HCV Epidemiology in the United States

HCV Incidence in the United States

Definitions of HCV Incidence

The incidence of hepatitis C virus (HCV) infection is defined as number of new infections in a specific region in a specific time period; the incidence data is typically reported out for a 1-year period, often in conjunction with cumulative and comparative multi-year 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 number of cases per 100,000 persons).

Method of Estimating HCV Incidence

Most patients with acute hepatitis C do not have an acute 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 have undiagnosed 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

The CDC HCV surveillance data from 1982 to 2017 shows a peak in the estimated number of acute HCV cases in 1989, a steady decline from 1990 to 2005, a relative leveling off between 2006 and 2010, and then an increase from 2010 to 2017 (Figure 3).[2] In 2017, a total of 3,216 new cases of acute hepatitis C were reported to the CDC from 43 states; based on this number, the CDC estimated a total of 44,700 new acute cases of HCV in 2017.[2] From 2010 to 2017, the number of estimated annual acute HCV infections increased approximately 2.8-fold (Figure 4).[2] This steady and significant increase in new HCV infections from 2010 to 2017 is attributed primarily to the opioid epidemic, and associated injection drug use, particularly among young adults.[3,4,5,6] The following summarizes CDC HCV surveillance data in 2017 based on specific groups and demographic factors.[2]
• **Sex:** The number of acute HCV infections in 2017 was higher in males (1,775) than in females (1,499), with males accounting for 55% of the acute HCV infections in 2017 (Figure 5).[2] The gap in the rate of infections in men and women has existed during the past 3 years.

• **Age Group:** For 2017, the number and rate of acute HCV infections and the rate of acute HCV infections was highest among persons aged 20-29 years followed by those 30-39 years of age; the lowest number and rate was among those 0-19 years of age (Figure 6).[2]

• **Race/Ethnicity:** In 2017, the highest number of reported cases of acute HCV by race/ethnicity occurred in whites, followed by Hispanics and blacks (Figure 7).[2] Among all reported acute cases in 2017, whites comprised 69% of the cases.[2] The highest rate for acute cases was in American Indian/Alaska Natives, followed by whites (Figure 8).[2]

• **State:** For 2017 in the United States, the 7 states with the most number of reported cases of acute HCV were Florida (357), Massachusetts (327), Pennsylvania (224), Indiana (191), New York (188), Ohio (159), and Michigan (152).[2] Together, these 7 states comprised approximate 50% of the total number reported number of acute cases in the United States (1,598 of a total of 3,216 cases). In 2017, the 7 states with the highest rate (reported cases of acute HCV per 100,000 persons in the state) were (in descending order): West Virginia, Massachusetts, Indiana, Utah, South Dakota, Tennessee, and Kentucky.[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 any implemented plans, and identifying focal outbreaks or regional patterns of infection. In addition, valuable information emerges when data is categorized by age group, gender, race/ethnicity, and risk factor for acquiring hepatitis C virus; these data may inform major 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 observed infected with HCV (Figure 9). Most often, the HCV prevalence specifically refers to persons living 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 spontaneous cure of HCV, (3) number of treatment cures, (4) number of deaths, and (5) number of persons cured who become reinfected (Figure 10). 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) (Figure 11).[7,8,9,10,11] The NHANES surveys require some adjustments since they do not sample certain populations, including the incarcerated, homeless, nursing home residents, persons on active military duty, and immigrants. The most recent estimate of HCV prevalence in the United States was generated from analysis of 2013 to 2016 NHANES survey data.[11] In this time period, there were an estimated 4.1 million persons living in the United States who were HCV antibody positive and 2.4 million persons who were HCV RNA positive (1% prevalence among adults).[11] When compared with earlier NHANES studies, the number of persons with a positive HCV antibody has remained relatively stable whereas the number of HCV RNA positive persons has decreased significantly from the estimated 3.2 million HCV RNA-positive persons in the 1999 to 2002 time period.[8,11] The declining HCV RNA-positive prevalence likely has resulted from a significant number of persons obtaining cure of chronic HCV infection with direct-acting antiviral therapy.

