

# Epidemiology and Natural History

This is a PDF version of the following document:

Module 8: [HCV Test and Cure](#)

Lesson 1: [Epidemiology and Natural History](#)

You can always find the most up-to-date version of this document at

<https://www.hepatitisC.uw.edu/go/test-cure/natural-history-epidemiology/core-concept/all>.

---

## Welcome Video

[Activity] B. Welcome Video

## Background

Hepatitis C (HCV) is an RNA virus in the *Flaviridae* family ([Figure 1](#)). Chronic HCV infection remains one of the most common causes of liver disease and liver cancer in the United States, and is a leading indication for liver-related deaths worldwide. In the United States, there are currently more than 2 million individuals living with this potentially deadly infection, many of whom remain unaware of their HCV infection.[\[1\]](#) The annual number of new HCV infections in the United States steadily increased from 2013-2020 and then plateaued with more than 65,000 estimated acute hepatitis C cases each year.[\[2\]](#) The rise and persistence of a high number of acute HCV infections has been fueled in large part by increasing rates of opioid and other forms of injection drug use nationally.[\[2,3\]](#)

## Low HCV Treatment Rates

In the United States, among insured adults who were newly diagnosed with HCV (positive HCV RNA test) during 2019-2020, fewer than one-third were treated within 12 months of their HCV diagnosis; treatment initiation rates in adults were lowest in younger age groups (20-29 years of age and 30-39 years of age) ([Figure 2](#)).[\[4\]](#) These overall low HCV treatment rates have occurred despite the availability of safe and well-tolerated oral antiviral therapy that cures more than 98% of those who complete it. Strategies to improve the low treatment rates have included simplifying treatment protocols, removing eligibility criteria for treatment, integrating HCV treatment into primary care services, and expanding the number of primary care clinicians who have the core competency to treat most individuals with chronic HCV.[\[4,5,6\]](#)[\[Q\]](#) Effectiveness of HCV Therapy

## Key Role for Primary Care Clinicians in HCV Treatment

Primary care medical providers and non-specialty clinicians can effectively treat the majority of people with chronic HCV infection. In 2019, the American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) generated simplified HCV treatment algorithms for treatment-naïve adults without cirrhosis or with compensated cirrhosis.[\[5,6\]](#) The AASLD-IDSA guidance provides a practical and easy-to-implement framework for treating persons with chronic HCV.[\[5,6\]](#) This online training will provide the fundamental knowledge base and skills needed by clinicians to screen and diagnose persons with HCV, evaluate cirrhosis status, and provide antiviral treatment to most people with chronic HCV based the AASLD-IDSA simplified treatment guidance.

# Epidemiology of HCV in United States

## People Living with Chronic HCV (HCV Prevalence)

The HCV prevalence is defined as the number of persons in the total population living with HCV. In the United States, there are an estimated 2.2 million people with current HCV infection (HCV RNA positive); this translates to approximately 0.9% of the adult United States population living with HCV infection.[7] This estimate is based on the 2017–2020 National Health and Nutrition Examination Survey (NHANES).[7] The HCV prevalence has not significantly decreased in recent years, which is very disappointing given the availability of curative HCV therapy for nearly a decade.[1] The graphic below summarizes several key demographic findings from the most recent NHANES HCV prevalence survey ([Figure 3](#)).[7]

## High HCV Prevalence Groups

Multiple studies have identified three key high HCV prevalence groups in the United States: people who inject drugs (PWID); men who have sex with men, particularly men with HIV who have sex with men (MSM); and the baby boomer birth cohort (born 1945-1965).[8] The HCV prevalence in each of these groups is significantly higher than the overall estimated HCV prevalence in the general United States population ([Figure 4](#)).[8] Among PWID, the HCV (anti-HCV positive) seroprevalence, which includes persons with chronic and cleared HCV, is estimated to range from 25-70% in the United States, depending on geographic locale and duration of injection drug use.[9,10,11] More recently, primarily as a result of the United States opioid epidemic, young adults in the millennial age cohort (born 1981-1996) have also emerged as a high HCV prevalence group.[12,13,14,15]

## New HCV Infections (HCV Incidence)

The HCV incidence is the number of acute cases of HCV that occur in a year. The CDC surveillance data includes the actual and estimated number of acute cases reported in one year, taking into account that most cases of acute HCV are not diagnosed, since many people are asymptomatic (or mildly symptomatic) and do not present for medical care.[2] National surveillance data estimates that 69,000 new HCV infections occurred in the United States in 2023.[2] From 2013 to 2021, there was a steady increase in acute HCV infections in the United States, driven primarily by the opioid crisis, but the number of new infections has remained relatively stable from 2020-2023.[2] Key HCV incidence surveillance findings are summarized in the figure below ([Figure 5](#)) and include the following:[2]

- The rate of new infections is twice as high in males as in females
- The highest rates occur in young adults 30–39 years of age
- There are significant differences in rates based on geographic regions of the United States

