Hepatitis C Among Women of Reproductive Age in Allegheny County, Pennsylvania: A Vulnerability-Focused Report

by

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Abstract

Background/Objective: Hepatitis C, a liver condition caused by bloodborne hepatitis C virus (HCV), can cause permanent liver damage. According to CDC, most new cases are associated with injection drug use (IDU). Hepatitis C is concerning among women of reproductive age (WRA), who can transmit HCV to their unborn children. The aims of this report are to describe the epidemiology of hepatitis C among women of reproductive age in Allegheny County and assess the association of the social vulnerability of the community at the ecological level.

Methods: Individual-level data was obtained from PA-NEDSS, Pennsylvania's version of the National Notifiable Disease Surveillance System. Social vulnerability at the census tract level was assessed using the CDC/ATSDR's Social Vulnerability Index (SVI), an index composed of 15 variables across 4 categories that seeks to quantify social vulnerability. After data cleaning was completed, Poisson regression analyses were performed using SAS EG to assess the degree of association between SVI and HCV case count at the census tract level.

Results: The majority of cases were classified as confirmed, White, non-Hispanic, in the 25-34-year-old age group. Risk factor information was unknown for 67% of cases, but for those who had risk factor information available, 26% reported close contact with an HCV case and 74% reported a history of IDU. Only 23% of cases reported that they were currently receiving medical care for their HCV and only 19% reported ever receiving treatment. The Poisson regression analyses showed that the overall SVI was a significant predictor of ecological case count, but when further broken down into its four component subcategories, the component SVI related to socioeconomic status proved to be the only significant predictor.

Discussion: Demographic, risk factor, and treatment characteristics of our population of interest aligned closely with characteristics described in the literature. This report holds public health significance because it has quantified the association of poverty and HCV infection at the census tract level in Allegheny County, providing the foundation for individual-level focused research and better-informed intervention programs in the future.

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Frequently used abbreviations are listed and defined below:

HCV – Hepatitis C Virus

WRA – Women of Reproductive Age

PWID – People Who Inject Drugs

SVI – Social Vulnerability Index

The phrase "Women of Reproductive Age (WRA)" is used throughout this essay instead of the more gender-inclusive "Pregnant People". This is because "WRA" is the term most frequently used in the literature to describe pregnant people their reproductive years. The use of "WRA" instead of "pregnant people" is not at all meant to be gender exclusive or erase the experiences of pregnant people who do not identify as women, but rather to use consistent terminology.

I would like to thank both the Allegheny County Health Department and Dr. Lauren Orkis from the Pennsylvania Department of Health for offering me an opportunity to begin the work that was the foundation for this essay. Thank you to Dr. Hill, Dr. Elias, and Rachael Bieltz for their valuable feedback and guidance during the writing process. I also need to thank my academic adviser, Dr. Nancy Glynn, who has guided me academically, professionally, and personally and has played an instrumental role in my success during my graduate education. Lastly, I would like to thank my great friend, Nate Setar, for helping me think through the statistical analysis.

1.0 Introduction

1.1 Natural History of Hepatitis C

Hepatitis C is a liver condition caused by the hepatitis C virus (HCV). The virus is spread primarily when someone comes into contact with blood from an infected person, although sexual transmission is possible. HCV infections are categorized either as acute or chronic. Acute infections are those that occur during the six months following an exposure to the virus. Acute infections are often asymptomatic and therefore go unnoticed by the infected person, but can cause abdominal pain, nausea, flu-like symptoms, and jaundice. Spontaneous clearance, the innate elimination of an HCV infection without treatment, occurs in 15-45% of all acute cases (Seo et al., 2020). Chronic infections are defined as those for which HCV RNA still persists in the blood for greater than six months following the onset of an acute infection. Acute infections transition to chronic infections in 55-85% of cases, and the probability of spontaneous clearance of a chronic infection is low (Lingala & Ghany, 2015). It is estimated that 2.4 million Americans were living with hepatitis C from 2013-2016 (Hofmeister et al., 2019). Chronic HCV infection can lead to serious liver issues such as progressive fibrosis, eventually resulting in cirrhosis, end-stage liver disease, and hepatocellular carcinoma. Over an infection period of 25 to 30 years, 20-30% of individuals with chronic hepatitis C will develop cirrhosis (Lingala & Ghany, 2015).

1.2 Risk Factors for Hepatitis C

In the United States (U.S.), injection drug use is the most commonly reported risk factor for hepatitis C infection. For those with drug use information available in the most recent U.S. data, 67% of cases disclosed a history of injection drug use. No risk factors were reported by 15% of cases while 39% of cases reported at least one risk factor. Currently, HCV transmission associated with surgery, dialysis, and transfusions are exceedingly rare, so recent procedures are not a frequently observed risk factor. Concerningly, risk factor data was missing for 45% of all cases in 2019 U.S. data (*Viral Hepatitis Surveillance Report - United States, 2019*, 2021). This high level of missing data makes it incredibly difficult to accurately describe and understand risk factors and the magnitude of their influence. This understanding provides a strong foundation for well-informed, targeted interventions. Without comprehensive and accurate risk factor data, interventions are more likely to miss both breadth and depth of understanding, which could certainly impact a program's success.

The correlation between hepatitis C infection and the opioid crisis is significant and it is clear that the increase in intravenous opioid use drove the increase in hepatitis C cases. "Significant and concurrent" increases occurred simultaneously in both reported cases of hepatitis C and reported admissions for injection drug use. For both HCV infections and IDU, the largest increases were observed among the same demographic groups: 18-39-year-olds and non-Hispanic, white individuals (Zibbell et al., 2018). The geographic distribution of hepatitis C cases is similar to that of fatal opioid overdoses, with the highest infection rates occurring in the Appalachian region and rural counties outside of Appalachia, although the majority of cases (78%) are among people who reside in urban areas *(Viral Hepatitis Surveillance Report - United States, 2019, 2021).*

This national geographic trend provides further evidence of the established relationship between IDU and HCV infection.

