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Changes Over Time in Awareness of Hepatitis C Infection in the United States 2007-2018

Jennifer Mezzo

ABSTRACT

Changes over time in awareness of hepatitis C infection in the United States 2007-2018

By

Jennifer Lynn Mezzo

December 4, 2020

INTRODUCTION: An estimated 115 million people worldwide and 2.4-3.5 million people in the United States are infected with Hepatitis C infection. The majority of these individuals are unaware of their infection due to the asymptomatic nature of the disease and are therefore at greater risk for advanced-staged complications such as cirrhosis or liver cancer.

AIM: This study aimed to measure changes over time in awareness of hepatitis C infection among a housed, non-institutionalized representative sample within the United States.

METHODS: National Health and Examination Survey (NHANES) data spanning years 2007 – 2018 were compiled into one dataset. After eligibility restrictions were applied the final dataset contained N=387 respondents. Bivariate and multivariate logistic regression models were conducted to explore the associations between our independent variables and awareness of HCV infection as well as to assess possible confounders and mediators of the relationship between time (primary exposure variable) and awareness of HCV infection (outcome variable). Bivariate linear regression was used to estimate linear trends to estimate linear trends in awareness of HCV infection over time. We also assessed the percent of those aware of their HCV infection to clearly define the outcome variable.

RESULTS: Awareness of one's HCV infection increased from 24.53% in the 2007-2008 survey cycle to 63.48% in the 2017-2018 survey cycle (β for trend 0.09, $p<0.0001$). The odds of reporting a positive HCV diagnosis in the second survey period (2013-2018) was 3.71 times the odds in the first time period ($p <0.0001$).

CONCLUSION: Diagnosed hepatitis C is increasing, however, remains suboptimal in the US. Recent efforts may have contributed to these increases, bringing us closer to achieving DHHS and WHO goals of viral hepatitis elimination.

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by

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Author's Statement Page

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Introduction:

1.1. Background

According to the World Health Organization (WHO), an estimated 115 million people worldwide are infected with Hepatitis C (HCV) (WHO, 2016). In the US, an estimated 4.1 million Americans are living with a past or current HCV infection, approximately 2.4-3.5 million of whom have a current HCV infection (DHHS, 2017; Hofmeister, 2019). The majority of individuals infected are baby boomers, or those born between 1945 and 1965; however, there has been an increase in the number of individuals younger than 30 infected due to injection drug use, contributing to a bimodal age distribution of HCV burden (Bush, 2019; Hofmeister, 2019). Chronic HCV infection is a major cause of liver cirrhosis and liver cancer and claims the livers of approximately 15,000 Americans each year (Al-Tayyib, 2009; Trooskin, 2015).

The majority of individuals infected with HCV are unaware of their infection due to the silent nature of the disease in its early stages, and are therefore at greater risk for developing cirrhosis, liver cancer, and premature mortality (Valdisermi, 2014). Several studies have found that awareness of one's HCV infection among Americans is suboptimal, between 50-55% (Kim, 2018; Volk, 2009; Zhou, 2020). The asymptomatic nature of the disease makes screening essential to identify and get into treatment those individuals who are infected (Zhou, 2020). In 2014, several new drugs called direct-acting antivirals (DAAs) were approved by the FDA to treat HCV (Trooskin, 2015). DAAs have a cure rate over 95% with fewer severe side-effects than previous interferon treatments (Barua, 2015; Douglass, 2018; Trooskin, 2015). The emergence and high cure rate of these DAAs increases the importance of screening for and diagnosing HCV.

The largest barrier to increasing HCV and screening treatment is lack of diagnosis (Clark & Muir, 2012). In addition to the asymptomatic nature of the disease, a lack of awareness about the disease among providers, policymakers and the general public; the price of HCV treatment; and lack of affordable treatment have been cited as barriers to accessing HCV screening and care (Bruggmann, 2015; Clark, 2012; Ditah, 2015; Stopka, 2017; Valdisermi, 2014).

On March 23, 2010, the Patient Protection and Affordable Care Act (ACA) was signed into law and intended to increase overall insurance coverage in the US (French, 2016). The ACA utilized multiple strategies to increase access, including allowing young adults to remain on parents insurance until age 26, requiring large employers to offer healthcare, requiring individuals without employer sponsored insurance to purchase insurance or pay a penalty, and the ACA also expanded Medicaid eligibility (French, 2016; McIntyre, 2019). McIntyre et al. reported that since the law's implementation in 2010, the number of uninsured people in the US has fallen by about 20 million (2019). Additionally, significant improvements have been seen in access to primary care services and medications since the ACA has been implemented (French, 2016).

Another factor that may affect diagnosis of HCV infections is injection drug use (IDU) and the current opioid epidemic. The estimated global prevalence of HCV among PWID is 67%, and the countries with the greatest number of HCV injected PWID include China with 1.6 million, the US with 1.4 million, and Russia with 1.3 million affected (Bruggmann, 2015). In the US, IDU is currently the primary risk factor for HCV transmission and the leading cause of HCV incidence (Zibbell, 2018). Since 2009, the number of new HCV cases has risen dramatically, largely among white adults in their twenties and thirties and particularly among those residing

in nonurban areas (Liang and Ward, 2018; Zibbell, 2018). Abara et al. reported that 55% of people who inject drugs (PWID) in 8 US cities were found to also have been infected with HCV, including almost half of young PWID (18-35 years) (2019). Research evidence indicates that there has been a significant increase in HCV infections among young people age 18-39, with IDU being indicated in more than 80% of the HCV infections in one analysis (Zibbell, 2018).

Currently, there are few studies that assess awareness of one's HCV infection, and none that assess changes in awareness over time. Researchers have used National Health and Nutritional Examination Survey (NHANES) data to determine awareness of participants' HCV infection (Kim, 2019; Zhou, 2020). NHANES conducts lab tests for HCV antigen and antibody on survey respondents in addition to asking respondents whether they've been diagnosed or have seen a doctor for their HCV diagnosis. This allows researchers to match the biomarkers from the lab results with the survey questionnaires to estimate the percentage of people with HCV infection who have been diagnosed, or are aware of their HCV infection. Kim (2019) found that overall awareness of chronic HCV among NHANES participants was 55.6%, and Zhou (2020) found there was a 49% awareness of HCV infection among respondents. Both authors used NHANES survey years 2013-2016 to conduct their analysis and did not assess change over time.

