An Actuarial Approach to the Incremental Cost of Hepatitis C in the Absence of Curative Treatments

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Commissioned by Pharmaceutical Research and Manufacturers of America (PhRMA)

September 2015

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EXECUTIVE SUMMARY

Hepatitis C Virus (HCV) infects nearly 1% of the non-institutionalized population in the United States,[1] with peak prevalence of about 3.5% among males ages 55-59. HCV is the leading cause of both liver-related deaths and liver transplants in the United States.[2,3] The high cost of new antiviral medicines has sparked debate over the cost of treating HCV, and some payers are seeking ways to minimize their spending on these medicines.[4] This paper uses actuarial analysis to estimate the incremental (or extra) cost associated with HCV in the absence of curative treatment. This incremental cost is the difference between the direct medical and non-antiviral prescription drug costs of patients with naturally progressing HCV and those cured of the disease.

Incremental cost is useful when comparing the burden of particular diseases. For instance, it may be a valuable measure for payers as they evaluate the cost-benefit of treating a disease. Incremental cost is not an accounting item—generally health insurers do not report or account for their costs on a condition-by-condition basis. However, risk adjustment does affect many insurers' revenue on a condition-by-condition basis, and the risk adjusters used for Affordable Care Act (ACA) qualified health plans and Medicare Advantage plans do recognize HCV. We used these HCV related risk score components to simulate the extra costs associated with HCV.

To forecast the incremental cost of HCV, we simulated a cohort of representative HCV infected individuals for ten years considering aging, disease stage progression, payer coverage, and mortality. Two hypothetical scenarios were used, one in which there is no cure for HCV and HCV patients progress naturally through the stages of the disease and have increased mortality, and one in which all HCV infected individuals are assumed to be cured of the virus with no further progression and reduced mortality. Our analysis does not consider the cost of antiviral medicines.

Our simulation forecasts that, in the absence of a cure for HCV, 350,000 more patients would be living with advanced stages of HCV between 2015 and 2025, which includes 100,000 more patients with cirrhosis of the liver and nearly 250,000 more patients with end stage liver disease (ESLD). We estimate that the aggregate US annual incremental cost of HCV in the absence of a cure will total $115 billion over the 2015 to 2025 forecast period.

These aggregate cost estimates represent incremental direct healthcare costs for 2015-2025 attributable to today's HCV infected population in the absence of a cure. In reality, many patients are receiving curative treatments. We provide these estimates to illustrate the costs of HCV that will be potentially avoided with curative treatments. These curative treatments come with a cost, which we do not quantify.

Aside from not examining the cost of current curative treatments, other limitations of this report include future changes in therapies, inflation, and the uncertainties inherent in many of our assumptions. We did not consider the relatively small number of newly infected individuals, estimated at about 29,700 new cases in 2013.[5] Our paper also does not consider the prison population, for which the prevalence of HCV is much higher, estimated at 23-39%.[2]

This report was commissioned by Pharmaceutical Research and Manufacturers of America (PhRMA), whose members manufacture and sell products for viral infectious diseases. This report should not be interpreted as an endorsement of any particular treatment or legislation by Milliman. Two of the authors, Bruce Pyenson and Andrew Bochner, are Members of the American Academy of Actuaries and meet its qualification standards for issuing this report. The report reflects the authors' findings and opinions. Because extracts of this report taken in isolation may be incomplete or misleading, we ask that this report be distributed only in its entirety.

BACKGROUND

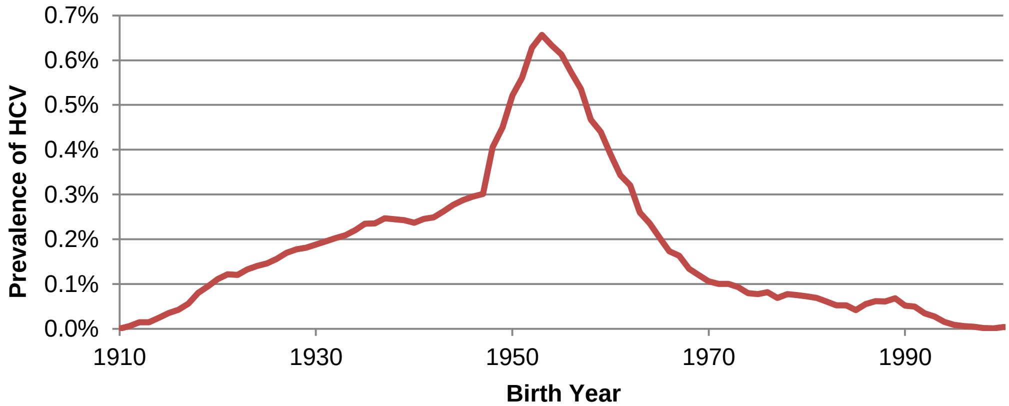
HCV is typically acquired through contact with infected blood, frequently through injection drug use.[3] Transmission via blood transfusions from medical procedures was more common prior to 1992, but has been nearly eliminated due to improved screening of the blood supply.[5] HCV often takes many years to become symptomatic, with liver inflammation as the primary complication.[6] Scarring of the liver (fibrosis) can progress to cirrhosis, which develops in approximately 20 to 30% of chronically infected patients.[7] Advanced liver diseases, such as decompensated cirrhosis and hepatocellular carcinoma, pose a serious threat to the lives of infected patients and may necessitate liver transplantation.[8]

With a standard course of treatment of 12 to 24 weeks, the new antivirals can produce sustained virologic response (SVR), a measure of HCV cure, in over 95% of previously untreated patients with minimal side-effects.[9] Antiviral treatments available prior to 2013 required longer treatment courses than today's antivirals, had lower SVR rates, and were frequently accompanied by severe flu-like side effects, such as fever, fatigue and headaches.[10] Many patients discontinued use of these earlier treatments.[11]

SVR has been associated with liver health improvement, which contributes to reduced health care costs.[12] Both fibrosis and inflammation tend to regress following achievement of a cure and complete elimination of fibrosis has been reported in some cases.[13] The probability of progressing to decompensated cirrhosis or hepatocellular carcinoma is nearly eliminated, except in cases with highly advanced liver disease prior to treatment.[14] Additionally, the reduction in long-term health consequences contributes to increased life expectancy following a cure.[15,16]

HCV prevalence in the U.S. is not uniform across various demographic and economic measures. Baby boomers account for approximately 80% of the chronically infected population.[1] Figure 1 shows the prevalence of diagnosed HCV for commercially insured and Medicare patients by birth year, exhibiting a sharp peak among the baby boomers. In response to this concentration, the U.S. Preventive Services Task Force (USPSTF) recently adopted the Centers for Disease Control's (CDC) recommendation for a one-time screening for individuals born between 1945 and 1965 in an effort to reduce the number of undiagnosed individuals and open access to treatment.[2,17, 18] Since HCV can take decades to manifest symptoms, many infected patients are unaware of their illness.[3,19] However, the impact of increased screening and the eventual development of symptomatic liver complications will likely lead to a growing number of diagnosed patients.

Figure 1: Base Prevalence of Diagnosed HCV by Birth Year



Source: Authors' analysis of 2012 MarketScan and 2012 Medicare 5% Sample.

HCV patients are more likely to have lower income[1], and, in 2013, a large portion of infected individuals were uninsured. Uninsured patients may have avoided treatment due to high out of pocket costs, making the ACA's expansion of Medicaid eligibility and subsidized coverage in the Exchanges an opportunity to insure a large segment of the HCV population. As shown in Figure 2, both Medicare and Medicaid each have a large number of HCV patients, but individuals eligible for both Medicare and Medicare have higher prevalence. Although it has relatively low total membership, Veterans Affairs has the highest prevalence among payers.

