VIRAL HEPATITIS B AND C INFECTION AND STATE-LEVEL READINESS TO REDUCE HEPATITIS-RELATED DIFFERENCES IN CARE AND TREATMENT IN THE UNITED STATES

by

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(Under the Direction of M. MAHMUD KHAN and DONGLAN ZHANG)

ABSTRACT

Hepatitis B and C infection is a severe health problem in the United States that persists even with the available clinical interventions, diagnostic tests, and therapeutics that exist such as a highly effective vaccine for hepatitis B and better tolerated treatment for hepatitis C. Only acute hepatitis B and C infection can lead to chronic infection, and these two types of hepatitis have many similarities regarding the need for improved testing to diagnose infection and linkage to care. This study focuses on acute hepatitis B virus and hepatitis C virus infection in the United States and assesses state-level readiness to achieve national viral hepatitis elimination goals. The main objective of this study is to 1) assess the relationship between acute hepatitis B and C infection at the state level and the socioeconomic factors associated with high infection rates, and 2) compare and assess state-level readiness to eliminate viral hepatitis. Acute hepatitis B and hepatitis C infection rates at the state-level were significantly associated with substance use, opioid related variables, and socioeconomic factors like the rate of homelessness in the state. Efforts to eliminate hepatitis at the state level are multidimensional. Common strengths of hepatitis elimination efforts were identified among selected states to include robust harm

reduction programs, accessible wrap around services, and improved access to testing and treatment services. Similarly, weaknesses of hepatitis elimination efforts included having no harm reduction programs in place or having programs that do not go far enough in preventing disease transmission, persistent barriers in access to testing and treatment services, and a lack of wrap around services particularly among at risk populations. More remains to be done to at the state and national level to accelerate progress towards achieving national viral hepatitis elimination goals in the United States.

INDEX WORDS: Viral hepatitis, Hepatitis B virus, Hepatitis C virus, Hepatitis elimination, Infectious diseases, Substance use, Opioid use.

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DEDICATION

Dedicated to Dr. Ukeatabuchi Ogar, my cheerleader extraordinaire. Your kind heart, diligence, and example served as a constant guide and comfort through many challenges. I could tell you each one, but you already know!

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CHAPTER 1

INTRODUCTION AND BACKGROUND

Acute and chronic hepatitis infection is a severe health problem in the United States (U.S.). The U.S. Department of Health and Human Services (DHHS) report that an estimated 2.4 million people are living with hepatitis C virus (HCV or HepC) infection; at least 850,000, and possibly as many as 2.4 million are living with hepatitis B virus (HBV or HepB) infection (Department of Health and Human Services, 2018; Wong et al., 2021). Many persons living with hepatitis are unaware of their infection, are at an increased risk for liver disease, cirrhosis, and death, and can unknowingly transmit the disease to others (HHS, 2018). The most common types of hepatitis in the U.S are hepatitis A, hepatitis B, and hepatitis C; however, only hepatitis B and C lead to chronic infection.

Therefore, this study focuses on acute hepatitis B virus (HBV or HepB) and acute hepatitis C virus (HCV or HepC) infection in the U.S. and assesses state-level readiness to achieve national viral hepatitis elimination goals. Populations affected by each hepatitis type differ, but both hepatitis B and C are ideal for preventive screening for the following reasons: an early asymptomatic period, high prevalence and low diagnosis rate, highly sensitive and specific tests, and promising treatments for hepatitis C with improved clinical outcomes (Chak, Sarkar, & Bowlus, 2016).

According to 2018 data from the Department of Health and Human Services (DHHS), 67% of persons living with HBV infection and 51% of persons living with HCV infection do not know they are infected. According to 2019 surveillance data from the Centers for Disease

Control and Prevention (CDC), there were 3,192 reported cases of acute HBV infection representing an estimated 20,700 new HBV infections; and 4,136 acute hepatitis C cases reported representing an estimated 57,500 new HCV infections (CDC 2019 Viral Hepatitis Surveillance Report).

In 2020, to address the national hepatitis burden, the U.S. Department of Health and Human Services (DHHS) released the Viral Hepatitis National Strategic Plan for the United States: A Roadmap to Elimination (2021-2025). The national plan provides a comprehensive framework for stakeholders and guides strategies and approaches needed for viral hepatitis elimination by 2030 (HHS, 2021). The HHS plan includes five main goals that have associated objectives:

Goal 1: Prevent new viral hepatitis infections

Goal 2: Improve viral hepatitis-related health outcomes of people with viral hepatitis

Goal 3: Reduce viral hepatitis-related disparities and health inequities

Goal 4: Improve viral hepatitis surveillance and data usage

Goal 5: Achieve integrated, coordinated efforts that address the viral hepatitis epidemics among all partners and stakeholders

Additionally, the CDC released a Viral Hepatitis 2025 Strategic Plan with goals and strategies to reduce infections, morbidity, and mortality and address viral hepatitis-related health disparities (CDC, 2021). The four main goals of the CDC's 2025 strategic plan align with HHS goals: 1) Reduce new viral hepatitis infections, 2) reduce viral hepatitis-related morbidity and mortality, 3) reduce viral hepatitis-related disparities, and 4) establish comprehensive national viral hepatitis surveillance for public health action. Possible national elimination of viral

hepatitis in the U.S. is an exciting but challenging goal; nonetheless, progress towards meeting goals in each plan is reported and monitored annually.

As shown in Table 1.1, certain populations are disproportionately affected by higher infection rates and have trouble accessing proper care and treatment (Yeo & Nguyen, 2020; Wong et al., 2018).

Table 1: Groups at-risk for hepatitis infection

Hepatitis Type	Incidence (Acute Infection)	Prevalence (Chronic Infection)	Mortality (At-risk Groups)
HBV	-Persons who inject drugs -Persons with multiple sexual partners	-Asian and Pacific Islanders -non-Hispanic Blacks	-Asian and Pacific Islanders -non-Hispanic Blacks
HCV	-People who inject drugs -non-Hispanic Whites -American Indian/Alaska Native	-People who inject drugs -non-Hispanic Blacks -People born 1945-1965 -People with Human Immunodeficiency Virus (HIV)	-American Indian/Alaska Native -non-Hispanic Blacks -People born 1945-1965

Prior to the current national hepatitis plan, other national viral hepatitis plans were directed towards harmonizing the efforts of stakeholders, federal partners, and collaboration among agencies (DHHS, 2020). However, challenges in the health system and the delivery of health services persist, requiring an integrated approach. In an article published in The New Yorker magazine, Dr. Atul Gewande – a renowned professor of public health and surgeon, talks about improving public health systems and integrating healthcare delivery into public health practice. He emphasizes the high rate of hepatitis infections among groups who have trouble accessing medical care, including injection drug users, the poor, immigrant populations (particularly Asians), and African Americans. He also notes the importance of ensuring that

effective treatments, vaccines, and targeted screenings are equitably provided to prevent infection and eliminate disease incidence through expanded health services (Gewande, 2021).

Acute hepatitis B and C infection can lead to chronic infection. These two types of hepatitis have many similarities regarding the need for improved testing to diagnose infection and linkage to care. However, each hepatitis type has its unique challenges. A common thread between managing hepatitis-related illness is the need for innovative approaches, including community-based outreach, improved information technology to increase access to screening and other health services, and expanded government programs (Chak, Sarkar, & Bowlus, 2016).

Study Objective and Justification

Due to the increasing incidence of acute hepatitis infection and the increased prevalence of chronic infection among different groups, this study has the following objectives:

1) To assess the relationship between acute hepatitis infection at the state level and the social and economic factors associated with high acute B and C hepatitis infection rates.
2) Given the known risk factors of acute hepatitis infection to identify and compare the three states with high calculated ratios for infection and the three states with low calculated ratios for infection for (a total of six identified states each hepatitis type).
3) Examine state-level program and policy prevention efforts to reduce the rate of new infections, hepatitis-related illness, and death in the selected high and low calculated ratio states.
4) Descriptively analyze prevention efforts and recommend additional approaches, strategies, and opportunities for action to achieve national goals, particularly in the states with high rates of hepatitis infection.

Rationale and Relevance of Study

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections can lead to chronic liver conditions such as cirrhosis and hepatocellular carcinoma (HCC), the most common type of primary liver cancer (Lavanchy, 2008; Chak, Sarkar, & Bowlus, 2016). Annually, viral hepatitis infection accounts for over one million deaths per year globally and about 20,000 deaths in the United States, more deaths than HIV/AIDS, malaria, or tuberculosis. Yet, awareness of chronic viral hepatitis infection, particularly among patients at risk for significant fibrosis, is low (Kim, Yang, El-Serag, and Kanwal, 2019).

At the state level, prevention and elimination efforts of viral hepatitis focus on multiple approaches, including increasing hepatitis B immunization coverage, raising knowledge and awareness of viral hepatitis infection, and increasing testing, linkage-to-care, and engagement in care and treatment for hepatitis C infections. Gaps in patient and physician knowledge create barriers in patient access to screening and linkage to care. For example, in a survey conducted among Chinese immigrants in the United States, only about 65% knew about a hepatitis B vaccine. Many wrongly believed that a person could get infected with hepatitis B by ingesting contaminated food, stress, or casual contact with a positive individual (Chak, Sarkar, & Bowlus, 2016). Physician knowledge of the screening for hepatitis infection and the care and management of infected patients are additional barriers to prevention.

Advances in hepatitis research have led to strategies and technologies that improve hepatitis prevention and care. For example, the guidance on screening, diagnosis, monitoring, and managing infected persons is updated periodically as new knowledge from research becomes available (CDC, 2021). Targeted prevention efforts such as large-scale hepatitis B vaccination,

hepatitis testing with linked treatment for HBV, and a cure for HCV infections have substantially reduced incidence and prevalence (CDC, 2020).

However, these interventions need to be more broadly adopted and sustained to achieve national elimination goals. The nation is presented with a unique opportunity to implement national plans to guide policy development at the state and regional levels; from providing support for implementing effective interventions to conducting health promotion activities that influence behaviors and social norms; and tracking progress towards goals needed for hepatitis elimination (CDC, 2019). Therefore, understanding elimination challenges at the state level is crucial to inform local efforts, practical regional strategies, and approaches.

Pathways to infection: a brief description of clinical aspects of infection

Viral hepatitis infection is characterized by an inflammation of the liver caused by a virus that affects liver function. For hepatitis B and C, an infection can be short-term (acute) or long-term (chronic). Overall, symptoms of hepatitis infection include nausea, fever, loss of appetite, abdominal pain, joint pain, dark urine, jaundice, fatigue, vomiting, and light-colored stools (Department of Health and Human Services, 2020). Many infected people do not have symptoms and are unaware of their infection. In most acute infection cases, symptoms develop between two weeks to six months after infection (CDC, 2021). Depending on the type, hepatitis can spread through contact with contaminated food or water (hepatitis A) or through contact with an infected person's blood and other body fluids (hepatitis B and C).

Hepatitis B Virus (HBV)

Specifically, symptoms of acute hepatitis B infections include body aches and pains, abdominal pain, nausea, headaches, vomiting, rash, fever, dark-colored urine, light stools, and jaundice (yellowing of skin and eyes). Infants and children who become infected with hepatitis B

at a young age are more likely to develop chronic infection later in life compared to adults, leading to serious health complications. HBV spreads through contact with body fluids of an infectious person, and no specific treatments currently exist for HBV infection, but there are highly effective vaccines used to prevent HBV.

There are many risk factors for chronic hepatitis B virus infection. These include being born to a hepatitis B infected mother, household exposures, sexual exposure to partners with hepatitis B infection, sharing drug injection equipment, exposure to hepatitis B contaminated blood or other bodily fluids. Hepatitis B virus infection is diagnosed with specific serologic markers: hepatitis B surface antigen (HBsAg), anti-HBs (antibody to HBsAg), immunoglobulin class M (IgM) hepatitis B core antibody (anti-HBc), and immunoglobulin class G (IgG) anti-HBc; and at least one of these markers is present during HBV infection (Haber & Schille, 2015). Anti-HBc indicates previous HBV infection; HBsAg indicates current chronic infection; and anti-HBs indicates immunity (Roberts et al., 2016).

HBV Vaccine History

The first plasma-derived hepatitis B vaccine called Heptavax manufactured by Merck Pharmaceuticals was licensed in 1981 by the Food and Drug Administration (FDA). The United States discontinued this vaccine in 1990, and a new vaccine, Recombivax HB, was licensed in the United States in 1986; a second vaccine, Engerix-B, was approved in 1989. Both vaccines are a three-dose series given at 0, 1, and 6 months. Hepatitis B virus became a nationally notifiable infection during the 1970s, and before the introduction of the vaccine, there were approximately 9.6 per 100,000 cases per year in the U.S. (Haber & Schille, 2018).

In 1991, the Advisory Committee on Immunization Practices (ACIP) recommended that the HepB vaccine be included as part of the routine vaccination schedule for all infants born in

the United States (MMWR, November 22, 1991). In 1994, the ACIP expanded its recommendation to include previously unvaccinated children between the ages of 11-12 years and all unvaccinated children ages 0 -18 years in 1997. The vaccine was made available through the Vaccine for Children (VFC) program (MMWR, January 22, 1999). The introduction of the hepatitis B vaccine and the national recommendation on infant vaccination from the ACIP decreased the rate of acute HBV infection by 90% to about 1 per 100,000 cases in 2018 (Haber & Schille, 2018).

HBV Infection Trends

Acute HBV Infection Trends

Data from the National Notifiable Diseases Surveillance System indicates that although the rate of hepatitis B infection has trended downwards slowly, infection remains highest among persons aged 40 - 49 years, with a rate of 2.7 cases per 100,000 people in 2019. Overall, the rate of acute hepatitis B infection has varied for all age groups 20 years and above since 2015 (CDC NNDSS, 2019). In 2015, the rate of acute HBV infections reported to CDC was at 1.1 cases per 100,000 population; recent 2019 reports show acute HBV infection rate of 1.0 cases per 100,000 population (CDC, 2020). Across states, the rates of reported cases for hepatitis B infection ranged from the highest of 4.3 cases per 100,000 population in Maine to the lowest of 0.1 cases per 100,000 population in Connecticut.

Chronic HBV Infection Trends

Between 1980-1991, an estimated 200,000-300,000 new hepatitis B infections occurred each year, with an estimated 4,000-5,000 HBV-related deaths annually from cirrhosis or chronic hepatitis-B-related liver infection (MMWR, February 1990). The prevalence of chronic HBV infection decreased by about 79% among persons aged 6-19 years between 1999-2006 (Roberts

et al., 2016). The AIDS epidemic slowed the initial adoption of the hepatitis vaccine in the 1980s; however, since the early 1990s, vaccination has successfully reduced disease burden and conferred immunity against hepatitis B infection (Meireles, Marinho, & Van Damme, 2015). In the United States, acute HBV infection is slowly increasing with reported cases between 2014 and 2015, going from 2,791 cases to 3,370 cases, respectively (Yeo & Nguyen, 2020), particularly among at-risk groups such as among persons who inject drugs.

Challenges with decreasing the rate of infection and eliminating HBV are amplified with the migration to the U.S. of persons from HBV endemic regions in East Asia and sub-Saharan Africa. Immigrants may already be chronically infected with hepatitis B, increasing disease prevalence in the U.S. (Roberts et al., 2016). Among Medicare beneficiaries aged 65 and older, chronic hepatitis B infection burden is highest among Asians, African refugees, and Pacific Islanders (Yeo & Nguyen, 2021); this increases the demand for healthcare resources needed to manage and treat comorbidities.

Hepatitis C Virus (HCV) Infection

Hepatitis C is spread primarily through contact with an infected person's blood. Most infections occur among people who inject drugs because of sharing needles or other drug paraphernalia (CDC, 2020). The estimated incidence of hepatitis C virus infection before 1965 was low; infection incidence increased steadily in the 1980s and stayed high with about 230,000 infections occurring each year (MMWR, August 17, 2012, p.3). The 2012 MMWR also reported that an analysis of data from a national health survey showed that before July 1992, 55% of persons ever infected with HCV reported having an exposure risk through injection drug use or blood transfusion and 45% reported no known exposure risk. Other potential exposures include being born to an HCV-infected mother, having received prolonged hemodialysis, intranasal drug

use, having received invasive healthcare procedures, being incarcerated, health worker exposures (i.e., getting stuck by a needle), and getting a tattoo (MMWR, August 17, 2012, p.3).

While some persons may clear the infection from their bodies without treatment, over half of those infected with hepatitis C who do not receive treatment will develop a lifelong chronic infection. Injection drug use (IDU) is the most recognized behavior strongly associated with HCV infection. Due to the lack of national-level IDU data, some research studies have used reported acute HCV infection as a proxy outcome for IDU (Van Handel et al., 2016; Sharareh et al., 2020; Wesner et al., 2020; Bergo et al., 2021). There is no vaccine for hepatitis C, but recent advances in research have led to advanced treatment therapies for HCV infection that can cure the disease in 8 to 12 weeks.

The introduction of direct-acting antivirals (DAAs) changed the care cascade for hepatitis C treatment in the U.S (Chhatwal, Chen, Bethea, Hur, Spaulding, & Kanwal, 2019). Since December 2013, hepatitis C treatment has become more accessible with the release of innovative, affordable therapies that have revolutionized care for people infected with HCV (Henry, 2018). In the U.S. Sovaldi™ and Olysiso™ were "the first oral, interferon-free treatments with minimal side effects" and combined with other drugs used to complete antiretroviral therapy for hepatitis C treatment.

Treatment of infected persons has increased the rate of sustained virologic response (SVR) to very high levels, curing over 90% of infections (Hagan, Sulkowski, and Schinazi, 2014). However, certain factors such as the implementation of universal screening and treatment restrictions, and controlling the rate of new infections, affect improvements in the hepatitis C care cascade (Chhatwal et al., 2019). Although treatment for HCV is highly effective, people can become re-infected. As a result, the U.S. Preventive Services Task Force recommends screening

for all adults aged 18 to 79 years. Furthermore, the CDC recommends that persons engaged in risky behaviors and people on dialysis get tested for hepatitis regularly. An HCV antibody test is used to detect exposure to HCV infection, this test is also called the anti-HCV test. A positive anti-HCV test is followed by a virologic detection assay, typically a nucleic acid test, the HCV RNA test, or a PCR test to detect active infection.

