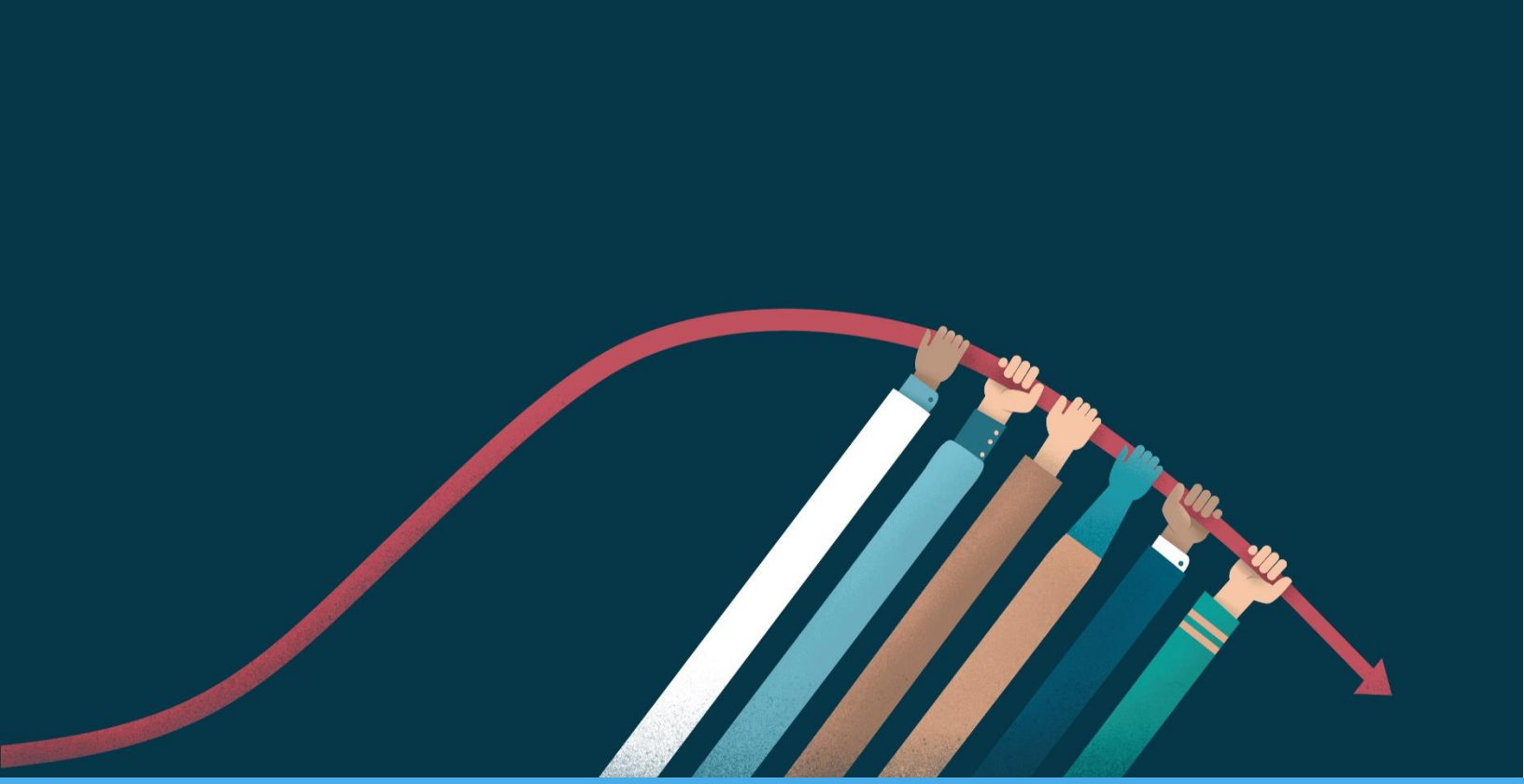

Public health impact of a population-based approach to hepatitis C treatment in Iowa

Authorship – Bureau of HIV, STD, and Hepatitis
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Protecting and Improving the Health of Iowans

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This is a summary of the key outcomes of a hepatitis C virus (HCV) disease-burden analysis undertaken by the CDA Foundation's Polaris Observatory, in collaboration with ASTHO, CDC, the Iowa Department of Public Health, University of Iowa, UnityPoint Health, the Iowa Harm Reduction Coalition, the HIV and Hepatitis Community Planning Group, and the Iowa Department of Corrections.

This analysis was funded by a CDC cooperative agreement with ASTHO.

Note: The analysis was created in 2017.

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Executive Summary and Key Recommendations

Hepatitis C virus (HCV) infection is a blood-borne infectious disease that causes substantial liver-related morbidity and an increased risk of liver cancer and liver-related death.[1] HCV is often known as a "silent disease," as there are few noticeable symptoms, especially in early-stage infection.[2] Because of this, many individuals are unaware of their HCV until more serious, late-stage complications arise. Treatment is available for HCV, with success measured by the sustained viral response (SVR) rate at 12 to 24 weeks post treatment (i.e., no detectable virus). Prior to 2014, an average of 48 to 70% of people achieved SVR with the available therapies; however, recent advances in therapeutic medications increased SVR rates to more than 95% in 2018.[3] Achieving SVR can reverse the effects of early-stage fibrosis and slow the progression of cirrhosis to decompensation or hepatocellular carcinoma (HCC).[4,5] This reduces liver-related mortality by 20-fold and all-cause mortality by 4-fold.[6] Transmission of HCV can be prevented by avoiding direct exposure to contaminated blood or blood products, including objects that may have come in contact with contaminated blood, such as syringes and other drug paraphernalia.

Over the last 14 years, the HCV epidemic has drastically changed in the U.S. Originally a disease affecting "baby boomers" (people born between 1945 and 1965), HCV has reemerged as a syndemic with opioid use and overdoses, methamphetamine use, and HIV.[7] In 2010, approximately 3.5 million Americans were living with chronic HCV.[8] According to CDC data, HCV now kills more Americans than any other infectious disease.[9] In addition, HCV is the leading cause of cirrhosis and liver cancer, and the most common reason for liver transplantation in the U.S.[10] In 2013, deaths from HCV-related causes surpassed the total combined numbers of deaths from 60 other infectious diseases reported to the CDC, including HIV and tuberculosis. In 2014, HCV-related deaths reached an all-time high with more than 19,600 deaths reported.[11] At the same time, there has been a marked simultaneous increase in the number of people newly diagnosed with HCV across the US, particularly among people with a history of injection drug use.[12] The U.S. experienced marked increases in hospital admissions for acute HCV and for opioid injection between 2004 and 2014, with the number of people newly diagnosed with HCV more than doubling between 2010 and 2014.[13]

