HEPATITIS C SURVEILLANCE

Hepatitis C is a reportable disease in Virginia and nationwide. The Code of Virginia and the Board of Health Regulations for Disease Reporting and Control govern notifiable conditions within the Commonwealth of Virginia, including laboratory results consistent with HCV infection.

VDH uses a version of the National Electronic Disease Surveillance System (NEDSS) developed by CDC and designed for reporting infectious diseases, most of which can be confirmed by a single laboratory test. Hepatitis C cases can be classified as chronic or acute and further designated as probable or confirmed, as determined by laboratory test results. A positive result from an HCV antibody (HCV Ab) test is interpreted as a probable chronic case. A positive HCV Ab test is an indicator of exposure and does not always mean that there is a present infection (CDC, 2016). A person who has been exposed to the virus and is not presently infected (i.e. has cleared the infection naturally or through treatment) will continue to test positive for HCV Ab. A positive result for HCV Nucleic Acid Test (NAT), which confirms the presence of HCV RNA, is interpreted as a confirmed chronic case (CDC, 2016). A positive result from an HCV Ab test in conjunction with any sign or symptom of acute viral hepatitis and jaundice or elevated serum alanine aminotransferase (ALT) and does not have a documented positive HCV test within 12 months is interpreted as a probable acute case (CDC, 2016). A positive result for HCV NAT or HCV antigen (HCV Ag) in conjunction with any sign or symptom of acute viral hepatitis and jaundice or elevated serum ALT or a documented negative HCV Ab, HCV Ag or HCV NAT test followed within 12 months by a positive result is interpreted as a confirmed acute case (CDC, 2016). Classification of perinatal hepatitis C cases in infants differs from case classification in adolescents and adults. Infants who have a positive HCV RNA nucleic acid amplification test (NAAT), HCV Ag, or detectable HCV genotype at ≥2 months and ≤36 months of age and have no known HCV exposure other than perinatal is interpreted as a confirmed perinatal HCV case (CDC, 2018). Limited local and state resources prevent the majority of hepatitis C cases from being investigated. Because only 20-30% of acute infections are symptomatic (CDC, 2017), incidence of acute hepatitis C would likely still be underestimated even if resources allowed for more thorough investigation. Many individuals infected with hepatitis C may not know their infection status until they have symptoms of chronic disease, at which point it may be difficult to determine the approximate time of initial infection. According to CDC, about 75% to 85% of people infected with the HCV will develop chronic hepatitis C (CDC, 2017).

The Virginia Electronic Disease Surveillance System (VEDSS) received 11,570* reports of hepatitis C in 2017. VDH guidelines specify that local health departments (LHDs) should investigate likely cases of acute HCV infection, while others are to be investigated as resources permit. In 2013, two health districts in Southwest Virginia began allocating resources to investigate the majority of both acute and chronic hepatitis C cases after hepatitis C case management and prevention was prioritized at the local level. Surveillance data for those two districts are presented in the Appalachia section of this profile.

** Cases reported as of April 9, 2018.*

Because LHDs are not required to investigate every newly identified case of chronic hepatitis C, data entry and management of newly reported hepatitis C cases is most often performed at the state health department. A nearly decade-long backlog of hepatitis C data awaiting verification peaked in the spring of 2015, when quality improvement

methods were initiated on cases from 2011-2015. Quality improvement actions added more than 3,000 new hepatitis C cases, de-duplicated more than 1,000 cases, and corrected discrepancies within specific fields in over 3,000 cases. Prior to 2016, reports lacking a patient address were not included in surveillance data; however, as of 2016, these cases are included in surveillance data if the medical provider and/or performing laboratory is located in Virginia. This change may have contributed in part to the increase in cases seen in 2016.

Despite these efforts, there are also challenges in data management and analysis of hepatitis B and C with VEDSS. Specifically, risk factor information are sometimes documented as text within comments fields in VEDSS making these data difficult to capture during statistical analysis, and risk factor information documented in risk factor-specific fields in VEDSS did not align exactly with risk factor fields collected on paper-based case report forms (CRFs). In 2017, Page Builder was implemented in VEDSS that now align the risk factor questions in VEDSS with the risk factor information collected on paper-based Hepatitis B/C CRF, allowing for risk factor analysis that was not possible before. Even with the implementation of Page Builder, the data is still limited by information that is not reported.