HCV Infection Trends

Acute HCV Infection Trends

Data from the National Notifiable Diseases Surveillance System indicates that although the rate of hepatitis C infection remains highest among persons aged 20 - 30 years, the acute infection rate has increased for all age groups 20 years and above since 2010 (CDC NNDSS, 2019). In 2015, the rate of acute HCV infections reported to CDC was at 0.81 cases per 100,000 population which required a reduction of 69.1% to meet 2020 goals (CDC, 2017). Recent 2019 reports show acute HCV infection rate as 1.3 cases per 100,000 population, much higher than the 2015 rate.

Chronic HCV Infection Trends

Chronic HCV infection can be asymptomatic for many years while slowly harming the liver. In 2019, 123,312 newly reported cases of chronic hepatitis C were reported to the CDC, with chronic cases from 4 states (Ohio, Pennsylvania, Tennessee, and Florida) accounting for one-third of the total number. The highest rate of newly reported cases in West Virginia, Alaska, Tennessee, and New Mexico (CDC 2019 Surveillance Report). According to the 2019 report, persons aged 30-39 years accounted for 25% of the total cases; 64% occurred among males and 78% among persons in urban areas. The rate of HCV infection in the U.S. has increased mainly

among males, American Indians/Alaska Natives, and persons aged 20-29 (Rosenberg, Hall, Sullivan, Sanchez, Workowski, Ward, and Holtzman, 2017).

Data from the National Health and Nutrition Examination Survey (NHANES), a survey that collects blood specimens to test for antibodies and RNA, provides prevalence estimates of HCV infection in the United States. Between 2003 -2010, the NHANES survey data estimates indicated that about 3.6 million people in the United States had HCV antibodies, and of these, 2.7 million people were infected (Edlin, Eckhardt, Shu, Holmberg, and Swan, 2015). Edlin and colleagues specified three potential sources of underestimation in the NHANES data, including omitting several large populations, poor representation of groups at an increased risk for HCV infection, and nonresponse bias from persons who opt-out of participating in all parts of the survey. In 2015, the prevalence of HCV infection in the United States ranged from 3.4 million to 6.0 million, of which about 3.5 million were infected (Edlin et al., 2015).

The Chronic Hepatitis Cohort Study (CHeCS) is a racially diverse longitudinal multicenter cohort study among hepatitis B and C patients from 4 geographically distinct health systems across the country. CHeCS data helps assess access to care and care outcomes in persons infected with viral hepatitis. Lu and colleagues (2019) examined the trends of chronic hepatitis B virus infection and found that between 2006 and 2015, the incidence rates among patients in the Asian American/American Indian/Pacific Islander category were 20.5 times higher compared with non-Hispanic Whites and 2.8 times higher than African American patients (Lu et al., 2019). Additionally, patients aged less than or equal to 40 years old or between 61-70 years old and non-White minority populations had the fastest decline in incidence rates (Lu et al., 2019).

Mortality from Chronic Hepatitis

In 2013, deaths associated with HCV infection surpassed the total mortality from 60 other nationally notifiable diseases (Edlin, Eckhardt, Shu, Holmberg, and Swan, 2015). Using data from three publicly available sources, Rosenberg, and colleagues (2017) estimated state-level prevalence of HCV infection and found that states in the West and South of the U.S. were most impacted (Rosenberg et al., 2017).

Table 2: Groups most affected by acute hepatitis

	Groups Most Affected by Acute Hepatitis Infections in 2019			
Hepatitis Type	**Age**	**Sex**	**Race/Ethnicity**	**Risk**
HBV	40-47 years (2.7 cases per 100,000)	Males (1.3 cases per 100,000)	White, non-Hispanic (1.0 cases per 100,000)	Injection Drug Use (IDU)
HCV	30-39 years (3.2 cases per 1000,000)	Males (1.6 cases per 100,000)	American Indian/Alaska Native (3.6 cases per 100,000)	Injection Drug Use (IDU)

In 2019, CDC's surveillance report data indicate that 14,242 hepatitis C-associated deaths were reported among residents. Persons aged 55-74 years had the highest mortality rates, and Whites accounted for 64%. Still, the rates among American Indian/Alaska Native persons and non-Hispanic Blacks were 2.8 times and 1.8 times respectively higher than those among non-Hispanic White persons.

Current HBV and HCV Trends

National NHANES surveillance data indicate that an estimated 862,000 adults were living with hepatitis B virus (HBV) infection in 2016, while 2.4 million adults were estimated to be living with hepatitis C virus (HCV) infection. The most recent 2019 CDC national surveillance reports 20,700 estimated acute HBV infections and about 57,500 estimated acute HCV infections. Agreeably, the interventions needed to stop hepatitis-associated mortality are

different from the interventions required to halt transmission of viral hepatitis for each type of infection.

Risk factors for hepatitis infection

The opioid epidemic and injection drug use (IDU) have increased the rates of infectious diseases, including viral hepatitis and HIV infections across the country, due to the lack of data on injection drug use and the high correlation between drug use and hepatitis C infection. Researchers have used HCV infections as a proxy to measure injection drug use among persons in research studies (Van Handel et al., 2017). Van Handel and colleagues (2017) conducted a multi-step analysis that identified county-level vulnerabilities for the rapid spread of new and increasing HCV infections and HIV infections associated with drug use. The study identified six indicators associated with acute HCV infections: prescription opioid sales, drug-related overdose deaths, unemployment, per capita income, white (race), non-Hispanic race/ethnicity, and buprenorphine prescribing.

Challenges and missed opportunities for reducing and viral hepatitis infections and preventing disease persist. In addition to individual risk, factors such as testing limitations, treatment barriers, insufficient surveillance data, and a lack of awareness of infection contribute to the slow progress over the years. Successful strategies and approaches should include efforts to address discrimination against positive individuals, stigma, and the social determinants that affect health outcomes.

Prevention Strategies and Approaches

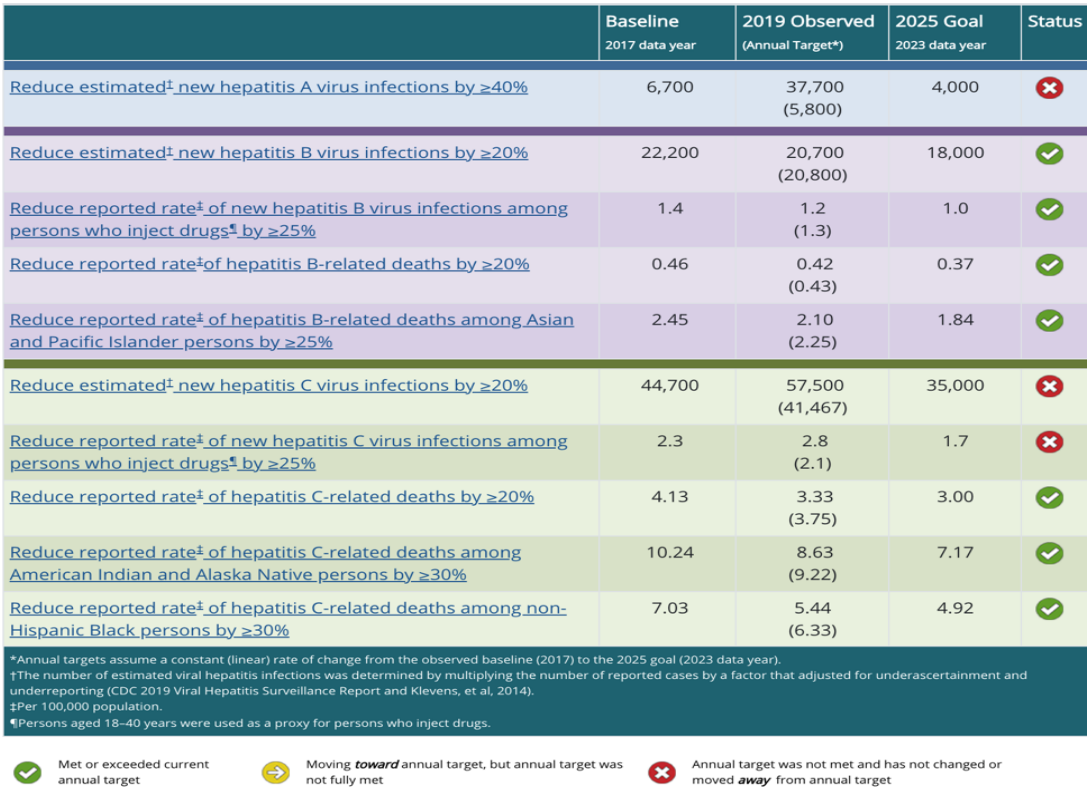
In collaboration with other national partners, the CDC supports state, city, and local health departments to improve existing prevention programs, mobilize community health advocates, and educate health care providers and the local community to prevent viral hepatitis

infections (CDC, 2020). These programs promote recommendations by the Advisory Committee on Immunization Practices (ACIP) on universal hepatitis B vaccinations for adults aged 19 to 59 years, as well as the CDC and the U.S. Preventive Services Taskforce (USPTF) recommendation on testing/screening, care, and treatment for both hepatitis B and hepatitis C infection (CDC 2020).

Because injection drug use is the most common risk factor for HBV and HCV infection, some states have enacted public health laws and regulations to help address high infection rates across the U.S. (Campbell et al., 2017). In an analysis of state laws to govern access to safe injection equipment, Campbell, and colleagues (2017) found that only three states had comprehensive laws and Medicaid policies with full access to preventive and treatment services for persons who inject drugs without any restrictions. These laws provide people who inject drugs (PWIDs) with access to clean needles and syringes and specifically include 1) authorizing syringe exchange programs; 2) retail sale of syringes and needles to PWIDs; 3) removing needles and syringes from the definition of drug paraphernalia (CDC, 2019).

Preventive health services coverage efforts inform the CDC's, Division of Viral Hepatitis, 2025 Strategic Plan and set priorities for the preventive health services needed to end the viral hepatitis epidemics in the United States. The plan outlines strategic approaches, goals and objectives, and outcome measures to reduce disparities, infection, related illness, and deaths caused by viral hepatitis in the United States by 2025.

The DHHS's Roadmap to Elimination (2021 – 2025) outlines a comprehensive plan to eliminate viral hepatitis through five high-level goals. Similarly, international organizations like the World Health Organization (WHO) set a goal to reduce viral hepatitis-related mortality by 65% globally by 2030.



	Baseline 2017 data year	2019 Observed (Annual Target*)	2025 Goal 2023 data year	Status
Reduce estimated‡ new hepatitis A virus infections by ≥40%	6,700	37,700 (5,800)	4,000	✗
Reduce estimated‡ new hepatitis B virus infections by ≥20%	22,200	20,700 (20,800)	18,000	✓
Reduce reported rate‡ of new hepatitis B virus infections among persons who inject drugs¶ by ≥25%	1.4	1.2 (1.3)	1.0	✓
Reduce reported rate‡of hepatitis B-related deaths by ≥20%	0.46	0.42 (0.43)	0.37	✓
Reduce reported rate‡ of hepatitis B-related deaths among Asian and Pacific Islander persons by ≥25%	2.45	2.10 (2.25)	1.84	✓
Reduce estimated‡ new hepatitis C virus infections by ≥20%	44,700	57,500 (41,467)	35,000	✗
Reduce reported rate‡ of new hepatitis C virus infections among persons who inject drugs¶ by ≥25%	2.3	2.8 (2.1)	1.7	✗
Reduce reported rate‡ of hepatitis C-related deaths by ≥20%	4.13	3.33 (3.75)	3.00	✓
Reduce reported rate‡ of hepatitis C-related deaths among American Indian and Alaska Native persons by ≥30%	10.24	8.63 (9.22)	7.17	✓
Reduce reported rate‡ of hepatitis C-related deaths among non-Hispanic Black persons by ≥30%	7.03	5.44 (6.33)	4.92	✓

*Annual targets assume a constant (linear) rate of change from the observed baseline (2017) to the 2025 goal (2023 data year).
†The number of estimated viral hepatitis infections was determined by multiplying the number of reported cases by a factor that adjusted for underascertainment and underreporting (CDC 2019 Viral Hepatitis Surveillance Report and Klevens, et al, 2014).
‡Per 100,000 population.
¶Persons aged 18–40 years were used as a proxy for persons who inject drugs.

✓ Met or exceeded current annual target
→ Moving ***toward*** annual target, but annual target was not fully met
✗ Annual target was not met and has not changed or moved ***away*** from annual target

Source: Progress toward viral hepatitis elimination in the United States, 2017. Available at: https://www.cdc.gov/hepatitis/policy/PDFs/NationalReport.pdf.

Figure 1: Indicators showing progress toward viral hepatitis elimination

Furthermore, Goal 3.3 of the United Nations 2030 Agenda for Sustainable Development calls for ending the epidemics of communicable diseases and precisely an action to "combat hepatitis" (United Nations, 2015). National strategic plans in the United States incorporate targets of the WHO global strategy to its 2030 elimination goal.

Monitoring Progress of Viral Hepatitis Infections

To objectively assess progress towards achieving national viral hepatitis goals, the CDC reports on ten selected indicators for hepatitis infection in the annual national surveillance progress report, as shown in Figure 1.

These indicators include 1) estimated new HAV infections, 2) estimated new HBV infections, 3) rate of new HBV infections among PWIDs, 4) rate of hepatitis B-related deaths, 5)

rate of hepatitis B-related deaths among Asians and Pacific Islanders, 6) estimated new HCV infections, 7) rate of new HCV infections among PWIDs, 8) rate of hepatitis C-related deaths, 9) rate of hepatitis C-related deaths among AI/AN, and 10) rate of hepatitis C-related deaths among non-Hispanic Blacks

A snapshot of the CDC's 2020 National Viral Hepatitis Progress Report (inserted above) shows measurable progress for seven out of ten key indicators. Indicators met or exceeded their targets based on set goals to prevent new infections and eliminate the viral hepatitis A, B, and C. For hepatitis B and C particularly, one indicator met the current annual target, three indicators did not meet their target, did not change, or moved away from the annual target. In 2019, reductions in incidence for HBV infections were minimal even with the progress of decreasing infection rates among high-risk groups, including persons who inject drugs (PWIDs), Asians, and Pacific Islanders. New HCV infections increased particularly among PWIDs (CDC 2021 National Viral Hepatitis Progress Report).

Racial/ethnic disparities in viral hepatitis infection are magnified by the knowledge, attitudes, and behaviors of minority populations with a high disease burden. A community-based participatory qualitative research study conducted among recent African immigrants in Minnesota indicated that study participants were unaware of viral hepatitis screening or testing, vaccination, and treatment services available in their community (Mohamed et al., 2020). This finding provides further evidence to support the need for culturally appropriate tools and strategies to address viral hepatitis-related disparities in different communities.

For example, the San Francisco Hep B Free Campaign provides free and low-cost hepatitis testing and vaccinations to Asian and Pacific Islanders throughout San Francisco. Additionally, the Hep Free 2030 Hawaii hepatitis elimination strategy has five priorities:

promoting equity and data use in decision-making, increasing awareness, access to care, and advocacy. Furthermore, to improve access to care for persons with HCV infection in underserved communities, the Extension for Community Health Outcomes (ECHO) effectively trained primary care providers to treat complex HCV-related conditions (Arora et al., 2011). This approach successfully increased access to specialized medical and health resources for populations in hard-to-reach communities.

Problem Statement

Viral hepatitis infection in the United States (U.S.) has been studied extensively, and the research on care, management, and treatment for chronic hepatitis B and C patients is well known. However, infections persist across the country, with disproportionate incidence, morbidity, and mortality rates among specific populations. Advances in treatment for HCV infection and practical strategies to further prevent hepatitis B virus (HBV) both present an opportunity to eliminate viral hepatitis in the United States and globally. Therefore, it is essential to understand the persistent challenges and obstacles to eliminating hepatitis in the United States. A deep-dive analysis into prevention efforts in states with high infection rates for hepatitis B and hepatitis C will help identify gaps in current efforts leading to more targeted prevention efforts.

CHAPTER 2

LITERATURE REVIEW

Introduction and History of Viral Hepatitis Prevention

Each year, about 1.5 million deaths are caused by viral hepatitis globally, higher than other infectious diseases like tuberculosis, malaria, or HIV. International and national agencies recognize the immense burden of viral hepatitis infection and the need to work towards elimination. The World Health Organization calls for eliminating viral hepatitis as a public health threat by 2030, while Goal 3.3 of the United Nations (UN) Sustainable Development Goals is to end the epidemics of communicable diseases and combat hepatitis by 2030 (United Nations, 2020). In the United States, the Health and Human Services (HHS) developed an action plan with goals and priorities for hepatitis elimination. Additionally, the Centers for Disease Control and Prevention (CDC) published the 2025 strategic plan, aligning with the HHS national plan.

Individual state-level efforts to achieve national elimination goals in the United States align with the goals and priorities of the HHS national action plan and the CDC's strategic plan. In a paper published by Lazarus and colleagues (2018) titled the "*Association between national viral hepatitis policies/programmes and country-level socioeconomic factors: a sub-analysis of data from the 2013 WHO viral hepatitis policy report,*" researchers found that with the existence of key national hepatitis prevention policies and programs, there was no difference in the reduction of the burden of hepatitis infection between countries with higher and lower socioeconomic status indicators (Lazarus et al., 2018). This research found that to effectively

reduce the burden of hepatitis infection, a better understanding of the local environment, including multiple interactions of socioeconomic factors, service delivery methods, and improved health outcomes are needed. As a result, it is vital to examine state-level readiness to reduce the incidence and prevalence of hepatitis infection to achieve set elimination goals.

