

HCV Epidemiology in the United States

This is a PDF version of the following document:

Module 1: Screening and Diagnosis of Hepatitis C Infection

Lesson 1: <u>HCV Epidemiology in the United States</u>

You can always find the most up-to-date version of this document at https://www.hepatitisC.uw.edu/go/screening-diagnosis/epidemiology-us/core-concept/all.

HCV Incidence in the United States

Definitions of HCV Incidence

The incidence of hepatitis C virus (HCV) infection is defined as the number of new infections in a specific region over a specific time period; the incidence data is typically reported for a 1-year period, often in conjunction with cumulative and comparative multiyear data (Figure 1). The Centers for Disease Control and Prevention (CDC) defines the incidence of HCV in the United States (or in each state) as the number of acute HCV cases that occur per year, which is the closest proxy of actual new infections. The incidence rate is the number of cases per total population (typically defined as the number per 100,000 persons).

Method of Estimating HCV Incidence

Most individuals with acute HCV infection do not have a clinically evident illness, and most do not seek medical care. In addition, many cases of diagnosed acute hepatitis C are not reported. Thus, determining the true incidence of new HCV infections per year based on the number of reported cases requires highly complex epidemiology modeling techniques.[1] For each new acute HCV case that is reported in the United States, the CDC estimates there are approximately 13.9 actual new acute HCV cases (reported and unreported) that have occurred.[1,2] This high ratio (total estimated cases to actual reported cases) is primarily a result of the large proportion of persons with acute HCV who have asymptomatic or minimally symptomatic infection and do not seek medical care, or they have undiagnosed HCV infection (Figure 2); the passive HCV reporting system likely also contributes to the low number of reported acute HCV cases. The CDC provides several numbers related to the incidence of hepatitis C in the United States, including number of reported acute cases, estimated number of acute clinical cases, estimated number of new infections, and rates per 100,000 persons at the state and national level.[2]

HCV Incidence Data

In 2021, a total of 5,023 new cases of acute hepatitis C were reported to the CDC from 44 states; based on this number, the CDC estimated there was a total of 69,800 new acute cases of HCV in 2021.[2] From 2010 to 2021, the number of estimated annual acute HCV infections has steadily increased, with an overall increase of 492%.[2] The increase in new HCV infections from 2010 to 2021 is primarily attributed to the opioid epidemic and associated injection drug use, particularly among young adults.[3,4,5,6] The following summarizes CDC HCV surveillance data for 2021 based on specific groups and demographic factors (Figure 3).[2]

• Sex: The number of reported cases of acute HCV infections was higher in males (3,348) than in



females (1,669), with males accounting for two-thirds of the acute HCV infections.[2]

- **Age Group**: Most reported acute infections involved persons 20-49 years of age, with the highest number among persons 30-39 years of age.[2]
- Race/Ethnicity: The highest number of reported cases of acute HCV by race/ethnicity occurred in White persons, followed by Hispanic and Black persons.[2] White persons comprised 72% (3,097 of the 4,329) cases for which race/ethnicity data was reported.[2] The highest rate of acute HCV (cases per 100,000 population) was in American Indian/Alaska Native persons, followed by White persons; this has been consistent since 2005.[2]
- **Urban/Rural**: Although 84% of cases were diagnosed in Urban areas, the rate of acute HCV (cases per 100,000 population) was slightly higher in rural areas (1.7) versus urban areas (1.3).[2]

Importance of HCV Incidence Data

The United States HCV incidence data provide important information for monitoring trends in transmission patterns, developing hepatitis C prevention strategies, monitoring the effectiveness of implemented prevention plans, and identifying focal outbreaks or regional patterns of infection. In addition, valuable information emerges when data is categorized by age group, sex, race/ethnicity, and risk factor for acquiring HCV, as these data may inform major population-specific prevention strategies.



HCV Prevalence in United States

Definition of HCV Prevalence

The HCV prevalence is defined as the number (or percent) of persons in the total population living with HCV. Typically, HCV prevalence specifically refers to persons with active (HCV RNA-positive) HCV infection. The HCV prevalence in the United States is dynamic and is impacted by five factors: (1) number of new HCV infections, (2) number of persons who experience a spontaneous HCV cure, (3) number of treatment cures, (4) number of deaths, and (5) number of persons cured who acquire HCV again (Figure 4). Less frequently, the HCV prevalence data is given for all individuals who have ever been infected with HCV, which includes those with active HCV, persons who spontaneously resolved HCV, and those with HCV treatment-related cure. The prevalence rate of chronic hepatitis C is the number of persons living with HCV per population (typically defined as number of persons per 100,000 population).

HCV Prevalence Estimates

In the United States, HCV infection is the most common bloodborne infection. The best estimates of HCV prevalence derive from analysis of serum specimens taken from participants in the National Health and Nutrition Examination Survey (NHANES).[7,8,9,10,11,12] The NHANES surveys require some adjustments since they do not sample certain populations, such as persons who are incarcerated, persons without housing, nursing home residents, and persons on active military duty. The most recent estimate of HCV prevalence in the United States was generated from analyses of 2017 to 2020 NHANES survey data.[12] In this time period, there were an estimated 2.2 million persons who were HCV RNA positive (0.9% prevalence among adults).[12] The following summarizes NHANES HCV prevalence estimate by sex, age group, and race ethnicity (Figure 5).[12]

- **Sex**: In the United States, the estimated HCV prevalence for adult males is 1.4%, which is 2.8-fold higher than the 0.5% prevalence in adult females; among people living with HCV, males account for 73% and females 27%.[12]
- **Age Group**: More than 50% of people living with HCV are 55 years of age or older. Persons 55-64 years of age account for the highest number of people living with HCV, with an HCV prevalence of 2.4% .[12]
- Race/Ethnicity: Based on race/ethnicity, White people have the highest HCV prevalence, accounting for roughly 80% of people living with HCV.[12] The prevalence rate among White people was 5.0%, which is only slightly higher than the 4.8% prevalence rate in Black people.[12]
- State and Region: In the United States, 9 states each have more than 65,000 persons living with HCV; these states are California (318,900), Texas (202,500), Florida (151,000), New York (116,000), Pennsylvania (93,900), Ohio (89,600), Michigan (69,100), Tennessee (69,100), and North Carolina (66,400).[13] Five of these states (New York, Pennsylvania, Ohio, Tennessee, and North Carolina) are in the Appalachian region.[13] Together, these 9 states account for an estimated 52% of all persons living with HCV nationally.[13]

Newly Reported Chronic Hepatitis C Cases

In 2021, the CDC reported 107,540 persons in the United States with a new diagnosis of chronic HCV.[2] Persons 30-39 years of age had the highest numbers of reported new diagnoses of HCV, followed by persons 60 years of age and older.[14] Among the newly reported chronic HCV cases, 64% were male and 36% female.[14] (Figure 6)