- **Sex:** In the United States, the estimated HCV prevalence for adult males is 1.31%, which is 2.3-fold higher than the 0.57% prevalence in adult females; this corresponds with a male to female HCV prevalence ratio of 2.3.[12]
- **Birth Cohort:** Age data for HCV prevalence has been typically analyzed and reported as birth cohort prevalence. Recent analysis of birth cohort HCV prevalence estimates in the United States showed highest rates in persons born 1945-1965 (1.63%), followed by persons born after 1965 (0.51%), and lowest in persons born prior to 1945 (0.21%). These data are consistent with earlier published data that also show highest HCV prevalence among persons born during 1945 to 1965 (Figure 12).[9,13] The relatively high prevalence of HCV infection among persons born during 1945 to 1965 corresponds with the high HCV incidence (new infections) that occurred among young adults using or experimenting with injection drugs in the 1970s and 1980s.[2] In recent years, the proportion of cases involving persons born after 1965 has steadily increased.
- **Race/Ethnicity:** In the United States, during the years 1999-2016, the highest HCV prevalence, based on race/ethnicity was among blacks and next highest in whites (Figure 13).[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).[12] Five of these states (New York, Pennsylvania, Ohio, Tennessee, and North Carolina) are in the Appalachian region.[12] Together, these 9 states account for an estimated 52% of all persons living with HCV nationally.[12]

Awareness of HCV Infection Status
Using the most recent NHANES data, investigators estimated only 55.6% of persons infected with HCV in the United States were aware of their HCV infection status.[14]. Awareness of infection status was lower in persons who were foreign-born and in persons with income below poverty level.[14] 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.[15] 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.[16]

**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% genotypes 4, 5, or 6.[17,18,19] Among the genotype 1 infections, genotype 1a is more common than 1b.[19]
HCV-Related Deaths

The CDC reports for HCV-related deaths in the United States are based on death certificate data and are likely underestimate the true number of HCV-related deaths.[20] From 1999 to 2007, the number of annual deaths related to hepatitis C increased substantially and in 2007, the number of deaths related to hepatitis C had exceeded those related to HIV (Figure 14).[21] A subsequent study that analyzed HCV-related deaths in the United States from 2003 to 2013 concluded the annual HCV-related deaths continued to increase since 2007, with an estimated 19,368 HCV-related deaths in 2013.[22] During 2010 to 2017, the annual HCV-related deaths in the United States peaked in 2014 and 2015, with slight declines in 2016 and 2017 (Figure 15).[2] Approximately 71% of the deaths were in males versus 29% in females (Figure 16).[2] The number of HCV-related deaths was highest in whites (Figure 17), but the death rate was highest in American Indian/Alaskan Natives (Figure 18).[2]
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 a solid organ transplantation, hemophilia with receipt of factor concentrates made before 1987, male-to-male sex, body tattoos, and intranasal cocaine use. Among these, injection drug use is the most common and important risk factor for acquiring HCV in the United States. Several studies have indicated that approximately 45% of persons with HCV infection do not report an exposure. Many of these patients, after undergoing careful questioning, eventually identified injection drug use as a risk factor. 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 introduction of blood screening tests in the early 1990s, the proportion of new HCV cases caused by contaminated blood or organs dramatically declined.

Persons in different ethnic groups may have relatively different routes of acquiring HCV.

Injection Drug Use

Injection drug use remains the most common risk factor for acquiring HCV in the United States, accounting for more than 60% of all cases of HCV. 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. Transmission risk is greatest with “direct sharing” of needles and syringes, but may also occur indirectly via sharing of injection paraphernalia, such as water, cookers, and cotton filters. The incidence of HCV in persons who inject drugs markedly declined from the early 1992-2002, likely due to increased availability of needle exchange programs that arose in response to the HIV epidemic. Since about 2002, however, multiple reports have documented a surge in HCV infections in the United States among young persons who inject drugs. This surge in HCV infections in the United States is intricately connected with the ongoing opioid epidemic and its associated injection drug use. These reports identified a new cohort of persons diagnosed with HCV who inject drugs and have the following characteristics: age younger than 30, white race, residence in non-urban areas, and use of oral prescription opiates prior to using heroin. Regions of the United States east of the Mississippi River have been most heavily impacted, with a particularly high intensity of new HCV cases in the central Appalachian region.

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. 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 noninjection drug users ranges from 2.3 to 35.3%. It is possible that use of noninjection drugs is a surrogate for other risk behaviors associated with HCV acquisition.

Sexual Exposure

The risk of acquiring HCV through sexual contact with a person who has HCV infection remains highly controversial. Overall, sexual transmission has accounted for up to 15% of cases of HCV in the United States, but with very close interrogation most of these 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 less than 1% per year. In a study involving 500 anti-HCV-positive, HIV-negative subjects and their long-term monogamous heterosexual partners, investigators reported transmission of HCV by sex at a rate of 0.07% per year among the couples, which translates to approximately 1 per 190,000.
In recent years, multiple reports have identified cases of sexual transmission among men who have sex with men (MSM), particularly among MSM who have HIV infection. Particular risk 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 use of shared sex toys.