## How People Acquire HCV in the United States

### Injection Drug Use and HCV

People who inject drugs (PWID) are at high risk of acquiring HCV from shared needles and other contaminated drug preparation equipment.[2,3] In the United States, there are approximately 3.7 million people who inject drugs; most of these individuals are male and white ([Figure 6](#)).[3] The CDC hepatitis C surveillance data does not routinely include transmission categories for persons newly diagnosed with HCV, but available data indicate that injection drug use is the primary factor associated with HCV acquisition in the United States.[2,8] Further, in recent years, the opioid epidemic has played a major role in new HCV infections. Because addiction, by definition, involves continued activities despite harmful consequences, PWID can repeatedly engage in injection behaviors (e.g., sharing equipment, water, or other paraphernalia) that place them at risk of contracting viral hepatitis. In addition, PWID may be reluctant to engage with the medical system, including

for HCV testing or treatment.[[16](#),[17](#)]

## **Sexual Transmission**

Sexual transmission of HCV among heterosexual couples is rare. In contrast, transmission of HCV among MSM, particularly those with HIV, is significantly higher when compared with rates for men who have sex with women and in the general population.[[18](#)] The overall estimated global HCV prevalence among MSM is 3.4%, and the prevalence is significantly higher in MSM with HIV (6.3%) compared to MSM without HIV (1.5%).[[18](#)] The mechanism for the higher rate of sexual transmission of HCV among MSM is not entirely clear, but is thought to be related to the mucosal microtrauma that can occur with anal sex.[[19](#)]

## **Other**

There are other routes for HCV acquisition, but these now play a minor role overall. These include perinatal HCV transmission, chronic hemodialysis, receipt of contaminated blood products, organ and tissue transplantation, tattoos, piercing, nasal cocaine, and household contact.[Q] HCV Transmission in the United States

## Natural History

### Progression of Disease in Untreated Chronic HCV Infection

The following summarizes the natural history and progression of disease in untreated HCV infection ([Figure 7](#)).

- With acute HCV infection, most individuals are asymptomatic or have only mild symptoms.
- Following acute infection, a subset of individuals (15 to 45%) mount a robust immune response that spontaneously clears HCV from their liver and blood. After clearing HCV, these individuals will have a positive HCV antibody test but a negative HCV RNA.
- Approximately 55 to 85% of persons who acquire HCV infection do not achieve spontaneous resolution and will develop chronic HCV infection. Therefore, chronic infection needs to be confirmed by detecting virus in the blood, to differentiate between those who spontaneously clear and those who have persistent infection.
- Of those with persistent viremia (chronic infection), approximately 20 to 30% will develop cirrhosis. If cirrhosis develops, it typically occurs 20 to 30 years after HCV acquisition.
- Of those with cirrhosis, approximately 1 to 4% per year are at risk of developing liver cancer—the most common type being hepatocellular carcinoma (HCC).
- Of those with cirrhosis, approximately 2 to 5% per year are at risk of developing end-stage liver disease (ESLD), which is when liver failure or decompensation occurs. Clinical events that can mark ESLD are ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, and variceal hemorrhage.

### Factors that Impact Progression of Disease

In the presence of certain factors, some individuals with chronic HCV will have an accelerated disease progression. The following factors have been identified that can predispose to faster liver disease progression ([Figure 8](#)).<sup>[20]</sup>

- Acquisition of HCV at an older age (older than 40 years)
- Current older age (independent of duration of infection)
- Male sex
- Heavy alcohol use
- Coinfection with HIV
- Coinfection with hepatitis B virus
- Metabolic dysfunction-associated steatotic liver disease (MASLD)
- Insulin resistance

[Q] Cirrhosis in Untreated HCV

## Summary Points

- HCV is an RNA virus in the *Flaviviridae* family and is one of the most common causes of chronic liver disease worldwide.
- Left untreated, HCV infection can progress to cirrhosis, hepatocellular carcinoma, and end-stage liver disease.
- Fewer than one-third of persons newly diagnosed with HCV in the United States are treated within 12 months of diagnosis, despite availability of direct-acting oral antiviral therapy with cure rates of greater than 98%.
- HCV treatment rates (within 12 months of initial HCV diagnosis) are lowest in younger age groups (20–29 years of age and 30–39 years of age).
- The AASLD-IDSA guidance generated simplified HCV treatment algorithms that primary care medical providers and non-specialty clinicians can use to effectively treat most people with chronic HCV infection.
- HCV prevalence has not significantly decreased in recent years and an estimated 2.2 million people are living with chronic HCV in the United States. Injection drug use and the opioid crisis are the main drivers of current HCV incidence in the United States.
- Sexual transmission of HCV among men who have sex with men, particularly those with HIV, is significantly higher than in the general population, whereas sexual transmission of HCV among heterosexual couples is rare.

