

HEPATITIS C CLINICAL TRAINING

# Hepatitis C: Epidemiology, Natural History and Diagnosis

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## Training Development and Funding

- This training is designed in collaboration with the NYC Department of Health and Mental Hygiene (DOHMH)
- This training is funded by the NYC City Council

## Housekeeping Notes

### **Have a question for the presenter**

- Type the question into the chat box and Meg will read them aloud to the presenter at the end

### **Claiming CE**

- After the training, you will receive an e-mail with instructions, the course number, and the access code
- CE certificate can be printed or stored in your account
- Questions about CEs, contact [Joycambe@empireliverfoundation.org](mailto:Joycambe@empireliverfoundation.org)

### **For Additional Information**

- Visit <https://empireliverfoundation.org/about-us/cme-accreditation/>

## Disclosures

Consultant- Gilead

Speaker's Bureau- Gilead

# Learning Objectives

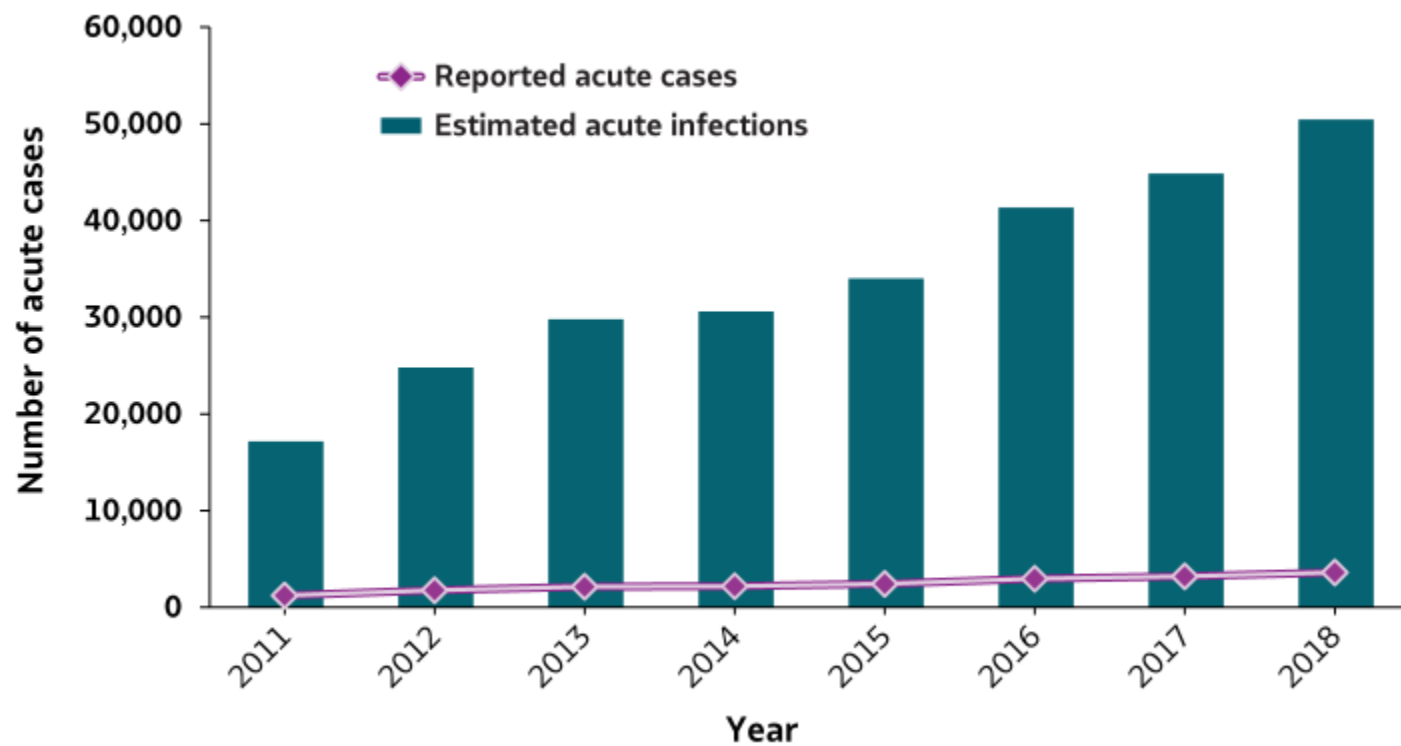
By the end of this presentation, participants will be able to:

- Recall the epidemiology and natural history of the hepatitis C virus (HCV)
- Identify and interpret diagnostic tests for HCV
- Explain pre-therapy assessment of HCV patients, including assessment of liver fibrosis
- Describe the impact of HCV treatment on patient outcomes



