Hospitalizations of Persons with Hepatitis B and C in Allegheny County, Pennsylvania, 2016-2019

by

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Abstract

Background/Objective: Several million people in the United States are infected with Hepatitis B virus (HBV) or Hepatitis C virus (HCV), both viral liver infections that can lead to cirrhosis or liver cancer. Characteristics of Allegheny County residents hospitalized with HBV or HCV from 2016 through 2019 were examined in order to identify groups at highest risk.

Methods: Statistical Analysis Software (SAS) was used to analyze patient de-identified data from the Pennsylvania Health Care Cost Containment Council datasets, which include up to 18 diagnosis codes. Only hospitalizations of Allegheny County residents with an HBV or HCV ICD-10 diagnosis code, and an admission date from 2016 through 2019, were included. SAS was used to determine the number of hospitalizations for each infection type, sex, race, and age group. The rate of hospitalizations per 100,000 population was calculated, and the percentage of hospital admissions that had an HBV or HCV diagnosis code was calculated for each year.

Results: Hospitalizations with an HCV diagnosis were more common than those with an HBV diagnosis (290.8 hospitalizations per 100,000 population versus 24.4 per 100,000 population). Few HCV and HBV hospitalizations were classified as acute (0.7% for HCV and 2.3% for HBV). Both HCV and HBV hospitalizations were more common in men than women (M:F ratio of 1.4:1 for HCV and 1.7:1 for HBV), and were more common in Black residents than in White (B:W ratio of 2.8:1 for HCV and 2.6:1 for HBV). For both HCV and HBV, hospitalizations were most common in the 55 to 64 year age group. Finally, the percentages of

hospitalizations with an HBV diagnosis were constant between 2016 and 2019 at around 0.2%, while the percentage of hospitalizations with an HCV diagnosis decreased, from 2.7% in 2016 to 1.8% in 2019.

Conclusion: Overall, this study highlights the public health burden of hospitalizations with an HCV infection and HBV infection in Allegheny County, and illuminates groups that are most affected and that need more support.

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Preface

I would like to thank all of my readers and advisors for their help and recommendations while working on this essay. Nancy Glynn, PhD, Kristen Mertz, MPH, MD, Ashley Hill, MPH, DrPH, and Martha Terry, PhD, have been great guides. I would also like to thank everyone in the Agnihotri Lab for their support while I have been a lab technician there; Sameer Agnihotri, PhD, Brian Golbourn, PhD, Kate Halligan, MD, PhD, Matt Halbert, Taylor Gatesman, and Andrea Cruz. Finally, I would love to thank my parents and my brothers. I love you all very much!

1.0 Introduction

Viral hepatitis is a group of infections that cause inflammation of the liver. Inflammation can lead to further complications, including scarring of the liver, called cirrhosis, and liver cancer such as hepatocellular carcinoma.[1] There are five types of viral hepatitis (A, B, C, D, and E). All five types have an acute phase, which has a rapid onset and comparatively short course. Hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis D virus (HDV) also have a chronic phase, which can last until treatment or until death.[1] Globally, HBV and HCV are of more concern than hepatitis A virus (HAV), hepatitis D virus (HDV), or hepatitis E virus (HEV), as HBV and HCV infections are more common and cause an estimated 96% of viral hepatitis related deaths.[1] An estimated 292 million people globally had a chronic HBV infection in 2016, and an estimated 71.1 million people had a chronic HCV infection in 2015. Comparatively, only 3.4 million people had an HAV infection, and 20.1 million people had an HEV infection.[1] HDV requires an HBV infection in order to replicate, and so it is difficult to separate HDV cases from HBV infections, though an estimated 5-10% of HBV infected individuals globally also have an HDV infection.[1,2] Additionally, HBV caused an estimated 799,008 deaths in 2017 and HCV caused an estimated 580,052 deaths, compared to comparatively lower 18,642 deaths caused by HAV and 14,686 deaths caused by HEV.[2] In the United States (US), HAV, HBV, and HCV are the most common types of viral hepatitis.[3] In fact, in the United States, HDV and HEV are not notifiable diseases.[4] This essay focuses on HBV and HCV, as they are important public health issues in the United States, both for the burden of infections and for the liver complications and death they cause.

1.1 Hepatitis B virus transmission, health problems, and treatment

Hepatitis B virus is a partly double-stranded DNA virus that is about 3.2 kilobases long.[5] There are 10 genotypes of HBV, with more than 30 subtypes.[6] HBV is transmitted from an infected person's bodily fluids, and is most commonly transmitted sexually, perinatally, or through unsafe needle use.[5] It is also transmitted via unscreened blood donations.[7] Due to these primary forms of transmission the United States has been screening blood donations for HBV since 1972.[8]

HBV can cause either an acute or a chronic infection. To be considered an acute case, the patient must have a positive hepatitis B surface antigen test (HBsAg), as well as either jaundice or serum alanine aminotransferase levels above 100 IU/L.[9] However, acute cases are often asymptomatic. Infections in children in particular are largely asymptomatic, and only 30% of adults have jaundice.[5] This is one of the reasons HBV infections are often not identified and are underreported, and the true number of acute cases is estimated to be 6.5 times as much as the reported cases in the United States.[10]

Chronic hepatitis B infection is also largely asymptomatic and a person needs two positive test results six months or more apart to be considered a confirmed chronic case.[6] Positive test results can include an HBsAg test, an HBV DNA test, or a hepatitis B e antigen test (HBeAg).[11] A person with acute HBV is at much higher risk of infecting others as compared to a person with chronic HBV.[12] Acute cases also can develop into chronic cases, though this is dependent on the infected person's age. Acute infections obtained perinatally will develop into chronic infections in 95% of cases. Comparatively, children between the ages of one and five years have a 20-30% chance of developing a chronic infection, while this percentage lowers to 5% for adults.[5] Chronic cases do not need an acute diagnosis before being considered a chronic case.

HBV infections, particularly chronic HBV infections, are a major public health concern because of the long term health problems that they cause. In untreated chronic cases, the cumulative five year incidence for cirrhosis is between 8 and 20%, and for hepatocellular carcinoma is between 2 to 5%.[6] In fact, half of all hepatocellular carcinoma cases are caused by HBV,[6] and half of all liver cancer mortality worldwide in 2010 was due to HBV.[5] In the United States, roughly 15% of adults with chronic HBV and an estimated 25% of children with chronic HBV will die prematurely from cirrhosis or hepatocellular carcinoma.[6,13] Acute cases can also cause mortality, albeit more rarely than in chronic cases. In 1% of acute cases worldwide, HBV causes fulminant hepatitis, which without a liver transplant will lead to death in 80% of cases.[5]

Fortunately, there are vaccines and treatments for HBV. The first vaccine for HBV was invented in 1981, and there are now several types available. In the United States, the vaccine series is recommended for infants within 24 hours of birth, for any unvaccinated children,[6] for all adults aged 19 to 59,[14] and for any adults over 60 who are at risk of contracting HBV,[6] including but not limited to healthcare workers, household contacts of those with HBV, and people who travel to where HBV is endemic.[10] These vaccines are effective, and between 75% and 100% of people will develop an antibody response, depending on the vaccine and age of the patient.[15] While current treatments cannot completely rid the body of the virus, HBV DNA can be suppressed, and patients who were initially HBsAg positive or HBeAg positive can test negative. Lifelong monitoring of chronic cases is necessary, however, as HBV infection can be reactivated.[6] Perinatal infections can also be prevented. Infants born to HBsAg positive mothers can be given the HBV vaccine within 24 hours after birth, which will prevent a hepatitis B infection in 75% to 95% of cases. These infection rates can be decreased to nearly 1% if the infant is also given hepatitis B immunoglobulin, and if the vaccination series is finished.[16]