Tordrup and colleagues (2019) agree that hepatitis elimination can be achieved with sufficient levels of health coverage for the delivery of core interventions (Tordrup et al., 2019). Core interventions from many years of research include immunizing infants against hepatitis B, timely administration of hepatitis B vaccination at birth to prevent mother-to-child hepatitis B virus (HBV) transmission, and the provision of harm reduction services for people who inject drugs to prevent hepatitis C virus (HCV) infection, including blood and injection safety, and improved testing, linkage-to-care, and treatment for HBV and HCV infections (WHO, 2017).

Most people infected with hepatitis are asymptomatic and unaware of their infection at the onset; therefore, routine testing for viral hepatitis help to identify patients for treatment to prevent disease spread. For hepatitis B, about 60% of those infected are unaware of their infection and remain unaware until the onset of end-stage liver disease or cirrhosis (Krist et al., 2020). The United States Preventive Services Task Force (USPSTF) recommends screening and testing for hepatitis B infection in adolescents at an increased risk for infection (*JAMA.* 2020;324(23):2415-2422).

Similarly, screening for hepatitis C virus infections is recommended for all adults aged 18 to 79 years; medical evaluation and treatment as needed depending on the status or phase of infection (the United States Preventive Services Task Force, 2020). The tables below show the laboratory tests and phase of infection (status) for hepatitis B virus (Table 1) and hepatitis C virus (Table 2), respectively.

Table 3a: Hepatitis B tests and status

HBsAg	Anti-HBs	Anti-HBc	Phase of Infection (Status)
Negative	Negative	Negative	Susceptible to the infection
Negative	Positive	Negative	Immunity due to HBV vaccination
Negative	Positive	Positive	Immunity due to natural infection
Positive	Negative	Positive	Infected with HBV

Table 3b: Hepatitis C tests and status

HCV antibody	HCV RNA	Status
Negative	~	Non-reactive
Positive	Not Detected	Exposed, No current HCV infection
Positive	Detected	Current HCV infection

Hepatitis C virus (HCV) infection is the most common form of viral hepatitis in the United States, followed by hepatitis B virus (HBV) infection. Advances in research and drug development have led to significant progress in disease elimination. These advances include: a highly effective vaccine that prevents hepatitis B, improvements in blood safety and infection control, hepatitis B treatment options to avoid death, and curable therapies for hepatitis C infection with a shorter, more tolerable treatment course (National Academy of Sciences, Engineering, and Medicine Report, 2017).

Hepatitis C infections can be cured with antiviral treatments that are over 90% effective in achieving a sustained virologic response (SVR). Although there is no cure for hepatitis B, therapies reduce mortality risk by 50%. Also, there is a safe and effective vaccine that prevents infection and proven medical interventions that can significantly mitigate the significant effects of the infection (Lazarus et al., 2018).

Several interventions are being implemented to eliminate viral hepatitis as a public health threat by 2030. The interventions include increased hepatitis B vaccine coverage, prevention of mother-to-child transmission of hepatitis B infection, screening of blood donations with quality

assurance and injection safety, harm reduction services, and increased testing and treatment for persons infected with hepatitis B or C. Indicators for these interventions are tracked at state, national, and international levels.

Hepatitis B Trends in the United States

In 2019, the national acute infection rate for hepatitis B was 1.0 per 100,000 population. States or jurisdictions reported acute infection rates above the national average at 4.0 reported cases per 100,000 population (Maine, West Virginia, and Kentucky); rates ranged from 4.3 cases per 100,000 population (Maine) to 0.1 cases per 100,000 population in Connecticut, Montana, Wisconsin, and Hawaii (2019 CDC Surveillance Report). Notably, the availability of needed resources to conduct extensive surveillance and prevention activities in each state varies.

Vaccinations and advances in available treatment options help keep people from getting infected and patients living longer (Lu et al., 2019). Based on CDC surveillance data, universal vaccination campaigns started in the early 1990s and have successfully kept the rate of acute hepatitis B infection low among children and adolescents. In 2019, persons aged 30-49 years accounted for more than half of acute cases reported. Among those 0-19 years, zero acute cases were reported to CDC every year since 2015; the acute hepatitis B rate in 2019 among those 20-29 years was also relatively low at 0.5 reported cases per 100,000 population.

Using data from the Chronic Hepatitis Cohort Study (CHeCS) – a multicenter cohort study of chronic hepatitis B and C patients, Lu and colleagues (2019) found that between 2006 and 2014, the prevalence of chronic hepatitis B among patients in the United States increased, then decreased in more recent years. For newly reported cases of chronic infection, persons in the Asian American/American Indian/Pacific Islander category had 20.5 times higher rates than white patients, and among African Americans, 2.8 times higher compared with whites (Lu et al.,

2019). Hepatitis B prevalence is influenced by the large proportion of patients with chronic infection in the United States who have emigrated from endemic countries, particularly Asian and African migrant groups.

Hepatitis C Trends in the United States

The national hepatitis C rate across the United States increased every year since 2017 – with a rate of 1.2 acute cases per 100,000 in 2018 to 1.3 acute cases per 100,000 population in 2019 due to the impact of the nation's opioid crisis as the highest reported rate occurred among those 20-39 years (CDC, 2020). In the 2019 CDC surveillance report, the acute hepatitis C infection rate reported ranged from 4.8 cases per 100,000 population in Indiana to 0.2 cases per 100,000 population in South Carolina, Louisiana, Connecticut, Nebraska, and Texas.

The risk for hepatitis C infection varies by state (Rosenberg et al., 2017). Rosenberg and colleagues show that states with a high urban population, a high proportion of people who inject drugs, and states with a high proportion of Native Americans tended to have a high estimated anti-HCV prevalence. Therefore, to effectively identify and treat patients with hepatitis C and achieve elimination goals, state-level efforts should continue to address the high burden of infection in these groups disproportionately affected.

Screening and Treatment Strategies

Hepatitis B Screening and Vaccination

Because transmission of hepatitis B virus is through mucosal or percutaneous contact with infectious blood or body fluids, some populations are at increased risk of becoming infected with HBV. The CDC recommends targeted HBV screening, prevention, and linkage to care for at-risk groups, including people who inject drugs, people with HIV, men who have sex with men, infants born to HBV-infected mothers, people born in the United States but not vaccinated

as infants with parents who were born in regions with high rates of HBV infection, people born in areas with a high prevalence of HBV (countries with HBsAg prevalence ≥ 2%), people who require immunosuppressive therapy, household members and sexual contacts of HBV-infected people, blood and tissue donors, people with end-stage renal disease, pregnant women, and people with elevated alanine aminotransferase levels (≥ 19 IU/L for women, ≥ 30 IU/L for men).

Five hepatitis B vaccines are currently licensed in the United States, three single-antigen vaccines: ENGERIX-B®, RECOMBIVAX HB®, HEPLISAV-B™; and two combination vaccines: PEDIARIX®, TWINRIX® for persons six weeks through 6 years and 18 years and older respectively. Different vaccine dose formulations are recommended for persons 0-19 years, 11-15 years, and 20 years and older. The vaccine schedule often used is three intramuscular injections administered at 0, 1, and 4-6 months, respectively. Heplisav-B, a new formulation, is approved for two doses administered one month apart. (CDC, 2020).

The hepatitis B virus vaccine effectively prevents HBV infection and provides long-term protection from chronic hepatitis B virus infection and clinical illness (CDC, 2020).
The Advisory Committee on Immunization Practice (ACIP) recommends that all adults, particularly populations and groups at-risk for infection receive the hepatitis B vaccine. The groups include all infants, unvaccinated children under the age of 19 years, persons at risk for infection through sexual exposure, people at risk for infection by exposure to blood (percutaneous or mucosal), people infected with HCV or HIV, international travelers to countries known to have high or intermediate endemic hepatitis B infection levels (countries with HBsAg prevalence ≥2%), people with chronic liver disease, people who are incarcerated, and all other people who need protection from HBV infection.

The USPSTF's assessment of the magnitude of net benefit resolves with moderate certainty that HBV screening in adults and adolescents at an increased risk is of moderate net benefit. In a recent analysis to identify and summarize gaps and barriers for effective hepatitis B virus prevention, testing, and linkage to care in the United States, Yeo and Nguyen (2021) conducted a systematic review of hepatocellular carcinoma (HCC) surveillance adherence. This review found that data for proper care and retention in treatment was poor, with about 64.5 million high-risk adults having no evidence of hepatitis B virus immunity. The reasons for this lack of adherence are many, some of which were identified to include a lack of physician knowledge, lack of access to proper medical care, linguistic and cultural barriers and stigma, and a lack of patient awareness and health literacy (Yeo and Nguyen, 2021).

Some hepatitis B prevention programs target high-risk groups and introduce stigma to prevention efforts. To optimize the continuum of care and treatment options available for hepatitis B prevention, states across the country need to scale up their screening efforts and develop system-wide interventions. These include scaling up primary, secondary, and tertiary prevention efforts to lessen barriers in accessing vaccinations, proper care, and treatment for hepatitis B and hepatitis C infection.

Hepatitis C Screening

Many people affected with hepatitis C do not have symptoms. According to WHO data, globally, less than 5% of people infected are unaware of their infection, including several in the United States (Stasi, Silvestri & Voller, 2020; Ahmed et al., 2017). There is no vaccine to prevent HCV infection and no effective pre- or postexposure prophylaxis; over half of the people who become infected with HCV will develop chronic HCV infection (Schille et al., 2020). The USPSTF and the CDC recommend that all adults over 18 years receive one-time testing for

hepatitis C infection, all pregnant women receive testing at each pregnancy, and regular periodic testing for people with known risk factors, including people who inject drugs (Schille, Wester, Osborne, Wesolowski, & Ryerson, 2020).

Persons at an increased risk for HCV infection identified by the CDC are: current or former people who inject drugs, including those who have ever injected drugs no matter how long ago, people infected with HIV, prior recipients of blood transfusions or organ transplants (before July 1992), people with selected medical conditions such as those who ever received hemodialysis, children of mothers infected with HCV, and people working in health care, public safety, and emergency medical after exposure to HCV-positive blood through needle sticks, or sharp equipment. Ideally, testing is recommended for anyone who requests a hepatitis C test.

Hepatitis C prevention interventions for people who inject drugs are insufficient in capacity in many states across the United States to effectively prevent hepatitis C transmission and, in most cases, HIV (Larney et al., 2017). New York City recently authorized the nation's first supervised drug injection site to provide injection drug users with clean needles and options for addiction treatment (Mays & Newman, 2021).

Other interventions include opioid substitution therapy (OST) to help minimize opioid use and misuse and support complete cessation of injection practices and needle and syringe exchange programs to prevent disease spread through sharing injection paraphernalia. Compared to similar high-income countries, the United States coverage estimate for needle and syringe programs is low, with low-to-moderate coverage for opioid substitution therapy (Larney et al., 2017). These estimates highlight the need for improvements in interventions, care, and treatment options for hepatitis C infection among people who inject drugs.

Hepatitis C Treatment

Direct-acting antiviral (DAA) treatment for hepatitis C infections introduced in 2011 changed hepatitis C treatment with recent oral therapy medications that are tolerated better, shorter in duration, and have proven more effective in curing HCV infection (Schille et al., 2020). Current treatment for hepatitis C involves an 8–12-week oral therapy of pan-genotypic DAAs proven to be very effective in curing HCV infection with a sustained virologic response (SVR) rate of over 90%, regardless of the HCV genotype being treated (CDC, 2020). Therefore, the key to achieving HCV elimination is increased access to screening and affordable medicines and proper infection management by trained public health professionals (Tordrup, 2019) and among populations at risk.

In addition to proper healthcare management, access to medications is also a challenge. In a 2011 article titled "*Outcomes of Treatment for HCV Infection by Primary Care Providers,"* Arora and colleagues note that the number of persons receiving treatment for HCV infection was low. Prescriptions for HCV antiviral medications reduced by 34% between 2002 and 2007; additionally, older patients and racial and ethnic minorities were less likely to receive the care they needed (Arora et al., 2011).

Prevention efforts to screen patients and provide treatment for hepatitis C are similar across states in the United States. One initiative is the Extended Community Healthcare Outcomes (ECHO) project launched in New Mexico in 1993 that uses video conferencing technology to train primary care providers. It focuses on providing local healthcare providers in communities with no available specialized care with the knowledge, expertise, and guidance needed to treat patients infected with hepatitis C (Arora et al., 2011; Ahmed et al., 2017). The ECHO model improved access to care for populations in underserved areas (Arora et al., 2011)

and has successfully dismantled some barriers to accessing care and treatment for people living in areas with no specialized care available.

The United States can achieve elimination of hepatitis C with the delivery and administration of therapies proven to be effective to the patients who need them, ensuring their compliance with treatment and adequate follow-up (Ahmed, Almashhrawi, Ibdah, and Tahan, 2017). Also, preventing the vertical transmission of infection from mother to child is critical to help reduce disease prevalence and control disease spread.

Perinatal Hepatitis Prevention

Transmission of hepatitis B virus from an infected mother to her baby occurs through percutaneous or mucosal exposure to blood or body fluids, and 80-90% of infants infected at birth become chronically infected with the virus (CDC 2020). Infected infants usually do not have symptoms; however, about 25% of those chronically infected will develop liver cancer or cirrhosis leading to premature death. The perinatal hepatitis B prevention program (PHBPP), which began in 1990, was funded by the CDC to prevent perinatal hepatitis B in the United States. The program requires maternal screening for all pregnant women at each pregnancy, infant vaccination for infants born to HBsAg+ mothers, and post-vaccination serologic testing of infants 1-2 months after the final dose in the series is administered.

The PHBPP aims to quickly identify mothers infected with hepatitis B, ensure infants receive post-exposure prophylaxis promptly, confirm the infant's status with post-vaccination serologic tests, and provide re-vaccination for infants who do not respond to the vaccine initially. According to surveillance data from the National Notifiable Disease Surveillance System (NNDSS), the PHBPP has successfully reduced the rate of new hepatitis B cases.

According to CDC surveillance data, there is increasing perinatal hepatitis C exposure for infants born to infected mothers through vertical transmission. National guidelines recommend testing for infants exposed to hepatitis C infection. Between 2009 to 2014, the prevalence of hepatitis C virus among pregnant reached 3.4 per 1000 births in the United States (Lopata et al., 2020). In a recent study, researchers found that less than 1 in 4 infants exposed to hepatitis C received testing; this number was even lower among African American infants (Lopata et al., 2020).

The populations affected by hepatitis B and hepatitis C differ. Still, some conditions make HBV and HCV ideal for preventive screening, including increasing prevalence and low diagnosis rates, specific and highly sensitive tests, early asymptomatic period, effective therapy, and treatments that improve outcomes (Chak, Sarkar & Bowlus, 2016). Increasing access to screening, treatment, and vaccination (for hepatitis B) is critical to eliminating viral hepatitis by 2030.

Vaccination Coverage

Childhood Vaccine Coverage

The National Immunization Survey (NIS) collects provider-reported immunization records for children on vaccine coverage rates for hepatitis B and other vaccines in the United States. In 2018, the vaccine coverage rate for the recommended three doses for hepatitis B vaccine was at 91.9%, and coverage for hepatitis B birth dose vaccine was at 73.6% (Hill, Elam-Evans, Yankey, Singleton, and Sterrett, 2021). Only 1.0% of children received no vaccination before age 24 months; however, disparities in vaccine coverage were identified for poverty status, race/ethnicity, and health insurance status (Hill et al., 2021). Furthermore, childhood

vaccine coverage among children born in 2017-2018 was 2.1-4.5 percentage points higher compared to those born in 2015-2016 for the hepatitis B birth dose and other childhood vaccines.

Adult Vaccine Coverage

Vaccine administration and booster vaccination coverage rates for adults who may not have received the hepatitis B vaccine series at birth are not well documented in the United States. The National Health Interview Survey (NHIS) collects self-reported information for hepatitis vaccination among adults; adult coverage has remained low for most routinely recommended vaccines, including the hepatitis B vaccine (CDC MMWR, 2012). In the survey, the self-report of vaccine administration is unverified by medical records and is subject to recall bias (Lu, Bryd, Murphy, and Weinbaum, 2011).

An analysis of NHIS data by Williams et al. (2015) found that vaccination coverage (≥ 3 doses) among adults aged ≥ 19 years was at 25%, among adults aged 19-49 years, coverage was 32.6%, and among adults ≥ 50 years 16.1% (Williams et al., 2015). These rates varied (23.7%) compared to whites (35.2%) and Asians (39.3%). Vaccine coverage rates among adults are below the Healthy People target of 90%.

Similarly, Bhuiyan and colleagues (2020) used data from the National Health and Nutrition Examination Survey (NHANES) to examine hepatitis B vaccine coverage by race/ethnicity. For all races, vaccine coverage was at 23.3%. Mexican Americans and African Americans had lower vaccine coverage rates than Whites, men had lower coverage rates than women, and those ≥ 50 years) had lower coverage rates than those 18-29 years (Bhuiyan, Kabir, Mitra, Ogungbe, & Payton, 2020).

Prevalence of Viral Hepatitis Infection

The prevalence of chronic hepatitis B and C in the United States differs among different populations and settings. Between 2008-2019, a total of 25 hepatitis B outbreaks (19 occurring in long-term care facilities, six occurring in other settings) were reported to CDC. Additionally, a total of 43 hepatitis C outbreaks (16 occurring in outpatient or long-term care facilities, 22 in hemodialysis settings, and four because of drug diversion) were reported to CDC. Due to the long incubation period (up to 6 months) and asymptomatic nature of the infection, it is highly likely that only a fraction of outbreaks are detected, reported, and or investigated by health departments (CDC, 2020).

