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Projected Health Benefits and Health Care Savings from the United States National Hepatitis C Elimination Initiative

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ABSTRACT

The national hepatitis C elimination initiative provides an opportunity to dramatically expand access to hepatitis C virus (HCV) treatment and put the US on a path to eliminating hepatitis C. Our objective was to project the health benefits and cost savings of this initiative. A previously developed mathematical model was updated to simulate trends in HCV disease burden and cost of care in the US for the next 20 years under status quo and national hepatitis C elimination initiative. Within five years, the initiative will diagnose 92.5% of all persons with HCV and cure 89.6% of HCV infection. Over 10 years, compared with the status quo, the initiative will avert 20,000 cases of hepatocellular carcinoma, 49,100 cases of diabetes, and 25,000 cases of chronic kidney disease. The initiative will also avert 24,000 deaths adding 220,000 life years. These benefits in improved health will save $18.1 billion in direct healthcare spending, of which $13.3 billion would accrue to the federal government. Over 20 years, the health benefits would increase by more than 2-fold and cost savings by 3-fold. The cost savings would further increase if the HCV incidence rate decreases because of rapid decline in HCV prevalence. In conclusion, the national hepatitis C elimination initiative would substantially reduce HCV-related morbidity and mortality and would reduce healthcare spending at 10 years and beyond.

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Introduction

On March 9, 2023, the Biden Administration proposed a national hepatitis C elimination initiative to dramatically expand access to hepatitis C virus (HCV) treatment and put the US on a path to eliminating hepatitis C as a public health problem.[1] The Administration projects that this national initiative will treat over 1.5 million individuals over the next 5 years.

This bold initiative aims to overcome historic barriers to HCV elimination. Despite the availability of highly-effective oral drugs since 2014 — with a cure rate of more than 95%[2] — over 2 million Americans were estimated to have chronic HCV in 2020,[3] and about 14,000 people died from HCV-related complications.[4] In 2020, there were 66,700 estimated new HCV infections, a 100% increase from 2015.[4]

There are several reasons for the slow progress in addressing hepatitis C. First, 40% of the infected people have not been tested and so are unaware of their infection status.[5] Second, at the time of their market launch, the high price of HCV medications served as a major barrier to access and hence to HCV cure.[6] Third, Medicaid and other payers imposed treatment restrictions, including requiring evidence of advanced fibrosis and prolonged sobriety. Though the cost of treatment has come down to $20,000 or less, many Medicaid programs continue to restrict access to curative drugs.[7] Fourth, HCV disproportionately affects certain marginalized and/or minoritized communities, including those who are uninsured, American Indian and Alaska Native persons, non-Hispanic Black persons, incarcerated populations, and people who inject drugs who often have less access to medical care.[8] These populations have, in particular, experienced rising infection rates in recent years.[5]

The national initiative to eliminate hepatitis C will accelerate the development and deployment of point-of-care HCV diagnostic technologies in the US to enable “test and treat” in one visit; improve access to HCV treatment by establishing a novel national “subscription model” to competitively procure drugs for Medicaid, uninsured, Indian Health Service, and justice involved populations, and by removing

out-of-pocket costs for these drugs for certain Medicare beneficiaries; and expand outreach and capacity for screening and treatment.[9,10]

The FY 2024 President's budget requests $12.3 billion in mandatory funding for the national hepatitis C elimination initiative over 5 years, with a significant amount of the funding redirected from current hepatitis C expenditures.[11] At a time where macroeconomic concerns are focused on deficit reductions, it is important to evaluate how investment in this national initiative is not just associated with health benefits, and not just general cost savings to the health care system, but cost savings to the federal budget through reduction in liver-related complications[12] and extrahepatic manifestation of HCV.[13] Therefore, in this study, we estimate the health benefits and healthcare savings to the federal government from the national hepatitis C elimination initiative compared to the status quo.

METHODS

Overview

A previously developed mathematical model, *Hepatitis C Simulation Model* (HEP-SIM), was used to simulate temporal trends in HCV disease burden and cost of care in the US for the next 20 years under status quo and the national hepatitis C elimination initiative. The HEP-SIM synthesizes information on patient demographics, hepatitis C disease progression, screening and treatment for HCV, access to healthcare (including insurance status), and the cost of care and treatment. The model has been used to project the changing prevalence and outcomes of HCV in the US since 2001 and has been validated with published data and national surveys.[14-17] The model was developed in C++ programming language and analysis were performing using R, version 4.1.0.