Before universal testing began in 1992, donated blood and organs were a significant source of HCV infection. This contributed to a high burden of hepatitis C among the baby boomer generation, many of whom were recipients of donated blood and/or organs before 1992. With rigorous testing practices, HCV infection from donated blood and organs is now exceedingly rare (Klevens, Hu, Jiles, & Holmberg, 2012). Although the baby boomer birth cohort still experiences high rates of chronic hepatitis C, the association between injection drug use and HCV positivity was approximately ten times that of the association between being a member of the baby boomer birth cohort and HCV positivity (Dimova, Rude, & Talal, 2020). Another study found that a positive HCV test was most closely associated with a positive drug test, narcotic use, and opioid overdose although the distribution of cases still follow a bimodal distribution (Chan & Mangla, 2022).

1.3 Epidemiology of Hepatitis C

The epidemiology of hepatitis C in the United States has drastically changed in recent years. Currently, the age group most frequently diagnosed with hepatitis C in the United States is 20-39-year-olds (110 cases per 100,000 population); however, the age distribution of hepatitis C cases is bi-modal with 55-70-year-olds still bearing a significant burden. The high burden of HCV amongst 20-39-year-olds is due in large part to the ongoing opioid crisis that has increased transmission of bloodborne diseases among this age group due to the sharing of needles and other drug injecting equipment. Slightly more males than females are diagnosed with hepatitis C, and it is most common among white, non-Hispanic individuals in the U.S.

Generally, for cases of hepatitis C to be identified by surveillance, individuals must have been infected, showed symptoms, and then perceived those symptoms to be concerning enough to warrant seeking care, where they would then be tested, and their positive result reported. However, HCV infections are often asymptomatic or minimally symptomatic and a small proportion of total positive cases are actually captured by surveillance systems ("Hepatitis C Surveillance in the United States for 2019 | CDC," 2021). With that context in mind, the estimated prevalence of hepatitis C in the United States is estimated to be 2.4 million people which corresponds to 0.75% of the total population and 1% of adults (Hofmeister et al., 2019). While there were 4,136 acute cases of hepatitis C reported in 2017, the annual incidence of hepatitis C is estimated to be 57,500 cases after adjusting for under-reporting and under-ascertainment. From 2012 to 2018, there was a 133% increase in acute cases of HCV infection reported nationally (CDC, 2021).

The prevalence of hepatitis C in Pennsylvania is higher than that of the United States, with an estimated 93,900 Pennsylvanians currently infected or about 0.93% of the state population (Rosenberg et al., 2018). The 2019 incidence of acute HCV infection was 210, a large underestimation of the actual total (Rosenberg et al., 2018). In Allegheny County, the prevalence of hepatitis C is estimated to be higher than that of both the country and the state at 0.97% or 9,605 individuals as of 2016. Just 7 cases of acute hepatitis C were reported to the Allegheny County Health Department in 2017, although this is also a gross underestimate of acute HCV cases (Carr, Mertz, Fidner, & Seresin, 2020).

Nationally, deaths with hepatitis C listed as a contributing cause of death are trending down, having decreased from 4.91 per 100,000 in 2015 to 3.33 per 100,000 in 2019, a 32% decrease. Deaths associated with HCV are highest among 55-74-year-olds, with 76% of deaths occurring in this group. While non-Hispanic, white individuals account for 64% of the HCV-associated deaths, the highest death rate is observed among American Indian and Alaska Native individuals (*Viral Hepatitis Surveillance Report - United States, 2019*, 2021). In 2012, the number of deaths associated with hepatitis C surpassed the number of deaths associated with 60 other nationally notifiable infectious conditions (ONNICs) combined, illustrating the tremendous mortality burden caused by hepatitis C (Ly, Hughes, Jiles, & Holmberg, 2016).

In Pennsylvania, 10,848 cases of chronic hepatitis C were reported in 2019, corresponding to a rate of 84.7 per 100,000 that year. This is higher than the national rate of 56.7 new cases per 100,000 in that same year. Like the trend observed at the national level, deaths associated with hepatitis C are decreasing in Pennsylvania *(Viral Hepatitis Surveillance Report - United States, 2019, 2021).*

1.4 Testing and Treatment of Hepatitis C

Both the testing recommendations and available treatment for HCV infection have changed significantly in recent years. Prior to 2020, risk-based screening was the standard practice to determine who should be tested for hepatitis C. The main risk factors that would have warranted testing at the time would have been history of injection drug use and having received donated blood and/or organs before 1992. However, in 2020, the CDC amended their existing testing guidance, recommending that all adults be tested for HCV once in their life and pregnant people be tested during each pregnancy, in addition to risk based testing (Schillie, Wester, Osborne, Wesolowski, & Ryerson, 2020). These changes in testing guidance allowed more people to have access to HCV testing, ideally improving rates of diagnosis amongst already vulnerable populations.

Prior to the development and implementation of direct-acting antiviral (DAA) therapy to treat HCV infections, interferon-based treatment regimens were the standard. These regimens often lasted six months to one year and had low adherence due to sometimes severe adverse side effects and many contraindications. Even for those who did complete the treatment, infection clearance, or sustained virologic response (SVR), was low at approximately 50% (Deutsch & Hadziyannis, 2008). The current standard, DAAs, have much fewer side effects than interferon-based treatment, are completed in 8-12 weeks, and achieve SVR in more than 90% of cases, even for populations with HIV-coinfection and cirrhosis (Falade-Nwulia et al., 2017).

1.5 Economic Burden of Hepatitis C

Hepatitis C clearly has negative impacts on the health of individuals, but it also carries a significant economic burden in the United States. It is estimated that the total annual burden of HCV infections is almost $10 billion. One third of that burden is attributable to direct costs like DAA treatment and medical care for HCV associated conditions, while the remaining two thirds represents indirect costs like lost productivity and stress placed on infected individuals and their loved ones (Stepanova & Younossi, 2017).