Awareness of HCV Infection Status

Using the most recent NHANES data, investigators estimated only 56% of persons infected with HCV in the United States were aware of their HCV infection status.[15] Awareness of infection status was lower in



persons who were foreign-born and in persons with income below the poverty level.[15] These most recent NHANES data do not show a major improvement from a prior analysis of NHANES data (from 2001-2008) that reported 50% of persons infected with HCV were aware of their HCV infection status.[16] Awareness of HCV status may be higher among persons engaged in the private health care sector—a study involving persons with access to medical care in four private health care organizations during the years 2006 to 2008 showed an estimated 57% were aware of their HCV infection.[17]

HCV Genotype

In the United States, approximately 75% of chronic HCV infections are caused by hepatitis C genotype 1 (subtypes 1a or 1b), 15 to 20% by genotype 2 or 3, and less than 5% by genotypes 4, 5, or 6.[18,19,20] Among the genotype 1 infections, genotype 1a is more common than 1b.[20]



HCV-Related Deaths

The CDC reports for HCV-related deaths in the United States are based on death certificate data and likely underestimate the true number of HCV-related deaths.[21] During the years 2010 to 2021, the annual deaths attributed to HCV in the United States peaked in 2014 and 2015, followed by an overall decline from 2016 through 2021.[2] In 2021, there were 13,385 deaths with hepatitis C listed as the cause of death, and 71% of these deaths occurred in males.[2] The total number of HCV-related deaths was highest in White persons.[2] (Figure 8)



Risk Factors for Acquiring HCV

Overview of Risk Factors for HCV Acquisition

Investigators and public health officials have identified multiple risk factors for acquiring HCV in the United States: injection drug use, history of receiving a blood product transfusion prior to July 1992, receipt of solidorgan transplantation, hemophilia with receipt of factor concentrates made before 1987, male-to-male sex, body tattoos, and intranasal cocaine use.[18,22,23,24] Among these, injection drug use is the most common and important risk factor for acquiring HCV in the United States. In the 1970s and 1980s, receipt of HCV-infected blood products or organs accounted for nearly 50% of new cases of HCV, but after the discovery of HCV as the cause of non-A, non-B hepatitis in 1989 and the introduction of blood screening tests in the early 1990s, the proportion of new HCV cases caused by contaminated blood or organs dramatically declined.[7,23,25,26]

Injection Drug Use

Injection drug use remains the most common risk factor for acquiring HCV in the United States, and in 2021, among the 1,449 reported cases of acute HCV for which risk factor information on drug use was available, 57% reported injection drug use as their risk factor for acquiring HCV.[2] Approximately 20 to 30% of persons who inject drugs become infected with HCV within the first 2 years of starting to inject drugs, and 50% within 5 years.[27] Transmission risk is greatest with "direct sharing" of needles and syringes, but may also occur indirectly via sharing injection paraphernalia, such as water, cookers, and cotton filters.[28,29,30] The incidence of HCV in persons who inject drugs markedly declined from early 1992-2002, likely due to the increased availability of needle exchange programs that arose in response to the HIV epidemic.[29,31] Since 2002, however, multiple reports have documented a surge in HCV infections in the United States among young persons who inject drugs, owing to the ongoing opioid epidemic and continued high rates of receptive needle and syringe sharing (Figure 7).[3,4,5,32,33]

Noninjection Drug Use

The role of noninjection drug use, such as snorting crack cocaine, powder cocaine, methamphetamines, or heroin, as a risk factor for acquiring hepatitis C remains controversial.[34] The risk of acquiring HCV is plausible with use of pipes that may cause burns in the oral mucosa (with possible open mouth sores) or use of straws or tubing that causes erosion of nasal membranes (with bleeding in the nasal passage). Sharing these blood-contaminated devices could then lead to HCV transmission. The prevalence of HCV in people who use noninjection drugs ranges from 2.3 to 35.3%. In some people, the use of noninjection drugs is a surrogate for other risk activities associated with HCV acquisition.

Sexual Exposure

The risk of acquiring HCV through sexual contact with a person who has HCV infection depends on one's sex partners and the type of sex they engage in. Overall, sexual transmission has accounted for up to 15% of cases of HCV in the United States, but very close interrogation revealed that most cases of sexual transmission also involved injection drug use as a risk factor. Multiple studies involving monogamous heterosexual couples have shown a rate of HCV transmission of less than 1% per year, including one study among 500 serodifferent monogamous couples that reported a sexual transmission rate of 0.07% per year.[35,36,37,38,39] In recent years, however, multiple reports have identified cases of sexual transmission among men who have sex with men (MSM), particularly men with HIV who have sex with other men.[40,41,42,43] Specific factors identified with HCV transmission among MSM include coinfection with HIV, use of recreational drugs during sex, and certain sex practices that result in rectal bleeding or damage to the rectal mucosa, including fisting and sharing sex toys.[40,44]

Chronic Hemodialysis



The prevalence of HCV infection in persons receiving hemodialysis is approximately 8%, which is nearly 5-fold higher than the general United States population.[45] Several risk factors have been identified for dialysis patients acquiring HCV, including number of blood transfusions received, number of years on dialysis, mode of dialysis (hemodialysis poses a greater risk than peritoneal dialysis), and the prevalence of HCV in the dialysis unit. In the United States, multiple dialysis-associated HCV outbreaks have occurred. In most cases, HCV transmission likely resulted from inadequate infection control practices, particularly in situations when patients received dialysis immediately after a patient with HCV infection received dialysis.[46,47,48,49]

Receipt of Clotting Factor Concentrates

In the late 1970s through the mid-1980s, most persons with hemophilia acquired HCV infection via the receipt of contaminated plasma clotting factor concentrates.[50,51,52] In 1985, several companies introduced virus inactivation procedures for hemophilia blood products, and by 1987, these procedures were uniformly used, virtually eliminating the risk of transmission of HCV via clotting factor concentrates. Use of recombinant factor concentrate also provides an option for providing factor concentrate with no risk of viral contamination.

Receipt of Transfusion of Blood Products

In the 1960s, the risk of acquiring HCV from a blood transfusion was approximately 33%. The universal screening of blood and organ donors with the routine use of second-generation HCV antibody tests in 1992 nearly eliminated the subsequent risk of transfusion-associated HCV.[26,31,53] In 1999, the introduction of HCV nucleic acid testing (NAT) as a supplement to HCV antibody testing of blood products further reduced the risk of acquiring HCV from a blood transfusion.[26,54,55] The estimated risk of acquiring HCV from a blood transfusion decreased further following the introduction, in 1999, of HCV nucleic acid testing (NAT) as a supplement to HCV antibody testing of blood products.[54,55] Blood banks in the United States now use a combination of the third-generation enzyme-linked immunosorbent assay (ELISA) and NAT screening of minipool testing (16 samples). The current estimated risk of acquiring HCV from a transfusion in the United States is approximately 1 in 2 million.

Receipt of Immune Globulin

In the 1990s, scattered cases and outbreaks of HCV transmission via gamma globulin occurred in the United States and Europe.[56,57,58] Subsequently, advances in virus inactivation procedures have nearly eliminated any risk of HCV transmission with immune globulin, and the manufacturers of intravenous immune globulin use vigorous viral inactivation and removal procedures.