The Natural History of Hepatitis C

The natural history of hepatitis C is simulated as an individual-level state-transition model (**Figure 1**), where at any given time, an HCV infected person exists in one of the following states: acute HCV infection; spontaneously resolved acute infection; chronic HCV defined by one of the five METAVIR liver fibrosis states ranging from F0 (no fibrosis) to F4 (compensated cirrhosis); sustained virologic response, which is indicative of cure of HCV infection; decompensated cirrhosis; hepatocellular carcinoma; liver-transplant recipient; and liver-related death. HCV infected persons can progress to the next state or stay in their current state, according to the transition probabilities in **Table 1**. Patients in the F0 to F3 stages who are successfully treated with antivirals transition to 'cure' state. Patients with F4 state who are successfully treated with antivirals move to the 'F4-cure' state, with the likelihood of further progression to advanced liver disease state (decompensated cirrhosis or hepatocellular carcinoma) greatly diminished but still possible. Persons in the decompensated cirrhosis, hepatocellular carcinoma, or liver transplant states have a heightened risk of liver-related mortality. We also applied background mortality by age and sex to each health state.

HCV prevalence and incidence

National data were included to align the model to the US-specific HCV epidemic from 2015 onwards. **Table 1** summarizes the parameters and data sources used for the HCV prevalence and distribution by subpopulation, HCV genotype, fibrosis stage, incident cases, infection awareness rates, and age distribution by subpopulation.

The model was initialized with HCV prevalence in 2015 using multiple data sources and a national survey (**eTable 1**).[18] We also incorporated data on the justice-involved population size from HepCorrections (**eTable 2**).[19-21] In addition to the prevalent cases, the model simulates incident chronic HCV cases using the reported annual cases in the *CDC's Viral Hepatitis Surveillance Report* from 2011 to 2020 (**eTable 3**).[4] From 2021 to 2050, the number of new chronic HCV cases is extrapolated based on a linear trend between 2011 to 2020. These cases are then distributed between the high- and low-risk subpopulations in a 2.55 to 1 ratio by subpopulation (**eTable 4**).[4]

To confirm the validity of these projections, the simulation results were compared with published studies and national data, including the chronic HCV prevalence in 2015 (**eFigure 1a**) and liver-related deaths from 2015 to 2019 (**eFigure 1b**).[4,18]

Extrahepatic manifestations of HCV

Prevalence and incidence of diabetes and chronic kidney disease (CKD) is higher among those with an HCV infection than those without.[22-25] Furthermore, persons cured of HCV infection have lower rates of diabetes and CKD.[13] Because of this strong association between HCV treatment and diabetes and CKD, the model simulates incidence of diabetes and CKD separately for HCV-infected and cured persons (**Table 1**).

Cost of Illnesses Averted

To evaluate the economic impact of potential interventions, the model incorporates the cost of managing liver-related complications and diabetes and CKD. The annual cost of managing each

complication is based on previously published analyses (**Table 1**). All disease management costs were converted into 2023 USD.

Model Outcomes and Sensitivity Analysis

For each scenario, the status quo and national hepatitis C elimination initiative, the model simulated the number of people getting diagnosed and receiving HCV treatment, the incidence of hepatocellular carcinoma and extrahepatic manifestations, liver-related deaths, and years of life saved for 10 and 20 years post implementation.

For each scenario, we also evaluated total cost of illness averted. We further estimated the cost of illness averted to the federal government. We assume that Medicare savings accrue entirely to the federal government and 85% of Medicaid savings is attributable to the federal government because many HCV persons will be in an eligibility category that the federal government pays a 90% match. Because many persons who are uninsured, in corrections, or privately insured today may require Medicaid for care of complications of HCV, we assume that 70% of savings in care for the uninsured, 20% of privately insured, and 50% of those in corrections will accrue to Medicaid.

To estimate confidence in model outcomes, we conducted one-way sensitivity analysis by defining uncertainty in input parameters using the lower and upper bounds detailed in **Table 1.** We also evaluated outcomes by discounting future cost savings at 3% per year.