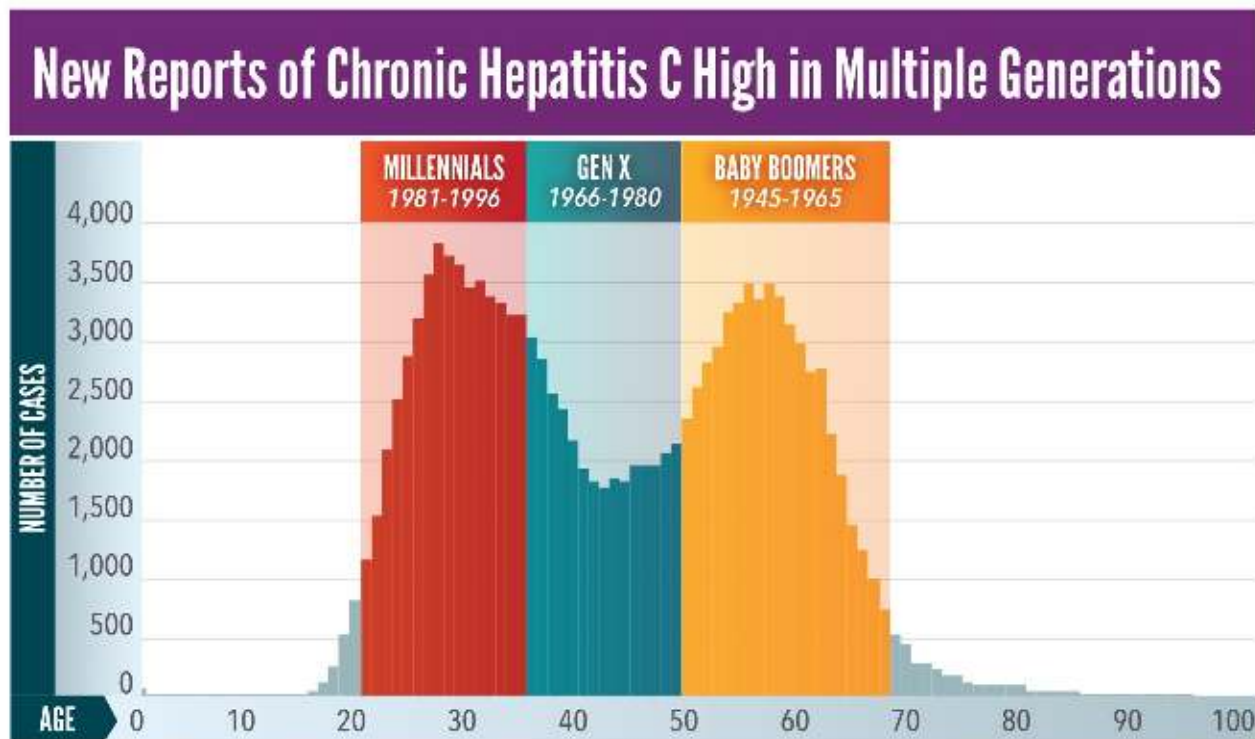
# Epidemiology

## Number of Reported Acute Hepatitis C Cases and Estimated Infections\* — United States, 2011–2018



Source: CDC, National Notifiable Diseases Surveillance System.

# Number of Newly Reported Cases of Chronic Hepatitis C by Age, 2018



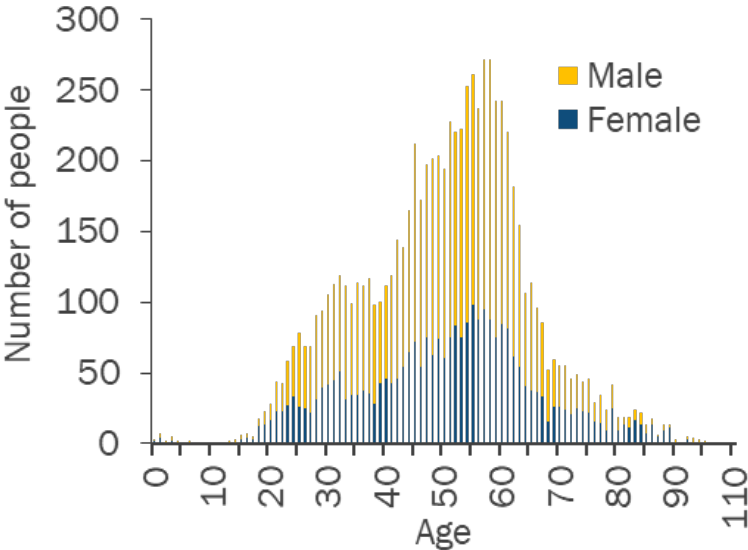
Source: CDC, National Notifiable Diseases Surveillance System.