1.2. Purpose of Study

For this study, we will examine whether there are changes over time in awareness of HCV infection using data from 6 NHANES survey cycles between 2007 and 2018 (2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2018 administration periods). We will also examine whether HCV diagnosis changed over time and look at potential confounders, effect modifiers, and mediators to determine if 1) the prevalence of awareness of HCV infection

increased over time; 2) if the increase was statistically significant; and 3) if there were any confounders, mediators, or effect modifiers that influenced the association between awareness of HCV infection and time.

Literature Review

2.1. Estimated Versus Actual Prevalence of HCV Infection

Hepatitis C is a leading cause of morbidity and mortality worldwide and represents a major global public health concern (Stone, 2018). Abadie et al. estimates that worldwide, there are an estimated 130 million people infected with HCV (2017). The World Health Organization (WHO) estimates that 1.5 million new HCV infections occur annually, and 170 million people worldwide are estimated to have chronic HCV (Douglass, 2018; Harris, 2013). In 2017, only 1.6 million patients were treated for HCV, speaking to the low number of individuals aware of their infection, striking, given that an estimated 350,000 persons worldwide die due to HCV-related liver diseases each year (Douglass, 2018; Harris, 2013).

Hepatitis C is the most common blood-borne infection in the US (Al-Tayyib, 2014; Trooskin, 2015). An estimated 2.7 to 3.9 million persons are living with HCV infection, and the majority do not know they are infected (Trooskin, 2015; Valdisermi, 2014). The Centers for Disease Control and Prevention (CDC) estimates that up to 75% of individuals with HCV are not aware of their infection, and this estimate is conservative as it is based on NHANES data and does not include homeless individuals, those with unstable housing, or incarcerated individuals, populations that are disproportionately affected by viral hepatitis (NASTAD, 2013). Further, it is estimated that 80% of all HCV-infected individuals in the US will develop chronic HCV infection and 20% will develop serious complications such as cirrhosis or HCC, requiring treatments such as medication, hospitalization, and liver transplant (Bush, 2019; CDC 2017; Trooskin, 2015; Valdisermi, 2014).

CDC estimates that there are approximately 17,000 new HCV infections each year in the US (Valdisermi, 2014). Without the necessary access to care and/or treatment, viral hepatitis can lead to chronic liver disease, cirrhosis, liver cancer and liver failure and complications from these chronic infections claim 15,000 lives annually (Al-Tayyib, 2014; NASTAD, 2013; Trooskin, 2015). The number of deaths attributed to HCV infection now surpasses the number of deaths attributed to HIV (Al-Tayyib, 2014). There is a lack of knowledge and awareness surrounding the seriousness of chronic viral hepatitis among healthcare providers, policy makers, and at-risk populations and this, in combination with inadequate resources to combat this epidemic, has impeded an effective national and global public health response (Valdisermi, 2014).

2.2. Viral Hepatitis Elimination Goals

Worldwide, chronic viral hepatitis accounts for more deaths than that from HIV/AIDS, tuberculosis, or malaria (Buckley, 2016; WHO, 2016). In the US, more than 20,000 deaths can be attributed to viral hepatitis annually (CDC, 2013). In response, both the WHO and US Department of Health and Human Services have developed viral hepatitis elimination plans (DHHS 2017; WHO, 2016). The WHO aimed to reduce viral hepatitis infections to less than one million and reduce deaths attributed to viral hepatitis to less than 500,000 worldwide by 2030 (WHO, 2016). One of the key areas of focus in the WHO plan is increasing viral hepatitis diagnosis from less than 5% of chronic hepatitis infections (2015 baseline estimate) to 90% in 2030 (WHO, 2016). To do this, the WHO recommends integration of viral hepatitis testing into national hepatitis policies, strengthening national laboratory systems so countries can provide quality diagnosis of viral hepatitis, as well as establishing key linkages between testing and other services to improve access to treatment and support services (WHO, 2016).

By 2020, the US Department of Health and Human Services (DHHS) aims to decrease the number of new HCV infections by at least 60% and increase the percent of persons aware of their HCV infection to 66% (DHHS, 2017). DHHS estimates that 45% of people with HCV have not been diagnosed (DHHS, 2017). The action plan calls for education of both providers and individuals about screening as a first step in increasing awareness of one's HCV infection status.

2.3. The Patient Protection and Affordable Care Act

On March 23, 2010, the Patient Protection and Affordable Care Act (ACA) was signed into law (French, 2016). The ACA built upon the existing employer-sponsored insurance system and created new requirements for individuals, employers, health care providers, and insurance companies to address access to health insurance, health care costs, and delivery of health care (French, 2016). Multiple strategies were employed with the goal of increasing overall insurance coverage: allowing young adults to remain on parents' insurance plans until age 26; requiring large employers to offer health insurance to full-time employees; requiring individuals without employer-sponsored insurance to purchase insurance or pay a penalty; and expand Medicaid eligibility to all individuals under age 65 with an annual income up to 400% of the federal poverty level (French, 2016; McIntyre, 2019). The ACA also imposed new regulations on insurance companies, including prohibiting companies from charging higher premiums or denying coverage due to preexisting conditions, requiring insurance companies to provide some preventive services without any cost sharing, and annual and lifetime limits on health benefits were abolished (French, 2016; McIntyre, 2019; NVHR, N.D.).

The ACA provides opportunities to help prevent new viral hepatitis infections, and also treat existing infections. Some of the features of the ACA related to viral hepatitis include access to

viral hepatitis vaccinations (hepatitis A and B), improved provision of essential care and treatment, a ban on denial of health coverage based on preexisting conditions, and required coverage of recommended preventive services such as hepatitis B and C screening for individuals in recommended risk categories (DHHS, 2017).

Early Findings

Several studies suggest that the ACA has substantially decreased the number of uninsured Americans (French, 2016; McIntyre, 2019). Since the implementation of the ACA in 2010, the number of individuals without insurance in the US has decreased by about 20 million people (McIntyre, 2019). Additionally, significant improvements in access to primary care services, medications, affordability of care, and self-reported health were reported as early findings in studies looking at the effectiveness of the ACA (French, 2016). The proportion of the population without a regular source of health care decreased from 29.8% in 2013 to 26% in 2014, however, French reported that 40% of respondents still had at least one access problem, especially for racial/ethnic minority and low income groups (French, 2016).