Table 1.1. Case definitions for Chronic Hepatitis C.

2016 Case Definition Hepatitis C, Chronic	*2012 Case Definition Hepatitis C, Past or Present*
No Clinical Criteria Laboratory Criteria: • Positive HCV-Ab Test • Positive NAT **Probable case** Positive HCV-Ab Test **AND** No test conversion within 12 months or no report at all **Confirmed case** Positive NAT **AND** No test conversion within 12 months or no report at all	No clinical criteria Laboratory Criteria (any one): • Positive HCV-Ab with true positive signal to cut-off ratio • HCV recombinant assay positive • Positive NAT **Probable case** • Positive HCV-Ab Test • Higher ALT or SGPT • Signal to cut-off ratio or HCV-Ab unknown

Table 2.1. Case definitions for Acute Hepatitis C.

2016 Case Definition Hepatitis C, Acute	*2012 Case Definition Hepatitis C, Acute*
Clinical Criteria • Symptoms including fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and/or abdominal pain • Jaundice or serum alanine aminotransferase level > 200 IU/L **Laboratory Criteria** • Positive HCV-Ab Test • Positive NAT **Probable case** • Meets clinical criteria • Positive anti-HCV Test • No seroconversion in 12 months **Confirmed case** Requires one of the following: • Positive NAT • Documented seroconversion within the past 12 months	**Clinical Criteria** • Symptoms including fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and/or abdominal pain • Jaundice or serum alanine aminotransferase level > 400 IU/L **Laboratory Criteria** Requires at least one of the following: • Positive HCV-Ab with true positive signal to cut-off ratio • HCV recombinant assay positive • Positive NAT AND Absence of IgM antibody to hepatitis A virus and hepatitis B antigen

Surveillance changes

Case definition changes implemented in 2016, quality assurance actions taken in 2015, and the decision to include lab reports without a known patient address in 2016 have impacted hepatitis C surveillance.

Tables 1.1 and 2.1 provide a comparison of the case definitions for hepatitis C issued in 2012 and 2016. The 2016 case definitions introduce criteria for classifying cases as probable or confirmed, depending on the type of test result and whether seroconversion was demonstrated in the past 12 months.

Key findings in Southwest Virginia

In late 2015, district epidemiologists at each of the four districts in the Southwest region of Virginia were interviewed to assess capacity for investigating and managing hepatitis B and hepatitis C cases and to compare local trends. While the findings from this region are not representative of the state as a whole, the epidemiologists' responses provide insight into the differences in procedures used even among neighboring districts. Furthermore, some districts have novel mechanisms for increasing local capacity for hepatitis C surveillance and connecting with patients that might be useful for other districts to consider adding to their protocols.

Of the four Southwest districts, one reported that they investigate all newly reported cases of hepatitis C, one stated they do not investigate any chronic hepatitis C cases, and two intend to investigate all chronic cases but are limited by insufficient staffing resources. The latter two districts prioritize investigations for specific groups, such as pregnant women, persons under 25 years of age, and people in congregate living situations. One district engages public health graduate students from a local university to assist with interviewing people with hepatitis C infection. Another district uses Disease Intervention Specialists (DIS), who usually perform partner services for individuals with sexually transmitted infections, for interviewing and contact investigation. Those two districts also have used social media or texting to connect with patients and attempt to conduct in-person interviews to gather more accurate information.

Challenges reported by these districts include:

- lack of access to electronic medical records or information from providers, which are needed to confirm acute cases;
- discrepancies between fields on CRFs and in VEDSS;
- patients' resistance (e.g., not reporting risk behaviors or avoiding phone calls);
- insufficient number of staff at the local level to keep up with the high number of cases;
- inadequate and overlapping CRFs for acute and chronic hepatitis B and C (e.g., history of tattoo not included on chronic hepatitis B or C forms).

Outbreaks

In addition to surveillance data, VDH collects and manages outbreak data for hepatitis C. The most recent hepatitis C outbreak in Virginia occurred in 2006. Since 2012, however, there have been two hepatitis B outbreaks in Virginia. Hepatitis B virus (HBV) is more easily transmitted than HCV, but has similar modes of transmission.

One of the two hepatitis B outbreaks was in a rural community in Southwest Virginia among IDU, while the other was in an assisted living facility in Central Virginia associated with an infection control breech involving shared blood glucose monitoring (BGM) devices. VDH assists with detection and mediation of infection control breeches at healthcare facilities and, from 2012-2015, seven infection control breeches involving BGM were identified in Virginia and warranted testing of exposed individuals.