SOURCE: National Notifiable Diseases Surveillance System, 2018

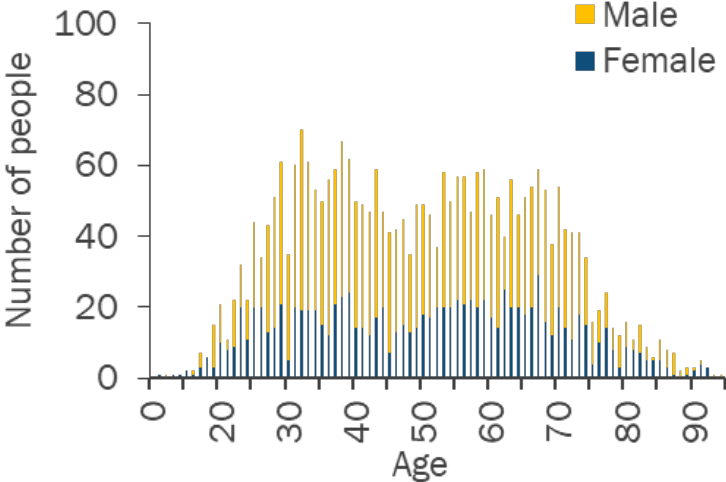


# Newly Reported Chronic HCV Age Distribution in New York City, 2011 and 2021

**2011**

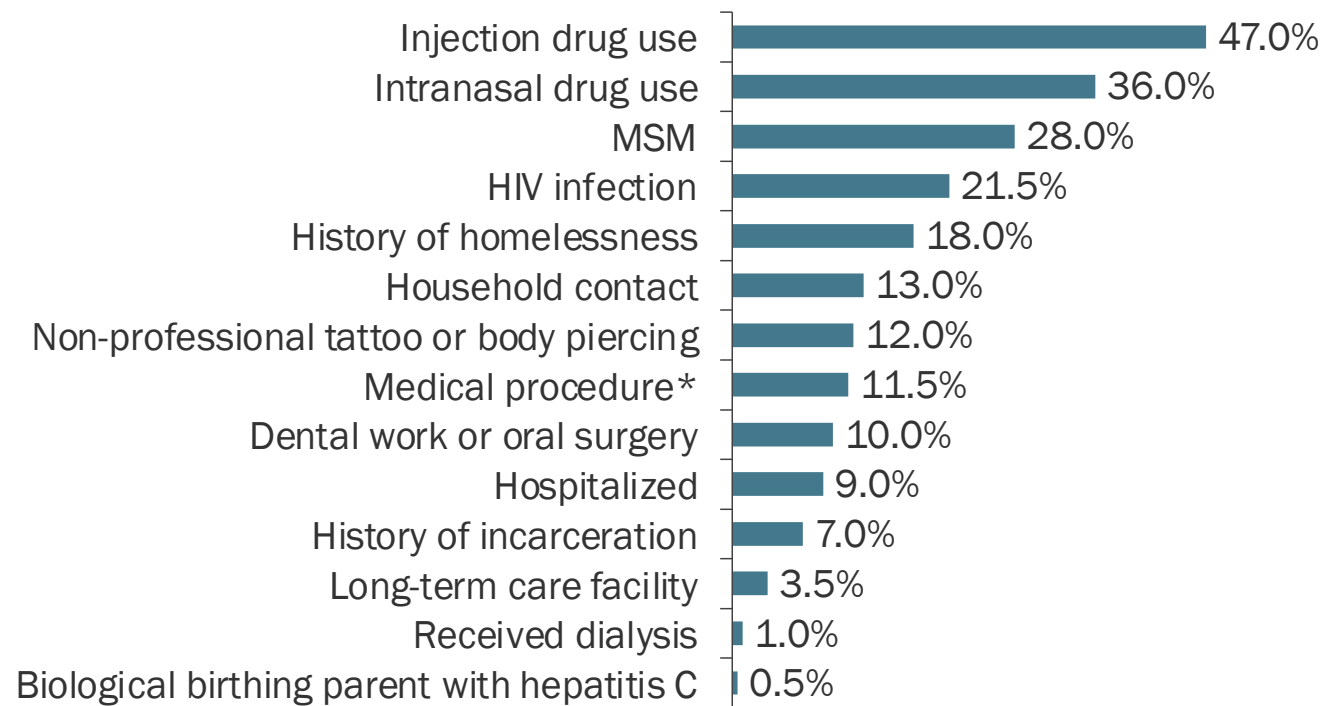


**2021**



NYC Health Department, 2022.

## Risk Factors for HCV Infection of People Ages 18–34 Newly Reported With Chronic HCV In NYC In 2021



\*Involving injections, anesthesia or blood  
NYC Health Department, 2022.

## Transmission of HCV

- Sharing supplies for injection or intranasal drug use
- Transfusion of blood/blood products prior to 1992
- Needle stick injury in health care settings
- Sharing personal care items (i.e. straight razors)
- Being born to a mother who has HCV
- Tattoos, body piercing in unlicensed setting (e.g. jails)
- Sex with an infected person, especially among MSM, and in particular, MSM who are HIV+

## Case Study 1

Patient is a 65-year-old man with a positive HCV antibody with reflex to RNA test, confirming active infection. He has a history of injection drug use once as a teenager. He reports feeling well but was noted to have ALT levels of 42 U/L on a routine PE. He was asked to return for additional blood work. Further testing showed his HCV RNA viral load to be 850,000 IU/mL. He currently drinks alcohol, mostly on weekends.

Think about what you would do next.  
We will review at end of presentation.

