REPORT

Assessing the Burden of Illness of Chronic Hepatitis C and Impact of Direct-Acting Antiviral Use on Healthcare Costs in Medicaid

M. Christopher Roebuck, PhD; and Joshua N. Liberman, PhD

ABSTRACT

OBJECTIVES: To quantify the burden of illness of chronic hepatitis C virus (HCV) infection and estimate the impact of interferon-free direct-acting antiviral treatment on healthcare costs in Medicaid.

STUDY DESIGN: Observational, retrospective analysis.

METHODS: Medicaid claims data from 2012 for nonelderly adult enrollees with chronic HCV in 16 states were used to estimate the burden of HCV in Medicaid. Annual measures of health services utilization and cost for patients with HCV were compared with a control group of patients without HCV exactly matched on a robust set of individual characteristics and stratified according to liver disease severity, Medicaid eligibility group, and plan type. Subsequently, HCV burden-of-illness estimates were used in a separate analysis of Medicaid State Drug Utilization Data on interferon-free drug utilization and expenditures to estimate the annual and cumulative impact of these curative medications on national Medicaid costs from 2013 through 2022.

RESULTS: Annual per-person Medicaid healthcare costs attributed to HCV infection were estimated to range from $10,561 for noncirrhotic disabled adults to $46,263 for nondisabled adults with end-stage liver disease. The costs were due mainly to inpatient hospitalizations and outpatient hospital visits, prescription drug utilization, outpatient physician's office/clinic visits, and laboratory tests. By 2014, the first full year following the approval of interferon-free treatment, an estimated 12,175 adults with HCV were cured in Medicaid nationwide, each avoiding an estimated $15,907 per year in healthcare costs associated with the disease. As more patients in Medicaid are treated and net savings continue to grow year after year—due to recurring avoidance of health services use and declining drug prices—total cumulative treatment costs since 2013 are expected to be fully offset by total cumulative healthcare expenditure reductions by the end of 2019. By 2022, the recurrent annual avoidance of healthcare costs will have delivered an estimated $12 billion in total cumulative savings to Medicaid, net of DAA drug expenditures.

CONCLUSIONS: The introduction of interferon-free HCV treatments enables the avoidance of significant healthcare costs previously associated with treating the disease year after year, producing annual cumulative Medicaid savings beginning in 2019. A main finding from this study is that the cost of a complete DAA treatment course, at 2018 estimated net prices, can be expected to be fully offset by healthcare cost savings after only 16 months, on average, on a per-person basis. Given the tremendous value provided by these curative drugs, Medicaid policies aimed toward restricting access to these treatments based on disease severity or other requirements would be shortsighted.

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For author information and disclosures, see end of text.

More than 2 million people are currently infected with the hepatitis C virus (HCV) in the United States.[1] For many, an HCV infection is an asymptomatic condition that often goes undiagnosed. If untreated, the virus increases an individual's risk of life-threatening conditions such as cirrhosis, hepatocellular carcinoma, and liver failure.[2] As such, HCV imposes substantial costs on society. Patients who are infected with HCV have poorer quality of life and decreased productivity,[3-5] consume more health services,[6-11] and have higher mortality rates.[12] Moreover, healthcare needs increase dramatically as HCV disease progresses.[7,13-16]

Until 2011, the primary treatment for chronic HCV infection was a combination of pegylated interferon and ribavirin. With this regimen, about 50% of patients were able to achieve "cure," defined by a sustained virologic response (SVR)—no measurable virus in the blood—12 or 24 weeks after the end of treatment.[17,18] The duration of treatment was long (up to 48 weeks) and associated with high discontinuation rates.[19] In May 2011, the FDA approved the first agent in a new therapeutic class known as direct-acting antivirals (DAAs). Unlike peginterferon and ribavirin, DAAs interfere with the growth and replication cycles of HCV itself.[20] DAAs were initially used in combination with peginterferon and ribavirin; however, since late 2013, interferon-free DAA regimens have been available. Clinical evidence indicates that these interferon-free DAA regimens are well tolerated and effective, achieving SVR in 92% or more of patients, although outcomes vary by genotype, prior treatment, and disease severity.[21]