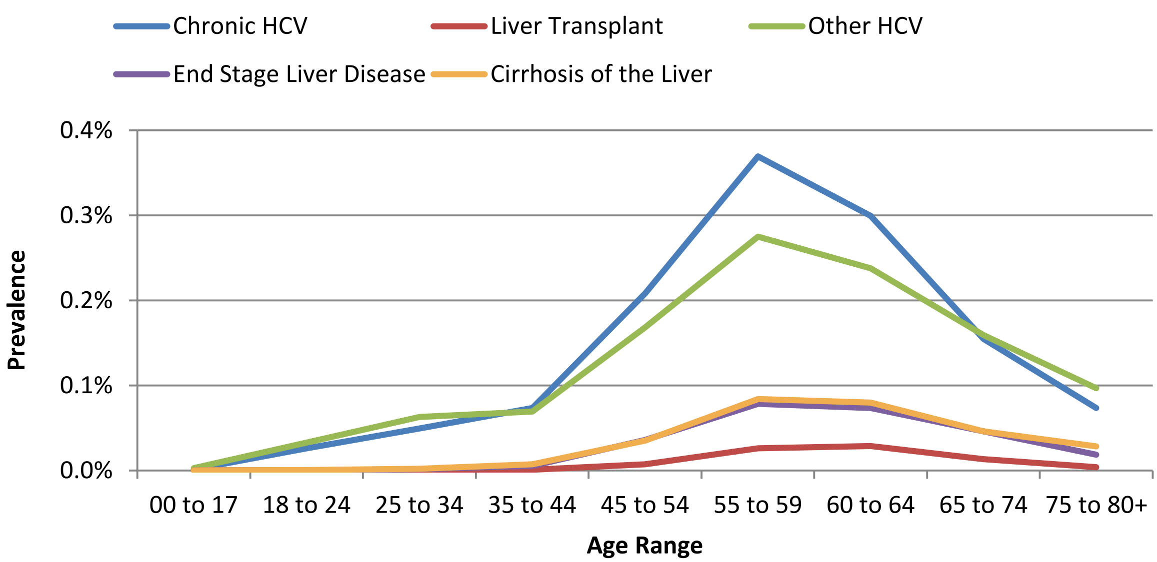
Figure 2: HCV Prevalence by Health Insurance Payer as of 2014 (pre-Exchange, pre-Medicaid Expansion)

Payer	Total U.S. Population (Thousands)	Estimated Prevalence of HCV	Estimated Number of HCV+ Patients (Thousands)
Uninsured	41,900	1.90%	796
Veteran Affairs	5,700	5.40%	307
Commercial	166,400	0.46%	767
Dual Medicare and Medicaid	5,100	2.91%	147
Medicare (Non-Dual)	41,800	0.43%	180
Medicaid	48,500	0.94%	457
Other Military	3,600	0.46%	16
Total	**313,000**	**0.85%**	**2,670**

Sources: Authors' analysis of 2005-2012 NHANES. Variable:LBXHCR - Hepatitis C RNA (HCV-RNA) in NHANES. 2014 CPS. Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver Int.* 2011;31(8):1090-1101. Dominitz JA, Boyko EJ, Koepsell TD, et al. Elevated prevalence of hepatitis C infection in users of United States veterans medical centers. *Hepatology.* 2005;41(1):88-96.

Annual medical costs for HCV patients vary greatly by stage, with advanced liver diseases contributing significantly to overall costs. Despite an expected decrease in the total number of HCV patients, growth in the number with advanced liver disease is expected to increase total medical costs.[20] As shown in Figure 3, the current number of patients at advanced stages of HCV, which include cirrhosis, ESLD (including decompensated cirrhosis and liver cancer) and liver transplants, is relatively low compared to the number with chronic and other HCV, a category used throughout this paper that includes less advanced forms of HCV, such as HCV carriers and acute or unspecified HCV. In the coming years, without treatment, many of these early stage patients will transition to more advanced stages of the disease and incur significantly higher costs. Liver complications drive these costs, but highly prevalent comorbidities, including diabetes and end stage renal disease (ESRD), contribute significantly to the costs in advanced stages as well.

Figure 3: Prevalence of Diagnosed HCV by Age Range and Stage

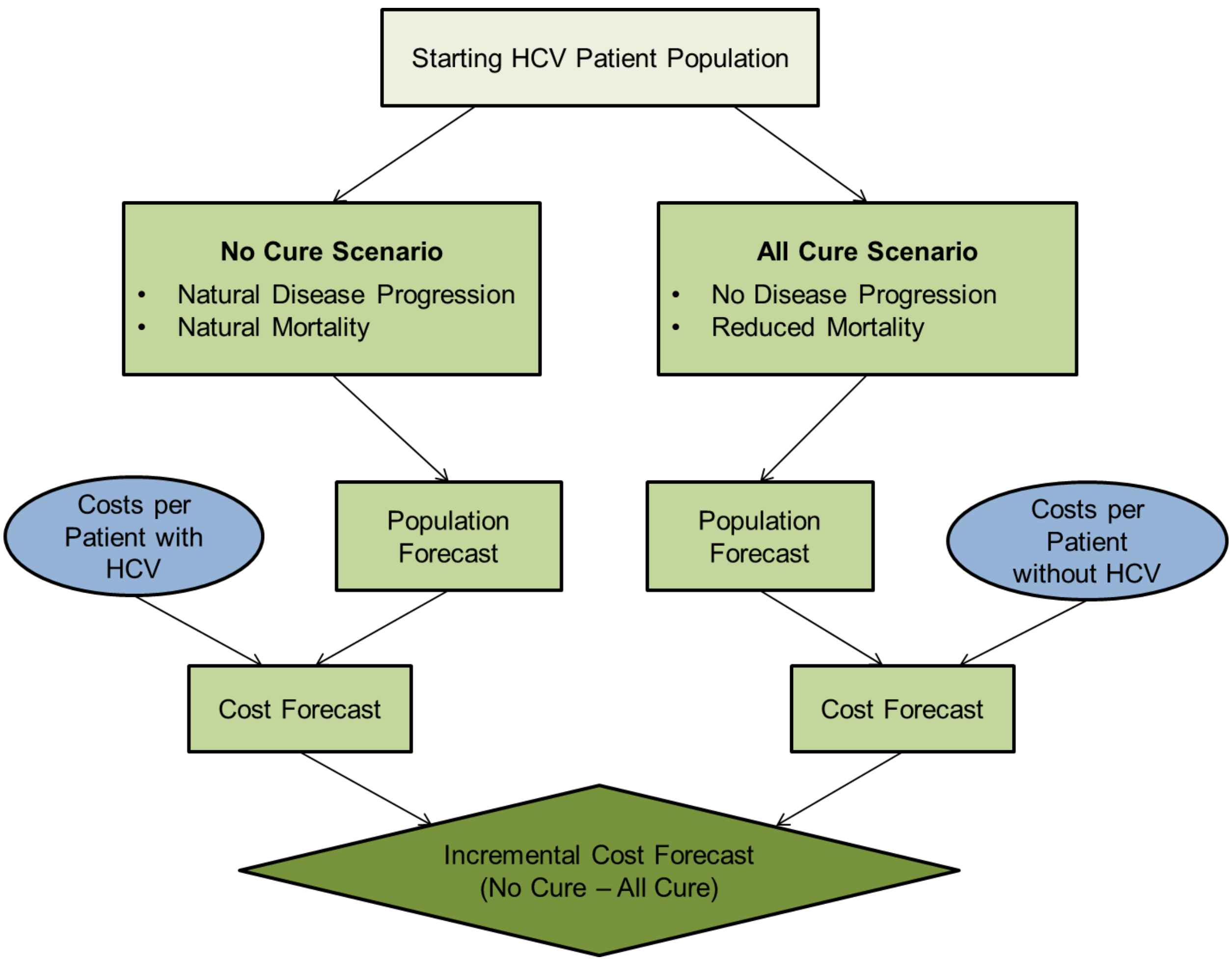


Source: Authors' analysis of 2012 MarketScan, 2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