2.4. The ACA and Access to Hepatitis Treatment

ACA and Hepatitis treatment

In 2014, several new drugs to treat HCV received FDA approval in the US (Trooskin, 2015). These direct-acting antivirals (DAAs) have a cure rate over 95% with a treatment duration of only 8-12 weeks and fewer and less sever side-effects than interferon treatments used previously (Barua, 2015; Douglass, 2018; Trooskin, 2015). These treatments, however, are extremely expensive (up to approximately $40,000 per treatment course), and given the large size of the population in need some insurers have restricted coverage (Douglass, 2018;

Trooskin, 2015). This issue is especially relevant to the Medicare and Medicaid programs because of the high burden of HCV infection in their covered populations, but other populations covered through governmental funding are also disproportionately affected by HCV, including those incarcerated and those receiving care through the VA (Bush, 2019; Trooskin, 2015).

While the ACA stipulates that no insurer may deny coverage to someone based on pre-existing or chronic health conditions, some insurers have included stipulations into their plans that place limits on the types and amount of coverage those with HCV receive for their condition, including excluding medications and placing drugs in the most expensive copay or coinsurance tiers, making the cost prohibitive for many patients seeking treatment for their HCV (NASTAD, 2013; Ryan, 2014). Additionally, insurers are not required to provide routine HCV screening for baby boomers, and HCV screening is only required to be covered for pregnant women (NASTAD, 2013).

Medicaid Coverage for HCV Treatment

One of the strategies employed in the ACA to expand health insurance coverage was the expansion of Medicaid. As of 2018, 32 states had expanded their Medicaid programs (KFF, 2018). A literature review conducted by the Kaiser foundation found that states that expanded their Medicaid programs experienced large reductions in uninsured rates beginning in 2014, and these reductions far exceeded reductions seen in states that did not expand their Medicaid programs (KFF, 2018). Kaiser also found that people with substance use disorders and people with HIV were two populations that saw large reductions in uninsured rates (KFF, 2018).

Despite these great strides seen in increasing health insurance coverage, individuals with HCV, and especially injection drug users, experience significant barriers in gaining access to HCV treatment while on Medicaid. Of the 42 states with known Medicaid reimbursement criteria for sofosbuvir, one of the new DAA drugs available with a >90% cure rate for HCV, 88% of states include drug or alcohol use in their eligibility criteria for reimbursement (Barua, 2015). This means that patients with current (or historical substance use depending on the state) will be ineligible for treatment, despite current clinical guidelines that have removed current IDU as an exclusion criteria for treatment and is inconsistent with FDA-approved labeling for sofosbuvir and evidence-based recommendations for treatment (Barua, 2015; Harris, 2013). Most states require urine drug screening before treatment (Harris, 2013).

2.5. The Opioid Epidemic and Hepatitis C

The US is currently in the midst of an opioid epidemic in which substantial challenges are tied to prescription opioid addition, elevated heroin use, and an increasing number of HCV infections, especially in younger populations, in addition to an overwhelming number of opioid overdose deaths (Stopka, 2017). IDU is currently the primary risk factor for HCV transmission, as well as the leading cause of incidence (Zibbell, 2018). The US saw a substantial increase in acute HCV infections between 2004 and 2014 in persons age 18 to 39 years, with IDU the most frequently cited risk factor in national surveillance data, and reported that 80% of case reports with an HCV-related risk indicated IDU in 2014 (Zibbell, 2018. Abara et al (2019) reported that 55% of people who inject drugs (PWID) in 8 US cities were found to also have been infected with HCV, including almost half of young PWID (18-35 years).

Methods and Procedures

3.1. Data Source and Sample

The National Center for Health Statistics (NCHS), part of the CDC, conducts the NHANES survey annually with approximately 5,000 individuals participating in interviews, questionnaires, and health examinations (NCHS, 2020a). NHANES is nationally representative, with a target population of the noninstitutionalized civilian resident population in the US. Several groups are oversampled, including Hispanic persons, Non-Hispanic Black persons, Non-Hispanic Asian persons, Non-Hispanic White and other persons at or below 185% poverty level, and Non-Hispanic White and other persons age 80 and older. NHANES utilizes a complex, multistage probability design, first selecting primary sampling units, then selecting segments within the primary sampling units that contain a cluster of households, then selecting specific households within those segments, and finally selecting individuals within a household (NCHS, 2020b).

For this analysis, six two-year survey cycles, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2018 were combined and compared to identify changes in hepatitis C diagnosis over time. For each of the survey periods, the following datasets were combined for analysis: 1) demographics, 2) hepatitis C (laboratory), 3) current health status, 4) health insurance, 5) hepatitis (questionnaire), 6) hospital utilization and access to care; 7) immunization, 8) medical conditions, and 9) drug use.

We applied restrictions on the initial sample of individuals included in the six datasets (N=57,414) to include only those participants who were age 20 and older and received a

positive HCV RNA test result. After applying our inclusion/exclusion criteria, there were a total of 387 respondents in our sample.

The datasets utilized contain secondary public use data and therefore do not require IRB approval. NHANES data is a pre-approved data source per IRB policies and guidelines at GSU (GSU, 2019). Secondary data were used for this study because it is cost-effective and less time consuming than it would be to conduct primary data collection for this topic. NHANES is nationally representative and collects data on measures that were used to conduct this analysis.

3.2. Key Variables of Interest

The following section presents the variables of interest for this study.

Dependent Variable

The dependent variable for this study is diagnosed hepatitis C infection, measured by diagnosis of HCV. To create this variable, we used the variable "ever told you have hepatitis C" for survey years 2013-2018 and the variable "seen a doctor about test result?" for survey years 2007-2012 for the numerator and divided this by the number of respondents with a positive RNA test. The outcome is expressed as a proportion.

Independent Variables

To answer our research questions, we looked at several independent variables, as described below. Our primary independent variable, or exposure of interest was survey period. We also assessed several additional variables as potential confounders. Finally, test our hypothesis that ACA implementation would increase awareness of HCV infection, we assessed health insurance coverage as a potential mediator of this association.

Primary Independent Variable

Survey Period: For our primary exposure variable we looked at the differences in diagnosed hepatitis C across survey periods (2007-2018). We also developed a dichotomous variable to compare survey periods between 2007-2012 and 2013-2018.