Some researchers argue that the incremental cost-effectiveness ratio (ICER) for DAA treatment is below the $50,000 per quality-adjusted life year (QALY) gained threshold. Therefore, direct-acting antiviral therapy to cure chronic hepatitis C is cost effective and should be pursued because the majority of DAA costs would be offset by preventing the cost of future liver disease (Wong, 2006). Conversely, other researchers believe that the cost per QALY gained for DAA treatments is much too high, and cheaper interferon-based treatments should be pursued instead (Stepanova & Younossi, 2017). Disagreement regarding the cost effectiveness of various ways to reduce HCV infections highlights that balancing economic constraints with patient-centered outcomes is not easily achieved.

1.6 Hepatitis C Follow-Up

Due to the risk of HCV-related adverse events, prenatal and postpartum visits are beneficial for both mother and child. Prenatal HCV testing allows for a unique opportunity for WRA to become aware of their HCV status, and if positive, be linked to postpartum treatment since they are having more frequent healthcare interactions than they likely would if they were not pregnant (Kushner, Chappell, & Kim, 2019). Although HCV treatment is not yet approved for use in pregnancy, prenatal diagnosis can lead to postpartum referral to treatment, potentially nullifying the risk of perinatal transmission in future pregnancies if SVR is achieved.

The follow-up monitoring and testing of at-risk children is crucial to identify and treat perinatal cases before progressive disease occurs. Delaying testing for 18 months after birth is likely to produce more accurate results and is advisable so long as the child has no indications of liver disease. Perinatal cases rarely experience signs or symptoms during their first 15 years of life, but it is important to identify and treat their infection early to prevent progressive disease in early or mid-adulthood. Treating young children with HCV has recently become more feasible with the FDA approving treatment for children as young as 3 (“FDA Approves New Treatment for Pediatric Patients with Any Strain of Hepatitis C | FDA,” 2020). Knowing the HCV status of an at-risk child is also important so they can avoid modifiable risk factors that place them at increased risk for progressive liver disease, like consuming alcohol and injecting drugs (Squires & Balistreri, 2017). A low proportion, approximately 16%, of at-risk children actually receive follow-up testing by 18 months (Kuncio, Newbern, Johnson, & Viner, 2016). The ability to intervene and alter the natural history of HCV infection in postpartum mothers and their at-risk children underscores the value of screening during every pregnancy.

1.7 Barriers to Testing and Treatment

Although current treatments have shown tremendous promise and have been proven to be very efficacious in the clinical-trial setting, their real-world effectiveness has been severely dampened by low uptake. A retrospective cohort study evaluating the actual effectiveness of DAAs found that less than 10% of people with chronic HCV infection receive treatment (Kwo et al., 2019). Predictive modelling has established that to achieve global eradication of HCV, 90% of individuals with hepatitis C need to be diagnosed and treated, making that 10% treatment rate even more concerning (Wiktor, 2019). Additionally, for those who did receive treatment, their median time to initiation was 300 days (Kwo et al., 2019). Delaying the initiation of curative treatment by 300 days would certainly contribute to sustained community spread, especially among people who inject drugs (PWID).

In a systematic review to assess any gaps in the chronic hepatitis C treatment cascade, it was discovered that only 50% of HCV positive individuals were diagnosed and aware of their status, 43% had access to outpatient care, 27% had confirmatory RNA testing, 16% were prescribed treatment, and just 9% achieved SVR (Yehia, Schranz, Umscheid, & Lo Re, 2014). Also, a retrospective cohort study of over 1000 hepatitis C positive individuals were less likely to receive treatment if they were lost to follow-up, had HIV-coinfection, or had significant cases of psychiatric illness. Many participants also reported the cost of the medication being a prohibitive factor even if they were insured (Al-Khazraji et al., 2020). These studies confirm that there are gaps and therefore opportunities for intervention at almost any point in the testing and treatment for individuals with hepatitis C.

In-depth interviews with women who were pregnant or recently became mothers that were simultaneously being treated for substance use disorder illuminated other barriers specific to that population. Chief among them, they reported competing demands like experiencing homelessness and not having reliable transportation or being able to miss work to attend numerous clinical visits. Many of them also believed that they were ineligible for treatment, based either on the type of insurance they had, or because they had not stopped using drugs for a long enough period (Adekunle et al., 2021). Additionally, current treatments are not approved to be administered during pregnancy, so pregnant people must wait until they have given birth and finished breastfeeding to begin treatment ("Test for Hepatitis C During Every Pregnancy | CDC," 2021). Understanding and addressing the barriers that exist regarding the testing and treatment of hepatitis C is vital to closing the gap between the proportion of people currently being treated, and the proportion needed to significantly reduce transmission or eradicate hepatitis C.

1.8 Social and Structural Determinants of Health and Hepatitis C

Broadly speaking, the most impactful social determinants of health for infectious diseases in the U.S. are income and education (Braveman, 2011). Income and education are both major upstream factors that influence and are influenced by everything from employment, health insurance coverage, diet, exercise, stress, safety, housing quality, etc. The nature of the influence of these factors is also highly dependent on the systems and structures under which they are operating.

Studies seeking to examine social determinants of health (SDOH) related to HCV infection in the U.S. are difficult to find in the literature. However, several studies have been undertaken to understand the SDOH related to HCV infection among PWID. As previously stated, PWID account for the majority of incident and prevalent cases of HCV in the U.S., so understanding the SDOH among this subgroup will be useful to understand the SDOH of HCV-positive individuals broadly. SDOH data was gathered from baseline questionnaires as a part of a clinical trial assessing an intervention program for PWID with hepatitis C in New York City. These questionnaires revealed that the majority of trial participants were enrolled in state Medicaid, reported not having enough money to cover their basic needs, and received food stamps. Almost half of participants received less than a high school diploma, over half had previously been incarcerated, almost half did not have access to reliable transportation, and nearly a quarter of participants reported being homeless (Corro et al., 2020). In summary, PWID with HCV had a low socioeconomic status, as evidenced by their qualification for Medicaid, inability to provide for themselves, and reduced educational achievement. Also, this subpopulation experienced transportation challenges and unstable housing.

