Public health impact of a population-based approach to HCV treatment in Alabama

This is a summary of the key outcomes of a hepatitis C virus (HCV) disease burden analysis undertaken by the CDA Foundation's (CDAF) Polaris Observatory, in collaboration with the Association for State and Territorial Health Officials (ASTHO), the Centers for Disease Control and Prevention (CDC), Alabama Department of Public Health (ADPH), University of Alabama at Birmingham, Alabama Medicaid Agency, Alabama Department of Corrections, Five Horizons Health Services and Jefferson County Department of Health.

August 2019

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

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Executive Summary and Key Recommendations

Hepatitis C virus (HCV) is a bloodborne 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 infected individuals are unaware of their HCV status until more serious, late stage complications arise. Treatment is available for HCV, with success measured by the sustained viral response (SVR) rate at 12-24 weeks post-treatment. Prior to 2014, an average of 48-70% of patients achieved SVR with the available therapies; however, recent therapeutic advances in 2018 have increased SVR rates to more than 95%.[3] Achieving SVR can reverse the effects of early stage fibrosis and slow the progression of cirrhosis into decompensation or hepatocellular carcinoma (HCC).[4,5] Achieving SVR reduces liver-related mortality by twenty-fold and all-cause mortality by four-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 needles and syringes.

Over the last 14 years, the HCV epidemic has drastically changed in the US. Originally a disease affecting "baby boomers" (people born between 1945 and 1965 according to the Center for Disease Control and Prevention's (CDC) definition), HCV has reemerged as a syndemic with opioid misuse, overdose and HIV.[7] In 2010, approximately 3.5 million Americans were chronically infected with HCV.[8] Additionally, HCV "is the leading cause of cirrhosis and liver cancer and the most common reason for liver transplantation in the US."[9] In 2013, HCV-related deaths surpassed the total combined numbers of deaths from 60 other infectious diseases reported to the CDC, including HIV and tuberculosis, and in 2014, HCV-related deaths reached an all-time high with more than 19,600 deaths reported.[10] At the same time, there has been a marked simultaneous increase in the number of persons newly diagnosed with HCV and in opioid injection across the US.[11] Increases in acute HCV and hospital admissions for opioid injection were seen between 2004 and 2014, with the number of persons newly diagnosed with HCV more than doubling between 2010 and 2014.[12]

National-level programs to control the burden of HCV have focused primarily on the older cohort of previously infected individuals. These programs include screening for HCV in the baby boomer birth cohort (1945-1965) as well as programs through the US Department of Veterans Affairs (VA) to diagnose and cure all veterans infected with HCV. Despite these efforts, barriers to treatment still exist at the state Medicaid level, as evidenced in many states by fibrosis requirements that preclude treatment for patients with early stage liver disease.[13] Universal procedures exist to prevent HCV transmission in medical settings across the US (though localized outbreaks may still occur when procedures fail). However, the recent opioid crisis presents a new challenge for HCV prevention efforts. As of 2016, policies to prevent transmission among drug users were entirely state-specific, and in many states these policies were non-existent.[14]

This report presents the outcomes of a multi-stakeholder collaboration to assess the HCV disease burden in the state of Alabama. This work follows a standard methodology (modified Delphi process) developed and facilitated by the CDAF's Polaris Observatory staff. It engages local stakeholders, including the Alabama Department of Public Health, the University of Alabama at Birmingham, Alabama Medicaid Agency, Alabama Department of Corrections, Five Horizons Health Services and Jefferson County Department of Health, to ensure the data used in the analysis represent the best available and 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, which can answer the basic questions needed for HCV policy development.

Key Insights and Recommendations

Who is affected?

- At the beginning of 2018, there were 45,100 HCV-RNA+ (viremic) infections accounting for 0.91% of the population in Alabama. Approximately 64% of infections were diagnosed previously (n=29,000), with 1,170 infections newly diagnosed, and 4% of persons infected were initiated on treatment (n=1,720) in 2018. There were an estimated 1,360 new infections, an incidence rate of 27 per 100,000 in 2018.
    - 57% of total infections were in the 1945 to 1965 birth cohort*
    - 10% of total infections were among women of childbearing age*
    - 7% of total infections were among people who inject drugs*
    - 4% of total infections were among the incarcerated population*
    - 20% of infections were among diagnosed patients on Medicaid*

    *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 current fibrosis-based HCV treatment restrictions (≥F2) in Alabama, the total number of HCV infections will decline 20% by 2030; liver-related deaths, HCC and cirrhosis will decrease by 40% as the infected population ages.

What needs to be done to eliminate HCV in Alabama?

- The World Health Organization (WHO) Elimination Targets (defined by the WHO as a 90% diagnosis and 80% treatment of all infections, an 80% reduction in incident cases and a 65% reduction in liver-related mortality by 2030) can be achieved in Alabama by taking one of the following approaches:
    - Harm reduction – Between 2020 and 2030, an additional 16,100 treatments are needed above and beyond current measures to treat an average of 2,600 patients annually (a total of 28,800). An additional 720 diagnoses are needed, an average of 890 annually (a total of 9,700). Furthermore, prevention efforts will need to be increased to lower the incidence rate from 27 per 100,000 cases in 2018 to 4.0 per 100,000 by 2030.
        - Strategies such as providing access to sterile needles and syringes, creating safe injection sites and treating persons who are actively injecting drugs for their HCV could all contribute to this prevention effort.
    - No harm reduction – In the absence of prevention efforts, between 2020 and 2030 an additional 40,000 treatments are needed above and beyond current measures for an average of 4,800 patients annually (a total of 52,700). An additional 15,000 diagnoses are needed, i.e., an average of 2,200 annually (a total of 24,200).