## Citations

1. Hofmeister MG, Rosenthal EM, Barker LK, et al. Estimating Prevalence of Hepatitis C Virus Infection in the United States, 2013-2016. *Hepatology*. 2019;69:1020-31.  
[[PubMed Abstract](#)] -
2. Centers for Disease Control and Prevention (CDC). Hepatitis C Surveillance 2023. Published April 2025.  
[[CDC](#)] -
3. Bradley H, Hall EW, Asher A, et al. Estimated Number of People Who Inject Drugs in the United States. *Clin Infect Dis*. 2023;76:96-102.  
[[PubMed Abstract](#)] -
4. Thompson WW, Symum H, Sandul A, et al. Vital Signs: Hepatitis C Treatment Among Insured Adults - United States, 2019-2020. *MMWR Morb Mortal Wkly Rep*. 2022;71:1011-17.  
[[PubMed Abstract](#)] -
5. AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults With Compensated Cirrhosis.  
[[AASLD-IDSA Hepatitis C Guidance](#)] -
6. AASLD-IDSA. HCV Guidance: Recommendations for testing, management, and treating hepatitis C. Simplified HCV Treatment for Treatment-Naive Adults Without Cirrhosis.  
[[AASLD-IDSA Hepatitis C Guidance](#)] -
7. Lewis KC, Barker LK, Jiles RB, Gupta N. Estimated Prevalence and Awareness of Hepatitis C Virus Infection Among US Adults: National Health and Nutrition Examination Survey, January 2017-March 2020. *Clin Infect Dis*. 2023;77:1413-5.  
[[PubMed Abstract](#)] -
8. Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. *MMWR Recomm Rep*. 2020;69:1-17.  
[[PubMed Abstract](#)] -
9. Kapadia SN, Katzman C, Fong C, Eckhardt BJ, Guarino H, Mateu-Gelabert P. Hepatitis C testing and treatment uptake among young people who use opioids in New York City: A cross-sectional study. *J Viral Hepat*. 2021;28:326-33.  
[[PubMed Abstract](#)] -
10. Nelson PK, Mathers BM, Cowie B, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet*. 2011;378:571-83.  
[[PubMed Abstract](#)] -
11. Ozga JE, Syvertsen JL, Pollini RA. Hepatitis C antibody prevalence, correlates and barriers to care among people who inject drugs in Central California. *J Viral Hepat*. 2022;29:518-28.  
[[PubMed Abstract](#)] -
12. Suryaprasad AG, White JZ, Xu F, et al. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012. *Clin Infect Dis*. 2014;59:1411-9.  
[[PubMed Abstract](#)] -
13. Zibbell JE, Asher AK, Patel RC, et al. Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014. *Am J Public Health*.

2018;108:175-181.

[\[PubMed Abstract\]](#) -

14. Zibbell JE, Hart-Malloy R, Barry J, Fan L, Flanigan C. Risk factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. *Am J Public Health*. 2014;104:2226-32.  
[\[PubMed Abstract\]](#) -
15. Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged  $\leq 30$  years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012. *MMWR Morb Mortal Wkly Rep*. 2015;64:453-8.  
[\[PubMed Abstract\]](#) -
16. Neale J, Tompkins C, Sheard L. Barriers to accessing generic health and social care services: a qualitative study of injecting drug users. *Health Soc Care Community*. 2008;16:147-54.  
[\[PubMed Abstract\]](#) -
17. Motavalli D, Taylor JL, Childs E, et al. "Health Is on the Back Burner:" Multilevel Barriers and Facilitators to Primary Care Among People Who Inject Drugs. *J Gen Intern Med*. 2021;36:129-37.  
[\[PubMed Abstract\]](#) -
18. Jin F, Dore GJ, Matthews G, et al. Prevalence and incidence of hepatitis C virus infection in men who have sex with men: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6:39-56.  
[\[PubMed Abstract\]](#) -
19. Centers for Disease Control and Prevention (CDC). Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men--New York City, 2005-2010. *MMWR Morb Mortal Wkly Rep*. 2011;60:945-50.  
[\[PubMed Abstract\]](#) -
20. Lingala S, Ghany MG. Natural History of Hepatitis C. *Gastroenterol Clin North Am*. 2015;44:717-34.  
[\[PubMed Abstract\]](#) -

## References

- Centers for Disease Control and Prevention (CDC). Hepatitis C Surveillance 2022. Published April 2024.  
[\[CDC\]](#) -
- Centers for Disease Control and Prevention. 2023 Viral Hepatitis National Progress Report.  
[\[CDC\]](#) -
- Cepeda JA, Thomas DL, Astemborski J, et al. Impact of Hepatitis C Treatment Uptake on Cirrhosis and Mortality in Persons Who Inject Drugs: A Longitudinal, Community-Based Cohort Study. *Ann Intern Med*. 2022;175:1083-91.  
[\[PubMed Abstract\]](#) -
- Ghany MG, Morgan TR. Hepatitis C Guidance 2019 Update: American Association for the Study of Liver Diseases-Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. *Hepatology*. 2020;71:686-721.  
[\[PubMed Abstract\]](#) -
- Handanagic S, Finlayson T, Burnett JC, Broz D, Wejnert C. HIV Infection and HIV-Associated Behaviors Among Persons Who Inject Drugs - 23 Metropolitan Statistical Areas, United States, 2018. *MMWR Morb*



Mortal Wkly Rep. 2021;70:1459-65.