Independent Variables Assessed as Potential Confounders or Mediators

Demographics: Demographic variables included age, gender, marital status, race/ethnicity, poverty income ratio (PIR), and education level. Age was reported as the respondent's age in years at the time of the interview. Gender was classified into two groups, male and female. Race/ethnicity was reported as Mexican American, Other Hispanic, non-Hispanic White, Non-Hispanic Black, and other race-including multi-racial. NHANES asks respondents their highest level of education completed or highest degree received. For this analysis, education level was categorized as the following: less than 5^{th} grade education; less than 9^{th} grade education; some high school completed; high school diploma (or equivalent); some college; or college graduate. For marital status, NHANES collects information about whether participants are married, widowed, divorced, separated, never married, or living with a partner. For this analysis, we classified marital status into two groups: married or not married. Finally, poverty income ratio (PIR) was calculated using family income, and poverty guidelines by family size dependent on state of residence and year. For this analysis, PIR was divided into two categories: at or below poverty level (0-4.00) and above poverty level (greater than 4.00).

Drug Use: Drug use variables included lifetime illicit drug use (cocaine, heroin, methamphetamine) and lifetime IDU. Lifetime use of cocaine/heroin/methamphetamine and IDU were reported as yes or no.

Health Insurance: Health insurance variables included health insurance coverage and type of health insurance. Health insurance coverage was reported as yes or no. To collect the type of health insurance a participant has, NHANES asks a series of questions to determine the type of insurance plan by which a participant is covered. Response options include private insurance, Medicare, Medi-Gap, Medicaid, CHIP, military health care, state-sponsored health plan, other government insurance, Indian Health service, single service plan, or no coverage of any type.

Access to Healthcare: The access to care variable used for this analysis was routine place to go for healthcare. For this variable, NHANES reported the following response options: yes, there is no place, and there is more than one place. We created a dichotomous variable combining options for yes and there is more than one place.

Hepatitis Vaccinations: Hepatitis vaccination variables included hepatitis A and hepatitis B vaccinations. For hepatitis A, NHANES categorized responses as those who received at least 2 doses, those who received less than 2 doses, and those who received no doses. For hepatitis B, NHANES categorized responses as those who received at least 3 doses, those who received less than 3 doses, and those who received no doses. For both HAV and HBV vaccinations we created a dichotomous variable with options yes (those who received at least one dose of the vaccine) and no (those who did not receive any doses of the vaccine).

Ever tested for HIV virus: This variable was used as a proxy for sexual risk. NHANES reported responses as yes or no.

Blood Transfusion: For this category we looked at receipt of a blood transfusion. Response options for this variable included yes or no.

Chronic Disease: Chronic disease variables included asthma, coronary heart disease, emphysema, bronchitis, and liver condition. For each of these variables, responses were categorized as yes or no.

3.3. Statistical Analysis

SAS version 9.4 was used to conduct all analyses. Descriptive statistics were conducted for all participant characteristics including age, gender, race, marital status, education, income, and insurance coverage. Bivariate analyses were conducted using Chi-square tests and were reported as odds ratios.

Bivariate and multivariate logistic regression models were conducted to explore the associations between our independent variables and awareness of HCV infection as well as to assess possible confounders and mediators of the relationship between time (primary exposure variable) and awareness of HCV infection (outcome variable). Bivariate linear regression was used to estimate linear trends to estimate linear trends in awareness of HCV infection over time. Survey years were combined to develop a dichotomous variable (2007-2012 and 2013-2018) for measuring time as exposure of interest. Potential confounders and mediators were evaluated for the relationship between time and awareness of HCV infection, our outcome variable. Findings were reported as unadjusted and adjusted odds ratios. Statistical significance was determined using 95% confidence intervals and p-values<.05.

Results

4.1. Study Sample

Of the 387 individuals included in our study, 32.82% were female. The mean age of participants was 54.46 (95% CI: 53.38,55.53), and the racial/ethnic make-up of the sample included 39.53% non-Hispanic Black, 37.73% non-Hispanic White, 9.56% Mexican American, 8.53% Other Hispanic, and 4.65% other race. One hundred and twenty five (32.30%) of the 387 participants reported being married, and 215 (55.84%) reported having attended some college or having received a college degree or higher. Table 1 below provides demographic and risk factor characteristics of study participants.

There were 142 participants (36.69%) who reported awareness of their HCV infection. We divided the NHANES survey cycles into 2 time periods, the first using survey cycles between 2007 and 2012 and the second survey cycles between 2013 and 2018. The odds of reporting a positive HCV diagnosis in the second survey period (2013-2018) was 3.71 times the odds in the first time period ($p < 0.0001$). In the first survey period, 2007-2012, 52 (23.74%) respondents reported a positive HCV diagnosis, while in the second survey period, 2013-2018, 90 (53.57%) respondents reported a positive HCV diagnosis. Among those reporting lifetime injection drug use, 51.34% reported being aware of their positive HCV infection (OR 1.8, $p=0.02$). Among those who were older than 50 years of age, 40.68% reported awareness of their HCV infection (OR 1.74, $p=0.02$), and 40.08% of those who were not married reported being aware of their HCV infection (OR 1.59, $p=0.04$). Finally, the odds of reporting a positive HCV diagnosis among those covered by health insurance was 0.55 times the odds of those not covered by health insurance ($p =0.01$).