Scenario analysis: Decreasing HCV Incidence

In the base case, HCV incident cases are assumed to increase annually from 2021 to 2050 based on an extrapolation of the CDC's estimated incident case counts from 2011 to 2020 (**eTable 3**).[4] An additional scenario where the incidence of HCV decreases proportionally to prevalence, under the national hepatitis C elimination initiative, was modeled.

RESULTS

HCV diagnosis and treatment

In 2022, an estimated 59.7% of all persons with HCV were aware of their infection, and 57.0% had been successfully treated. Because of the implementation of the national hepatitis C elimination initiative, 92.5% of all HCV persons would get diagnosed and 89.6% of all would achieve cure within five years of the initiative. **eFigure 3** shows the annual number of HCV persons projected to receive treatment in the next 5 years under this initiative. Among those, 1.05 million (69%) of the patients treated for HCV would be in Medicare or Medicaid, 195,000 (13%) private insurance 103,000 (7%) under corrections; the program would include 171,000 (11%) persons without health insurance.

Reduction in HCV disease burden

From 2024 to 2034, the national HCV initiative will decrease the number of persons with HCV in the US by 94% from 1.6 million to about 100,000. In comparison, in the absence of a program, the number of persons with HCV infection would be 1.3 million.

In the next 10 years, the national hepatitis elimination initiative will reduce the hepatocellular carcinoma incidence rate by 53% to 1.28 cases per 100,000. In the absence of a program, the hepatocellular carcinoma incidence rate will decrease by 27% to 2.07 cases per 100,000. Cumulatively, the initiative will prevent an additional 20,000 cases of hepatocellular carcinoma over 10 years and 43,000 cases over 20 years **(Figure 2**). For liver-related deaths, the annual mortality rate would decrease by 46% from 5.02 to 2.70 per 100,000 in the first 10 years of the initiative. In total, the initiative will prevent over 24,000 additional liver-related deaths within 10 years and 69,000 deaths over 20 years. The initiative is also projected to prevent the need for 2,500 liver transplants over 10 years and 9,100 transplants over 20 years. With the reductions in HCV-related liver disease, the national initiative is projected to save 217,000 years of life compared to the status quo over the next 10 years. This difference continues to grow substantially, with 3,036,000 life years saved at 20 years.

In addition to the reductions in liver-related disease, the national hepatitis C elimination initiative is projected to prevent 49,100 cases of diabetes over 10 years and 112,000 cases over 20 years **(Figure 2**). The initiative would also prevent 25,000 cases of chronic kidney disease in 10 years and 66,000 cases over 20 years**.**

Cost savings

Over 10 years, total cost savings attributable to averted liver-related complications and extrahepatic manifestation amount to $18.1 billion ($13.3 billion, if discounted; **eTable 5**) for uninsured, private, Medicare, Medicaid, and justice-involved populations **(Figure 3 and eTable 6)**. Of this $18.1 billion, the federal government will accrue $13.3 billion (73%) ($9.8 billion, if discounted) of the cost savings. Over 20 years, cost savings will accrue to $57.1 billion in total ($31.0 billion, if discounted), of which $44.2 billion ($24.0 billion, if discounted) will accrue to the federal government.

Scenario: reduction in HCV incidence

If HCV incidence decreases at the rate of reduction in HCV prevalence, the national initiative would avert an additional 25,000 liver-related deaths and save $41.9 billion in 10 years, with $32.0 billion of savings accrued to the federal government (**eFigure 4** and **eTable 7**). The corresponding benefits over 20 years would increase to 70,000 liver-related deaths averted and $233.6 billion saved ($185.9 billion accrue to federal government).

One-way sensitivity analysis

Figure 4 shows the ten model parameters that the cost savings and deaths averted outcomes are most sensitive to. We found that the national initiative remained cost saving when accounting for uncertainty within each parameter. Additionally, we found the anticipated impact on the HCV-related disease burden was relatively robust.