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. 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 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 and with 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. The CDC does not recommend using dedicated dialysis machines for patients with HCV, but recommends universal precautions and strict sterilization procedures for all dialysis machines.

Receipt of Clotting Factor Concentrates

Two types of clotting factor concentrates are used in clinical practice: plasma factor concentrate and recombinant factor concentrate. Most often, these involve use of factor VIII or factor IX 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. 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 routine use of second-generation HCV antibody tests in 1992 nearly eliminated subsequent risk of transfusion-associated HCV. In the mid-1990s the risk of acquiring HCV from a blood transfusion had declined to less than 0.3%. 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. 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

Scattered cases and outbreaks of HCV transmission via gamma globulin have occurred in the United States and in Europe. In 1993 and 1994, a major outbreak of HCV transmission in the United States occurred following patient receipt of HCV-contaminated lots of intravenous immune globulin, with a total of 23 persons infected with HCV through receipt of contaminated immunoglobulin. Advances in virus inactivation procedures have nearly eliminated any risk of HCV transmission with immune globulin and manufacturers of intravenous immune globulin use vigorous viral inactivation and removal procedures. No cases of HCV transmission have been documented with administration of intramuscular immune globulin. All immune globulin products undergo solvent detergent.

Organ and Tissue Transplantation
Rare cases of inadvertent HCV transmission via organ or tissue transplantation have occurred in the United States.[61,62] Most cases of transmission have involved HCV antibody-negative, HCV RNA-positive donors.[61,62] Among transplant recipients who receive HCV-infected organs or tissues, the risk of developing chronic HCV infection is high. With the advent of more accurate testing methods for donors, the risk of HCV transmission in this setting has markedly declined. In 2013, the U.S. Public Health Service drafted updated guidelines for prevention of HCV transmission through organ transplantation and these guidelines recommend HCV RNA testing (NAT) of all organ and tissue donors.[63]

**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 for a potential significant increase in perinatal HCV infections.[64,65] Among pregnant women with chronic HCV infection, approximately 6% will transmit HCV to their child.[66,67,68] 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.[66] The risk of HCV transmission via breastfeeding appears to be negligible.[66,67,68]

**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.[69,70] 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.[71] The risk in unregulated and unlicensed tattoo centers, such as with tattoos applied by friends or in prison, increases the risk for HCV acquisition.[71,72]
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—2016 Case Definition

The CDC 2016 Case Definition for Acute Hepatitis C infection includes clinical and laboratory criteria (Figure 19), along with a case classification as probable or confirmed (Figure 20).[73] Of note, a patient can have a confirmed case of acute hepatitis C 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 of any of these tests). Symptomatic cases often go unreported and for multiple reasons, including many symptomatic patients 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.

Chronic Hepatitis C Virus Infection—2016 Case Definition

The CDC 2016 Case Definition for Chronic Hepatitis C includes clinical and laboratory criteria (Figure 21), as well as a case definition(Figure 22).[74] These cases pertain to persons with current (active) hepatitis C infection and do not represent persons who spontaneously cleared hepatitis C 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 definition.[75] A confirmed case definition 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 hepatitis C 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) hepatitis C infection should be interviewed to determine lifetime risk factors for hepatitis C. The Viral Hepatitis Case Report form should be filled out for persons identified with either acute hepatitis C infection or past/present hepatitis C. Cases of hepatitis C 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 following summarizes the epidemiology of HCV in the United States:

- The estimated number of annual acute HCV infections in the United States increased significantly from 11,800 in 2010 to 44,700 in 2017.
- The recent increases in new HCV infections have primarily resulted from the ongoing opioid epidemic and the associated injection drug use.
- From 2013-2017, the highest rates of new infections have occurred in persons 20-39 years of age.
- Based on CDC estimates, 2.4 million persons are living with active HCV infection, corresponding to a 1.0% 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.
- Approximately 45% of persons with HCV infection are unaware of their HCV status.
- 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 infection.
- The number of annual HCV-related deaths is approximately 17,000 persons, with the majority (69%) 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


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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. The HCV incidence rate is the number of infections per 100,000 persons in the group being described.

Illustration: David H. Spach, MD

**HCV Incidence:** The number of people who become newly infected with HCV in a defined time period, typically reported for 1-year period.
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. The CDC estimates a ratio of 13.9 total acute HCV infections for every 1 reported case of acute HCV infection.

Figure 3 Estimated Acute Cases of HCV, United States, 1982-2017

This graphic represents the estimated number of new hepatitis C infections per year.