National-level programs to control the burden of HCV have focused primarily on the older cohort of people with HCV. These programs include screening for HCV in the baby-boomer cohort (born 1945 to 1965) and programs offered through the Veteran's Administration (VA) to diagnose and cure all veterans with HCV. Despite these efforts, barriers to treatment still exist at the state Medicaid level, as evidenced in many states by restrictions on treatment, including fibrosis scarring requirements that preclude treatment for people with early-stage liver disease.[14] Universal procedures exist to prevent HCV transmission in medical settings across the U.S. (though localized outbreaks may still occur when procedures fail). However, the recent opioid crisis combined with increased methamphetamine usage in some parts of the country present new challenges for HCV prevention efforts. At present, policies to prevent transmission among drug users are entirely state-specific, and in many states, these policies simply do not exist.[15]

This report presents the outcomes of a multi-stakeholder collaboration to assess the HCV disease burden in the state of Iowa. This work follows a standard methodology (modified Delphi process) developed and facilitated by the CDA Foundation's Polaris Observatory staff. It engages local stakeholders, including the Iowa Department of Public Health, doctors from the University of Iowa and UnityPoint Health, the Iowa Harm Reduction Coalition, the HIV and Hepatitis Community Planning Group, and the Iowa Department of Corrections. The stakeholders ensured that the data used in the analysis were the best available and they helped to develop momentum and consensus toward a common goal. The tool used in this work is a

Microsoft Excel-based Markov model, populated with consensus estimates that answer the basic questions needed for HCV policy development.

Key Insights and Recommendations

Who is affected?

- At the beginning of 2017, there were 26,900 Iowans with chronic HCV (HCV RNA+ viremic infections) in Iowa. Approximately 59% of people with chronic HCV were previously diagnosed (n= 15,900), with around 1,500 people being diagnosed annually, and 8% of people with diagnosed HCV (n=2,200) being initiated on treatment annually. There were an estimated 870 people acquiring HCV annually, an incidence rate of 57.8 per 100,000 in 2017. In addition,
    - 52% of people with chronic HCV were in the 1945 to 1965 birth cohort*
    - 14% of people with chronic HCV were women of child bearing age*
    - 4% of people with chronic HCV were people who inject drugs*
    - The number of people with chronic HCV in prisons was unknown
    - The number of people with chronic HCV in Medicaid was unknown

    *Percentages do not sum to 100% because overlap exists across groups and not all subpopulations are considered here.

What is the impact of current policies?

- If current policies continue and there is no change to the HCV treatment paradigm in Iowa, the total number of people with chronic HCV will decline by 40% by 2030. In addition, liver-related deaths and incidence of hepatocellular carcinoma (HCC) and cirrhosis will decrease by 75-85% as the population ages.

What needs to be done to eliminate HCV in Iowa?

- To eliminate HCV (defined as a 90% reduction in the number of people who acquire HCV, diagnosis of 90% people with HCV, and a 65% reduction in liver related mortality) by 2030 in Iowa, fibrosis restrictions on treatment need to be removed by 2018. Between 2018 and 2030, 25,800 people need to be treated, an average of 2,000 people annually.
- In addition, prevention efforts need to increase, to lower the incidence rate from 27.8 per 100,000 people in 2017 to around 2.6 per 100,000 by 2030.
    - Strategies such as providing access to sterile needles and syringes and treating people who are actively injecting drugs could all contribute to this prevention effort.

Background

HCV globally

Today, an estimated 71 million individuals globally are living with hepatitis C, a curable disease that can lead to cirrhosis, liver cancer, and liver-related death. Approximately 400,000 people die each year from causes related to HCV. These deaths can be eliminated through coordinated efforts for prevention and treatment. Unfortunately, as of 2017, only 20% of those people living with HCV have ever been diagnosed and currently, only 2% of people with HCV are being treated for the disease annually.

The CDA Foundation and the Polaris Observatory

The CDA Foundation (CDAF) is a non-profit organization that specializes in the study of complex and poorly understood diseases to provide countries and states with the data and information to create and implement successful elimination strategies. The Polaris Observatory, an initiative of CDAF, provides epidemiological data, modeling tools, training, and decision analytics to support eliminating hepatitis B and C globally by 2030. The observatory offers the most up-to-date estimates for hepatitis B and C disease burden and economic impact, and offers strategies for elimination of each virus, along with financing options. An independent advisory board with representatives from global health organizations, academia, civil societies, and donors oversees the activities of the observatory. The Polaris Observatory's teams of epidemiologists work directly with stakeholders in over 100 countries to assess the current and future disease burdens of hepatitis, model economic impact, and develop strategies that can achieve country- or state-defined elimination targets. By developing partnerships at country and regional levels, the observatory collects and analyzes data for its platform and publishes key findings to enable policies for hepatitis elimination.

How this model has been used globally

This work has resulted in the adoption of national hepatitis elimination strategies in countries such as Egypt and Mongolia. In Egypt, this included an economic analysis that accounted for direct costs (healthcare, screening, diagnostic and antiviral therapy costs) and indirect costs (costs based on disability-adjusted life years). The analysis showed that it would cost Egypt U.S. $90 billion over a 15-year period if the government kept the status quo. A plan of action was then developed to begin in 2014 with a goal of treating 300,000 persons annually, including cost subsidies for four years. After seeing successes, the plan continued each year. In 2016, Egypt treated 577,000 people, and the plan expanded to include people at all stages of disease, including those without any HCV-related consequences.

In Mongolia, CDAF and its Polaris Observatory team worked with the World Health Organization's Regional Office for the Western Pacific (WPRO) to design an economic analysis and understand the disease burden. Working with partners including WPRO, the president of the Mongolian Association on Study of Liver Diseases, a physician professor, and a group of other researchers, the team developed the co-payment method based on income level. The Mongolian government subsidized part of drug treatment and as prices declined, treatment became even less expensive for people. CDAF also worked with the WPRO to develop a national screening program in urban and rural areas after reaching the conclusion that, even if the prevalence of HCV goes down in the next decade, there will still be more transmission and deaths unless there is an increase in screening and diagnosis.

How this model has been used in the United States

In 2014, this work expanded to include state-based analyses within the U.S. Through collaborations with a combination of state health departments, the CDC Foundation, the Association of State and Territorial Health Officials (ASTHO), and state collaborators, this model has been used to encourage the removal of Medicaid fibrosis restrictions (Colorado), to publish the HCV epidemiology and an elimination scenario (Rhode Island), and to inform the development of state elimination strategies (District of Colombia and New York, *in progress*). In addition, the results for five states (California, Colorado, Louisiana, Rhode Island and Washington) are included on the Polaris Observatory website (https://cdafound.org/dashboard/polaris/dashboard.html). Ongoing analyses include collaborations with ASTHO, CDC, and state partners to identify the disease burden and associated elimination strategies in Georgia, Iowa, Maryland, New Mexico, Pennsylvania, and Tennessee.

