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: HCV Epidemiology in the United States

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HCV Incidence and Prevalence

Definitions of HCV Incidence

The incidence of hepatitis C is defined as number of new infections in a specific region in a specific time period. The CDC typically defines the incidence of hepatitis C in the United States (or in each state) as the number of new hepatitis C virus infections that occur per year. The incidence rate is the number of cases per total population (typically defined as number of cases per 100,000 persons).

Incidence Data

The CDC generates estimates for the total number of new cases that occur each year based on reporting data. For each new symptomatic acute HCV case that is reported, an estimated 3.3 cases of symptomatic acute HCV actually occur. In addition, for each new HCV case that is symptomatic and reported, the actual number of acute cases is approximately 13 times the number of new HCV infections reported. In 2014, a total of 2194 new cases of hepatitis C were reported to the CDC from 40 states; based on this number, the CDC estimates 30,500 persons were newly infected with hepatitis C in 2014.[1] The number of estimated new annual HCV infections increased from 16,500 in 2011 to 30,500 in 2014, but the number of annual new infections in recent years is markedly lower than during the 1980’s, when an estimated 230,000 persons were newly infected with HCV each year (Figure 1).[1]

Importance of Incidence Data

The United States hepatitis C 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.

Method of Estimating 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 incidence of new infections per year requires sophisticated epidemiologic modeling techniques that use surveillance data to generate estimates for the number of new infections per year. 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 the national rates per 100,000 persons.

Definition of HCV Prevalence
The HCV prevalence is defined as the number (or percent) of persons in the total population observed infected with hepatitis C. Most often, the HCV prevalence specifically refers to persons living with active (chronic) hepatitis C infection. Less frequently, the HCV prevalence data is given for all individuals with anti-HCV (number of persons living who have been infected with hepatitis C), 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 Data Based on NHANES Data**

In the United States, hepatitis C virus 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 2).[0,2,3,4] The first estimate of HCV prevalence in the United States was generated from NHANES III, which was conducted between 1988 and 1994 and estimated 2.7 million persons had chronic HCV in the United States.[2] In a subsequent NHANES analysis based on information collected between 1999 and 2002, investigators estimated 3.2 million persons had chronic HCV and this corresponded to a prevalence rate of approximately 1.3% of the United States population.[3] A more recent follow-up NHANES included data from 2003 to 2010 and estimated a prevalence of 2.7 million persons chronically infected with HCV in the United States, corresponding to a population prevalence of chronic hepatitis C of 1.0%.[4] These NHANES surveys, however, did not sample certain populations, including the incarcerated, homeless, nursing home residents, persons on active military duty, and immigrants.

**CDC Current HCV Prevalence Estimate**

Other investigators have estimated a higher HCV prevalence (up to 5.2 million) in the United States, based on the knowledge that the NHANES surveys did not include certain populations in the survey, including incarcerated, homeless, nursing home residents, hospitalized individuals, and persons on active military duty.[0,5,6] The CDC, after adjusting for populations not included in the NHANES surveys, estimates that 3.5 million persons are living with HCV infection in the United States.

**HCV Prevalence by Year of Birth**

The HCV prevalence is highest among persons born during 1945 to 1965 (Figure 3). Indeed, the CDC estimates that approximately three-fourths of all persons living with HCV infection in the United States were born during 1945 to 1965. 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 in the 1970s and 1980s.

**Awareness of HCV Infection Status**

An estimated 40 to 85% of persons infected with HCV are unaware of their HCV infection status.[7] One study reported that among HCV-infected injection drug users who were 15 to 30 years old, 72% were unaware of their HCV infection status. A more recent analysis of NHANES data from 2001 through 2008 found that 50.3% of persons infected with HCV were unaware of their hepatitis C infection.[8] In a study involving persons with access to medical care in four private health care organizations during the years 2006 to 2008, an estimated 43% were unaware of their HCV infection.

**HCV Genotype**

In the United States, approximately 70% of chronic HCV infections are caused by hepatitis C genotype 1, 15 to 20% by genotype 2, 10 to 12% genotype 3, 1% genotype 4, and less than 1% genotype 5 or 6. Among the genotype 1 infections, approximately 55% are genotype 1a and 35%
1b.
Risk Factors for Acquiring HCV

Overview of Risk Factors for HCV Acquisition

Investigators 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 1970’s and 1980’s, 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 1990’s, 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.

Hemodialysis

The incidence of HCV infection in dialysis patients decreased from 1.7 to 0.2% during 1982 to 1997. The overall prevalence of HCV among persons receiving dialysis is approximately 8% (nearly 5-fold higher than the general population). Several risk factors have been identified for dialysis patients acquiring HCV, including number of blood transfusion 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, recent dialysis-associated outbreaks have occurred and HCV transmission most likely resulted from inadequate infection control practices, particularly in situations when patients received dialysis immediately after an HCV-infected patient 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.

