.

Prevention

Prevention

- Preventing viral hepatitis involves several strategies:
- **Vaccination:** Vaccines are available for Hepatitis A and B.
- **Safe Practices:** Avoid sharing needles, ensure safe sex practices, and avoid sharing personal items that might be contaminated.
- **Hygiene:** Practice good hand hygiene and ensure clean drinking water.
- **Regular Screening:** For those at risk, regular screening can help catch infections early.

Viral Hepatitis: Summary

- Viral hepatitis is one of the most frequent cause of liver disease
- Viral hepatitis is the most common cause of cirrhosis and liver cancer
- Viral hepatitis A and B can be prevented by vaccine
- Treatment for chronic viral hepatitis B and C can be effective

Questions?

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THANK YOU SO MUCH



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AETC Resources

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