SIMULATION FRAMEWORK

Our model simulates the progression of representative HCV infected individuals through ten annual transitions, taking into account aging, disease stage progression, payer coverage, and mortality. Two hypothetical scenarios were used: a "No Cure" scenario in which we assume natural disease progression through the stages of HCV and an "All Cure" scenario in which we assume there is no further disease progression and patients are maintained at their starting (year 1) stage of HCV with reduced mortality. The All Cure scenario is a device to understand the total cost burden of the disease, not a projected real-world outcome. We modeled HCV population forecasts for 2015-2025 under each scenario. These population forecasts were combined with per-patient cost estimates to forecast total annual cost for each scenario. We calculated the incremental cost of HCV as the difference between the total annual costs for the two scenarios. This model framework is summarized in Figure 4.

Figure 4: Simulation Model Flow



We define five stages of diagnosed HCV:

- Chronic hepatitis C
- Cirrhosis of the liver
- End stage liver disease (ESLD), including hepatocellular carcinoma and decompensated cirrhosis
- Liver transplant status/complications
- Other HCV, including HCV carriers and acute HCV and unspecified HCV with or without hepatic coma

The first four HCV disease stages are defined according to the Hierarchical Condition Category (HCC) risk adjusters used by Medicare Advantage plans and by commercial insurers selling qualified health plans on the Exchanges.[21,22] The fifth stage, “Other HCV”, contains individuals identified as having HCV but not otherwise included in the HCC system. We define a sixth stage for HCV infected patients who are unaware that they have the virus. We refer to patients in this stage as “Undiagnosed” throughout the paper.

For each year, in addition to the number of patients at each stage of HCV, we calculated the expected number of patients with HCV who died. Additional details about our assumptions and methodology are available in the Methodology section and Appendix C.

The incremental cost is intended to represent the extra cost of HCV for patients in the absence of curative antiviral treatment. While therapeutic cures for HCV are possible for many patients, the reader should understand that the two scenarios were constructed only for the sake of the difference between them—the individual scenarios have limited value on their own and neither represents a realistic forecast. Appendices D and E contain additional forecasts and analyses for each scenario.

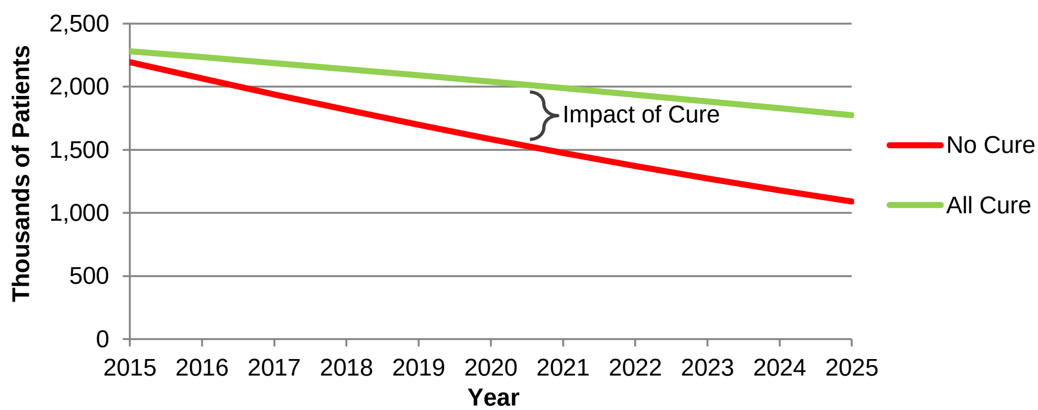
KEY FINDINGS

Disease Progression

Without curative treatment, we project that hundreds of thousands of HCV infected patients will shift from early to advanced stages of disease as the virus progresses over the forecast period. For the All Cure Scenario, individuals are more highly concentrated in the early stages (undiagnosed, other or chronic HCV) than in the more advanced stages (cirrhosis, ESLD, and liver transplant), because disease progression is halted in this scenario. By 2025, about 94% of patients in the All Cure scenario are in the early stages of the disease versus 70% in the No Cure Scenario.

Figure 5 depicts the decline in the number of patients in the early stages of HCV over the forecast period. While the total number of patients declines in the All Cure scenario due to mortality and no new entrants, the total number falls more sharply in the No Cure scenario due to both higher mortality and disease progression. In 2015, there are projected to be nearly 100,000 more patients in the early stages of HCV in the All Cure scenario than in the No Cure scenario. This difference grows to nearly 700,000 by 2025.

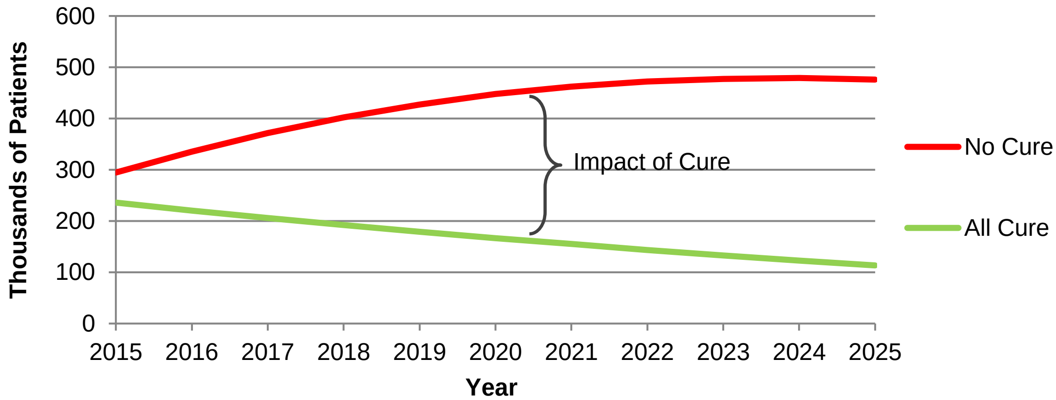
Figure 5: Forecast Comparison of Patients in Early HCV Stages



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

Figure 6 shows the projected number of HCV infected patients in the advanced stages of HCV over the forecast period for both scenarios. In the All Cure scenario, the number of patients declines due to mortality and lack of new entrants. However, for the No Cure scenario, the number progressing to advanced stages outweighs the higher mortality, and the total number of patients in advanced stages rises over the forecast period. The difference in the number of advanced stage HCV patients between the scenarios grows from approximately 60,000 in 2015 to over 350,000 by 2025.

Figure 6: Forecast Comparison of Patients in Advanced Stages of HCV



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

Important drivers of the incremental cost of HCV are the differential progression to more advanced and more expensive stages and the interplay of those transitions with differential mortality. Cost differentials between the scenarios are largely driven by the number of individuals over the forecast period surviving with more advanced and more expensive disease stages. We project that in the absence of curative treatment, 350,000 more individuals will be living with advanced stage HCV by 2025, with 100,000 more patients with cirrhosis of the liver and nearly 250,000 more patients with ESLD.