Research shows a higher rate of hepatitis infection among people infected with HIV/AIDS and people born outside the United States; for example, hepatitis B surveillance data indicate that up to 12% of people living with hepatitis B in the United States were born in Africa. Other groups with high levels of exposure to infection include health care providers, people who inject drugs, men who have sex with men, people with diabetes, and people experiencing homelessness. Similarly, chronic hepatitis C infection rate is high among people infected with HIV/AIDS. In 2014-2015, an injection of prescription opioids was linked to an outbreak of HIV infection in a rural county in the United States; 92% of those infected were also co-infected with hepatitis C virus (Van Handel et al., 2016).

States at Risk for HBV and HCV Transmission

In a 2017 CDC Morbidity and Mortality Weekly Report (MMWR) publication, Campbell and colleagues examined state HCV incidence and policies related to services aimed at persons who inject drugs in the United States from 2015-2016. The study found that seventeen states had above average HCV incidence rates compared to the national average. Only three states had

Medicaid policies or state laws considered capable of preventing and treating infections among people who inject drugs. Increases in HCV incidence across the United States are primarily attributed to increases in injection drug use. Many states enacted public health laws and treatment policies to mitigate the transmission risk of HCV, particularly among injection drug users (Campbell et al., 2017).

Van Handel and colleagues sought to understand the growing epidemic of injection drug use, opioid abuse, and high rates of hepatitis C infection and help identify communities vulnerable to a possible outbreak. Researchers identified 220 counties in 26 states as most vulnerable with six indicators associated with acute hepatitis infection, including buprenorphine prescribing potential by waiver, prescription opioid sales, drug overdose deaths, non-Hispanic race/ethnicity, white, per capita income, and unemployment. (Van Handel et al., 2017). This study emphasizes the need for further exploration and targeted interventions to prevent disease transmission and spread.

Factors Affecting Viral Hepatitis Infection Rates

In 2019, 80% of acute hepatitis B cases reported to the CDC were among people aged 30-59 years, and the highest rate of infection occurred among non-Hispanic Whites (1.0 cases per 100,000 population). On the other hand, 63% of the reported acute hepatitis C cases occurred among people aged 20-39 years, and the highest rate of infection was among American Indians/Alaska Natives (AI/AN) (3.6 cases per 100,000) and Whites (1.4 per 100,000 population) (CDC, 2020). Across the different demographic groups, the lack of awareness of infection and the restrictions to treatment access based on disease severity are barriers to receiving treatment (Kim et al., 2019; Greenwald, Waters, & Cayer, 2020).

To identify the societal and cultural barriers to prevention, screening, and treatment of hepatitis infection among African immigrants and refugees living in the United States, Mohamed and colleagues (2020) assessed knowledge, attitudes, and behaviors. This community-based study further emphasized the need for targeted approaches to increase knowledge and awareness of viral hepatitis infection in the African immigrant and refugee community (Mohamed et al., 2020). Culturally appropriate prevention strategies will be more effective in educating hard-to-reach groups.

Several factors account for the differences in acute infection rates in different groups. Surveillance data from the CDC notes that non-Hispanic Whites, non-Hispanic Blacks, and American Indian/Alaska Natives have a higher incidence, prevalence, and mortality (CDC, 2020). This inequity in infection rate adversely affects racial and ethnic minorities who are more likely to be uninsured, limiting their access to screening and treatment. Other barriers to accessing health services can include homelessness or unstable housing, lack of trust in providers, discrimination, racism, communication challenges, language barriers, lack of vacation time from work, and lack of transportation and childcare (HHS, 2020).

Hepatitis C Vulnerability Studies

Certain communities or environments are vulnerable to the rapid spread of hepatitis C infection and IDU-associated HIV infection. As mentioned, opioid use and injection drug use is a significant risk factor for hepatitis C infection and increases the spread of infections (Sharareh et al., 2020). In an extensive vulnerability county-level analysis, Van Handel, and colleagues (2017) used confirmed acute hepatitis C infection cases as a proxy for injection drug use due to their strong correlation. This multi-step analysis identified indicators associated with injection

drug use and increasing hepatitis C or HIV infection rates across the United States. It highlighted 220 counties in 26 states as most vulnerable to hepatitis C infections (Van Handel et al., 2017).

Other researchers have employed the same methodology to identify state-level indicators potentially associated with hepatitis C infection. State-level analysis helps to identify targeted strategies to achieve elimination goals. For example, in South Dakota, with 69% reservation counties and 62% rural counties, the minority counties had four times higher hepatitis C infection rates than non-minority counties (Wesner et al., 2020). Another study examined hepatitis C risk in Illinois at the zip code level and identified rural counties as having a high risk for hepatitis C infection (Bergo et al., 2021). Additionally, social/economic/physical environment, access and resources, and health outcome variables were predictive of high risk for hepatitis C transmission (Bergo et al., 2021).

Consequences of Infection and Disparity in Outcomes

The Chronic Hepatitis Cohort Study (CHeCS) funded by a CDC Foundation grant began in mid-2010. It is a multicenter longitudinal observational cohort study that monitors hepatitis B and C patients and currently serves over 2 million racially diverse patients receiving ongoing care and treatment from 4 geographically distinct health systems in the United States. Study participants are mostly urban hepatitis B and C infected patients. The CHeCS database collects information from multiple sources, including electronic medical records (EMRs), patient intake interviews, billing information, ancillary data from death registries, and related infectious disease reporting systems (i.e., HIV/AIDS). CHeCs data is used for research and allows for longitudinal assessments of hepatitis B and C infection, access to care, comorbidities, adherence to treatment, and disease outcomes (CDC Foundation, 2020).

Viral Hepatitis and HIV Co-infection

The co-infection of hepatitis infection among HIV-infected people creates a hepatitis B virus, hepatitis C virus, and HIV/AIDS infection syndemic. In sub-Saharan Africa, for example, many HIV-positive people are co-infected with hepatitis B or C (Barth, Huijgen, Taljaard, Hoepelman, 2010). This association is less evident in Western countries like the United States, even though a significant number of people are co-infected with hepatitis and HIV, particularly among people involved in high-risk activities such as people who inject drugs and persons who use opioids.

Hepatitis B is prevalent in sub-Saharan Africa and Asia, the origin of most immigrants in Western countries. In these countries, most hepatitis B virus infection are acquired at birth or during early childhood (Barth et al., 2010), but regional variability in the prevalence of infection, particularly in sub-Saharan Africa (Hung et al., 2021). In a recent study, researchers in the United Kingdom determined the prevalence of hepatitis B and C among 2,473 HIV-infected people of African descent; 6.2% were also co-infected with HIV/hepatitis B and 1.3% co-infected with HIV/hepatitis C (Hung et al., 2021).

In the United States, patterns of immigration have changed over time with increases in immigration from hepatitis B endemic regions as foreign-born persons make up a substantial number of the hepatitis burden in the country (Wong et al., 2021). Wong and colleagues (2021) updated a 2011 study and estimated the burden of foreign-born persons infected with chronic hepatitis B virus in the United States. Among those infected, 59% emigrated from Asia, 19% from the Americas, and 15% from Africa. However, researchers found no consistent patterns between hepatitis B infection rates for foreign-born and those in-country (Wong et al., 2021).

Determinants of Increasing Hepatitis Infection Rate

The 2017 national strategy for the elimination of hepatitis B and C report by the National Academies of Sciences, Engineering, and Medicine (NASEM) identifies hard-to-reach people infected with viral hepatitis. This list includes the uninsured, those born outside the United States, people who have mental health problems and substance use disorders, and those who have been incarcerated. Still, some infected people are even less accessible, like those with unstable housing or those experiencing homelessness (NASEM Report, 2017).

Health delivery in the United States is unique because there are separate systems for different classes of people; Medicaid for the poor, Medicare for the elderly, private insurance for most Americans mainly through employment, and government health programs for veterans, active and retired military (Kulesher & Forrestal, 2014). In 2019, about 9.2% of the population was uninsured (Kaiser Family Foundation, 2021) with a health system that stresses freedom of choice, individual responsibility, and pluralism of society.

Disparities in health delivery introduce healthcare access and treatment inequities for hepatitis virus infection. For example, treatment for hepatitis C is about 18.7% in the United States compared to 34% in Europe, and the price of hepatitis C treatment drugs, access to screening for both hepatitis B and C, and availability of medical care is affected by insurance status (Vutien et al., 2017). The Department of Veterans Affairs - one public health system in the United States has successfully reduced treatment inequities. The VA is the largest single HCV care provider in the U.S., with approximately 165,000 veterans in care for diagnosed HCV. To align with the USPSTF and CDC recommendations, in January of 2018, more than 80% of veterans were screened and engaged in care, with over 100,000 initiating treatments for hepatitis C with direct-acting antivirals (DAAs) (Park et al., 2018).

Achieving the goals outlined in the national plans to eliminate viral hepatitis depend on overcoming the identified barriers and enhancing operational interventions, including testing, linkage to care, treatment uptake and adherence, viral suppression, or cure (Zhou et al., 2016). In a systematic review of existing operational interventions, the promotion of hepatitis B testing by lay health workers and scheduled reminders to prompt hepatitis C testing by clinicians increased testing rates. A coordinated approach of substance use, mental health, and treatment services for hepatitis significantly increased treatment uptake, adherence to the treatment regimen, and cure compared to routine care (Zhou et al., 2016).

Current Disease Elimination Activities

In 2021, the CDC provided funds through a competitive cooperative agreement with 59 state, county, and city health department jurisdictions over five years to support an integrated approach to viral hepatitis surveillance and prevention program across the country. Three key strategies emphasized in the agreement include core viral hepatitis outbreak response and surveillance activities (*Component 1*); core viral hepatitis prevention activities (*Component 2*); and special projects-prevention, diagnosis, and treatment related to the infectious disease consequence of drug use (*Component 3*). Fourteen jurisdictions received additional funds for component 3 activities.

The 14 jurisdictions with additional funds include Baltimore City, Florida, Indiana, Iowa, Kentucky, Los Angeles County, Massachusetts, New York City, Oregon, Philadelphia, Rhode Island, Utah, Washington State, and West Virginia. Components 1 and 2 funding focus on surveillance and implementation of prevention projects. Component 3 funds account for the burden of viral hepatitis infection associated with injection drug use in the 14 identified jurisdictions.

The vision for 2021-2025 Health and Human Services National Strategic Plan and the Centers for Disease Control and Prevention's 2025 Strategic plan is to eliminate viral hepatitis in the United States for all people irrespective of their sex, age, sexual orientation, gender identity, religion, race, ethnicity, disability, socioeconomic status, and geographic location (HHS, 2020) and contribute to creating a world without hepatitis. Advanced research and treatment options have led to effective strategies and tools to achieve these goals. Additionally, different national, state, and specialty organizations are working together to achieve viral hepatitis elimination.

For example, the Harm Reduction Coalition focuses on reducing injection drug use by bringing harm reduction strategies such as syringe access implementation, overdose prevention, and treatment activities to scale in different locations. The National Alliance of State and Territorial Aids Directors (NASTAD) is a non-profit association working to end the intersecting epidemics of viral hepatitis, HIV, and other related conditions. And, the National Viral Hepatitis Roundtable is a coalition of advocates, including patients, community-based organizations, health care providers, and public health partners fighting together for an equitable world free of viral hepatitis.

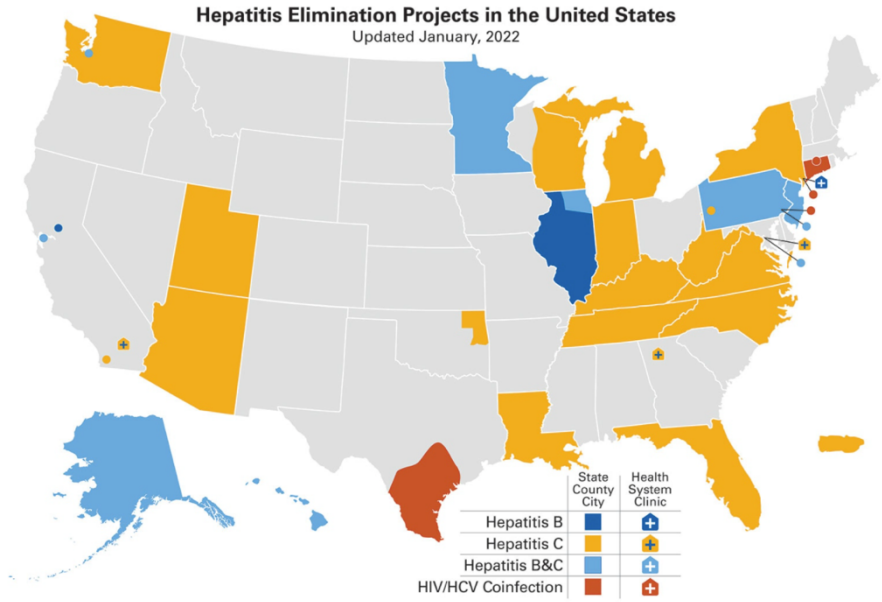
The CDC funds provided to all jurisdictions seek to address focus areas in the recently updated Healthy People 2030 related to immunization and infectious diseases, specifically to: reduce the rate of acute hepatitis B (IID-11); reduce the rate of acute hepatitis C (IID-12); increase the proportion of people who know they have chronic hepatitis B (IID-13), and increase the proportion of people who no longer have hepatitis C (IID-14).

Research Gaps and Study Significance

Viral hepatitis elimination in the United States and globally is achievable with sustained efforts to prevent new infections and treat chronic patients. The WHO encourages countries to

develop and implement national strategic plans (NSPs) to guide appropriate elimination strategies; plans that include strategies from the Global Health Sector Strategy (GHSS) on viral hepatitis elimination by 2030 (Njuguna, Hiebert, Jacques-Carroll, Gupta, & Ward, 2021). A review of global national strategic plans identified gaps such as having a national committee oversight, including elimination cost estimates, having financing plans, having monitoring and evaluation plans, and integration with other infectious diseases.

In the United States, states have individual elimination plans and are implementing strategies to reduce infection. However, based on 2019 surveillance data, minimal progress has been made towards achieving national elimination goals. States, local jurisdiction, non-government organizations, and health systems are collaborating in innovative ways to establish elimination projects across the nation (HHS, 2022). The Department of Health and Human Services recently developed a national map of promising efforts with a wide variety of stakeholders.



Source: U.S. Department of Health and Human Services, January 2022

Figure 2: Hepatitis elimination projects in the United States

At the national level, several agencies and organizations are working to reduce hepatitis incidence, prevalence, and death. For example, the Asian Liver Center at Stanford University established in 1996 by Dr. Samuel So is a non-profit organization that seeks to address high rates of hepatitis B infection among Asians and Asian Americans. The Addiction Technology Transfer Center (ATTC) Network Coordinating Office at the national and network of Regional ATTCs established an initiative, *HCV Current,* with the goal of increasing knowledge of hepatitis C virus among health professionals particularly among people with mental health issues and substance use disorders.

Also at the national level, "Curing Hepatitis among HIV/HCV Coinfected People of Color" is a multi-pronged initiative that supports the expansion of health services for hepatitis C prevention, testing, care, and treatment. In addition, the Jurisdictional Approach to Curing Hepatitis C among HIV/HCV Coinfected People of Color supports jurisdictions in increasing their capacity to provide health services in the continuum of care for HIV/HCV coinfected patients. The FOCUS program created by Gilead facilitates the development and sharing of best practices among partners to overcome barriers and stigma related to the delivery of preventive health services. Local Elimination Programs Leading to Global Action in HCV (LEGA-C) Platform, is also funded by Gilead as part of its hepatitis C and HIV/HCV coinfection investigator sponsored research (ISR) that supports hepatitis C patients with unmet needs in the United States.

Help-4-Hep, a program of The Hepatitis C Association, is a non-profit, peer-counselor, nationwide helpline provided free of charge to anyone who needs support and information. Hep B United is a national coalition that supports local hepatitis B elimination efforts across the country. The Coalition is co-chaired by the Association of Asian Pacific Community Health

Organization and the Hepatitis B Foundation, it comprises over 40 national organizations as well as local hepatitis B community coalitions across 20 states. "*HepVu*" is an online platform that provides state-level data, interactive maps, and educational resources on the burden and impact of viral hepatitis across the United States. This collaborative effort between researchers at Emory University Coalition for Applied Modeling for Prevention (CAMP) project and the CDC, is a great resource in understanding the hepatitis landscape in each state in attempts to focus efforts aimed at eliminating hepatitis B and C infections.

Further research and sustained efforts are needed to understand the challenges at the state and local levels with implementing practical strategies and approaches. In states with exceptionally high infection ratios given the risk factors, this study seeks to examine and explore additional prevention strategies and approaches needed to reduce the rate of acute hepatitis.

CHAPTER 3

METHODS

Conceptual Framework

The conceptual framework illustrated in Figure 3 shows a visual representation of viral hepatitis elimination efforts at the national level using an adaptation of the Donabedian model (1988) for examining health care services and evaluating health care quality. The national viral hepatitis elimination efforts in the United States and the strategies and approaches being implemented at the state-level, guide the conceptual framework for in this study. National elimination efforts are illustrated in three levels: structures, processes, and outcomes. Structures include the resources and needs for improving hepatitis infection surveillance; Processes consist of the evidence-based strategies and interventions adopted to advance hepatitis B and C elimination goals; and the outcomes outline the national elimination goals laid out by the CDC and the HHS.