1.1.1 HBV prevalence worldwide

Despite the vaccines and treatment available, HBV is still a major health concern worldwide. It is considered one of the most common chronic infection in the world, with an estimated 350 million chronic infections worldwide.[5] About 1.5 million people are newly infected each year.[17] In 2017, it is estimated that nearly 800,000 people worldwide died due to HBV, mostly due to HBV-related liver cirrhosis or liver cancer.[2] It is highly endemic, with a prevalence of above 8%, in many parts of the world, including southeast Asia, most of Africa, and most of the Pacific Islands.[5]

1.1.2 HBV prevalence and disparities in the United States

While not as common in the United States, HBV is still an important public health issue because of the large number of infections and associated liver complications and deaths. Between 2,791 and 3,409 acute cases were reported each year between 2012 and 2019 to the National Notifiable Disease Surveillance System (NNDSS). The estimated burden of acute cases is much higher, however, and there were an estimated 18,100 to 22,200 acute cases in that same time period.[18] While it is harder to determine the prevalence of chronic HBV, as NNDSS captures only newly reported chronic cases and not ongoing cases from previous years,[18] between 850,000 to 2.2 million people are living in the United States with chronic HBV.[6] In addition, an estimated 1,000 perinatal cases occur annually in the US.[6] Finally, HBV is a major public health concern in the United States because of the deaths it causes. In 2019 in the United States, 1,662 deaths had HBV listed as a cause of death, or 0.42 deaths per 100,000 population.[18]

This burden of the disease is why public health systems need to study and perform surveillance on HBV. Not only do acute HBV cases have to be found, in order to identify and prevent outbreaks, but trends in the disease also have to be analyzed. Acute HBV infections have been a national notifiable disease since 1966, and chronic infections have been nationally notifiable since 2003.[19,20] The rate of reported acute hepatitis B infections has remained relatively stable over the last decade, at around 1.0 and 1.1 cases per 100,000 population per year in the 2010s.[18] It is important to note that these reported rates might not indicate the true burden of acute hepatitis B in the US, as many cases go unreported.[10] Trends of chronic infections in the US are much harder to identify. The CDC does not keep track of already existing chronic cases, only cases that are newly reported in a year of interest.[18]

Another reason for surveillance and monitoring is to identify disparities present in HBV infections, so that outreach programs and prevention campaigns can better focus on more affected groups. See Table 1 for acute and chronic incidence rates by sex, race, and age group. Both acute and chronic HBV infections are more common in men than women at the national level. For reported acute cases, the male to female ratio was between 1.5:1 and 1.8:1 from 2011 through 2019. For newly reported chronic cases, the male to female ratio was 1.4:1 in 2019. Similarly, males had a higher mortality rate than females, at a ratio of 3.1:1 (Table 2).[18]

Another important disparity in HBV infections is differences by age groups. In the United States, people in their mid-life, between 30 and 59 years old, have a higher burden of both acute and chronic HBV infections. In fact, people in the 30 to 49 age range account for 47% of all newly reported chronic cases. Childhood HBV vaccine series were not implemented until 1991, which is one of the reasons those above the age of 30 have higher rates than those under. For those in the 20 to 29 age group, the rate of acute infections has decreased steadily and substantially over the

past two decades, from 3.5 cases per 100,000 population in 2004 to 0.5 cases per 100,000 population in 2019, largely due to vaccinations.[18]

Another important factor to pay attention to is race data. There are many racial disparities in the United States in HBV infection rates. The rates of reported acute HBV infections are highest among non-Hispanic White and non-Hispanic Black people, and lowest among Asian and Pacific Islander people (Table 1). However, these disparities are starkly different for chronic cases (Table 1). Rates of newly reported chronic infections are highest among Asian and Pacific Islander people, at a ratio of 10.5:1 as compared to non-Hispanic White people. Rates among non-Hispanic Black people are also high, at a ratio of 3.7:1 as compared to non-Hispanic White people. It is lowest among Indigenous people, at a ratio of 0.6:1 as compared to non-Hispanic White people.

There are similar trends for mortality rates. Asian and Pacific Islander people had higher mortality rates as compared to non-Hispanic White people (ratio of 7.5:1) and non-Hispanic Black people also had higher mortality rates as compared to White people (ratio of 3:1) (Table 2).[18] These disparities further illustrate the importance of collecting race data, so that these trends can be identified and new campaigns can be launched to better support these affected groups.

Other disparities among HBV infections in the United States are related to immigration status. One study in 2011 estimated that 95% of new chronic HBV infections were among foreign born people in the United States, as opposed to US born people.[21] However, it is difficult to analyze HBV infection rates in the foreign born as compared to the US born, as immigration status is often not asked for in surveys or reported on.

In addition to race and immigration status, another factor that needs further investigation is hospitalization status. Among acute case reports to the CDC in 2016, 42.0% did not include information on whether the patient was hospitalized or not.[22] Of those acute HBV cases with

hospitalization data in 2019, 1,427 patients were hospitalized. This number includes only HBV cases that were reported to the CDC for the first time, and not individuals who were hospitalized with chronic HBV or who were previously reported as acute.[18] Hospitalization data for HBV are often difficult to find, but they are an important measure of the burden of the disease, especially for the sickest patients. When hospitalization data do exist, they often do not examine the demographics of those hospitalized. This study aims to address this gap in knowledge.

1.1.3 HBV prevalence and disparities in Pennsylvania

Pennsylvania varies slightly from the national trends of HBV infections. Pennsylvania alone in 2019 had 91 reported acute cases, two confirmed perinatal cases, and 926 newly reported chronic cases; these numbers do not include any undetected estimates.[18] Pennsylvania had a lower mortality rate due to HBV as compared to the national average, at 0.25 deaths per 100,000 population.[18] Pennsylvania has submitted information about its acute cases to the CDC every year, and it too has had a stable rate of acute hepatitis B cases, just like at the national level, but at slightly lower levels. From 2014 to 2018, there were 0.5 cases per 100,000 population, though this number jumped to 0.7 cases per 100,000 population in 2019.[18,22,23,24,25,26] According to the Pennsylvania Department of Health, the acute incidence of hepatitis B has remained relatively stable, at between 0.3 and 0.7 per 100,000 between 2014 and 2019.[27] In Allegheny County, a county in the western part of the state that contains the city of Pittsburgh, the acute HBV incidence rate was 0.8, and the chronic HBV incidence rate of newly reported chronic cases was 7.7 in 2019.[28]

In Pennsylvania, males also had consistently higher overall incidence rates of HBV than females. According to the Healthy People 2020 report, from 2015 to 2019, the male to female ratio

ranged from 1.3:1 to 2.3:1.[27] The incidence rates among other people of color were not analyzed.[27] This study aims to examine these understudied demographics, in hospitalizations of those with HBV in Allegheny County.