Medical and Pharmaceutical Costs

Without considering the cost of antivirals, HCV is associated with high medical and high non-antiviral prescription drug costs. Costs vary significantly by disease stage and payer. Figure 7 shows the allowed per patient per year (PPPY) costs in 2015 dollars split by payer under the No Cure and All Cure scenarios as well as the HCV contribution to costs for the undiagnosed, other, chronic, cirrhosis and ESLD stages of HCV. Allowed costs are the total of insurer-paid and patient-paid amounts. Note that costs related to liver transplant patients are excluded as described in the Methodology section.

The costs associated with the advanced stages of HCV are substantially higher than those of the early stages. The cost of ESLD is over three times that of chronic HCV for many of the payers. Undiagnosed individuals incur costs that are substantially lower than those of diagnosed patients, but are still much higher than a typical individual without HCV. Costs also vary significantly by payer, with the per-patient costs for individuals dually eligible (a person with both Medicare and Medicaid benefits) being the highest. The HCV contribution to costs also varies by payer and disease stage, with HCV having the smallest percentage impact on ESLD patients in Medicaid and the largest percentage impact on other patients with commercial insurance.

Figure 7: Per Patient per Year (PPPY) Allowed Costs (in 2015 Dollars) by Payer, Disease Stage, and Scenario

HCV Stage	Scenario	Commercial	Medicaid	Dual Medicare and Medicaid	Medicare Non-Dual	Other Military	Uninsured	Veteran Affairs
Undiagnosed	No Cure	12,159	7,854	18,752	15,572	12,159	6,080	18,752
	All Cure	9,686	6,892	15,584	12,487	9,686	4,843	15,584
	HCV Contribution	20%	12%	17%	20%	20%	20%	17%
Other	No Cure	18,763	12,629	33,111	27,469	18,763	9,382	33,111
	All Cure	14,482	11,058	27,642	22,168	14,482	7,241	27,642
	HCV Contribution	23%	12%	17%	19%	23%	23%	17%
Chronic	No Cure	19,609	13,179	29,495	24,230	19,609	9,804	29,495
	All Cure	15,953	11,573	24,393	19,267	15,953	7,976	24,393
	HCV Contribution	19%	12%	17%	20%	19%	19%	17%
Cirrhosis	No Cure	30,317	21,217	36,701	25,700	30,317	15,159	36,701
	All Cure	27,038	19,764	31,658	21,650	27,038	13,519	31,658
	HCV Contribution	11%	7%	14%	16%	11%	11%	14%
ESLD	No Cure	61,702	36,558	56,558	42,427	61,702	30,851	56,558
	All Cure	58,672	35,429	50,727	37,292	58,672	29,336	50,727
	HCV Contribution	5%	3%	10%	12%	5%	5%	10%

Source: Authors' analysis of 2012 MarketScan, 2012 Medicare 5% Sample, 2012 Medicaid CHSD, 2014 Final Medicare Advantage Notice, 2014 HHS Risk Adjustment Model, and 2013-2023 CMS NHE data

Allowed cost differences between the scenarios represent the per patient incremental cost of HCV independent of other decrements, such as mortality and disease progression. To measure the aggregate incremental impact over the forecast period, each scenario's per patient cost must be combined with the population forecasts that incorporate mortality and patient migration between stages and payers.

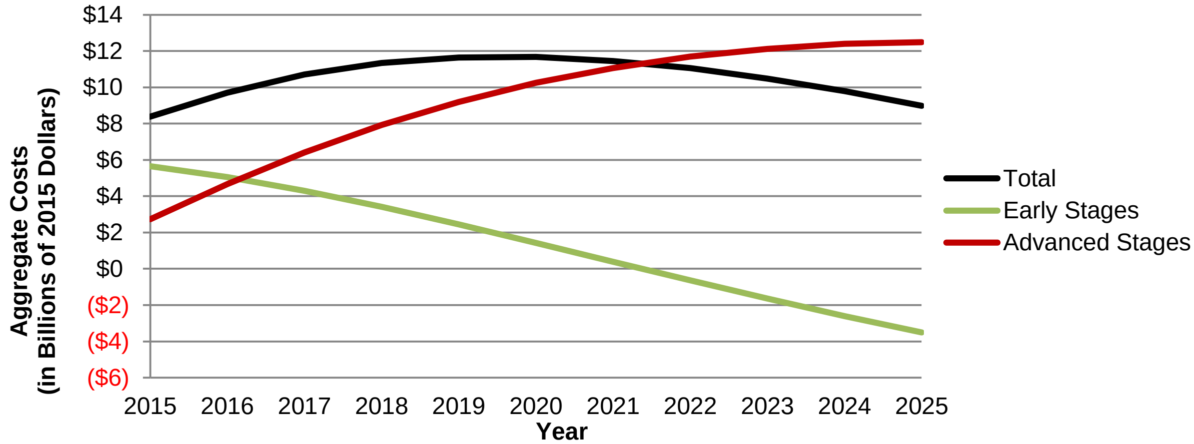
Incremental Cost Forecast

The total incremental costs over the forecast period (shown in Figure 8) amount to $115 billion. The rapid increase in the early years of the projection is due to disease progression among the chronically infected and the associated higher costs. After 2020, the incremental cost declines due largely to mortality.

Disease Progression Cost Trends

HCV costs vary by disease stage. Figure 8 shows the 2015-2025 incremental cost forecast (in 2015 dollars) split between early and advanced stages of HCV. Comparing the incremental cost trends for the early and advanced stages explains why total incremental costs for the 10-year period appear as a U-shape. While incremental costs for the early stages decrease steadily throughout the forecast period from almost $6 billion in 2015 to approximately $1.5 billion in 2020 to about –$3.5 billion by 2025, incremental costs of advanced stages increase sharply in the first five years from under $3 billion in 2015 to just over $10 billion by 2020 and then, at a slower pace, to $12.5 billion by 2025. Without a cure, patients in early stages shift into the more advanced and more costly stages. However, due to the higher mortality for advanced stages, the increase in incremental costs for advanced stages is tempered over time. This interaction of disease progression and mortality explains the decline in total incremental costs from 2020 to 2025 as the costs for the early stages decline faster than costs for the advanced stages rise. Appendix E provides further detail.

Figure 8: Incremental Cost of HCV Infected Patients by Disease Stage



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, 2012 Medicaid CHSD, 2014 Final Medicare Advantage Notice, 2014 HHS Risk Adjustment Model, and 2013-2023 CMS NHE data

How Costs Vary By Payer

HCV incremental costs vary by payer, which reflects different reimbursement levels and populations. The total incremental cost by payer over the forecast period is shown in Figure 9. Medicare (including people with dual, Medicare and Medicaid eligibility) exhibits the highest incremental cost and uninsured shows the lowest incremental cost.