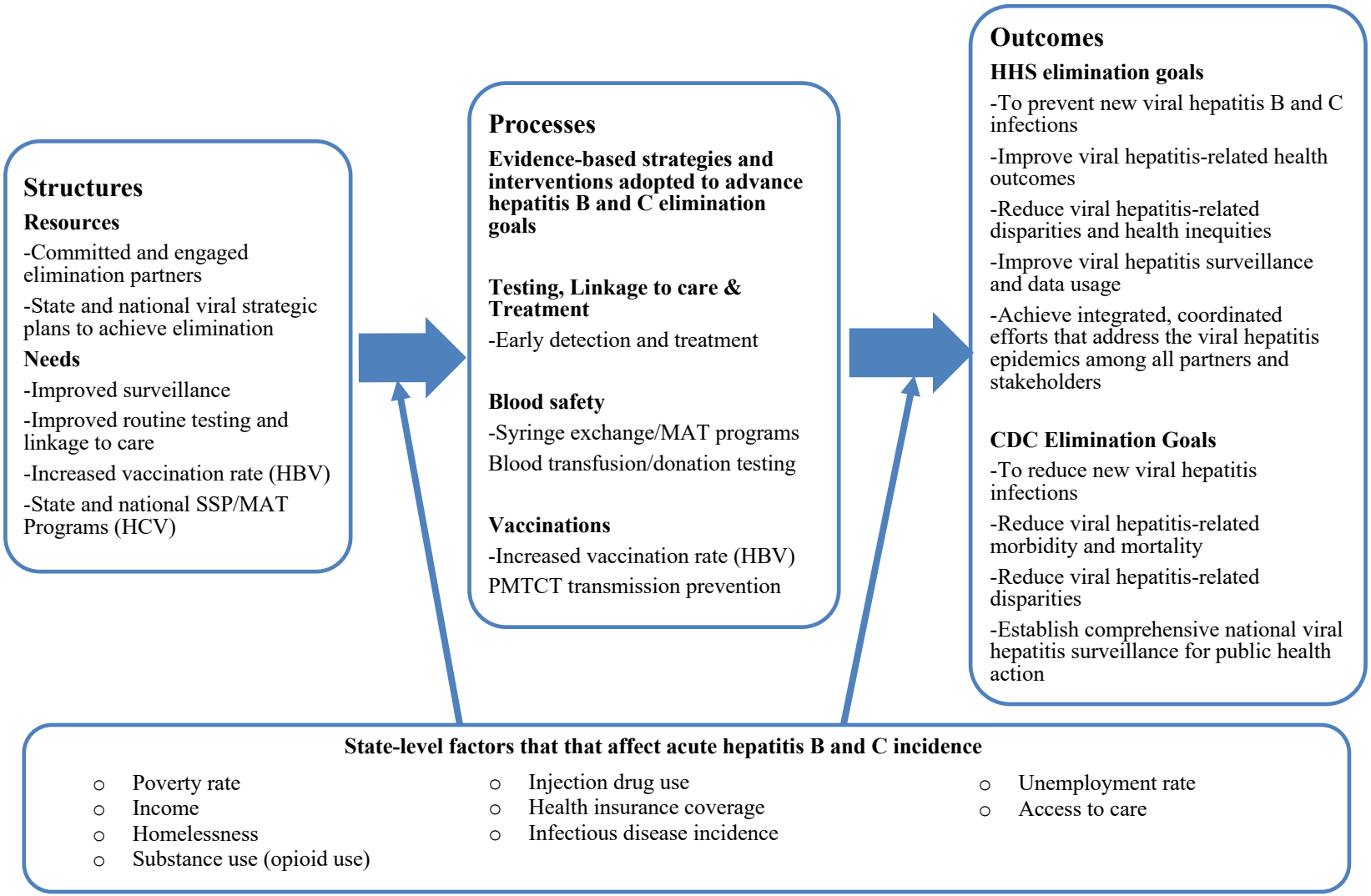
Similarly, the conceptual framework for this study illustrated in Figure 4, shows a stepwise process to examine the relationship between risk factor variables and acute hepatitis infection and identify states with higher or lower calculated ratios given the risk factors. The identified states are examined further to compare state-level efforts to achieve elimination goals. This approach seeks to assess, compare, and understand individual state efforts and their readiness to achieve viral hepatitis elimination.

Study Design and Data Sources

This cross-sectional study used data from multiple sources. Reported state-level surveillance data on acute hepatitis B and hepatitis C infection was obtained from the Centers for Disease Control and Prevention (CDC) 2019 Viral Hepatitis Surveillance Report (CDC, 2021). Data for the risk factors or covariates the was obtained from the Kaiser Family Foundation (KFF) State Health Facts Report (KFF, 2022) and other CDC surveys and reports including the Annual Surveillance Report of Drug Related Risk and Outcomes, the Sexually Transmitted Diseases Surveillance Report, and the Behavioral Risk Factor Surveillance System (BRFSS) survey (CDC, 2021).

The CDC hepatitis surveillance report provides a national profile for all three types of hepatitis infection. Data is collected annually through the National Notifiable Diseases Surveillance System (NNDSS). Each week, state health departments across the United States submit case reports of viral hepatitis to the CDC. The CDC collates, summarizes, and publishes an annual surveillance report showing trends of reported cases for hepatitis A, hepatitis B, and hepatitis C infection. Similarly, other national surveys and reports published by the CDC collate and summarize state-level data to monitor health in the United States. Each report is used by public health partners to improve health outcomes and help focus efforts on disease prevention, develop policy, allocate resources, plan services, and identify and respond to clusters or outbreaks nationally.

The Kaiser Family Foundation (KFF) State Health Facts compiles health data for all states and territories in the United States. The State Health Facts is a project of the KFF that provides free updated health-related data by state comprising more than 800 health indicators from various public and private sources. These sources include internal KFF reports, government



*Framework is an adaptation of the Donabedian model (1988) for examining health care services and evaluating health care quality.

Figure 3: National Viral Hepatitis Elimination Framework*

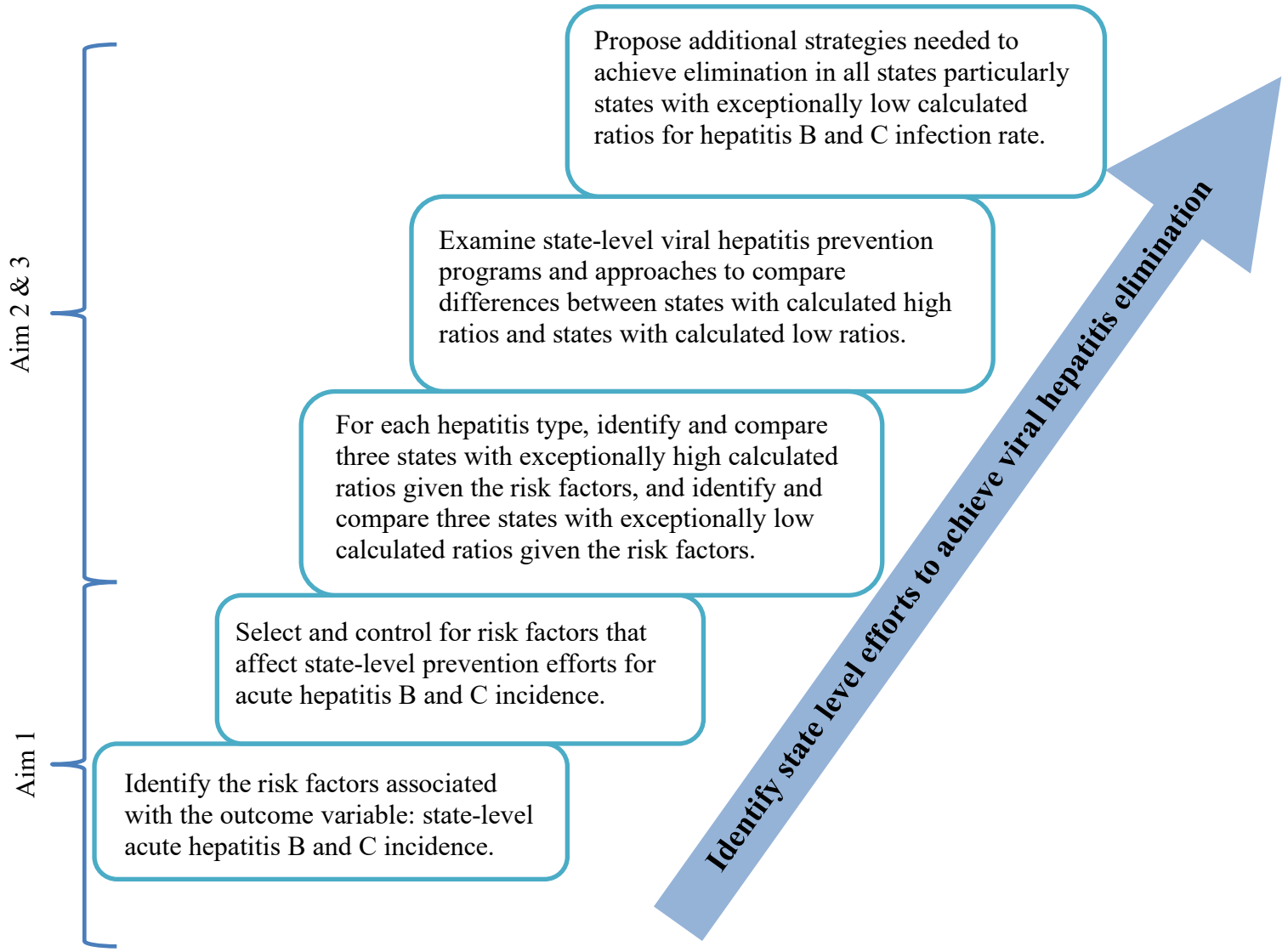


Figure 4: Study Conceptual Framework

surveys and reports, public websites, and private organizations. The data can be viewed by state and is organized into categories, subcategories, and indicators.

Variable Selection

A list of the selected variables, their definitions, and data source is listed on Table 1a in the results section. Only hepatitis B and hepatitis C acute infections leads to chronic conditions. Therefore, this study focused on the incidence of acute hepatitis B and C across states as the dependent variable. Annual incidence of viral hepatitis infection reported to the CDC by each state is estimated using three parameters, 1) the proportion of those infected with symptoms, 2) the proportion of those seeking care, and 3) the proportion of persons diagnosed and reported to hepatitis surveillance (Klevens, Liu, Roberts, Jiles, and Holmberg, 2019). Although the incidence rate for acute hepatitis B and C infection in each state remained relatively stable from year to year with little variability, data was collected for the most recent three years 2017, 2018, and 2019.

Due to varying state laws, infrastructure, laboratory resources, and the COVID-19 pandemic, hepatitis B and C cases were not regularly reported to CDC leading to missing data in some states. Additionally, because the symptoms of hepatitis infections can be mild, people who do not seek care or those who do not get recommended for testing by their health provider do not get reported.

Selection of Risk Factors

Hepatitis B and C infections are bloodborne infections and the selected independent variables are associated state-level indicators and risk factors for viral hepatitis incidence based on research from the field, experts' opinion, and existing literature (Van Handel et al., 2016; Sharareh et al., 2020; Moorman et al.,2013; Wesner et al., 2020; Degenhardt et al., 2017; and

CDC, 2020). Data from 2017 through 2019 for each risk factor were obtained from various sources. This methodology mirrors the approach used by Wesner et al (2020), Sharareh et al. (2020), and Van Handel et al. (2016) to assess county and regional level vulnerability for acute hepatitis infections in the United States and diseases associated with injection drug use.

Risk Factors and Hepatitis Infection

The identified risk factors hinder successful implementation of the approaches, strategies, and practices needed to achieve hepatitis elimination goals set by the CDC and HHS. These sociodemographic, and environmental factors include poverty rate, income, homelessness, substance or opioid use, health insurance coverage, injection drug use, unemployment rate, access to care, and other sexually transmitted infections (STIs) such as Syphilis, Chlamydia, and Gonorrhea.

Sociodemographic Factors

Poverty rate, income, health insurance coverage, unemployment rate, and access to care are social determinants of health that affect many health outcomes including many infectious diseases like viral hepatitis. These factors differ across regions and affect individual risk for acute hepatitis B and C infection. Individual level determinants and high-risk behaviors like drug injection use and unsafe sexual practices are chief drivers of bloodborne disease transmission (Dean & Fenton, 2010).

Other social, structural, economic, and environmental factors further influence the prevalence of hepatitis infection and the effectiveness of the preventive measures and control interventions put in place to reduce the rate of illness. For example, access to care and treatment for infected patients is influenced by their health insurance coverage, uninsured and underinsured persons have difficulty access screenings and preventive health services. As a result, it is

expected that states with a high percentage of uninsured or underinsured, including non-Medicaid expansion states have high rates of viral hepatitis infection.

Environmental Factors

Furthermore, persons experiencing homelessness are a hard-to-reach population and have difficulty accessing health services in their community. This makes it difficult to implement effective prevention strategies (i.e., testing, vaccination, and treatment) to prevent hepatitis incidence and prevalence. Therefore, states with high percentage of persons experiencing homelessness are inclined to have high hepatitis infection rates.

Also, ongoing surveillance and research show that the incidence of viral hepatitis B and C is high among persons who are both homeless and inject drugs as infections occur through the sharing of syringes and other drug paraphernalia (CDC, 2020). The HCV epidemic in counties across the United States have been occurring among young people engaged in high-risk behaviors like injection drug use and substance use, particularly opioids – again, most hepatitis C cases are related to injection drug use (Sharareh et al., 2020).

Although models of infectious disease transmission highlight the interaction between the individual, the infectious agent, and the environment, the success of individual level interventions and approaches like counseling, screening, and testing has been slow in achieving desired progress. Thus, a wider and broader focus on the higher-level factors that affect health outcomes is essential.

Dataset Compilation

For this study, data was compiled to include the dependent variables - acute hepatitis b and C incidence by state in the United States from 2017 through 2019. Next, state-level data for each selected risk factor identified for acute hepatitis B and C incidence was collected for the

same consecutive years (2017 – 2019). The compiled dataset data was cleaned and merged by state and year for each hepatitis type. We performed a simple relational analysis of the dataset to identify missing values which occurred at random. The states with missing acute hepatitis B or hepatitis C incidence data were deleted and only states with complete data were included in the analysis. Deleting the states with missing values did not bias the results of the analysis. For each year, states with missing data are listed in Table 1c.

The purpose of this study is to examine the association between acute hepatitis infection and the identified risk factors at the state level. Additionally, given the differences and variations in the risk factors within states, this study will identify states with exceptionally high and exceptionally low infection ratios compared to what is expected.

Empirical Method

A simple regression analysis was conducted to observe the association between the dependent and independent variables.

Dependent Variables

There are two dependent variables, estimated acute hepatitis B infection incidence rates per 100,000 and estimated acute hepatitis C infection incidence rates per 100,000 by state for the years 2017 -2019.

Independent Variables

Based on expert's opinion, an in-depth review of existing literature and the conceptual models, the independent variables in this study include state-level indicators for the same years as the dependent variables (2017 – 2019) obtained from various data sources. These variables include:

1) Access to care - operationalized by

   a. percentage of adults reporting not having a personal doctor (percentages were weighted to reflect population characteristics) and
   b. percentage of need unmet due to primary care health professional shortage

2) State-level economic factors
   a. state poverty rate
   b. median annual household income by state
   c. percent of uninsured persons by state
   d. seasonally adjusted state unemployment rate within the civilian non-institutional population aged 16 years and over
   e. State homelessness rate per 10,000 people (2019) obtained from the National Alliance to End Homelessness data

3) Infectious disease rates
   a. Syphilis rate per 100,000
   b. Gonorrhea rate per 100,000
   c. Chlamydia rate per 100,000

4) Substance use factors
   a. Percent distribution of the number of clients in treatment for substance use by state
   b. substance use indicators, including
      i. percentage of people in each state reporting needing but not receiving treatment for illicit drug use in the past year (non-treatment for illicit drug use),

ii. percentage of people reporting past year opioid use disorder (opioid past year use)

iii. percentage of people reporting past year opioid misuse (opioid past year misuse)

c. Opioid prescription rate per 100 by state for 2019 obtained from CDC's 2019 Annual Surveillance Report of Drug-Related Risk and Outcomes

d. Death rates

i. opioid overdose death rate

ii. all drug overdose death rate

Each independent variable was assessed independently for association with acute hepatitis B rate and acute hepatitis C rate outcome variables respectively. Regression analysis was used to assess the correlation between indicators. All analysis was performed using SAS version 9.4 software package (SAS Institute, Cary, North Carolina).

Qualitative Data Collection

State-level qualitative information on viral hepatitis prevention policies, programs, and activities for the identified 12 states were obtained from each Department of Public health website. The state health department is the lead agency for the entire state in preventing disease and promoting overall health and well-being. Additional updated information on current strategies and approaches to prevent hepatitis infection was requested from viral hepatitis coordinators in the health department through email with follow up phone call discussions as needed.

We followed with state viral hepatitis coordinators with assistance from the National Alliance of State and Territorial AIDS Directors (NASTAD), “a leading non-partisan, non-profit

association that represents public health officials who administer HIV and hepatitis programs in the U.S.", which provided contact details for health department staff. We sent an email to the viral hepatitis coordinator for each of the 12 states to request responses to the following questions:

1. Does (state) have a current published elimination plan? If yes, please share the link to the plan.
2. Is (state) currently implementing programs or policies to reduce acute hepatitis B and C infection in different populations?
    i. What are the major components of the program or policy related to:
        a) adult HBV vaccination policies,
        b) HCV testing and treatment (Treatment as Prevention for HCV),
        c) harm reduction laws and policies such as SSPs? Counseling and education for substance use,
        d) key interventions to disrupt transmission
    ii. What strengths and weaknesses are identified in the implementation of the programs and/or policies?
    iii. What efforts are in place to address challenges and gaps in program/policy implementation?
3. In general, what are the problems, barriers, and concerns in the elimination of hepatitis B and C in (state)?
    a. Is it possible to achieve? What do you think will be needed to achieve elimination?

b. Are the current interventions in-place adequate? If not, what else would you suggest?
c. Do you think that the state has the right mix of personnel and other resources to address this issue?

Data Analysis

We performed descriptive analysis using chi-square tests on all the variables and calculated the mean and standard deviation for each variable. Next, we performed a linear regression to explore the associations between each dependent variable - acute hepatitis B and acute C infection rates and the independent variables - the sociodemographic, economic, and environmental factors.

In the regression model, we fitted a cross sectional regression model and included all the independent variables mentioned above to explore the association between the covariates with the outcome. Years (2018, 2019 vs. 2017) when the data was collected was modeled as dummy variables. We also conducted a multicollinearity test - variance inflation factor analysis to assess whether the variables are highly correlated. Statistical significance was determined as $p\ value < 0.05$.