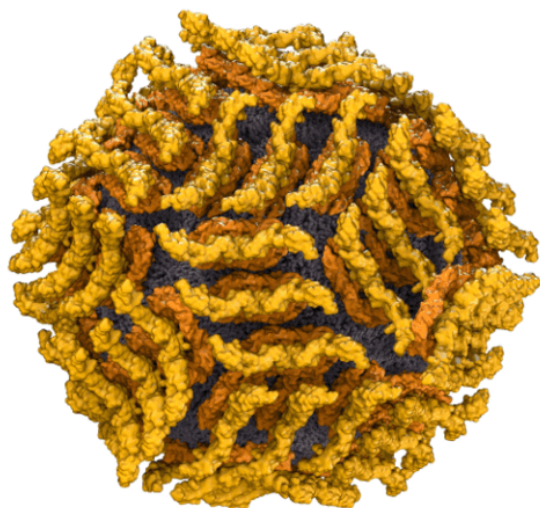
[\[PubMed Abstract\]](#) -

- Liang TJ, Rehermann B, Seeff LB, Hoofnagle JH. Pathogenesis, natural history, treatment, and prevention of hepatitis C. Ann Intern Med. 2000;132:296-305.  
[\[PubMed Abstract\]](#) -
- National Academy of Medicine of the National Academies of Sciences, Engineering and Medicine. A National Strategy for the Elimination of Hepatitis B and C: Phase Two Report (2017)  
[\[National Academies\]](#) -
- Office of HIV/AIDS and Infectious Disease Policy (OHAIDP). National Viral Hepatitis Action Plan. 2017-2020. January 2017.  
[\[HHS\]](#) -
- Oru E, Trickey A, Shirali R, Kanters S, Easterbrook P. Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. Lancet Glob Health. 2021;9:e431-e445.  
[\[PubMed Abstract\]](#) -
- Ryerson AB, Schillie S, Barker LK, Kupronis BA, Wester C. Vital Signs: Newly Reported Acute and Chronic Hepatitis C Cases - United States, 2009-2018. MMWR Morb Mortal Wkly Rep. 2020;69:399-404.  
[\[PubMed Abstract\]](#) -
- Schillie SF, Canary L, Koneru A, et al. Hepatitis C Virus in Women of Childbearing Age, Pregnant Women, and Children. Am J Prev Med. 2018;55:633-41.  
[\[PubMed Abstract\]](#) -
- Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C virus infection: host, viral, and environmental factors. JAMA 2000;284:450-6.  
[\[PubMed Abstract\]](#) -
- Thomas DL, Seeff LB. Natural history of hepatitis C. Clin Liver Dis. 2005;9:383-98.  
[\[PubMed Abstract\]](#) -
- U.S. Department of Health and Human Services. 2020. Viral Hepatitis National Strategic Plan for the United States: A Roadmap to Elimination (2021-2025). Washington, DC.  
[\[HHS\]](#) -
- Wester C, Osinubi A, Kaufman HW, et al. Hepatitis C Virus Clearance Cascade - United States, 2013-2022. MMWR Morb Mortal Wkly Rep. 2023;72:716-20.  
[\[PubMed Abstract\]](#) -
- World Health Organization. Updated recommendations on simplified service delivery and diagnostics for hepatitis C infection. Policy Brief. Geneva: World Health Organization; 2022.  
[\[WHO\]](#) -
- World Health Organization. Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics. Geneva: World Health Organization; 2022.  
[\[WHO\]](#) -

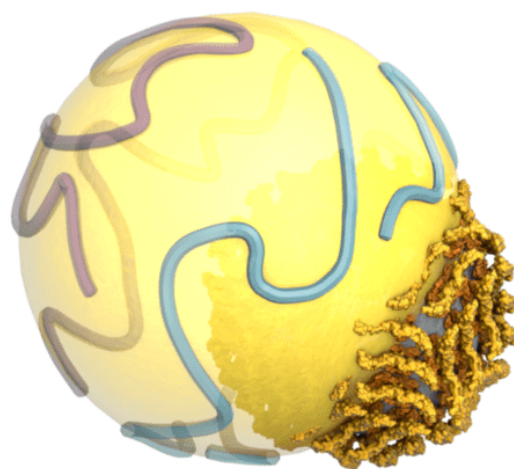
## Figures

### Figure 1 Hepatitis C Virus

Illustration: Cognition Studio, Inc.