1.9 Special Populations

1.9.1 Women of Reproductive Age

The concerning epidemiologic trends of hepatitis C among women of reproductive age (WRA) and pregnant women are even more pronounced than those of the general population. Infections among WRA are particularly concerning because the main cause of childhood HCV infection is perinatal transmission from a hepatitis C positive mother before, during or after birth, which occurs in approximately 6% of cases (Le Campion, Larouche, Fauteux-Daniel, & Soudeyns, 2012).

Women of reproductive age (15-44) accounted for 40% of the women with confirmed HCV infection from 2006-2014. Among this age cohort, acute HCV cases increased by 3.4 times, and past or present cases doubled over that same time period. Non-Hispanic, white individuals accounted for 57% of all acute infections among WRA. For those WRA with risk factor information available, 63% reported a history of injection drug use (IDU). Between 2011 and 2014, it is estimated that 29,000 women gave birth each year, resulting in 1,700 infants born with HCV infection annually during that time (Ly et al., 2017).

Infections among pregnant women have increased by at least 261% from 2001-2017, involving it in 0.24% of all live births during that period. Maternal HCV infection affected 1.8 out of every 1000 lives births in 2001, but that figure rose to 4.7 per 1000 live births by 2017. The estimated prevalence of maternal HCV increased by 147% from 2013 to 2014 and has annually increased approximately 110% each year since then (Rahal et al., 2020). White, non-Hispanic race and ethnicity, being covered by Medicaid, and living in Appalachia or another rural area were found to be significant social determinants influencing maternal HCV infection

(Rossi et al., 2020). In Allegheny County, the number of cases of HCV among WRA has increased from 2005-2018. Although some of this increase may be due to a change in the case definition that occurred in 2016, this trend is unlikely to be artifactual since some of this increase is likely also related to the ongoing opioid crisis (Carr et al., 2020).

1.9.2 Perinatal Hepatitis C Transmission

Perinatal transmission is the main cause of childhood hepatitis C infection in the U.S. (Le Campion et al., 2012). Perinatal transmission occurs in approximately 6% of births involving an infected mother, but that figure may increase to 11% if the mother is also HIV-coinfected. A mother's history of injection drug use is also an independent predictor of perinatal transmission (Benova, Mohamoud, Calvert, & Abu-Raddad, 2014). Maternal HCV infection at the time of birth is associated with several adverse birth outcomes such as preterm birth, ICU admission for mother and neonate, low birth weight, neonates requiring assisted ventilation, and neonatal death (Rossi et al., 2020). Due in large part to the increase in HCV infections among WRA, it is estimated that perinatal cases of hepatitis C have increased by 245% from 2001 to 2017 (Rahal et al., 2020). This increase has also been observed at the state level in Pennsylvania with 20 perinatal cases being reported in 2019 alone, the second most in the country behind only Ohio (*Viral Hepatitis Surveillance Report - United States, 2019*, 2021). This rise in perinatal HCV infection, if unaddressed, could lead to an increase of progressive liver disease among young adults.

1.10 Gaps in Knowledge and Public Health Significance

Current gaps in the knowledge surrounding hepatitis C are largely driven by sometimes poor data availability. Specifically, risk factor data is unavailable for almost half of HCV cases in 2019, which greatly reduces our ability to understand the breadth and depth of the situation. Also, race and ethnicity data are missing for a large proportion of HCV cases, limiting our ability to identify, understand, and mitigate any disparities or inequities that may exist. The poor data quality, specifically among WRA, is especially influential since understanding the social and structural influences on HCV in this subgroup can have implications not only for case rates among WRA but also perinatal case rates. Additionally, a general knowledge gap regarding the social determinants of health contributing to HCV infection generally and among WRA exists.

Having a detailed understanding of the epidemiology of hepatitis C among women of reproductive age in Allegheny County, PA holds public health significance. Significant treatment gaps and a significant rise in HCV cases among WRA warrants a granular look at the local epidemiology because of the increased risk to both infected WRA in the county and their current and future children.

2.0 Objectives

The primary objective of this report is to describe the epidemiology of hepatitis C among women of reproductive age in Allegheny County, Pennsylvania. The secondary objective is to indirectly assess the social vulnerability of these cases by examining the social vulnerability associated with the census tracts they resided in from January 2020 to July 2021.

3.0 Methods

3.1 Data Sources

3.1.1 PA-NEDSS

Allegheny County Health Department (ACHD) conducts hepatitis C surveillance through Pennsylvania's version of the National Notifiable Disease Surveillance System (PA-NEDSS). Hepatitis C cases are identified according to the Centers for Disease Control and Prevention's case definitions for acute and chronic hepatitis C. Both acute and chronic cases are further classified as probable and confirmed cases. Probable acute cases must meet the clinical criteria and have presumptive laboratory evidence, but not have a positive anti-HCV or HCV-RNA test in the previous year. Probable chronic cases do not meet the clinical criteria but have presumptive laboratory evidence and do not have a positive HCV test in the previous year. Confirmed acute cases must meet the clinical criteria and have confirmatory laboratory evidence or have a negative HCV test followed within one year by a positive HCV test. Confirmed chronic cases do not meet the clinical criteria but have confirmatory laboratory evidence and does not have a positive HCV test in the previous year ("Hepatitis C, Acute 2020 Case Definition | CDC," 2021); ("Hepatitis C, Chronic 2020 Case Definition | CDC," 2021).

To complete this report, a dataset was created using data in PA-NEDSS for all HCV cases who met the inclusion criteria. The inclusion criteria to be included in this dataset was being marked as a "Hepatitis C infection" in PA-NEDSS, Allegheny County being listed as the reporting jurisdiction, the PA-NEDSS investigation initiation date falling between January 1, 2020, and July

13, 2021, being listed as a "Confirmed" or "Probable" case of hepatitis C, having sex listed as "Female", and age falling between 15 and 44 years. The time period of January 1, 2020-July 13, 2021 was selected because during this time, additional resources were available to conduct case investigation interviews for WRA with HCV in Allegheny County. This means that the completeness of the PA-NEDSS data for those cases reported during this time period will likely be greater and not reflect the completeness of data for hepatitis C cases reported outside of this time period. Only hepatitis C cases with their sex listed as "Female" were included because the purpose of this report was the specifically examine HCV among WRA, not the general population.

