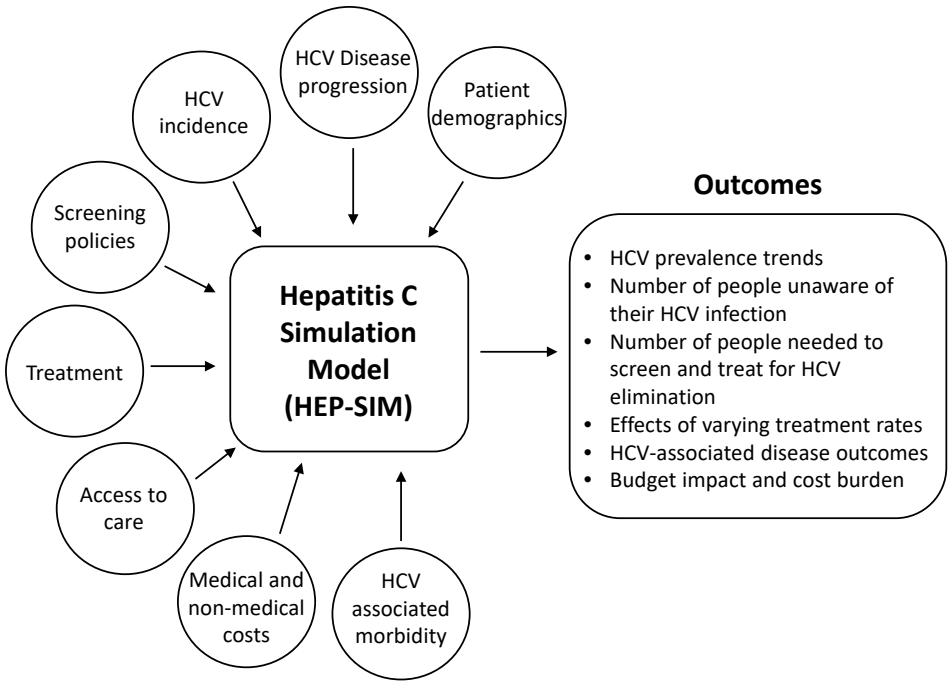
Hep C State Policy Simulator

Model Structure and Parameter Estimates in Brief

Underlying Model

The *Hep C State Policy Simulator* (hereafter, the *Simulator*) uses a previously validated mathematical model, HEP-SIM, which includes information on patient demographics, hepatitis C disease progression, hepatitis C screening, therapeutic advancement, access to healthcare (including insurance status), and the cost of care and treatment to assess temporal trends in hepatitis C disease burden and cost burden from 2018 to 2030 (Figure 1, adapted from Chhatwal et al.[1]).[1-3] The HEP-SIM model has been used to project the changing prevalence and various outcomes of hepatitis C virus (HCV) infection in the United States since 2001, and has been validated with multiple studies and national surveys.[4-7]

Figure 1: Key components and outcomes of HEP-SIM:

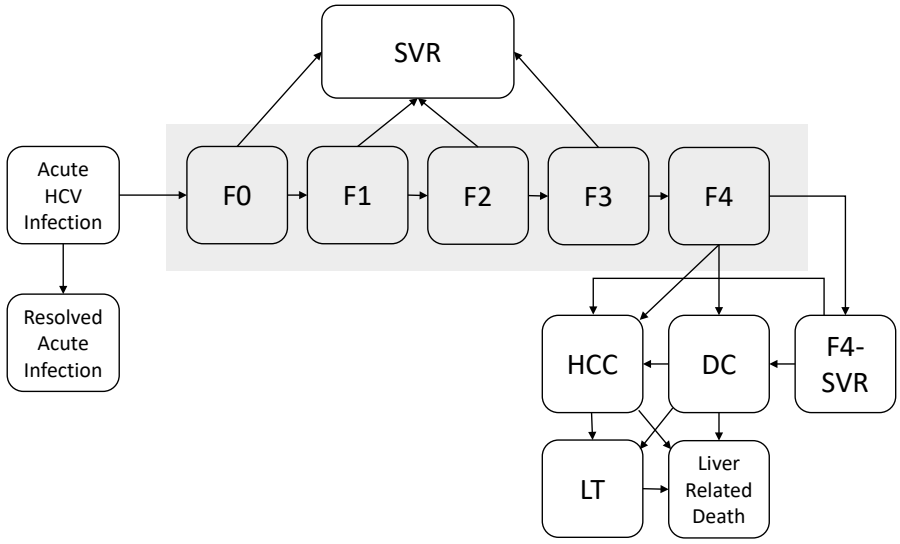


The natural history of hepatitis C development is simulated as a state-transition model (Figure 2, adapted from Chhatwal et al.[1]). At any given time, a patient will be in one of the health states represented in the boxes. The health states include infection stages (acute HCV infection and resolved HCV infection) as well as chronic

disease stages (F0, no liver fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, many septa without cirrhosis; and F4, cirrhosis). Patients can transition to different health states, as illustrated by arrows. Patients whose disease is successfully treated transition to the sustained virologic response (SVR) state from states F0 to F3 and are assumed to be cured. In contrast, patients in F4 state who are successfully treated (illustrated as F4-SVR state) may develop further complications. In addition, patients in hepatocellular carcinoma (HCC), decompensated cirrhosis (DC), and liver transplantation (LT) states have higher mortality rates than do people in the general population. All other patients have the same mortality rates as that of the general population.

We also account for new HCV infections. However, our model explicitly excludes re-infection. Available data, while limited, suggest reinfection rates are generally low.[8,9] Moreover, incident cases, which are captured in the model, indirectly account for re-infections to some extent.

Figure 2: State-transition model of the natural history of hepatitis C:



Estimating Model Parameters

We used a variety of data sources to estimate model parameters. The information below describes the different components of model inputs and their data sources.

