Projected U.S. national Hepatitis C treatment costs and estimated reduction to medical costs

A 10-year nationwide projection of pharmacy costs related to the treatment of chronic Hepatitis C infection with direct-acting antivirals and an estimate of the reduction in medical costs

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Executive Summary

Hepatitis C virus (HCV) is a common and costly infection of the liver affecting millions of Americans and resulting in a high cost burden due to both direct healthcare costs and indirect costs resulting from impaired quality of life and loss of productivity.[1] Prior to the availability of direct-acting antivirals, HCV treatment options were limited to injection-based regimens with limited efficacy and serious adverse effects. The approval of interferon-free direct-acting antivirals (DAAs) brought considerable improvements in efficacy, safety, and tolerability compared to existing regimens, while also generating public debate about their costs and associated long-term value.

In this report, we estimate the U.S. national and per-patient net cost impact of HCV treatment with DAAs on HCV-related medical costs over a 10-year period (from 2021 to 2030). We estimate a national net savings of $49.2 billion over 10 years.

Our analysis produced the following key findings:

- Assuming 25% of diagnosed HCV patients are treated annually with an interferon-free DAA treatment, the aggregate estimated national HCV DAA net* treatment cost is $21.7 billion from 2021 to 2030. The reduction in national HCV-related medical costs is estimated as $70.8 billion over the same period. This results in a national net savings of $49.2 billion over the 10-year projection.
- The cumulative 10-year per-patient HCV-related medical costs are estimated to reduce following DAA treatment by $57,000 for patients with non-cirrhotic disease (NCD), $37,500 for patients with compensated cirrhosis (CC), and $199,500 for patients with end-stage liver disease (ESLD).
- The breakeven point of national HCV treatment costs and the HCV-related medical costs reduced by treated patients generally occurs between years 2 and 3.

* We define HCV DAA net treatment cost as the wholesale acquisition cost (WAC) less pharmacy discounts, patient assistance, and manufacturer funded price concessions, such as rebates, coverage gap discounts in Medicare, federal and supplemental rebates in Medicaid, and 340B drug pricing.

Background

OVERVIEW OF HEPATITIS C AND HCV TREATMENTS

Hepatitis C virus (HCV), a viral infection of the liver, is a leading cause of serious liver disease in the United States resulting in increased morbidity and mortality and a large financial burden for both patients and the healthcare system. HCV is a bloodborne illness that is usually spread through blood or bodily fluids that contain blood. HCV can be spread through sharing needles or syringes, perinatal transmission at birth, healthcare exposures, and other methods that involve coming into contact with blood from an infected individual.[2] Prior to the widespread screening of the blood supply in 1992, HCV was also spread through blood transfusions and organ transplants, though this occurs with much lower frequency today. Currently, the majority of new acute HCV cases are in persons who inject drugs, and the highest rates now occur in persons 20-39 years.[3] The Centers for Disease Control and Prevention (CDC) reported 123,312 total new confirmed cases of chronic hepatitis C in the United States in 2019.[3] However, because HCV is often asymptomatic, roughly four in 10 people are unaware of their diagnosis, indicating the actual number of chronic cases is likely much higher.[4] The most recent large-scale epidemiologic study using 2013-2016 data estimated roughly 1% of the U.S. adult population has HCV, suggesting there were approximately 2.4 million people in the United States living with HCV in 2016.[5] In 2020, the CDC updated its recommendations for HCV screening to include one-time screening for all adults and with each pregnancy, while the U.S. Preventive Services Task Force (USPSTF) recommended screening for adults aged 18 to 79. Both organizations have expanded screening recommendations compared to the prior screening recommendations for adults born between 1945 and 1965.[6,7]

Until the last decade, HCV treatment options were limited to interferons and ribavirin-based regimens. These treatments were injection-based, had limited efficacy, and were associated with serious side effects, including influenza-like symptoms, depression, neutropenia, and anemia. Victrelis® and Incivek®, approved in 2011, were the first-generation DAAs and showed slightly improved efficacy. However, their use was limited to a subset of HCV patients (genotype 1), and interferons and ribavirin were required for use in conjunction with the DAAs. In 2013, second-generation DAAs, Sovaldi® and Olysio®, were approved. Regimens including these products resulted in fewer side effects and higher cure rates than prior existing options, measured by sustained virologic response (SVR12), or no detectable amount of HCV after 12 weeks post-treatment.[8] Since then, multiple interferon-free and ribavirin-free regimens have become available (e.g., Harvoni®, Zepatier®, Epclusa®, Vosevi®, Mavyret®). These newer therapies have further improved the HCV treatment landscape, resulting in cure rates over 95%, improved tolerability, expanded indications to cover all virus genotypes, shorter treatment duration (typically eight to 12 weeks), and increased price competition.