Organ and Tissue Transplantation

Rare cases of inadvertent HCV transmission via organ or tissue transplantation have occurred in the United States.[59,60] Most cases of transmission have involved HCV antibody-negative, HCV RNA-positive donors.[59,60] In 2013, the U.S. Public Health Service drafted updated guidelines for preventing HCV transmission through organ transplantation, and these guidelines recommend HCV RNA testing of all organ and tissue donors, which has further reduced the risk of inadvertent HCV transmission.[61] It should be noted, however, that owing to the safety profile and effectiveness of direct-acting antivirals for HCV, some institutions now allow for HCV-positive organ donations, with a plan to treat organ recipients post-transplant.

Perinatal

In the United States, due to the opioid epidemic, there has been a significant increase in HCV infection in recent years among women of childbearing age; this trend has raised concerns about a potentially significant increase in perinatal HCV infections.[62,63,64] Among pregnant women with chronic HCV, approximately 6% will transmit HCV to their child.[65,66,67] Nearly all cases of perinatal HCV transmission have involved mothers who had detectable HCV RNA in plasma during pregnancy. Women coinfected with HIV and HCV



have an approximately twofold higher risk of perinatal HCV transmission when compared with women who have HCV monoinfection.[65] The risk of HCV transmission via breastfeeding appears to be negligible.[65,66,67]

Household Contact

Acquiring HCV via nonsexual household contact with a person infected with HCV can occur, but the number of documented cases is extremely low.[68,69] Transmission in this setting would most likely involve sharing a razor or toothbrush, since this process could involve transmission via a blood-tainted device.

Tattoos and Piercings

In the United States, the risk of acquiring HCV from a licensed, regulated professional tattoo or piercing center is extremely low.[70] Tattoos performed in unregulated and unlicensed tattoo centers, such as with tattoos applied by friends or in prison, increase the risk for HCV acquisition.[70,71]



CDC Case Definitions and Reporting

CDC Hepatitis C Case Definitions

The CDC has established case definitions and reporting criteria for acute and for past (resolved) or present (chronic) hepatitis C infection.

Acute Hepatitis C-2020 Case Definition

The CDC 2020 Case Definition for Acute Hepatitis C infection includes clinical and laboratory criteria (Figure 9), along with a case classification as probable or confirmed.[72] Of note, a patient can have a confirmed case of acute HCV based on laboratory data alone (a hepatitis test conversion documented by a negative HCV antibody, HCV antigen, or NAT laboratory test result, followed within 12 months by a positive result with any of these tests). Symptomatic cases often go unreported for multiple reasons: many persons with symptomatic acute HCV do not seek medical care, the diagnosis may be missed, and medical providers may fail to report diagnosed cases. It is important not to report cases that have already been reported. A more detailed discussion of the Acute Hepatitis C 2020 Case Definition is included in the lesson *Diagnosis of Acute HCV Infection*.

Chronic Hepatitis C Virus Infection—2020 Case Definition

The CDC 2020 Case Definition for Chronic Hepatitis C includes clinical and laboratory criteria (<u>Figure 10</u>), as well as a case classification.[73] These cases pertain to persons with current (active) HCV infection and do not represent persons who spontaneously cleared HCV infection. Also, it is important not to report cases that have already been reported.

Perinatal Infection Hepatitis C Infection—2018 Case Definition

The CDC 2018 Case Definition for Hepatitis C, Perinatal Infection includes clinical criteria, laboratory criteria for diagnosis, criteria to distinguish a new case from an existing case, and a case classification.[74] A confirmed case requires the following:

• Infant who has a positive test for HCV RNA nucleic acid amplification test (NAAT), HCV antigen, or detectable HCV genotype at ≥2 months and ≤36 months of age and is not known to have been exposed to HCV via a mechanism other than perinatal.

Reporting Criteria

Persons identified with acute HCV should undergo an interview to determine an identifiable risk factor in the 2-week to 6-month time frame that preceded the onset of their illness. Similarly, the individual with past (resolved) or present (chronic) HCV infection should be interviewed to determine lifetime risk factors for HCV. The <u>Viral Hepatitis Case Report</u> form should be filled out for persons identified with either acute HCV infection or past/present HCV. Cases of HCV should be reported to a health department, which in turn submits reporting data to the CDC via the Nationally Notifiable Diseases Surveillance System (NNDSS).



Summary Points

- The estimated number of annual acute HCV infections in the United States increased significantly from 11,800 in 2010 to 69,800 in 2021.
- The recent increases in new HCV infections have primarily resulted from the ongoing opioid epidemic and the associated injection drug use.
- In 2021, the highest number of new HCV infections occurred in persons 30-39 years of age.
- In 2021, American Indian/Alaskan Native, White, and Black individuals were among the top three groups with the greatest prevalence rate of new HCV infections.
- Based on CDC estimates, there are 2.2 million persons living with HCV infection, corresponding to a 0.9% HCV prevalence among the adult population in the United States.
- The HCV prevalence is dynamic and impacted by the number of new HCV infections, the number of persons that spontaneously resolve their infection, the number of treatment cures, the number of deaths, and the number of cured persons who become reinfected.
- It is estimated that approximately 56% of persons with HCV infection are aware of their infection in the United States.
- Injection drug use is the most common risk factor for HCV acquisition; sexual transmission of HCV can occur, but this most often involves MSM; the risk among MSM is substantially higher in those with HIV.
- The number of annual deaths attributed to HCV has declined significantly in recent years, falling from 19,613 in 2014 to 13,895 in 2021, with most of the deaths involving males.
- The CDC has established a clear definition of acute, chronic, and perinatal HCV infection for reporting purposes as well as reporting guidelines.



Citations

- 1. Klevens RM, Liu S, Roberts H, Jiles RB, Holmberg SD. Estimating acute viral hepatitis infections from nationally reported cases. Am J Public Health. 2014;104:482-7. [PubMed Abstract] -
- Centers for Disease Control and Prevention (CDC). Hepatitis C Surveillance 2021. Published August 2023.
 [CDC] -
- 3. 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] -
- 4. 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] -
- Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years - Kentucky, Tennessee, Virginia, and West Virginia, 2006-2012.
 MMWR Morb Mortal Wkly Rep. 2015;64:453-8.
 [PubMed Abstract] -
- 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] -
- 7. Ditah I, Ditah F, Devaki P, et al. The changing epidemiology of hepatitis C virus infection in the United States: National Health and Nutrition Examination Survey 2001 through 2010. J Hepatol. 2013;60:691-8.

 [PubMed Abstract] -
- 8. Denniston MM, Jiles RB, Drobeniuc J, Klevens RM, Ward JW, McQuillan GM, Holmberg SD. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med. 2014;160:293-300.

 [PubMed Abstract] -
- 9. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. Ann Intern Med. 2006;144:705-14. [PubMed Abstract] -
- 10. Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. N Engl J Med. 1999;341:556-62.