3.1.2 CDC/ATSDR Social Vulnerability Index (SVI)

The Centers for Disease Control and Prevention in collaboration with the Agency for Toxic Substances and Disease Registry created a Social Vulnerability Index (SVI) that uses 15 separate variables at the U.S. county and census tract level to identify communities that may be particularly vulnerable to external community events like natural disasters or infectious disease outbreaks ("CDC/ATSDR's Social Vulnerability Index (SVI)," 2022). The overall SVI is composed of four component categories of variables: Socioeconomic Status, Household Composition and Disability, Minority Status and Language, and Housing Type and Transportation. Figure 3 shows the breakdown of the four SVI component categories and how the 15 variables are distributed across them. An overall ranking and the four component SVI rankings range from 0-1 and represent the proportion of counties or census tracts that are equally or less vulnerable. For example, an SVI ranking equal to 0.40 means that 40% of counties or census tracts are less vulnerable, and 60% of counties or census tracts are more vulnerable.

3.2 Data Cleaning

Once the PA-NEDSS dataset was created using hepatitis C surveillance, extensive data cleaning and verification was required. This included the removal of duplicate cases from the PA-NEDSS dataset, manual address verification, and merging of the SVI dataset with the PA-NEDSS dataset. Minimal data cleaning, comprised of removing census tracts that contained missing values for the SVI indices, was required for the SVI data set. Figure 2 describes in detail the number and reason for the removal of cases and/or census tracts at each level of analysis. The initial data extraction from PA-NEDSS yielded 343 hepatitis C cases that met the inclusion criteria, however 15 of them were removed from the dataset due to them being a duplicate case, not living in Allegheny County, or being classified as "Not a Case" in PA-NEDSS. The data for the remaining 328 cases were analyzed to understand the demographics characteristics, risk factors, and treatment uptake among cases. Census tract data was unknown, missing, or incomplete for 137 (42%) cases, so manual address verification was conducted through the Census Bureau. Of those 328 cases who met the inclusion criteria, manual address verification could not be completed for 42 cases for a variety of reasons. Once manual address verification was completed, the PA-NEDSS dataset was merged with the SVI dataset by census tract. Of the remaining 286 cases who resided in 189 unique census tracts, 18 census tracts containing 21 cases did not have matching census tracts in the SVI dataset. This may be due to small changes made to census tracts between 2010 and 2020 since the SVI dataset uses 2010 census data and the Census Bureau's manual geocoder uses 2020 census data. An additional 12 census tracts in the SVI dataset were missing values for the overall SVI ranking and were removed. At the conclusion of all data cleaning, a dataset containing 171 census tracts with 265 cases and 219 census tracts with 0 cases was used for regression analysis.

3.3 Statistical Analysis

SAS Enterprise Guide (EG) was used to create all datasets and perform all statistical analyses. Charts were created using Microsoft Excel. Summary statistics were calculated for demographics variables, self-reported risk factors, and treatment initiation. Poisson regression analysis was performed to determine the association between SVI and hepatitis C case rate at the census tract level. An ecological, census tract level analysis was chosen because matching controls on an individual level was not feasible for this report, but SVI data did exist for census tracts that contained no cases and could act as ecological controls. Poisson regression was chosen because the response variable in these models is a census-tract-level case rate that do not follow the normal distribution that would be required to use other regression analyses, and the mean case rate is approximately equal to the variance of the case rates.

4.0 Results

4.1 Hepatitis C Cases Over Time

Hepatitis C cases among women of reproductive age were reported to ACHD during every month between January 2020 and July 2021. A total of 328 cases were reported across this timeframe with the minimum of 2 cases reported in July 2020 and the maximum of 38 cases reported in August 2020 (Figure 1).

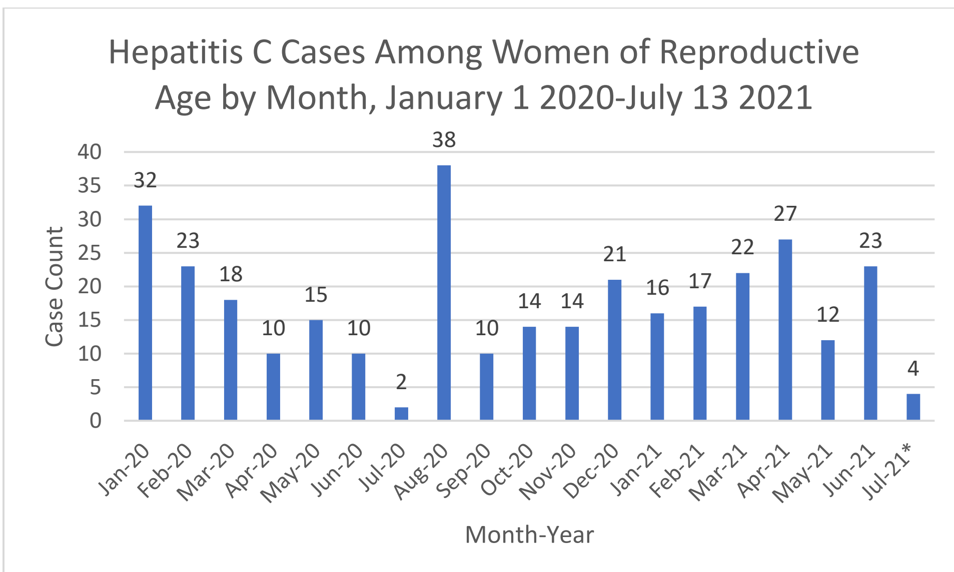

Figure 1. Hepatitis C Cases Among WRA by Month, January 1, 2020-July 13, 2021 (N=328)

*Only cases reported from July 1-13, 2021, are plotted

4.2 Descriptive Characteristics of Cases

Over three quarters (78%) of the hepatitis C cases among WRA reported to ACHD during the timeframe of interest were confirmed cases. The majority of cases self-reported their race and ethnicities as White and Non-Hispanic, respectively, although much of the race and ethnicity data is unknown. The average age of HCV cases was 32.7 years (range: 15-44) and approximately half of them were a part of the 25-34-year-old age group (Table 1)