Table 1: Participant Characteristics by Awareness of HCV Infection

Variable Frequency (unweighted %)	Aware of HCV Infection+ N=142	Not Aware of HCV Infection+ N=245	OR*	P-value
NHANES Survey Implementation Period				
Survey Cycles 2007-2012	52 (23.74)	167 (76.26)	1	<0.0001
Survey Cycles 2013-2018	90 (53.57)	78 (46.43)	3.71	
Age				
Less than/equal to 50 years	35 (28.23)	89 (71.77)	1	0.02
Older than 50 years	107 (40.68)	156 (59.32)	1.74	
Sex				
Female	41 (32.28)	86 (67.72)	1	0.21
Male	101(38.85)	159 (61.15)	1.33	
Race				
Other, including Multi-racial	86 (36.75)	148 (63.25)	1	0.98
Non-Hispanic Black	56 (36.60)	97 (63.40)	0.99	
PIR				
Greater than 4.00	11 (39.29)	17 (60.71)	1	0.77
Less than or equal to 4.00	131 (36.49)	228 (63.51)	0.88	
Education				
Some college or above	80 (37.21)	135 (62.79)	1	0.75
High school diploma or below	53 (35.57)	96 (64.43)	0.93	
Marital Status				
Married	37 (29.60)	88 (70.40)	1	0.04
Not married	105 (40.08)	157 (59.92)	1.59	
Lifetime injection drug use				
No lifetime injection drug use	51 (36.96)	87 (63.04)	1	0.02
Yes, has ever injected drugs	57 (51.35)	54 (48.65)	1.8	
Lifetime Illicit drug use				
No	32 (36.36)	56 (63.64)	1	0.12
Yes	77 (46.67)	88 (53.33)	1.53	
Covered by health insurance				
Yes	109 (40.98)	157 (59.02)	1	0.01
No	33 (27.50)	87 (72.50)	0.55	
Type of health insurance				
Private insurance	26 (32.91)	53 (67.09)	1	0.09
Public insurance	82 (44.09)	104 (55.91)	1.6	
Routine place to go for healthcare				
Yes	118 (38.19)	191 (61.81)	1	0.23
No	24 (30.77)	54 (69.23)	0.72	
Received HAV vaccine				
Yes	34 (39.53)	52 (60.47)	1	0.51
No	94 (35.61)	170 (64.39)	0.85	
Received HBV vaccine				

Variable Frequency (unweighted %)	Aware of HCV Infection+ N=142	Not Aware of HCV Infection+ N=245	OR*	P-value
Yes	45 (45.92)	53 (54.08)	1	0.03
No	83 (33.20)	167 (66.80)	0.59	
Ever tested for HIV virus**				
No	34 (26.15)	96 (73.85)	1	0.0009
Yes	98 (43.95)	125 (56.05)	2.21	
Ever received blood transfusion				
No	93 (33.82)	182 (66.18)	1	0.07
Yes	44 (44.00)	56 (56.00)	1.54	
Risk factor: Chronic Asthma				
No	112 (35.22)	206 (64.78)	1	0.2
Yes	30 (43.48)	39 (56.52)	1.41	
Risk factor: CHD				
No	137 (36.73)	236 (63.27)	1	0.98
Yes	4 (36.36)	7 (63.64)	0.98	
Risk factor: Chronic Emphysema				
No	133 (36.14)	235 (63.86)	1	0.32
Yes	9 (47.37)	10 (52.63)	1.59	
Risk factor: Chronic Bronchitis				
No	124 (35.33)	227 (64.67)	1	0.18
Yes	16 (47.06)	18 (52.94)	1.63	

+ Awareness of HCV infection variable developed by using NHANES hepatitis questionnaire variables HEQ030 (2013-2018) or HCQ070 (2007-2012) and dividing by the number of RNA positives (NHANES laboratory variable LBXHCR)

* Reference value is 1.00

** Proxy measure for sexual risk

4.2. Changes Over Time in Awareness of HCV Infection

Table 2 below provides the percent of awareness of HCV infection in our sample and corresponding 95% confidence intervals for each 2-year survey cycle. Awareness of HCV infection increased from 24.53% (95% CI: 10.40, 38.66) in the 2007-2008 survey cycle to 63.48% (95% CI: 48.03, 78.93) in the 2017-2018 survey cycle, and this increase was significant (β for trend 0.09, $p<0.0001$).

Table 2: Percent of Awareness of HCV Infection by NHANES Survey Period

NHANES Survey Period	Percent Aware+	95% Confidence Interval
2007-2008	24.53%	(10.40, 38.66)
2009-2010	16.10%	(2.66, 29.55)
2011-2012	22.77%	(14.97, 30.57)
2013-2014	54.28%	(35.30, 73.25)
2015-2016	56.85%	(38.37, 75.32)
2017-2018	63.48%	(48.03, 78.93)

+Weighted percent using survey procedures in SAS

To assess change over time we compared participant characteristics in the first survey period (survey cycles between 2007 and 2012) and second survey period (survey cycles between 2013 and 2018) to identify any significant differences among people with chronic HCV between the time periods. Table 3 below describes participant characteristics and risk factors by NHANES survey period. Odds ratios and p-values were calculated for each characteristic measured. Several demographic characteristics were significantly associated with survey period, including age (OR 2.46, p <0.0001), poverty-to-income ratio (OR 3.83, p= 0.0046), and marital status (OR 1.93, p=0.0036). Type of health insurance, private vs. public, was also significantly associated with survey period (OR 1.92, p=0.018).

Table 3: Participant Characteristics and Risk Factors by NHANES Survey Period

Variable Frequency (unweighted %)	NHANES Survey Cycles 2007-2012 N=219	NHANES Survey Cycles 2013-2018 N=168	OR*	P-value
Aware HCV Positive+				
No	167 (76.26)	78 (46.43)	1	<0.0001
Yes	52 (23.74)	90 (53.57)	3.71	
Age				
Less than/equal to 50 years	88 (40.18)	36 (21.43)	1	<0.0001
Older than 50 years	131 (59.82)	132 (78.57)	2.46	
Sex				
Female	78 (35.62)	49 (29.17)	1	0.18
Male	141 (64.38)	119 (70.83)	1.34	
Race				
Other, including Multi-racial	130 (59.36)	104 (61.90)	1	0.61