Background

HCV globally

Today, an estimated 71 million individuals globally are infected with hepatitis C virus (HCV), 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, which can be eliminated through coordinated efforts for prevention and treatment. Unfortunately, as of 2017, only 20% of those infected patients have ever been diagnosed, and currently only 2% of infected patients are being treated for the disease annually.[15,16]

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 in order 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 the HCV and hepatitis B virus 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 burden of hepatitis, model economic impact and develop strategies that can achieve country- or state-defined targets to eliminate it. By developing partnerships at country and regional levels, the observatory collects and analyzes data for its platform and publishes key findings to enable policies around 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 both 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 US$90 billion over a 15-year period if the government kept the status quo. A plan of action was then developed beginning in 2014 with a goal of treating 300,000 patients annually, including cost subsidies for four years. After seeing successes, the plan continued each year. In 2016, Egypt treated 577,000 patients, and the plan expanded to include patients at all stages of disease, even those without any HCV-related consequences.

In Mongolia, CDAF and its Polaris Observatory team worked with the World Health Organization's (WHO) Regional Office for the Western Pacific (WPRO) to first 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 patients. 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 US. Through collaborations with a combination of state health departments, the Centers for Disease Control and Prevention (CDC) Foundation, 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 Columbia and New York, *in progress*). Additionally, the results for ten states (California, Colorado, Georgia, Iowa, Louisiana, New Mexico, Pennsylvania, Rhode Island, Tennessee, and Washington) are included on the Polaris Observatory website (http://cdafound.org/polaris-hepC-dashboard/). Ongoing analyses include collaborations with ASTHO, CDC and state partners to identify the disease burden and associated elimination strategies in Alabama.

Hepatitis C-Related Disease Burden – Alabama

The analysis presented here represents the work of stakeholders from Alabama Department of Public Health (ADPH), University of Alabama at Birmingham (UAB), Alabama Medicaid Agency, Alabama Department of Corrections, Five Horizons Health Services, Jefferson County Department of Health, ASTHO, CDC and CDAF. The primary objectives were to quantify the current and future disease burden of HCV in Alabama and identify the level of effort necessary to eliminate HCV in the state.

Based on the Edlin et al. adjustments of the National Health and Nutrition Examination Survey (NHANES) data, scaled specifically to Alabama (detailed later), it was estimated that 1.1% (0.8%-1.5%) of the Alabama population was chronically infected (RNA positive) with HCV in 2010. This equates to approximately 54,100 (38,700-72,800) infected individuals in 2010. [17]

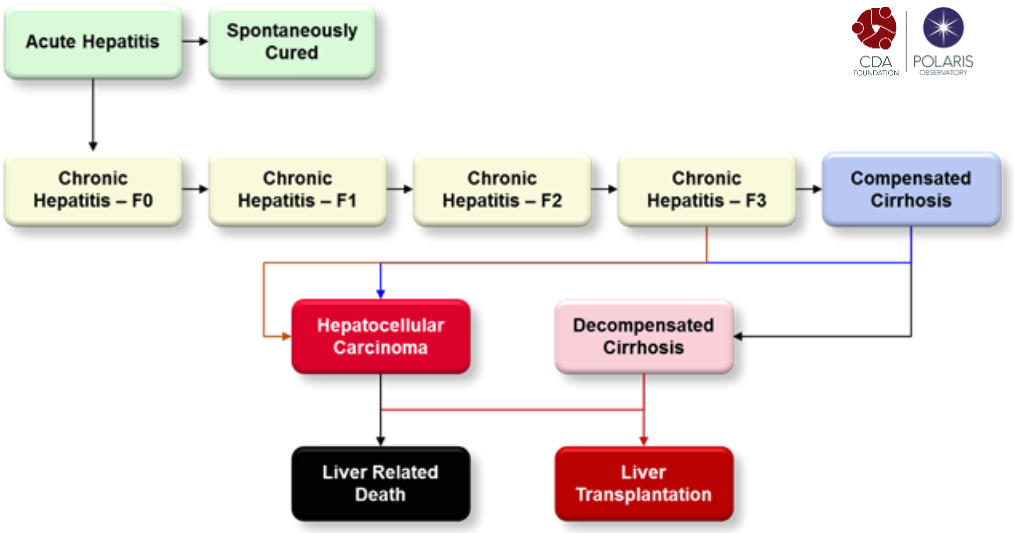
Achieving a sustained virologic response (SVR) to HCV treatment can reverse the effects of early stage fibrosis and slow the progression of cirrhosis into decompensation or hepatocellular carcinoma (HCC).[18,19] This impact on disease trajectory reduces liver-related mortality by twenty-fold and all-cause mortality by four-fold.[20] Direct acting antivirals (DAA) can achieve SVR in >90% of patients with HCV.[21]

Similar to the US as a whole, in Alabama, 75% of known infected individuals with genotyping results have genotype 1.[22] Though previously genotype 1 chronic infection was the most difficult to treat, DAAs have become the standard of care and are safe for the treatment of genotype 1 patients. For this modeling exercise, based on input from expert meetings, we assumed an SVR rate of 90% among patients for all genotypes initiating treatment.

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 captures new (acute) infections by age and sex starting in 1950, and then follows the annual progression from acute to spontaneous clearance or through the stages of chronic infection. Additionally, the model accounts for age-specific mortality as well as patients who maintain an SVR. Based on state-specific inputs, the model is used to forecast the disease burden by HCV-sequelae, including fibrosis, cirrhosis, decompensated cirrhosis, HCC and liver-related death from 1950-2030.

Input Data

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

Table 1.