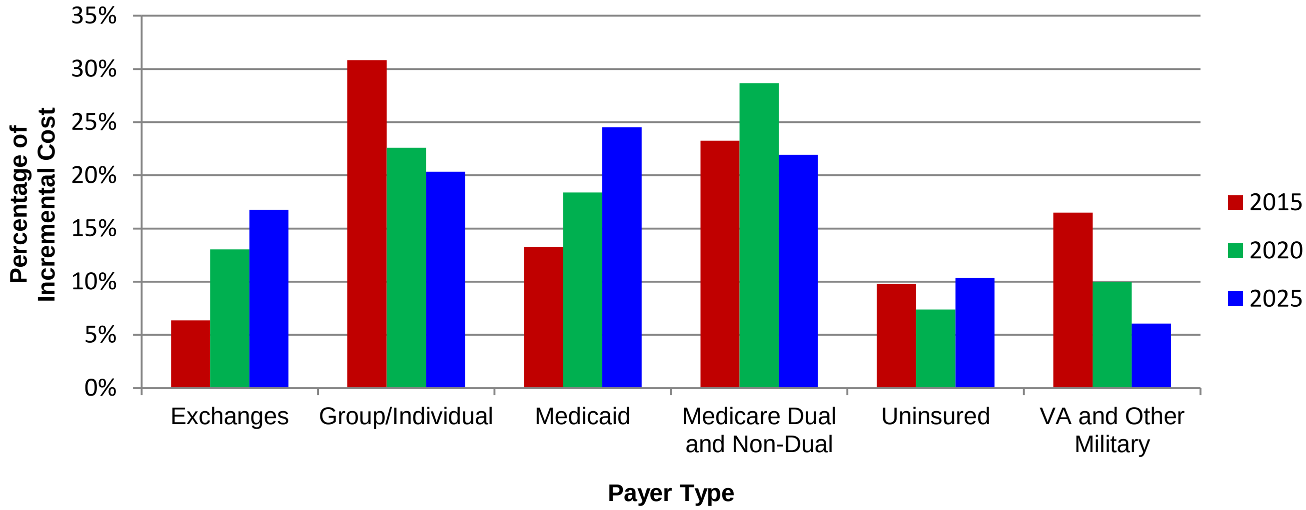
Figure 9: Total Incremental Cost of HCV by Payer from 2015-2025

Payer	Incremental Cost (Millions)	Percentage of Total Incremental Cost
Exchanges	$14,700	13%
Group/Individual	$27,100	24%
Medicaid	$21,500	19%
Medicare Dual and Non-Dual	$30,400	26%
Uninsured	$9,400	8%
VA and Other Military	$11,900	10%
Total	$115,000	100%

Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, 2012 Medicaid CHSD, 2014 Final Medicare Advantage Notice, 2014 HHS Risk Adjustment Model, and 2013-2023 CMS NHE data

Figure 10 shows the incremental costs split by each payer's portion in 2015, 2020, and 2025. Costs as a percentage of total incremental costs for the commercially insured group and individual HCV patients and those insured through Veteran Affairs or other military payers are projected to decline over the forecast period as a large portion of patients age into Medicare. Unsurprisingly, due to expanded coverage under the ACA, the portion of incremental costs for HCV patients insured through the Exchanges is estimated to increase from about 6.5% in 2015 to nearly 17% in 2025. The proportion due to the uninsured declines as individuals transition into the Exchanges/Medicaid in the early years, and then increases as fewer uninsured individuals obtain insurance.

Figure 10: Forecast of Distribution of Incremental Cost of HCV by Payer



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, 2012 Medicaid CHSD, 2014 Final Medicare Advantage Notice, 2014 HHS Risk Adjustment Model, and 2013-2023 CMS NHE data

Some irregular patterns appear in the forecast, such as the sharp increase in the Medicaid proportion of incremental cost and the decrease from 2020 to 2025 for Medicare. Even though the portion of HCV infected patients in Medicaid declines for both population forecasts, the proportion of projected HCV costs increases from just over 13% in 2015 to almost 25% by 2025. This is due to the sharp increase in the number of Medicaid patients in costly advanced stages coupled with the decrease in the number of Medicaid patients in less costly early stages in the No Cure scenario. Although the HCV-infected Medicare population increases throughout from 2015 to 2025 as HCV infected baby boomers age into Medicare or individuals under 65 move into Medicare through disability, the Medicare portion of total costs increases from 23% in 2015 to nearly 29% in 2020 before falling to about 22% in 2025. This drop is due to the mix of Medicare patients shifting toward more individuals in the early stages. While the portion of individuals in the early stages decreases for other payers, there is a sharp increase for Medicare as many relatively healthier chronically infected patients age into Medicare. While the number of Medicare patients in the more advanced stages also increases, this increase is at a slower rate due to higher mortality.

METHODOLOGY

Mortality

We estimated the mortality of HCV patients by stage using the 2010-2012 Medicare 5% Sample. The population used to calculate mortality rates includes individuals with an HCV diagnosis in 2012 that either died in 2012 or had 12 months of eligibility. Each individual's assigned stage was determined by the individual's highest HCV diagnosis (based on the HCC hierarchy) for 2010 and 2011. The undiagnosed stage is composed of individuals who had 24 months of eligibility and no HCV diagnosis in 2010 and 2011, followed by a diagnosis of HCV in 2012.

We estimated mortality load factors as the average actual mortality rate for each HCV stage divided by the average expected mortality rate for the same population. The actual mortality rate is calculated as 2012 deaths divided by eligible HCV population for each sex and stage. The expected mortality rate is calculated by applying the general population mortality rates from the 2010 Periodic Life Table to calculate expected deaths based on the age and sex distribution of the sample HCV population and then dividing by the same eligible HCV population used to calculate the actual mortality rate.

The mortality rates by stage were then calculated by multiplying mortality rates for the general U.S. population for each age/sex combination by the load factor for each stage/sex combination. These rates were used in the model across all payers to estimate the mortality of HCV patients.

Progression Rates between Disease Stages

We estimated annual progression (or transition) rates between HCV stages for commercially insured and Medicare patients using 2010-2012 MarketScan and Medicare 5% Sample data as well as information from NHANES series 2005-2012. Separate methods were used to calculate transition rates for diagnosed and undiagnosed patients.

Diagnosed Patients

We identified patients with an HCV diagnosis in 2010 who had 12 months of eligibility each year from 2010-2012. For 2010-2011, and, for each patient, identified the highest HCV stage based on the HHS-HCC staging hierarchy. Other and chronic HCV were grouped into one stage. We did not allow an individual to transition backwards to a less severe stage on the HCC staging hierarchy. For all stages other than liver transplant, we used the combined commercial and Medicare rates shown in Figure 11 in our simulation. Liver transplants transitions are lower for Medicare patients, as it is harder for Medicare patients to qualify for a transplant due to age.[23] Therefore, we used separate rates for transition to liver transplant for Medicare and commercial rates were used for all other payers.

Figure 11: Annual Probabilities of Transitions between Diagnosed HCV Stages by Payer

	End of Year HCV Stage		
Beginning of Year HCV Stage	Cirrhosis (Combined)	ESLD (Combined)	Transplant (Commercial / Medicare)
Other/Chronic	2.97%	1.20%	0.15% / 0.06%
Cirrhosis		12.56%	0.86% / 0.14%
ESLD			6.07% / 2.84%

Source: Authors' analysis of 2010-2012 MarketScan and 2010-2012 Medicare 5% Sample

Undiagnosed Patients

For the transition probabilities from undiagnosed to diagnosed HCV, we used 2009-2012 MarketScan and 2005-2012 NHANES. We first estimated the prevalence of diagnosed HCV patients based on total nationwide prevalence by payer reduced by the estimated percentage of these individuals that are assumed to be undiagnosed based on NHANES. We identified newly diagnosed HCV patients in 2012 MarketScan with a look-back to 2009 and 2010 for the absence of HCV diagnoses in years prior to 2012. We estimated the percentage of patients that were first diagnosed in 2012 as a portion of all diagnosed patients using both the two and three year look-backs. These estimated percentages were then extrapolated over a virtual nine year look-back period to produce a 10% new diagnosis rate. This new diagnosis rate was multiplied by the prevalence rate of total diagnosed HCV to calculate the prevalence rate of newly diagnosed HCV. The resulting transition rate by payer is the prevalence rate of newly diagnosed patients divided by the prevalence rate of previously undiagnosed. These rates were then multiplied by the other/chronic transition rates shown in Figure 11 to calculate transition rates from undiagnosed to each diagnosed HCV stage.