DISCUSSION

Untreated hepatitis C causes hepatic and extrahepatic complications and leads to substantial morbidity and premature mortality. The national hepatitis C elimination initiative aims to treat over 1.5 million individuals over the next 5 years by overcoming historic barriers to HCV cure. The initiative requires upfront commitment of resources, and we projected substantial health benefits and cost savings from those resources. Over 10 years, this analysis finds that the national hepatitis C initiative will avert 20,000 cases of hepatocellular carcinoma, 49,100 cases of diabetes, and 25,000 cases of chronic kidney disease. This reduction in HCV related disease will prevent 24,000 deaths and add 220,000 life years. These benefits in improved health would save $18.1 billion in direct healthcare spending, of which $13.3 billion would accrue to the federal government. Over 20 years, the health benefits of the national initiative would increase by more than 2 fold and cost savings by 3 fold.

The President's budget estimates $12.3 billion for a national five-year hepatitis C elimination initiative. However, this budget is not all new resources. A substantial portion is shifted from existing expenditures from the Medicaid program for hepatitis C medications. Our estimates predict that by preventing disease and reducing healthcare utilization, the hepatitis C elimination initiative would save the federal government an additional $13.3 billion within a 10-year time frame. Thus, at 10 years, the initiative will simultaneously reduce federal costs and save lives; these savings will increase substantially over a 20-year time frame.

Of note, the cost savings from our model provides a conservative estimate of the value of the national initiative. Several government agencies use the concept of "value of a statistical life" to convert mortality risk reductions into dollar terms for economic and social benefit overall. The US Department of Health and Human Services recommends using $11.4 million (in 2020 dollars) as the value of a statistical life.[26] Multiplying this estimate of a value of a statistical life with liver-related deaths averted provides an estimate of the health benefits in dollar value of $275.6 billion over 10 years and $784.6 billion over 20 years—far in excess of the cost of the initiative.

Though previous studies did not evaluate the health and economic impact of the national hepatitis C initiative, our findings are consistent with other studies showing that HCV interventions are cost-saving and prevent associated mortality. A systematic review identified 24 relevant cost-effectiveness studies and concluded that antiviral treatment both save lives and reduce costs.[12] A 2023 Milliman white paper found savings from HCV elimination ranging from $28 to $46 billion over 10 years.[27] Over 30 years, the savings were even greater between $226 and $257 billion. Another study estimated that antiviral use in the US Veterans Affairs health care would result in cost savings between $7 and $9 billion over 50 years.[28] In addition, costs savings were achieved in their program as early as 5 years after treatment begins. A modeling study of six WHO world regions estimated that HCV elimination scenario would prevent 2.1 million liver-related deaths and 10 million new HCV infections globally between 2018 and 2030.[29]

There are several limitations to this study. First, in the base case, we did not dynamically model reduction in HCV transmission because of reduction in HCV prevalence under the elimination scenario; however, we simulated an additional scenario accounting for reduction in HCV incidence that showed substantially higher cost savings than our base case results. Second, while we accounted for HCV prevalence in correctional population, we did not account for HCV prevalence in other groups excluded from the NHANES; therefore, we may have underestimated national HCV prevalence. Third, we did not consider fibrosis regression after HCV cure, which underestimated the health benefits and cost savings of the national hepatitis C initiative. Fourth, we did not explicitly model HCV re-infection, but this was incorporated via inclusion of HCV incident cases. Fifth, we underestimated the potential cost savings of the national hepatitis C elimination plan by not modeling the association of HCV treatment with other extrahepatic manifestations including depression, cardiovascular disease, stroke, and lymphoma.

Conclusion

The national hepatitis C elimination initiative is both feasible and economically grounded. This initiative will have a large impact on improving health by averting 24,000 liver-related deaths, adding 220,000 life

years, and saving $18.1 billion in costs over the next 10 years. Over five years, the national program will virtually eliminate HCV as a public health threat in the US while reducing healthcare spending of the federal government at 10 years and beyond.