To rank and compare the three states with the highest calculated ratios and the three states with the lowest calculated ratios given the related risk factors, we conducted a multi-step analysis:

1) We took the log of the outcome variable – acute hepatitis B and hepatitis C infection rate for each state

2) Then, we conducted a regression analysis by using the log transformed hepatitis B and C acute infection rates as the outcome variables and the above-mentioned independent variables as predictors
3) We predicted the outcome values for each state using the fitted regression model in step 2
4) Next, we took the exponentials of the predictor values and then calculated the ratio which is the predicted value divided by the actual value of hepatitis B and hepatitis C infection rate in each state
5) Finally, we ranked the states based on the calculated ratio values to identify the states with better-than-expected ratios and the states with worse than expected ratios

Upon identification of the 12 states (six states for HBV and six states for HCV), additional state level data was collected from state health department websites and other publicly available sources including discussions with state hepatitis coordinators to assess hepatitis elimination readiness. In addition, we noted any updated information on ongoing state level programs, practices, and policies currently being implemented to reduce and eliminate hepatitis B and hepatitis C infection in the state.

CHAPTER 4

RESULTS

State-level Determinants of Acute Hepatitis Infection

Table 4.1a lists the dependent and independent variables included in the analysis, their definition, and the data source for each variable. The mean and standard deviation for each variable is presented in Table 4.1b, and the list of states with missing data for hepatitis B and hepatitis C for each year is listed in Table 4.1c. States with missing incidence rates were deleted from the dataset, only the complete sample used in the analysis.

Table 4.2a shows the regression results for acute hepatitis B virus and the covariates and Table 4.2b shows regression results for acute hepatitis C virus and the covariates. The median income variable was dropped from the regression due to its collinearity with poverty rate. For each hepatitis type, a significant association was observed between the dependent variable and covariates.

Association with Acute HBV Rates

For acute hepatitis B infection, a significant association was observed between the outcome variable and opioid past year use (β = 1.035; 95% CI 0.57 – 1.50; p = 0.000), opioid prescription rate per 100 (β = 0.290; 95% CI 0.19 – 0.38; p =0.000), opioid overdose death rate (β = 0.1618; 95% CI 0.00 -0.32; p = 0.043) and clients in treatment for substance use (β = 1.144; 95% CI 0.48 – 1.81; p = 0.001). We did not observe a significant observation between the outcome variable and other covariates; however, a positive but insignificant association was observed between acute hepatitis B incidence and poverty rate (β = 0.0056; 95% CI -0.04 –

0.05), unemployment rate (β = 0.0404; 95% CI -0.12 – 0.20), and percent of adults reporting no personal doctor (β = 0.0200; 95% CI -0.04 – 0.08). A negative but insignificant association was observed between acute hepatitis B and percent uninsured (β = -0.0017; 95% CI -0.04 – 0.04), homelessness rate (β = -0.0430; 95% CI -0.17 – 0.09), nontreatment for illicit drug use (β = -0.1281; 95% CI -0.51 -0.25), Chlamydia rate per 100,000 (β = -0.0034; 95% CI -0.04 – 0.03), Gonorrhea rate per 100,000 (β = -0.0028; 95% CI -0.02 – 0.02), and Syphilis rate per 100,000 (β = -0.0342; 95% CI -0.12 – 0.05). In addition, compared with data in 2017, acute hepatitis B infection rates in 2018 is on average 2.74 percentage points higher and 4.55 percentage points higher in 2019.

Association with Acute HCV Rates

For acute hepatitis C infection, a significant association was observed between the outcome variable and percent uninsured (β = 0.0683; 95% CI 0.03 – 0.19; $p = 0.011$;), Syphilis rate per 100,000 (β = -0.167; 95% CI -0.27 - -0.07; $p = 0.001$), Chlamydia rate per 100,000 (β = -0.91; 95% CI -0.13 - -0.05; $p = 0.000$), opioid prescription rate per 100 (β = 0.237; 95% CI 0.13 – 0.35; $p = 0.000$), opioid overdose deaths (β = 0.266; 95% CI 0.07 – 0.46; $p = 0.007$), clients in treatment for substance use (β = 2.376; 95% CI 3.24 – 10.39; $p = 0.000$), and percent of adults reporting no personal doctor (β = 0.109; 95% CI -0.03 – 0.07; $p = 0.005$). We did not observe a significant observation between the outcome variable and other covariates; however, a positive but insignificant association was observed between acute hepatitis C incidence and poverty rate (β = 0.022; 95% CI -0.03 – 0.08), homelessness rate (β = 0.071; 95% CI -0.08 – 0.22), Gonorrhea rate per 100,000 (β = 0.004; 95% CI -0.02 – 0.03), and opioid past year use (β = 0.188; 95% CI = -0.38 – 0.76). A negative but insignificant association was observed between

acute hepatitis C rate and unemployment rate (β = -0.065; 95% CI -0.26 – 0.13) and non-treatment for illicit drug use (β = -0.283; 95% CI -0.75 – 0.18). Additionally, compared with acute hepatitis C infection rates in 2017, the rates in 2018 is on average 3.81 percentage points higher and 6.82 percentage points higher in 2019.

Identification of Exceptional States

Tables 5.1a and 5.1b show results from the multi-step analysis comparing qualitative data for the states with exceptional calculated ratios. Table 5.1a shows the states doing worse than expected for hepatitis B acute infection with the lowest calculated ratios are Florida, Iowa, and Minnesota while the states doing better than expected with the highest calculated ratios are Montana, Connecticut, and Wisconsin. Similarly, Table 5.1b shows that the states doing worse than expected for hepatitis C acute infection. States with the lowest calculated ratio are Indiana, South Dakota, and Wisconsin while the states doing better than expected with the highest calculated ratios are Nebraska, Louisiana, and South Carolina.

Table 5.2a and 5.2b show the status of each state for having an evaluation plan, harm reduction practices, improved surveillance and data usage, and Medicaid expansion. States with high calculated ratios are identified as doing better than expected while the states with low calculated ratios are doing worse than expected given the risk factors. For both states with high and low calculated ratios, additional qualitative information and follow up discussions was conducted with the state hepatitis coordinators.

The additional information obtained identified the strengths and weakness in state-level hepatitis infection prevention programs and policies. In-depth state level examination compared the differences between states with high calculated ratios doing better than expected and states with low calculated ratios doing worse than expected given the risk factors.

Table 4.1a: Definition and data source of dependent and independent variables

Health Outcome	Definition	Data Source
Dependent variables		
Acute hepatitis B infection (HBV) rate	Rate of acute hepatitis B virus infection by state of jurisdiction in the United States	Centers for Disease Control and Prevention 2019 Viral Hepatitis Surveillance Report
Acute hepatitis C infection (HCV) rate	Rate of acute hepatitis C virus infection by state of jurisdiction in the United States	Centers for Disease Control and Prevention 2019 Viral Hepatitis Surveillance Report
Independent variables		
Poverty rate	Estimate of poverty rate by state	KFF estimates based on the 2008-2019 American Community Survey, 1-Year Estimates.
Percent uninsured	Percent of persons without health insurance and persons with coverage under the Indian Health Service only	KFF estimates based on the 2008-2019 American Community Survey, 1-Year Estimates
Unemployment rate	Unemployment within the civilian non-institutional population aged 16 years and older	KFF estimates seasonally adjusted based on Bureau of Labor Statistics (BLS) data
Homelessness rate per 10,000	State-level homelessness rate per 10,000 population	National Alliance to End Homelessness data based on the Census Bureau's Population Estimates Program (Population and Housing Unit Estimates data tables, 2019 version)
Syphilis rate per 100,000	Number of Syphilis infections identified and reported	Centers for Disease Control and Prevention (CDC). 2019 Sexually Transmitted Diseases Surveillance. Atlanta: U.S. Department of Health and Human Services
Chlamydia rate per 100,000	Number of Chlamydia infections identified and reported	Centers for Disease Control and Prevention (CDC). 2019 Sexually Transmitted Diseases Surveillance. Atlanta: U.S. Department of Health and Human Services
Gonorrhea rate per 100,000	Number of Gonorrhea infections identified and reported	Centers for Disease Control and Prevention (CDC). 2019 Sexually Transmitted Diseases Surveillance. Atlanta: U.S. Department of Health and Human Services
Non-treatment for illicit drug use	Number of individuals aged 12 or older reporting needing but not receiving treatment for illicit drug use in the past year	KFF estimate of data collected from Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality
Median Annual Household Income	State median annual household income	KFF data based on U.S. Census Bureau, 2019 American Community Survey, 1-Year Estimates
Opioid past year use	Number of individuals aged 12 or older reporting past year opioid use disorder	KFF analysis of Substance Abuse and Mental Health Services Administration (SAMHSA)'s restricted online data analysis system (RDAS), National Survey on Drug Use and Health (NSDUH), 2018 and 2019, Substance Abuse and Mental Health Data Archive
Opioid past year misuse	Number of individuals aged 12 or older reporting past year opioid misuse	KFF analysis of Substance Abuse and Mental Health Services Administration (SAMHSA)'s restricted online data analysis system (RDAS), National Survey on Drug Use and Health (NSDUH), 2018 and 2019, Substance Abuse and Mental Health Data Archive

Opioid prescription rate per 100	Number of opioid prescriptions dispensed in the United States per 100 persons	Centers for Disease Control and Prevention 2019 Annual Surveillance Report of Drug Related Risks and Outcomes
Opioid overdose death rate	Deaths per 100,000 population (age-adjusted)	KFF analysis of Centers for Disease Control and Prevention (CDC) National Center for Health Statistics
Drug overdose death rate	Drug overdose deaths classified using the International Classification of Diseases 10th Revision (ICD-10)	KFF analysis of Centers for Disease Control and Prevention (CDC) National Center for Health Statistics
Clients in-treatment for substance use	Percent distribution of clients in treatment for substance use by state	Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, National Survey of Substance Abuse Treatment Services (N-SSATS), 2020
Medicaid Expansion	State Medicaid expansion enrollment	KFF analysis of Medicaid enrollment data collected from the Centers for Medicare and Medicaid Services (CMS)
Primary care physician shortage (Percent of need met)	Number of physicians available to serve the population	KFF estimate of Bureau of Health Workforce, Health Resources and Services Administration (HRSA), U.S. Department of Health & Human Services
Percent of adult reporting no personal doctor	Percent of adults reporting not having a personal doctor	KFF analysis of the Centers for Disease Control and Prevention (CDC)'s 2013-2019 Behavioral Risk Factor Surveillance System (BRFSS)

*KFF = Kaiser Family Foundation

Table 4.1b: Mean and standard deviations for each variable

Parameter	Mean	Standard Deviation
Acute HBV rate	1.15	1.53
Acute HCV rate	1.34	1.14
Poverty rate	0.13	0.03
Percent uninsured	0.08	0.03
Unemployment rate	0.04	0.01
Homelessness rate per 10,000	15.52	14.77
Syphilis rate per 100,000	27.36	22.04
Chlamydia rate per 100,000	527.15	166.95
Gonorrhea rate per 100,000	175.92	93.45
Non-treatment for illicit drug use	0.03	0.01
Median Annual Household Income ($)	65,511	11,171
Opioid past year use	0.01	0.01
Opioid past year misuse	0.04	0.01
Opioid prescription rate per 100	55.51	16.47
Opioid overdose death rate	16.25	10.17
Drug overdose death rate	22.75	10.37
Clients in treatment for substance use	1.95	1.78
Percent of adult reporting no personal doctor	0.22	0.05

Table 4.1c: States with missing acute hepatitis data

2017		2018		2019	
HBV	HCV	HBV	HCV	HBV	HCV
DC	AK	DC	AK	DC	AK
HI	DC	RI	AZ	NE	AZ
NH	HI		DE	ND	DE
ND	IA		DC	RI	DC
RI	MS		HI		MS
	RI		IA		ND
			MS		RI
			RI		

Table 4.2a: Regression results for acute hepatitis B infection (HBV) rate and covariates

Parameter	Coefficient	p-value	95% CI
Poverty rate	0.0056	0.807	- 0.04 – 0.05
Percent uninsured	- 0.0017	0.936	- 0.04 – 0.04
Unemployment rate	0.0404	0.621	- 0.12 – 0.20
Homelessness rate per 10,000	- 0.0430	0.511	- 0.17 – 0.09
Syphilis rate per 100,000	- 0.0342	0.420	- 0.12 – 0.05
Chlamydia rate per 100,000	- 0.0034	0.852	- 0.04 – 0.03
Gonorrhea rate per 100,000	- 0.0028	0.786	- 0.02 – 0.02
Non-treatment for illicit drug use	- 0.1281	0.507	- 0.51 – 0.25
Opioid past year use	1.0358	0.000	0.57 – 1.50
Opioid prescription rate per 100	0.2901	0.000	0.19 – 0.38
Opioid overdose death rate	0.1618	0.043	0.00 – 0.32
Clients in treatment for substance use	1.1443	0.001	0.48 – 1.81
Percent of adults reporting no personal doctor	0.0200	0.529	- 0.04 – 0.08
2018 Year	2.7469	0.036	0.18 – 5.30
2019 Year	4.5548	0.003	1.61 – 7.49

*Median income dropped from regression analysis due to collinearity with poverty rate

Table 4.2b: Regression for acute hepatitis C infection (HCV) rate and covariates

Parameter	Coefficient	p-value	95% CI
Poverty rate	0.0224	0.422	- 0.03 – 0.08
Percent uninsured	0.0683	0.011	0.03 – 0.19
Unemployment rate	- 0.0656	0.511	- 0.26 – 0.13
Homelessness rate per 10,000	0.0716	0.369	- 0.08 – 0.22
Syphilis rate per 100,000	- 0.1678	0.001	- 0.27 – - 0.07
Chlamydia rate per 100,000	- 0.0907	0.000	- 0.13 – - 0.05
Gonorrhea rate per 100,000	0.0043	0.728	- 0.02 – 0.03
Non-treatment for illicit drug use	- 0.2837	0.228	- 0.75 – 0.18
Opioid past year use	0.1885	0.515	- 0.38 – 0.76
Opioid prescription rate per 100	0.2376	0.000	0.13 – 0.35
Opioid overdose death rate	0.2666	0.007	0.07 – 0.46
Clients in treatment for substance use	2.3763	0.000	3.24 – 10.39
Percent of adults reporting no personal doctor	0.1099	0.005	- 0.03 – 0.07
2018 Year	3.8155	0.017	0.69 – 6.93
2019 Year	6.8225	0.000	3.24 – 10.39

*Median income dropped from regression analysis due to collinearity with poverty rate

Table 5.1a: Calculated ratio for acute hepatitis B infection rate by state

State*	Ratio**	
Florida	0.203	States with worse than expected ratios
Iowa	0.404	
Minnesota	0.418	
West Virginia	0.439	
Mississippi	0.523	
North Carolina	0.535	
Utah	0.538	
Maine	0.557	
Indiana	0.577	
South Carolina	0.582	
Alaska	0.588	
Michigan	0.594	
Maryland	0.636	
Washington	0.709	
Vermont	0.786	
South Dakota	0.786	
Virginia	0.787	
California	0.835	
Arizona	0.865	
Oregon	0.886	
Pennsylvania	0.980	
Tennessee	0.989	
Georgia	1.008	
Ohio	1.024	
Colorado	1.037	
Arkansas	1.043	
New York	1.105	
New Jersey	1.124	
Massachusetts	1.151	
Kentucky	1.180	
Kansas	1.220	
Delaware	1.235	
Louisiana	1.313	
Missouri	1.335	
Alabama	1.383	
Idaho	1.426	
Nevada	1.460	
Hawaii	1.541	
Texas	1.589	
New Mexico	1.635	
New Hampshire	1.639	
Oklahoma	1.915	
Illinois	2.115	
Wyoming	2.375	
Wisconsin	2.443	States with better- than-expected ratios
Connecticut	4.596	
Montana	4.825	

*Missing data for District of Columbia, Nebraska, North Dakota, and Rhode Island

**Ratio was calculated in a multi-step analysis, first we took the log of the HBV/HCV acute rate for the most recent year (2019). Next, we conducted a regression analysis using the log transformed rates and predicted the outcome variable for each state using the fitted regression model. Then, we took the exponentials of the predictor values and calculated the ratio by dividing the predicted value by the actual value.

Table 5.1b: Calculated ratio for acute hepatitis c infection rate by state

State*	Ratio**	
Indiana	0.339	States with worse than expected ratios
South Dakota	0.347	
Wisconsin	0.358	
Utah	0.367	
West Virginia	0.370	
Minnesota	0.402	
Florida	0.424	
Arkansas	0.492	
New York	0.497	
New Hampshire	0.577	
Montana	0.676	
Kentucky	0.706	
Michigan	0.706	
North Carolina	0.722	
Colorado	0.792	
Washington	0.827	
Maine	0.828	
Maryland	0.875	
Missouri	0.887	
Oklahoma	0.914	
Tennessee	0.950	
Alabama	0.971	
Idaho	0.972	
New Jersey	0.981	
Massachusetts	1.001	
Ohio	1.004	
Georgia	1.061	
Kansas	1.071	
Pennsylvania	1.078	
Virginia	1.170	
Texas	1.201	
California	1.281	
Nevada	1.310	
Oregon	1.314	
Illinois	1.445	
Hawaii	1.486	
New Mexico	1.645	
Wyoming	1.92	
Vermont	2.778	
Iowa	2.860	
Connecticut	2.989	
South Carolina	4.036	States with better- than-expected ratios
Louisiana	5.041	
Nebraska	6.924	

*Missing data for District of Columbia, Alaska, Arizona, Delaware, Mississippi, North Dakota, and Rhode Island

**Ratio was calculated in a multi-step analysis, first we took the log of the HBV/HCV acute rate for the most recent year (2019). Next, we conducted a regression analysis using the log transformed rates and predicted the outcome variable for each state using the fitted regression model. Then, we took the exponentials of the predictor values and calculated the ratio by dividing the predicted value by the actual value.