HCV Epidemiology

- State-level HCV prevalence
    - This parameter captures the number of adults living with HCV infection in each US state and the District of Columbia. The input values are based on recently published work[10] that leverages multiple data sources and advanced statistical models to estimate the prevalence of current HCV infection in each state from 2013 to 2016 (Appendix Table A.1). While users can change the default value, the model limits user adjustments to between -50% and +200% of the default value. This range balances user flexibility within a reasonable uncertainty range for default values and application speed online.
- State-level estimates of HCV prevalence by incarceration and insurance coverage

- Incarcerated population: Estimates for HCV prevalence in state prisons are taken from the Hep Corrections,[11] which brings together data from both peer-reviewed publications and other sources. Most notably, the site uses data contributed by Siraphob Thanthong-Knight, whose findings about access to hepatitis C treatment in prisons are featured in a 2018 Kaiser Health News special article,[12] and a previously conducted survey.[13,14]

- Non-incarcerated population: For each state, this parameter captures the breakdown of patients with HCV by insurance status: *Medicaid, Medicare, privately insured,* and *uninsured*. Input values are based on a recent CDC analysis of 2012-2015 state-level data on ambulatory, inpatient, and urgent care visits available through the National Center for Health Statistics (NCHS) and the Healthcare Cost and Utilization Project (HCUP) (Appendix Table A.2). CDC combined these data with evidence on frequency of seeking medical care among patients with HCV[15] and those with opioid abuse/dependence[16] to estimate the number of patients with HCV in each insurance category. Where state-level estimates are not available, the corresponding estimates from the census division/region level are used (Appendix Table A.2).

- Combined estimates: For each state, the estimates of HCV prevalence[10] are combined with the estimated breakdown of patients with HCV by insurance status and incarceration to compute the number of HCV-infected individuals within each subpopulation: Medicaid, Medicare, privately insured, uninsured, and incarcerated (Appendix Table A.1). If users choose to change the default value for HCV prevalence, then the estimated breakdown by subpopulation is applied to the updated prevalence value.

- HCV genotype

  - The HCV genotype distribution is assumed to be the same for all states and is obtained from Mapping Hep C.[17]

- HCV fibrosis stage distribution

  - The HCV fibrosis stage distribution is assumed to be the same for all states and is obtained from Mapping Hep C.[17]

- HCV incidence

  - Estimates of the new (incident) cases of HCV infection by year are obtained from CDC reports for the years 2010–2016. Data from 2007 to 2016 are downloaded from the CDC website.[18] Where state-level estimates are not available, an estimate applying the national rate to the state population is used (Appendix Table A.3). For the years between 2017 and 2028, we projected trends in HCV incidence by assuming that annual incidence continues to trend upward at the rate observed between 2006 and 2016. From 2029 onwards, we assumed that incidence rates stabilize and remain flat (Appendix Table A.4).

- HCV Awareness

  - The probability that an HCV-infected person was aware of his/her infection at the start of the model simulation depended on their age and insurance status. We relied on information from published studies of NHANES data for this information (Appendix Table A.5).[5,19]

Interventions

For each state, the user can define a hepatitis C screening strategy, an annual treatment rate, treatment restrictions (if any), and cost of hepatitis C treatment with direct-acting antivirals (DAAs).

- Screening strategy

  - Provider-driven diagnostic and risk-based testing: This strategy is equivalent to diagnostic and risk-based testing for high-risk individuals, as defined in the CDC's 1998 Recommendations, before birth cohort screening was recommended. The estimated annual testing rate for all persons was set to approximately 3%.[20] Within that overall or average rate, individual probabilities for testing varied by disease stage (so, for example, we assume providers were more likely to initiate testing for individuals with symptoms of advanced liver disease)

  - Birth cohort screening: This strategy is equivalent to risk-based testing (as outlined above, under the first screening strategy option) plus one-time screening for all individuals born between 1945 and1965 (i.e., Baby Boomers), as defined in the 2013 U.S. Preventive Services Task Force's Hepatitis C Screening Recommendation. Under this strategy, the estimated annual screening rate for Baby Boomers was set to 9%;[20] for those born before 1945 or after 1965, the annual screening rate remained 3%. We further assume that the annual screening rate will remain elevated among Baby Boomers until 90% of individuals chronically infected with HCV have been diagnosed. Past this threshold, the diagnostic benefit would decrease.

  - Universal screening: This strategy assumes one-time screening, recommended for all adults 18 years of age and older, with repeat testing for those at high risk for infection.[21] The default annual screening rate for universal, one-time screening of adults is 9%. This default rate reflects an assumption on our part that annual one-time screening rate for all adults will not be materially different from that achieved for Baby Boomers under current birth cohort recommendations. However, given the lack of available real-world data, users are also given the option to enter the rate of their choice. As is true of the birth-cohort screening strategy, we assumed that the annual rate will persist until 90% of all individuals 18 years of age and older who are chronically infected with HCV have been diagnosed. Past this threshold, the diagnostic benefit would decrease.

- Annual treatment rate

  - This captures the annual percentage of all *diagnosed* individuals within given subpopulation(s) who are expected to receive treatment. It thus attempts to quantify, in a single number, the combined effects of patient treatment seeking behaviors and health system capacity to provide treatment in a given year. Factors to consider when setting this rate for a subpopulation include, but are not limited to, patient awareness of treatment, provider restrictions (e.g., requirements that treatment be managed by a specialist), and availability and accessibility of trained providers. Based on limited data and expert opinion, the *Simulator* provides default values for each subpopulation. However, users are also given the option to enter the rate of their choice.

