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

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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).[20]

- 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

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2. Centers for Disease Control and Prevention (CDC). Hepatitis C Surveillance 2023. Published April 2025.
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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.
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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] -

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[[AASLD-IDSA Hepatitis C Guidance] -

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Figures

Figure 1 Hepatitis C Virus

Illustration: Cognition Studio, Inc.

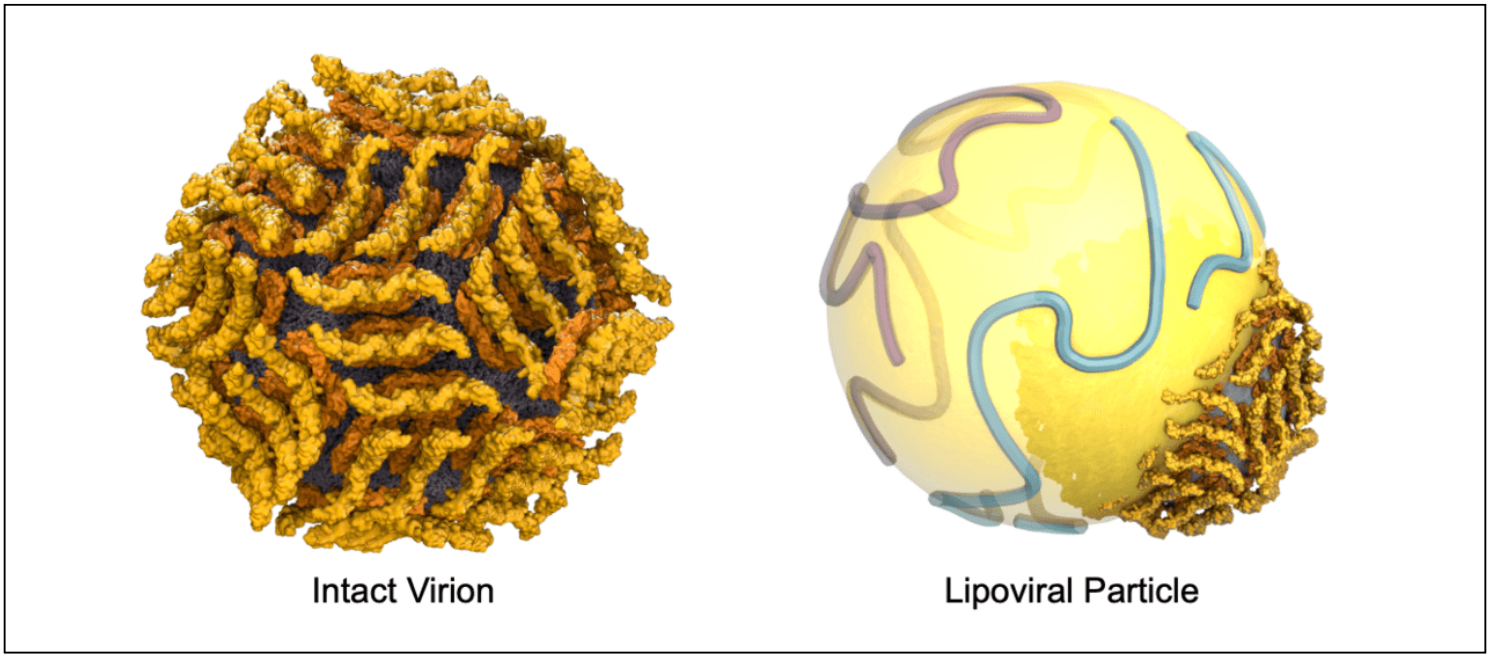


Figure 2 Hepatitis C Treatment Among Insured Adults, United States, 2019-2020

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.