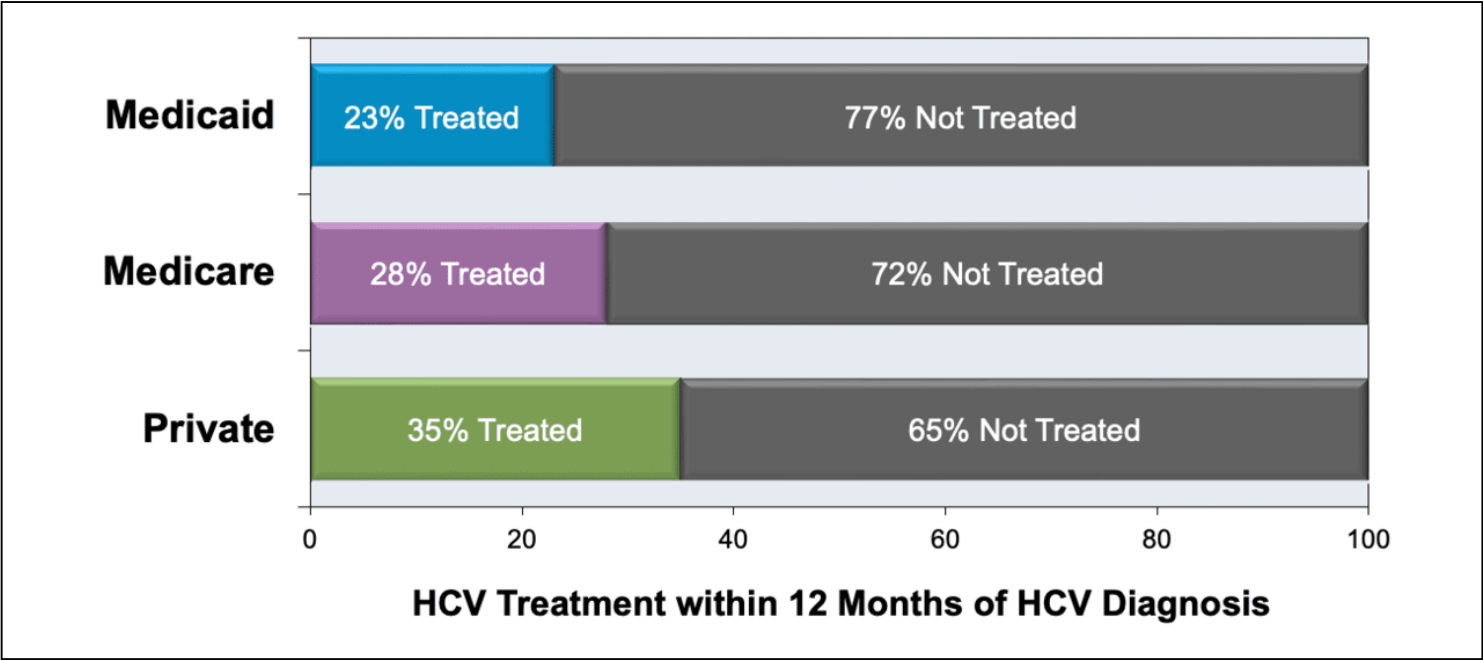
Intact Virion



Lipoviral Particle

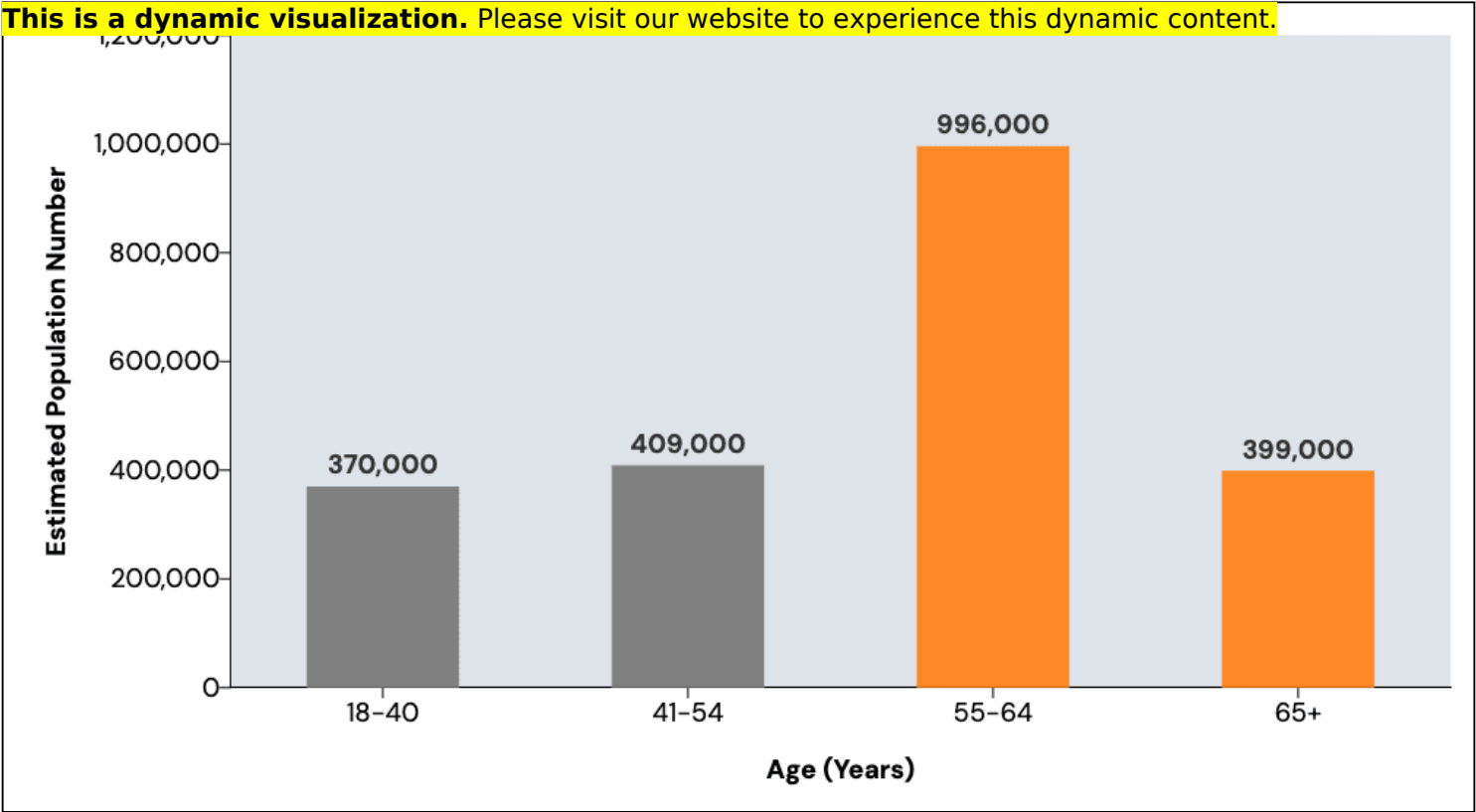
**Figure 2 Hepatitis C Treatment Among Insured Adults, United States, 2019-2020**