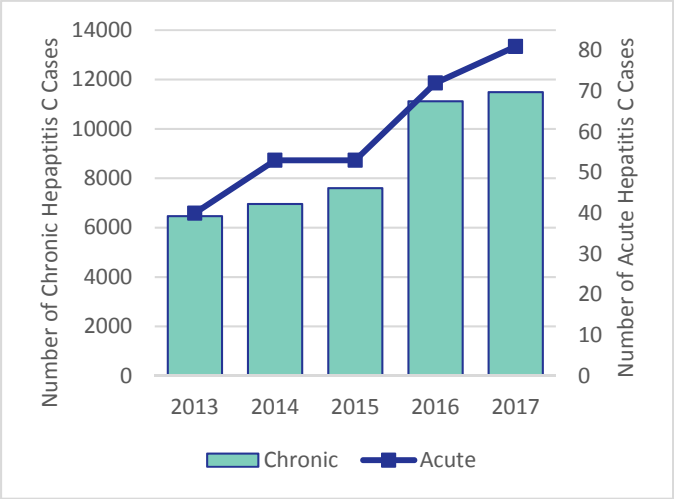
Community outbreaks might not be identified because most people with hepatitis C are not aware of their infection and only 20-30% of people develop symptoms of acute hepatitis C (CDC, 2017). Additionally, those who have been exposed might not seek care or report their potential exposure, particularly when exposure is via illegal IDU (Zibbell, 2015). The 2015 HIV outbreak in Indiana revealed that over 92% of those with HIV were also co-infected with HCV (Peters, 2016). Because HCV tends to be transmitted more easily than HIV among IDU, HCV infections are considered a potential indicator for predicting IDU-related HIV outbreaks (Shavor, 2015).

Robust federally-funded HIV prevention, surveillance, and treatment programs help facilitate public health action for persons living with HIV/AIDS, but parallel programs do not exist for hepatitis C (Valdiserri, 2014). There is heightened concern for future hepatitis C outbreaks in the Appalachian region given the increasing incidence of opioid abuse, injection drug use, and concomitant increase in acute hepatitis C rates (MMWR Appalachia 2015).

Longitudinal trends

Acute hepatitis C cases represent less than 1% of all hepatitis C cases reported to VEDSS, which is likely reflective of the inherent underestimation of acute cases by the current surveillance system. Figure 2.1 illustrates the trends in acute hepatitis C cases relative to the number of chronic cases reported to VDH between 2013 and 2017. The dramatic increase in reported cases may be attributed to both the decision to include laboratory diagnoses from individuals with unknown addresses and the new case definition.

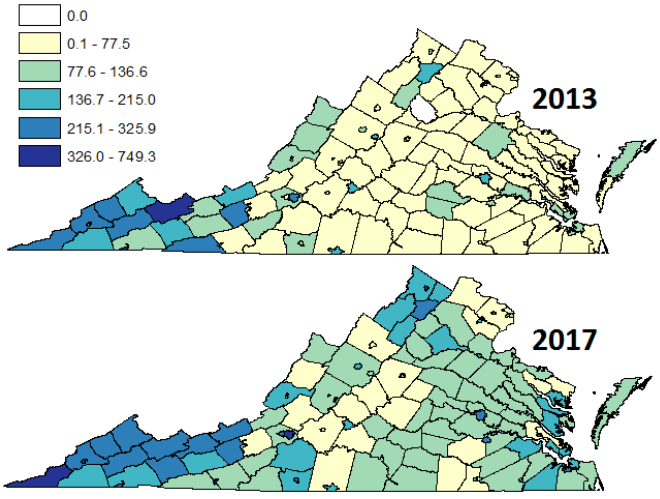
Figure 2.1. Acute and chronic hepatitis C cases reported in VEDSS, 2013-2017.



Geographic distribution

Figure 2.2 depicts the rate of cases of acute and chronic hepatitis C per 100,000 persons by city/county of residence. The southwestern Appalachian region of Virginia has the highest incidence of newly reported chronic and acute hepatitis C.