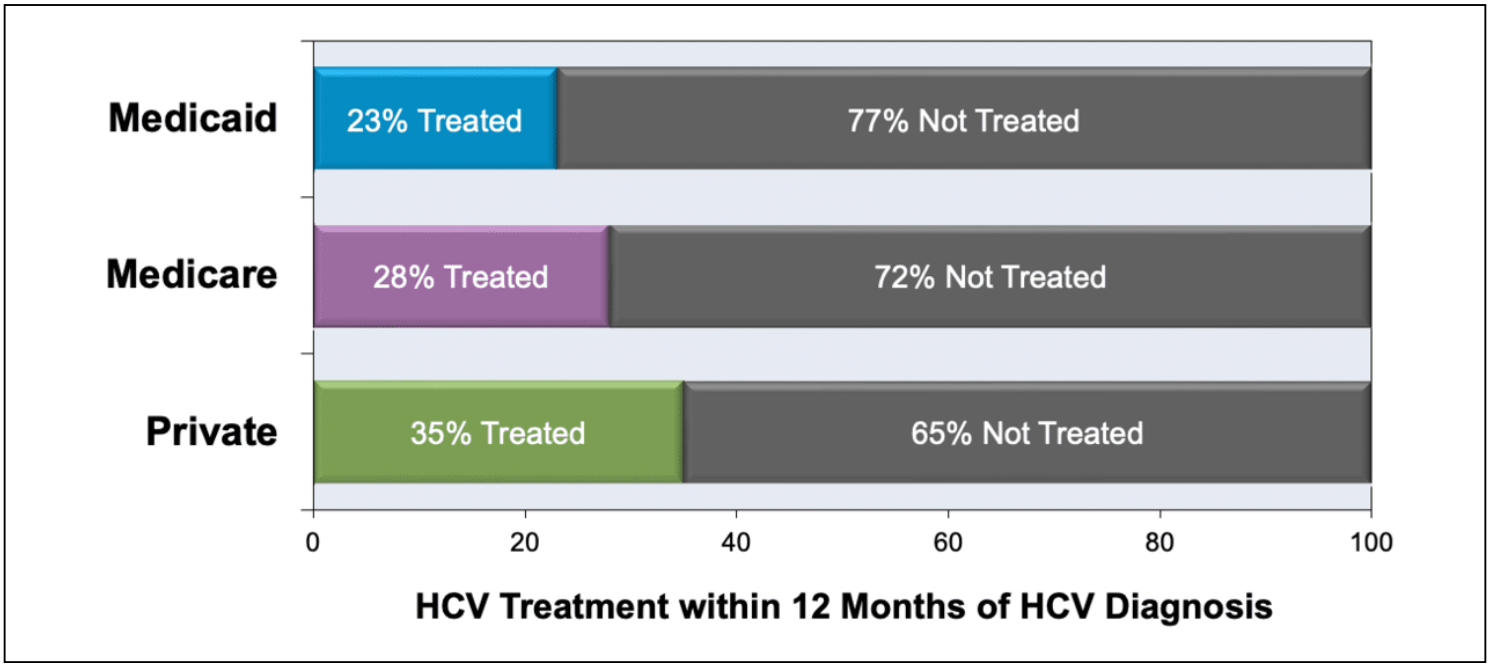


Figure 3 Hepatitis C Virus Prevalence Features in the United States

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.