Source: Thompson WW, Symum H, Sandul A, et al. Vital Signs: Hepatitis C Treatment Among Insured Adults - United States, 2019-2020. MMWR Morb Mortal Wkly Rep. 2022;71:1011-17.



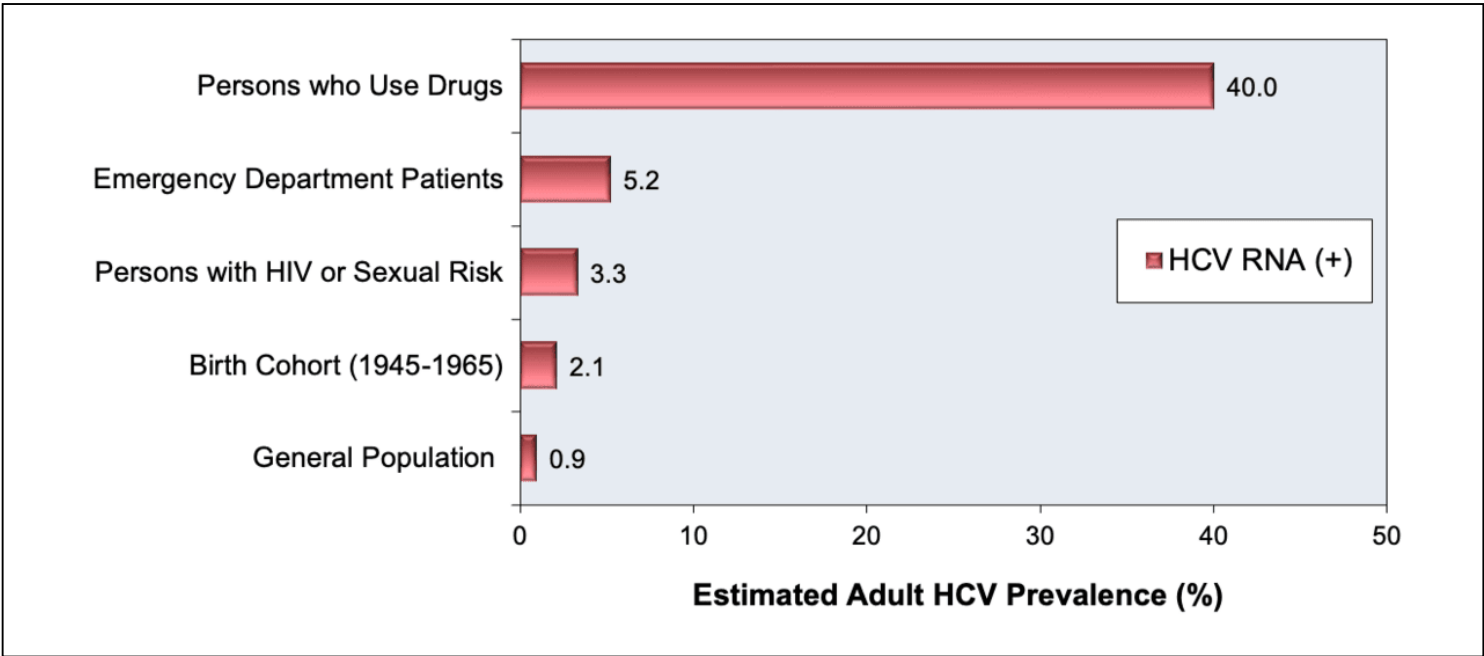
**Figure 3 Hepatitis C Virus Prevalence Features in the United States**

Source: Lewis KC, Barker LK, Jiles RB, Gupta N. Estimated Prevalence and Awareness of Hepatitis C Virus Infection Among US Adults: National Health and Nutrition Examination Survey, January 2017-March 2020. Clin Infect Dis. 2023;77:1413-5.