Liver Transplants and Incremental Cost

In the No Cure scenario, the number of ESLD patients requiring liver transplants will be higher than in the All Cure Scenario. If there were an unlimited supply of livers for transplant, the incremental cost of these HCV-related transplants would be about $30 billion over the ten year forecast period. However, the nationwide number of liver transplants may not decline even if HCV is cured, because the demand for transplants will continue to exceed the limited supply.[23] Consequently, we have not included incremental costs associated with liver transplants in this analysis.

Medicare Disability Rates

In our model, HCV infected individuals can gain Medicare eligibility in two ways: by aging at age 65 or through disability for those under age 65. We estimated the disability rates for transition into the Medicare population for HCV patients under age 65 using the 2011-2012 Medicare 5% Sample and NHANES 2007-2012. To calculate these rates, we first identified the HCV entrants under age 65 that were new to the Medicare 5% Sample in 2012. This number was projected to the total nationwide Medicare population. To calculate rates, we divided by the non-Medicare HCV population at each age, which was derived from NHANES. Disability rates were smoothed for individuals below age 41 using a 3-year rolling average and exponential smoothing to adjust for the lower and more volatile incidence of HCV at younger ages.

Payer Type Migration

We estimated transition probabilities for the expected migration of HCV infected patients between payer types. We used data from the Congressional Budget Office (CBO) (January 2015 Baseline), the Health Insurance Marketplaces 2015 Open Enrollment Period: January Enrollment Report and the U.S. Census Bureau's Current Population Survey tool to determine insurance status by age, gender, income and health status. The primary transitions we modeled were from uninsured, individual, and small group coverage to Medicaid or Exchanges based on CBO projections through 2018. Additionally, we modeled transitions to Medicare throughout the forecast period through two separate avenues: reaching age 65 or gaining eligibility through disability for HCV patients below age 65. Non-Medicaid Patients were assigned to Non-Dual Medicare, while Medicaid patients were assigned to a dual membership category.

Medical and Pharmaceutical Costs

We tabulated costs as of 2012 (before the current curative therapies had launched and excluded antivirals available then) and trended costs to 2015. For simplicity, we kept costs on a 2015 basis throughout the forecast period. We estimated these costs for the five HCV stages used in this analysis as well as for the undiagnosed HCV infected individuals for each scenario. These costs are combined with the population forecast for our two scenarios. We combined the per-patient projected costs for each scenario with the population forecasts to calculate a total cost forecast for each scenario. We then calculated the incremental cost by taking the difference between the costs for the two scenarios.

Diagnosed Patients

We estimated the cost of HCV for diagnosed HCV-infected patients using 2012 MarketScan, the 2012 Medicare 5% Sample and Milliman's 2012 CHSD. For the No Cure scenario, we produced 2012 medical and prescription drug average allowed costs split by HCV stage. We excluded the costs of claims associated with HCV antiviral drugs as defined by National Drug Code (NDC) for prescription drug claims and associated Healthcare Common Procedure Coding System (HCPCS) for medical claims.

We also produced average 2014 HCC risk scores by HCV stage for each payer. Risk scores were based on the HHS gold metal level risk score for commercially insured patients, the CMS HCC and RxHCC risk scores for Medicare patients, and the HHS platinum metal level risk score for Medicaid patients. For the All Cure scenario, we reduced the risk score for each stage by removing the age-weighted 2014 Chronic Hepatitis risk score component (based on the HCC staging methodology) from the average risk score from the claims data. We then calculated an allowed cost for the reduced risk score by multiplying the average allowed cost from the No Cure scenario by the ratio of the reduced risk score to the average risk score. This risk score reduction methodology is summarized in Figure 12 for commercially insured patients. We used a similar methodology for Medicare (Dual and Non-Dual) and Medicaid HCV infected patients.

Figure 12: Development of Commercial PPPM Costs through Risk Score Reduction

HCV Stage	No Cure Scenario Allowed PPPM (1)	Average Risk Score (2)	Chronic Risk Score Component (3)	Reduced Risk Score (4) = (2) - (3)	All Cure Scenario Allowed PPPM (5) = (4)/(2)*(1)
Chronic HCV	$1,606.71	6.580	1.227	5.353	$1,307.16
Other HCV	$1,564.74	5.369	1.225	4.144	$1,207.76
Cirrhosis	$2,485.75	11.352	1.228	10.124	$2,216.89
ESLD	$5,178.11	24.995	1.228	23.767	$4,923.75

Source: Authors' analysis of 2012 MarketScan and 2014 HHS Risk Adjustment Model

Since we could not identify Medicare Part D costs using the Medicare 5% Sample, we used an indirect methodology. For the No Cure scenario, we increased the average 2012 Part D allowed PPPM from the June 2014 Medicare Payment Advisory Commission (MEDPAC) Data Book based on the ratio of the 2014 CMS RxHCC risk scores for HCV infected people to the average risk score (1.0). We then adjusted these downward for the All Cure scenario by removing the 2014 Chronic Hepatitis RxHCC risk score component.

These costs were converted from a PPPM to a PPPY basis by multiplying by the average number of patient months per year observed in the claims data. They were then trended to 2015 based on 2013-2023 per enrollee CMS National Health Expenditure (NHE) projections split by payer to develop the costs shown in Figure 7.

Undiagnosed Patients

We estimated costs for undiagnosed commercial and Medicare patients using claims from 2010-2012 MarketScan and 2010-2012 Medicare 5% Sample data. We first identified patients with other or chronic HCV in 2012 who also had 12 months of eligibility in 2010 and 2011. We considered the 2012 HCV patients who did not have an HCV diagnosis in 2010 or 2011 to be undiagnosed HCV patients in 2010 and 2011. We then compared the cost of these undiagnosed HCV patients to HCV patients previously diagnosed (in 2010 or 2011) with other or chronic HCV to obtain a claims ratio that was used to produce per-capita costs for undiagnosed patients. Figure 13 shows the ratios we obtained from this analysis.

Figure 13: Development of Diagnosed to Undiagnosed Cost Ratio

Payer	Total Diagnosed PPPM	Total Undiagnosed PPPM	Ratio
Commercial	1,083	684	1.584
Medicare	1,665	998	1.668
Combined	1,412	862	1.639

Source: Authors' analysis of 2010-2012 MarketScan and 2010-2012 Medicare 5% Sample

LIMITATIONS

This report was commissioned by PhRMA. The authors are employed by Milliman, Inc. Milliman does not intend to endorse any product or benefit any third party through this report; the report reflects the findings of the authors.

As with any claim analysis, our results and conclusions are based on the underlying data and cannot capture all influences or all real world conditions. In particular, our analysis is based on recent historical experience but may not reflect present day experience for many reasons including new drug therapies and clinical guidelines.

Future experience will vary from the estimates presented in this report for reasons including random fluctuation. In addition, we present national average costs for typical populations and benefit designs, but the reader should note that considerable variation from the average results often occur in specific populations.

Additional limitations and potential areas for future research include that the simulation is based on a closed population with no new entrants, does not account for the incarcerated population and uses the same payer migration between the two simulation scenarios in our simulation.

We suggest that this report be distributed in its entirety, as material taken out of context can be misleading.

APPENDIX A: DESCRIPTION OF KEY DATA SOURCES

Milliman's 2012 Consolidated Health Cost Guidelines Source Database (CHSD) Medicaid Data

This database is a body of proprietary historical claims experience consisting of data collected from several of Milliman's Health Cost Guideline (HCG) data contributors. The dataset represents over 7 million lives and is comprised of medical and prescription drug claims on a line-item level of detail along with a complete history of per-individual eligibility for all covered lives. Approximately 96% of the lives covered are actively-employed commercial lives. Other groups represented include COBRA, Medicare Supplement and Medicaid.