1.2 Hepatitis C virus transmission, health problems, and treatment

Hepatitis C virus is an enveloped single-stranded RNA virus, and is about 9.6 kilobases in length.[29] There are eight reported genotypes.[30] Like HBV, it can be transmitted perinatally. While it can be transmitted sexually, of greater concern is percutaneous exposure, such as needlestick injuries or unsafe use of needles during drug use.[31] Historically, poor screening of blood donations and transplant organs has caused HCV infections,[30] though in the United States proper screening methods have been implemented and those risks have decreased substantially.[32] Acute HCV infections are largely asymptomatic,[29] with fewer than 25% of cases showing clinical symptoms,[30] and as such it can be difficult to separate acute cases from chronic, which are also largely asymptomatic.[29]

To confirm a chronic infection, a positive HCV antigen test or positive nucleic acid test is needed.[33] To confirm an acute infection, the same positive tests are needed, along with symptoms of an HCV infection and no previous positive tests.[34] Acute cases are generally defined as short term, within the first six months of HCV exposure, while chronic cases are long-term infections.[35] While there is currently no vaccine for HCV, treatment for chronic HCV is effective. Over 90% of patients with chronic HCV can be cured within eight to 12 weeks, through oral therapy.[36] However, since chronic HCV is largely asymptomatic, many people do not know they have HCV and so do not get treatment, leading to liver complications.

Between 70 and 80% of patients with acute infections will develop chronic HCV,[30,31,37] and of those between 10 and 20% will develop further liver diseases, such as cirrhosis and hepatocellular carcinoma.[30,31] Cirrhosis due to chronic HCV can lead to acute liver failure known as hepatic decompensation. If hepatic decompensation occurs, the patient has a 15-20% chance of dying.[30] Due to these liver complications, HCV is the leading cause of liver transplants in the United States.[31] In addition, mothers with HCV transmit HCV to their infants during birth 6% of the time, and this rises to 11% when the mother is coinfected with HIV.[30]

1.2.1 HCV prevalence worldwide

As with HBV, HCV is a major public health concern, both because of the number of cases and the further complications it causes. As one of the most common bloodborne pathogens,[31] it is estimated that between 71.1 and 200 million people in the world are infected,[30,31] and six countries (China, India, Russia, Pakistan, Nigeria, and Egypt) account for more than 50% of all infections.[30] An estimated 1.5 to 3 million new infections occur annually.[17,29,31]

1.2.2 HCV prevalence and disparities in the United States

In the United States, there were 4,136 reported acute HCV infections and 57,500 estimated acute HCV infections in 2019. There were also 123,312 newly reported chronic cases, at 56.7 cases per 100,000 population. As with HBV, it is difficult to determine the true prevalence of HCV as NNDSS notes only newly reported chronic cases. In the United States in 2019, there were 217 reported perinatal HCV infections.[18]

HCV infections are on the rise in the United States. The number of reported acute HCV infections has more than doubled in the past decade. In 2012, 1,778 acute infections were reported, and this number consistently increased each year to 4,136 cases in 2019, which is a rate of 1.3 acute infections per 100,000 population. This increase was present in all age groups above 19 years of age, for all races, and for both men and women.[18] However, acute cases are underreported, and so the true incidence is estimated to be 13.9 times higher.[38] The trends in chronic cases are hard to identify, in part because not all states report their chronic cases to the CDC every year.[39] The trends both for acute and chronic HCV infections are important to identify, especially since HCV cases are on the rise due to injection drug use and the opioid epidemic.[40] This is further proof of the need for accurate and timely surveillance, so that better interventions and outreach campaigns can be created and implemented, especially considering that there is currently no HCV vaccine.

Another reason for surveillance of HCV infections is the disparities within HCV infection distributions. Infections occur at higher rates in males than females, at a ratio of 1.6:1 for acute cases and 1.9:1 for newly reported chronic cases.[18] Consult Table 3 for acute and chronic incidence rates by sex, race, and age group. Males were also more likely to have HCV as a cause of death as compared to females, at a ratio of 2.7:1 (Table 4).[18] HCV also affects people of disparate ages differently. The most affected age group for acute infections is the 20 to 29 year age group and the 30 to 39 year age group, at 2.9 and 3.2 reported acute cases per 100,000 population. For newly reported chronic cases, the most affected age group is the 30 to 39 year age group, with 109.1 newly reported chronic cases per 100,000 population. The 20 to 29 year, the 40 to 49 year, and the 50 to 59 year age groups all have similar rates, at 72.3, 72.1, and 79.6 newly reported chronic cases per 100,000 population respectively.[18]

Racial disparities are another important area in need of study. Acute HCV infection rates are highest in Indigenous people in the US, at a ratio of 2.5:1 as compared to non-Hispanic White people, as of 2019. Non-Hispanic White people had the next highest rate, and non-Hispanic Black people and Hispanic people had ratios of 0.5:1 and 0.4:1 as compared to non-Hispanic White people. Asian people and Pacific Islanders had the lowest rate, at a ratio of 0.14:1 as compared to non-Hispanic White people. These trends were similar for newly reported chronic cases. Indigenous people were the most affected, at a ratio of 2.6:1 as compared to non-Hispanic White people. Non-Hispanic Black people had similar rates to non-Hispanic White people, at a ratio of 0.9:1. Asian people and Pacific Islanders had the lowest rates, at a ratio of 0.2:1 as compared to non-Hispanic White people (Table 3).[18] Trends were slightly different for mortality rates, however. Indigenous people were still the most affected group, at a ratio of 2.8:1 as compared to non-Hispanic White people. Both non-Hispanic Black people and Hispanic people were the next most affected groups (1.8:1 and 1.2:1 as compared to non-Hispanic White people, respectively). Asian people and Pacific Islanders were the least affected, with a ratio of 0.5:1 as compared to non-Hispanic White people.[18]

One area that needs further study is hospitalizations with HCV, in part because hospitalization data are often missing. For example, in 2017, 46.4% of acute HCV cases reported to the CDC did not mention whether the patient was hospitalized or not.[22] In 2019, of those cases that had hospitalization data reported to the CDC, 1,041 patients with acute HCV were hospitalized. However, this number includes only cases that were reported to the CDC for the first time. It does not include chronic cases or patients who were previously reported as acute cases.[18] In addition, the number of overall hospitalizations that have an HCV diagnosis is also hard to find, and the demographics of these patients are typically not analyzed. Hospitalization data are

important, because they are one measure of the burden of the disease, especially for those who are the most ill. This study aims to help address this knowledge gap.

1.2.3 HCV prevalence and disparities in Pennsylvania

Pennsylvania consistently reported its known acute cases to the CDC, and the incidence of acute cases has increased substantially, from 0.2 cases per 100,000 population in 2010 to 1.6 cases per 100,000 in 2019. This is slightly higher than the national average in 2019. There were also 10,848 reported chronic cases in 2019, at a rate of 84.7 cases per 100,000 population, which is higher than the national average.[18] In Pennsylvania, the incidence of acute HCV has ranged from 1.8 to 1.2 per 100,000 population from 2016 through 2020, with a high of 1.9 per 100,000 population in 2018.[41] In Allegheny County in 2019, there were 12 reported cases of acute HCV and 1,125 confirmed or probably chronic HCV cases. For both acute and chronic, 58% of cases were male, and for chronic HCV the 25 to 39 year age groups and the 55 to 69 year age groups were most affected.[38] This study aims to further examine these demographics in hospitalizations with HCV in Allegheny County.

2.0 Objectives

The objectives of this essay are to calculate the percentage of hospitalizations among Allegheny County residents with an HBV or HCV diagnosis; describe the incidence of hospitalizations with an HCV or HBV diagnosis code; and compare the incidence of hospitalizations with HBV and HCV diagnosis codes by gender, race, and age group.