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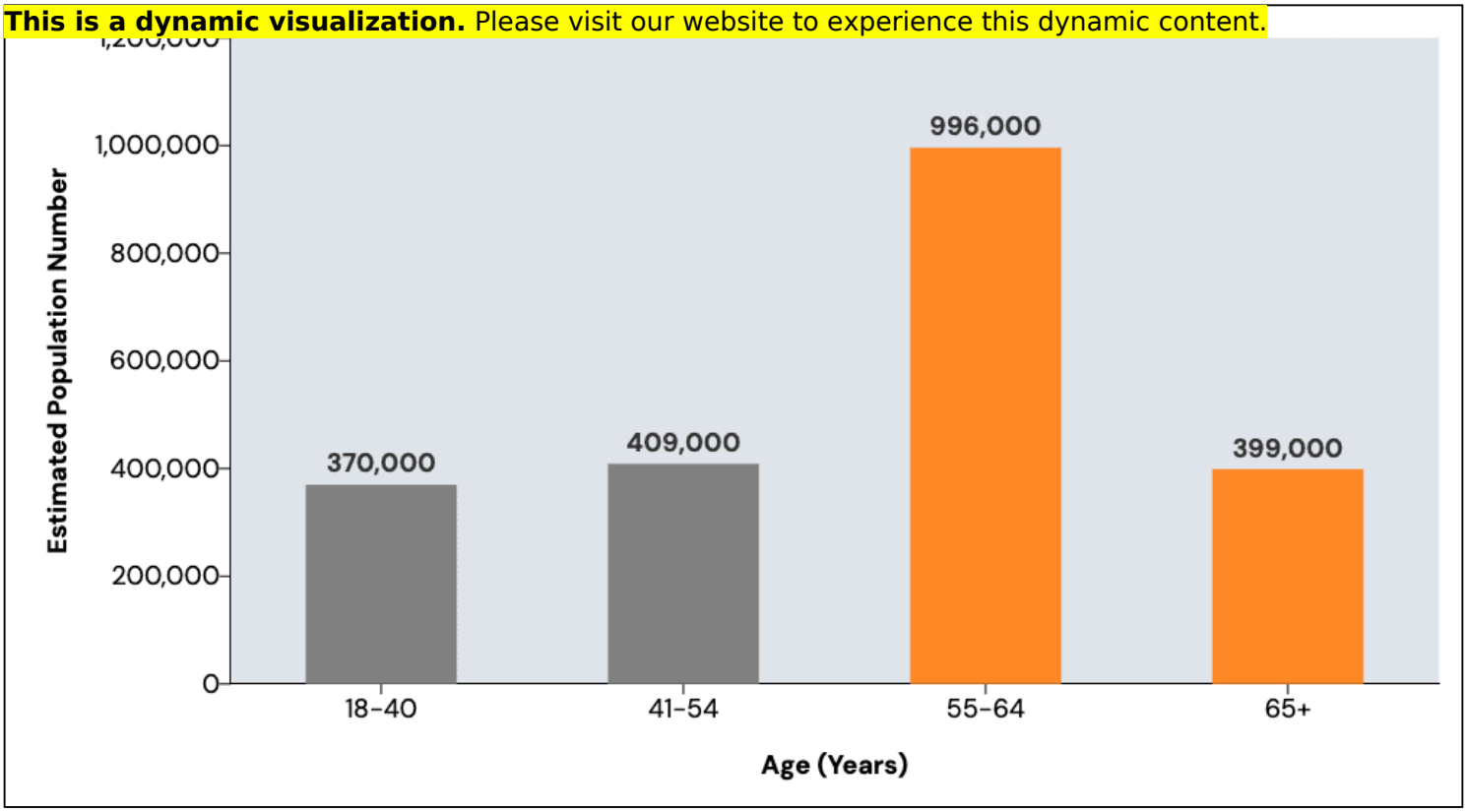


Figure 4 Estimated HCV RNA Prevalence in the United States

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.