Variable Frequency (unweighted %)	NHANES Survey Cycles 2007-2012 N=219	NHANES Survey Cycles 2013-2018 N=168	OR*	P-value
Non-Hispanic Black	89 (40.64)	64 (38.10)	0.9	
PIR				
Greater than 4.00	23 (10.50)	5 (2.98)	1	0.0046
Less than or equal to 4.00	196 (89.50)	163 (97.02)	3.83	
Education				
Some college or above	112 (55.45)	103 (63.58)	1	0.12
High school diploma or below	90 (44.55)	59 (36.42)	0.71	
Marital Status				
Married	84 (38.36)	41 (24.40)	1	0.0036
Not married	135 (61.64)	127 (75.60)	1.93	
Lifetime injection drug use				
No lifetime injection drug use	62 (57.94)	76 (53.52)	1	0.49
Yes, has ever injected drugs	45 (42.06)	66 (46.48)	1.2	
Lifetime Illicit drug use				
No	39 (35.45)	49 (34.27)	1	0.84
Yes	71 (64.55)	94 (65.73)	1.05	
Covered by health insurance				
Yes	145 (66.21)	121 (72.46)	1	0.19
No	74 (33.79)	46 (27.54)	0.74	
Type of health insurance				
Private insurance	52 (35.86)	27 (22.50)	1	0.018
Public insurance	93 (64.14)	93 (77.50)	1.92	
Routine place to go for healthcare				
Yes	180 (82.19)	129 (76.79)	1	0.19
No	39 (17.81)	39 (23.21)	1.4	
Received HAV vaccine				
Yes	50 (25.38)	36 (23.53)	1	0.69
No	147 (74.62)	117 (76.47)	1.11	
Received HBV vaccine				
Yes	59 (29.95)	39 (25.83)	1	0.4
No	138 (70.05)	112 (74.17)	1.23	
Ever tested for HIV virus**				
No	76 (37.62)	54 (35.76)	1	0.72
Yes	126 (62.38)	97 (64.24)	1.08	
Ever received blood transfusion				
No	154 (72.30)	121 (74.69)	1	0.6
Yes	59 (27.70)	41 (25.31)	0.88	
Risk factor: Chronic Asthma				
No	180 (82.19)	138 (82.14)	1	0.99

Variable Frequency (unweighted %)	NHANES Survey Cycles 2007-2012 N=219	NHANES Survey Cycles 2013-2018 N=168	OR*	P-value
Yes	39 (17.81)	30 (17.86)	1	
Risk factor: CHD				
No	212 (97.25)	161 (96.99)	1	0.88
Yes	6 (2.75)	5 (3.01)	1.1	
Risk factor: Chronic Emphysema				
No	210 (95.89)	158 (94.05)	1	0.41
Yes	9 (4.11)	10 (5.95)	1.48	
Risk factor: Chronic Bronchitis				
No	200 (91.32)	151 (90.96)	1	0.9
Yes	19 (8.68)	15 (9.04)	1.05	

+ HCV diagnosis variable developed by using NHANES hepatitis questionnaire variables HEQ030 (2013-2018) or HCQ070 (2007-2012) and dividing by the number of RNA positives (NHANES laboratory variable LBXHCR)
* Reference value is 1.00
** Proxy measure for sexual risk

4.3. Factors Associated with HCV Diagnosis

We used bivariate and multivariate logistic regression models to assess the association between the outcome (awareness of HCV infection) and exposure (survey implementation period) in the analysis described above Multivariate logistic regression models were used to assess potential confounders and mediators. Potential confounders identified and included in our model were age and marital status. In the bivariate analysis, being older than 50 years was associated with HCV diagnosis (OR=1.74, 95% CI: 1.10, 2.77). Not being married was also associated with HCV diagnosis (OR=1.59, 95% CI: 1.01, 2.51). Other demographic and risk factor variables examined, including race/ethnicity, lifetime injection drug use, type of health insurance, receipt of hepatitis A or B vaccine, and poverty-to-income ratio were not significantly associated with HCV diagnosis in this population. After adjusting for potential confounders, neither age nor marital status remained significant factors in the association between NHANES

survey implementation period and awareness of HCV infection. Table 4 below provides the unadjusted and adjusted odds ratios for the bivariate and multivariate analysis.

To examine our hypothesis that implementation of the ACA mediated the relationship between time and awareness of one's HCV infection, health insurance coverage was examined as a potential mediator. However, the increase in HCV diagnosis was not mediated by increases in health insurance coverage.

Table 4: Factors Associated with Awareness of HCV Infection

Variable	Unadjusted OR+ (95% CI*)	P-value**	AOR+ (95% CI)	P-value**
NHANES Survey Implementation Period				
Survey Cycles 2007-2012	1.00		1.00	<0.0001
Survey Cycles 2013-2018	3.71 (2.40,5.72)	<0.0001	4.633 (2.49,8.62)	
Age				
Less than/equal to 50 years	1.00		1.00	0.76
Older than 50 years	1.74 (1.10,2.77)	0.02	1.11 (0.58, 2.10)	
Marital Status				
Married	1.00		1.00	0.13
Not married	1.59 (1.01,2.51)	0.04	1.52 (0.88, 2.61)	

*CI – confidence interval
** p-value statistically significant when *P* is 0.05 or less
OR – Odds Ratio
AOR – Adjusted Odds Ratio

Discussion

This study examined NHANES data for years 2007-2018 to assess changes in HCV diagnosis and demographics and risk factors associated with HCV diagnosis over time. This analysis demonstrates that HCV diagnosis has been increasing over time in the US. We found that in all survey periods (2007-2018), 36.69% of participants reported knowledge of their HCV diagnosis. We saw a significant increase in HCV diagnosis over time, with 24.53% of participants reporting HCV diagnosis in the 2007-2008 NHANES survey cycle, compared to 63.48% of participants reporting an HCV diagnosis in the 2017-2018 survey cycle. These findings illustrate progress toward DHHS and WHO viral hepatitis elimination goals (DHHS, 2017; WHO 2016).

We tested for mediation of the relationship between time and awareness of HCV infection by insurance status. However, in this analysis the increase of awareness of HCV infection was not mediated by health insurance coverage. It is possible the increase we saw can be attributed to participant misreporting of self-reported survey items, measurement error in the analysis, or the small sample size, which did not provide enough power to see an association that may have been present.

While our analysis could not attribute a specific factor to the increase in HCV diagnosis, there are several potential factors that could explain this significant increase in HCV awareness. First, the ACA was implemented in 2010 with options and implementation commencing throughout 2011-2013 (Cauchi, 2013). The purpose of the ACA was to increase the number of Americans with health insurance, thereby increasing their access to care. If more Americans are able to access healthcare they may be more likely to ask for, or have a provider recommend, HCV screening. However, this was not borne out of this analysis. It's possible this is because the

NHANES survey does not collect data on a representative sample of those most affected by HCV, for example IDU, homeless individuals, or those who are incarcerated. So, it's possible we did not capture enough individuals with HCV infection to see an increase in awareness that was due to increased health insurance coverage or access to care. It's also possible that since neither our health insurance coverage nor access to health care variables were significantly associated with survey period, those who participated in the NHANES survey already had health insurance and a place to go for healthcare prior to the implementation of the ACA.

Additionally, the current opioid epidemic and associated increases in injection drug use has been attributed to increases in HCV infections (Zibbell, 2018) and may be associated with increased awareness of HCV diagnosis, even though we were not able to show that with this analysis.