Table 1. Annual transition probabilities for hepatitis C virus natural history model

Input	Parameter	Range for Sensitivity Analysis	Reference
HCV Transition Probabilities (Annual)			
F0 to F1	0.117	0.104 - 0.130	30
F1 to F2	0.085	0.07 - 0.096	30
F2 to F3	0.120	0.109 - 0.133	30
F3 to F4	0.116	0.104 - 0.129	30
F4 to DCC	0.039	0.010 - 0.079	31
F4 to HCC	0.014	0.010 - 0.079	31
F4-cure to DCC	0.008	0.002 - 0.036	32
F4-cure to HCC	0.005	0.002 - 0.013	32
DCC to HCC before DAA	0.068	0.030 - 0.083	33
DCC to LT	0.023	0.010 - 0.062	34,35
DCC to HCC Adjustment	0.700	0.600 - 0.800	Calibrated
DCC to LRD Adjustment	0.700	0.600 - 0.800	Calibrated
DCC (first year) to death from liver disease before DAA	0.182	0.065 - 0.190	33
DCC (subsequent years) to death from liver disease before DAA	0.112	0.065 - 0.190	33
HCC to Liver transplant	0.040	0.000 - 0.140	16,36
HCC to death	0.427	0.330 - 0.860	31
Liver transplant (first year) to death	0.116	0.060 - 0.420	37
Liver transplant to death	0.044	0.024 - 0.110	37
Extrahepatic Disease Probabilities			
Diabetes			
Prevalence (HCV infected)	0.179	0.112 - 0.275	22
Prevalence (not HCV infected)	0.138	0.128 - 0.149	23*
Incidence (untreated)	0.037	0.0366 - 0.0379	13
Incidence (DAA treated)	0.030	0.0289 - 0.0315	13
CKD			
Prevalence (HCV infected)	0.201	0.150 - 0.250	24
Prevalence (not HCV infected)	0.131	0.121 - 0.144	25*
Incidence (untreated)	0.034	0.0335 - 0.0347	13
Incidence (DAA treated)	0.031	0.0299 - 0.0322	13
Disease Management Costs (Annual)			
F0–F2	$976	$732 - $1,220	38-40
F3	$2,005	$1,504 - $2,506	38-40
Compensated cirrhosis	$2,492	$1,869 - $3,115	38-40
Decompensated cirrhosis	$26,014	$19,511 - $32,518	38-40
Hepatocellular carcinoma	$47,794	$35,846 - $59,743	38-40
Liver transplant (Year 1)	$138,205	$103,654 - $172,756	38-40
Liver transplant (Year 2+)	$38,635	$28,976 - $48,294	38-40
Diabetes	$11,826	$8,870 - $14,783	41
Chronic Kidney Disease	$30,410	$22,808 - $38,013	42**
Initialization Parameters			
HCV Prevalence	See eTable 2 for calibrated values	--	18***
Prevalence by Subpopulation			
Justice-Involved	See eTable 2	--	19
Medicare, Medicaid, Private, Uninsured	See eTable 2	--	CDC analysis*

HCV genotype (national estimates)	G1: 75.7%, G2: 10.7%, G3: 11.9%, G4-6: 1.7%	--	43
HCV fibrosis stages (national estimates)	Calibration Parameter	--	Calibrated
HCV incidence	See eTable 3	--	4
HCV awareness rates	See eTable 8 for insurance status and age-specific values	--	44
Age Distribution by Subpopulation	See eTable 10	--	10,11*

Abbreviations. F0 to F4: Metavir liver fibrosis stage; DAA: direct-acting antiviral; LT: liver transplant; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LRD: liver-related death

* These parameters were estimated through a linear extrapolation through 2023 that used the midpoint year of each NHANES cycle and the prevalence estimate.

** The annual cost of managing CKD was calculated as a weighted average combined the frequency and cost of managing each CKD stage.