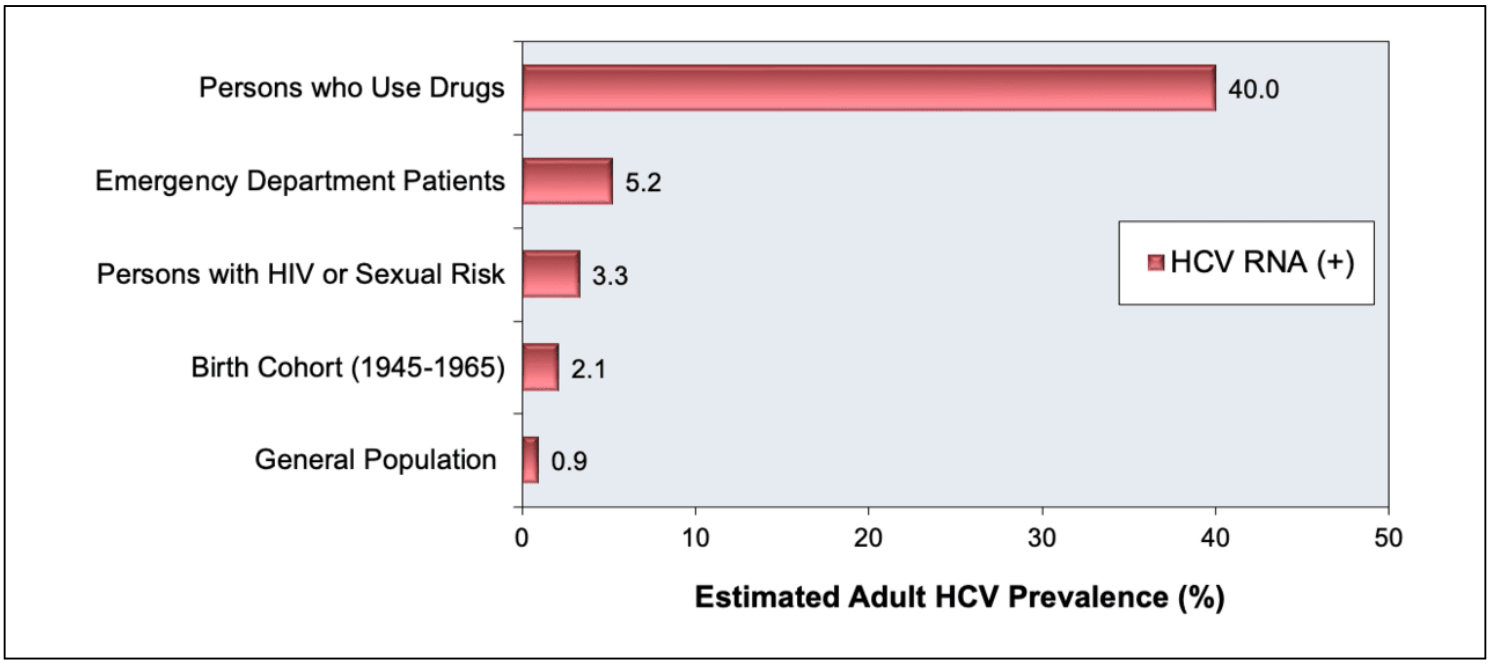


Figure 5 Hepatitis C Incidence, United States, 2023

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

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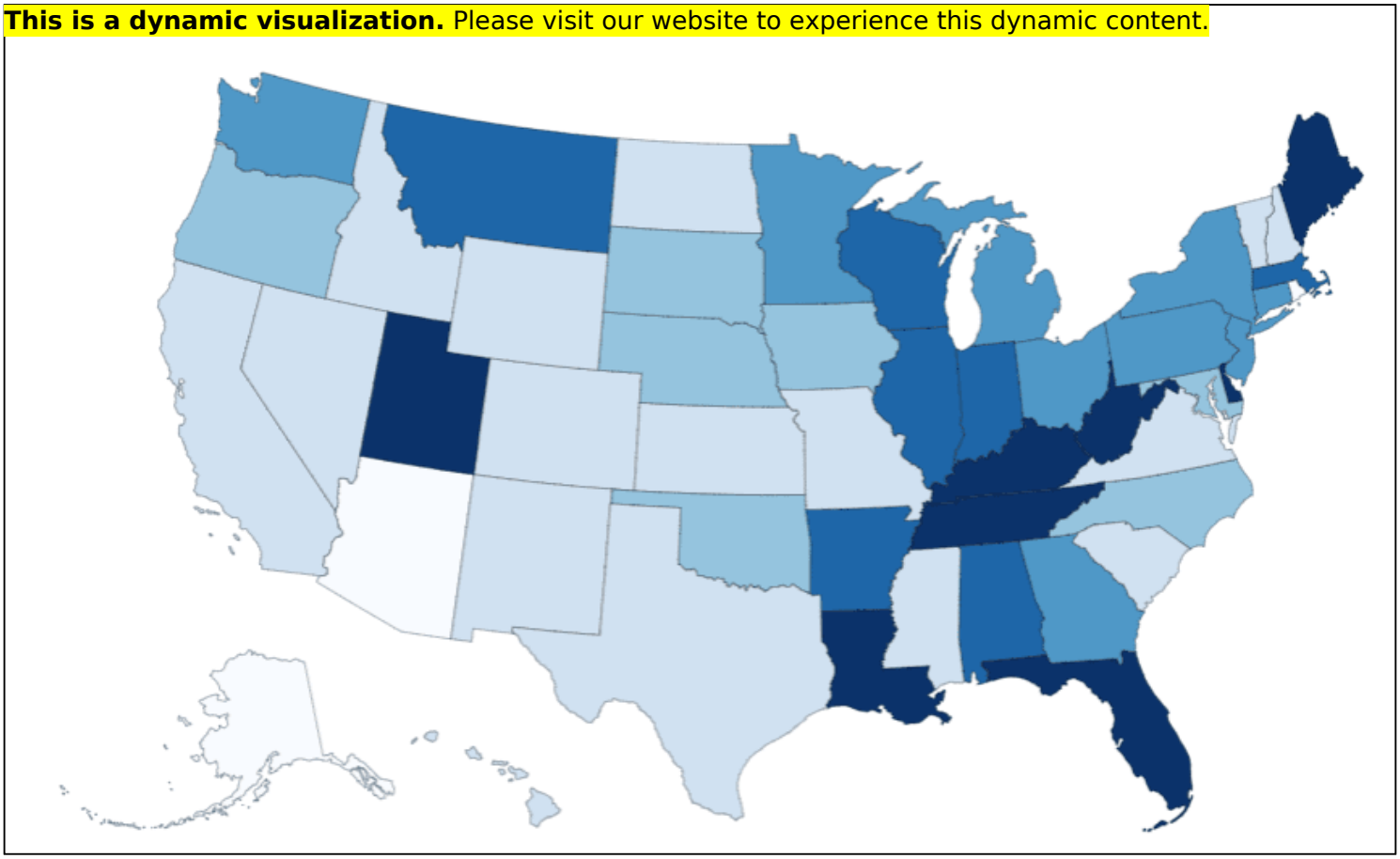