Historical Input	Estimate (Range)	Estimate Year	References	Source Description
HCV-RNA+ Infections	54,100 (38,700-72,800)	2010	[24]	NHANES data adjusted for Alabama specific homeless and incarcerated populations
Anti-HCV Prevalence by Age and Sex	See Figure 2	2006	[25]	Analysis of NHANES data
HCV-RNA Prevalence by Age and Sex	See Figure 3	2018	[26,27]	Denniston 2014, scaled to the Alabama prevalent population and aged through the model accounting for patients with lab results reported to the ADPH in the under 40 population
HCV Genotype	See Table 2	2016-2018	[28]	ADPH mostly electronically laboratory reported data
Total Diagnosed (HCV-RNA)	29,000	2017	[29]	Unpublished data from a statewide test and treat program (ACTIVE-C), assuming it accounts for 90% of all patients
Annual Newly Diagnosed (HCV-RNA)	1,650	2017	[30]	~3% of the US infected population are newly diagnosed annually, scaled to the AL population
Annual Number Treated	2,079	2016	[31]	Aggregate data from a statewide test and treat program (ACTIVE-C) from January 2011 to March 2017, assuming it accounts for 50% of treated patients statewide. Data distributed annually based on national treatment trends during the same years

HCV Prevalence

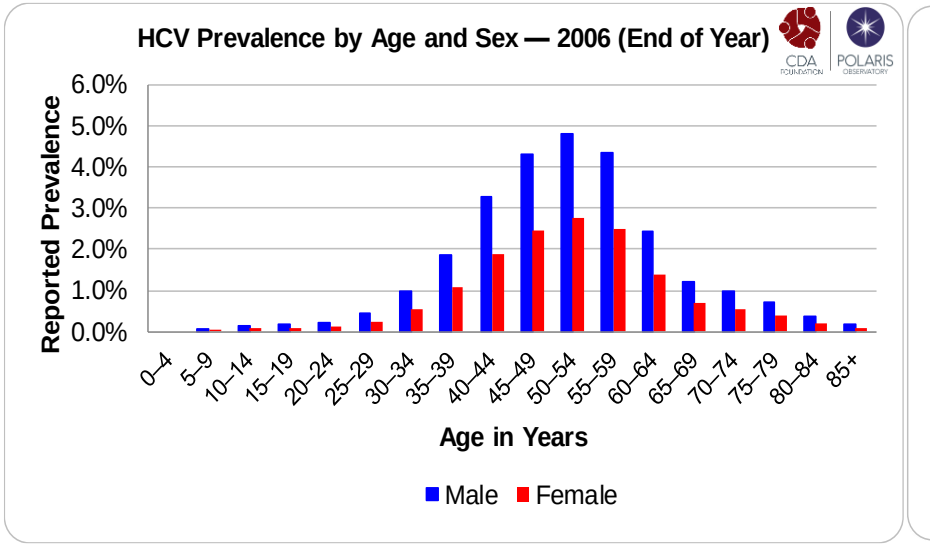
Prevalence of HCV in Alabama was estimated for 2010 based on adjustments made to the National Health and Nutritional Examination Survey (NHANES) data. Edlin et al. details several high-risk groups (such as incarcerated, homeless, active military, etc.) that were excluded from the NHANES data. Taking those groups into consideration, and based on this analysis, it was estimated that 1.1% (range 0.8%-1.5%) of the population, or approximately 54,100 (range 38,700-72,800) individuals, were chronically infected with Hepatitis C in 2010.[32] Uncertainty intervals from Edlin et al. were used in the sensitivity analysis.

Due to a lack of Alabama-specific data, the historical age and sex distribution of the infected population in Alabama was assumed to be similar to the US as a whole, so data reported from NHANES 2003-2010 were chosen for the baseline prevalence by age and sex in 2006.[33] Specifically, published US prevalence by age and sex was multiplied by the Alabama population by age and sex in 2006, with extrapolations for younger age groups (Figure 2a). Next, this distribution was scaled to match the overall number of HCV infections estimated in 2010. The HCV infected population was aged through the model by 12 years to

estimate the age and sex distribution of the infected population in 2018. Additionally, the incidence by age after 2010 was adjusted to ensure the age and sex distribution exceeded notified cases (surveillance data provided by the ADPH) for those under 40 years of age.[34]

The distribution of total viremic patients by age group for Alabama in 2018 is shown in Figure 3a. As injection drug use grows in the United States, the number of infected individuals increases between the ages of 25 and 39 years. More so, in Figure 3b, there is an increasing parity among males and females in the younger age groups (15-39 years).

Fig. 2a and 2b. Historical reported viremic prevalence and cases distributed by age and sex and applied to the Alabama population in 2006.[35,36]