HCV-RELATED MEDICAL COSTS

While HCV may be asymptomatic in the early stages, the severity and speed of disease progression is highly variable. Chronic HCV can result in liver damage, cirrhosis (scarring of the liver), liver failure, and liver cancer, resulting in an estimated fivefold increase in all-cause mortality and 20fold increase in liver-related mortality when compared to the general population.[9] In addition to increased mortality, chronic HCV is accompanied by economic burden, including both direct medical costs and indirect costs resulting from loss of work productivity and impaired quality of life.

Several studies evaluated the medical costs associated with chronic HCV and found patients with HCV have higher all-cause medical costs than control populations with similar characteristics.[10,11,12] In a study of HCV-related medical costs (costs directly associated with HCV or liver disease), Gordon et al. (2012) found the weighted average per patient per month (PPPM) HCV-related medical costs in 2010 U.S. dollars were $917.48 across all HCV patients studied, or $11,010 per year.[13] When broken down by disease severity, the study found HCV-related PPPM medical costs of $466.68 for patients with NCD, $663.31 for patients with CC, and $3,328.05 for patients with ESLD.[13] This equates to 2010 annual HCV-related costs of roughly $5,600, $7,960, and $39,937 for NCD, CC, and ESLD, respectively. Similarly, other studies found medical costs increase significantly with increased disease severity.[14,15] Despite the often asymptomatic nature of HCV, the ability to prevent disease progression accompanied by substantial medical costs emphasizes the potential value of treating HCV in all stages of disease severity as recommended by the American Association for the Study of Liver Diseases (AASLD).[16]

Although DAAs offer improved efficacy, safety, and tolerability compared to the previous standard of care, they have been a source of debate among payers, regulators, manufacturers, and other stakeholders regarding the cost, associated value, and affordability of the treatments.[17] A number of pharmacoeconomic studies and models assessed the value of DAA treatment and total cost of care.[18,19,20] Less common are studies focusing on the HCV-related medical offsets attributable to avoided liver disease progression from DAA usage.

The purpose of our study is to estimate the 10-year HCV-related medical cost savings associated with the treatment of HCV with second-generation DAAs, utilizing recent estimates of net DAA treatment costs and published HCV-related medical costs and prevalence.

HCV-related medical cost is evaluated across the entire adult U.S. population, among three levels of disease severity: NCD, CC, and ESLD, with ESLD including conditions like decompensated cirrhosis and hepatocellular carcinoma.

Results

HCV-RELATED MEDICAL COSTS

Figure 1 shows the estimated disease-severity distribution of the HCV population as of 2021 and the estimated annual HCV-related medical costs assumed in the model. We define HCV-related medical costs as any medical costs attributed to HCV itself or liver disease. We estimated the disease severity distribution from numerous published studies.[10-15,21] We also derived the annual HCV-related medical costs from the literature, including the Gordon study and others.[13-15] For year 1 of our study, we used information by disease severity from the literature and trended costs to 2021 U.S. dollars using historical Consumer Price Index for All Urban (CPI-U) data as a measure of medical inflation.[22]

FIGURE 1: ESTIMATED 2021 DISTRIBUTION AND HCV-RELATED MEDICAL COSTS BY DISEASE SEVERITY

Disease Severity	Estimated Percentage of Diagnosed HCV Population	2021 HCV-related Medical Costs
Non-Cirrhotic Disease (NCD)	78.2%	$6,043
Compensated Cirrhosis (CC)	7.4%	$8,957
End-Stage Liver Disease (ESLD)	14.3%	$47,711

U.S. NATIONAL HCV-RELATED COSTS

In Figure 2, we provide the projected number of HCV patients, as well as the breakouts of diagnosed and DAA-treated patients by disease severity for 2021 through 2030. The estimated HCV prevalent population changes annually by adding new HCV cases, removing patients assumed to be cured after treatment with DAAs, and reflecting annual mortality applied at each disease severity. As a result, the distributions noted below differ slightly than those shown in Figure 1 after 2021. We used a 25% treatment rate for purposes of our projection, which we believe produces a conservative estimate of national reduction in HCV-related medical costs. See Appendix A for additional model assumptions and their sources.