Hepatitis C-related disease burden – Iowa

Iowa is a Midwestern U.S. state that is mid-sized both geographically and in population. According to the recent HCV epidemiological profile of Iowa, there are few specialists who have the skills and capacity to treat hepatitis C in counties with the highest rates of the disease. [16]

The analysis presented here represents the work of stakeholders from the Iowa Department of Public Health (IDPH), the University of Iowa, UnityPoint Health, the Iowa Harm Reduction Coalition, the HIV and Hepatitis Community Planning Group, the Iowa Department of Corrections, ASTHO, CDC, and CDAF. The primary objectives were to quantify the current and future disease burden of HCV in Iowa and to identify the level of effort necessary to eliminate HCV in the state.

Based on the Edlin et al. adjustments of NHANES data scaled specifically to Iowa, it was estimated that 1.1% (0.9% to 3.5%) of the population of Iowa was living with chronic HCV (RNA positive) in 2010. This equates to approximately 34,400 (range of 28,700 to 108,800) Iowans in 2010. [17] These estimates are also supported by the Iowa Department of Health prevalence calculations. [18]

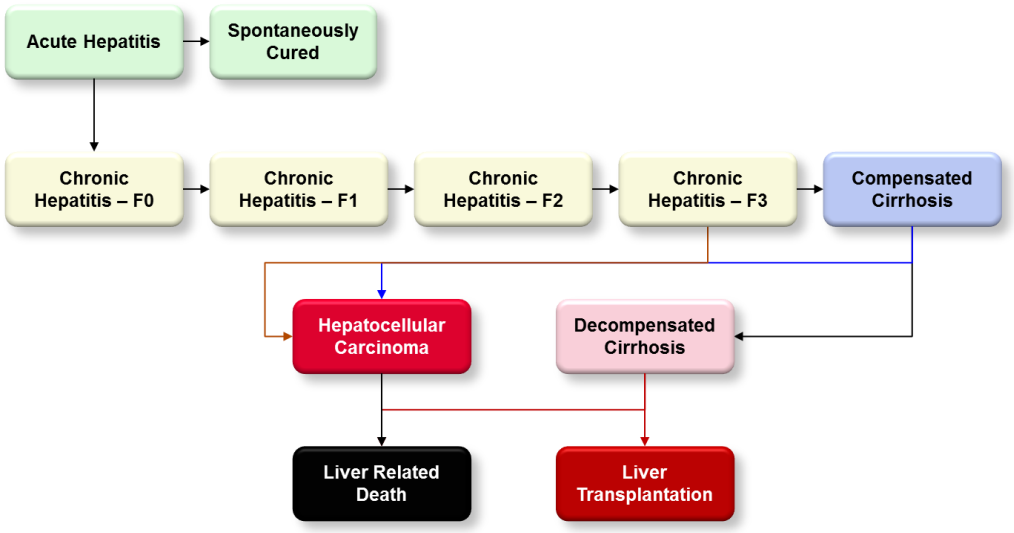
Achieving a sustained virologic response (SVR) to HCV treatment can reverse the effects of early stage fibrosis and slow the progression of cirrhosis to decompensation or HCC.[19,20] This reduces liver-related mortality by 20-fold and all-cause mortality by 4-fold.[21] Direct acting antivirals (DAA) can achieve SVR in >95% of people with HCV.

Similar to the United States, almost 70% of Iowans with HCV have genotype 1.[22] Although genotype 1 was previously the most difficult type of HCV to treat, DAAs have become the standard of care and are safe for the treatment of genotype 1. For this modeling exercise and based on input from expert meetings, we assumed a SVR rate of 97% for all genotypes.

The model

The mathematical model is an Excel-based disease progression model that was calibrated using reported, state-specific, epidemiologic data. The progression is as follows (Figure 1):

Figure 1.



The details of the model have been described previously in Blach 2016.[23] Briefly, a Markov disease progression model grounded in population, mortality, and state-specific HCV data was developed. The model was then used to forecast the disease burden by HCV-sequelae, including fibrosis, cirrhosis, decompensated cirrhosis, hepatocellular carcinoma (HCC), and liver-related death from 1950 to 2030. Inputs to the model include the annual numbers of people with acute infections that progressed to chronic infection, accounting for spontaneous clearance, mortality, and cure, by age and sex from 1950 onward. The age and sex distribution of people with newly acquired HCV was back-calculated to match the reported prevalence.

Input data

The following epidemiologic data were inputted into the model (Table 1):

Table 1.

Historical Input	Estimate (Range)	Estimate Year	Source	Source Description
People with HCV RNA+	34,400 (28,700-108,800)	2010	[24]	Edlin 2015
Anti-HCV Prevalence by Age and Sex	See Figure 2	2006	[25,26,27]	Denniston 2014
HCV-RNA Prevalence by Age and Sex	See Figure 3	2016	[28,29,30]	Denniston 2014, scaled to the IA prevalent population and aged through the model accounting for people reported to the IDPH in the under 30 population
HCV Genotype	See Table 2	2014-2017	[31]	CDC data for US
Total Diagnosed (HCV-RNA)	16,810	2016	[32]	Surveillance data provided by the Iowa Department of Health
Annual Newly Diagnosed (HCV-RNA) People	1,599	2016	[33]	Surveillance data provided by the Iowa Department of Health
Annual Number People Treated	2,229	2016	[34]	Drug sales & Gilead investor Reports for the US, scaled to Iowa