- Treatment restrictions

  - The *Simulator* layers treatment restrictions on top of the selected treatment rate. In other words, the annual treatment rate parameter represents system capacity to treat all diagnosed individuals *in the absence of any treatment restrictions*. The actual treatment rate (a percentage of all diagnosed individuals who are treated in a given year) will be lower if a user subsequently adds a treatment policy restriction (e.g., F2 and above). For example, a state with 50% treatment capacity and policies restricting treatment to individuals with advanced liver disease (F3 or above) within Medicaid might ultimately only treat 20% of all Medicaid beneficiaries diagnosed with hepatitis C in a given year. The treatment restriction options available for application include the following:

- F3 and F4 only: Only individuals with advanced liver disease (stage 3 fibrosis or worse) are eligible for treatment

- F2 and above: Only individuals with moderate to severe liver disease (stage 2 fibrosis or worse) are eligible for treatment

- No restrictions: All individuals, regardless of the current extent of damage to their livers (includes individuals with stages 0 and 1 disease) are eligible for treatment

- Treatment efficacy

    - In accordance with current standards of care,[22] treatment is assumed to consist of all-oral DAA combinations for both treatment naïve and treatment experienced patients (including those for whom initial DAA therapies did not work). Based on data from multiple clinical trials, as well as published outcomes reported by the TRIO and TARGET studies, the *Simulator* varies rates of sustained virologic response (SVR) by viral genotype, stage of fibrosis, treatment regimen, and treatment history (Appendix Table A.6).[2]

Cost Parameters

To evaluate the economic impact of interventions such as screening and treatment, we incorporate the cost of antiviral treatment with DAAs, cost of diagnosing infection, and cost of management of HCV-related diseases (e.g., cirrhosis, hepatocellular carcinoma, and liver transplant). All costs have been adjusted to 2018 dollar values.

- Cost of DAA treatment

    - This captures the average total cost for a curative course of therapy. Treatment costs vary widely by payer and DAA medication. The default value set for all populations is $20,000, which is generally in line with some payers' net purchase costs (post any negotiated rebates or discounts) for the newest pangenotypic regimens.[23-26]

- Cost of diagnosing infection

    - This captures the totality of resources involved in efforts to identify and diagnose one HCV-infected patient, including the costs of initial (e.g., antibody) and confirmatory (e.g., RNA) tests. Because the prevalence of infection varies, depending on the population targeted by a given screening strategy, the cost of diagnosing an HCV infection also varies by screening strategy. Based on previously published analyses, [21] the estimated cost per diagnosed infection is $2,500 for birth-cohort screening and $4,400 for universal screening. For provider-driven diagnostic and risk-based testing, we use a value of $357 per diagnosed infection. This estimate is calculated assuming at least one-time testing of individuals at high risk for HCV infection (e.g., persons who inject drugs) having HCV (viremic) prevalence of 15.48%,[21] the cost of antibody test of $35, and the cost of HCV RNA test of $98.

- Cost of management of HCV-related disease outcomes

    - The costs associated with managing diagnosed HCV infection vary, depending on the severity of liver disease present. Based on previously published assessments,[27] we assume annual management costs associated with each health state range from a low of $809 (for those with fibrosis scores between F0 and F2) to $21,553 (for those with decompensated cirrhosis) and $114,505 (for those who receive a liver transplant, at least in the first year, when the transplant occurs). Importantly, disease management related

costs only begin to accrue once an individual's HCV infection has been diagnosed. Individuals who achieve SVR do not accrue any cost in the SVR state. However, if individuals progress to advanced liver disease (e.g., HCC) after achieving cure, they accrue the costs associated with the corresponding state.

Understanding Results

When users change default parameter values, these changes are applied at the start of 2019 and in all subsequent years. However, we include 2018 model outputs for all temporal trend graphs. Those 2018 results are generated based on the default parameter values for each state, so they offer users a baseline for which they can evaluate the immediate effects of changes in assumed policy or disease burden.

Limitations

The *Simulator* is based on a mathematical model HEP-SIM, which projects future disease and economic burden associated with HCV.[1-3] The HEP-SIM model is subject to a number of limitations. First, because HEP-SIM is a microsimulation model, model outcomes are affected by simulation noise. To reduce the noise, the *Simulator* runs the simulation for states with smaller HCV populations up to 25 times, depending on state HCV prevalence. Nonetheless, simulation noise could generate unexpected results in some cases. For instance, increasing treatment rates typically reduce HCV prevalence. In a few rare cases, a minor adjustment in treatment rates (e.g., from 20% to 21%) can cause a slight increase in the prevalence. However, with a more significant change in the treatment rate (e.g., from 20% to 25%), the expectant trend in hepatitis C prevalence will be recovered.

Second, we assumed that future HCV screening rates under 'diagnostic and risk-based' and 'birth-cohort' screening strategies are the same as the rates observed in year 2017. If future screening rates are lower than current rates, the Simulator may overestimate the benefits of screening and underestimate future disease burden. If future screening rates are higher than current rates, the Simulator may underestimate the benefits of screening. Third, we used state-reported cases of acute hepatitis C to estimate incident infections, although actual acute cases may significantly exceed reported cases in a given state or year. Fourth, our model did not include extrahepatic benefits resulting from HCV treatment, so the Simulator likely underestimates the cost-related benefits of HCV curative therapy. Finally, the *Simulator* does not allow users to conduct sensitivity analyses to assess the impact of input parameters' uncertainty on outcomes.