Receiving a diagnosis, being aware of one's HCV infection, is an important first step toward achieving elimination goals laid out by the US DHHS (DHHS, 2017) and the WHO (WHO, 2016b). There have been several initiatives focusing on enhancing HCV screening and diagnosis in the US. For example, in 2020 the CDC revised previous birth cohort screening recommendations to provide guidance that all adults age 18 and older should receive HCV screening at least once in their lifetime and that women should receive HCV screening during each pregnancy except where the prevalence of HCV is less than 0.1% (Schillie, 2020). There have also been a number of awareness campaigns implemented recently to increase HCV screening among high-risk populations. (CDC Foundation, N.D.; Veterans Affairs, 2020). But, the benefits of knowing one's diagnosis may extend beyond receipt of antiviral treatment. Left untreated, individuals with

chronic hepatitis C may be at greater risk for developing cirrhosis, liver cancer, and even premature mortality (Valdisermi, 2014).

There are several limitations to this study. First, NHANES sampling does not capture several groups of individuals, including institutional populations and homeless individuals. Additionally, groups with a higher risk of viral hepatitis, injection drug users as an example, are generally underrepresented or not captured. Second, NHANES uses a cutoff of 20 years and older for "adult". This does not account for the rising viral hepatitis infections among young injection drug and opiate users. This likely leads to an underestimation of the proportion of the population that is unaware of their HCV diagnosis, which may have skewed the results of our analysis. Third, because NHANES utilizes a self-report design, it is possible that stigmatized behaviors, such as injection or illicit drug use are underreported. Fourth, the small sample size in our study may have resulted in an inability to show some important associations that would have been apparent had our sample been larger. Fifth, between the 2011-2012 and 2013-2014 survey administration periods, NHANES changed the hepatitis questionnaire, and therefore, the variable we used to develop the numerator for our outcome variable changed from "seen a doctor about a test result" (HCQ070) to "Ever told you have hepatitis C?" (HEQ030). Because of the use of different variables at different time points, it's possible this change introduced measurement error into our analysis. Finally, the two variables we hypothesized would mediate the relationship between time and awareness of HCV infection, insurance status and injection drug use, did not. These are both self-reported and are subject to mis-reporting and measurement error/information bias.

This study provides a snapshot of the current progress of eliminating hepatitis C in the US. As discussed, diagnosis of one's HCV infection remains inadequate at 63.48% in this analysis. This finding is supported by previous research highlighting the low awareness of viral hepatitis infections in this country (Kim, 2018; Volk, 2009; Zhou, 2020). Our analysis found an increasing trend in HCV diagnosis, which is encouraging. As this analysis did not include institutionalized populations or homeless individuals, and individuals at high risk for HCV (e.g., injection drug users) are often underrepresented in NHANES surveys, it is important for additional studies to build on these findings by including those populations in the analysis. This will build a more complete picture of the true gaps between the prevalence of HCV and awareness of one's HCV infection in the US. Future research and interventions should also focus on scaling-up screening and linkage to care campaigns across the US and educating healthcare providers about the revised CDC recommendation (Schillie, 2020) that all adults should be screened for HCV in order to increase awareness of HCV infection and get infected individuals into care for appropriate HCV treatment.

References

Abadie, R., Welch-Lazoritz, M., Khan, B., & Dombrowski, K. (2017). Social determinants of HIV/HCV co-infection: A case study from people who inject drugs in rural Puerto Rico. *Addictive Behaviors Reports*, 5, 29-32.

Abara, W. E., Trujillo, L., Broz, D., Finlayson, T., Teshale, E., Paz-Bailey, G., ... & Sey, E. K. (2019). Age-related differences in past or present hepatitis C virus infection among people who inject drugs: National Human Immunodeficiency Virus Behavioral Surveillance, 8 US Cities, 2015. *The Journal of infectious diseases*, *220*(3), 377-385.

Al-Tayyib, A. A., Thiede, H., Burt, R. D., & Koester, S. (2015). Unmet health care needs and hepatitis C infection among persons who inject drugs in Denver and Seattle, 2009. *Prevention science*, *16*(2), 330-340.

Barua, S., Greenwald, R., Grebely, J., Dore, G. J., Swan, T., & Taylor, L. E. (2015). Restrictions for Medicaid reimbursement of sofosbuvir for the treatment of hepatitis C virus infection in the United States. *Annals of internal medicine*, *163*(3), 215-223.

Bruggmann, P., & Grebely, J. (2015). Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. *International Journal of Drug Policy*, *26*, S22-S26.

Buckley, G.J., &Strom, B.L. (2016). What stands in the way of making hepatitis B and C rare diseases in the US? *Ann Intern Med*, 165(4), 284-285.

Bush, H., Paik, J., Golabi, P., de Avila, L., Escheik, C., & Younossi, Z. M. (2019). Impact of hepatitis C virus and insurance coverage on mortality. *Am J Manag Care*, *25*(2), 61-67.

Cauci,R. (2013). 2011-2014 health insurance reform enacted state laws related to the affordable care act. Retrieved from: https://www.ncsl.org/research/health/health-insurance-reform-state-laws-2013.aspx.

CDC Foundation (No Date). Viral hepatitis action coalition: Helping CDC shine new light on a silent epidemic. Retrieved from: https://www.cdcfoundation.org/sites/default/files/files/VHACAchievements.pdf.

Centers for Disease Control and Prevention (2017). HIV and Viral Hepatitis. Retrieved from: https://www.cdc.gov/hiv/pdf/library/factsheets/hiv-viral-hepatitis.pdf

Centers for Disease Control and Prevention (2013). Surveillance for viral hepatitis – United States, 2013. Retrieved from: https://www.cdc.gov/hepatitis/statistics/2013surveillance/

Clark, P.J. & Muir, A.J. (2012). Overcoming barriers to care for hepatitis C. *New England Journal of Medicine*, 366(26), 2436-2438.

Department of Health and Human Services (2017). National viral hepatitis action plan 2017-2020. Retrieved from: https://www.hhs.gov/sites/default/files/National%20Viral%20Hepatitis%20Action%20Plan%202017-2020.pdf.

Ditah, I., Al Bawardy, B., Gonzalez, H.C., Saberi, B., Ditah, D., Kamath, P.S., & Charlton, M. (2015). Lack of health insurance limits the benefits of hepatitis C virus screening: Insights from the national health and nutrition examination hepatitis C follow-up study. *Am J Gastroenterol*, 110, 1126-1133.