## Case Study 2

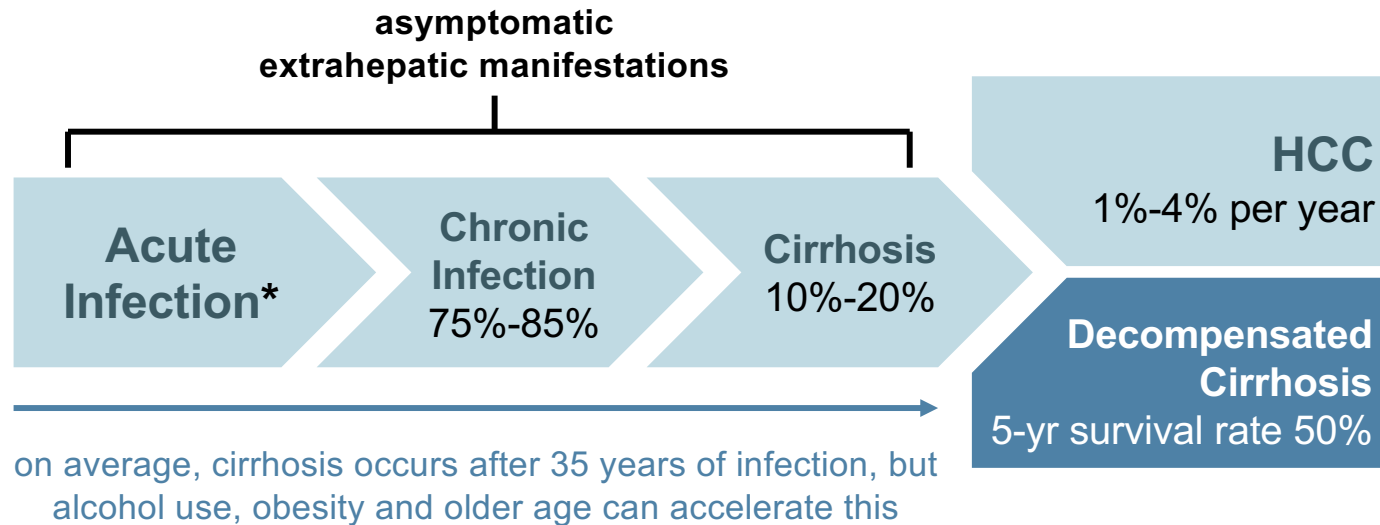
Patient is a 28-year-old woman with a positive HCV antibody with reflex to RNA test, confirming active infection. She reports being an active intravenous drug user. She reports feeling well but was noted to have ALT levels of 87 U/L on a routine PE. She was asked to return for additional blood work. Further testing showed her HCV RNA viral load to be 550,000 IU/mL.

Think about what you would do next.  
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# Natural History of Hepatitis C

# Natural History of HCV



\*Most have minimal symptoms

# Liver Cancer Screening in People with HCV

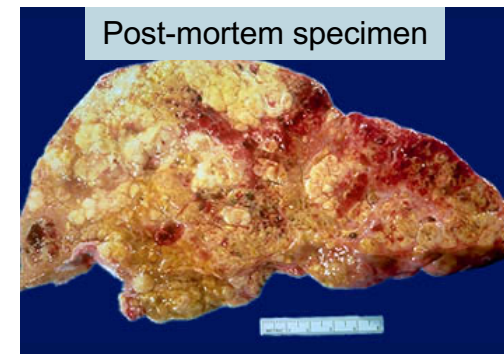
- Approximately 1/3 of liver cancer cases in the US are from HCV
- HCV-related HCC is related mostly to fibrosis/cirrhosis

## Who should be screened for liver cancer?

- Patients with hepatitis C with cirrhosis (or stage 3 fibrosis) should be screened **every 6 months with ultrasound and AFP.**

## Liver cancer is curable if caught early:

- Resection cases: cure rate is about 50%
- Transplant cases: cure rate is about 80%