2009-2012 Truven MarketScan Commercial Claims Research Database

This is an annual medical database that includes private sector health data from approximately 100 payers. The dataset contains more than 35 million commercially insured lives. It represents the medical experience of insured employers and their dependents for active employees, early retirees, COBRA continues and Medicare-eligible retirees with employer-provided Medicare Supplemental plans. The dataset consists of person-specific clinical utilization, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services from a selection of large employers, health plans, and government and public organizations. The MarketScan databases link paid claims and encounter data to detailed patient information across sites and types of providers, and over time.

2010-2012 Medicare 5% Sample Data

This limited data set contains all Medicare Part A and Part B paid claims generated by a statistically-balanced sample of Medicare beneficiaries. Information includes county of residence, diagnosis codes, procedure codes, and DRG codes, along with site of service information as well as beneficiary age, eligibility status and an indicator for Medicare Advantage enrollment.

2014 U.S. Census Bureau, Current Population Survey

The Current Population Survey (CPS), sponsored jointly by the U.S. Census Bureau and the U.S. Bureau of Labor Statistics (BLS), is the primary source of labor force statistics for the population of the United States. The CPS is the source of numerous high-profile economic statistics, including the national unemployment rate, and provides data on a wide range of issues relating to employment and earnings. The CPS also collects extensive demographic data that complement and enhance our understanding of labor market conditions in the nation overall, among many different population groups, in the states and in sub state areas.

2005-2012 Centers for Disease Control and Prevention (CDC), National Health and Nutrition Examination Survey (NHANES)

The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations. NHANES is a major program of the National Center for Health Statistics (NCHS). NCHS is part of the Centers for Disease Control and Prevention (CDC) and has the responsibility for producing vital and health statistics for the Nation.

APPENDIX B: IDENTIFICATION OF HCV POPULATION

To identify patients with HCV in the source databases, we included individuals with at least one inpatient, one emergency room, or one non-laboratory/non-radiology professional claim with an allowed amount greater than $0 and with one of the ICD-9 Diagnosis Codes (in any position on claim) below:

Appendix B: Hepatitis C Virus Diagnosis Codes

ICD9 Diagnosis Code	Description
070.41	Acute hepatitis C with hepatic coma
070.44	Chronic hepatitis C with hepatic coma
070.51	Acute hepatitis C without mention of hepatic coma
070.54	Chronic hepatitis C without mention of hepatic coma
070.70	Unspecified viral hepatitis C without hepatic coma
070.71	Unspecified viral hepatitis C with hepatic coma
V02.62	Hepatitis C carrier

To identify HCV stages, we used the CMS-HCC and HHS-HCC risk adjustment models. These risk adjustment models include four stages of disease progression related to Hepatitis C: chronic HCV, cirrhosis of the liver, end stage liver disease, and liver transplant. People identified as having HCV who were not staged according to the HCC risk adjustment models are reported in the other HCV category. This group includes HCV carriers as well as individuals with acute HCV and unspecified HCV with or without hepatic coma (diagnosis codes 070.41, 070.51, 070.70, 070.71, and V02.62).

We could not identify the undiagnosed patients based on diagnosis codes in our claims data. We used NHANES series 2005-2012 to determine the number of undiagnosed individuals based on the NHANES question HCQ030 (“Was the test result in our letter the first time you were told (you had/SP has) hepatitis C?”). The results varied by payer, with over 70% of uninsured individuals and one-third of commercially insured individuals reporting that it was the first time. We treated these as the percentages of HCV infected patients that were undiagnosed in our simulation model.

APPENDIX C: SIMULATION MODEL DETAIL

Starting Population Characteristics

To determine the characteristics of the HCV population for the beginning of the simulation, we used the U.S. Census Bureau's Current Population Survey tool to stratify the non-incarcerated U.S. population as of the beginning of 2014 by age, sex, income-to-poverty ratio, health status and health insurance status. The age and gender distribution of diagnosed HCV patients was calculated using 2012 MarketScan, the 2012 Medicare 5% Sample and 2012 CHSD. Then, we calibrated the prevalence of HCV to the nationwide distribution by birth year, gender, income, and payer (series 2005-12).

We calibrate the HCV prevalence derived from our 2012 claims databases to the nationwide prevalence based on NHANES and adjusted for under-sampled populations, such as homeless people and individuals in nursing homes,[2] and underrepresented payers, such as Veteran Affairs.[24] We started by summarizing the number of patients by HCV stage including those without HCV ("HCV Free") in the claims data. Distributions from the claims data were then adjusted so that the undiagnosed prevalence matches the estimated nationwide undiagnosed prevalence based on NHANES. The distributions for the other stages were then redistributed proportionally so that the total distribution added up to 100%.

Model Parameters

Our simulation modeled one million individual patients with HCV with varying characteristics. Each simulated patient was assigned a weight of 2.67 in order to reproduce the nationwide starting HCV population shown in Figure 2. From 2014 to 2025, each patient was aged one year and exposed to the following decrements: mortality, disease transition, disability and payer migration. For an individual patient's age, sex and stage in a given year, an annual mortality rate was applied against a randomly assigned uniform variable. Surviving patients' progression to more advanced disease stages was similarly determined. We constrained the number of HCV-related liver transplants to approximately 5,000 per year to correspond with the limited supply of livers available for HCV patients in the U.S.[23] We then applied payer migration probabilities to determine if that patient's insurance coverage shifted.

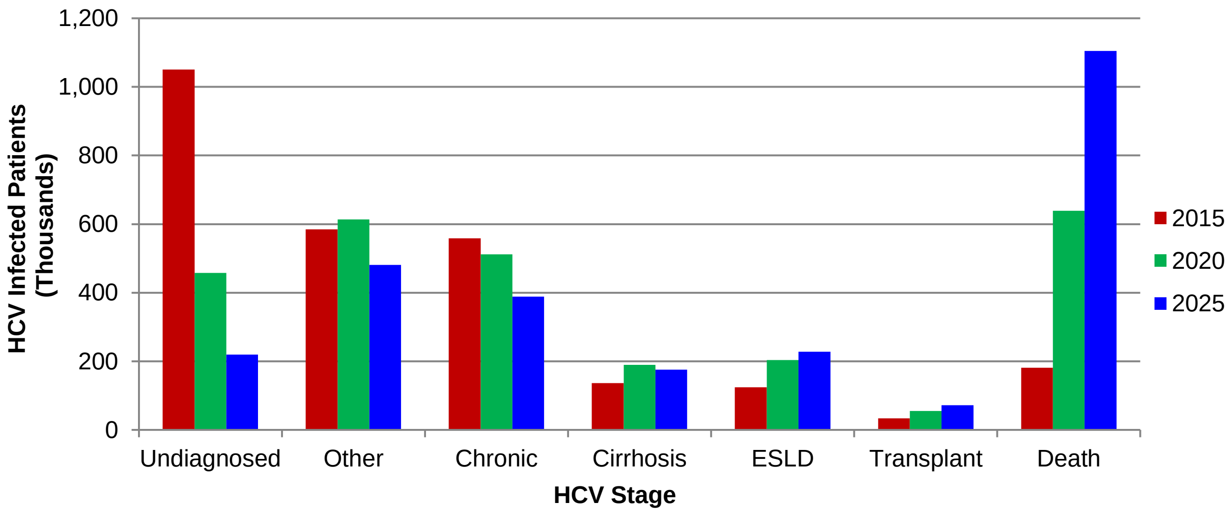
To capture the incremental cost of HCV, we simulated two hypothetical scenarios. The No Cure scenario modeling the natural progression of the disease and an All Cure scenario, which uses the mortality and transition rates described above. The All Cure scenario uses modified progressions appropriate for patients whose HCV has been cured. Many sources indicate that SVR has a beneficial effect on patients' survival.[12,14,16] A hazard ratio of 70% for mortality between SVR and non-responders was used to reduce the mortality rates for patients in the All Cure scenario. Additionally, we eliminated transitions between stages.[12] Since patients with liver fibrosis may not see a reversal of this damage, we retained the original stage for each patient.