 [PubMed Abstract] -
- 11. 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] -
- 12. 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.



13. Bradley H, Hall EW, Rosenthal EM, Sullivan PS, Ryerson AB, Rosenberg ES. Hepatitis C Virus Prevalence in 50 U.S. States and D.C. by Sex, Birth Cohort, and Race: 2013-2016. Hepatol Commun. 2020;4:355-70.

[PubMed Abstract] -

14. Centers for Disease Control and Prevention (CDC). 2019 Viral Hepatitis Surveillance Report—Hepatitis C. Published May 2021.

[CDC] -

- 15. Kim HS, Yang JD, El-Serag HB, Kanwal F. Awareness of chronic viral hepatitis in the United States: An update from the National Health and Nutrition Examination Survey. J Viral Hepat. 2019;26:596-602. [PubMed Abstract] -
- 16. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001-2008. Hepatology. 2012;55:1652-61.

 [PubMed Abstract] -
- 17. Spradling PR, Rupp L, Moorman AC, et al. Hepatitis B and C Virus Infection Among 1.2 Million Persons With Access to Care: Factors Associated With Testing and Infection Prevalence. Clin Infect Dis. 2012;55:1047-55.

 [PubMed Abstract] -
- 18. Guss D, Sherigar J, Rosen P, Mohanty SR. Diagnosis and Management of Hepatitis C Infection in Primary Care Settings. J Gen Intern Med. 2018;33:551-7.

 [PubMed Abstract] -
- 19. Germer JJ, Mandrekar JN, Bendel JL, Mitchell PS, Yao JD. Hepatitis C virus genotypes in clinical specimens tested at a national reference testing laboratory in the United States. J Clin Microbiol. 2011;49:3040-3.

 [PubMed Abstract] -
- 20. Manos MM, Shvachko VA, Murphy RC, Arduino JM, Shire NJ. Distribution of hepatitis C virus genotypes in a diverse US integrated health care population. J Med Virol. 2012;84:1744-50. [PubMed Abstract] -
- 21. Mahajan R, Xing J, Liu SJ, et al. Mortality among persons in care with hepatitis C virus infection: the Chronic Hepatitis Cohort Study (CHeCS), 2006-2010. Clin Infect Dis. 2014;58:1055-61. [PubMed Abstract] -
- 22. Bragg DA, Crowl A, Manlove E. Hepatitis C: A New Era. Prim Care. 2017;44:631-642. [PubMed Abstract] -
- 23. Williams I. Epidemiology of hepatitis C in the United States. Am J Med. 1999;107(6B):2S-9S. [PubMed Abstract] -
- 24. Alter MJ. Epidemiology of hepatitis C. Hepatology. 1997;26(3 Suppl 1):62S-65S. [PubMed Abstract] -
- 25. Stramer SL. Current risks of transfusion-transmitted agents: a review. Arch Pathol Lab Med. 2007;131:702-7. [PubMed Abstract] -



- 26. Alter HJ, Houghton M. Clinical Medical Research Award. Hepatitis C virus and eliminating post-transfusion hepatitis. Nat Med. 2000;6:1082-6.

 [PubMed Abstract] -
- 27. Hagan H, Pouget ER, Des Jarlais DC, Lelutiu-Weinberger C. Meta-regression of hepatitis C virus infection in relation to time since onset of illicit drug injection: the influence of time and place. Am J Epidemiol. 2008;168:1099-109.

 [PubMed Abstract] -
- 28. Pouget ER, Hagan H, Des Jarlais DC. Meta-analysis of hepatitis C seroconversion in relation to shared syringes and drug preparation equipment. Addiction. 2012;107:1057-65.

 [PubMed Abstract] -
- 29. Holtzman D, Barry V, Ouellet LJ, et al. The influence of needle exchange programs on injection risk behaviors and infection with hepatitis C virus among young injection drug users in select cities in the United States, 1994-2004. Prev Med. 2009;49:68-73.

 [PubMed Abstract] -
- 30. Hagan H, Thiede H, Weiss NS, Hopkins SG, Duchin JS, Alexander ER. Sharing of drug preparation equipment as a risk factor for hepatitis C. Am J Public Health. 2001;91:42-6.

 [PubMed Abstract] -
- 31. Klevens RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. Clin Infect Dis. 2012;55 Suppl 1:S3-9.

 [PubMed Abstract] -
- 32. Centers for Disease Control and Prevention (CDC). Hepatitis C virus infection among adolescents and young adults: Massachusetts, 2002-2009. MMWR Morb Mortal Wkly Rep. 2011;60:537-41. [PubMed Abstract] -
- 33. 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] -
- 34. Scheinmann R, Hagan H, Lelutiu-Weinberger C, Stern R, Des Jarlais DC, Flom PL, Strauss S. Non-injection drug use and hepatitis C virus: a systematic review. Drug Alcohol Depend. 2007;89:1-12. [PubMed Abstract] -
- 35. Terrault NA. Sexual activity as a risk factor for hepatitis C. Hepatology. 2002;36(5 Suppl 1):S99-105. [PubMed Abstract] -
- 36. Kao JH, Liu CJ, Chen PJ, Chen W, Lai MY, Chen DS. Low incidence of hepatitis C virus transmission between spouses: a prospective study. J Gastroenterol Hepatol. 2000;15:391-5. [PubMed Abstract] -
- 37. Tahan V, Karaca C, Yildirim B, et al. Sexual transmission of HCV between spouses. Am J Gastroenterol. 2005;100:821-4. [PubMed Abstract] -
- 38. Vandelli C, Renzo F, Romanò L, et al. Lack of evidence of sexual transmission of hepatitis C among monogamous couples: results of a 10-year prospective follow-up study. Am J Gastroenterol. 2004;99:855-9.



39. Terrault NA, Dodge JL, Murphy EL, Tavis JE, Kiss A, Levin TR, Gish RG, Busch MP, Reingold AL, Alter MJ. Sexual transmission of hepatitis C virus among monogamous heterosexual couples: the HCV partners study. Hepatology. 2013;57:881-9.

[PubMed Abstract] -

40. 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] -

- 41. Hoornenborg E, Achterbergh RCA, Schim van der Loeff MF, et al. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. AIDS. 2017;31:1603-1610. [PubMed Abstract] -
- 42. Jin F, Matthews GV, Grulich AE. Sexual transmission of hepatitis C virus among gay and bisexual men: a systematic review. Sex Health. 2017;14:28-41.

 [PubMed Abstract] -
- 43. Urbanus AT, Van De Laar TJ, Geskus R, et al. Trends in hepatitis C virus infections among MSM attending a sexually transmitted infection clinic; 1995-2010. AIDS. 2014;28:781-90. [PubMed Abstract] -
- 44. Gorgos L. Sexual transmission of viral hepatitis. Infect Dis Clin North Am. 2013;27:811-36. [PubMed Abstract] -
- 45. Patel PR, Thompson ND, Kallen AJ, Arduino MJ. Epidemiology, surveillance, and prevention of hepatitis C virus infections in hemodialysis patients. Am J Kidney Dis. 2010;56:371-8.