Hemophilia

Clotting factor concentrates used to treat patients with hemophilia (Factor VIII and Factor IX) are plasma-based products. In the late 1970s through the mid 1980s, an estimated 6,000 to 10,000 persons with hemophilia acquired HCV infection via the receipt of contaminated 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.

Household Contact

The number of persons acquiring HCV via household contact with a person infected with HCV is extremely low. These cases would most likely involve sharing a razor or toothbrush, since this process could involve transmission via a blood-tainted device.

Injection Drug Use

Injection drug use remains the most common risk factor for acquiring HCV in the United States, accounting for more than 50% of all cases of HCV. A recent study identified injection drug use as the risk factor for 84% of individuals diagnosed with acute HCV. Approximately 20 to 30% of persons who inject drugs are infected with HCV within the first 2 years of starting to inject drugs and 75 to 90% of persons who inject drugs are anti-HCV positive. Transmission risk is greatest with “direct sharing” of needles and syringes, but may also occur indirectly via sharing of injection paraphernalia, such as syringes, cookers, and cotton filters. The incidence of HCV in persons who inject drugs has
markedly declined in the past 20 years, likely secondary to use of needle exchange programs that arose in response to the HIV epidemic and saturation of HCV infection in the population of persons who inject drugs. Recent reports have identified a new cohort of HCV-infected injection-drug users with the following characteristics: age 24 or younger, white race, residence in non-urban areas, and use of oral prescription opiates prior to using heroin. The prototypical new heroin user initiates some type of substance abuse, such as alcohol or marijuana at about age 13, transitions to using oral opiates, most often oxycodone, around age 17, then eventually starts using cheaper and widely available heroin by about age 18.

Immune Globulin

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. This outbreak involved more than 100 persons. Other reports involving a smaller number of patients have documented HCV transmission with receipt of intravenous immune globulin. 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.

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.

Organ and Tissue Transplantation

Rare cases of inadvertent HCV transmission via organ or tissue transplantation continue to occur in the United States. Most cases of transmission have involved HCV-antibody negative, HCV RNA positive donors. 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 2011, the U.S. Public Health Service drafted guidelines that recommended HCV RNA testing of all organ and tissue donors.

Perinatal

Among pregnant women with chronic HCV infection, approximately 5% (range 4 to 10%) will transmit HCV to their child. Nearly all cases of perinatal HCV transmission have involved mothers who had detectable HCV RNA in plasma during pregnancy, but rare cases of perinatal HCV transmission have occurred in HCV antibody positive, HCV RNA negative women. The major risk of transmission occurs at the time of birth and the HCV RNA levels at the time of delivery correlate with the relative risk of transmission. Women coinfected with HIV and HCV have an approximately twofold higher risk of perinatal HCV transmission when compared with women who have HCV monoinfection. The risk of HCV transmission via breastfeeding appears to be negligible.

Receipt of Infected Blood Transfusion

In the 1960’s, the risk of acquiring HCV from a blood transfusion was about 33%. The universal
screening of blood and organ donors with routine use of second-generation HCV antibody tests in 1992 nearly eliminated the risk of transfusion-associated HCV. In the mid 1990’s 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 the 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 3rd 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.

**Sexual Exposure**

The risk of acquiring HCV through sexual contact with another HCV-infected person 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. Indeed, four large prospective studies involving monogamous heterosexual couples have shown extremely low risk of HCV transition in this setting. In a recent 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 sexual contacts. Among the bona fide cases of sexual transmission of HCV, most have involved either men who have sex with men or heterosexuals with high numbers of sexual contacts. For heterosexual HCV transmission, the number of sexual partners, not the number of sexual acts, appears to have the greatest impact. Recently, researchers have investigated a significant number of new HCV cases among HIV-infected men who have sex with men and have identified unprotected receptive anal intercourse with ejaculation and having sex while high on methamphetamine as important risk factors for acquiring HCV.

**Tattoos and Piercings**

In the United States, the risk of acquiring HCV from a licensed, regulated professional tattoo or piercing center is extremely low. The risk in unregulated and unlicensed tattoo centers may be significant, such as with tattoos applied by friends or in prison.
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 4), along with a case classification as probable or confirmed (Figure 5).[9] 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 6), as well as a case definition (Figure 7).[1] These cases pertain to persons with current (active) hepatitis C infection and do not represent persons who spontaneous cleared hepatitis C infection. Also, it is important not to report cases that have have already been reported.

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).
HCV Disease Burden

Deaths Related to Hepatitis C

Persons with HCV infection have all-cause mortality greater than twice that of HCV-negative persons. In the United States, hepatitis C is the cause of death or contributing cause of death in approximately 15,000 people per year. From 1997 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 8). A more recent study that analyzed HCV-related deaths in the United States from 2003 to 2013 concluded the annual HCV-related deaths have continued to increase since 2007, with an estimated 19,369 HCV-related deaths in 2013. Persons with chronic hepatitis C infection have an estimated mortality rate 12 times higher than the general population. In addition, the number of hepatitis C-related deaths are at least 8-fold greater than those related to hepatitis B. Investigators have identified factors associated with an increased risk of death in persons with chronic hepatitis C infection: chronic liver disease, coinfection with hepatitis B virus, alcohol-related conditions, minority status, and coinfection with HIV. Among the HCV-related deaths in recent years, more than 70% have involved persons 45 to 64 years of age.