Table 1. Summary of input parameters used in *Hep C State Policy Simulator*

Parameter	Default Value	User Adjustment to Values Allowed	Source
HCV Epidemiology			
State-level HCV prevalence	See Appendix Table A.1 for default state values	Yes	[10]
State-level prevalence by subpopulation			
Incarcerated population	See Appendix Table A.1 for state values	No	[11]
Non-incarcerated population (Medicare, Medicaid, Private, Uninsured)	See Appendix Table A.1 for state values	No	CDC analysis*
HCV genotype (national estimates)	G1: 75.7%, G2: 10.7%, G3: 11.9%, G4-6: 1.7%	No	[17]
HCV fibrosis stages (national estimates)	F0-F1: 44.2%, F2: 28.5%, F3: 11.2%, F4: 16.1%	No	[17]
HCV incidence	See Appendix Tables A.3 and A.4 for state values	No	[18]
HCV awareness rates	See Appendix Table A.5 for insurance status and age-specific values	No	[19]
Transition probabilities (annual)			
F0 to F1	0.117	No	[28]
F1 to F2	0.085	No	[28]
F2 to F3	0.120	No	[28]
F3 to F4	0.116	No	[28]
F4 to DC	0.039	No	[29]
F4 to HCC	0.014	No	[29]
F4-SVR to DC	0.008	No	[30]
F4-SVR to HCC	0.005	No	[30]
DC to HCC	0.068	No	[31]
DC to LT	0.023	No	[32,33]
DC (first year) to death from liver disease	0.182	No	[31]
DC (subsequent years) to death from liver disease	0.112	No	[31]
HCC to LT	0.040	No	[6,34]
HCC to death from liver disease	0.427	No	[29]
LT (first year) to death from liver disease	0.116	No	[35]
PLT to death from liver disease	0.044	No	[35]
Interventions			
Screening Strategy			
Provider-driven diagnostic and risk-based testing rate (annual)	3%	No	[20,36]
Birth-cohort screening rate (annual)	9%	No	[20,36]
Universal screening rate (annual)	9%	Yes	[20,36] **
Treatment rate (annual)			
Medicaid	50%	Yes	Unpublished data

Medicare	50%	Yes	Unpublished data
Privately insured	50%	Yes	[37]
Incarcerated	State-specific	Yes	[11]
Uninsured	10%	Yes	Unpublished data
Treatment restrictions			
Medicaid	State-specific	Yes	[38]
Medicare	No restrictions	Yes	[39]
Privately insured	No restrictions	Yes	Subject matter expertise
Incarcerated	F3 and above	Yes	[40]
Uninsured	F2 and above	Yes	Subject matter expertise
HCV treatment efficacy	See Appendix Table A.6 for SVR rates by viral genotype, stage of fibrosis, treatment regimen, and treatment history	No	[2]
Cost Parameters			
Cost of DAA treatment	$20,000	Yes	[23-26]
Cost of disease management (annual)			
F0–F2	$809	No	[27,41,42]
F3	$1,661	No	[27,41,42]
Compensated cirrhosis	$2,065	No	[27,41,42]
Decompensated cirrhosis	$21,553	No	[27,41,42]
Hepatocellular carcinoma	$39,598	No	[27,41,42]
Liver transplant (Year 1)	$114,505	No	[27,41,42]
Liver transplant (Year 2+)	$32,010	No	[27,41,42]
Cost of diagnosis (per case)			
Diagnostic and risk-based testing	$357	No	[43] ***
Birth-cohort screening	$2,500	No	[21]
Universal screening	$4,400	No	[21]

*Based on unpublished recent CDC analysis that used multiple state- and national-level datasets.[44-48] (Appendix Table A.2).
**Based on the assumption that universal screening rate is equal to the birth-cohort screening rate.
***Based on the assumption that HCV (viremic) prevalence in high-risk groups is 15.48%,[43] cost of HCV RNA test is $98, cost of antibody test is $35, the cost of per HCV (viremic) case detected is $357.

Abbreviations: HCV, hepatitis C; F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, numerous septa without cirrhosis; F4, cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; LT, liver transplantation (first year); PLT, post liver transplantation (> 1 year), DAA treatment, direct-acting antiviral treatment.

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Appendix

Table A.1. State-Level Estimates of Hepatitis C Prevalence by Insurance Status and Incarceration, United States

State	HCV Prevalence[a]	Breakdown by Insurance Status and Incarceration, %[b]				
	No. of Viremic People	Medicaid	Medicare	Private	Uninsured	Incarcerated
Alabama	30,623	37%	27%	15%	14%	7%
Alaska	5,608	38%	29%	16%	4%	14%
Arizona	64,251	47%	26%	14%	4%	9%
Arkansas	21,976	30%	30%	27%	6%	6%
California	335,355	42%	32%	16%	5%	6%
Colorado	38,555	41%	29%	18%	4%	8%
Connecticut	19,244	44%	27%	15%	4%	9%
District of Columbia	12,012	47%	27%	18%	7%	1%
Delaware	6,159	30%	30%	16%	15%	9%
Florida	148,541	26%	32%	16%	21%	5%
Georgia	56,195	31%	29%	19%	14%	7%
Hawaii	6,917	47%	28%	13%	3%	9%
Idaho	11,100	45%	29%	17%	6%	4%
Illinois	57,616	40%	25%	20%	6%	9%
Indiana	39,819	38%	28%	18%	10%	5%
Iowa	12,626	41%	31%	18%	4%	6%
Kansas	14,424	32%	31%	18%	15%	4%
Kentucky	44,005	56%	20%	12%	5%	6%
Louisiana	50,638	24%	30%	21%	18%	6%
Maine	7,370	42%	23%	15%	14%	6%
Maryland	41,489	52%	26%	13%	4%	4%
Massachusetts	38,196	48%	30%	16%	3%	2%
Michigan	70,527	39%	33%	17%	6%	5%
Minnesota	25,070	41%	25%	27%	3%	4%
Mississippi	22,771	37%	27%	15%	14%	7%
Missouri	41,576	38%	24%	14%	15%	10%
Montana	7,669	44%	28%	16%	6%	5%
Nebraska	7,938	18%	34%	36%	7%	6%
Nevada	23,272	39%	30%	17%	6%	8%
New Hampshire	8,087	46%	28%	16%	5%	5%
New Jersey	47,727	38%	28%	25%	7%	2%
New Mexico	29,046	49%	26%	13%	4%	7%
New York	119,646	50%	27%	14%	5%	4%
North Carolina	66,244	27%	27%	22%	20%	4%
North Dakota	2,787	37%	19%	24%	8%	11%
Ohio	101,577	39%	25%	16%	6%	14%
Oklahoma	55,826	28%	31%	16%	18%	7%
Oregon	51,870	45%	30%	15%	4%	5%
Pennsylvania	100,939	43%	26%	17%	5%	9%
State	HCV Prevalence[a]	Breakdown by Insurance Status and Incarceration, %[b]				