3.0 Methods

3.1 Study population

This was a descriptive statistics study. The study population included any residents of Allegheny County who were hospitalized between 2016 and 2019, and had either an HCV or HBV ICD-10 diagnosis code. The ICD-10 codes used are shown in Table 5. Data were pulled from the Pennsylvania Health Care Cost Containment Council (PHC4) datasets,[42] which contain patient de-identified data for hospitalizations in Pennsylvania for each year. The PHC4 datasets give one primary diagnosis and up to 17 secondary diagnoses for each hospitalization. Occasionally, a hospitalization had two HBV codes or two HCV codes. Only one of these codes was used in the analysis. When this happened, acute codes were used over chronic or unspecified codes, and chronic codes were used over unspecified codes. This study analyzed only the years 2016 to 2019, as hospitals in Allegheny County switched over from using ICD-9 diagnosis codes to ICD-10 diagnosis codes in late 2015, and using only ICD-10 codes allows for easier case comparison.

3.2 Measurements and statistical analysis

The statistical software SAS Version 9.4 (SAS Institute Inc., Cary, NC) was used to determine the number of hospitalizations with either an HCV or HBV ICD-10 diagnosis code. Of those, the number of hospitalizations by sex, by race, by age group, and by infection type were calculated. The rate of hospital admissions per 100,000 population was then calculated for each

sub-group. The rates were calculated using 2019 US Census estimates for Allegheny County. The percentage of total hospital admissions that had an HBV or HCV diagnosis was also calculated for each year.

To examine how many HCV or HBV infections co-occurred with liver cancer, the number of hospitalizations with an HBV or HCV diagnosis code that had liver cancer as the primary diagnosis was also determined. The ICD-10 codes C22.xx were used to identify liver cancer hospitalizations, where xx is any number. Other kinds of liver diseases as the primary diagnosis were also examined, and include K74.xx through K77.xx. The ICD-10 codes K70.xx through K73.xx also pertain to liver diseases, but these codes were not included in the analysis because they were specific to alcohol use, drug poisoning, or explicitly excluded viral hepatitis. Delivery (*i.e.*, giving birth to a baby) as a primary diagnosis was also examined, using the ICD-10 codes O80 and O82.[43] Viral hepatitis complicating childbirth, which is the ICD-10 code O98.42, was also used as a measure of delivery.[43] Additionally, the ten most common primary diagnoses for hospitalizations with an HBV or HCV secondary diagnosis were also found.

4.0 Results

4.1 HBV

The percentage of hospitalizations in Allegheny County with an HBV diagnosis was relatively consistent from 2016 to 2019, with a high of 0.21% in 2017 and a low of 0.17% in 2018 (Fig. 1). The counts of hospitalizations are summarized in Table 6. HBV hospitalizations occurred at a rate of 24.4 hospitalizations per 100,000 population. Unspecified infection types were most common, at 68.9% of all HBV diagnoses, at a rate of 16.8 infections per 100,000 hospitalizations (Fig. 2). Acute infections made up 2.3% of all HBV infections and chronic infections made up 28.8%. HBV diagnoses were more likely to be secondary diagnoses, as 98.4% were secondary diagnoses and 1.6% were primary. Over this four year period, 14 hospitalizations had two HBV diagnosis codes, which is 1.2% of all hospitalizations with an HBV diagnosis code. Only one of these codes was used in the analysis.

HBV hospitalizations were more common in men than in women, with a male to female ratio of 1.7:1 (Fig. 3). Race data were missing for 69 (5.8%) hospitalizations of 1,188 hospitalizations with an HBV diagnosis. Of those hospitalizations with race data, hospitalizations were more common in Black residents than in White at a ratio of 2.6:1 (Fig. 4). The age group with the highest burden of hospitalization with an HBV diagnosis is the 55-64 year age group, at 57.1 hospitalizations per 100,000 population (Fig. 5). Rates were lowest in the 0-24 year age range at 1.2 hospitalizations per 100,000 population, but were also comparatively low in the 25-34 year age range at 12.6 hospitalizations per 100,000.

Of all the hospitalizations with an HBV secondary diagnosis between 2016 and 2019, 1.9% had a primary diagnosis of liver cirrhosis, and 1.5% had a primary diagnosis of liver cancer. Additionally, 0.4% had a primary diagnosis of some other liver disease, including nonalcoholic steatohepatitis (NASH), inflammatory liver disease, and autoimmune hepatitis. None had a primary diagnosis of delivery, though 12 had a primary diagnosis of viral hepatitis complicating childbirth. Additionally, the most common primary diagnosis for hospitalizations with an HBV secondary diagnosis was sepsis (6.3%), followed by hypertension (3.7%) and alcoholic and toxic liver disease (3.3%) (Table 7).

4.2 HCV

From 2016 to 2019, the percentage of overall hospitalizations in Allegheny County that had an HCV diagnosis had a consistent, slight decrease from year to year, starting at 2.7% in 2016 to 1.8% in 2019 (Fig. 6). The counts of hospitalizations are summarized in Table 8. Overall, there were 290.8 hospitalizations with an HCV diagnosis per 100,000 population (Fig. 7). Of these, an unspecified infection type was most common, at 68.7% of all HCV diagnoses, for a rate of 199.8 infections per 100,000 hospitalizations. Chronic infections made up 30.6% of the HCV diagnoses, and acute infections represented only 0.7% of all diagnoses. HCV diagnoses were more commonly secondary diagnoses, with 99.4% secondary diagnoses and 0.6% primary diagnoses. In addition, 123 hospitalizations (0.87%) of all hospitalizations with an HCV diagnosis over the four year period had two HCV diagnosis codes. When this happened, only one diagnosis code was used in the analysis.

HCV diagnoses were more common in men than women at a male to female ratio of 1.4:1 (Fig. 8). Out of the 14,147 hospitalizations with an HCV diagnosis over the four year period, 208 hospitalizations (1.5%) were missing race data. Of those that had race data, hospitalizations were more common in Black residents than White residents at a ratio of 2.8:1 (Fig. 9). The age group most affected is the 55-64 year age group, at 685.2 hospitalizations per 100,000 population (Fig. 10). Comparatively, the 0-24 year age group and the 75 year and up age group had much smaller rates, at 25.1 and 89.0 hospitalizations per 100,000 population (Fig. 10).

Out of all hospitalizations with an HCV secondary diagnosis, 0.95% had a primary diagnosis of liver cirrhosis and 0.80% had a primary diagnosis of liver cancer. Additionally, 0.09% had another liver disease, including NASH, portal tension, and chronic passive congestion of the liver. No hospitalizations with an HCV diagnosis code were found to have childbirth as a primary diagnosis. However, 44 hospitalizations had the primary diagnosis of viral hepatitis complicating childbirth. The most common primary diagnosis of hospitalizations with an HCV secondary diagnosis was drug poisoning and use, including opioid use, at 6.9% (Table 9). Depression (6.3%) and alcohol use (4.7%) were the next most common primary diagnoses.

Finally, some hospitalizations included both an HBV diagnosis code and an HCV diagnosis code. Over the four year period, 358 hospitalizations had both an HBV and an HCV diagnosis codes, which is 30.1% of all hospitalizations with an HBV diagnosis and is 2.5% of all hospitalizations with an HCV diagnosis.

5.0 Discussion

5.1 Comparing HBV and HCV hospitalizations

Hospitalizations in Allegheny County with an HCV diagnosis were nearly 12 times as common as those with an HBV diagnosis, at 290.8 hospitalizations per 100,000 population as compared to 24.4 hospitalizations per 100,000 population. There was overlap between hospitalizations with an HCV diagnosis and with an HBV diagnosis. Nearly a third of hospitalizations with an HBV diagnosis also had an HCV diagnosis, though only 2.5% of all hospitalizations with an HCV diagnosis also had an HBV diagnosis. For both HCV and HBV, fewer than 2.5% of hospitalizations had an acute diagnosis. The majority, nearly 70%, of hospitalizations had an unspecified diagnosis.