FIGURE 2: PROJECTED U.S. HCV PREVALENCE, DIAGNOSED, AND DAA TREATED POPULATION 2021 TO 2030 (IN MILLIONS)

	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
HCV Prevalent Population	2.14	1.71	1.37	1.13	0.94	0.81	0.70	0.62	0.55	0.50
HCV Diagnosed Population (56% of HCV population)	1.20	0.96	0.77	0.63	0.53	0.45	0.39	0.34	0.31	0.28
NCD	0.95	0.77	0.63	0.52	0.44	0.37	0.32	0.29	0.26	0.23
CC	0.09	0.07	0.06	0.05	0.04	0.03	0.03	0.03	0.02	0.02
ESLD	0.16	0.12	0.09	0.07	0.05	0.04	0.04	0.03	0.03	0.03
DAA Treated Population (25% of diagnosed population)	0.30	0.25	0.20	0.17	0.14	0.12	0.10	0.09	0.08	0.07
NCD	0.24	0.20	0.16	0.14	0.11	0.10	0.08	0.07	0.07	0.06
CC	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
ESLD	0.04	0.03	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01

In Figure 3, we provide a 10-year projection of a reduction in HCV-related medical costs as a result of HCV treatment compared to HCV DAA treatment costs for the U.S. population. The amount of estimated HCV-related medical cost reduction increases each year as more patients are treated and continue to accumulate avoided HCV-related medical costs. HCV-related medical cost reductions include costs avoided from the patients treated in the current year and patients treated in prior years. Total national HCV treatment costs are projected to slowly decline after 2022 as the size of the population eligible for treatment decreases. The national estimates include a small portion (4%) of patients requiring a second course of DAA treatment to reach a cure and applies mortality assumptions by disease severity.

Figure 3 shows that the reductions in HCV-related medical costs begin to offset the cost of HCV DAA treatment starting in 2023 (year 3 of the model).

FIGURE 3: PROJECTED U.S. POPULATION MEDICAL COSTS REDUCED AND HCV TREATMENT COSTS 2021 TO 2030 (IN BILLIONS)

	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	Total
HCV-related Medical Costs Avoided	$0.5	$2.5	$4.3	$5.7	$7.0	$8.2	$9.2	$10.2	$11.1	$12.0	$70.8
Net HCV Treatment Costs	$4.3	$3.6	$2.9	$2.4	$2.0	$1.7	$1.5	$1.3	$1.1	$1.0	$21.7
Costs / (Savings)	$3.7	$1.0	($1.4)	($3.4)	($5.0)	($6.5)	($7.7)	($8.9)	($10.0)	($11.0)	($49.2)

HCV TREATMENT MEDICAL COST OFFSET AT THE PATIENT LEVEL

Figure 4 provides a more granular view of the projection, showing a reduction in HCV-related medical costs at the patient level by disease severity, assuming 10 years of survival and a single course of DAA treatment. A course of DAA treatment is typically between eight and 12 weeks, therefore we use an average treatment course of 10 weeks for our model. During each year of projection (including 2021 as year 1), we assume that a portion of HCV-related medical costs can be reduced once a patient has been cured. Patients with NCD are assumed to have larger reductions in costs than patients with CC or ESLD due to the less severe nature of their disease and liver damage. Please refer to the methodology section for additional detail.

For patients with non-cirrhotic disease, compensated cirrhosis, and end-stage liver disease, the reduction in medical costs begins to offset the cost of HCV DAA treatment by 2024, 2025, and 2022, respectively. The weighted average of cumulative net savings per patient across all disease severities is $57,447 over 10 years.