Figure 4 Estimated Acute Cases of HCV, United States, 2010-2017

Figure 5 Estimated Acute Cases of HCV, by Sex, United States, 2017


Reported Cases of Acute HCV

- **Male**: 55% (n = 1,775)
- **Female**: 45% (n = 1,431)
Figure 6 Estimated Acute Cases of HCV, by Age Group, United States, 2017

Figure 7 Estimated Acute Cases of HCV, by Race, United States, 2017

Figure 8 Estimated Rate of Acute Cases of HCV, by Race, United States, 2017

Figure 9 Concept of HCV Prevalence

The HCV prevalence in the United States refers to the estimated number of people living with hepatitis C in the United States. This number may refer to the number of persons who have ever been infected or those with current active HCV infection. This graphic represents a conceptual view of HCV prevalence and does not represent actual numbers. The prevalence rate is the number of persons with HCV per 100,000 persons in the population.

Illustration: David H. Spach, MD
Figure 10 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, including number of new infections, spontaneous resolution of new infections, deaths, treatment-related cure, and reinfection.

Source: Illustration by David H. Spach, MD
Figure 11 Estimated Number of Persons Infected with HCV in the United States.

This graphic shows data representing seroprevalence (anti-HCV) and chronic infection (HCV RNA) from four distinct NHANES studies. The numbers on the bar graph represent millions of persons.

**Figure 12 Prevalence of HCV Antibody, by Year of Birth**

The HCV prevalence is highest among persons born from 1945 to 1965. This graphic shows prevalence studies performed during two separate time periods: 1988-1994 (blue line) and 1999-2002 (purple line).

Figure 13 HCV Prevalence, by Race/Ethnicity, 2013-2016

**Figure 14 Mortality Rates* from HBV, HCV, and HIV in United States, 1999-2007.**

This graphic shows that after determining age-adjusted mortality rates for HBV, HCV, HIV (when listed as cause of death), HCV-related deaths surpassed HIV-related deaths by 2007. *Because decedent can have multiple causes of death, a record listing more than 1 type of infection was counted for each type of infection.

Figure 15 Annual Deaths Associated with Chronic Hepatitis C Infection, 2010 to 2017

Figure 16 HCV as Cause of Death, by Sex, United States, 2017

Deaths Caused by HCV

- Male: 71% (n = 12,287)
- Female: 29% (n = 4,966)

Total = 17,253

Figure 17 HCV as Cause of Death, by Race/Ethnicity, United States, 2017

Figure 18 HCV as Cause of Death (Rate), by Race/Ethnicity, United States, 2017


Rate of Deaths Caused by HCV (per 100,000 population)
### Acute Hepatitis C: 2016 Case Definition

#### Clinical Criteria

An illness with discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), AND

(a) jaundice, OR

(b) a peak elevated serum alanine aminotransferase (ALT) level >200 IU/L during the period of acute illness.

#### 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)*

* When and if a test for HCV antigen(s) is approved by FDA and available.
**Acute Hepatitis C: 2016 Case Definition**

**Criteria to Distinguish a New Case from an Existing Case**

A new acute case is an incident acute hepatitis C case that meets the case criteria for acute hepatitis C and has not previously been reported.

**Case Classification**

**Probable**

- A case that meets clinical criteria and has a positive anti-HCV antibody test, but has no reports of a positive HCV NAT or positive HCV antigen tests,

  **AND**

- Does not have test conversion within 12 months or has no report of test conversion.

**Confirmed**

- A case that meets clinical criteria and has a positive hepatitis C virus detection test (HCV NAT or HCV antigen),

  **OR**

- A documented negative HCV antibody, HCV antigen or NAT laboratory test result followed within 12 months by a positive result of any of these tests (test conversion).
### Chronic Hepatitis C: 2016 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)*

* When and if a test for HCV antigen(s) is approved by FDA and available.
Figure 22 Chronic Hepatitis C: 2016 Case Definition—Case Classification as Probable or Confirmed

Source: Centers for Disease Control and Prevention (CDC)

<table>
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<tr>
<th>Chronic Hepatitis C: 2016 Case Definition</th>
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<td><strong>Criteria to Distinguish a New Case from an Existing Case</strong></td>
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<tr>
<td>A new chronic case is an incident chronic hepatitis C case that meets the case criteria for chronic hepatitis C and has not previously been reported.</td>
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**Case Classification**

**Probable**
- A case that does not meet clinical criteria or has no report of clinical criteria, **AND**
- Does not have test conversion within 12 months or has no report of test conversion, **AND**
- Has a positive anti-HCV antibody test, but no report of a positive HCV NAT or positive HCV antigen test.

**Confirmed**
- A case that does not meet clinical criteria or has no report of clinical criteria, **AND**
- Does not have test conversion within 12 months or has no report of test conversion, **AND**
- Has a positive HCV NAT or HCV antigen test.