Douglass, C. H., Pedrana, A., Lazarus, J. V., FM't Hoen, E., Hammad, R., Leite, R. B., ... & Hellard, M. (2018). Pathways to ensure universal and affordable access to hepatitis C treatment. *BMC medicine*, *16*(1), 1-9.

French, M. T., Homer, J., Gumus, G., & Hickling, L. (2016). Key provisions of the Patient Protection and Affordable Care Act (ACA): a systematic review and presentation of early research findings. *Health services research*, *51*(5), 1735-1771.

Georgia State University: University Research Services and Administration. (2019). Institutional review board policies and procedures for faculty, staff and student researchers. Retrieved from: https://ursa.research.gsu.edu/download/irb-manual/

Harris, M. & Rhodes, T. (2013). Hepatitis C treatment access and uptake for people who inject drugs: A review mapping the role of social factors. *Harm Reduction Journal*, 10(1), 7.

Hofmeister, M.G., Rosenthal, E.M., Barker, L.K., Rosenberg, E.S., Barranco, M.A., Hall, E.W… & Ryerson, A.B. (2019). Estimating prevalence of hepatitis C virus infection in the United States, 2013-2016. *Hepatology*, 69(3), 1020-1031.

Kaiser Family Foundation. (2018). Medicaid expansion enrollment. Retrieved from: https://www.kff.org/health-reform/state-indicator/medicaid-expansion-enrollment/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D#notes.

Kim, H., Yang, J.D., El-Serag, H.B., & Kanwal, F. (2019). Awareness of chronic viral hepatits in the United States: An update from the National health and nutrition examination survey. J *Viral Hepat*, 26, 596-602.

Liang, T.J, & Ward, J.W. (2018). Hepatitis C in injection-drug users – A hidden danger of the opioid epidemic. *NEJM*, 378, 1169-1171.

McIntyre, A. & Song, Z. (2019). The US Affordable Care Act: Reflections and directions at the close of a decade. *PLoS Med*, 16(2), e1002752.

Murdock, R.M., Brizzi, M.B., Perez, O., & Badowski, M.E. (2019). Public health considerations among people who inject drugs with HIV/HCV co-infection: A review. *Infect Dis Ther*, 8, 23-32.

National Alliance of State & Territorial AIDS Directors (NASTAD). (2013). The affordable care act and the silent epidemic: Increasing the viral hepatitis response through health reform.

National Center for Health Statistics. (2020a). National Health and Nutrition Examination Survey. Retrieved from: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/overview.aspx?BeginYear=2015

National Center for Health Statistics (2020b). National Health and Nutrition Examination Survey 2017-2018. Retrieved from: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/overview.aspx?BeginYear=2017

National Viral Hepatitis Round Table. How the affordable care act (ACA) helps people with hepatitis B and C. Retrieved from: https://nvhr.org/sites/default/files/.users/u33/How%20the%20ACA%20Helps%20People%20with%20Hepatitis%20B%20and%20C_fact%20sheet%20FINAL.pdf.

Ryan, B. (2014). Obamacare: Not so affordable for people with HIV and Hep C. Retrieved from: https://www.hepmag.com/article/unaffordable-care-25227.

Schillie, S., Wester, C., Osborne, M., Wesolowski, L. & Ryerson, A.B. (2020). CDC recommendations for hepatitis C screening among adults – United States 2020. *MMWR*, 69(2), 1-17.

Stone, J., Fraser, H., Lim, A.G., Walker, J.G., Ward, Z., MacGregor, L… & Vickerman, P. (2018) Incarceration history and risk of HIV and hepatitis C virus acquisition among people who inject drugs: A systematic review and meta-analysis. *The Lancet Infectious Diseases*, 18(12), 1397-1409.

Stopka, T. J., Hutcheson, M., & Donahue, A. (2017). Access to healthcare insurance and healthcare services among syringe exchange program clients in Massachusetts: qualitative findings from health navigators with the iDU ("I do") Care Collaborative. *Harm Reduction Journal*, *14*(1), 26.

Trickey, A., Fraser, H., Lim, A.G., Peacock, A., Colledge, S., Walker, J.G… &Vickerman, P. (2019). The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: A modelling study. *Lancet Gastroenterol Hepa*tol, 4(6), 435-444.

Trooskin, S.B., Reynolds, H., & Kostman, J.R. (2015). Access to costly new hepatitis C drugs: Medicine, money, and advocacy. *Clinical Infectious Diseases*, 61(15), 1825-1830.

US Department of Veterans Affairs (2020). Hepatitis C testing and treatment awareness campaign. Retrieved from: https://www.hepatitis.va.gov/news/campaign-test-treat-cure.asp.

Valdisermi, R., Khalsa, J., Dan, C., Holmberg, S., Zibbell, J., Holtzman, D., Lubran, R., & Compton, W. (2014). Confronting the emerging epidemic of HCV infection among young injection drug users. *American Journal of Public Health*, 104(5), 816-821.

Volk, M.L., Tocco, R., Saini, S., & Lok, A.S. (2009). Public health impact of antiviral therapy for hepatitis C in the United States. *Hepatology*, 50(6), 1750-1755.

World Health Organization. (2019). Hepatitis C: Key facts. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c.

World Health Organization. (2016). More than 2 million people coinfected with HIV and hepatitis C. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c.

World Health Organization (2016a). Global health sector strategy on viral hepatitis 2016-2021. Retrieved from: https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf?sequence=1

Yehia, B.R., Herati, R.S., Fleishman, J.A., Gallant, J.E., Agwu, A.L., Berry, S.A… & Gebo, K.A. (2014). Hepatitis C virus testing in adults living with HIV: A need for improved screening efforts. *PLoS ONE*, 9(7), e102766.

Zhou, K. & Terrault, N.A. (2020). Gaps in viral hepatitis awareness in the United States in a population-based study. *Clinical Gastroenterology and Hepatology*, 18, 188-195.

Zibbell, J.E., Asher, A.K., Patel, R.C., Kupronis, B., Iqbal, K., Ward, J.W., & Holtzman, D. (2018). Increases in acute hepatitis C virus infection related to a growing opioid epidemic and associated injection drug use, United States, 2004-2014. *AJPH*, 108, 175-181.