	No. of Viremic People	Medicaid	Medicare	Private	Uninsured	Incarcerated
Rhode Island	10,535	49%	30%	11%	4%	5%
South Carolina	36,790	25%	33%	16%	20%	6%
South Dakota	3,876	34%	25%	18%	11%	12%
Tennessee	71,342	32%	29%	15%	19%	5%
Texas	205,802	21%	30%	21%	20%	8%
Utah	12,604	32%	26%	21%	14%	7%
Vermont	3,842	52%	27%	13%	3%	5%
Virginia	45,331	27%	26%	15%	13%	19%
Washington	58,277	42%	29%	19%	4%	6%
West Virginia	21,111	52%	21%	12%	10%	5%
Wisconsin	28,336	40%	31%	15%	5%	9%
Wyoming	3,853	31%	27%	15%	18%	9%

[a]Default estimates for HCV prevalence (for the year 2015) were obtained from a recently published work[10] that leverages multiple data sources and advanced statistical models to estimate the prevalence of current HCV infection in each state. In the *Hep C State Policy Simulator*, users can change the default prevalence value (from -50% to +200% of the default value).

[b]Estimates for HCV prevalence in state prisons are obtained from the Hep Corrections website (www.HepCorrections.org). For non-incarcerated population, estimates of the breakdown of HCV prevalence by insurance status were based on a recent CDC analysis. This analysis incorporates evidence on frequency of seeking medical care among persons with diagnosed HCV[15] and those with opioid abuse/dependence[16] (a proxy for probable recent HCV infections) as well as state-level data for 2012–2015 from a variety of data sources[44-48] (Table A.2) to estimate the number of patients with HCV in each insurance category. If users choose to change the default value for HCV prevalence (reported in column "HCV Prevalence, No. of Viremic People"), then the estimated breakdown by subpopulation (i.e., Medicaid, Medicare, privately insured, uninsured, and incarcerated) is applied to the updated prevalence value.

Table A.2. Data Sources for Inpatient, Emergency Rooms, and Ambulatory Care Visits, United States

State	HCV-Related Visits[a]			Opioid-Related Visits[b]		
	Ambulatory Care[c]	Inpatient Care[d]	Emergency Room Care[e]	Ambulatory Care[c]	Inpatient Care[d]	Emergency Room Care[e]
Alabama	census region	census division	census region	census region	census division	census region
Alaska	census region	census division	census region	census region	census division	census region
Arizona	state level	state level	state level	census region	state level	state level
Arkansas	census region	state level	state level	census region	state level	state level
California	state level	state level	census region	state level	state level	census region
Colorado	census region	state level	census region	census region	state level	census region
Connecticut	census region	census division	census region	census region	census division	census region
District of Columbia	census region	census division	census region	census region	census division	census region
Florida	state level	state level	state level	state level	state level	state level
Georgia	state level	census division	census region	state level	state level	census region
Hawaii	census region	state level	state level	census region	state level	state level
Illinois	census region	state level	census region	census region	state level	census region
Indiana	census region	state level	census region	census region	state level	census region
Iowa	census region	state level	state level	census region	state level	census region
Kansas	census region	state level	census region	census region	state level	census region
Kentucky	census region	state level	state level	census region	state level	state level
Louisiana	census region	census division	census region	census region	census division	census region
Maine	census region	state level	census region	census region	state level	census region
Maryland	census region	state level	state level	census region	state level	state level
Massachusetts	census region	state level	state level	census region	state level	state level
Michigan	census region	state level	census region	census region	state level	census region
Minnesota	census region	state level	state level	census region	state level	state level
Mississippi	census region	census division	census region	census region	census division	census region
Missouri	census region	state level	census region	census region	state level	census region
Montana	census region	census division	census region	census region	census division	census region
Nebraska	census region	state level	state level	census region	state level	state level
Nevada	census region	state level	state level	census region	state level	state level
New Hampshire	census region	census division	census region	census region	census division	census region
New Jersey	census region	state level	state level	census region	state level	state level
New Mexico	census region	state level	census region	census region	state level	census region
New York	census region	state level	census region	census region	state level	census region
North Carolina	census region	state level	state level	census region	state level	state level
North Dakota	census region	state level	census region	census region	state level	census region
Ohio	census region	census division	census region	census region	census division	census region
Oklahoma	census region	state level	census region	census region	state level	census region
Oregon	census region	state level	census region	census region	state level	census region
Pennsylvania	census region	census division	census region	census region	census division	census region
Rhode Island	census region	state level	state level	census region	state level	state level

	HCV-Related Visits[a]	Opioid-Related Visits[b]

State	Ambulatory Care[c]	Inpatient Care[d]	Emergency Room Care[e]	Ambulatory Care[c]	Inpatient Care[d]	Emergency Room Care[e]
South Carolina	census region	state level	state level	census region	state level	state level
South Dakota	census region	census division	census region	census region	census division	census region
Tennessee	census region	state level	census region	census region	state level	census region
Texas	state level	state level	census region	census region	state level	census region
Utah	census region	state level	census region	census region	state level	census region
Vermont	census region	state level	state level	census region	state level	state level
Virginia	census region	census division	census region	census region	census division	census region
Washington	state level	state level	census region	state level	state level	census region
West Virginia	census region	state level	census region	census region	state level	census region
Wisconsin	state level	state level	census region	census region	state level	census region
Wyoming	census region	state level	census region	census region	state level	census region

[a]HCV-related visits are defined as those with ICD-9[i] diagnosis codes for acute HCV (ICD-9 codes 070.41, 070.51[15,49-51]), chronic HCV (ICD-9 codes 070.44, 070.54[15,49-51]), and unspecified HCV (ICD-9 codes 070.70, 070.71, V02.62[15,49,51]) noted as the principal or any of 29 secondary diagnoses.