*** Based on unpublished recent CDC analysis that used multiple state- and national-level datasets.[45-49]

Figures

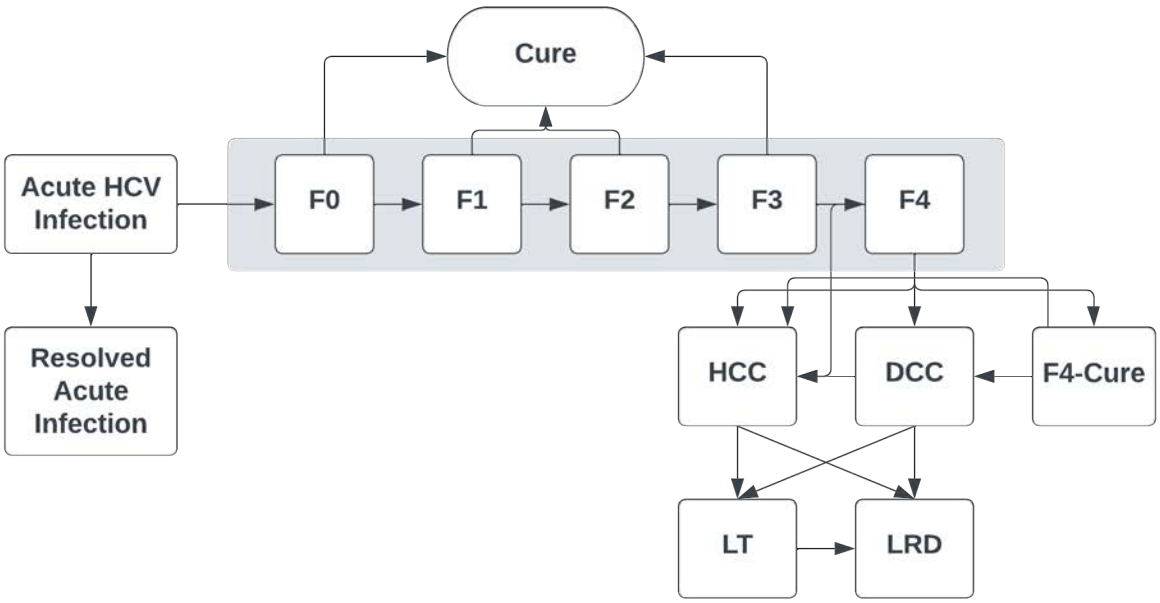

Figure 1. Schematic of the HCV Natural History Model.

Each square represents a health state that a patient can exist in. The arrows between states represent annual transition probabilities that can occur. In each state, competing-cause mortality, the background risk of dying from other causes, exists. F0, F1, and F2 represent no fibrosis, portal fibrosis without septa and portal fibrosis with few septa, respectively. F3 indicates severe septal fibrosis, and F4 represents compensated fibrosis.

Abbreviations: LT: liver transplant; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LRD: liver-related death