DAAs were initially more expensive than older treatment options; however, these costs have declined substantially over time with increased competition. Indeed, within a year of the approval of the first interferon-free regimen, additional interferon-free DAAs entered the market, which enabled payers to negotiate large discounts and/or rebates in exchange for favorable formulary placement. Largely because of this increased competition, negotiated supplemental rebates have risen from about 22% off list price in 2014 to as high as 60% in ensuing years.[22,23] Moreover, list prices for DAAs themselves have declined drastically, from nearly $100,000 per treatment course in 2014 to as low as $24,000 per treatment course today.[24]

Despite a reduction in the costs of DAAs, state Medicaid programs have expressed concerns over allowing universal access to these new therapies because of the unique dual challenge of having both the financial constraints of annual public budgets and high numbers of HCV-infected enrollees.[25] Consequently, many Medicaid programs have chosen to restrict coverage of DAAs, based on parameters of fibrosis stage (ie, degree of liver damage), abstinence from alcohol and substance use, and prescriber type.[26,27] From an economic efficiency standpoint, the appropriateness of these access restrictions depends not only on the costs of DAAs but also on the benefits derived from their use.

Several economic evaluations of DAAs have been published.[28-31] Moreover, burden-of-illness studies have been conducted on populations of patients with HCV in commercial insurance,[7,10,13,14,32,33] Medicare,[9] and the general US population.[8,11] However, comparable research in Medicaid is scant, with only 1 published study on a single state's experience.[15] The present study estimates the healthcare costs associated with chronic HCV infection in Medicaid using detailed data from 16 states and more than 5 million Medicaid enrollees, paired with actual interferon-free DAA utilization and expenditure data to measure the annual and cumulative impact of these curative medications on Medicaid costs from 2013 through 2022.

Methods

This study was conducted in 2 separate stages using 2 distinct data sources to estimate Medicaid costs attributable to HCV infection and to Medicaid savings resulting from curative DAA treatment. These sources were Medicaid Analytic eXtract (MAX) files, which were used to quantify the per-patient cost burden of HCV infection, and Medicaid State Drug Utilization Data (SDUD) files, which were used to project the number of Medicaid beneficiaries cured of HCV following the release of interferon-free DAAs and to simulate the expected savings associated with these curative therapies.

Medicaid Analytic eXtract Data

MAX files were obtained under a Data Use Agreement from CMS with institutional review board (IRB) approval and oversight (Advarra IRB; Columbia, MD). Created primarily to support research and policy analysis, MAX data include pharmacy and medical claims and encounter records, as well as eligibility information, on all individuals enrolled in Medicaid.[34,35] MAX files for the year 2012 from 16 states—Alabama, California, Connecticut, Florida, Illinois, Indiana, Louisiana, Michigan, New Hampshire, New Mexico, New York, Ohio, Oregon, Pennsylvania, Virginia, and Washington—were utilized for this study. Participants were aged between 18 and 64 years as of December 31, 2012, with unrestricted Medicaid benefits and without an annual gap in coverage of more than 30 days. After these criteria were imposed, 5,210,249 adult Medicaid recipients remained. Participants were then segmented according to their Medicaid basis of eligibility: either adults who were blind/disabled (hereafter "disabled") or adults who were other nonblind/disabled (hereafter "nondisabled"). They were further stratified by plan type: either fee-for-service (FFS) or managed care (see **Appendix Figure**).

Medicaid State Drug Utilization Data

The SDUD files contain precise information on the counts and reimbursement amounts for all prescriptions dispensed in Medicaid nationwide.[36] Specifically, data were obtained on all interferon-free DAA (hereafter just "DAA") fills from the fourth quarter of 2013 through the second quarter of 2018. Package inserts for each DAA product, which specify recommended dosage amounts and treatment durations by cirrhosis status and treatment naïvety, were used to determine the average number of prescriptions filled per treated patient with HCV infection and were applied to the SDUD to calculate the annual number of patients treated with DAAs. Subsequently, expected DAA-specific SVR rates were used to determine the estimated annual number of patients cured of the virus, accounting for treatment nonadherence. See **Appendix** for details.

HCV Burden-of-Illness Analysis

MAX claims and encounter data were analyzed to estimate Medicaid costs attributable to an HCV diagnosis in 2012. Patients with chronic HCV were identified using an algorithm employed by Gordon et al.[14] Individuals were required to have at least 1 medical claim with a diagnosis of chronic HCV; at least 2 medical claims on different dates for unspecified HCV or HCV carrier; or 2 or more medical claims at least 6 months apart for unspecified HCV, HCV carrier, or acute HCV. Records for HCV testing were excluded from this case-finding definition to avoid basing HCV status on rule-out procedures. Using these criteria, a total of 72,109 individuals were classified as having chronic HCV during the study period. Patients were then assigned to 1 of 3 liver disease severity cohorts: noncirrhotic, cirrhosis, or end-stage liver disease (ESLD), based on the work of Gordon et al.[14] See the Appendix for details.