[b] Opioid-related visits were used as a proxy for new Hepatitis C infections among persons who inject drugs who might have not yet been diagnosed. Opioid-related visits are defined as those with ICD-9 diagnosis codes for overdose (ICD-9 codes 965.00- 965.02, 965.09[49,52] or E850.0-E850.2[49,52]), opioid dependence (ICD-9 codes 304.00-304.02, 304.70-304.72[49]), opioid abuse (ICD-9 codes 305.50-305.52[49]), and opiates or opiate antagonists causing adverse therapeutic effects (ICD-9 codes 970.1; E935.0-E935.2, E940.1[49]), where such codes were noted as the principal or any of 29 secondary diagnoses. Patient records with ICD-9 codes for both HCV and Opioids were classified only as HCV visits.

[c] Estimates of ambulatory care visits were based on data from the National Ambulatory Medical Care Survey (NAMCS),[44] from the National Center for Health Statistics (NCHS). State-level estimates were used where available (2012-2015 data for California, Florida, Georgia, Texas, and Wisconsin; 2014-2015 data for Arizona and Washington). Alternatively, we used 2014-2015 data to obtain estimates at the census region level, and applied the appropriate census region level value to each jurisdiction.

[d] Estimates of inpatient visits were based on data for January-September of 2015 from the Healthcare Cost and Utilization Project (HCUP). For states that allow the release of their data for public use, we used data from HCUPnet (https://hcupnet.ahrq.gov) online query system.[45] For all other jurisdictions, we used data from the National Inpatient Sample (NIS)[46] to obtain estimates at the census division level, and applied the appropriate census division level value to each jurisdiction.

[d] Estimates of emergency room visits were based on HCUP data for January-September of 2015. For states that allow releasing their data for public use , we used data from the State Emergency Department Databases (SEDD).[47] For all other jurisdictions, we used data from the National Emergency Department Sample (NEDS) [48,53] to obtain estimates at the census region level, and applied the appropriate census region level value to each jurisdiction.

Data Sources:
NAMCS:[44]

- For the years of 2012-2015, NAMCS includes a random sample of 25,000-28,000 unweighted visits to nonfederally employed office-based physicians primarily engaged in direct patient care. NAMCS provides estimates of the use of ambulatory care at the national level and at the state level for the most populous states (ranging from 34 states in 2012 to 16 states in 2015).

HCUPnet:[45]

- HCUPnet is an on-line query system that includes state-level health care statistics for hospital inpatient settings. HCUPnet is based on the State Inpatient Databases (SID)[54] ─ an HCUP's dataset that contains all inpatient care

[i] For this analysis, we used only ICD-9 codes and did not use ICD-10 codes. According to a recent study by Heslin et al. (2017; DOI: https://doi.org/10.1097/MLR.0000000000000805), the transition to ICD-10-CM codes, effective October 2015, could result in substantial changes in the number of visits with the same medical condition. For instance, in October-December 2015, the number of inpatient visits involving opioid abuse and poisoning decreased by 21.1% and 12.4%, respectively, compared to July-August 2015, with the greatest decreases observed in Medicare-eligible populations. Since the impact of the ICD-10-CM codes transition on other medical conditions is not well understood, we excluded records for October-December 2015 and focused on the time periods that used ICD-9 codes only (January 2012-September 2015).

records from community hospitals in 48 participating states, of which 36 states allow releasing their data for public use.

NIS:[46]

- NIS randomly samples 20% of SID visits and contains approximately 7 million unweighted observations per year.

SEDD:[47]

- SEDD contains all ER visits that do not result in an admission from 36 participating states, of which 16 states released their data for public use.

NEDS:[48,53]

- Sampled from SEDD and SID, NEDS represents a 20-percent sample of US hospital-based ER visits and contains 30-31 million unweighted visits per year.

Table A.3. Number of Reported Acute HCV Cases by State and Year, United States

State	2008	2009	2010	2011	2012	2013	2014	2015	2016
Alabama	13	10	7	23	24	30	35	70	32
Alaska	2	2	2	3	4	5	5	6	7
Arizona	21	21	21	28	42	49	49	56	70
Arkansas	1	2	1	0	5	30	13	2	0
California	30	43	32	48	63	72	73	59	60
Colorado	14	28	20	28	42	21	33	40	35
Connecticut	19	53	37	47	34	25	25	29	17
District of Columbia	3	3	3	4	6	7	7	4	25
Delaware	2	1	2	3	4	5	5	6	7
Florida	32	53	56	64	107	134	93	126	236
Georgia	16	31	32	53	82	48	57	84	93
Hawaii	4	4	4	6	9	10	10	11	14
Idaho	3	7	11	12	11	14	6	4	7
Illinois	10	6	1	6	26	37	27	31	21
Indiana	13	22	27	84	110	175	122	138	146
Iowa	0	11	0	0	3	22	22	25	31
Kansas	1	1	2	8	16	17	28	22	15
Kentucky	68	64	109	142	178	226	176	119	103
Louisiana	9	9	4	7	11	19	22	24	5
Maine	3	2	2	12	8	8	31	30	25
Maryland	22	23	24	35	39	53	42	38	35
Massachusetts	13	10	13	23	37	174	228	249	424
Michigan	129	35	45	32	76	74	78	83	107
Minnesota	22	15	16	17	32	47	40	37	51
Mississippi	9	9	9	12	18	21	21	24	30
Missouri	2	0	6	8	4	6	6	8	24
Montana	6	1	4	9	9	16	13	15	20
Nebraska	2	3	2	2	3	2	2	8	2
Nevada	22	5	7	10	12	9	6	12	16
New Hampshire	4	4	4	5	8	9	9	11	13
New Jersey	61	7	28	53	71	106	113	130	122
New Mexico	5	6	14	14	21	12	16	40	18
New York	43	53	50	52	93	131	126	121	179
North Carolina	46	24	39	60	63	79	111	144	82
North Dakota	0	2	0	0	0	4	0	0	1
Ohio	40	26	10	6	7	116	105	122	187
Oklahoma	20	27	41	53	80	40	45	35	32
Oregon	23	19	19	20	37	14	15	13	19
Pennsylvania	27	39	26	35	66	81	69	129	225
Rhode Island	10	10	10	13	20	23	23	27	33
South Carolina	4	1	1	1	1	0	4	5	10