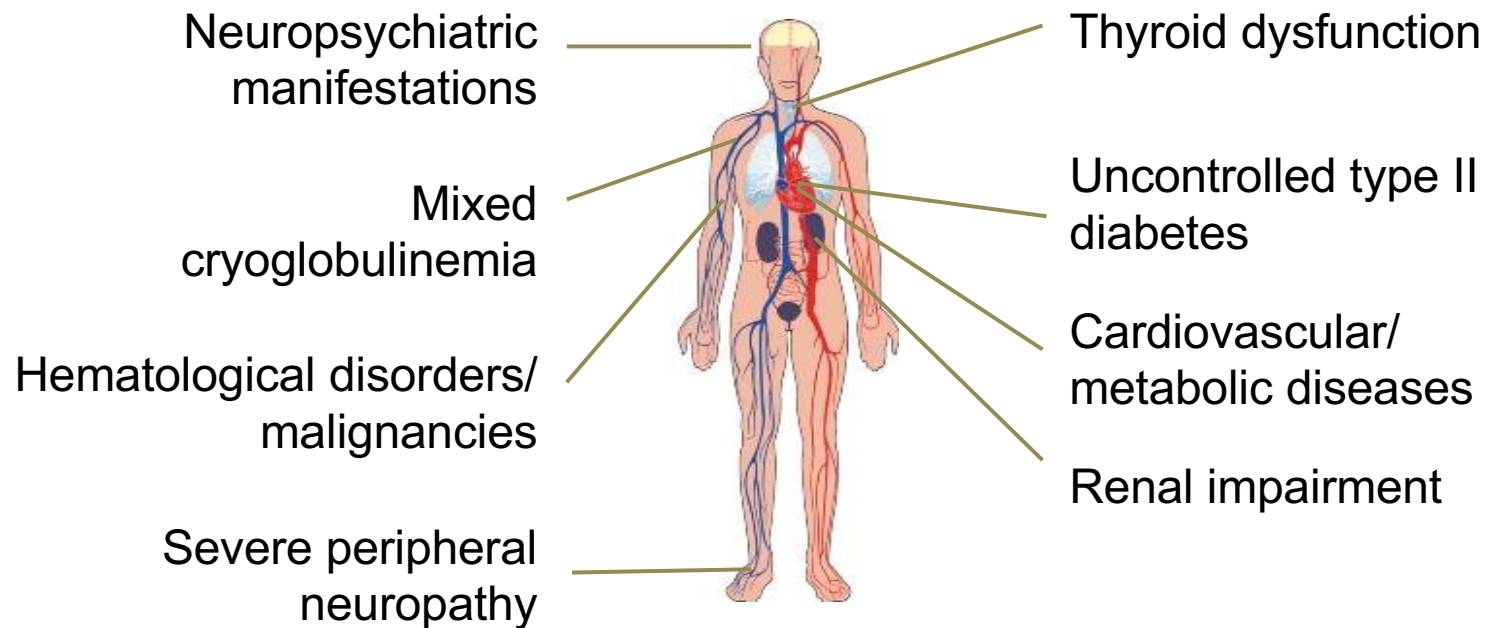


# Liver Cancer 101



- If there is a suspected nodule on ultrasound → refer for MRI
- Most HCC diagnoses are made radiologically

# Extrahepatic Manifestations of HCV Infection





# **Pre-Therapy Assessment**

## Acute HCV: Interpretation of Tests

Test	Interpretation
<b>HCV Ab</b>	<ul style="list-style-type: none"><li>• Test may be negative during first 6 weeks after exposure</li><li>• Seroconversion may be delayed or absent in immunosuppressed individuals</li><li>• Presence of HCV Ab alone does not distinguish between acute and chronic infection</li></ul>
<b>HCV RNA</b>	<ul style="list-style-type: none"><li>• Viral fluctuations <math>&gt; 1 \log_{10}</math> IU/ml may indicate acute HCV infection</li><li>• HCV RNA may be transiently negative during acute HCV infection</li><li>• Presence of HCV RNA alone does not distinguish between acute and chronic infection</li></ul>
<b>ALT</b>	<ul style="list-style-type: none"><li>• Fluctuating ALT peaks suggests acute infection</li><li>• ALT may be normal during acute HCV infection</li><li>• ALT may be elevated due to other liver insults, such as ETOH use and NAFLD</li></ul>

# HCV Screening Recommendations

- March 2020 USPSTF Grade B recommendation - one-time HCV screening of all asymptomatic adults ages 18-79 years, including pregnant women.<sup>1</sup>
- AASLD-IDSA Screening Recommendations:<sup>2</sup>
  - Universal screening over 18 years
  - Risk based screening if under 18 years
  - Prenatal HCV testing as part of routine prenatal care
  - Periodic screening with risk factors for HCV
  - Annual screening PWID, men with HIV who have unprotected sex with men, MSM taking PrEP

1. JAMA, 2020. <https://jamanetwork.com/journals/jama/fullarticle/2762186>

2. HCVGuidelines.org, 2021. <https://www.hcvguidelines.org/evaluate/testing-and-linkage>

## HCV Testing Recommendations

- Since 2017, NYC Health Code requires labs to automatically perform HCV RNA confirmatory test on all positive antibody test for HCV (reflex test)
- Since 2015, NYS Department of Health recommends reflex testing and provides resources for implementation:  
[https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis\\_c/providers/reflex\\_testing.htm](https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_c/providers/reflex_testing.htm)

# Counsel to Prevent Transmission

Risk	More Information	Prevention Messages
<b>Sharing drug use equipment</b>	<ul style="list-style-type: none"> <li>• Transmission rate can exceed 40%</li> <li>• Both injection drug use and snorting</li> </ul>	<ul style="list-style-type: none"> <li>• Use new equipment (needles, cookers, cutters) for drug use</li> </ul>
<b>Sex</b>	<p>Not common but can happen. Risk factors:</p> <ul style="list-style-type: none"> <li>• Coinfection with HIV</li> <li>• Unprotected anal intercourse</li> <li>• Coincident ulcerative STDs (e.g. syphilis)</li> <li>• Practices that predispose to bleeding</li> </ul>	<ul style="list-style-type: none"> <li>• Get partner tested and cured if needed, until then, practice safe sex (use condoms every time)</li> </ul>
<b>Household</b>	<p>Risk factors:</p> <ul style="list-style-type: none"> <li>• Sharing razors, toothbrushes, nail clippers</li> <li>• Contact with blood</li> </ul>	<ul style="list-style-type: none"> <li>• Clean up blood spills with bleach</li> <li>• Avoid sharing personal care items (such as razors, toothbrushes, nail clippers)</li> </ul>
<b>Perinatal</b>	<p>5% transmission rate from HCV+ mothers to infants</p>	<ul style="list-style-type: none"> <li>• Screen and treat (if needed) all women of childbearing age prior to pregnancy</li> </ul>