Patients with chronic HCV were exact-matched 1:1 to control individuals (those without evidence of HCV) on the following demographic and plan characteristics: basis of eligibility, age, gender, race, ethnicity, state of residence, plan type, any months enrolled in primary care case management, and any months receiving cash maintenance assistance. Individuals were also exact-matched on the presence of diagnoses for asymptomatic HIV or symptomatic HIV/AIDS because these often cooccur with, but are not caused by, HCV infection. Because patients with HCV were exactly matched to patients without HCV, no statistically significant differences in mean values of any of the matching variables were present. Additional details are provided in the Appendix.

Five count measures of annual health services utilization (HSU) were constructed from the claims data: inpatient hospitalizations,

hospital days, emergency department (ED) visits, physician's office/clinic visits, and prescription drug fills (adjusted to 30-day equivalents). For individuals enrolled in FFS plans, healthcare cost variables were generated using the amounts paid by Medicaid. Cost measures were not created for managed care plan enrollees because their health services are routinely covered on a capitated basis. In the process of building the MAX files, CMS classifies Medicaid expenditures into 33 specific types of service. For the present analysis, a subset of 14 of these were retained; the remaining 19, which contained little to no spending, were summed to form an "other" category. Costs were aggregated into drug and nondrug subtotals, as well as total healthcare costs. Because HCV prescription drug costs were expected to be a significant part of the burden of illness in 2012, spending on peginterferon and ribavirin—and the proportion of chronic HCV patients treated with this regimen—was measured and reported separately. The costs associated with the first 2 DAAs on the market (boceprevir and telaprevir), which were used concomitantly with peginterferon and ribavirin in 2012, were itemized.

Differences in mean values for the HSU and cost variables were tested between the chronic HCV and control groups, as well as across liver disease severity cohorts using the nonparametric Kruskal-Wallis equality of populations test.[37] All analyses were conducted using Stata/MP version 15.1 (StataCorp LP; College Station, TX).

Impact of DAA Use on Healthcare Costs Simulation

The impact of DAA utilization on overall healthcare costs in Medicaid from 2013 through 2022 was projected by combining the results from the burden-of-illness analysis with DAA costs and utilization data from the SDUD files.

Patients with HCV who were cured of the disease were expected to have HSU similar to that of otherwise comparable individuals without the infection. Specifically, it was assumed that 90% of the estimated average burden of illness would be eliminated by the cure. The remaining 10% of HCV costs would likely be more than sufficient to cover the recommended posttreatment monitoring of some individuals cured of the infection, which may include HCV testing, ultrasound examination, and endoscopy.[38] Patients were classified as cured based on DAA product-specific expected SVR rates, assuming a 90% medication adherence rate.[39]

The total cost of DAA treatment equaled total annual reimbursements (derived from the SDUD) minus expected rebates. Estimated rebates took into account the federally mandated Medicaid Drug Rebate,[40] any state-negotiated supplemental rebates, and competition from new products, which together produced a range of 23.1% to 59.5%. Total DAA expenditures (net of rebates) were subtracted from total avoided healthcare costs due to curing of HCV infection to yield the net financial impact of DAA use on Medicaid costs, derived annually and cumulatively from 2013 through 2022. Projected costs for the remainder of 2018 through 2022 assumed that DAA prices and utilization rates will not change from the levels exhibited in the first half of 2018. All costs were inflated to 2017 dollars using the Consumer Price Index for Medical Care[41] (the Appendix includes further details).

Results

HCV Burden of Illness

Based on the sample selection process, the implied prevalence of diagnosed chronic HCV infection was 1.4% among nonelderly adults in Medicaid. This rate was substantially higher among disabled enrollees (3.0%) relative to the cohort of nondisabled enrollees (0.6%). In comparison with a recent estimate of HCV prevalence in the entire adult US population of 1.0%, the present results reflect a somewhat greater overall proportion of infected individuals in Medicaid.[1] Descriptive statistics for all variables employed in the matching process are provided in **Appendix Table A1**. As reflected in **Tables 1** and **2**, 71.6% of the disabled cohort and 86.8% of the nondisabled cohort were classified as having noncirrhotic liver disease. Furthermore, disabled patients with chronic HCV had higher percentages of both cirrhosis (8.8% vs 4.8%) and ESLD (19.6% vs 8.4%) than nondisabled patients with chronic HCV. Among both eligibility groups, these percentages varied only slightly between FFS and managed care Medicaid plans.