APPENDIX D: DISEASE PROGRESSION BY STAGE AND SCENARIO

Appendices D-1 and D-2 describe the disease progression between HCV stages over the forecast period for each scenario.

Appendix D-1 shows a forecast of the number of HCV infected patients in 2015, 2020 and 2025 who are undiagnosed or in the five diagnosed stages of HCV, as well as the cumulative number of deaths for the No Cure scenario. Our simulation projects that the undiagnosed will make up over 40% of HCV infected patients in 2015. However, as the disease progresses with no cure and screening improves, we project that these patients will compose less than 15% of HCV infected patients by 2025. Many of these undiagnosed patients are projected to transition to other/chronic stages, leading to a projected increase in these stages from 46% of the HCV infected population in 2015 to 56% by 2025. However, patients in the other/chronic stages will also transition in the absence of a cure. As a result, the portion of HCV patients in more advanced stages will increase over the forecast period. From 2015 to 2025, the portion of HCV infected patients with cirrhosis is projected to more than double from 5% to 11%, the portion with ESLD is forecast to triple from 5% to 15%, and the portion with liver transplants would more than triple from 1.4% to 4.6%.

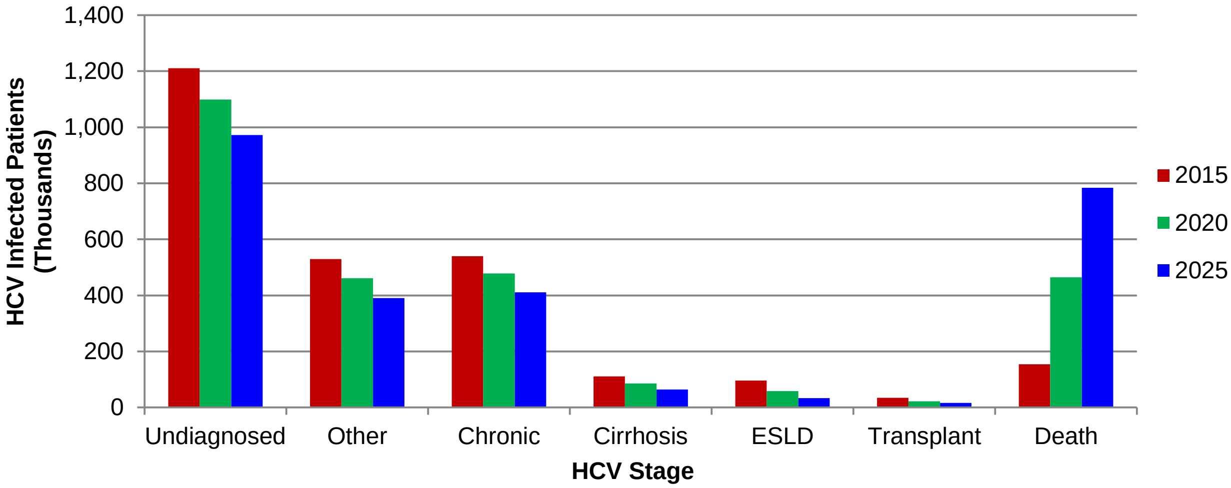
Appendix D-1: No Cure Scenario Forecast of HCV Infected Patients by Disease Stage



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

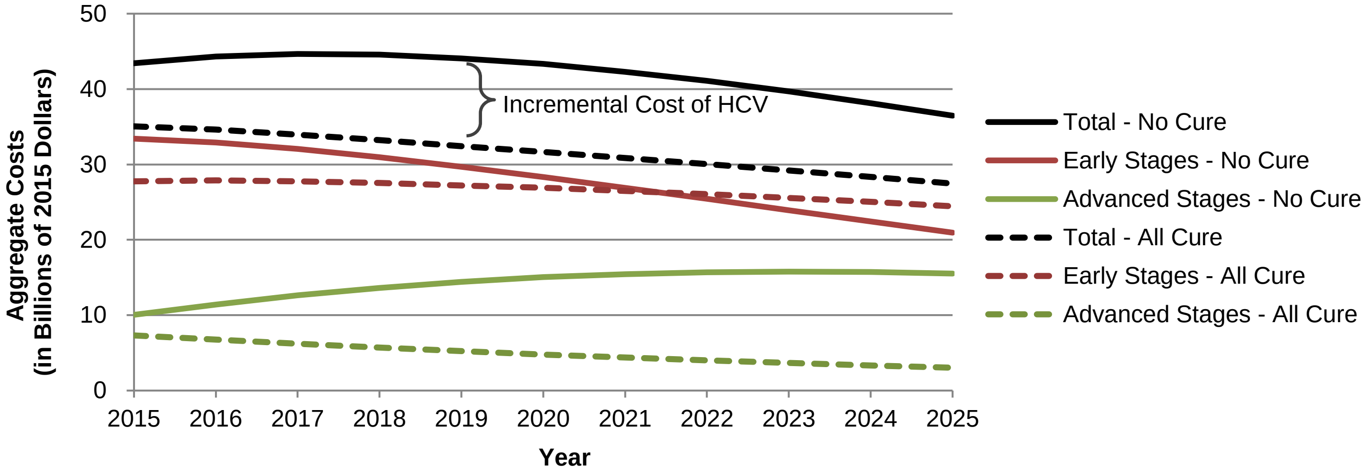
Appendix D-2 shows a similar forecast for the All Cure scenario. In this scenario, there is no movement between disease stages. Any change in a stage's population is due to mortality. Therefore, much of the HCV population remains concentrated in the early stages with little change in stage distribution over the forecast period.

Appendix D-2: All Cure Scenario Forecast of HCV Infected Patients by Disease Stage



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

APPENDIX E: AGGREGATE HCV COSTS BY STAGE AND SCENARIO



Source: Authors' analysis of 2005-2012 NHANES, 2014 CPS, 2009-2012 MarketScan, 2010-2012 Medicare 5% Sample, and 2012 Medicaid CHSD.

The figure above shows a direct comparison of aggregate costs (in 2015 billions of dollars) between the two scenarios split by early and advanced stages of HCV. The incremental cost is represented by the difference between the total costs corresponding to the solid black and dotted black lines. In the No Cure scenario, costs will increase from about $43.5 billion in 2015 to a peak of almost $45 billion in 2017 and then decline sharply to just under $36.5 billion by 2025. In the All Cure scenario, costs will decrease throughout the forecast period from about $35 billion in 2015 to just under $27.5 billion by 2025.

The cost movement of each scenario can be understood by separately examining the costs for the early and advanced stages of HCV. The red lines portray the costs for the early stages. Costs for the No Cure scenario are projected to decrease rapidly from almost $33.5 billion in 2015 to just under $21 billion by 2025 due to patients progressing into more advanced stages and mortality. By contrast, the All Cure scenario costs are forecast to decrease gradually, exclusively due to mortality, from about $28 billion in 2015 to about $24.5 billion by 2025. Without treatment, patients shift from the early stages to the more advanced and more costly stages. This is clear from the green lines, which represent estimated costs for advanced stages. For the All Cure scenario, projected costs decline throughout the forecast period from about $7 billion in 2015 to just $3 billion by 2025. Costs are projected to increase for the No Cure scenario from about $10 billion in 2015 to just over $15.5 billion by 2025.

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