## HCV Provider Responsibilities

### Obtain Basic Blood Tests

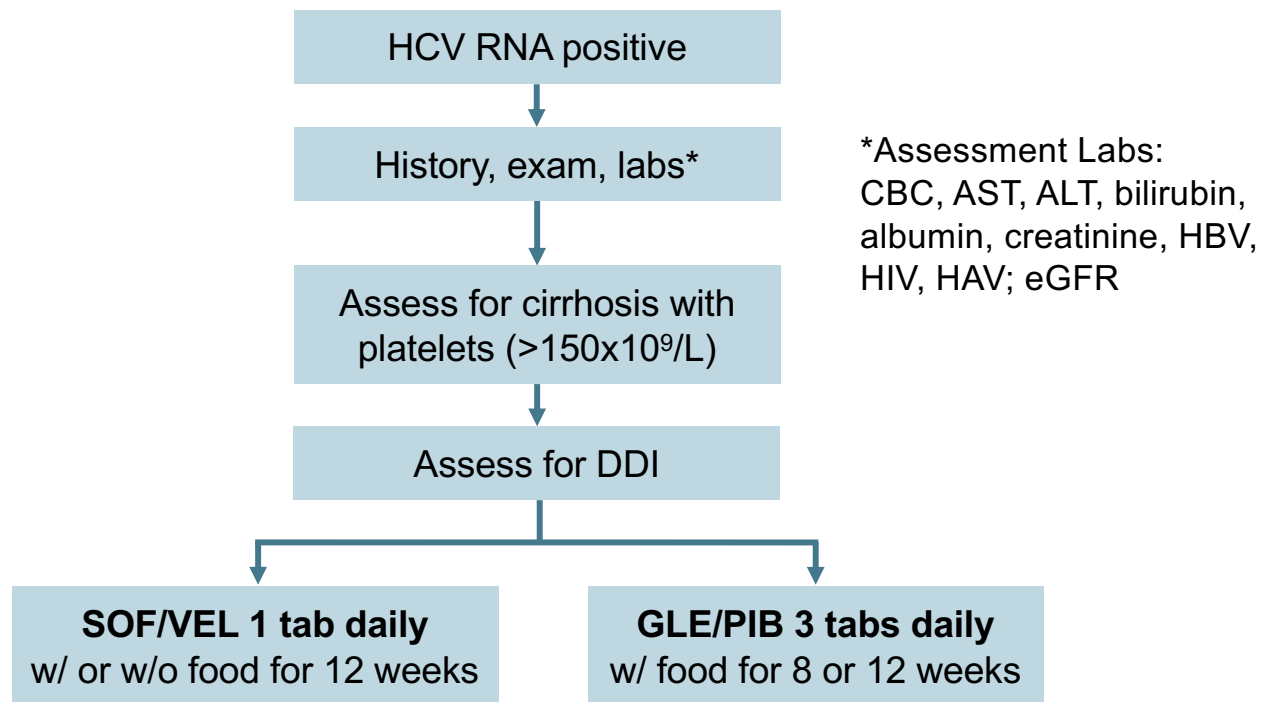
- **CBC, platelets**
- **Comprehensive metabolic profile**
  - Renal function
  - Liver chemistries
    - Albumin
    - Total bilirubin
    - Alkaline phosphatase
    - Aspartate aminotransferase
    - Alanine aminotransferase
- **INR**
- **Viral studies**
  - HIV Ab
  - HAV Ab (total, not IgM!)
  - HBcAb (total, not IgM!)
  - HBsAg
  - HBsAb
  - HCV RNA



## Reactivation of Hepatitis B

- Patients with prior, resolved, or active HBV infection are at risk of reactivation on DAA therapy
- FDA issued black box warning in 2016
  - 29 reactivations reported since 2013
  - 2 died, 1 required liver transplant

# How Simple Can HCV Treatment Be For Most Patients?



# Pre-Therapy Assessment

- Basic labs should include:
  - Genotype at least once in the past
  - Viral load relatively recent
    - Most insurances require within 3 months
  - Assessment of liver function
  - Assessment of renal function (creatinine, GFR)
- Assessment of liver fibrosis
- Drug/alcohol screening only if required by payers

## Pre-Therapy Assessment: Drug-Drug Interactions (DDIs)

- **Very important** element in pre-therapy assessment
- List of prohibited drugs is relatively short
- Be alert for interactions with common drugs
  - Statins, acid reducing agents, birth control preparations, amiodarone, rifampin
- No herbs!
  - In particular, no St. John's Wort
- Use online tools to help assess DDI's
  - *<https://www.hep-druginteractions.org/checker>*