Regardless of insurance plan type, severity of liver disease, or basis of Medicaid eligibility, individuals with chronic HCV infection had significantly (P <.001) greater use of hospitals, physicians, EDs, and prescription drugs (Tables 1 and 2). For example, patients with chronic HCV averaged at least 1 additional hospitalization and 3 to 5 more inpatient hospital days annually compared with Medicaid enrollees without the disease. Although HSU did not radically differ between the noncirrhotic and cirrhotic cohorts, individuals with ESLD had 2 to 3 times more hospitalizations and twice as many ED visits compared with patients with less severe disease (see the Appendix for more details).

Higher rates of HSU translated into significantly (P <.001) greater healthcare costs (**Table 3**). Mean annual total costs were $53,159 per disabled patient with chronic HCV and $35,280 for their controls without the disease, for a difference of $17,879. Nearly two-thirds of this difference was attributable to inpatient hospitalizations ($11,142). Drug costs were greater by $5370, of which $1849 (34.4%) was for boceprevir and telaprevir and $1237 (23.0%) was for peginterferon and ribavirin, the older treatments supplanted by interferon-free DAAs. Chronic HCV infection was also associated with higher costs for physician visits ($1203), outpatient hospital visits ($1146), laboratory and x-ray services ($810), clinic visits ($589), psychiatric services ($365), and transportation services ($313). Across liver disease severity cohorts, total healthcare costs were similar for patients with noncirrhotic and cirrhotic disease; however, costs were 69.6% higher for those with ESLD.

TABLE 1. Health Services Utilization Means by Liver Disease Severity for Disabled Adults Cohort by Plan Type

Fee-for-Service										
	Noncirrhotic (n = 6899)		Cirrhosis (n = 978)		End-Stage Liver Disease (n = 2248)		Total Chronic HCV (N = 10,125)		Control Group (N = 10,125)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inpatient hospitalizations	1.4	3.4	1.2	3.8	3.0	4.8	1.7	3.9	0.5	1.7
Inpatient hospital days	5.9	31.7	4.0	28.9	12.0	44.1	7.1	34.7	2.5	24.0
Emergency department visits	3.1	6.2	3.0	5.7	5.7	8.7	3.7	6.9	1.7	3.8
Physician's office/clinic visits	7.6	9.0	9.8	9.7	11.6	11.8	8.7	9.9	6.1	8.4
Prescription drug fills	73.2	53.0	76.5	50.7	86.7	58.4	76.5	54.3	67.7	58.4
Managed Care										
	Noncirrhotic (n = 29,983)		Cirrhosis (n = 3555)		End-Stage Liver Disease (n = 7849)		Total Chronic HCV (N = 41,387)		Control Group (N = 41,387)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inpatient hospitalizations	1.1	3.3	1.3	3.5	3.0	5.9	1.5	4.1	0.4	1.9
Inpatient hospital days	3.9	20.2	4.4	20.7	9.1	31.1	4.9	22.8	1.6	13.8
Emergency department visits	2.9	5.5	3.2	5.8	6.1	9.2	3.5	6.5	1.6	3.6
Physician's office/clinic visits	10.7	9.4	12.5	11.4	13.3	10.9	11.4	10.0	7.0	8.2
Prescription drug fills	67.6	55.6	72.2	57.6	79.3	58.8	70.2	56.6	60.1	58.4

HCV indicates hepatitis C virus.
All differences in variable means across liver disease severity groups, and between total chronic HCV and control groups, are statistically significant (P <.001) using the Kruskal-Wallis equality of populations test.