| State | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |

South Dakota	3	3	3	3	5	6	6	7	20
Tennessee	28	33	46	83	129	98	123	173	150
Texas	59	36	35	37	44	28	47	48	40
Utah	12	6	10	10	17	11	38	30	76
Vermont	1	1	2	6	6	3	4	1	5
Virginia	8	10	13	25	76	41	54	52	43
Washington	25	22	25	41	54	63	82	63	62
West Virginia	22	31	21	46	55	58	62	63	94
Wisconsin	3	3	10	15	26	40	49	64	103
Wyoming	0	0	0	2	3	4	4	5	6

Data from 2007 to 2016 are downloaded from the CDC website.[18] Where state-level estimates are not available (i.e., Alaska, Arizona, Delaware, Hawaii, Iowa, Mississippi, New Hampshire, North Dakota, South Carolina, South Dakota, and Wyoming), the national rate was applied to the state population to generate a state estimate.

Data Source: Viral Hepatitis: Statistics and Surveillance, Centers for Disease Control and Prevention.[18]

Table A.4. Projected Acute HCV Cases by State for Years 2017–2030, United States

State	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029+
Alabama	52	57	61	66	71	76	81	85	90	95	100	105	105
Alaska	7	8	9	9	10	10	11	12	12	13	14	14	14
Arizona	69	74	80	85	91	97	102	108	113	119	125	130	130
Arkansas	11	11	12	13	14	15	16	17	18	19	20	21	21
California	68	70	72	75	77	79	82	84	86	89	91	93	93
Colorado	40	42	44	47	49	51	53	55	57	60	62	64	64
Connecticut	17	17	17	17	17	17	17	17	17	17	17	17	17
District of Columbia	15	16	17	19	20	22	23	25	26	28	29	31	31
Delaware	7	8	8	9	10	10	11	11	12	13	13	14	14
Florida	196	214	233	252	271	290	309	328	347	365	384	403	403
Georgia	97	105	113	121	130	138	146	154	163	171	179	187	187
Hawaii	14	15	16	17	18	19	21	22	23	24	25	26	26
Idaho	9	9	10	10	10	10	10	11	11	11	11	12	12
Illinois	32	35	37	40	43	45	48	50	53	55	58	61	61
Indiana	186	205	223	241	260	278	296	315	333	352	370	388	388
Iowa	31	34	38	41	45	48	52	55	59	62	66	69	69
Kansas	27	30	32	35	38	41	44	47	49	52	55	58	58
Kentucky	187	199	211	223	235	247	259	271	283	295	306	318	318
Louisiana	19	20	22	23	25	26	27	29	30	31	33	34	34
Maine	31	34	38	41	45	48	52	55	58	62	65	69	69
Maryland	49	51	54	57	60	63	66	69	72	75	78	80	80
Massachusetts	350	392	435	477	519	561	604	646	688	730	772	815	815
Michigan	81	82	83	84	86	87	88	89	90	91	92	93	93
Minnesota	49	52	55	59	62	65	68	72	75	78	82	85	85
Mississippi	28	30	32	34	36	38	40	42	44	46	48	50	50
Missouri	15	17	18	20	21	23	25	26	28	29	31	32	32
Montana	20	22	24	26	28	30	32	34	36	38	40	42	42
Nebraska	4	5	5	5	5	6	6	6	7	7	7	7	7
Nevada	11	11	11	11	11	11	11	11	11	11	11	11	11
New Hampshire	13	14	15	16	17	18	19	20	21	22	23	24	24
New Jersey	129	138	147	156	165	175	184	193	202	211	220	229	229
New Mexico	29	31	34	36	39	41	44	46	49	51	54	56	56
New York	169	184	198	213	228	242	257	271	286	300	315	329	329
North Carolina	127	139	150	161	172	183	194	205	216	227	238	249	249
North Dakota	1	1	1	1	1	1	1	2	2	2	2	2	2
Ohio	157	174	191	208	225	242	258	275	292	309	326	343	343
Oklahoma	44	45	45	46	46	46	47	47	48	48	48	49	49
Oregon	19	19	19	19	19	19	19	19	19	19	19	19	19
Pennsylvania	166	183	199	216	233	250	267	284	300	317	334	351	351
Rhode Island	33	36	38	41	44	47	49	52	55	58	60	63	63
South Carolina	6	7	8	8	9	10	10	11	12	12	13	14	14
South Dakota	13	14	16	17	18	19	21	22	23	25	26	27	27

State	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029+

Tennessee	179	196	212	228	245	261	277	293	310	326	342	358	358
Texas	40	40	40	40	40	40	40	40	40	40	40	40	40
Utah	53	58	64	70	75	81	87	92	98	104	109	115	115
Vermont	5	5	5	5	5	5	5	5	5	5	5	5	5
Virginia	66	72	77	83	89	95	101	107	113	119	125	131	131
Washington	82	88	95	102	108	115	121	128	135	141	148	154	154
West Virginia	89	96	104	111	119	126	134	141	149	156	164	172	172
Wisconsin	87	97	108	118	128	138	148	158	169	179	189	199	199
Wyoming	6	7	8	9	9	10	11	12	12	13	14	15	15

These estimates are modeled based on CDC data on the reported acute HCV cases for the period of 2007-2016[18] (see Table A.3). For the years between 2017 and 2028, we assumed HCV incidence continues to increase at the rate observed between 2006 and 2016. From 2029 onwards, we assumed that incidence rates stabilize and remain flat.