FIGURE 4: PROJECTED PER PATIENT AVERAGE REDUCTION IN HCV-RELATED MEDICAL COSTS AND HCV TREATMENT COSTS 2021 TO 2030 BY DISEASE SEVERITY

	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Non-Cirrhotic Disease (NCD)										
Annual HCV-related Medical Costs Avoided	$1,511	$5,575	$5,714	$5,857	$6,003	$6,153	$6,307	$6,465	$6,627	$6,792
Cumulative Reduction in HCV-related Medical Costs	$1,511	$7,086	$12,800	$18,657	$24,660	$30,814	$37,121	$43,586	$50,212	$57,005
Average DAA Treatment Costs	$14,250	$0	$0	$0	$0	$0	$0	$0	$0	$0
Cumulative Costs / (Savings)	$12,739	$7,164	$1,450	($4,407)	($10,410)	($16,564)	($22,871)	($29,336)	($35,962)	($42,755)
Compensated Cirrhosis (CC)										
Annual HCV-related Medical Costs Avoided	$896	$3,672	$3,764	$3,858	$3,955	$4,054	$4,155	$4,259	$4,365	$4,474
Cumulative Reduction in HCV-related Medical Costs	$896	$4,568	$8,332	$12,190	$16,145	$20,198	$24,353	$28,612	$32,977	$37,451
Average DAA Treatment Costs	$14,250	$0	$0	$0	$0	$0	$0	$0	$0	$0
Cumulative Costs / (Savings)	$13,354	$9,682	$5,918	$2,060	($1,895)	($5,948)	($10,103)	($14,362)	($18,727)	($23,201)
End-Stage Liver Disease (ESLD)										
Annual HCV-related Medical Costs Avoided	$4,771	$19,561	$20,050	$20,552	$21,065	$21,592	$22,132	$22,685	$23,252	$23,834
Cumulative Reduction in HCV-related Medical Costs	$4,771	$24,332	$44,383	$64,934	$86,000	$107,592	$129,724	$152,409	$175,661	$199,495
Average DAA Treatment Costs	$14,250	$0	$0	$0	$0	$0	$0	$0	$0	$0
Cumulative Costs / (Savings)	$9,479	($10,082)	($30,133)	($50,684)	($71,750)	($93,342)	($115,474)	($138,159)	($161,411)	($185,245)

Discussion

Our study findings are consistent with similar conclusions made by other pharmacoeconomic studies and models. A recent study by Roebuck et al. estimated the impact of DAA treatment on healthcare costs in Medicaid specifically, finding that a course of DAA treatment, on a per-person basis, can be expected to be fully offset by healthcare cost savings after 16 months, on average.[11] Another study by Chou et al. estimated the budget impact of removing HCV treatment restrictions in four state Medicaid programs, finding that all treatment scenarios modeled achieved breakeven costs in four to eight years.[23] Jung and colleagues evaluated the changes in medical costs for 30 months following DAA treatment for Medicare patients, finding DAA treatment was associated with a reduction in HCV-related medical costs, but that DAA treatment was not cost-saving at that time, as a result of the high cost of DAAs assumed and shorter study period compared to our study.[15] While both the Chou and Jung studies applied discounts to DAA list prices, the net prices utilized in the studies are higher than recent DAA price estimates, which may explain why our findings differ.[24]

Data, Methodology, and Limitations

DATA SOURCES

We relied on published literature and HCV-related studies of medical costs and epidemiology. Medical cost estimates developed in past years' studies were trended to 2021 using the Consumer Price Index for All Urban (CPI-U) and then projected from 2021 to 2030 using the Milliman Medical Index.[22,26]

METHODOLOGY

We referenced published literature regarding HCV-related medical costs and HCV epidemiology in the United States to create a model estimating the medical cost offset associated with a reduction in HCV-related costs and avoided liver disease progression from treatment of HCV with DAAs.