Figure 6 People Who Inject Drugs in the United States

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.

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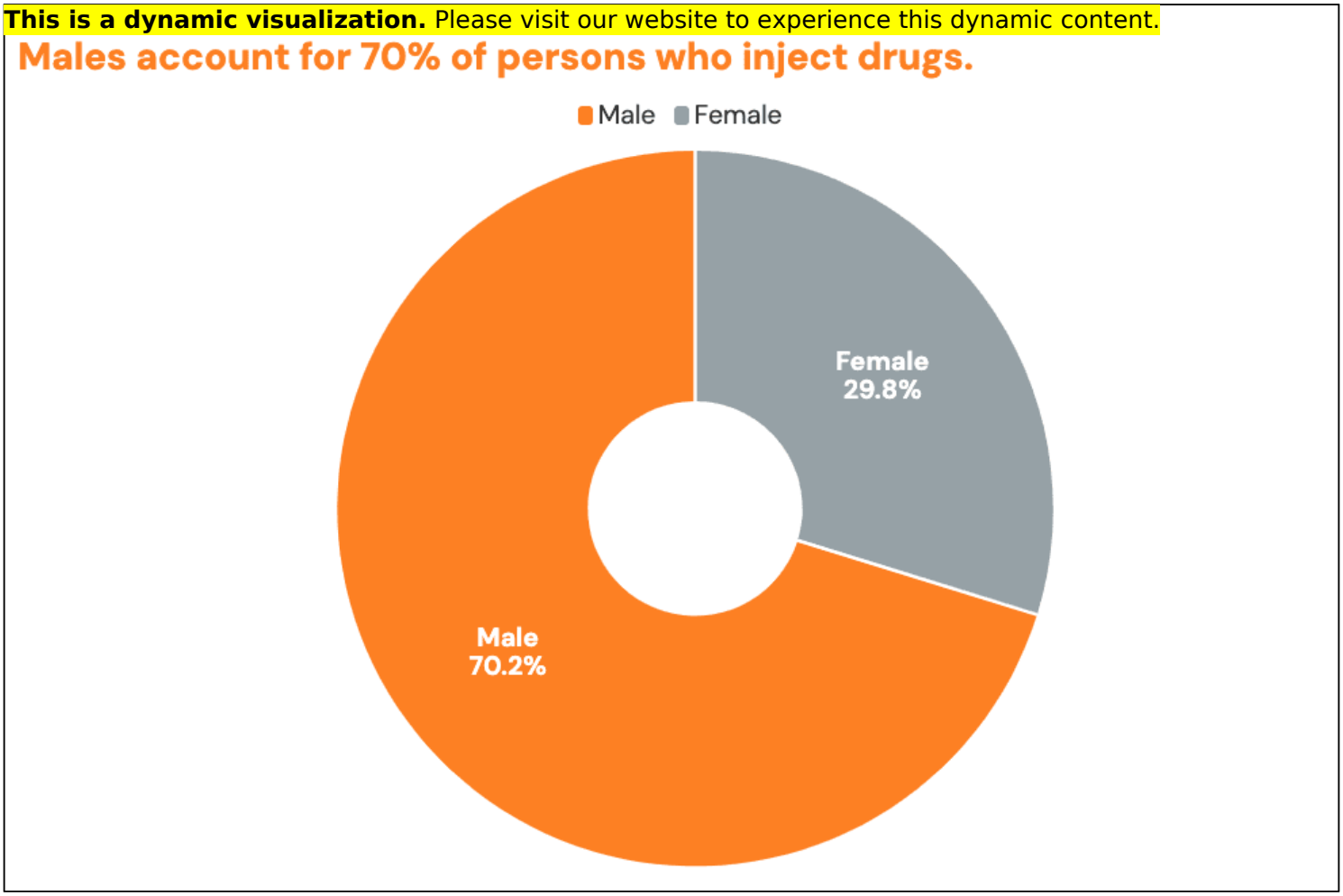