 [PubMed Abstract] -
- 46. Thompson ND, Novak RT, Datta D, et al. Hepatitis C virus transmission in hemodialysis units: importance of infection control practices and aseptic technique. Infect Control Hosp Epidemiol. 2009;30:900-3.

- 47. Nguyen DB, Gutowski J, Ghiselli M, et al. A Large Outbreak of Hepatitis C Virus Infections in a Hemodialysis Clinic. Infect Control Hosp Epidemiol. 2016;37:125-33.

 [PubMed Abstract] -
- 48. Centers for Disease Control and Prevention (CDC). Hepatitis C virus transmission at an outpatient hemodialysis unit--New York, 2001-2008. MMWR Morb Mortal Wkly Rep. 2009;58:189-94. [PubMed Abstract] -
- 49. Muleta D, Kainer MA, Moore-Moravian L, et al. Notes from the Field: Hepatitis C Outbreak in a Dialysis Clinic--Tennessee, 2014. MMWR Morb Mortal Wkly Rep. 2016;64:1386-7. [PubMed Abstract] -
- 50. Zoulim F, Bailly F. New approaches to the management of hepatitis C in haemophilia in 2012. Haemophilia. 2012;18 Suppl 4:28-33. [PubMed Abstract] -
- 51. Witkop ML, Peerlinck K, Luxon BA. Medical co-morbidities of patients with haemophilia: pain, obesity and hepatitis C. Haemophilia. 2016;22 Suppl 5:47-53.



52. Troisi CL, Hollinger FB, Hoots WK, et al. A multicenter study of viral hepatitis in a United States hemophilic population. Blood. 1993;81:412-8.

[PubMed Abstract] -

53. Donahue JG, Muñoz A, Ness PM, et al. The declining risk of post-transfusion hepatitis C virus infection. N Engl J Med. 1992;327:369-73.

- 54. Busch MP. Transfusion-transmitted viral infections: building bridges to transfusion medicine to reduce risks and understand epidemiology and pathogenesis. Transfusion. 2006;46:1624-40. [PubMed Abstract] -
- 55. Perkins HA, Busch MP. Transfusion-associated infections: 50 years of relentless challenges and remarkable progress. Transfusion. 2010;50:2080-99.
 [PubMed Abstract] -
- 56. Bresee JS, Mast EE, Coleman PJ, et al. Hepatitis C virus infection associated with administration of intravenous immune globulin. A cohort study. JAMA. 1996;276:1563-7. [PubMed Abstract] -
- 57. Bjøro K, Frøland SS, Yun Z, Samdal HH, Haaland T. Hepatitis C infection in patients with primary hypogammaglobulinemia after treatment with contaminated immune globulin. N Engl J Med. 1994;331:1607-11.

 [PubMed Abstract] -
- 58. Centers for Disease Control and Prevention (CDC). Outbreak of hepatitis C associated with intravenous immunoglobulin administration--United States, October 1993-June 1994. MMWR Morb Mortal Wkly Rep. 1994;43:505-9.

 [PubMed Abstract] -
- 59. Centers for Disease Control and Prevention (CDC). Transmission of hepatitis C virus through transplanted organs and tissue--Kentucky and Massachusetts, 2011. MMWR Morb Mortal Wkly Rep. 2011;60:1697-700.

 [PubMed Abstract] -
- 60. Tugwell BD, Patel PR, Williams IT, et al. Transmission of hepatitis C virus to several organ and tissue recipients from an antibody-negative donor. Ann Intern Med. 2005;143:648-54. [PubMed Abstract] -
- 61. Seem DL, Lee I, Umscheid CA, Kuehnert MJ. PHS guideline for reducing human immunodeficiency virus, hepatitis B virus, and hepatitis C virus transmission through organ transplantation. Public Health Rep. 2013;128:247-343.

 [PubMed Abstract] -
- 62. Ly KN, Jiles RB, Teshale EH, Foster MA, Pesano RL, Holmberg SD. Hepatitis C Virus Infection Among Reproductive-Aged Women and Children in the United States, 2006 to 2014. Ann Intern Med. 2017;166:775-782.

 [PubMed Abstract] -
- 63. Koneru A, Nelson N, Hariri S, et al. Increased Hepatitis C Virus (HCV) Detection in Women of Childbearing Age and Potential Risk for Vertical Transmission United States and Kentucky, 2011-2014. MMWR Morb Mortal Wkly Rep. 2016;65:705-10.



64. Panagiotakopoulos L, Sandul AL, Conners EE, Foster MA, Nelson NP, Wester C. CDC Recommendations for Hepatitis C Testing Among Perinatally Exposed Infants and Children - United States, 2023. MMWR Recomm Rep. 2023;72:1-21.

[PubMed Abstract] -

- 65. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. Clin Infect Dis. 2014;59:765-73. [PubMed Abstract] -
- 66. Page CM, Hughes BL, Rhee EHJ, Kuller JA. Hepatitis C in Pregnancy: Review of Current Knowledge and Updated Recommendations for Management. Obstet Gynecol Surv. 2017;72:347-355.

 [PubMed Abstract] -
- 67. Post JJ. Update on hepatitis C and implications for pregnancy. Obstet Med. 2017;10:157-160. [PubMed Abstract] -
- 68. Diago M, Zapater R, Tuset C, et al. Intrafamily transmission of hepatitis C virus: sexual and non-sexual contacts. J Hepatol. 1996;25:125-8.

 [PubMed Abstract] -
- 69. Ackerman Z, Ackerman E, Paltiel O. Intrafamilial transmission of hepatitis C virus: a systematic review. J Viral Hepat. 2000;7:93-103. [PubMed Abstract] -
- 70. Tohme RA, Holmberg SD. Transmission of hepatitis C virus infection through tattooing and piercing: a critical review. Clin Infect Dis. 2012;54:1167-78.

 [PubMed Abstract] -
- 71. Carney K, Dhalla S, Aytaman A, Tenner CT, Francois F. Association of tattooing and hepatitis C virus infection: a multicenter case-control study. Hepatology. 2013;57:2117-23.

 [PubMed Abstract] -
- 72. Centers for Disease Control and Prevention (CDC). National Notifiable Diseases Surveillance System (NNDSS). Hepatitis C, Acute: 2020 Case Definition.

 [CDC and NNDSS] -
- 73. Centers for Disease Control and Prevention (CDC). National Notifiable Diseases Surveillance System (NNDSS). Hepatitis C, Chronic: 2020 Case Definition.

 [CDC and NNDSS] -
- 74. Centers for Disease Control and Prevention (CDC). National Notifiable Diseases Surveillance System (NNDSS). Hepatitis C, Perinatal Infection: 2018 Case Definition.

 [CDC and NNDSS] -

References

 Binka M, Paintsil E, Patel A, Lindenbach BD, Heimer R. Survival of Hepatitis C Virus in Syringes Is Dependent on the Design of the Syringe-Needle and Dead Space Volume. PLoS One. 2015;10:e0139737.



- Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. Liver Int. 2011;31:1090-101.

 [PubMed Abstract] -
- Chhatwal J, Wang X, Ayer T, et al. Hepatitis C Disease Burden in the United States in the era of oral direct-acting antivirals. Hepatology. 2016;64:1442-1450.
 [PubMed Abstract] -
- Durham DP, Skrip LA, Bruce RD, et al. The Impact of Enhanced Screening and Treatment on Hepatitis C in the United States. Clin Infect Dis. 2015;62:298-304.
 [PubMed Abstract] -
- Edlin BR, Eckhardt BJ, Shu MA, Holmberg SD, Swan T. Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015;62:1353-63.
 [PubMed Abstract] -
- Gish RG, Cohen CA, Block JM, et al. Data supporting updating estimates of the prevalence of chronic hepatitis B and C in the United States. Hepatology. 2015;62:1339-41.
 [PubMed Abstract] -
- Ioannou GN, Green PK, Berry K. HCV eradication induced by direct-acting antiviral agents reduces the risk of hepatocellular carcinoma. J Hepatol. 2017. pii: S0168-8278(17)32273-0. [PubMed Abstract] -
- Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising Mortality Associated With Hepatitis C Virus in the United States, 2003-2013. Clin Infect Dis. 2016;62:1287-8.

 [PubMed Abstract] -
- Paintsil E, Binka M, Patel A, Lindenbach BD, Heimer R. Hepatitis C virus maintains infectivity for weeks after drying on inanimate surfaces at room temperature: implications for risks of transmission. J Infect Dis. 2014;209:1205-11.
 [PubMed Abstract] -
- Rosenberg ES, Rosenthal EM, Hall EW, et al. Prevalence of Hepatitis C Virus Infection in US States and the District of Columbia, 2013 to 2016. JAMA Netw Open. 2018;1:e186371.
 [PubMed Abstract] -
- Singer AW, Reddy KR, Telep LE, et al. Direct-acting antiviral treatment for hepatitis C virus infection and risk of incident liver cancer: a retrospective cohort study. Aliment Pharmacol Ther. 2018;47:1278-1287.



Figures

Figure 1 Concept of HCV Incidence

The HCV incidence refers to the number of people with new infection (acute HCV cases) reported over a specific period of time, typically a 1-year period (as shown by red box).

Illustration: David H. Spach, MD

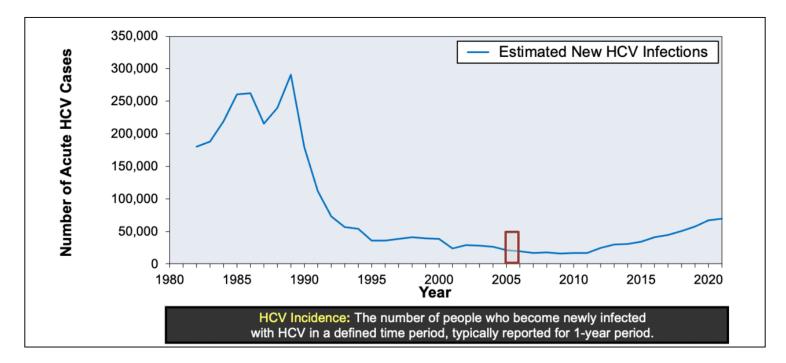




Figure 2 Conceptual View of Reported Cases Versus Actual Infections

As shown in this conceptual model, only a minor proportion of persons with acute (new) HCV infection have their case reported.

Source: modified from Klevens RM, Liu S, Roberts H, Jiles RB, Holmberg SD. Estimating acute viral hepatitis infections from nationally reported cases. Am J Public Health. 2014;104:482-7.

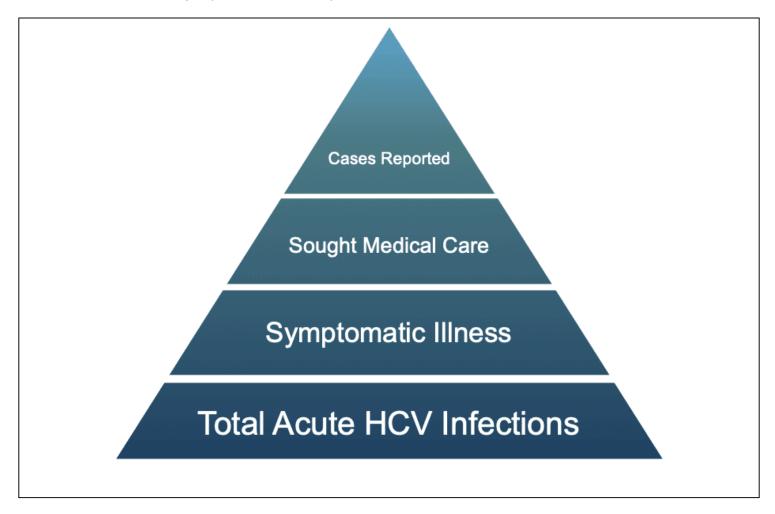




Figure 3 (Image Series) - Acute Cases of HCV, United States (Image Series) - Figure 3 (Image Series) - Acute Cases of HCV, United States Image 3A: Acute Cases of HCV, United States, 2010-2021

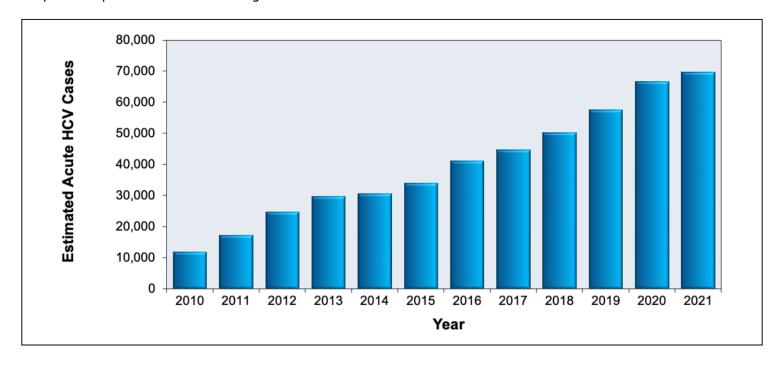




Figure 3 (Image Series) - Acute Cases of HCV, United States Image 3B: Reported Cases of Acute HCV, by Sex, 2021

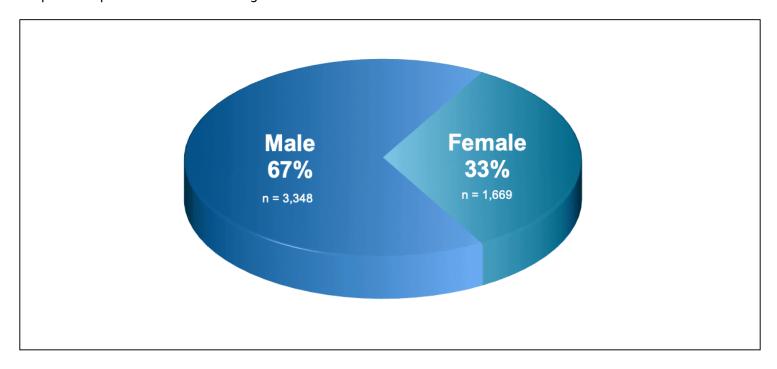




Figure 3 (Image Series) - Acute Cases of HCV, United States Image 3C: Reported Cases of Acute HCV, by Age Group, 2021