- Population: We derived the national HCV population using CDC-reported HCV prevalence of 1% of U.S. adults and the U.S. population.[2,5] Because the most recent prevalence estimates are from 2016 data, we adjusted the 2016 HCV population to 2021 by assuming a decrease in diagnosed patients as a result of patients being treated and cured and applying mortality assumptions, resulting in a starting HCV population of 2.14 million. An estimated 56% of patients with HCV have been diagnosed; therefore, we assumed that 56% of the total HCV population would be eligible for treatment.[4] The population is segmented into three disease severities: non-cirrhotic disease (NCD), compensated cirrhosis (CC), and end-stage liver disease (ESLD). Starting distribution among the disease severities is derived from the literature.[6-11,16] Among each disease severity, we assumed differing levels of annual mortality.[25] We did not explicitly apply any factors for timing of disease progression or growth in U.S. population, which may change the estimates for treatment costs and HCV-related medical costs.
- Medical costs: In year 1 of the model, we calculated a weighted mean of the annual HCV-related medical costs by disease severity as reported in the literature. We applied inflation adjustments to bring historical estimates to 2021 U.S. dollars using the CPI-U.[22] We trended medical costs forward from 2021 to 2030 using the average annual per person medical cost trend from the Milliman Medical Index.[26] During each year of projection (including 2021 as year 1), we assume a portion of HCV-related medical costs can be reduced. For NCD, we assume 25% of the medical costs are avoided in year 1 and 90% in subsequent years. For CC and ESLD, we assume 10% of the costs are avoided in year 1 and 40% in subsequent years. The proportions account for patients treated midyear in the first year, and some patients may have lingering HCV-related or liver-related medical needs, depending on disease progression. Higher reductions are assumed for patients with NCD as their liver damage is typically reversible and disease is less severe, therefore we expect a majority of HCV-related costs will go away following DAA treatment. We assume lower reductions in HCV-related medical costs for CC and ESLD patients due to the irreversible nature of their liver damage.
- Treatment costs: We referenced a previous Milliman study for the net cost of treatment courses of roughly $200 per day and used an equal blend of eight-week and 12-week treatment regimens, resulting in 10-week treatment costs of $14,250 per treatment course.[24] The prior study showed historical decreases in net cost; however, for this projection we assume DAA treatment net costs will remain level in future years and therefore did not assume negative future cost trends from 2020 and forward.

LIMITATIONS

Our 10-year model utilizes a number of assumptions derived from the literature to inform the results described herein. We note that these assumptions may vary for a variety of reasons, one notable reason being the COVID-19 pandemic. Since the start of the COVID-19

pandemic in March 2020, utilization of healthcare services has changed in unpredictable ways. Specific to HCV, diagnostic testing for HCV decreased substantially and, as a result, diagnosis rates and DAA prescription volume have also decreased.[27] Kaufman et al. found that, in 2020, HCV treatment prescriptions decreased by 43% in May, 37% in June, and 38% in July compared to the corresponding months in 2018 and 2019. Because of the lack of predictability and available information regarding COVID-19 and its ongoing impact on HCV diagnosis and treatment, our model does not include adjustments for COVID-19.

Our analysis and methodology are limited to information available in the literature. Our analysis did not account for the following:

- Variations in cost (including medical costs and DAA net costs) across different U.S. lines of business (commercial, Medicare, Medicaid) or the uninsured.
- Fluctuations in diagnosis and treatment rates as a result of the COVID-19 pandemic, changing testing recommendations, and other factors, such as further decreases to the net cost of DAA treatment.
- Historical analysis of HCV patient cost changes compared to model estimates.
- Adjustments to account for speed of disease progression in HCV patients.

This report was prepared for Gilead Sciences, Inc., a life sciences company that manufactures several HCV therapies. Our findings are based on a review of available literature regarding the medical costs associated with chronic HCV. Results from this analysis may not be applicable to other therapeutic areas or markets.

The results presented herein are estimates based on the best information available as of the date of publication. Differences between our results and other analyses may arise due to variations in definitions, methodology, or data updates.

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APPENDIX A

Model Assumptions and Sources

Appendix A Model Assumptions and Sources		
Metric	**Assumption**	**Source(s)**
Diagnosis Rate	56%	4
Treatment Rate	25%	15, 25, 28, 29, 30
Treatment Success Rate	96%	31
Re-Treatment Rate	4%	31
Overall U.S. Mortality (annual)	0.9%	32
NCD Mortality (annual)	4.8%	25
CC Mortality (annual)	6.5%	25
ESLD Mortality (annual)	14.6%	25

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