Table 1 Characteristics of Hepatitis C Cases Among WRA in Allegheny County between January 1, 2020, and July 13, 2021 (N=328)

Characteristics*	n (%)
Case Status	
Confirmed	257 (78)
Probable	71 (22)
Race	
White	239 (73)
Black	33 (10)
Asian	2 (0.6)
American Indian	1 (0.3)
Pacific Islander	0 (0)
Multiple Race Categories Selected	3 (0.9)
Unknown	50 (15)
Ethnicity	
Non-Hispanic	147 (45)
Hispanic	3 (0.9)
Unknown	178 (54)
Age (years)	
15-24	32 (10)
25-34	161 (49)
35-44	135 (41)

*Percentages may not add to 100% due to rounding

The PA-NEDSS case investigation interview collects information regarding many risk factors relevant to the spread of HCV but being a close contact of a hepatitis C case and having a history of injection drug use were the only risk factors for this group of WRA that were self-reported with any regularity. Contact with a known case of HCV was unknown for 74% and history of injection drug use was unknown for 61% of the 328 total cases in the dataset. However, for those cases for whom risk factor information was known, 26% reported close contact with a hepatitis C case and 74% reported a history of injection drug use (Table 2).

Table 2 Summary Statistics for Self-Reported Risk Factors of Hepatitis C Cases Among Wog WRA in Allehgheny County between January 1, 2020, and July 13, 2021 with Known Risk Factor Information

Risk Factor*	n (%)
Contact of HCV case	
Yes	22 (26)
No	64 (74)
History of injection drug use	
Yes	95 (74)
No	33 (26)

*Percentages may not add to 100% due to rounding

Medical care information was unknown for 55% and treatment information was unknown for 56% of the 328 total cases in the dataset. However, for those cases for whom risk factor information was known, 52% of cases were currently receiving medical care for their hepatitis C at the time of interview and 42% reported they had ever received treatment (Table 3). Among the 61 cases that self-reported having received medication, 45 of them had plausible treatment initiation dates listed in PA-NEDSS. An additional 7 cases had treatment initiation dates that occurred before their positive test result was reported to ACHD, so they were excluded from the time to treatment analysis. Among those 45 cases with plausible treatment initiation dates, the average time from when their positive HCV test was reported to when they reported initiating treatment was 81 days (range: 0-390 days).

Table 3 Summary Statistics for Medical Care and Treatment Uptake of Hepatitis C Cases Among WRA in Allegheny County between January 1, 2020, and July 13, 2021 with Known Risk Factor Information

HCV Care and Treatment*	n (%)
Currently receiving care?	
Yes	77 (52)
No	71 (48)
Ever received medication/treatment?	
Yes	61 (42)
No	84 (58)

*Percentages may not add to 100% due to rounding

At the time of interview, 5% of HCV cases reported being currently pregnant, though pregnancy status is unknown for over fifty percent (Table 4).

Table 4 Summary Statistics for Pregnancy Status of Hepatitis C Cases Among WRA in Allegheny County between January 1, 2020, and July 13, 2021 (N=328)

Pregnancy Status*	n (%)
Pregnant at time of interview?	
Yes	17 (5)
No	130 (40)
Unknown	181 (55)

*Percentages may not add to 100% due to rounding

4.3 Ecological Relationship Between SVI and Census Tract

A one sample t-test showed that the average overall SVI of the 265 HCV cases with manually verified addresses that had corresponding census tracts in the SVI data set was 0.4745. This average overall SVI was statistically significantly different than the average overall SVI for Allegheny County of 0.2121. The Poisson regression analysis using the four component SVIs as parameters showed that SVI-1 (corresponding to socioeconomic variables) and SVI-4 (corresponding to housing and transportation variables) were statistically significant predictors of hepatitis C case rate (Table 5). Additionally, the Poisson regression analysis using SVI-1 and SVI-4 as the parameters showed that SVI-1 and SVI-4 were statistically significant predictors of increased hepatitis C case rate, and the magnitude of their effect is approximately equal to their effect in the model that included all four component SVIs (Table 6). The variance inflation factors (VIF) are reported to assess the presence of collinearity among the four component SVIs in the first model and SVI-1 and SVI-4 in the second model (Tables 7,8).

Table 5 Poisson Regression Results for HCV Case Rate Using the Four Componenet SVIs as Parameters (N=265)

Parameter	Estimate (Standard Error)	Confidence Intervals
Constant	0.4475 (0.0872)	(0.3066, 0.6483)
Socioeconomic Status	1.3666 (0.1562)*	(1.0604, 1.6728)
Household Composition & Disability	-0.0512 (0.1294)	(-0.3048, 0.2024)
Minority Status and Language	-0.0970 (0.1593)	(-0.4093, 0.2152)
Housing Type & Transportation	-0.4316 (0.1315)*	(-0.6892, 0.1739)

*Indicates significance at the 95% confidence level

Table 6 Poisson Regression Results for HCV Case Rate Using Component SVI-1 and SVI-4 as Parameters (N=265)

Parameter	Estimate (Standard Error)	Confidence Intervals
Constant	0.4439 (0.0741)	(0.2987, 0.5891)
Socioeconomic Status	1.3060 (0.1172)*	(1.0764, 1.5357)
Housing Type & Transportation	-0.4497 (0.1246)*	(-0.6939, -0.2055)

*Indicates significance at the 95% confidence level

Table 7 Variance Inflation Factors (VIF) as a Measure of Collinearity for the Poisson Regression Model Using the Four Component SVIs as Parameters (N=265)

Parameter	Variance Inflation Factor (VIF)
Constant	0
Socioeconomic Status	1.9199
Household Composition & Disability	1.6186
Minority Status and Language	1.2901
Housing Type & Transportation	1.2999