Table A.5. Percentage of HCV-Infected People Aware of Their Disease Status, United States, 2015

Age	Awareness Rate by Insurance Status[19]	
	Insured	**Uninsured**
<40	18%	6%
40-49	60%	20%
50-59	55%	16%
>60	35%	6%

The likelihood of persons living with HCV infection who are aware of their infection depends on their insurance status and age. [19] Table A.5 summarizes this information and presents the age- and insurance-specific HCV awareness rates used in HEP-SIM.

Table A.6. SVR Rates by Treatment, Genotype, Treatment History, and Fibrosis State, United states

Treatment History and Fibrosis State	GT1	GT2	GT3	GT4–6
PEG+RBV				
Treatment naïve				
F0-F3	0.54	0.82	0.70	0.58
F4	0.36	0.64	0.49	0.32
Contraindicated with modifiable reasons				
F0-F2	-	0.66	0.56	0.46
F3	0.43	0.66	0.56	0.46
F4	0.28	0.51	0.40	0.26
Failed PEG+RBV: relapse				
F0-F3	0.27	0.71	0.66	0.31
F4	0.13	0.56	0.52	0.24
Failed PEG+RBV: partial response				
F0-F3	0.18	0.69	0.64	0.31
F4	0.10	0.55	0.51	0.24
Failed PEG+RBV: null response				
F0-F3	0.10	0.54	0.50	0.31
F4	0.05	0.42	0.39	0.24
BOC/TEL+PEG+RBV (GT1 only)				
Treatment naïve				
F0-F3	0.75	-	-	-
F4	0.62	-	-	-
Contraindicated with modifiable reasons				
F0-F2	-	-	-	-
F3	0.5	-	-	-
F4	0.36	-	-	-
Failed PEG+RBV: relapse				
F0-F2	0.87	-	-	-
F3	0.85	-	-	-
F4	0.84	-	-	-
Failed PEG+RBV: partial response				
F0-F2	0.72	-	-	-
F3	0.56	-	-	-
F4	0.56	-	-	-
Failed PEG+RBV: null response				
F0-F2	0.41	-	-	-
F3	0.39	-	-	-
F4	0.14	-	-	-
DAA non-NS5A*				
Treatment naïve				
F0-F3	0.9	0.9	0.85	0.9
F4	0.8	0.8	0.6	0.8

	GT1	GT2	GT3	GT4–6

Treatment History and Fibrosis State				
Contraindicated with modifiable and non-modifiable reasons				
F0-F3	0.9	0.9	0.9	0.9
F4	0.7	0.7	0.6	0.7
Failed PEG+RBV: relapse				
F0-F3	0.9	0.9	0.85	0.9
F4	0.8	0.7	0.6	0.75
Failed PEG+RBV: partial and null response				
F0-F3	0.9	0.9	0.85	0.9
F4	0.75	0.7	0.6	0.75
Failed first-generation PI				
F0-F3	0.9	-	-	-
F4	0.7	-	-	-
Failed DAA NS5A (during 2015-2018)				
F0-F3	-	-	-	-
F4	0.8	0.8	0.6	0.8
DAA NS5A**				
Treatment naïve, contraindicated, failed PEG+RBV, failed BOC/TEL+PEG+RBV (GT1 only), failed DAA non-NS5A, failed DAA nonNS5A				
F0-F3	0.95	0.99	0.95	0.99
F4	0.9	0.99	0.9	0.99
DAA NS5A-next generation**				
All conditions				
F0-F3	0.95	0.99	0.95	0.99
F4	0.9	0.99	0.9	0.99

*DAA1 non-NS5A includes the following drug combinations: SOF+IFN+/-RBV, SOF+/-RBV, SOF+SMV+/-RBV, and SMV+IFN+/-RBV.
**DAA1 NS5A includes the following drug combinations: SOF+LDV+/-RBV, SOF+DCV, DCV+IFN+/-RBV, OBV/PTV/r+DSV+/-RBV, OBV/PTV/r+/-RBV, EBR+GZR, and SOF+VEL.
***DAA2 NS5A includes the next wave of potential drug combinations such as SOF/VEL/VOX, grazoprevir/ruzasvir/uprifosbuvir, glecaprevir/pibrentasivr, and odalasvir+AL-335+/SMV

Abbreviations: GT, genotype; PEG, peginterferon; RBV, ribavirin; F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, numerous septa without cirrhosis; F4, cirrhosis; BOC, boceprevir; TEL, telaprevir; DAA, direct-acting antiviral; NS5A, nonstructural protein 5A; PI, protease inhibitor; SOF, sofosbuvir; IFN, interferon; SMV, simeprevir; LDV, ledipasvir; DCV, daclatasvir; OBV, ombitasvir; PTV, paritaprevir; r, ritonavir; DSV, dasabuvir; EBR, elbasvir; GZR, grazoprevir; VEL, velpatasvir; VOX, voxilaprevir

Data Source: All estimates in this tables are adapted from Chhatwal et al.[2]