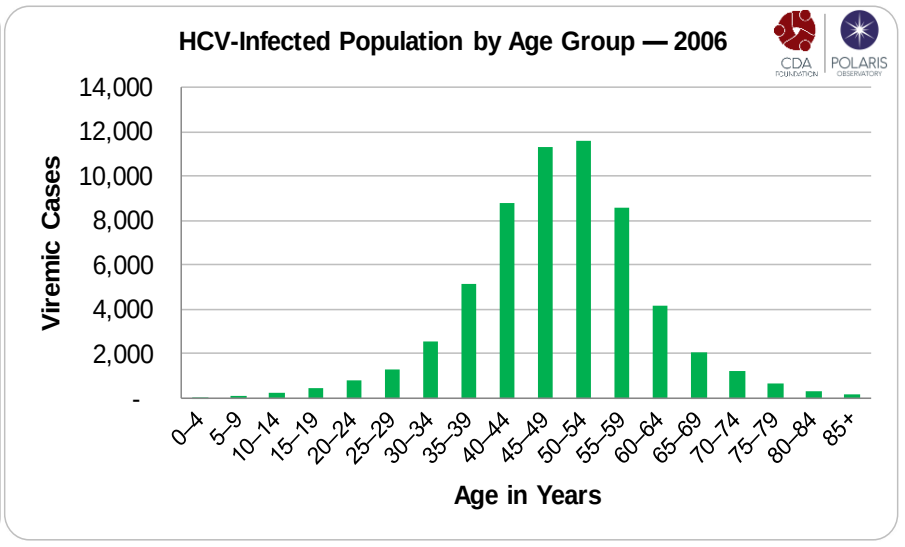
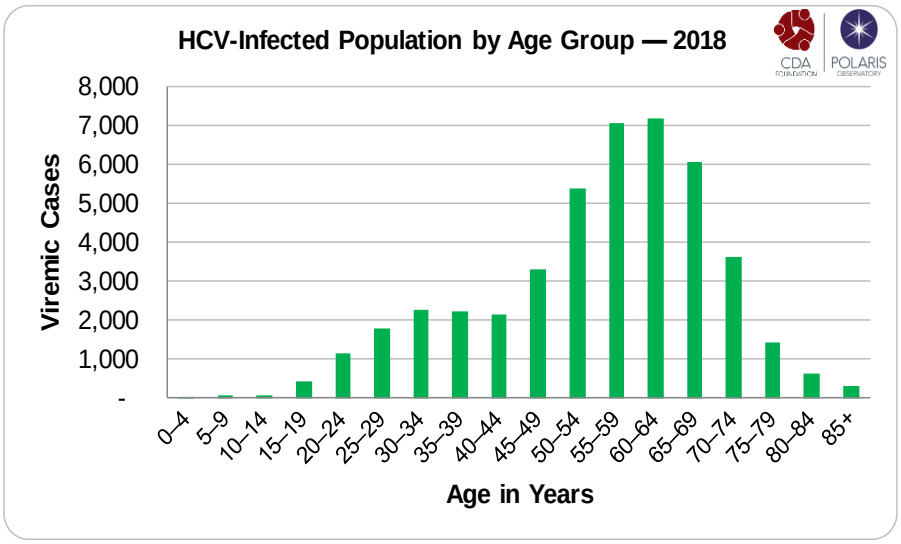
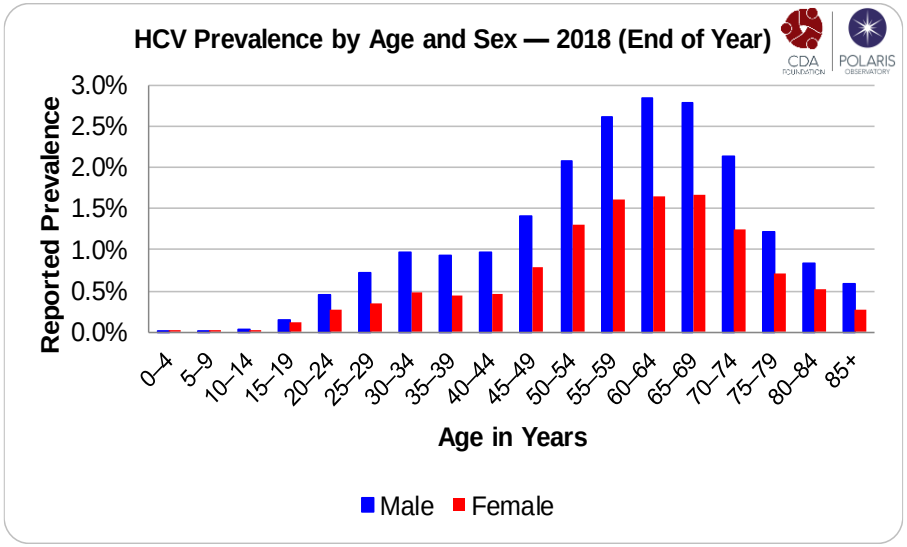


Fig. 3a and 3b. Modeled viremic prevalence and cases, adjusting for aging, incidence, mortality and cures over time and accounting for notification data.[37,38,39]





Genotype

The genotype distribution in Alabama is based on laboratory results reported to ADPH from 2016 to 2018.[40]

Table 2.

Genotype	G1	G2	G3	G4	G5	G6	Mixed/ Other
ADPH	75.0%	12.8%	9.1%	0.6%	0.0%	0.1%	2.4%

Incidence

Incidence was back-calculated to fit the number of infections in 2010 and adjusted to best match cases aged 40 years and younger. Prior to 2012, the incidence trend in Alabama was assumed to mirror that of the United States.[41] Acute notification data from ADPH averaged 35 reported acute cases annually in years 2012-2016 and 2018,[42,43] however this was determined to likely make up a very small fraction of new infections.

Diagnosis

According to data reported electronically to ADPH from 140 facilities across the state and analyzed in corroboration with the Alabama Coalition for Testing, Interventions & Engagement in Hepatitis C Care (ACTIVE-C) and UAB, 26,098 unique patients had positive RNA results between the beginning of 2011 and March of 2017.[44] This database captures ~90% of test results statewide with the other 10% coming from manual reporting (experts' input), and assuming the same test positivity rate in testing not captured by this database, it is estimated that there were 28,998 people living in Alabama with a positive test result for viremic HCV in 2017. It is estimated that approximately 3% of the HCV-infected population in the US is diagnosed each year, and this rate was scaled to the Alabama infected population to estimate the number of newly diagnosed patients in 2017 (N=1,650).[45]

Treated

Data from ADPH electronic and manual reporting, analyzed in conjunction with ACTIVE-C and UAB, were available for the number of patients treated between 2011 and March of 2017.[46] These data (n=3,618) were assumed to account for 50% of treated patients in Alabama (the other 50% accounting for patients already diagnosed prior to 2011 (experts' input)), thus it was assumed that ~7,236 patients may have been treated statewide over this time period. To estimate the number of patients treated annually, the distribution and proportion of annual treatment data from the US over the same time period was applied to the total number of patients treated in Alabama, resulting in an estimated 2,079 patients treated in 2016.[47] Future years were also estimated based on the projected decline in the number of patients annually treated over time at the national level (1,720 treated patients in Alabama in 2017).[48]

Based on Medicaid guidelines, treatment for Medicaid recipients in Alabama is only available to those patients that are of a fibrotic stage F2 or later.