Table 8 Variance Inflation Factors (VIF) as a Measure of Collinearity for the Poisson Regression Model Using SVI-1 and SVI-4 as Parameters (N=265)

Parameter	Variance Inflation Factor (VIF)
Constant	0
Socioeconomic Status	1.9199
Housing Type & Transportation	1.2999

5.0 Discussion

This report details the sociodemographic, risk factor, and medical care/treatment characteristics as well as census tract level social vulnerability predictors for hepatitis C cases among women of reproductive age in Allegheny County. Despite its preliminary nature, the results described in this report are foundational to understanding the epidemiology and social and structural determinants of hepatitis C among this population. Many of the demographic characteristics seen among this population were expected based on what was found in the literature review, such as the prominent age group being 25-34-year-olds and the prominent race/ethnicity group being White, non-Hispanic individuals *(Viral Hepatitis Surveillance Report - United States, 2019, 2021)*. Additionally, several studies have found that individuals with HCV rarely received treatment and those that did had to wait a very long time (Kwo et al., 2019). The same was observed in this analysis, though much of the data is unknown. Also, history of injection drug use was referenced extensively in the literature as the main risk factor for hepatitis C infection among people younger than 40 (Zibbell et al., 2018). This is also true of those in our population of interest. Lastly, the high degree of unknown data seen throughout the literature was also observed in this analysis. The increase in reported cases in August 2020, however, was not expected. One contributing factor to this increase could be the impact that the COVID-19 pandemic had on HCV testing services in Allegheny County. Availability of these services may have been paused during the first few months of the pandemic and resumed around August 2020, potentially leading to increased testing and positive cases being reported at that time.

The results from the t-test and Poisson regression models are each significant in their own way to help us understand how social vulnerability is associated with hepatitis C case counts.

Based on the t-test, we concluded that the average overall SVI of census tracts where cases resided is statistically significantly different than the Allegheny County average overall SVI. Based on the first model, we concluded that only SVI-1 and SVI-4 were significant predictors of HCV case rate at the census tract level while SVI-2 and SVI-3 were not. Based on the second model, we concluded that SVI-1 and SVI-4 remained significant predictors of HCV case rate of approximately the same magnitude when the nonsignificant predictors from the previous model were removed. These results demonstrate that poverty status, unemployment, lower income, not having a high school diploma, living in multi-unit structures, mobile homes, or group/crowded quarters, and not having a vehicle are the strongest predictor variables out of the 15 total variables that are included in the overall SVI. This finding is consistent with the literature which underscores the influence of socioeconomic variables, particularly income and education, on infectious disease. Further, housing and transportation is highly dependent on income, so it is reasonable that those variables are also significant predictors. Examining socioeconomic variables and other SDOH when performing foundational analyses like this one is vital to understand the systemic and societal influences on disease which underpins any successful advocacy work that public health officials may be a part of.

These nine variables related to socioeconomic status and housing type and transportation are all modifiable at the individual, interpersonal, and community level. However, substantive change to any one of them would require individual behavioral change and, more impactfully, systemic changes aiming to increase equity of opportunity to better one's socioeconomic situation and establishing a social safety net for those who are not able to do so.

5.1 Strengths and Limitations

Firstly, the individual level data we did have had high proportions of unknown and missing values. This could have led us to make incorrect conclusions about the demographics and self-reported behaviors of the population of interest, especially if those for who we have data are fundamentally different than those for who we do not. Also, the nature of the four component SVIs used as parameters in the larger Poisson regression model may cause them to have some degree of collinearity. There is disagreement in the literature on what value of VIF should cause concern for collinearity, but most suggest using 5 or 10 as a cutoff point *(Hair Jr, Anderson, Tatham, & Black, 1992).* The VIFs of the four component SVIs used in the first model and the VIFs of SVI-1 and SVI-4 are below those proposed cutoff points. However, the variables that comprise each of the component SVIs often affect and are affected by each other, so the indexes may still be collinear without the statistical support. Additionally, since this is an ecological, census tract level report, the data may not accurately reflect the individual data of the people in that area. This has been mitigated slightly by using census tract level data instead of zip code or county level data, but the possibility for ecological fallacy still exists.

Despite these limitations, this extensive surveillance report has gone into great detail describing the social and structural determinants of health related to hepatitis C among women of reproductive age in Allegheny County. Also, assessing these trends and associations at the ecological level allows for a foundational understanding of the relationship between social vulnerability and hepatitis C in our population of interest, justifying further investigation and investment to understand this relationship in a more nuanced way. Additionally, the SVI data from CDC and ATSDR is regarded as being highly accurate and complete, which strengthened this analysis.

5.2 Future Directions

This ecological report has laid the foundation for higher level studies to be conducted to understand the individual level relationship between social vulnerability and hepatitis C case status among women of reproductive age in Allegheny County. Moving forward, an individual level study, like a case-control study, could be undertaken for this purpose. Additionally, the variables related to socioeconomic status and housing type and transportation proved to be the most significant predictors of case rate, so they should be given special attention in any further studies. Due to its ecological nature, this report has produced a list of census tracts in Allegheny County in which HCV positive WRA are living (Table 9). Since these communities have been identified, they may benefit from increased preventative and testing outreach in the future. Linkage to care and treatment was found to be low among this population, so future work should be committed to understanding why this failure to link is occurring in these women and what can be done to increase linkage.

Data collection and entry issues in PA-NEDSS should also be examined. Many cases had verified addresses listed in PA-NEDSS that were actually rehabilitation facilities, correctional facilities, or other institutional facilities. This may be because of inaccurate address collection at the time of testing, but this should be explored further to understand and fix this problem. Also, since so many cases were found to be living in institutional settings, further research could be conducted with that geographic subgroup as the focus. Additionally, race data is difficult to summarize and understand among this group because many cases have a race category and "Unknown" simultaneously selected in PA-NEDSS. This may be because PA-NEDSS often checks "Unknown" as the default race status, and if it is not unchecked at the time of interview, both will be selected. This issue should also be examined further to understand and mitigate the issue.