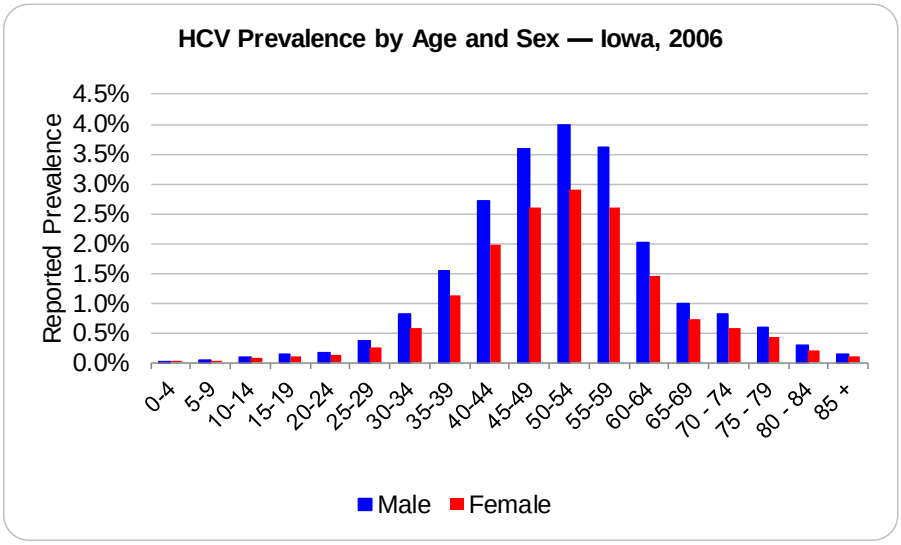
HCV Prevalence

Prevalence of HCV in Iowa was estimated for 2010 based on adjustments made to the National Health and Nutritional Examination Survey (NHANES) data. Edlin et al. details several high-risk groups (such as incarcerated, homeless, active military, etc.) that were excluded from the NHANES data. Using the adjustments for populations excluded in the NHANES data, it was estimated that 1.1% (0.9% to 3.5%) or approximately 34,500 (28,700 to 108,900) individuals were living with hepatitis C in 2010.[35] The Iowa Department of Public Health estimated ranges were used in the sensitivity analysis.

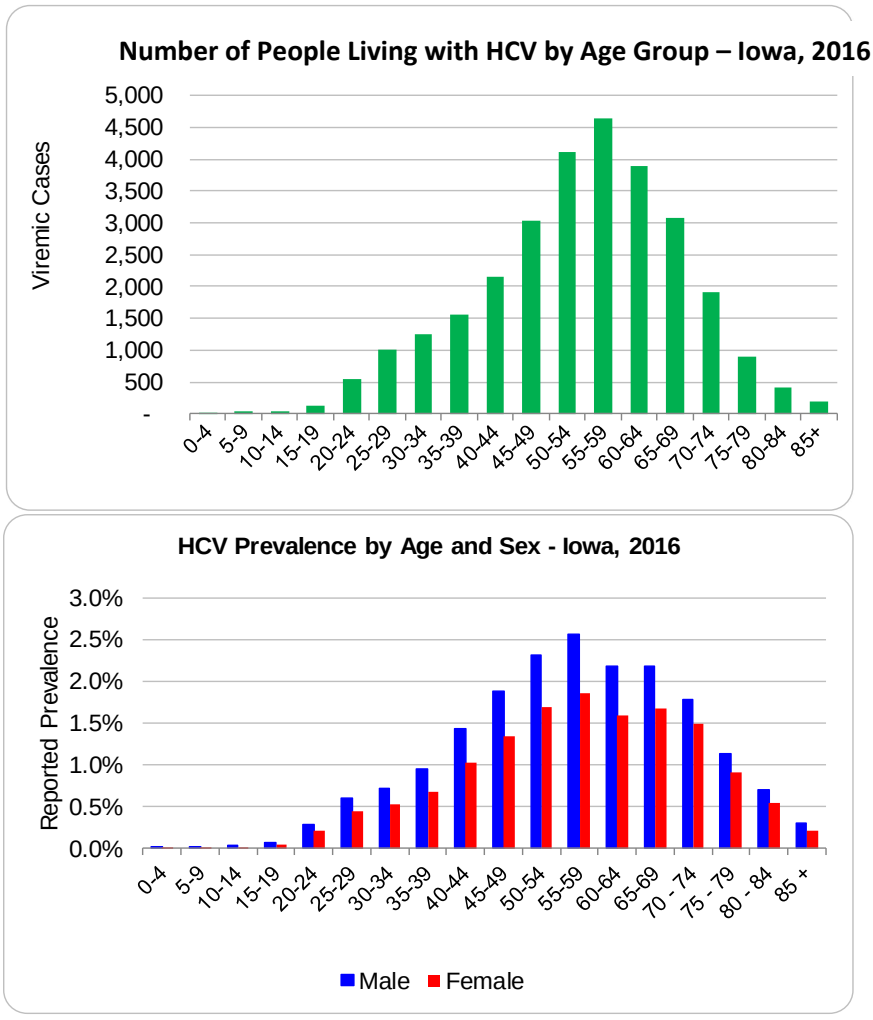
The historical age and sex distribution of the population with HCV in Iowa was assumed to be similar to the U.S. as a whole, so data reported from NHANES 2003-2010 were chosen for the baseline prevalence by age and sex, in 2006.[36] Specifically, published U.S. prevalence by age and sex was multiplied by the Iowa population by age and sex in 2006, with extrapolations for younger age groups (Figure 2). Next, this distribution was scaled to match the overall number of people with HCV infections reported by IDPH in 2016. The population with chronic HCV was aged through the model by 10 years to estimate the age and sex distribution of the population in 2016. Additionally, the incidence by age from 2010-2016 was adjusted to ensure the age and sex distribution exceeded notified cases (surveillance data provided by the Iowa Department of Public Health) among those under 30 years of age.[37]

The distribution of people with viremic HCV by age group for Iowa in 2016 can be seen in Figure 3a. As the opioid epidemic grows in the United States, we see an increase in the number of people with chronic HCV between the ages of 25 and 39. More so, in Figure 3b, we see that males between the ages of 25-49 are approximately two times more likely to have HCV than females in that age group.

Figure 2.



Figures 3a and 3b.



Genotype

The genotype distribution in Iowa was assumed to match the overall genotype distribution of the U.S., as reported by the 2003-2014 combined NHANES survey. [38]

Table 2.

Genotype	G1	G2	G3	G4	G5	G6	Mixed/ Other
NHANES 2003-2014, US	79.6%	10.9%	8.14%	0.8%	0.0%	0.5%	0.0%

Incidence

Incidence was back calculated to fit the total number of cases in 2016 and adjusted to best match the number of reported cases among those aged 30 years and younger. Prior to 2010, the incidence trend in Iowa was assumed to mirror that of the entire United States. [39] Data on acute cases were not available from the Iowa Department of Public Health at the time of the analysis.

Diagnosis

According to surveillance data provided by the Iowa Department of Public Health, 23,072 unique people with confirmed or probable HCV cases were reported between 2000 and 2016.[40] People were aged from the year of report until 2016, adjusting for viremia (80%, except for 2016 where actual RNA+ cases were reported), age- and sex-standardized mortality rates, and the number of people cured each year (in total, 14,220 people treated and 10,060 cured). The resulting number of individuals estimated to be diagnosed, alive, and with chronic infection (HCV-RNA+) in 2016 was 16,810.