Figure 7 Natural History of Untreated Hepatitis C Infection

Illustration: David H. Spach, MD

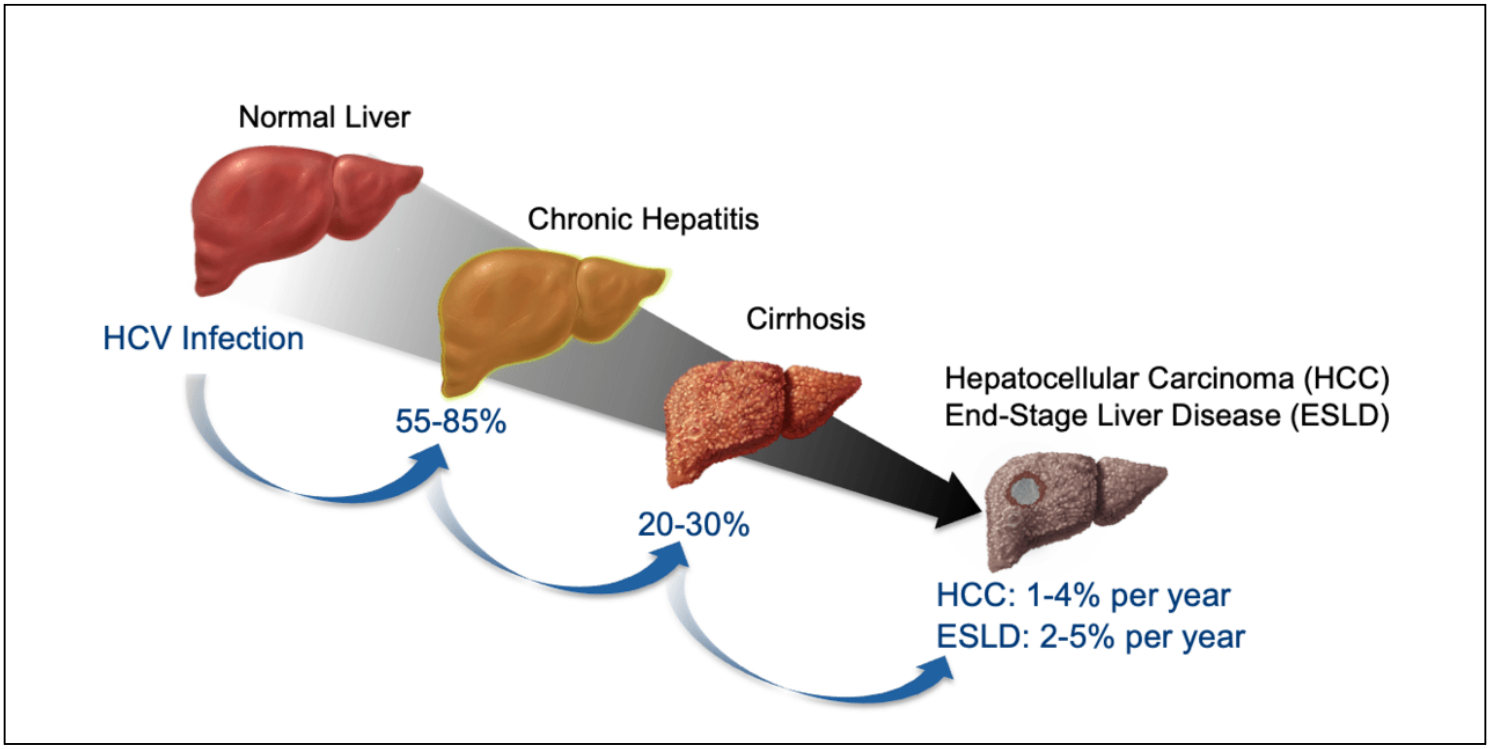


Figure 8 Typical and Accelerated Progression of Untreated Hepatitis C Infection

Illustration: David H. Spach, MD