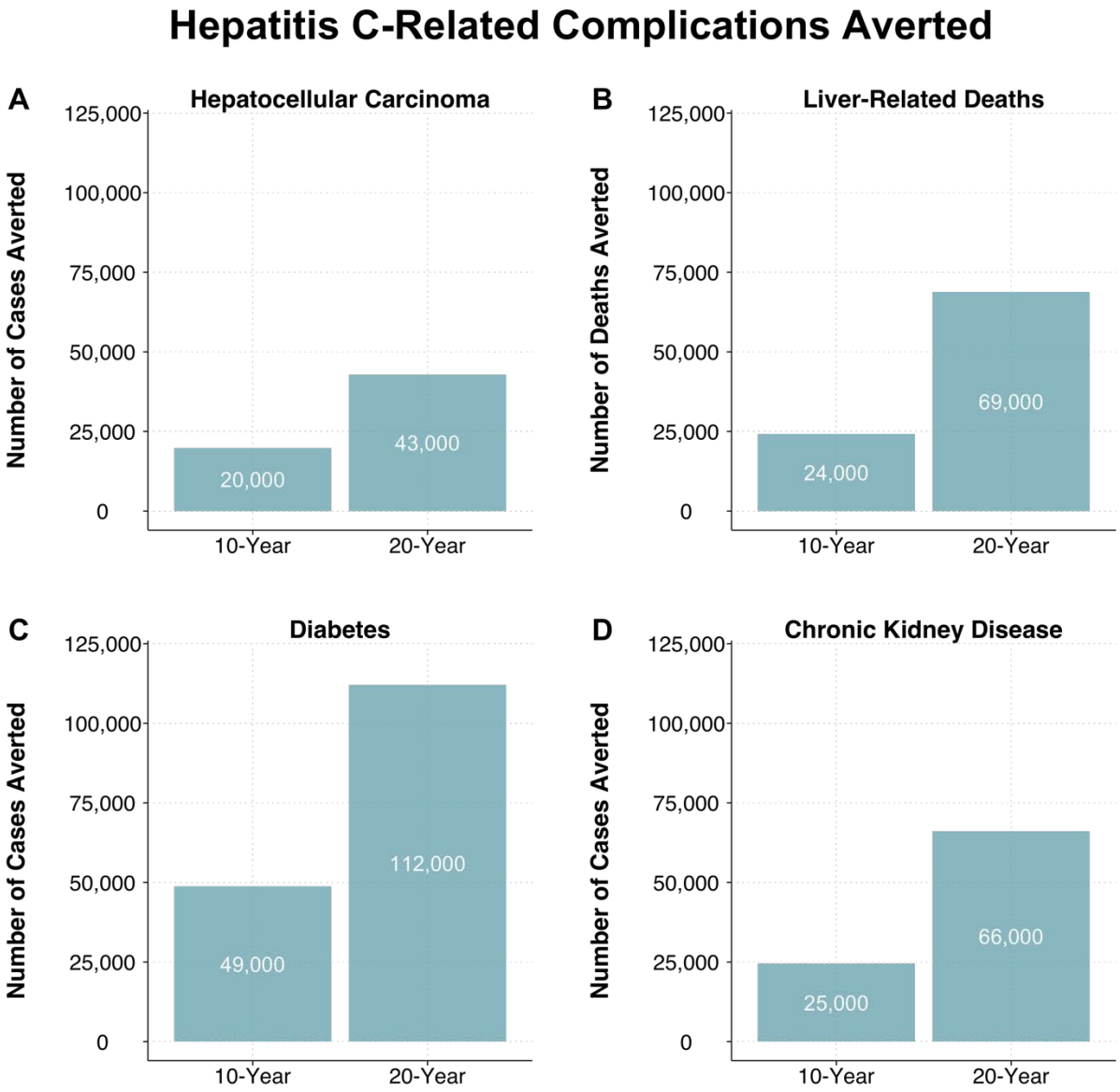

Figure 2. Reduction in HCV-related hepatocellular carcinoma (A), liver-related deaths (B), diabetes (C), and chronic kidney disease (D) because of the national hepatitis C initiative over 10 and 20 years.