In 2016 alone, IDPH received reports of 2,246 Iowans who tested antibody positive for HCV and 1,599 of those people were also confirmed to be RNA+ in that year.[41]

Treated

Between 2008 and 2016, annual U.S. treatment rates were applied to the Iowa population to estimate the number of people treated per year. Specific treatment data for Iowa were difficult to obtain. The Iowa Department of Public Health reached out to providers from all over the state, but some were reluctant to share data, while others had incomplete data sets. Treatment data available from the Veterans Administration included veterans from other states with no way to distinguish which were Iowa residents.

According to these estimates, arrived at with expert consensus, an estimated 2,200 Iowans were treated annually in 2016. Based on insurance and Medicaid guidelines, treatment in Iowa is only available for people with a fibrotic stage of F3 or F4 (i.e., advanced disease).

Subpopulations

Approximately 20% of the total population of Iowa is currently on Medicaid.[42] The prevalence of HCV in the Medicaid population was unavailable at the time of the analysis.

Universal screening for anti-HCV in the prison population began in 2004 for all incoming offenders. In 2014, over 91% of the prison population was screened for HCV antibodies with a 5.6% positivity rate. Iowa's prison population is estimated at 8,400 in 2017 and is expected to continue to increase over the next 10-years. [43] Of offenders with HCV, 16 received treatment in 2016, and a goal was set to treat 40 inmates in 2017.

There were an estimated 4,500 people who inject drugs (PWID) in Iowa in 2011 (0.2% of the population). It was assumed that approximately 43% of this population was HCV antibody positive. [44]

In 2017, approximately 22% of the total population in Iowa was women of childbearing age (WoCBA) (females aged 15 to 49 years). The prevalence of HCV in this population was unavailable at the time of this analysis, but could be estimated by the HCV disease burden model.

Results

Past and Present Burden of Disease

Annual incidence was estimated to peak in 1989, around the time systematic blood screening began. It was then modeled to increase again in 2010 to capture the increase in opioid use in the United States. In 2017, it was estimated that there were approximately 870 Iowans who acquired HCV (27.8 per 100,000).

In 2017, 59%, or 15,900, of the 26,900 people with viremic infections were diagnosed. Of the total population with HCV, only 8% (2,200) were treated. Of the 2,200 treated, 97% (2,160) were cured. This cascade of care in 2017 can be seen in Figure 4. The distribution of Iowans with HCV by fibrosis stage, which is calculated by the model, can be seen in Figure 5. More than 30% of people with HCV in 2017 were estimated to be fibrosis stage F1, while almost 50% had more advanced disease (F2, F3, or cirrhosis).

The prevalence in subpopulations was also considered. Within the incarcerated population, there were more than 2,200 offenders who were HCV-RNA+ in 2017. This was calculated by applying the anti-HCV (i.e., antibody) prevalence (5.6%) and a viremic rate of 80% to the number of incarcerated people (8,400). In 2017, 1.4% of all viremic infections (376/26,900) were among people who were incarcerated.

The prevalence among people who inject drugs (PWID) was also estimated. Assuming 20,150 total PWID in Iowa in 2011, and applying an anti-HCV rate of 43% and a viremic rate of 75%, there would be a total of 1,100 PWID who were HCV-RNA+, approximately 4% of all Iowans with viremic infections.[45]

The model was used to calculate the prevalence among WoCBA and among baby boomers (people born in the 1945 to 1965 birth cohort) in 2017. The prevalence by age in the WoCBA population ranged from 0.5% to 1.39% in 2017, with the peak prevalence in women aged 45 years. In total, 14% of all viremic infections were estimated to be among WoCBA. The prevalence by age in the baby boomer population ranged from 1.1% to 1.9% in 2017. In total, 52% of all viremic infections were estimated to be among baby boomers.

Figure 4.

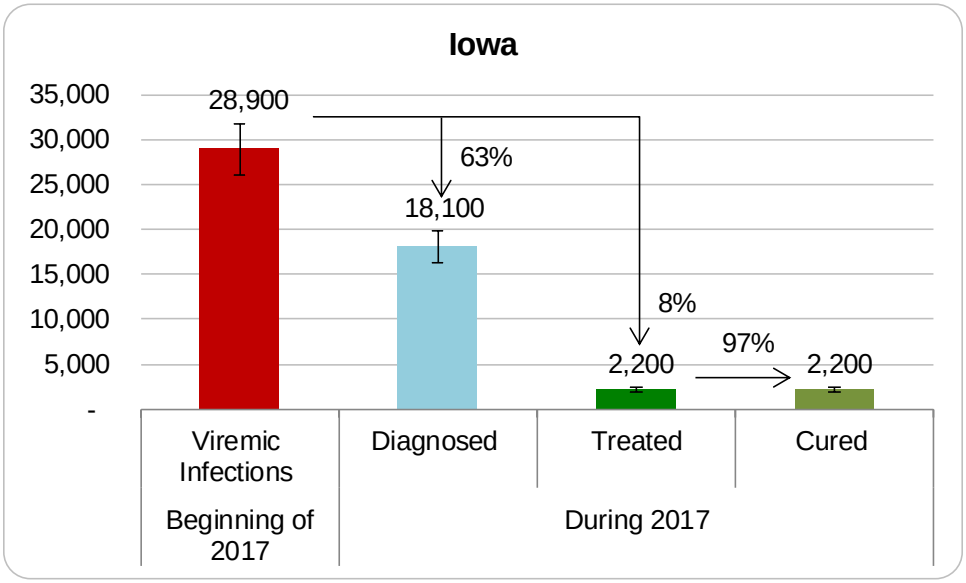
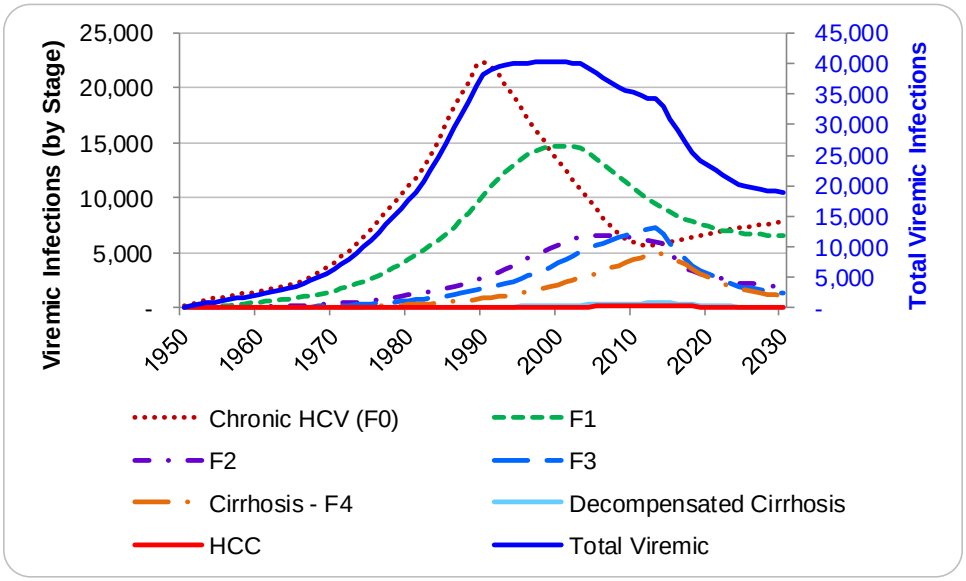


Figure 5.