Subpopulations

Approximately 15-25% of the population of Alabama is currently on Medicaid.[49,50] The prevalence rate of HCV in the Medicaid population was unavailable at the time of this analysis, however a total 9,131 recipients were considered to have chronic HCV between 2013 and 2018 (at least two paid claims on different dates of service in the year).[51] The majority of these patients were white (59%), followed by black

(24%), other (16%) and Hispanic (5%). There were more female than male recipients by 52% to 48%. The majority of this patient population is accounted for by 50-64 year olds (60%), followed by 35-49 year olds (24%), 20-34 year olds (12%), >64 year olds (10%) and <20 year olds (1%). Treatment claims data were also available for Medicaid recipients with 561 initiating treatment between 2013 and 2018 and 477 completing treatment (defined as having at least 56 days of HCV medications and SVR lab drawn between 120 and 270 days after their last prescription fill date).[52] Annual treatment initiation was still increasing in 2018 at 150 patients while treatment completion had peaked in 2015 at 138 patients.

The Alabama prison system conducts symptom screening upon intake, followed by antibody testing if symptomatic (expert input). As of the beginning of 2019, there were 2,237 known HCV-antibody positive cases within the Alabama prison system, out of 20,318 incarcerated people; accounting for viremia (75%), 1,678 would be RNA positive.[53] The Alabama Department of Corrections is in the process of implementing testing protocol for all incarcerated persons upon intake (whether symptomatic or not), therefore the number of positive cases is expected to increase.[54] Due to cost barriers, few inmates are currently being treated (expert input).

There were an estimated 14,400 people who inject drugs in Alabama in 2011 (based on data reporting a rate of 0.3% in the US population).[55] It was assumed that approximately 43% of this population was anti-HCV positive.[56] Among Medicaid recipients, approximately 14,000 opioid use-related claims were made in each of 2016 and 2017 with about 650 hepatitis-C patients among these claimants, though it is unclear what percentage of these claims are related to injection drug use.[57]

In 2018, approximately 23% of the population in Alabama was women of childbearing age (WoCBA) (females aged 15-49 years). The prevalence of HCV in this population was unavailable at the time of this analysis but can be estimated by the HCV disease burden model (as reported in the Results section below).

Results

Past and Present Burden of Disease

Annual reported incidence was modeled with experts' input to peak in 1989, around the time systematic blood screening began. It was then modeled to increase again in 2012 in order to capture the increase in transmission due to higher rates of injection opioid usage in the United States. In 2018, it was estimated that there were approximately 1,360 Alabamans who acquired HCV (27.5 per 100,000). This number is higher than the number of acute cases reported to the state, even when using the CDC's method for accounting for underreporting by applying a multiplier of 14. More than 7,600 antibody positive cases under the age of 35 years have been newly reported between 2016 and 2018, which could indicate a higher rate of incidence in recent years.[58]

At the start of 2018, 64% (N=29,000) of the estimated 45,100 viremic infections were diagnosed. Of the infected population, only 4% (n=1,720) initiated treatment. Of the 1,720 who initiated treatment, 90% (n=1,550) were cured. This cascade of care in 2018 can be seen in Figure 4. The distribution of Alabamans with HCV by fibrosis stage, which is calculated by the model, can be seen in Figure 5. Nearly 45% of patients in 2018 were estimated to be fibrosis stage F0 or F1, while almost 55% were F2, F3 or cirrhotic.

The prevalence in subpopulations was also considered. Within the incarcerated population there were more than 1,600 known RNA positive infections in 2018. This was estimated by applying the viremic rate

(75%) to the reported number of known anti-HCV positive individuals (2,247).[59] In 2018, known viremic infections among incarcerated persons accounted for 4% of estimated viremic infections (1,678/45,100).

The prevalence among people who inject drugs was also estimated. Assuming 14,400 people who inject drugs in Alabama in 2011 and applying an anti-HCV rate of 43% and a viremic rate of 75%, there would be 3,000 HCV-RNA positive people who inject drugs, approximately 7% of all viremic infections.[60]

The model was used to calculate HCV prevalence among WoCBA and in baby boomers (persons born in the 1945 to 1965 birth cohort). The prevalence by 5-year age cohort in the WoCBA population ranged from 0.11% to 0.79% at the start of 2018, with the peak prevalence in those aged 45-49. In total, 10% of all viremic infections were estimated to be WoCBA. The prevalence by age in the baby boomer population ranged from 1.66% to 2.22% at the beginning of 2018 and represented 57% of all viremic infections.

Figure 4.