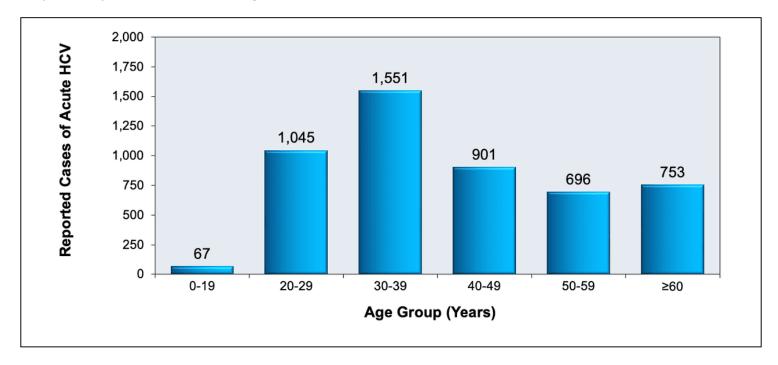




Figure 3 (Image Series) - Acute Cases of HCV, United States Image 3D: Reported Rates of Acute HCV, by Race/Ethnicity, 2005-2021

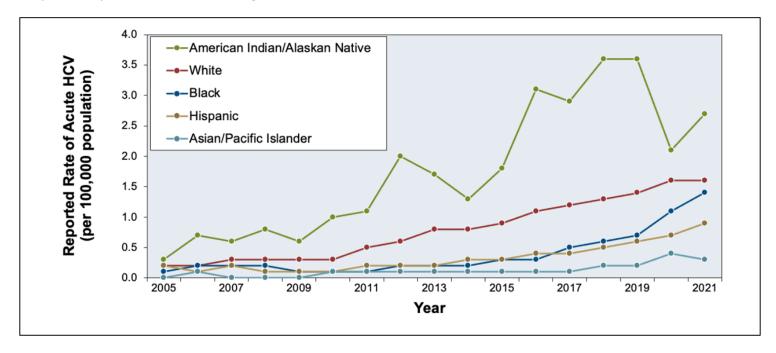




Figure 4 Dynamics of HCV Prevalence in the United States

This illustration shows the dynamics of HCV prevalence in the United States (persons living with chronic HCV infection) are impacted by multiple factors, as shown.

Source: Illustration by David H. Spach, MD

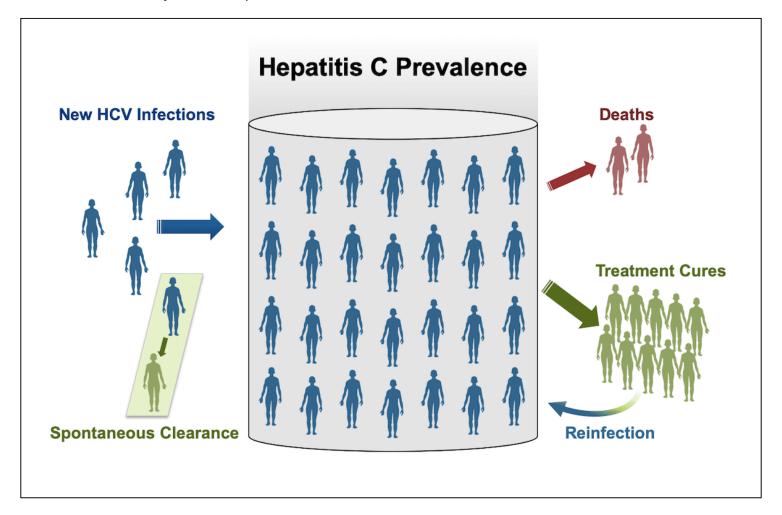




Figure 5 (Image Series) - NHANES HCV Prevalence Estimates, United States (Image Series) - Figure 5 (Image Series) - NHANES HCV Prevalence Estimates, United States Image 5A: NHANES Estimates HCV Prevalence, 2017-2020, by Sex

Source: Lewis KC, Barker LK, Jiles R, Gupta N. Estimated prevalence and awareness of hepatitis C virus infection among U.S. adults- National Health and Nutrition Examination Survey, January 2017-March 2020. Clin Infect Dis. 2023 Jul 7;ciad411.

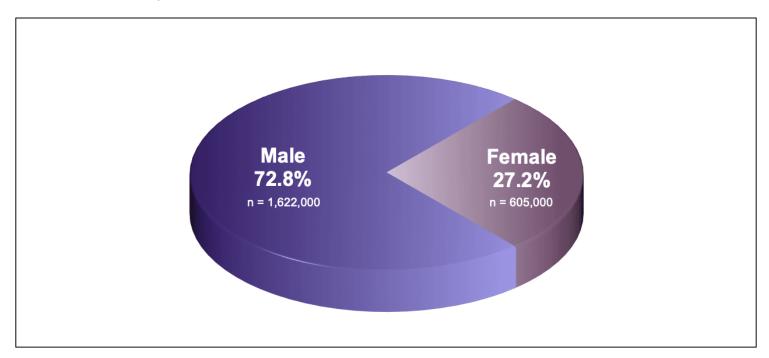




Figure 5 (Image Series) - NHANES HCV Prevalence Estimates, United States Image 5B: NHANES Estimates HCV Prevalence, 2017-2020, by Age Group

Source: Lewis KC, Barker LK, Jiles R, Gupta N. Estimated prevalence and awareness of hepatitis C virus infection among U.S. adults- National Health and Nutrition Examination Survey, January 2017-March 2020. Clin Infect Dis. 2023 Jul 7;ciad411.