For both HCV and HBV, hospitalizations were more common in men than in women, which matches infection trends at the national, statewide, and county level. Hospitalizations were also more common in Black residents than in White residents, which again matches national trends. The age group that is most affected is the 55 to 64 age group, which is expected considering that this age group tends to be hospitalized more than younger age groups. Additionally, 3.8% of hospitalizations with an HBV diagnosis and 1.8% of hospitalizations with an HCV diagnosis had some form of liver disease as a primary diagnosis. While this study cannot infer that HCV and HBV are the cause of those liver diseases, HCV and HBV are complicating factors with any liver disease.

The percentages of hospitalizations with an HBV diagnosis were constant between 2016 and 2019, which is similar to the relatively constant national and statewide HBV infection rates

throughout the past decade. However, the percentage of hospitalizations with an HCV diagnosis decreased, from 2.7% in 2016 to 1.8% in 2019. This does not completely match national or statewide infection rates, as while the number of newly reported chronic cases decreased during this time period, the number of acute cases increased. The range of years examined in this study is not wide enough to determine if this is a true trend, or merely a temporary decrease. However, the Allegheny County Health Department has been working to reduce HCV infections, with programs such as Hep C Free Allegheny County,[44] and this downward trend in hospitalizations with an HCV diagnosis may indicate the success of these programs.

5.2 Strengths and limitations

One strength of this study is the strong external validity, as it includes all Allegheny County residents hospitalized with an HCV or HBV diagnosis. All hospitalizations in the dataset had sex and age information, which also increases the external validity of this study. The use of ICD-10 codes also allows for consistent case definitions, which in turn allows for more reliable comparison between hospitalizations. While there were missing race data, the percentage of hospitalizations without a race designation was relatively low; it was missing in 1.5% of hospitalizations with an HCV diagnosis and in 5.8% of those with an HBV diagnosis.

This study also has several limitations. One limitation is that the data are patient de-identified. While this is important for protecting patient privacy, it also means that a single patient may be counted as several different hospitalizations in the dataset, if the patient was hospitalized multiple times. This could lead to overrepresentation of a subgroup, and limits the internal validity of this study. Another limitation is that nearly 70% of the hospitalizations had an unspecified

diagnosis. These diagnoses could be either acute or chronic infections in reality, but the dataset does not contain that information. This results in an underestimation of the true burden of acute and chronic infections during hospitalization.

A final limitation is that, occasionally, a hospitalization had two HBV diagnosis codes or two HCV diagnosis codes. For example, a hospitalization may have both an acute HBV diagnosis code and a chronic HBV diagnosis code, or a chronic HBV diagnosis code and an unspecified HBV diagnosis code. Since a person cannot have both chronic and acute HBV or HCV infection at the same time, only one code was used in the analysis, but this may result in an inaccurate estimation of the burden of hospitalizations with acute or chronic diagnoses. However, this happened relatively infrequently, at 0.9% of hospitalizations with an HCV diagnosis code and at 1.2% of hospitalizations with an HBV diagnosis code.

5.3 Recommendations

This study highlights areas that need further examination. Nearly 70% of the hospitalizations had an unspecified HBV or HCV diagnosis code, and about 1% of the hospitalizations had multiple HBV or HCV diagnosis codes. To increase the accuracy of the analysis, the diagnosis should either be acute or chronic, not unspecified, and there should be only one diagnosis code. Additionally, to lower percentages of hospitalizations with missing race information, hospitals should better elicit race information. While the percentage of hospitalizations with missing race data was relatively low in this study, the study would be more accurate if race data were present for every hospitalization.

Another important factor when studying HBV is immigration status, since HBV chronic infections are more common in foreign born individuals in the United States as compared to domestic born individuals. This study was not able to examine immigration status, because immigration status was not included in the dataset used for this study. Immigration status and its relation to HBV needs further study. However, confidentiality is paramount when examining immigration status, as undocumented immigrants are at risk for deportation.

The prevalence of HCV and HBV diagnoses among persons hospitalized is one measure of the burden of these diseases. The higher burden in Black residents, males, and the 55 to 64 year age group presents potential areas to focus on for interventions. Screening efforts for both HBV and HCV can focus on these more heavily affected groups. For HBV, vaccination efforts can focus on older adults who have not gotten the vaccine since it came out in 1981. For those hospitalized with HCV, the infection can be cured and efforts can focus on ensuring that people stick to the treatment regimen and providing financial relief, since the treatment is expensive. The much higher hospitalization rate for HCV as compared to HBV underscores the importance of developing an HCV vaccine. Overall, this study highlights the public health burden of hospitalizations with an HCV infection and HBV infection in Allegheny County, and illuminates groups that are most affected and that need more support.

6.0 Tables and Figures

Table 1. Incidence rate of acute and chronic hepatitis B virus infections in the United States, 2019*

Characteristic	Acute Incidence**	Chronic Incidence**
Total	1.0	5.9
Age (years)		
0-19	0.0	0.5
20-29	0.5	5.4
30-39	1.8	11.3
40-49	2.7	10.7
50-59	1.6	8.4
≥60	0.6	5.1
Sex		
Male	1.3	7.0
Female	0.7	4.9
Race/Ethnicity		
Indigenous	0.6	1.0
Asian or Pacific Islander	0.3	18.9
Black, non-Hispanic	0.9	6.7
White, non-Hispanic	1.0	1.8
Hispanic, any race	0.4	1.4

*Adapted from Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report–United States, 2019. https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm. Published May 2021. Accessed 23 Sept 21.

**All rates are per 100,000 population.

Table 2. Rates of death with hepatitis B virus infections listed as a cause of death, United States, 2019*

Characteristic	Mortality Rate**
Total	0.42
Age (years)	
0-34	0.03
35-44	0.26
45-54	0.62

55-64	1.18
65-74	1.54
≥75	1.18
Sex	
Male	0.66
Female	0.21
Race/ethnicity	
Indigenous	0.76
Asian or Pacific Islander	2.10
Black, non-Hispanic	0.64
White, non-Hispanic	0.28
Hispanic, any race	0.27

*Adapted from Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report–United States, 2019. https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm. Published May 2021. Accessed 23 Sept 21.

**Rates are per 100,000 population. Rates for total, sex, and race/ethnicity are age-adjusted per 100,000 US standard population during 2000.

Table 3. Incidence rate of acute and chronic hepatitis C virus infections in the United States, 2019*

Characteristic	**Acute Incidence****	**Chronic Incidence****
Total	1.3	56.7
Age (years)		
0-19	0.1	1.8
20-29	2.9	72.3
30-39	3.2	109.1
40-49	1.7	72.1
50-59	1.1	79.6
≥60	0.5	50.8
Sex		
Male	1.6	73.9
Female	1.0	39.7
Race/Ethnicity		
Indigenous	3.6	86.7
Asian or Pacific Islander	0.2	7.1
Black, non-Hispanic	0.7	31.0
White, non-Hispanic	1.4	34.0
Hispanic, any race	0.6	14.1

*Adapted from Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report–United States, 2019. https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm. Published May 2021. Accessed 23 Sept 21.

**All rates are per 100,000 population. All cases are newly reported in 2019.

Table 4. Rates of death with hepatitis C virus infections listed as a cause of death, United States, 2019*

Characteristic	Mortality Rate**
Total	3.33
Age (years)	
0-34	0.11
35-44	1.13
45-54	4.10
55-64	14.85
65-74	14.29
≥75	4.95
Sex	
Male	4.96
Female	1.83
Race/ethnicity	
Indigenous	8.63
Asian or Pacific Islander	1.43
Black, non-Hispanic	5.44
White, non-Hispanic	3.08
Hispanic, any race	3.84

*Adapted from Centers for Disease Control and Prevention. Viral Hepatitis Surveillance Report–United States, 2019. https://www.cdc.gov/hepatitis/statistics/2019surveillance/index.htm. Published May 2021. Accessed 23 Sept 21.