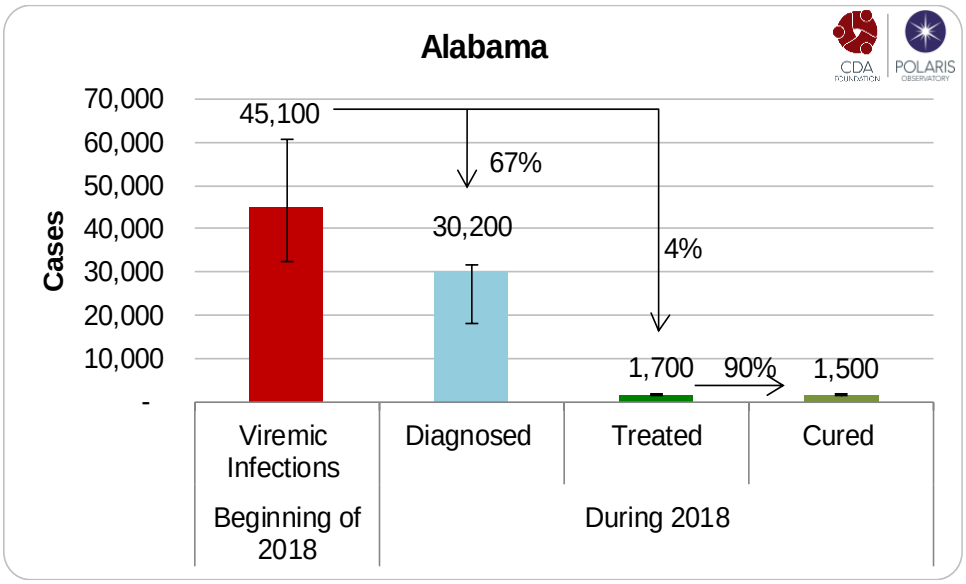
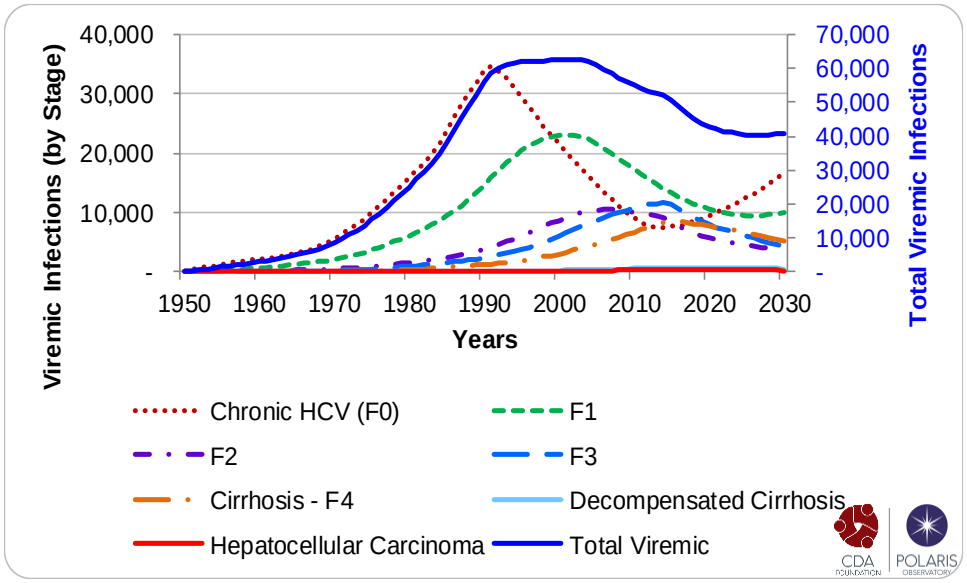


Figure 5.



Treatment Scenarios

We created four scenarios: 1) Base, the current standard of care, assuming a 40% drop in treatment between 2017 and 2020; 2) Unrestricted, a sustained annual treatment rate that is higher than in Base with the removal of fibrosis restrictions; 3) WHO elimination targets through harm reduction; 4) WHO elimination targets through treatment. The elimination scenarios are based on the WHO Elimination Targets, defined as an 80% reduction in new infections, 90% diagnosis of all infections and a 65% reduction in liver-related mortality by 2030. These strategies require the following numbers of patients to be diagnosed and treated for HCV:

Table 3.

Scenario	Model Parameter	2017	2018	2019	2020	2021	≥2022
Base	Incident Infections	1,300	1,400	1,400	1,500	1,600	1,700
	Treated	1,900	1,700	1,600	1,200	1,200	1,200
	Newly Diagnosed	1,700	1,200	1,200	820	820	820
	Fibrosis Stage*	≥F2	≥F2	≥F2	≥F2	≥F2	≥F2
	Treated Age	15-85+	15-85+	15-85+	15-85+	15-85+	15-85+
	SVR	90%	90%	90%	90%	90%	90%
Unrestricted	Incident Infections	1,300	1,400	1,400	1,500	1,500	1,600
	Treated	1,900	1,700	1,600	1,400	1,400	1,400
	Newly Diagnosed	1,700	1,200	1,200	820	820	820
	Fibrosis Stage*	≥F2	≥F2	≥F2	≥F0	≥F0	≥F0
	Treated Age	15-85+	15-85+	15-85+	15-85+	15-85+	15-85+
	SVR	90%	90%	90%	90%	90%	90%
WHO Targets,	Incident Infections	1,300	1,400	1,400	1,300	940	460
	Treated	1,900	1,700	1,600	1,600	2,000	2,800

Harm Reduction	Newly Diagnosed	1,700	1,200	1,200	820	820	900
	Fibrosis Stage*	≥F2	≥F2	≥F0	≥F0	≥F0	≥F0
	Treated Age	15-85+	15-85+	15-85+	15-85+	15-85+	15-85+
	SVR	90%	90%	90%	90%	90%	90%
WHO Targets, Treatment	Incident Infections	1,300	1,400	1,400	1,500	1,500	1,500
	Treated	1,900	1,700	1,600	2,500	3,000	5,800
	Newly Diagnosed	1,700	1,200	1,200	2,000	2,000	4,000
	Fibrosis Stage*	≥F2	≥F2	≥F0	≥F0	≥F0	≥F0
	Treated Age	15-85+	15-85+	15-85+	15-85+	15-85+	15-85+
	SVR	90%	90%	90%	90%	90%	90%

* As of 2018, fibrosis stage restrictions only remained for Medicaid patients in Alabama, thus the table indicates restrictions on this population. It is assumed that more advanced patients are prioritized for treatment even when restrictions are removed.