**Remember: Ask patients to tell you all the pills they are taking!**

## Importance of Assessing Fibrosis

- Patients with bridging fibrosis or cirrhosis need additional screening
  - Varices
  - Hepatocellular carcinoma
- Allows for selection of proper treatment plan and duration of therapy
- Determines post-treatment follow-up

## Methods for Staging Fibrosis

Method	Procedure	Advantages	Disadvantages
<b>Indirect serum markers</b>	APRI, FIB-4	Noninvasive; inexpensive	Limited ability to differentiate intermediate stages of fibrosis
<b>Direct markers</b>	FibroSure, FibroTest, FibroMeter, FIBROSpect II, HepaScore and Enhanced Liver Fibrosis (ELF) score	Noninvasive; easily accessible	Limited ability to differentiate intermediate stages of fibrosis
<b>VCTE</b>	Shear wave velocity	Noninvasive; assesses large volume of liver parenchyma	May be difficult to interpret in F2 and F3 liver disease; limited availability
<b>MRI elastography</b>	MRI with elastography	Non-invasive, evaluates entire liver	Not FDA approved in US, expensive

# Non-invasive Formulae to Assess Fibrosis

$$\text{APRI} = \frac{\frac{\text{AST Level (IU/L)}}{\text{AST (Upper Limit of Normal) (IU/L)}}}{\text{Platelet Count (10}^9\text{/L)}} \times 100 = \text{[ ]}$$

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



# Impact of Treatment on Natural History of Hepatitis C



# DAA Therapy Associated With Improved Survival in HCC Patients

**Methods:** Retrospective cohort study of 797 patients with HCV-related HCC from 31 health systems in U.S./Canada

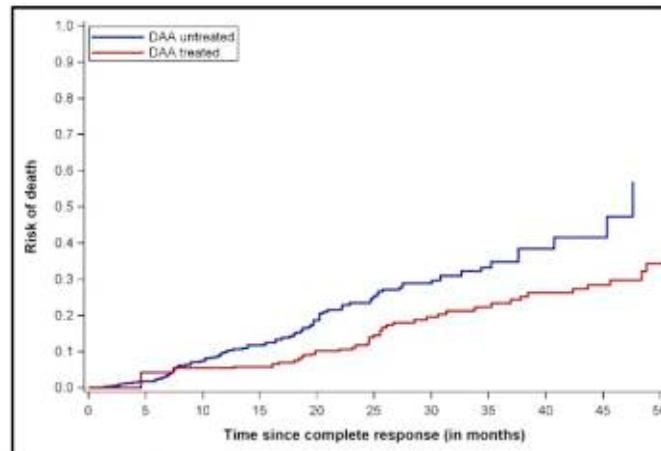
## Results:

DAA Treated:  
4.6 deaths per 100  
person-years follow-up

DAA Untreated:  
19.6 deaths per 100  
person-years follow-up

### Multivariable analysis

- Adjusted for site, age, sex, Child Pugh score, AFP, tumor burden and HCC treatment modality



DAA therapy associated with lower mortality:  
HR: 0.54; 95%CI: 0.33 – 0.90

## Case Study 1

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- What do you do next?

## Case Study 1

- Check HIV, HBV
- Confirm GFR > 30
- Confirm no cirrhosis (Plats > 150 or Fibroscan)
- Pregnancy - N/A
- Start anti-viral therapy
- Screen for hepatocellular carcinoma

## Case Study 2

Patient is a 28-year-old woman with a positive HCV antibody with reflex to RNA test, confirming active infection. She reports being an active intravenous drug user. She reports feeling well but was noted to have ALT levels of 87 U/L on a routine PE. She was asked to return for additional blood work. Further testing showed her HCV RNA viral load to be 550,000 IU/mL.

- What do you do next?

## Case Study 2

- Check HIV, HBV
- Confirm GFR > 30
- Confirm no cirrhosis (Plats > 150 or Fibroscan)
- Pregnancy check
- Start anti-viral therapy
- Provide referrals for:
  - harm reduction services (buprenorphine)
  - drug use treatment
  - write prescription for naloxone and syringes

## Summary of Key Messages

1. Estimated 3 million people with HCV in the US
2. All adults 18-79, including pregnant women, should be screened at least once
3. Increase in acute HCV cases likely secondary to opioid crisis
4. Oral pangenotypic DAAs cure greater than 95% of patients
5. All patients with bridging fibrosis or cirrhosis should be screened for HCC, even if HCV cured

# Hepatitis C Treatment Guidelines and Resources

- Treatment Guidelines - [HCVguidelines.org](http://HCVguidelines.org)
  - Includes a simplified treatment algorithm for use by primary care providers
- Drug-Drug Interactions - <https://www.hep-druginteractions.org/>