Morbidity Related to Hepatitis C

Overall, approximately 20% of persons infected with hepatitis C, if not treated, will develop cirrhosis after 20 years of infection and this number increases as the duration of infection increases. Hepatitis C-associated liver disease is the number one indication for liver transplantation and approximately one-third of all persons on liver transplantation waiting lists have hepatitis C-associated liver disease. In addition, Hepatitis C-associated liver disease is the number one cause of hepatocellular carcinoma, accounting for approximately 50% of cases of hepatocellular carcinoma.

Health Care Related Costs

In an analysis in a managed care setting, HCV-infected persons infected (when compared with controls) had markedly higher total health care utilization costs, hospitalization costs, and prescription costs. Persons infected with HCV have increased likelihood of requiring short-term or long-term disability.

Projected HCV-Related Deaths

Modeling studies have projected a dismal future in the next 40 to 50 years related to HCV-related disease burden. In general, these models make forecasts based on current conditions of low rates of screening and treatment and thus do not include a widespread program of identifying and treating the large proportion of undiagnosed HCV-infected individuals. When excluding the potential impact of treatment on future mortality, the projected HCV-related deaths will peak in 2030 to 2035, with approximately 36,000 deaths per year (Figure 9). Factoring in treatment gives lower estimates of death.

Projected End Stage Liver Disease Related to Hepatitis C

Investigators predict that 1.76 million persons with chronic HCV infection (if not treated) will develop cirrhosis during the next 40 to 50 years, with a peak prevalence of about 1 million in the mid-2020’s. The projected incidence peak (new cases) of end-stage liver disease will occur in 2030, with about 38,600 cases per year. The prevalence (number of people living) with end-stage liver disease also is predicted to peak in 2030, with an estimated 131,300 persons living with end-stage liver disease. Transplants would be expected to peak in 2032 to 2033 at level of 3200 HCV-related transplants per year.
Summary Points

In the United States:

- The number of estimated new HCV infections increased from 2011 (16,500) to 2014 (30,500).
- Based on CDC estimates, 3.5 million persons are living with HCV infection in the United States.
- An estimated three-fourths of persons living with HCV were born during 1945 to 1965.
- Approximately 50% 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 men who have sex with men.
- The number of annual HCV-related deaths is approximately 19,000 persons and this now exceeds the number of annual HIV-related deaths.
- The CDC has established a clear definition of acute and chronic HCV infection for reporting purposes as well as reporting guidelines.
Citations


References


[CDC and MMWR]

[CDC and NNDSS]

[CDC and MMWR]

[CDC and MMWR]

[CDC Surveillance]

[PubMed Abstract]

[PubMed Abstract]

[PubMed Abstract]

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Figures

Figure 1 Hepatitis C Incidence in United States, 1982-2014.

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

Source: Division of Viral Hepatitis. Statistics and Surveillance
Figure 2 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 three distinct NHANES studies. The numbers on the bar graph represent millions of persons.

Figure 3 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 4 Acute Hepatitis C: 2016 Case Definition—Clinical and Laboratory Criteria

Source: Centers for Disease Control and Prevention (CDC)

### 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.
**Figure 5 Acute Hepatitis C: 2016 Case Definition—Case Classification as Probable or Confirmed**

Source: Centers for Disease Control and Prevention (CDC)

<table>
<thead>
<tr>
<th>Acute Hepatitis C: 2016 Case Definition</th>
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<tbody>
<tr>
<td><strong>Criteria to Distinguish a New Case from an Existing Case</strong></td>
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<td>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.</td>
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<tr>
<td><strong>Case Classification</strong></td>
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<td><strong>Probable</strong></td>
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| • 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). |
Figure 6 Chronic Hepatitis C: 2016 Case Definition—Clinical and Laboratory Criteria

Source: Centers for Disease Control and Prevention (CDC)

### 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 7 Chronic Hepatitis C: 2016 Case Definition—Case Classification as Probable or Confirmed

Source: Centers for Disease Control and Prevention (CDC)

Chronic Hepatitis C: 2016 Case Definition

Criteria to Distinguish a New Case from an Existing Case
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.

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.
Figure 8 Mortality Rates from HBV, HCV, and HIV in United States, 1999-2007.

This graphic shows that when determining age-adjusted mortality rates, hepatitis C-related deaths surpassed HIV-related deaths in 2006. Abbreviations: PY = person years

Figure 9 Forecasted Annual Deaths Associated with Chronic Hepatitis C Infection.

Among persons with chronic hepatitis C infection and no liver cirrhosis, the hepatitis-C related deaths peak in 2030 to 2035.