The base case: Assume a 50% decrease in people treated and diagnosed by 2022

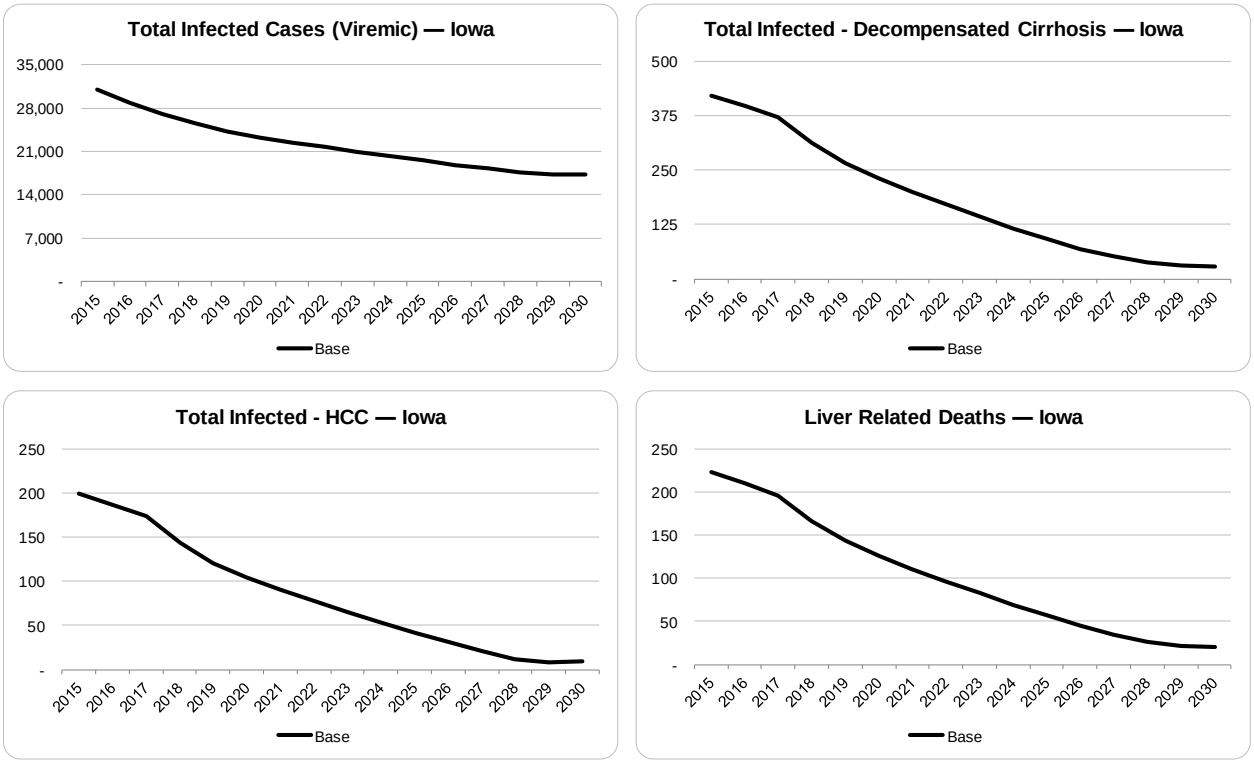
We calculated the impact on the number of HCV infections and mortality if HCV treatment and diagnosis were to decline by 50% by 2022:

	2016	2018	2019	2020	2022	2025
Treated	2,200	1,800	1,600	1,300	1,200	1,200
Newly Diagnosed	1,600	1,300	1,100	960	730	730
Fibrosis Stage*	≥F2	≥F2	≥F2	≥F2	≥F2	≥F2
New Infections	870	870	870	870	870	870
Treated Age	15-64	15+	15+	15+	15+	15+
SVR	97%	97%	97%	97%	97%	97%

* Although treatment in the Medicaid population is restricted to ≥F3, the expert panel assumed that there would be some people with other insurance types who are treated at an earlier stage. On average, ≥F2 was assumed for the state overall.

Under this scenario, the number of Iowans with viremic HCV peaked in 2000 and will continue to decline by 45% between 2015 and 2030, resulting in 18,800 Iowans with HCV by the end of 2030. Liver related deaths, hepatocellular carcinoma (HCC), and decompensated cirrhosis will also decrease by 90 to 95% as the population ages. Total cases of HCC will decrease from 200 in 2015 to 10 in 2030 (95% decrease). Total decompensated cirrhosis cases will decrease from 420 in 2015 to 30 in 2030 (95% decrease). Given the current standard of care in Iowa, there would be 200 fewer liver-related deaths by 2030, a 90% decrease from 2015.