5.3 Public Health Significance

Poverty is a well-known contributor and risk factor for many diseases, both chronic and infectious, especially since the widespread availability of improved sanitation, antibiotics, and vaccines. The effect of poverty on hepatitis C case rates at the census tract level is also evident and has now been quantified. Also, the opioid crisis is still ongoing, and getting hepatitis C transmission under control among people who inject drugs is important to reduce overall incidence and prevalence, and among WRA who inject drugs to reduce the risk of perinatal transmission. Identifying trends, risk factors, and ecological predictors of hepatitis C will help to provide a foundation for future research and interventions to pursue the goals of reducing the incidence and prevalence among women of reproductive age, neonates, people who inject drugs, and the general population.

Appendix A Figures

Figure 2. Data Cleaning and Creation of Usable Datasets

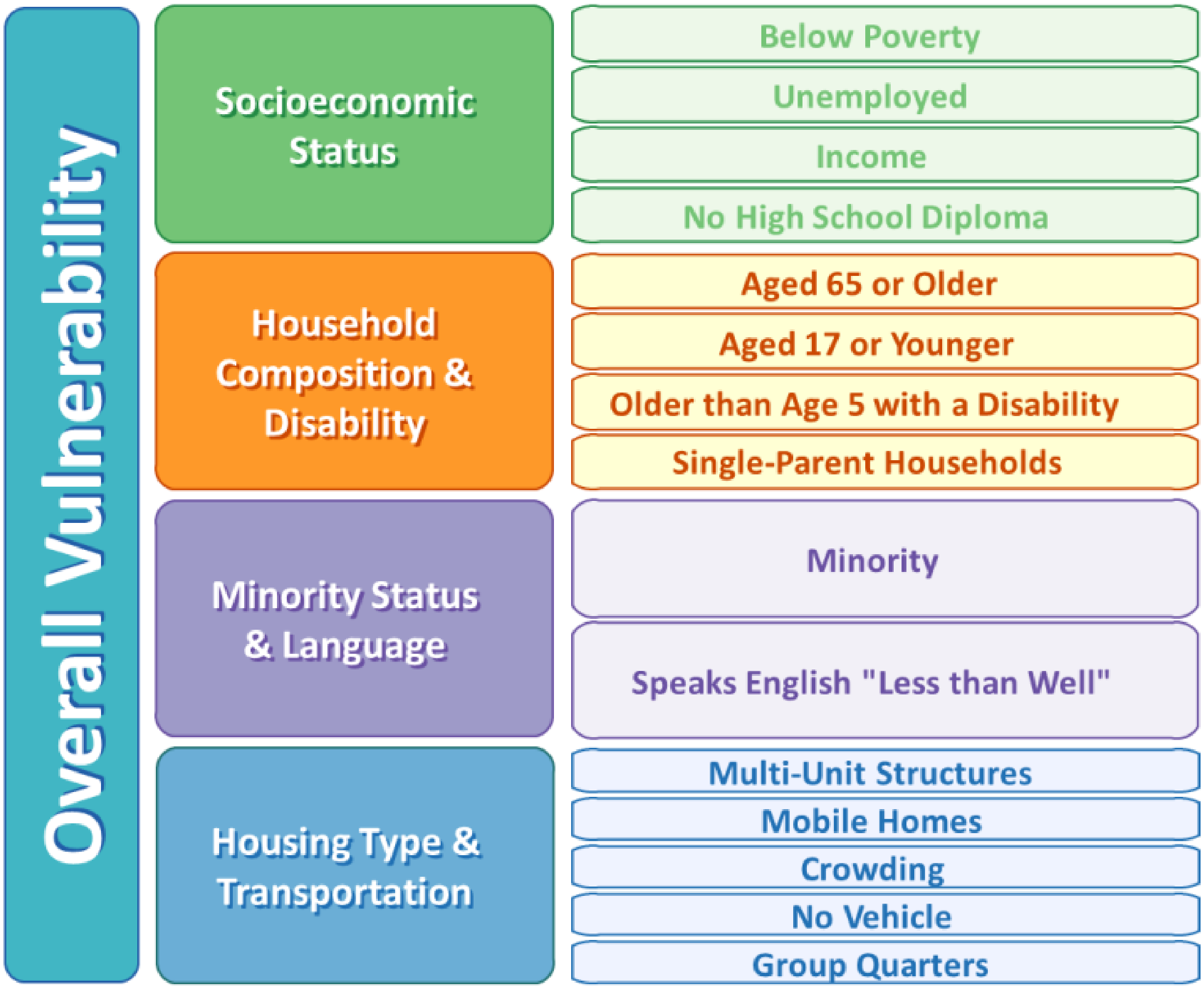

Figure 3. SVI Category Breakdown and Variable Distribution Adapted from CDC/ATSDR SVI 2018 Documentation

(“CDC SVI 2018 Documentation,” 2020)

Appendix B Tables

Table 9. HCV Case Counts by Census Tracts That Have 2 or More Cases

Census Tract	HCV Case Count
42003191600	4
42003401200	4
42003482500	4
42003484300	4
42003499400	4
42003170600	3
42003191500	3
42003191800	3
42003270300	3
42003271500	3
42003290200	3
42003403500	3
42003425000	3
42003470600	3
42003475101	3
42003475301	3
42003480300	3
42003481000	3
42003488200	3
42003519000	3
42003521301	3
42003522000	3
42003523200	3
42003523501	3
42003526202	3
42003563900	3
42003101100	2
42003111300	2
42003191700	2
42003202200	2
42003260700	2
42003290100	2
42003290400	2
42003320700	2
42003402000	2
42003406000	2
42003407001	2
42003407002	2
42003413500	2
42003423000	2

Census Tract	HCV Case Count
42003424000	2
42003428200	2
42003429202	2
42003429300	2
42003435000	2
42003450800	2
42003453003	2
42003453004	2
42003462600	2
42003465800	2
42003468900	2
42003471000	2
42003472100	2
42003476200	2
42003488400	2
42003489001	2
42003492900	2
42003515300	2
42003523800	2
42003551200	2
42003562500	2
42003564000	2
42003564400	2

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