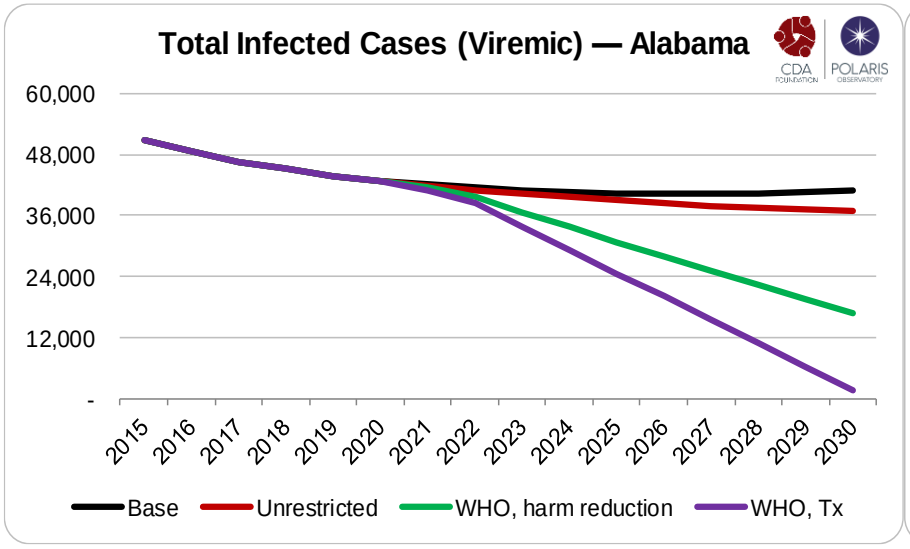
Under the base scenario, the number of Alabamans with viremic HCV peaked in 2001 and will decline by 20% between 2015 and 2030, resulting in 41,000 Alabamans with HCV by the end of 2030. Liver-related deaths, incident cases of hepatocellular carcinoma (HCC) and incidence of decompensated cirrhosis will also decrease by 40% as the population ages. Incidence of HCC will decrease from 300 in 2015 to 170 in 2030 (40% decrease). Decompensated cirrhosis cases will decrease from 240 in 2015 to 140 in 2030 (40% decrease). Given the current standard of care in Alabama, there would be 170 fewer liver-related deaths by 2030, a 40% decrease from 2015.

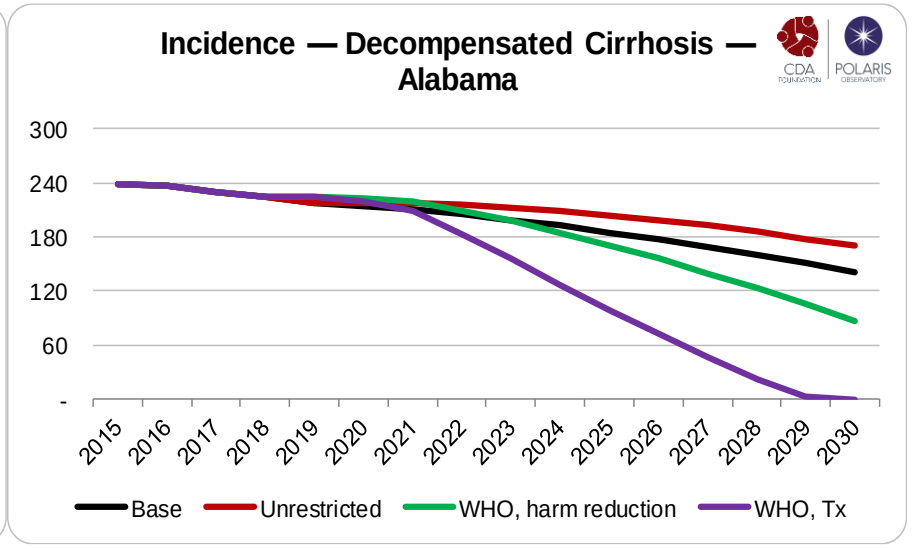
Under the unrestricted scenario, an additional 200 patients would be treated in 2020 due to the removal of fibrosis restrictions. Implementing these changes would result in a 25-30% reduction in cases of decompensated cirrhosis, HCC and liver-related deaths by 2030. Compared to the base, late stage outcomes are less optimistic due to the redistribution of treatments to some earlier stage patients.

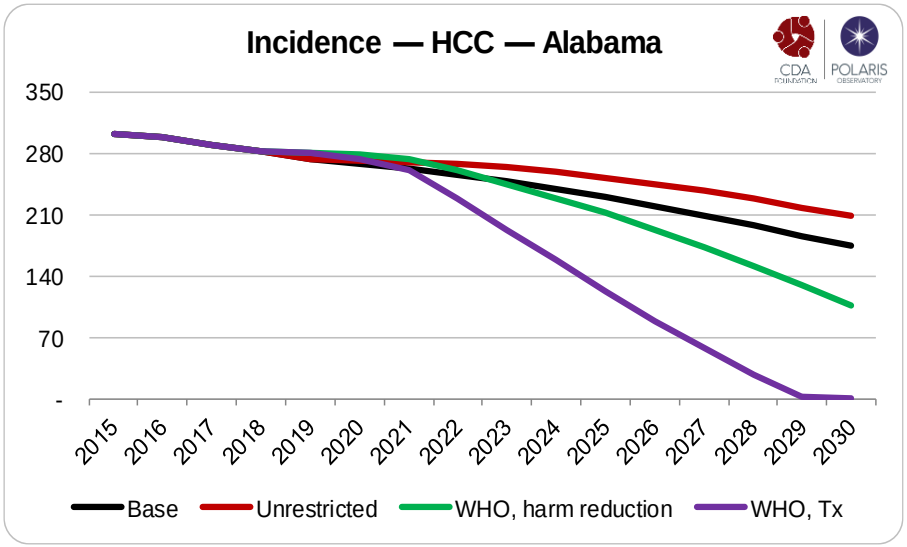
WHO Elimination can be achieved with an increase in treatment, diagnosis and prevention efforts. Increases in the numbers annually diagnosed and treated to peaks of 900 and 2,800, respectively, would result in a 65% reduction in liver-related deaths and incident cases of both decompensated cirrhosis and HCC by 2030. By achieving elimination, 230 cases of HCC and 180 cases of decompensated cirrhosis would be averted, and 390 lives would be saved between 2019 and 2030 (as compared to the base scenario).