Figure 6. The Base Case



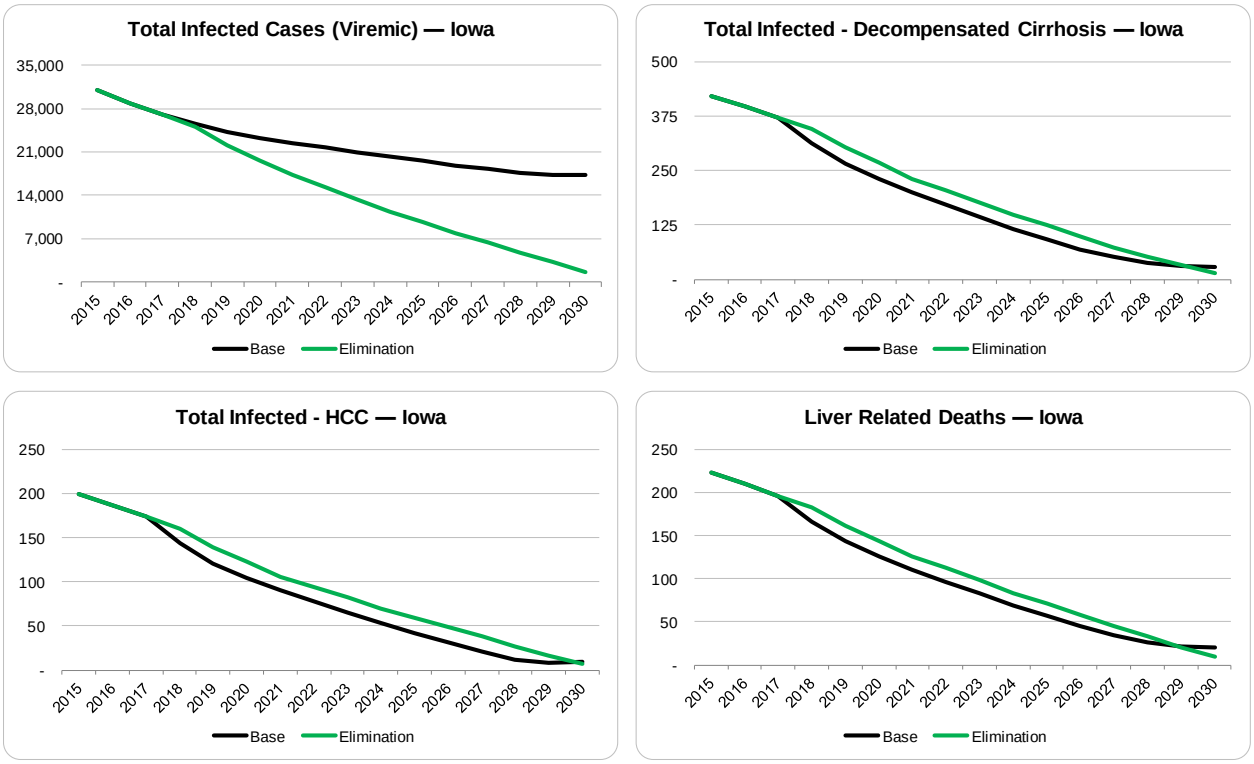
Elimination Strategy

We created an elimination strategy scenario based on the WHO Elimination Targets, defined as a 90% reduction in new infections, 90% diagnosis of all infections, and a 65% reduction in liver-related mortality by 2030. The base case is currently already meeting the targets for the reduction of liver related deaths, the remainder of the work necessary will be to reduce new infections by 90% and diagnose 90% of all people with HCV. This strategy requires the following numbers of people to be diagnosed and treated for HCV:

	2016-2018	2019	2020	2021	2022	2025
Treated	2,200	3,000	2,500	2,500	2,000	1,600
Newly Diagnosed	1,600	1,300	1,200	1,200	1,000	800
Fibrosis Stage	≥F2	≥F0	≥F0	≥F0	≥F0	≥F0
New Infections	870	780	620	430	220	90
Treated Age	15-64	15+	15+	15+	15+	15+
SVR	97%	97%	97%	97%	97%	97%

Under this scenario, 25,800 persons would need to be treated from 2018 to 2030, or an average of 2,000 persons per year. Implementing these changes would result in a 95% reduction in decompensated cirrhosis, HCC cases, and liver-related deaths by 2030. In 2030, 16 cases and 8 cases of decompensated cirrhosis and HCC, respectively, would remain. By achieving elimination, more than 45 incident cases of decompensated cirrhosis and more than 20 incident cases of HCC could be averted by 2030.

Figure 7. Elimination Strategy



Discussion

The ability to forecast the HCV disease burden in the presence and absence of interventions allows policy makers the ability to test hypotheses and quantify the impact of decisions. Using a Microsoft Excel-based Markov model, a team of state collaborators was able to develop consensus estimates to answer three primary questions: 1) Who in the state is most affected by HCV? 2) How do current policies positively or negatively impact indicators such as HCV prevalence, and HCV-related liver cancer and mortality? and 3) What level of effort will be necessary to eliminate HCV in Iowa?

Currently in Iowa, it is estimated that more people are being treated annually than are newly acquiring HCV. Alongside increased mortality from an aging population, this means that the number of people living with HCV is declining in the state. At the same time, the aging population is progressing to costly advanced liver disease, which can be prevented through timely treatment. Although the number of people with new HCV infections occurring annually is low compared with the number of people being treated, most people who acquire HCV are not diagnosed for many years. Without an active screening campaign to identify these individuals, they could remain silent carriers for decades, and may continue to transmit the virus and progress toward liver disease.

Elimination of HCV could be achieved in Iowa by diagnosing an average of 1,000 people and treating an average of 2,000 people per year. Although more than half of the population is estimated to be diagnosed, this does not imply that all diagnosed people have been linked to care. Efforts will be needed to screen and diagnose people with HCV, as well as to engage previously diagnosed people in care and treatment.

Lack of adequate funding for prevention and care and legislative barriers to syringe services programs have led to Iowa being slow to adopt policies and programs to address HCV; however, preventing transmission is integral for achieving elimination. Treatment coverage by Iowa's Medicaid program currently only extends to those that are in fibrotic stages F3 or F4. These kinds of restrictions will need to be removed to achieve elimination by 2030. Strategies such as improving access to sterile syringes, and test-and-treat programs for populations at risk (including people who inject drugs) could all contribute to these prevention efforts. Additional elimination efforts could also include the expansion of prevention and treatment programs in correctional settings.