**Rates are per 100,000 population. Rates for total, sex, and race/ethnicity are age-adjusted per 100,000 US standard population during 2000.

Table 5. HCV and HBV ICD-10 diagnosis codes used in the analysis

	Acute infection	Chronic infection	Unspecified
Hepatitis B virus	B16.0, B16.1, B16.2, B16.9	B18.0, B18.1	B19.10, B19.11
Hepatitis C virus	B17.10, B17.11	B18.2	B19.20, B19.21

Table 6. Summary of hospitalization counts with an HBV diagnosis code

	Hospitalization count
Total	1,188
Year	
2016	311
2017	337
2018	267
2019	273
Infection type	
Acute	27
Chronic	342
Unspecified	819
Sex	
Female	452
Male	736
Race	
Black	405
White	670
Other	113

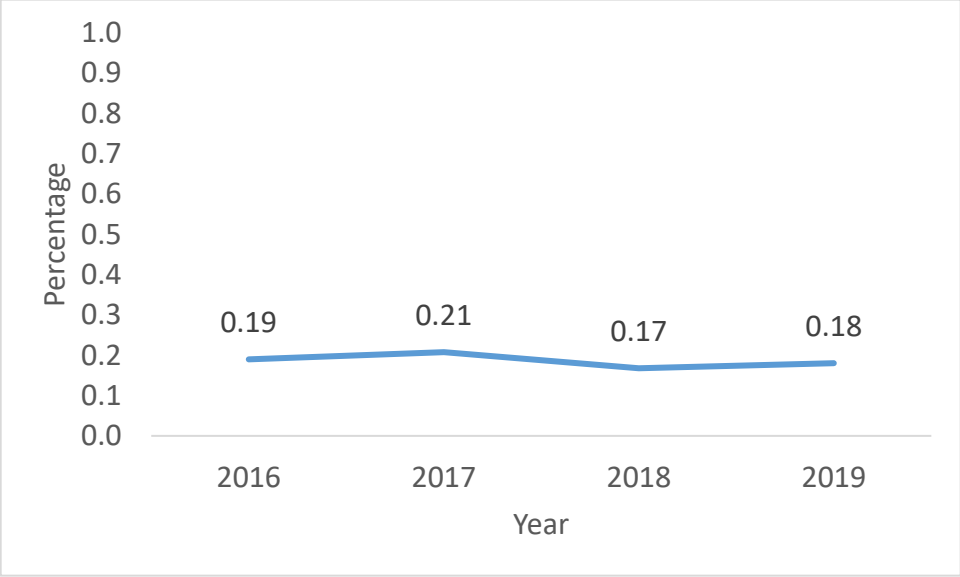

Figure 1. Percentage of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HBV, 2016-2019

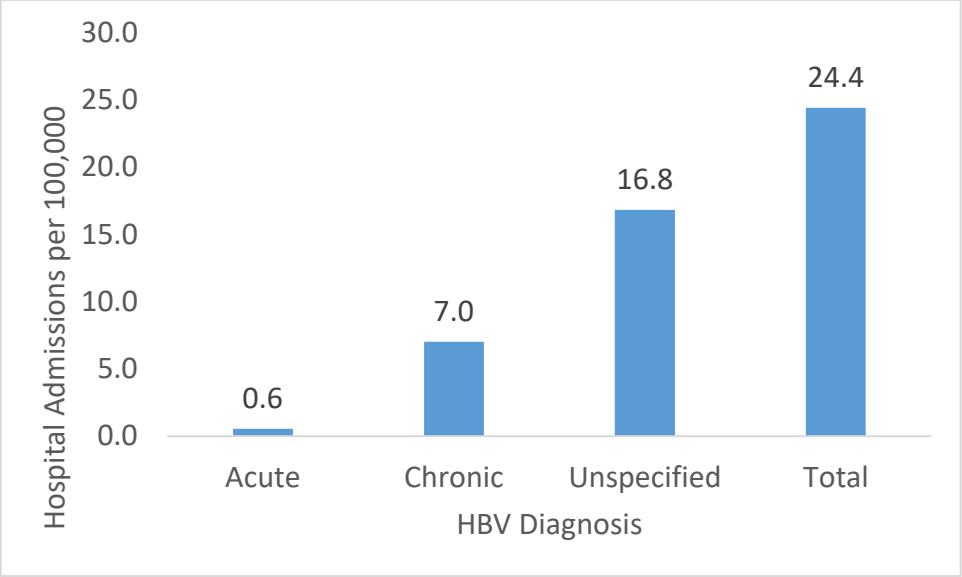

Figure 2. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HBV, by infection type, 2016-2019. Rates are per 100,000 population

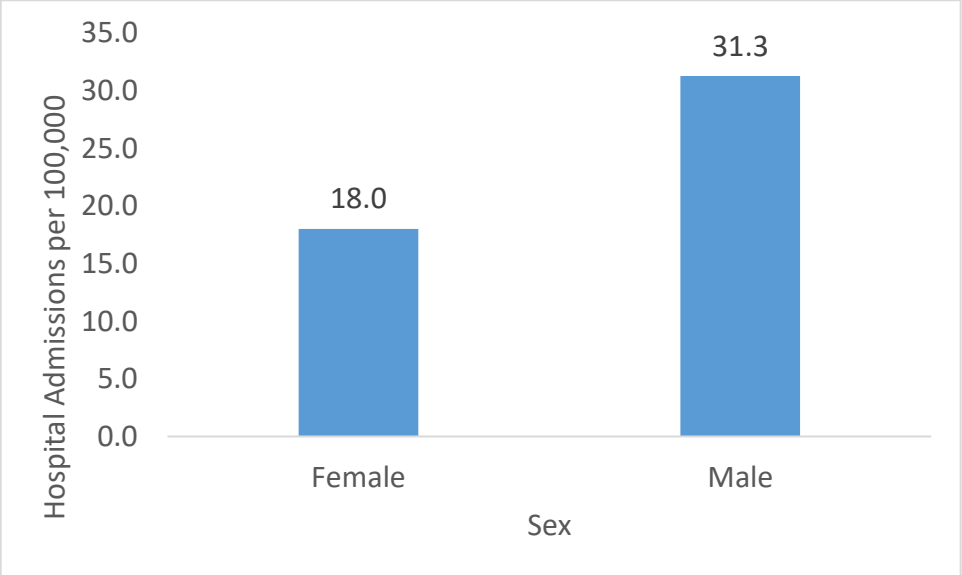

Figure 3. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HBV by sex, 2016-2019. Rates are per 100,000 population