**Figure 4 Estimated HCV RNA Prevalence in the United States**

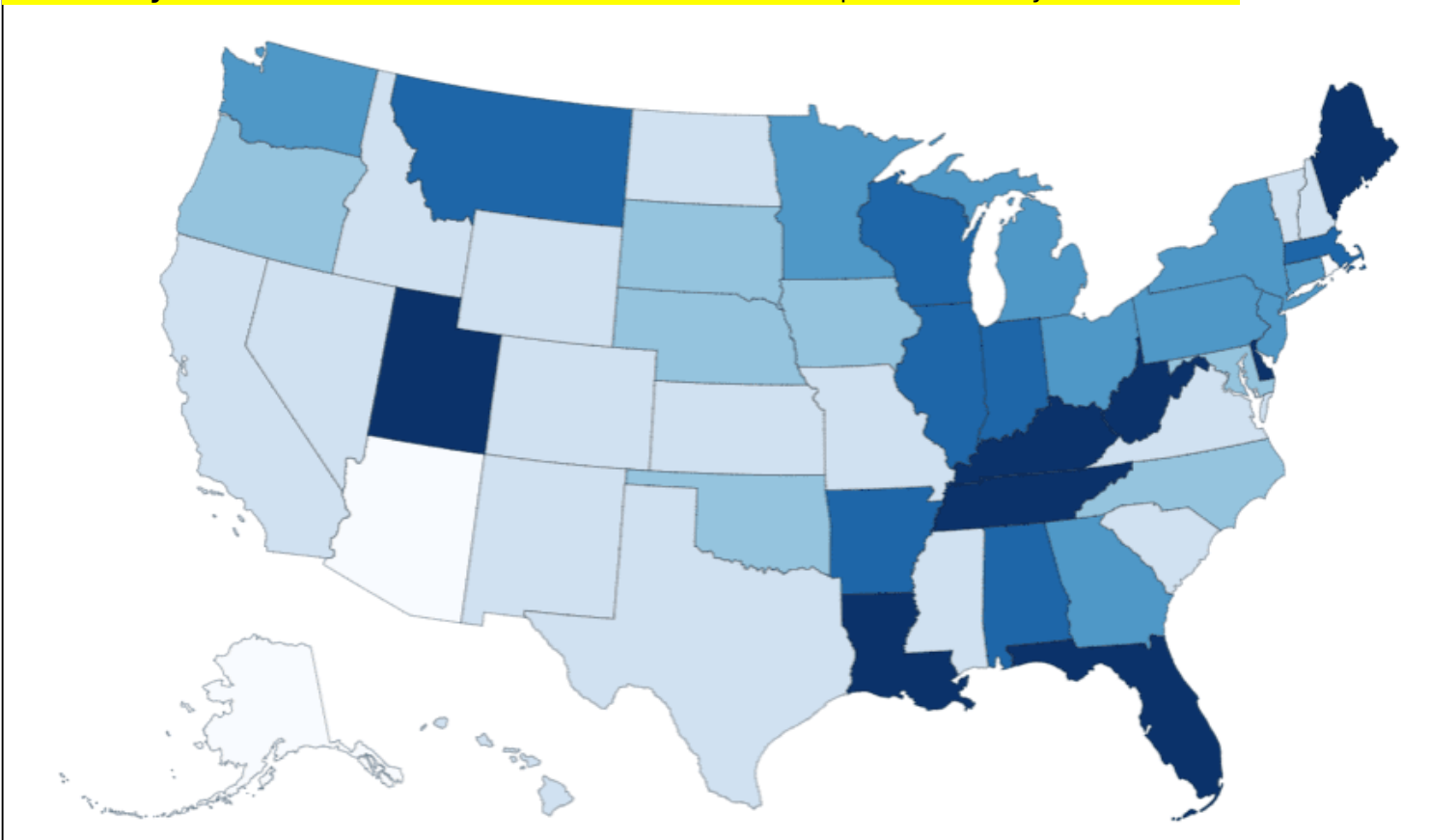
Source: Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. MMWR Recomm Rep. 2020;69:1-17.



## Figure 5 Hepatitis C Incidence, United States, 2023

Source: Centers for Disease Control and Prevention (CDC). Hepatitis C Surveillance 2022. Published April 2025.