[1] Stanaway JD, Flaxman AD, Naghavi M, et al., The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet 2016; 388: 1081-88.
[2] National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Viral Hepatitis. https://www.cdc.gov/hepatitis/hcv/index.htm
[3] Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, et al. ION-1 Investigators. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. N Engl J Med. 2014;370:1889–98. doi: 10.1056/NEJMoa1402454
[4] Poynard T., McHutchison J., Manns M., et al., "Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C." *Gastroenterology*. 2002. 122(5):1303-1313. Available at https://www.ncbi.nlm.nih.gov/pubmed/11984517. Accessed 5-01-2018.
[5] Aleman S., Rahbin N., Weiland O., et al. "A risk for hepatocellular carcinoma persists long-term after sustained virologic response in patients with hepatitis C-associated liver cirrhosis." *Clin. Infect. Dis*. 2013. 57(2): 230-236. Available at https://www.ncbi.nlm.nih.gov/pubmed/23616492. Accessed 5-01-2018.
[6] van der Meer AJ., Veldt BJ., Feld JJ. Et al., "The number needed to treat to prevent mortality and cirrhosis-related complications among patients with cirrhosis and HCV genotype 1 infection." *J Viral Hepat*. 2013. 21(8):568-77. Available at https://www.ncbi.nlm.nih.gov/pubmed/24118177. Accessed 5-01-2018.
[7] Perlman DC, Jordan AE. The Syndemic of Opioid Misuse, Overdose, HCV, and HIV: Structural-Level Causes and Interventions. Curr HIV/AIDS Rep. 2018;15(2):96-112.
[8] Edlin BR, Eckhardt BJ, Shu MA, et al., Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015: 62(5):1353-63.
[9] National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Hepatitis C Kills More Americans than Any Other Infectious Disease. Centers for Disease Control and Prevention. May 4, 2016.
[10] National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Increase hepatitis C infections linked to worsening opioid crisis. Centers for Disease Control and Prevention. December 21, 2017.
[11] ibid
[12] ibid
[13] ibid
[14] National Viral Hepatitis Roundtable. Hepatitis C: The State of Medicaid Access. Preliminary Findings: National Summary Report. November 2016. Available at: https://www.chlpi.org//wp-content/uploads/2013/12/HCV-Report-Card-National-Summary_FINAL.pdf. Accessed 5-01-2018.
[15] Campbell CA, Canary L, Smith N, Teshale E, Blythe Ryerson A, Ward JW. State HCV Incidence and Policies Related to HCV Preventive and Treatment Services For Persons Who Inject Drugs - United States, 2015-2016. Am J Transplant. 2017;17(7):1945-8.
[16] Iowa Department of Public Health. State of Iowa Hepatitis C Virus end-of-year 2016 Surveillance Report. Des Moines, IA: U.S. Bureau of HIV, STD, and Hepatitis, Iowa Department of Public Health. 2016.
[17] Edlin BR, Eckhardt BJ, Shu MA, et al., Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015: 62(5):1353-63.
[18] Iowa Department of Public Health. State of Iowa Hepatitis C Virus end-of-year 2016 Surveillance Report. Des Moines, IA: U.S. Bureau of HIV, STD, and Hepatitis, Iowa Department of Public Health. 2016.
[19] Poynard T., McHutchison J., Manns M., et al., "Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C." *Gastroenterology*. 2002. 122(5):1303-1313. Available at https://www.ncbi.nlm.nih.gov/pubmed/11984517. Accessed 5-01-2018.
[20] Aleman S., Rahbin N., Weiland O., et al. "A risk for hepatocellular carcinoma persists long-term after sustained virologic response in patients with hepatitis C-associated liver cirrhosis." *Clin. Infect. Dis*. 2013. 57(2): 230-236. Available at https://www.ncbi.nlm.nih.gov/pubmed/23616492. Accessed 5-01-2018.
[21] van der Meer AJ., Veldt BJ., Feld JJ. Et al., "The number needed to treat to prevent mortality and cirrhosis-related complications among patients with cirrhosis and HCV genotype 1 infection." *J Viral Hepat*. 2013. 21(8):568-77. Available at https://www.ncbi.nlm.nih.gov/pubmed/24118177. Accessed 5-01-2018.

[22] Centers for Disease Control and Prevention National Center for Health Statistics. National Health and Nutrition Examination Survey Data, 2003-2014. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.; 2015.
[23] Blach S., Zeuzem S., Manns M., et al., "Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study." *The Lancet Gastroenterology & Hepatology*. 2017. 2(3): p. 161-176. Available at https://www.ncbi.nlm.nih.gov/pubmed/28404132. Accessed 5-01-2018.
[24] Edlin BR, Eckhardt BJ, Shu MA, et al., Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015: 62(5):1353-63.
[25] ibid
[26] Denniston MM., Jiles RB., Drobeniuc J., et al., "Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010." *Ann Intern Med.* 2014;160(5):293-300. Available at https://www.ncbi.nlm.nih.gov/pubmed/24737271. Accessed 5-01-2018.
[27] Iowa Department of Public Health. Notification data 2000-2016. Des Moines, Iowa.
[28] Iowa Department of Public Health. State of Iowa Hepatitis C Virus end-of-year 2016 Surveillance Report. Des Moines, IA: U.S. Bureau of HIV, STD, and Hepatitis, Iowa Department of Public Health. 2016.
[29] Denniston MM., Jiles RB., Drobeniuc J., et al., "Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010." *Ann Intern Med.* 2014;160(5):293-300. Available at https://www.ncbi.nlm.nih.gov/pubmed/24737271. Accessed 5-01-2018.
[30] Iowa Department of Public Health. Notification data 2000-2016. Des Moines, Iowa.
[31] Centers for Disease Control and Prevention National Center for Health Statistics. National Health and Nutrition Examination Survey Data, 2003-2014. Hyattsville, MD: U.S. Department of Health and Human
[32] Iowa Department of Health. Notification data 1995-2016. Des Moines, Iowa.
[33] ibid
[34] Q4 2017 Earnings Results, February 6, 2018. Gilead Sciences Inc. http://investors.gilead.com/phoenix.zhtml%3Fc%3D69964%26p%3Dirol-earnings
[35] Edlin BR, Eckhardt BJ, Shu MA, et al., Toward a more accurate estimate of the prevalence of hepatitis C in the United States. Hepatology. 2015: 62(5):1353-63.
[36] Denniston MM., Jiles RB., Drobeniuc J., et al., "Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010." *Ann Intern Med.* 2014;160(5):293-300. Available at https://www.ncbi.nlm.nih.gov/pubmed/24737271. Accessed 5-01-2018.
[37] Iowa Department of Health. Notification data 2000-2016. Des Moines, Iowa.
[38] Centers for Disease Control and Prevention National Center for Health Statistics. National Health and Nutrition Examination Survey Data, 2003-2014. Hyattsville, MD: U.S. Department of Health and Human
[39] Armstrong, GL., Alter MJ., McQuillan GM., Margolis HS., "The past incidence of hepatitis C virus infection: implications for the future burden of chronic liver disease in the United States." *Hepatology*. 2000;31(3):777-82.
[40] Iowa Department of Public Health. Notification data 2000-2016. Des Moines, Iowa.
[41] ibid
[42] Preliminary Applications, Eligibility and Enrollment Data, May 21, 2018. Medicaid.gov. https://data.medicaid.gov/Enrollment/State-Medicaid-and-CHIP-Applications-Eligibility-D/n5ce-jxme/data
[43] Fineran, S. The Correctional Policy Project: Iowa Prison Population Forecast FY 2016-FY 2026, Iowa Department of Human Rights, Iowa Department of Human Rights. 2016.
[44] Lansky, A., et al. (2014). "Estimating the number of persons who inject drugs in the United States by meta-analysis to calculate national rates of HIV and hepatitis C virus infections." PLoS One **9**(5): e97596.
[45] Ibid