Figure 2.2. Reported Hepatitis C per 100,000, 2013 vs. 2017*



**This map excludes results from hepatitis C testing performed at correctional facilities to prevent false clustering of cases. Incarcerated individuals are not included in census population data for the counties where correctional facilities are located. Trends in hepatitis C in the incarcerated population are described separately*

Sex

Of people newly reported to have chronic hepatitis C from 2013-2017, 58% were male, 41% female, and 1% had unknown or missing information on sex. Of acute cases of hepatitis C in the same time period, 55% occurred in females and 45% in males. Surveillance data is insufficient for determining whether females are more likely than males to be present for care and testing during acute illness, or whether females are more likely to be identified during a contact investigation.

Race

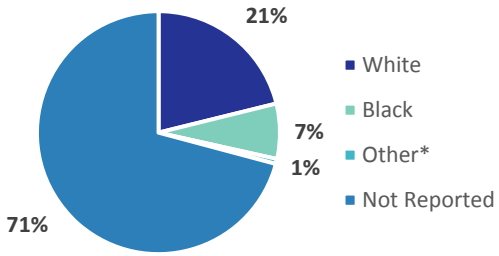
Among people with chronic hepatitis C, data on race are limited; 71% of chronic cases record race as "missing" or "unknown" in VEDSS (Fig. 2.3). Approximately 95% of reports are submitted via electronic laboratory report (ELR), which frequently do not include data on race. As most cases of chronic hepatitis C are not investigated, data available in VEDSS are often limited to data from the ELR. Data quality regarding race should improve as electronic case reporting is initiated in Virginia and nationwide in coming years.

Although race data reported for acute hepatitis C cases are more complete, 25% of acute cases have missing/unknown data on race. Acute hepatitis C cases are more likely to include additional demographic and epidemiologic information from CRFs used during a public health investigation.

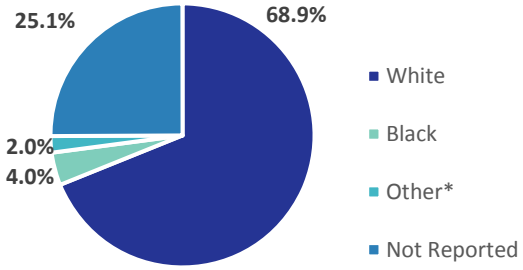
In Virginia from 2013-2017, White individuals comprised the majority of newly reported chronic hepatitis C cases of which there is known race and nearly 70% of acute hepatitis C cases (Fig. 2.3).

Figure 2.3. Reported hepatitis C percent by race, 2013-2017 (VEDSS).

Chronic Hepatitis C



Acute hepatitis C



**Other race includes American Indian or Alaska Native, Asian, Multi-race, and Native Hawaiian or Other Pacific Islander.*

Age

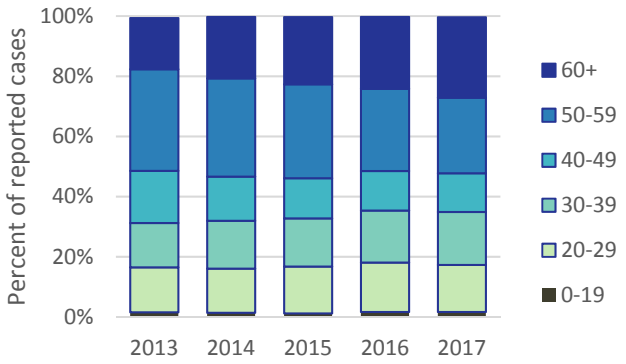
The median age of people with chronic hepatitis C is 50 years (IQR 34-59 years). The median age of people with acute hepatitis C is 32 years (IQR 27-44 years).

Acute or chronic hepatitis C reports are declining in persons aged 40-59 years and increasing in persons aged 20-39 years and 60 or more years (Fig. 2.4).

Because acute hepatitis C occurs within six months of exposure, approximate date of infection can be determined in those diagnosed with acute infection; however, acute infections comprise less than 1% of all hepatitis C cases in the VEDSS surveillance system. The median age of persons diagnosed with acute hepatitis C in Virginia has increased from 31 years of age in 2013 to 35 years of age in 2017 at an average of 18 years younger than those diagnosed with chronic hepatitis C. Age

at diagnosis of chronic hepatitis C cannot be used to estimate age at the time of infection.

Figure 2.4. Reported chronic hepatitis C, percent by age in years, 2013-2017 (VEDSS).



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