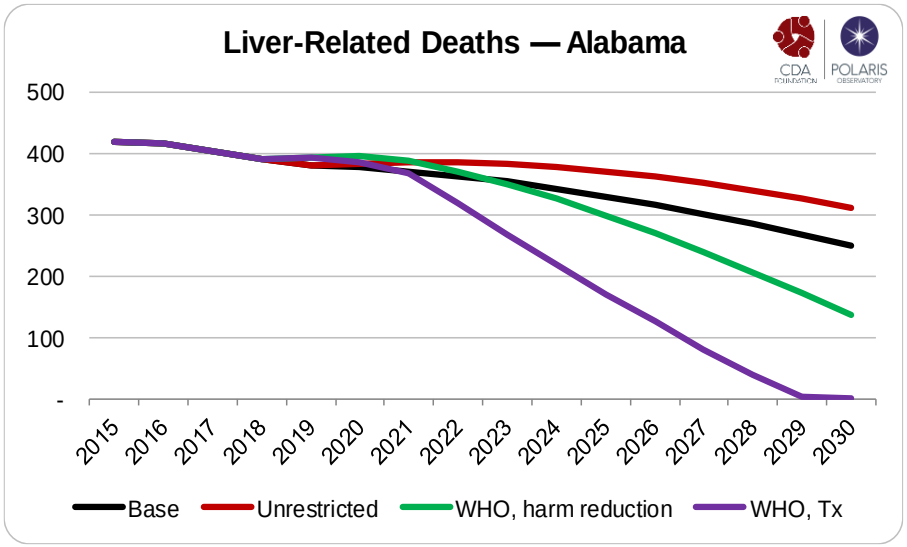
In the absence of harm reduction, WHO Elimination can be achieved through an aggressive treatment strategy. Treating an average of 4,800 patients annually would result in a >99% reduction in incidence of decompensated cirrhosis, HCC and in liver-related deaths by 2030. By achieving elimination, 860 cases of incident decompensated cirrhosis and 1,070 cases of HCC could be averted, and 1,570 lives would be saved (as compared to the base scenario).

Figure 6. Scenario Outcomes









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? 3) What level of effort will be necessary to eliminate HCV?

Currently in Alabama, it is estimated that more patients are being treated annually than are newly infected with HCV. Alongside increased mortality from an aging population, this means that the number of persons 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 new infections occurring annually is low compared with the number of patients being treated, most people who are newly infected 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 in their liver disease.

Elimination of HCV could be achieved in Alabama through a combination of moderate treatment scale-up and harm reduction or, in the absence of prevention measures, by treating an average of 4,800 patients per year. While treatments may be costly, treatment-based elimination significantly reduces the number of patients that progress to more costly stages of HCV. Although more than half of the HCV-infected population is estimated to be diagnosed, this does not indicate that all patients are linked to care. Efforts will be needed to screen and diagnose new patients as well as to engage previously diagnosed patients with services.

Alabama has yet to adopt policies and programs to adequately address HCV prevention and care; however, preventing new infections is integral for achieving elimination. Treatment coverage by Alabama's Medicaid program currently only extends to those that are fibrotic stage F2 or later. These restrictions will need to be removed in order to achieve elimination and reach all patients. Strategies such as improving access to sterile needles and syringes and test-and-treat programs for high risk populations (including people who inject drugs) could contribute to this prevention effort. Scientific research has shown that addiction is a medical condition among complex, multi-faceted individuals, and as a result, there has been a shift in how society deals with drug use away from punishment and marginalization and towards prevention and treatment.[61] This change in paradigm should apply to HCV as it relates to people who inject drugs as well. Additional prevention efforts could also include the expansion of treatment and prevention programs in Alabama prisons. Incarcerated people largely overlap with some of the most at-risk populations who are also the hardest to link to health care. Establishing a point of care in prisons would create an opportunity to prevent future infections through treatment of an otherwise difficult to reach population often with high transmission rates. Because the incarcerated population is very dynamic, there is a constant flow of patients living with HCV and treatment opportunities. The success of intervention would thus need to be measured by treatment and cure statistics and not by prevalence rate at intake.

Appendix A: Expert Panel Participants

The following individuals contributed to the content of this report through their participation in the expert panel discussions and in report revisions, and we are grateful for their efforts:

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Appendix B: Glossary of Terms

ACTIVE-C – Alabama Coalition for Testing, Interventions and Engagement in Hepatitis C Care

ADPH – Alabama Department of Public Health

ASTHO – Association of State and Territorial Health Officials

CDAF – Center for Disease Analysis Foundation

CDC – Centers for Disease Control and Prevention

DAA – Direct-acting antiviral

F1, F2, etc. – Fibrosis Score 1, 2, etc.

HCC – Hepatocellular carcinoma

HCV – Hepatitis C virus

HIV – Human immunodeficiency virus

NHANES – National Health and Nutrition Examination Survey

RNA – Ribonucleic Acid

SVR – Sustained virological response

Tx - Treatment

VA – US Department of Veterans Affairs

WHO – World Health Organization

WoCBA – Women of childbearing age

WPRO – Western Pacific Regional Office

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