**This is a dynamic visualization.** Please visit our website to experience this dynamic content.

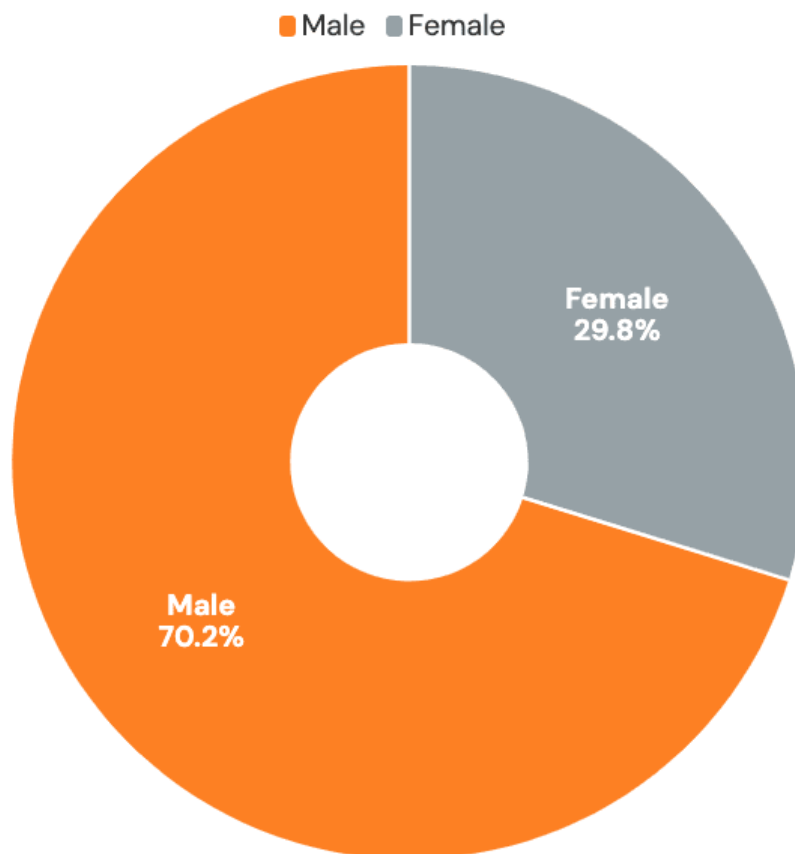


## Figure 6 People Who Inject Drugs in the United States

Source: Bradley H, Hall EW, Asher A, et al. Estimated Number of People Who Inject Drugs in the United States. Clin Infect Dis. 2023;76:96-102.

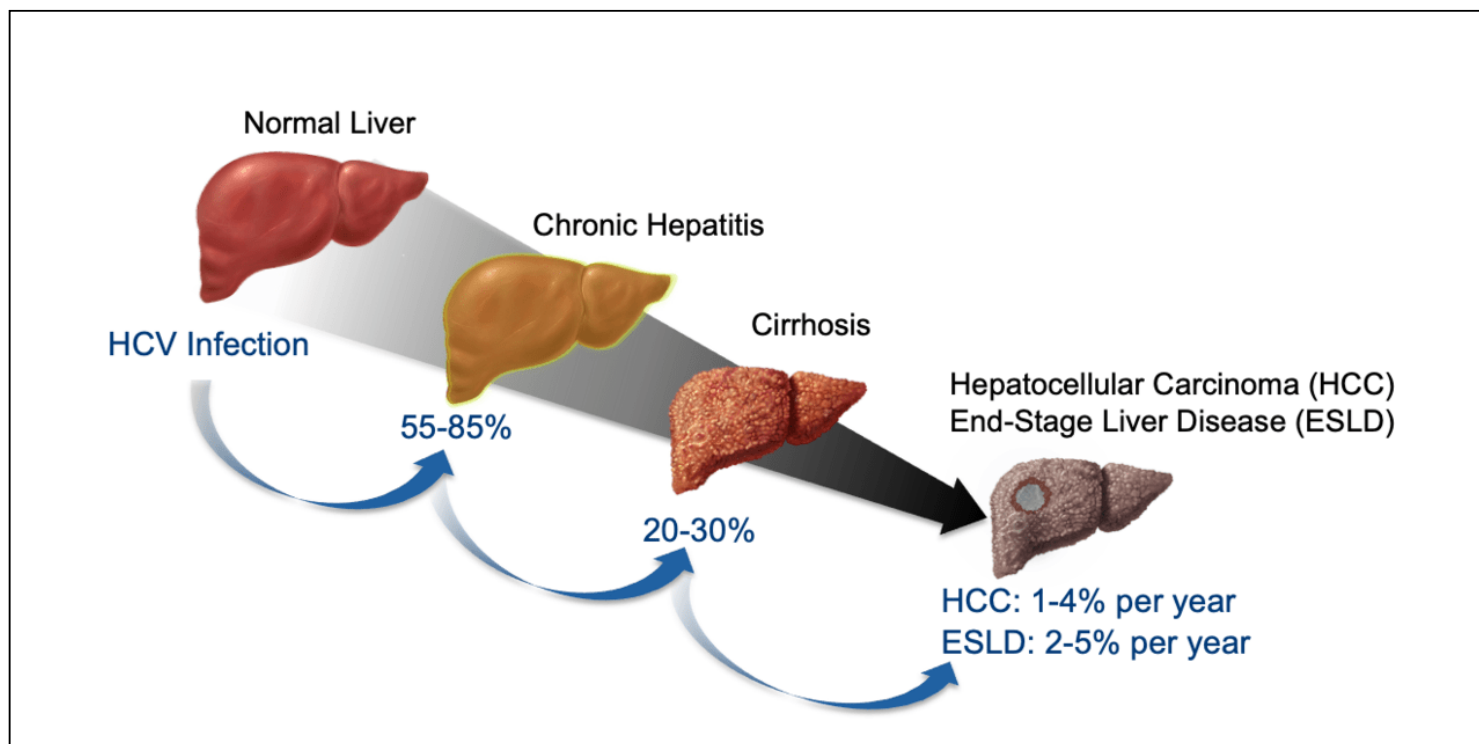
**This is a dynamic visualization.** Please visit our website to experience this dynamic content.

**Males account for 70% of persons who inject drugs.**



## Figure 7 Natural History of Untreated Hepatitis C Infection

Illustration: David H. Spach, MD





## Figure 8 Typical and Accelerated Progression of Untreated Hepatitis C Infection

Illustration: David H. Spach, MD