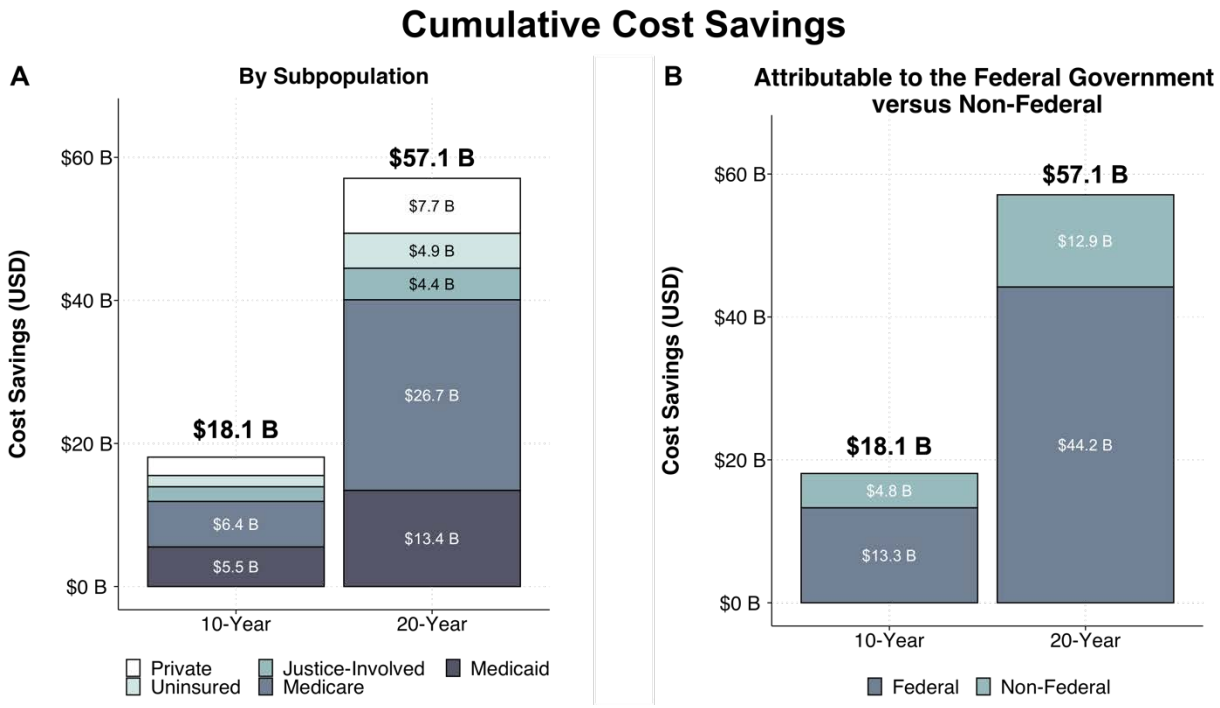

Figure 3. Cumulative cost savings (in billion US Dollar) of the national hepatitis C elimination initiative by subpopulation (A), and by whether they are attributable to the federal government or not (B).

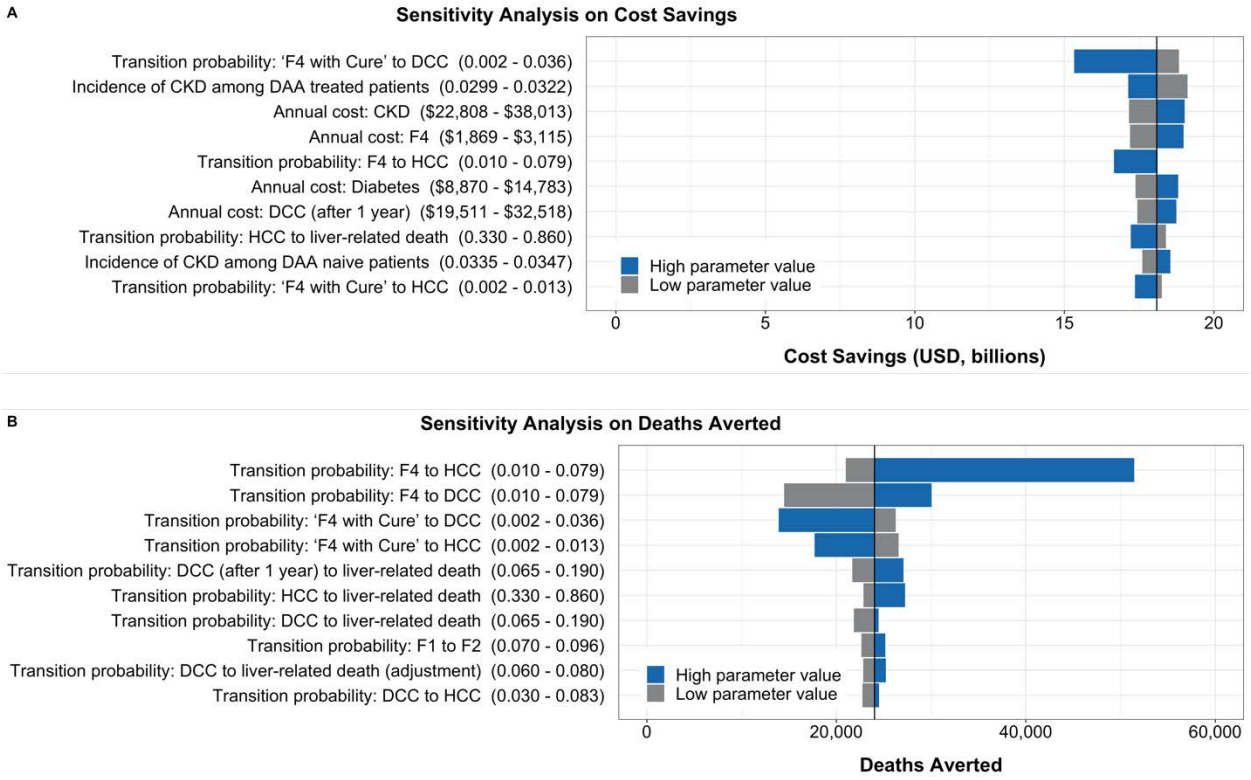

Figure 4. Tornado diagram showing top 10 most sensitivite model parameter for total 10-year cost savings (A) and liver-related deaths averted (B) associated with the national hepatitis C elimination initiative.

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