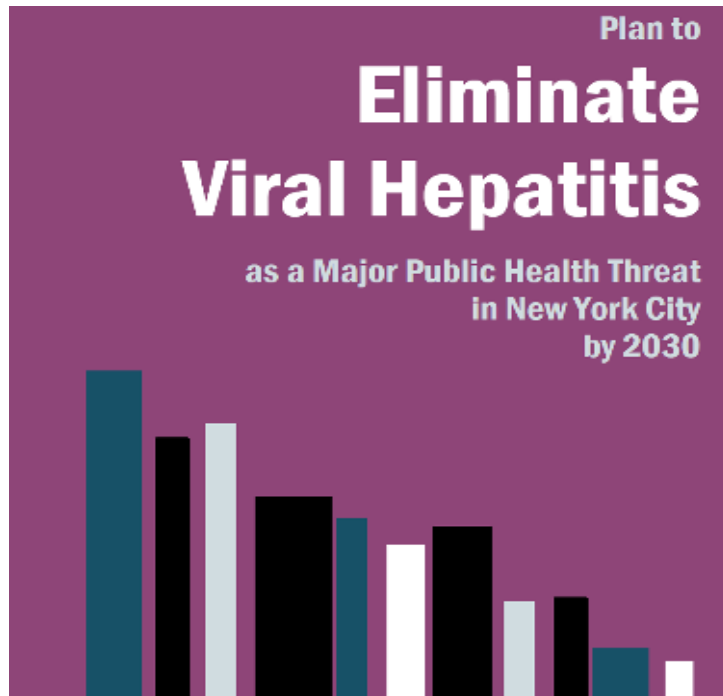
## Hepatitis C Resources in NYC

- NYS HCV CEI Clinical Consultation Hotline:  
(866) 637-2342 (leading hepatologist will answer questions)
- [www.HepFree.NYC](http://www.HepFree.NYC)
  - [Hep C Task Force](#)
  - [Clinical Resources](#)
  - [Capacity building tools](#)
  - [Advocacy Committee](#)
- Hepatitis C patient information page: [www.nyc.gov/health/hepc](http://www.nyc.gov/health/hepc)
  - Free or low-cost testing and treatment

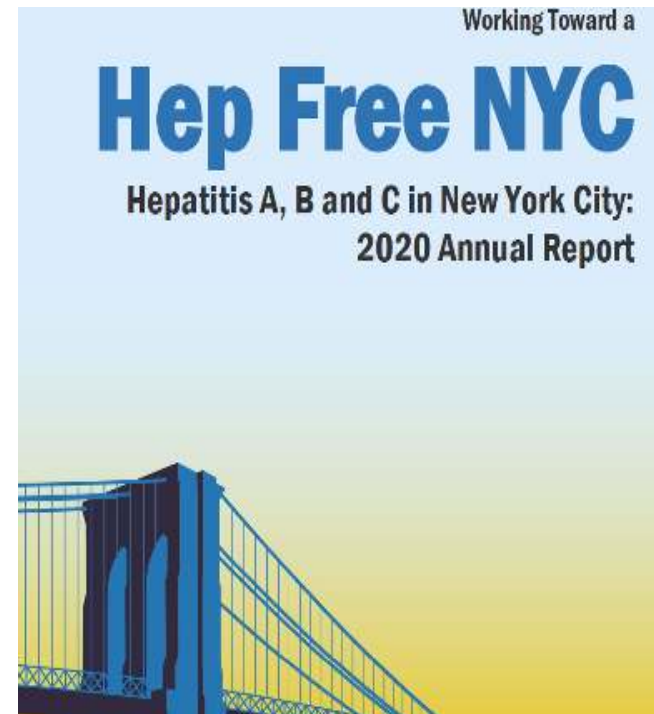


# Elimination Plan and Annual Report

Find on NYC.gov website [here](#)



Find on Hep Free NYC website [here](#)



## Contact Us

**For CMEs or educational opportunities, contact:**

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[megchappell@empireliverfoundation.org](mailto:megchappell@empireliverfoundation.org)  
[www.empireliverfoundation.org](http://www.empireliverfoundation.org)



**For questions about resources, contact:**

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[www.hepfree.nyc](http://www.hepfree.nyc)



## HCV Provider Training Series

<b>Date</b>	<b>Topic</b>
<b>October 6, 2022</b>	<b>Hepatitis C : Epidemiology, Natural History and Diagnosis with Dr. Sonal Kumar</b>
<b>October 13, 2022</b>	<b>Hepatitis C Treatment with Dr. Arun Jesudian</b>
<b>October 20, 2022</b>	<b>Hepatitis C Complications with Dr. David Bernstein</b>
<b>October 27, 2022</b>	<b>Hepatitis C Treatment in People Who Inject Drugs (PWID) with Dr. Sara Lorenz-Taki</b>

## Upcoming Webinars

### **Universal Hepatitis C Screening among Pregnant Persons to Reduce Stigma and Advance Elimination**

#### **PRESENTER**



Tatyana Kushner, MD, MSCE  
Assistant Professor of Medicine  
Division of Liver Diseases  
Icahn School of Medicine at Mount Sinai

#### **CONTINUING EDUCATION**

1 CME/CNE/CEU offered per webinar. Join both webinars or a single session!