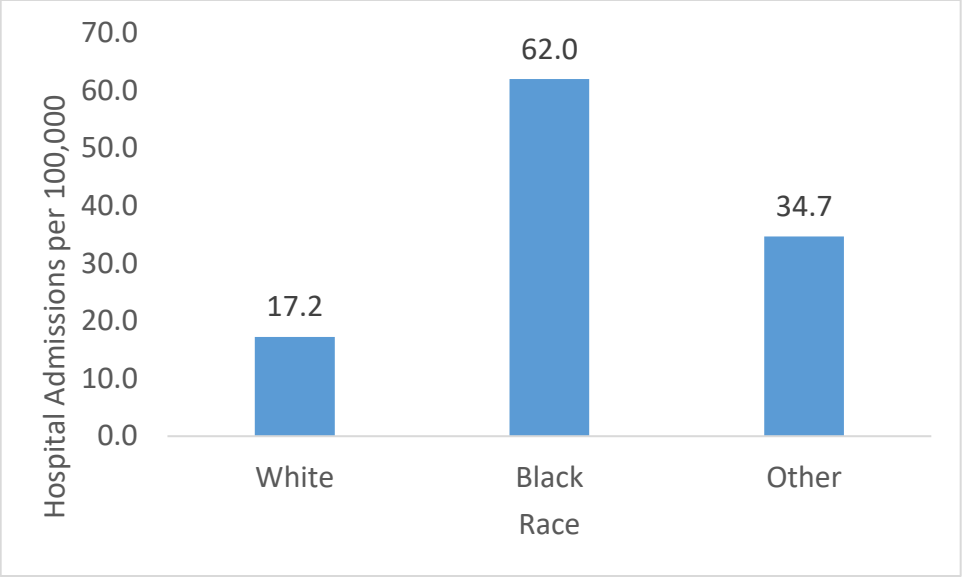

Figure 4. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HBV by race, 2016-2019. Rates are per 100,000 population

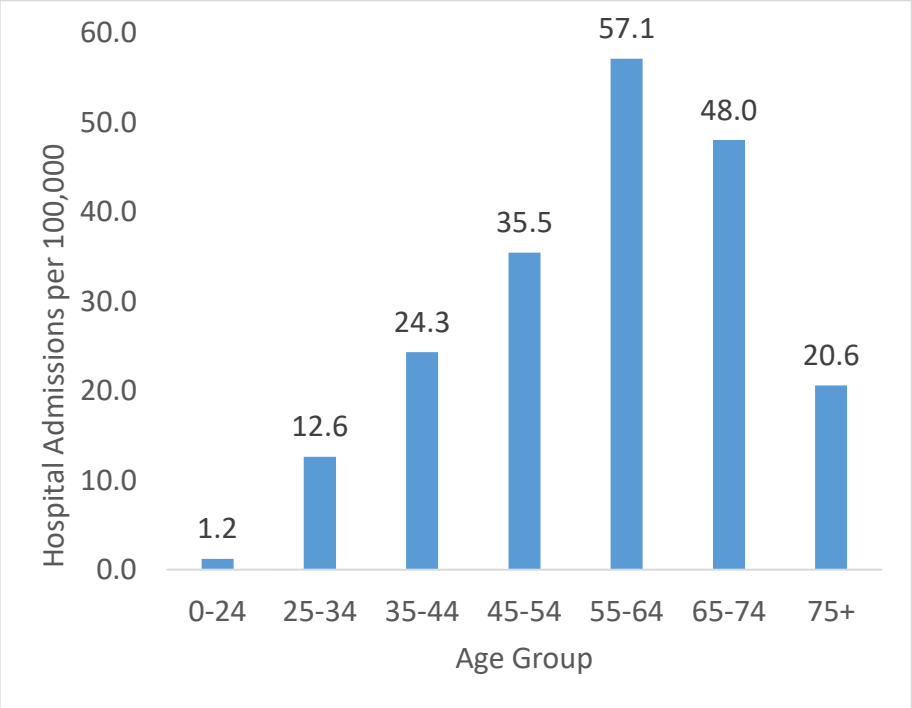

Figure 5. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HBV by age group, 2016-2019. Rates are per 100,000 population

Table 7. Top ten most common primary diagnoses for hospitalizations with an HBV secondary diagnosis

Rank	Primary Diagnosis (N=1,169)	n (%)
1	Sepsis	74 (6.3%)
2	Hypertension (including heart disease, chronic kidney disease, primary and secondary hypertension, and hypertensive crisis)	43 (3.7%)
3	Liver disease (alcoholic and toxic)	39 (3.3%)
4	Bone fracture	36 (3.1%)
5	Kidney failure	32 (2.7%)
6	Drug use and poisoning (including opioids)	31 (2.7%)
7	Respiratory failure	30 (2.6%)
8	Depression	28 (2.4%)
9	Pneumonia	25 (2.1%)
10	Complications from devices, implants, and grafts	24 (2.1%)
	All other primary diagnoses	807 (69.0%)

Table 8. Summary of hospitalization counts with an HCV diagnosis code

	Hospitalization count
Total	14,147
Year	
2016	4,506
2017	3,597
2018	3,289
2019	2,755
Infection type	
Acute	98
Chronic	4,329
Unspecified	9,720
Sex	
Female	6,020

Male	8,127
Race	
Black	4,386
White	9,432
Other	329

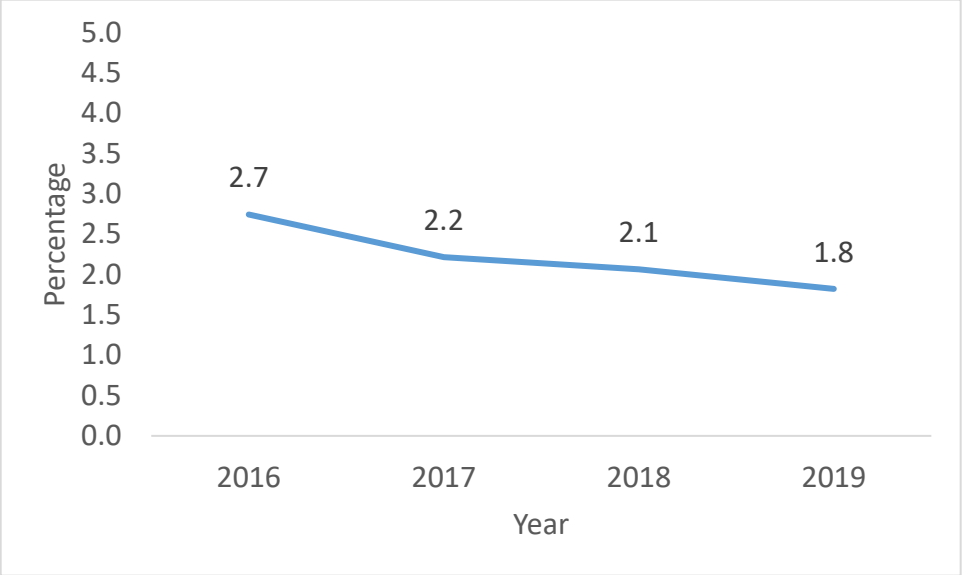

Figure 6. Percentage of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HCV, 2016-2019

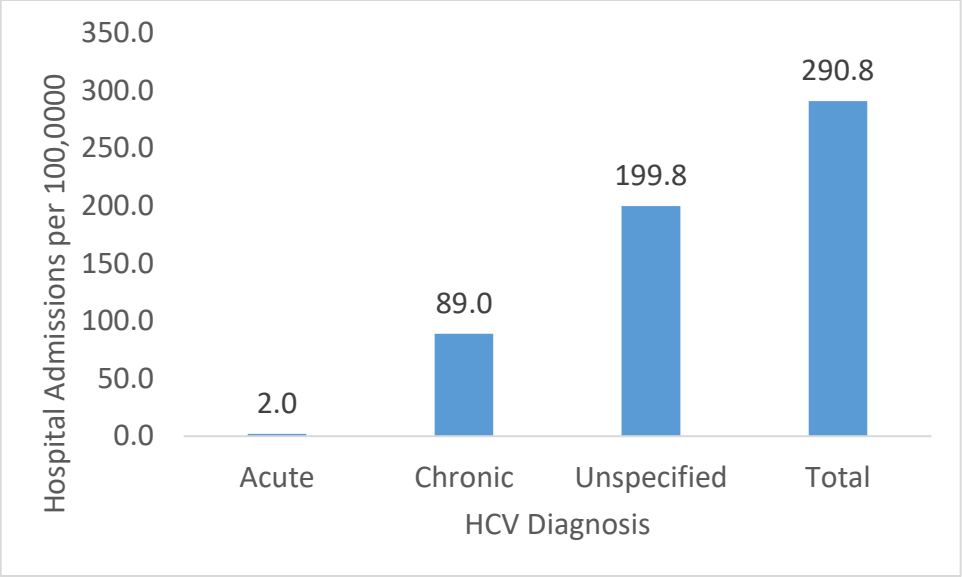

Figure 7. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HCV by infection type, 2016-2019. Rates are per 100,000 population