Table 5.2a: States with exceptional* high and low hepatitis B ratios

State	Acute HBV rate (2019)**	Elimination plan	Harm reduction practices (i.e., law legalizing SSPs)	Improved surveillance and data use	Medicaid expansion
Worse than expected states (low ratio)					
Florida	2.8	Yes^	Yes	Yes	No
Iowa	0.8	Yes^	No	Yes	Yes
Minnesota	0.3	None	Yes	Yes	Yes
Better than expected states (high ratio)					
Montana	0.1	None	Yes	Yes	Yes
Connecticut	0.1	None	Yes	Yes	Yes
Wisconsin	0.1	None	Yes	Yes	No

* Exceptional states are defined by significantly lower than expected incidence rates of diseases in the state or significantly higher than expected incidence, given the underlying factors affecting the incidence rates across states. Note that the states identified may not be the highest or lowest incidence rate states in the United States.
**Acute hepatitis rates are the reported cases of infections per 100,000 population.
^Elimination plan needs to be updated

Table 5.2b: States with exceptional* high and low hepatitis C ratios

State	Acute HCV rate (2019)**	Elimination plan	Harm reduction practices (i.e., law legalizing SSPs)	Improved surveillance and data use	Medicaid expansion
Worse than expected states (low ratio)					
Indiana	4.8	Yes	Yes	Yes	Yes
South Dakota	3.2	None	No	Yes	No
Wisconsin	1.9	None	Yes	Yes	No
Better than expected states (high ratio)					
Nebraska	1.3	None	No	Yes	Yes
Louisiana	1.3	None	Yes	Yes	Yes
South Carolina	0.2	None	No	Yes	No

* Exceptional states are defined by significantly lower than expected incidence rates of diseases in the state or significantly higher than expected incidence, given the underlying factors affecting the incidence rates across states. Note that the states identified may not be the highest or lowest incidence rate states in the United States.
**Acute hepatitis rates are the reported cases of infections per 100,000 population.
^Elimination plan needs to be updated

State-level analysis informs proposed additional strategies needed to reduce acute infection rates and achieve elimination goals at the state-level and nationally.

HBV High Calculated Ratio States

Montana

Montana has a calculated ratio of 4.82. In 2019, compared to the national rate of 1.0 cases per 100,000 population, the rate of reported acute hepatitis B incidence was 0.1 cases per 100,000 population, the lowest rate in the United States (CDC 2019 Hepatitis Surveillance Report). Currently, the state does not have a published viral hepatitis elimination plan to support elimination efforts. However, there is a needs-based syringe service program (SSP) aimed at reducing the transmission of infections. The Montana Department of Health website provides general information on hepatitis infection as well as training resources for health professionals, but there is no centralized page for viral hepatitis information for easy access.

Connecticut

The calculated ratio for Connecticut is 4.59, while the rate of reported acute hepatitis B infection rate in 2019 was also among the lowest rates at 0.1 cases per 100,000 population compared to the US rate of 1.0 cases per 100,000 population. the state does not have a published hepatitis elimination plan. The state has enacted practices and policies to support elimination efforts, with state laws in place authorizing a needs-based syringe service program and universal opt-out testing for hepatitis C testing in state corrections during intake. The state also provides direct acting antiviral (DAA) treatment to diagnosed persons in state correction facilities and supports partner organizations in providing wrap around services including targeted interventions and harm reduction services to populations at risk.

Wisconsin

Wisconsin's calculated ratio for hepatitis B infection is 2.44 and along with the other states in this category, the rate of reported acute hepatitis B in 2019 was 0.1 cases per 100,000 population. The state has legal laws authorizing syringe service programs (SSPs) on a needs-based model and an exemption is in place for the possession of syringes from SSPs. Also, Good Samaritan Laws protect those seeking medical assistance related to substance use, and persons who assist others with substance use medical emergencies. There is currently no published hepatitis elimination plan in Wisconsin, and the state did not expand Medicaid which limits access to hepatitis prevention, treatment, and care. However, current Medicaid beneficiaries and persons who are incarcerated no longer require prior authorization for HCV treatment.

Wisconsin like many other states, recently received viral hepatitis prevention funding from the CDC in 2021. State officials and other stakeholders are in the planning process for developing a comprehensive elimination plan, however, hepatitis prevention practices have been ongoing in the state. For example, the health department offers hepatitis B vaccine which is available to uninsured and underinsured adults and provides vaccines to the state Department of Corrections.

As with most states, designated funding for hepatitis prevention in Wisconsin has been lacking, as a result, funds are leveraged from other state and federal prevention programs such as the Tuberculosis prevention and the Ryan White (HIV) program. In 2020, the state health department established a Harm Reduction Unit within the Bureau of Communicable diseases unit and allocated funds for two additional staff including a Drug User Health Coordinator (for infectious diseases including viral hepatitis) and a Harm Reduction Response Team Coordinator.

HBV Low Calculated Ratio States

Florida

Florida's calculated ratio is the low at 0.20 with the rate of reported acute hepatitis B in 2019 of 2.8 cases per 100,000 population which is the fifth highest rate compared with the national reported rate of 1.0 cases per 100,000 population. In 2019, Florida was one of five states with the highest reported acute hepatitis B cases accounting for approximately half of the national hepatitis B burden of reported hepatitis cases. The Florida Hepatitis Prevention Plan 2016-2020 is yet to be updated by the elimination committee set up in 2019. A draft plan awaits inputs from the Florida Advisory Group consisting of diverse perspectives such as state clinicians, patient advocates, community organizers, and substance use treatment experts. Syringe service programs are legal in Florida, but the programs are restricted to a 1-for-1 exchange not a needs-based policy.

In 2019, Florida passed the Infectious Disease Elimination Act (IDEA) authorizing sterile needle and syringe exchange programs (SEPs) for persons who inject drugs. However, the law requires that SSPs or SEPs are funded through grants and donations from private resources and prohibits programs from using state, county, or municipal funds to run the program. Florida did not expand Medicaid and does not currently have a policy to provide treatment to persons with confirmed HCV infection diagnosis in state correction facilities. However, hepatitis B testing, and vaccination is provided to at-risk adults at no cost by the state health department. The health department also maintains an updated real-time resource provider list for all hepatitis treatment providers by county.

Iowa

The calculated ratio for Iowa given the risk factors was 0.40. In 2019, the rate of reported acute hepatitis B was 0.8 cases per 100,000 population. The 2017-2021 Hepatitis Action Plan released in 2018 needs to be updated and has two main goals – 1) To prevent new hepatitis C infections, and 2) Reduce deaths and improve the health of people living with hepatitis C. Although reducing hepatitis B infections is not directly mentioned in the plan, several strategies and activities included in the plan apply to hepatitis B infection and reduce overall disease incidence and prevalence.

Building capacity for telehealth delivery is one of many strategies in the Iowa Action Plan. The Project ECHO (Extension for Community Healthcare Outcomes) program run by the Iowa Primary Care Association helps to increase the capacity of health providers to provide care and treatment for viral hepatitis. The Project ECHO program has been effective in Iowa and many other states in increasing the knowledge and capacity of health professionals to provide care and treatment services.

There is no state law in place in Iowa authorizing Syringe Service Programs (SSPs) and no harm reduction policies to support populations at an increased risk for hepatitis transmission, but the state offers educational resources for persons who inject drugs. Iowa also runs an adult viral hepatitis vaccination program for hepatitis A and B administered through contracted integrated testing sites (ITS). These sites are chosen in a competitive process, they offer testing for hepatitis C to at-risk individuals as well as hepatitis A and B vaccines to qualified individuals. In addition to the success of integrated testing sites, area pharmacies and Federally Qualified Health Centers (FQHCs) recently started offering hepatitis C testing as well.

Minnesota

Minnesota's calculated ratio is 0.41 and in 2019, the rate of reported acute hepatitis B was 0.3 cases per 100,000 population. There is no published viral hepatitis elimination plan, but the state has laws authorizing syringe service programs that function on a needs-based policy as well as Good Samaritan Laws in place to protect those seeking medical assistance for substance use, and persons that assist others experiencing a medical emergency related to substance use. Hennepin Healthcare, a large integrated healthcare system across Hennepin County which is the most populous city in Minnesota, runs a Project ECHO program to expand access to care and services for vulnerable residents. Particularly, the Minnesota Viral Hepatitis ECHO includes a diverse group of stakeholders from the health care community, educational institutions, and community organizations that meets twice a month to increase knowledge and share resources to improve the health outcomes for persons infected with viral hepatitis.

HCV High Calculated Ratio States

Nebraska

Nebraska's calculated ratio is 0.33, and in 2019, the rate of reported acute hepatitis C was at 0.2 cases per 100,000 population compared to the national rate of 1.3 cases per 100,000 population. Nebraska was one of the states with the lowest hepatitis C rates in 2019 and it does not currently have a hepatitis elimination plan and no state assigned hepatitis coordinator to manage state hepatitis prevention and control activities.

Nebraska adopted and implemented Medicaid expansion services in October 2020, however, access to HCV treatment for Medicaid beneficiaries is restricted based on sobriety and severity of liver damage or fibrosis level. Syringe service programs (SSPs) are not legal but

Good Samaritan laws provide protection for those with substance use related medical assistance and persons who assist others with medical emergencies.

Louisiana

The calculated ratio in Louisiana is 5.04. Compared to the national acute hepatitis C rate in 2019 (1.3 cases per 100,000 population), the rate of reported acute hepatitis C in Louisiana was 0.2 cases per 100,000 population. In December 2019, the state released the "Hep C Free Louisiana: Louisiana Hepatitis C Elimination Plan: 2019-2024" to guide the HCV elimination efforts in the state. The plan consisting of seven strategies mainly address HCV elimination, however, strategies and activities also address reducing incidence and prevalence of other infectious diseases including hepatitis B. In 2015, Louisiana had the 5th highest rate of bile duct and liver cancer in the United States, driven mostly by hepatitis B and C infections (Hep C Free Louisiana, 2019).

Furthermore, syringe service programs are legal in Louisiana, it is illegal to possess a syringe. Medicaid has been expanded in the state and beneficiaries do not need prior authorization to access HCV treatment. Additionally, the state runs a Project ECHO (Expanding Capacity for Health Outcomes) program that trains and provides support for a diverse group of health professionals to provide HCV care, referrals, and treatment.

South Carolina

South Carolina's calculated ratio is 4.03, with a reported rate of acute hepatitis C rate in 2019 of 0.2 cases per 100,000 population. The state had the lowest 2019 rate nationally along with Louisiana, Nebraska, Connecticut, and Texas. A Viral Hepatitis Committee was recently formed to develop a strategic plan for hepatitis elimination and the viral hepatitis elimination plan for South Carolina is currently in development. The state did not expand Medicare and there

is no state law expressly authorizing syringe service programs, but Good Samaritan laws are in place. Lastly, the South Carolina Department of Health and Environmental Control website provides a concise overview on viral hepatitis infections and a downloadable link to resources on its infectious disease page for informational purposes.

HCV Low Calculated Ratio States

Indiana

Indiana's calculated ratio is 0.33, and a reported rate of acute hepatitis C of 4.8 cases per 100,000 population, the highest reported rate nationally. In 2021, Indiana released the Zero is Possible (ZIP) Plan to End HIV and HCV 2021-2030. This ZIP plan which has four main pillars - Diagnose, Treat, Prevent, and Response, and the activities included in the plan will strengthen health systems that address all types of viral hepatitis infection. Overall, the ZIP-Indiana plan seeks to "present nonbiased, appropriate, evidence-backed information that will empower both healthcare providers and legislators with a common understanding of challenges, opportunities, and barriers to proven harm reduction interventions in Indiana."

There are state has laws in place authorizing SSPs on a needs-based policy but there is no Good Samaritan law in place for persons seeking medical assistance for substance related issues or those who help persons experiencing substance related medical emergencies. Additionally, Indiana expanded Medicaid access providing HCV treatment to beneficiaries without requiring prior authorization. Prisoners are a key at risk group for hepatitis infection and disease transmission, consequently, guidance for HCV in state corrections provides treatment for persons with confirmed HCV diagnosis at intake. Also, Indiana is currently implementing programs such as the Indiana Peer Education Program (INPEP), an innovative approach aimed at providing health education to inmates in prisons. The INPEP program organized by the Health Foundation

of Greater Indianapolis Inc. as part of the tele-mentoring ECHO project, has successfully trained inmates to teach other inmates about harm reduction and disease transmission.

South Dakota

South Dakota has a calculated ratio of 0.34. The reported rate of acute hepatitis C in the state in 2019 was 3.2 cases per 100,000 population. No elimination plan exists and there is no current assigned state hepatitis coordinator to guide hepatitis elimination efforts; however, Good Samaritan laws are in place to protect persons seeking medical assistance for substance use or person assisting others experiencing medical emergencies, but there is no law authorizing syringe service programs (SSPs). Furthermore, South Dakota did not expand Medicaid and it has a minimum fibrosis requirement that restricts access to HCV treatment for Medicaid beneficiaries.

South Dakota is one of the most rural states in the United States. Population estimates in 2017 suggest a population of about 869,666, more than 80% of which are white and another over 8% American Indian/Alaska Native (Wesner et al., 2020). In a county-level vulnerability assessment for hepatitis C transmission, Wesner and colleagues observed a hepatitis C infection rate 4 times higher in minority counties compared to nonminority counties. The analysis also identified “structural and potentially modifiable” significant indicators of opioid-related disease vulnerability, signaling the need for strategic implementation of disease prevention efforts.

Wisconsin

Wisconsin’s calculated ratio for hepatitis C is 0.35 and in 2019, the rate of reported acute hepatitis C was 1.9 cases per 100,000 population. As mentioned under hepatitis B, groups at increased risk of infection benefit from the syringe service programs which are legal in the state. Also, Wisconsin provides hepatitis C-related provider trainings through their Education Center

plus the Midwest AIDS Training. Additionally, the Department of Corrections provides hepatitis C screening and treatment for all incarcerated persons. Recent 2020 data indicates that there were 1,942 newly reported cases and about 94% were chronic cases, however, the rates of newly reported hepatitis C cases were highest in northern Wisconsin among the rural counties.

The Wisconsin Division of Public Health within the state health department provides support for hepatitis C rapid testing and hepatitis C RNA reflex testing. That is, the laboratory first performs the antibody test, and if the result is positive, immediately follows with the RNA test. This accelerates the time between confirming an infection and treatment initiation and reduces the number of samples collected from patients. Other key interventions to disrupt disease transmission include providing mobile health care services for persons experiencing homelessness that includes outreach testing and HCV treatment on the streets, and Naloxone distribution from the 86 local public health departments in the state. Although the COVID-19 pandemic caused statewide disruptions in hepatitis C testing, state-level care cascade data shows that among persons with confirmed hepatitis C infection between 2018 – 2020, 26% had negative RNA results, indicating natural immunity or successful treatment for their infections.

CHAPTER 5

DISCUSSION

The main objective of this study was to 1) assess the relationship between acute hepatitis B and C infection at the state level and the socioeconomic factors associated with high infection rates, and 2) compare and assess state-level readiness to eliminate viral hepatitis - particularly hepatitis B and C in the United States by 2030. To understand the factors associated with the incidence rate of hepatitis B and C in different states, a dataset was generated by obtaining relevant information from multiple sources.

The data were obtained for the years 2017, 2018, and 2019. Literature review on the incidence of hepatitis B and C infection and the conceptual model developed for the study helped identify several variables likely to affect acute hepatitis incidence cases in a state. Using these explanatory variables, we used regression analysis to assess the association between these explanatory variables and the incidence of acute hepatitis B and C. The regression model indicates the variables that explained interstate variability in the incidence rates of these two hepatitis types.

The regression model was then used to identify the “exceptional” state experiences with hepatitis B and C. In this research, “exceptional states” are defined by significantly lower than expected incidence rates of diseases in the state or significantly higher than expected incidence, given the underlying factors that affect incidence rates across states. Note that the states identified may not be the highest or lowest incidence rate states because the research question is not related to the explanation of why the states show low or high incidence of hepatitis B and C

but to explore the question why do some states, despite showing high risk of hepatitis B and C acute infection, do not have high incidence rates, And, why do other states with low risk of hepatitis B and C incidence, show high incidence rates.

In the first part of our analysis, acute hepatitis B infection rates were significantly associated with opioid past year use, opioid prescription rate, opioid overdose death rate, and clients in treatment for substance use. According to CDC surveillance reports, injection drug or opioid use increase the risk and incidence of bloodborne infections like hepatitis, this helps to explain the association between increasing acute hepatitis B infection and opioid-related covariates. In 2019, injection drug use was the most common reported risk behavior among persons infected with hepatitis accounting for 35% of all reported cases. (CDC 2019 Surveillance Report).

We did find that although hepatitis B is commonly spread through sexual contact, we did not observe a significant association with the prevalence rates of other sexually transmitted infections (STIs) such as Syphilis, Chlamydia, and Gonorrhea. However, hepatitis incidence rates may not show correlation with other STI prevalence rates if other STIs show independent variability across states due to exposure factors not related to hepatitis infections. This may happen even when hepatitis B and other STIs show significant coinfections.

Acute hepatitis C infection rate was significantly associated with percent uninsured, Syphilis rate, Chlamydia rate, opioid prescription rate, opioid overdose deaths, clients in treatment for substance use, and percent of adults reporting no personal doctor. The observed association is in line with studies by Sharereh et al (2020) and Zibbell et al (2015), both of which found an association between acute HCV infection rate and buprenorphine prescription,

administered naloxone, and per capita income. Injection drug use is also identified as the most common reported risk behavior among cases of acute hepatitis C infection in 2019.

Interestingly, we observed a significant negative association between acute hepatitis C rate and syphilis and chlamydia rate. In 2019, sexual contact is listed as one of the top five exposure risk factors for hepatitis C infection and having multiple sexual partners is the second highest reported risk behavior after injection drug use (CDC, 2020). However, at the state-level we did not observe a positive association between acute HCV infection and sexually transmitted infections like Syphilis and Chlamydia.