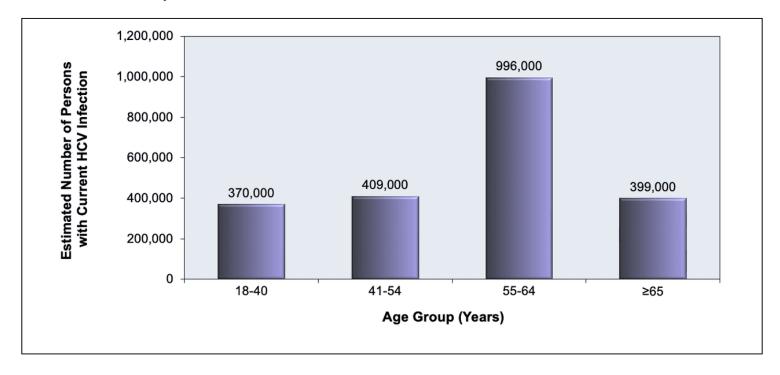




Figure 5 (Image Series) - NHANES HCV Prevalence Estimates, United States Image 5C: NHANES Estimates HCV Prevalence, 2017-2020, by Race/Ethnicity

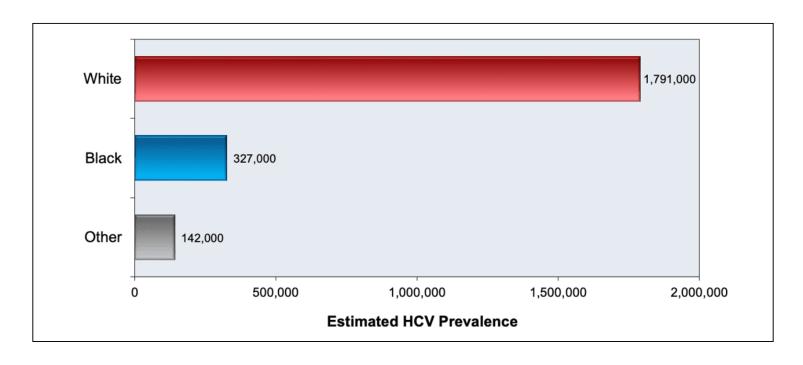




Figure 6 Newly Reported Cases Chronic HCV infection — United States, 2021

Source: Centers for Disease Control and Prevention (CDC). 2021 Viral Hepatitis Surveillance Report—Hepatitis C. Published August 2023.

This figure is not available in the PDF format.

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



Figure 7 Receptive Syringe or Needle Sharing Among People Who Inject Drugs (PWID) in the United States:

Source: 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.

This figure is not available in the PDF format.

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



Figure 8 (Image Series) - HCV as a Cause of Death, United States (Image Series) - Figure 8 (Image Series) - HCV as a Cause of Death, United States Image 8A: Annual HCV-Related Deaths, 2010 to 2021

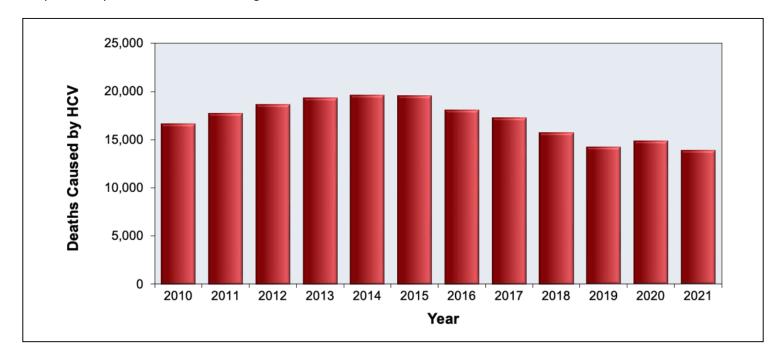




Figure 8 (Image Series) - HCV as a Cause of Death, United States Image 8B: HCV as Cause of Death, by Sex, 2021

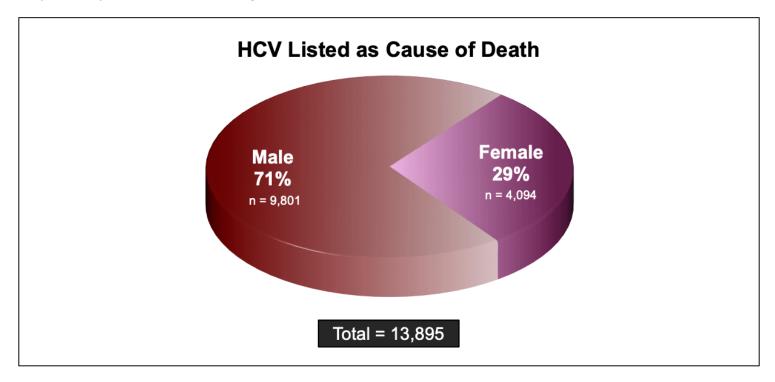




Figure 8 (Image Series) - HCV as a Cause of Death, United States Image 8C: HCV as Cause of Death, by Race/Ethnicity, 2021

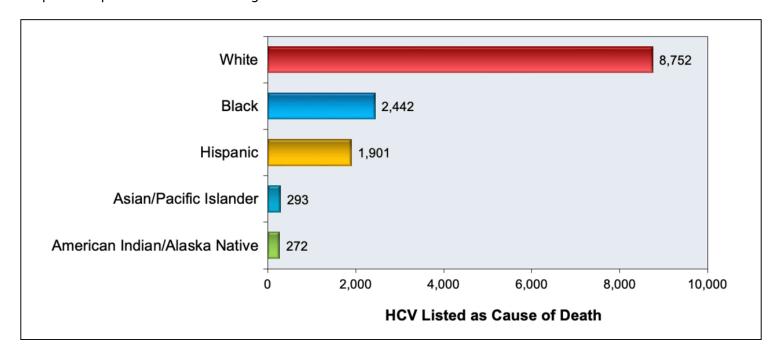




Figure 9 Acute Hepatitis C: 2020 Case Definition—Clinical and Laboratory Criteria

Source: Centers for Disease Control and Prevention (CDC)

Acute Hepatitis C: 2020 Case Definition

Clinical Criteria

All hepatitis C virus cases in each classification category should be >36 months of age, unless known to have been exposed non-perinatally.

One or more of the following:

- Jaundice, OR
- Peak elevated total bilirubin levels ≥3.0 mg/dL, OR
- Peak elevated serum alanine aminotransferase (ALT) level >200 IU/L

AND

The absence of a more likely diagnosis (which may include evidence of acute liver disease due to other causes or advanced liver disease due to pre-existing chronic HCV infection or other causes, such as alcohol exposure, other viral hepatitis, hemochromatosis, etc.)

Laboratory Criteria for Diagnosis

Confirmatory laboratory evidence:

- Positive hepatitis C virus detection test: Nucleic acid test (NAT) for HCV RNA positive (including qualitative, quantitative, or genotype testing), OR
- A positive test indicating presence of HCV antigen

Presumptive laboratory evidence:

• A positive test for antibodies to hepatitis C virus (anti-HCV)



Figure 10 Chronic Hepatitis C: 2020 Case Definition—Clinical and Laboratory Criteria

Source: Centers for Disease Control and Prevention (CDC)

Chronic Hepatitis C: 2020 Case Definition

Clinical Criteria

- No available evidence of clinical and relevant laboratory information indicative of acute infection.
- Most hepatitis C virus (HCV)-infected persons are asymptomatic; however, many have chronic liver disease, which can range from mild to severe.

Laboratory Criteria for Diagnosis

- A positive test for antibodies to hepatitis C virus (anti-HCV)
- Hepatitis C virus detection test:
 - Nucleic acid test (NAT) for HCV RNA positive (including qualitative, quantitative or genotype testing)
 - A positive test indicating presence of hepatitis C viral antigen(s) (HCV antigen)