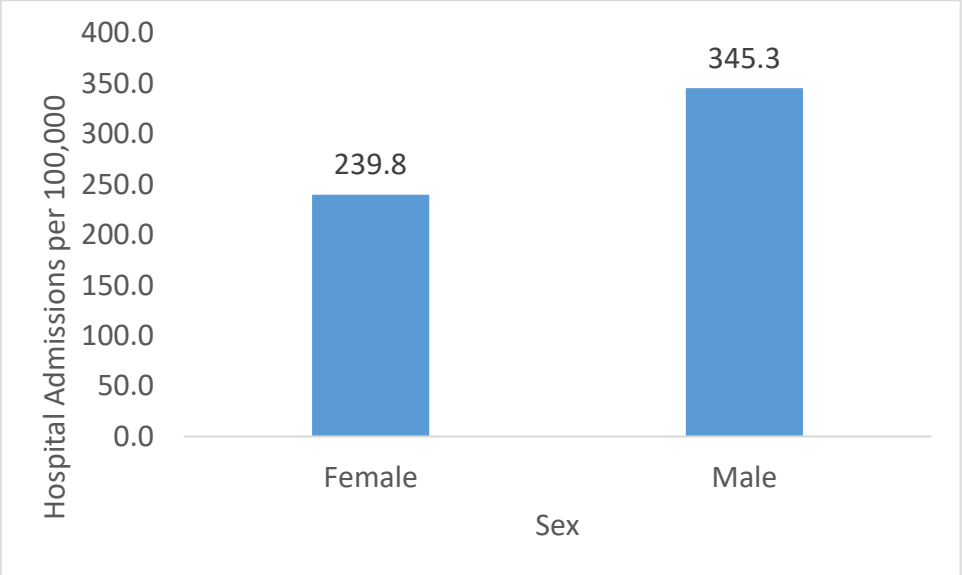

Figure 8. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HCV by sex, 2016-2019. Rates are per 100,000 population

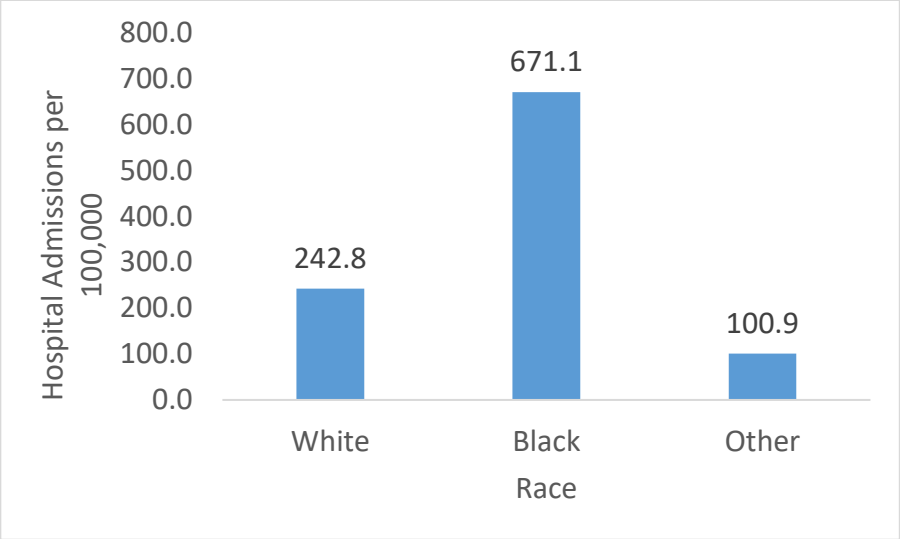

Figure 9. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HCV, by race, 2016-2019. Rates are per 100,000 population

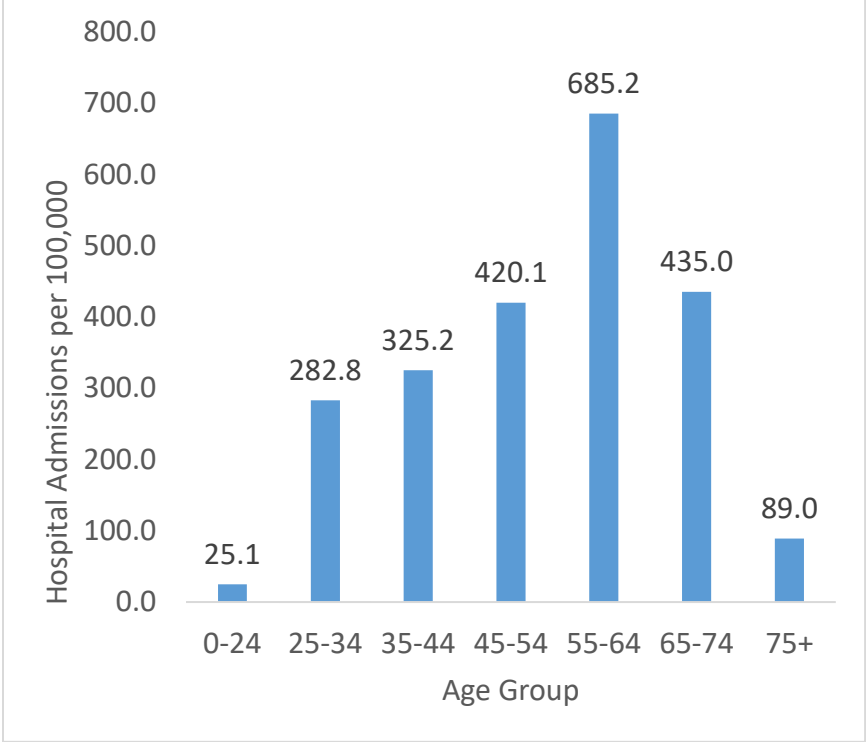

Figure 10. Rate of hospitalizations of Allegheny County residents with an ICD-10 diagnosis code for HCV, by age group, 2016-2019. Rates are per 100,000 population

Table 9. Top ten most common primary diagnoses for hospitalizations with an HCV secondary diagnosis

Rank	Primary Diagnosis (N=14,069)	n (%)
1	Drug use and poisoning (including opioids)	971 (6.9%)
2	Depression	885 (6.3%)
3	Alcohol use	667 (4.7%)
4	Sepsis	627 (4.5%)
5	Cellulitis and acute lymphangitis	396 (2.8%)
6	Hypertension (including heart disease, chronic kidney disease, primary and secondary hypertension, and hypertensive crisis)	377 (2.7%)
7	Liver disease (alcoholic and toxic)	354 (2.5%)
8	Bipolar disorder	339 (2.4%)
9	Obstructive pulmonary disease	316 (2.2%)
10	Kidney failure	297 (2.1%)
	All other primary diagnoses	8,840 (62.8%)

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