The second part of the analysis required the identification of these "exceptional" states, and we have arbitrarily decided to select three exceptional states at each end of the "exceptional" definition for both hepatitis B and hepatitis C incidence. In other words, to identify the exceptional states the incidence rates "expected" for the states were predicted using the explanatory variables included in the model and then we compared the expected incidence rates with the actual rates to identify how far the actual incidence rates were from the predicted rates. The highest deviations were considered to identify the "exceptionally low" and "exceptionally high" incidence rate states for hepatitis B and C separately.

Next, given the risk factors that affect hepatitis incidence, we identified three states with high calculated ratios and three states with low calculated ratio for each hepatitis type (a total of 12 states) to compare and assess state-level efforts towards elimination. Publicly available information on hepatitis elimination efforts in the 12 states were further examined and follow up discussions conducted with health department hepatitis staff.

This approach identified 12 states in total, six for hepatitis B and six for hepatitis C. An in-depth analysis of the identified states was performed to determine how the "exceptionally

good" and "exceptionally poor" states vary in terms of hepatitis prevention and control activities and policies. This process may help to better understand the reasons for relative success or failures of the states in controlling hepatitis B and C infection. Publicly available information on viral hepatitis elimination efforts in the 12 states were examined and follow up discussions conducted with health department staff.

For the second study objective, we conducted an in-depth analysis of viral hepatitis elimination efforts in each of the 12 states in the high and low calculated ratio categories. This analysis focused on ongoing effective approaches and strategies being implemented. Van Handel and colleagues (2016) identified 220 counties in 26 states as most vulnerable to hepatitis C infection, and state-level hepatitis elimination strategies and approaches are multi-pronged to include: developing and implementing a comprehensive hepatitis elimination plan to improve prevention, treatment, and outcomes for viral hepatitis infections; having harm reduction laws in place such as syringe service programs and Good Samaritan laws as well as programs that provide wraparound support services for at risk groups and underserved communities; and improved surveillance and data usage efforts to increase awareness beyond basic health-related information on the health department website.

Common strengths and weakness of hepatitis elimination efforts were identified in each state. Some of the strengths include: 1) buy-in from state leadership and state legislature to address increasing rates of acute hepatitis infection, 2) implementation of innovative programs and partnerships (i.e., Project ECHO, INPEP) that provides increased access in rural communities and hard to reach populations (i.e., incarcerated persons), and 3) robust harm reduction practices, referrals, and wraparound services for groups at an increased risk. These major strengths were more common among states with high calculated ratio.

On the other hand, major weaknesses were mostly found in states with low calculated ratio and include: 1) insufficient funding for dedicated staff in the hepatitis prevention unit within the health department, 2) lack of Medicaid expansion services including treatment restrictions for beneficiaries, and 3) inadequate harm reduction practices that do not go far enough in preventing the spread of new infections. These weaknesses delay progress towards reducing infection rate and achieving elimination goals.

State-level Hepatitis B Prevention Efforts

New and acute viral hepatitis infections have increased nationally, between 2014 to 2018, the rate of hepatitis B cases increased by 11%, this increase was highest among states hardest hit by the opioid crisis. The three states with high calculated ratios were Montana, Connecticut, and Wisconsin, while the states with low calculated ratios were Florida, Iowa, and Minnesota. Comparatively, all three states with high calculated ratios had harm reduction practices authorizing syringe service programs and Good Samaritan laws to protect persons seeking medical assistance for substance use as well as persons who assist those experiencing a substance use related medical emergency.

Among all six states, only two states – Florida and Iowa had published elimination plans. All six states reported improved surveillance and data use for decision making and targeted implementation of programs, practices, and policies. Among both high and low calculated ratio states, only Florida and Wisconsin are non-Medicaid expansion states.

State-level Hepatitis C Prevention Efforts

Between 2014 to 2018, the rate of acute hepatitis C increased nationally by 71% from 0.7 per 100,000 population to 1.2 per 100,000 population. The three states with better than expected or high calculated ratios for hepatitis C are Nebraska, Louisiana, and South Carolina while the

states with worse than expected or low calculated ratios were Indiana, South Dakota, and Wisconsin (which was also identified in HBV). Comparatively, there was no significant difference between the measures observed for the three states in each category. Among the six states, only Indiana has an updated elimination plan, the other states do not. Indiana, Wisconsin, and Louisiana have harm reduction practices in place, while Indiana along with Nebraska and Louisiana (better than expected states) are Medicaid expansion states.

Overall, states hepatitis prevention efforts include partnership with the Department of Corrections to provide viral hepatitis testing and screening as well as treatment for hepatitis C during intake for those who are incarcerated.

Harm Reduction Coverage

It is also important to explore harm reduction services and coverage particularly in states with exceptional calculated ratios for hepatitis C. In Indiana, eight counties and one city are approved to provide syringe service programs (SSPs). Over 16,000 participants are enrolled in the state and SSPs have provides over 83,200 doses of naloxone since 2019 according to information found on the health department website. In February 2020, the Wisconsin Department of Health Services conducted an assessment to identify geographic gaps in services to prevent and treat harms related to substance use and the opioid crisis. The assessment also included plans to address identified gaps in access to SSPs, naloxone, Medication- assisted treatment (MAT) and hepatitis C treatment.

Louisiana has six active SSPs across the state as well as hotlines and mail-based naloxone services. The New Orleans Syringe Access Program (NOSAP) is a Federally Qualified Health Center (FQHC) that provides safe sterile syringes and injection materials, syringe disposal

services, overdose prevention education, naloxone distribution and medication-assisted treatment referrals to members of the community.

Other hepatitis B states also have different harm reduction services and coverage. For example, syringe exchange programs were expanded in Florida in 2019 to allow county commissions permit SSPs in their county as well as contract with eligible entities to operate exchange programs. A syringe exchange program in Miami opened in 2016 enrolled over 1,000 participants, distributed approximately 1,900 Narcan kits and provided over 700 hepatitis C tests to participants. Florida also initiated their Naloxone program in 2016 with 112 organizations enrolled. Over 80,000 naloxone kits have been provided with about 2,860 overdose reversals reported in the community (Muller and Meaders, 2019).

The Iowa Harm Reduction Coalition has programs throughout the state and provides a discrete shipping option for persons outside of their service areas. Additionally, Iowa's Crisis HelpLine is available through call, text, or chat, 24 hours per day every day of the year.

National Viral Hepatitis Profile Overview

In 2021, the Coalition for Global Hepatitis Elimination, a program of The Task Force for Global Health developed a national elimination profile for the United States that outlines the ongoing progress towards hepatitis elimination based on the 2020 WHO elimination goals (30% reduction in hepatitis B and C infection, and 10% reduction in deaths from chronic hepatitis B and C infection). The updated 2030 goals include a 90% reduction in acute hepatitis cases and a 65% reduction in deaths from viral hepatitis.

Efforts to eliminate hepatitis in the United States are in place in all states across the country. However, more remains to be done in the progress towards HHS and CDC elimination goals. Nationally, between 2017 – 2019, the percentage change of new infections (incidence) for

hepatitis B decreased by -5% while that for hepatitis C between 2015 – 2019 increased substantially by +70% (CDC, 2019 Surveillance Report). These changes indicate that more support, resources, and innovations are needed in efforts to reduce the health burden of viral hepatitis infections.

In a partnership to study national efforts, the National Viral Hepatitis Roundtable (NVHR), the Center for Health Law and Policy Innovation (CHLPI), and the O'Neill Institute for National and Global Health Law at Georgetown University Law Center (O'Neill Institute) released an initial assessment of states' capacity for viral elimination efforts. The "Hep ElimiNATION" program assesses and grades the "policy landscape and programmatic strategies" that impacts hepatitis elimination in each state and offers guidance. Across the United States, state elimination efforts depend largely on differences in the current policy environment needed to achieve elimination. Broadly, this includes activities like 1) routine monitoring and communication of strategic information, 2) prevention of mother-to-child transmission (MTCT), 3) access to testing, diagnosis, and treatment, 4) health equity and addressing disparities in infection burden, and 5) financing and resources.

Communication of Strategic Information

In each of the 12 states, viral hepatitis is on the state notifiable disease list, and the state health department routinely collects and reports strategic information including incidence, prevalence, and mortality data to the National Notifiable Disease Surveillance System. However, the monitoring and surveillance data of diagnosis and treatment of hepatitis B and C is not routinely reported by states. For example, Iowa and Connecticut regularly update a public-facing website that reports on only hepatitis C data but not the other types of hepatitis, while Nebraska does not provide any hepatitis epidemiological data on their website.

Prevention of Mother-to-Child Transmission

Prevention of mother-to-child transmission of hepatitis B in each state is sustained by the national policy for hepatitis B vaccination of newborns. All 12 states receive federal funds to implement the national perinatal hepatitis B program. This program provides hepatitis B and hepatitis C testing for pregnant women and vaccination for all infants, particularly infants born to hepatitis B-positive mothers. This program has been tremendously successful in increasing infant vaccination rates nationally, as well as providing resources and education to pregnant women infected with, or at risk for hepatitis.

Testing and Diagnosis of Infection

Each states examined follow hepatitis B and C testing recommendations by the United States Preventive Services Task Force. These recommendations include risk-based testing for both hepatitis B and C, hepatitis B testing for persons born in regions with HBV prevalence above 2%, and one-time universal HCV testing for all adults. The Affordable Care Act (ACA) provides opportunities to prevent new infections, diagnose, and care for chronically infected persons (HHS, 2016), however, states like Florida, Wisconsin, South Dakota, and South Carolina are yet to fully adopt the health care law. Thereby, limiting access to testing particularly, HCV testing in emergency departments.

Hepatitis B and C Treatment

State health providers of counselling, and treatment services for hepatitis B follow the National treatment guidelines developed by the American Association for the Study of Liver Diseases (AASLD) (Terrault et al., 2018). Treatment for hepatitis C is affected by Medicaid access especially in states with fibrosis, sobriety, and prescribing restrictions. Among the states examined, Nebraska and South Dakota still have fibrosis restrictions in place, while Iowa and

South Dakota have sobriety restrictions. For hepatitis C particularly, all 12 states have adopted having less than 2 clinic visits by patients during treatment. They also either allow medications by prescriber, in consultation with prescriber, or no medication prescriber restrictions in place to simplify the care continuum. Other simplified care management guidelines in the care continuum such as having no treatment co-pays for patients is managed directly by the payer.

In underserved areas, care and treatment innovations like Project ECHO tele-mentoring provides an opportunity to expand access to services. For example, Iowa, Indiana, and Louisiana coordinate Project ECHO. Iowa has two ECHOs for hepatitis C and Behavioral health (Iowa Primary Care Association, 2020). Indiana's ECHO program to address the opioid epidemic is run by a partnership between the local primary care providers and a specialists-led team from Indiana University School of Medicine. Louisiana's Project ECHO, an initiative of Tulane University aims to mitigate effects of the opioid epidemic by reducing knowledge and treatment barriers among health professionals who treat patients (Louisiana Department of Health, 2020).

Louisiana also currently runs a "Hep C Free Louisiana" program started in 2019. Since inception of the program, about 9,821 Medicaid beneficiaries and state corrections inmates have received treatment for hepatitis C infection. Prior to 2019, this number stayed below 400 annually. Through the program, the hepcuredla.org website provides information on testing and treatment locations as well as training resources for providers to manage patients. Most of the program efforts however focus on testing and treatment for hepatitis C infection, not hepatitis B testing or vaccine information.

The availability of well-tolerated treatment therapy for hepatitis C has improved the rate of treatment. However, beyond primary care, the cost of testing and treatment in priority settings like the emergency department is a challenge. Annual Medicaid costs attributed to hepatitis C

infection ranges from $10,561 for noncirrhotic disabled persons to $46,263 for nondisabled persons with end-stage liver cancer (Roebuck & Liberman, 2019). Treatment for hepatitis B on the other hand is unaffordable for many patients due to the inequitable practices by insurance companies. Inequities also persist in hepatitis B and C testing, care, and management.

Addressing Health Equity and Disparities

Efforts to address disparities and inequities has been adopted to varying degrees in different states. Additionally, the Affordable Care Act (ACA) and the Americans with Disabilities Act (ADA) include provisions to protect persons living with chronic conditions like hepatitis (Hepatitis B Foundation, 2019). Recent recommendations from the ACIP include a national policy for adult vaccination against hepatitis B (Schille, et al., 2018), establishing syringe service programs in correction facilities and prisons, and harm reduction programs for persons who inject drugs (PWIDs).

Approaches within states to address persons disproportionately affected by hepatitis infection should include increased access to clean needles and syringes for people who inject drugs and increased number and availability of opioid substitution therapy recipients. Nationwide, only 3 states have partially adopted laws that decriminalize possession of syringes and other injection drug use paraphernalia. 12 states still have laws that criminalize hepatitis – Utah, Nebraska, Iowa, Missouri, Mississippi, Tennessee, Georgia, Indiana, Ohio, Pennsylvania, Virginia, and North Carolina. No state has adopted a law or policy to decriminalize drug use.

Limited access to safe drug use paraphernalia, harm reduction services, and opioid substitution therapy presents challenges in addressing disparities particularly among PWIDs. In 2021, the American Rescue Plan legislation permitted federal support and awarded funds for harm reduction. The appropriated funds led to increases in CDC support and funding for

activities to prevent, diagnose, and treat persons who inject drugs. States like California with community-based care, testing, and referral for persons experiencing homelessness, New York's Drug User Health hubs, and Washington state's HIT-B project are innovative programs targeting groups at an increased risk for infection (US-National Hepatitis Elimination Profile, 2021).

State Funding and Federal Financing

There is limited funding for state-level programs, activities, and the staff needed to successfully advance viral hepatitis elimination efforts, this is a major challenge for many states. For example, in Indiana, there is only one fully funded staff dedicated to hepatitis elimination efforts. Also, in addition to high turnover rates, health department staff originally focused on hepatitis have been redirected to dealing with the COVID-19 pandemic. Some states like Florida have secured additional state-level funds to expand services across the state. In 2021, the CDC released funds for the "Integrated Viral Hepatitis Surveillance and Prevention Funding for Health Departments (IVHSP) (CDC-RFA-PS21-2103)", this program provides funds for five years (2021 -2026) to support surveillance and prevention programs in all states, large cities, and territories across the United States. States will benefit from the released funds and are able to include a line item in their budgets specifically for hepatitis B and C prevention, testing, and treatment, as well as build statewide capacity to conduct hepatitis prevention and treatment activities.

Recommendations

In each state and across the United States, steps to advance hepatitis elimination goals should focus on a wide range of activities, program, practices, and policies. Reducing the incidence of acute hepatitis B and C can be achieved through improved state-level prevention program planning. First, having a comprehensive state elimination plan developed by a

multidisciplinary group of stakeholders' helps to outline plans to increase surveillance, inform specific actions on program activities and target the delivery of needed health services.

Also, it is important for states to prioritize partnerships needed to address health inequities. Among the states doing better than expected, there were wrap around services for persons who inject drugs and those who engage in high-risk behaviors. For example, partnerships with the state Department of Corrections to provide screening to inmates as well as mobile health services for people experiencing homelessness and persons with low income. Additionally, Medicaid adoption helps expand access to needed health services and increase access to robust harm reduction programs without sobriety or fibrosis restrictions for hepatitis C treatment for all adults. Decriminalization of possession of syringes obtained from SSPs will ensure that effective treatments and targeted screenings are equitably provided.

Lastly, states can leverage resources and innovation from the current response to the COVID-19 pandemic, for example, exploring ways to provide no-cost testing, screening, and vaccinations for hepatitis B to all eligible adults; and for hepatitis C, improvements in and expansion of reflex testing services, while also increasing linkage-to-care and treatment.

Public Health Implications

The study results highlight important public health implications that can help in efforts to eliminate viral hepatitis in states across the country. Hepatitis prevention activities are multidimensional and require adequate funds to effectively address increasing acute hepatitis infection rates. This includes improved surveillance systems and increasing staff capacity. beyond having a public facing website with periodically updated epidemiological data. State prevention programs can build on promising activities identified in states performing better than

expected to the expand testing infrastructure into hard-to-reach populations particularly in the rural parts of the state.

States would also benefit from integrating hepatitis prevention health services with prevention of other infectious diseases like HIV and TB; as well as the adoption of innovative programs and strategies like Project ECHO tele mentoring and telemedicine services. Findings from this study and similar studies nationally and globally show that harm reduction practices are a key strategy for reducing viral hepatitis and other bloodborne infections (Dengenhardt, 2020; Van Handel, 2016).

Limitations and Conclusion

This study highlights the need for in-depth assessment of all states across the country to understand hepatitis elimination challenges in the delivery of services. However, there were some limitations, first, for the years examined (2017 – 2019) few states had missing data for acute hepatitis B and C incidence and were not included in the sample. Future analysis should include recent acute hepatitis rates for all states and territories across the United States. Second, state-level data for other possible risk factors such as non-Hispanic race/ethnicity and percent of people in need of government food assistance included in similar studies were not considered. Third, results of this research and the interpretation was based on secondary data analysis and the primary data was initially collected for monitoring trends and surveillance purposes.

This multi-layered approach aimed to examine and compare states and to highlight viral hepatitis B and C elimination efforts across state health departments, health partners, and organizations working to reduce infection rate in all groups. Although challenges persist, some states are further along in reducing viral hepatitis infections and improving health outcomes. Although federal authorities and agencies like the CDC develop national recommendations for

hepatitis testing, prevention, and clinical management of patients, decisions around the capacity and how to deliver services occur at the state level. In addition to the implementation of effective programs, policies and practices, a comprehensive viral hepatitis elimination plan developed by a multidisciplinary group of stakeholders that highlights specific strategies, approaches, and activities is an important guide that helps advance needed progress towards achieving national elimination goals.

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