TABLE 2. Health Services Utilization Means by Liver Disease Severity for Nondisabled Adults Cohort by Plan Type

Fee-for-Service										
	Noncirrhotic (n = 3638)		Cirrhosis (n = 231)		End-Stage Liver Disease (n = 393)		Total Chronic HCV (N = 4262)		Control Group (N = 4262)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inpatient hospitalizations	1.2	4.4	1.4	5.9	2.9	6.4	1.4	4.8	0.4	2.2
Inpatient hospital days	5.9	27.2	5.5	21.0	13.4	37.5	6.6	28.1	2.0	17.0
Emergency department visits	2.3	5.4	2.7	5.6	4.8	8.3	2.6	5.8	1.2	3.3
Physician's office/clinic visits	4.4	5.5	6.1	6.3	7.7	8.7	4.8	6.0	3.1	4.8
Prescription drug fills	38.0	34.5	50.2	38.7	53.3	39.2	40.1	35.6	26.0	31.5
Managed Care										
	Noncirrhotic (n = 13,672)		Cirrhosis (n = 733)		End-Stage Liver Disease (n = 1282)		Total Chronic HCV (N = 15,687)		Control Group (N = 15,687)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inpatient hospitalizations	1.1	3.2	1.4	4.0	4.4	10.6	1.3	4.5	0.3	1.3
Inpatient hospital days	2.5	13.7	4.1	16.8	10.5	29.4	3.3	15.9	0.7	9.2
Emergency department visits	2.3	4.4	2.3	4.0	4.6	8.7	2.4	4.9	1.0	2.3
Physician's office/clinic visits	9.7	8.2	12.2	9.8	12.1	9.4	10.0	8.5	5.4	6.3
Prescription drug fills	40.5	39.6	51.1	44.6	53.9	45.4	42.1	40.6	26.6	35.6

HCV indicates hepatitis C virus.
All differences in variable means across liver disease severity groups, and between total chronic HCV and control groups, are statistically significant (P <.001) using the Kruskal-Wallis equality of populations test.

TABLE 3. Health Services Cost Means by MAX Type of Service by Liver Disease Severity for FFS Disabled Adults Cohort

	Noncirrhotic (n = 6899)		Cirrhosis (n = 978)		End-Stage Liver Disease (n = 2248)		Total Chronic HCV (N = 10,125)		Control Group (N = 10,125)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total healthcare costs	$45,841	$94,704	$46,347	$59,390	$78,582	$115,073	$53,159	$97,851**	$35,280	$63,108^^
Total drug costs	$13,106	$44,931	$16,891	$41,455	$14,501	$58,171	$13,782	$47,893*	$8412	$16,015^^
Peginterferon/ ribavirin costs	$1167	$4834	$2457	$7461	$918	$4666	$1237	$5128**	$0	$0^^
Percentage treated with peginterferon/ribavirin	8.36%	27.69%	14.11%	34.83%	5.74%	23.26%	8.34%	27.64%**	0.00%	0.00%^^
Boceprevir, telaprevir costs	$1806	$9396	$3850	$13,487	$1113	$7074	$1849	$9451*	$0	$0^^
Total nondrug costs	$32,735	$72,711	$29,456	$44,255	$64,081	$93,213	$39,378	$76,777**	$26,869	$59,336^^
Inpatient hospital	$11,943	$34,778	$9430	$25,838	$33,668	$60,439	$16,524	$42,234**	$5382	$20,421^^
Nursing facility services	$6090	$25,234	$6829	$26,142	$9980	$28,655	$7025	$26,165**	$7393	$29,204^
Outpatient hospital	$2051	$7614	$2324	$5054	$3866	$8606	$2480	$7679**	$1334	$5160^^
Physicians	$1736	$20,034	$1618	$2291	$3939	$13,349	$2214	$17,731**	$1011	$2919^^
Lab and x-ray	$1452	$2789	$1916	$3412	$2654	$3915	$1764	$3174**	$954	$3245^^
Clinic	$1446	$4368	$1194	$2250	$1683	$5409	$1474	$4472*	$885	$2929^^
Intermediate mental care facility	$1598	$46,062	$199	$6220	$949	$45,009	$1319	$43,579	$1998	$36,221
Psychiatric services	$1227	$3605	$1026	$3104	$883	$2972	$1131	$3431**	$766	$3174^^
Personal care services	$842	$5864	$694	$3838	$1011	$5345	$865	$5586	$1072	$6737
Home health	$800	$5631	$781	$4982	$968	$4809	$836	$5398**	$914	$6302^
Durable medical equipment	$727	$3100	$787	$3259	$1061	$3157	$807	$3131**	$712	$3052^^
Residential care	$795	$10,728	$765	$9636	$280	$4922	$678	$9633	$1762	$16,471
Transportation services	$467	$1755	$489	$2543	$958	$2199	$578	$1959**	$265	$1070^^
Other	$1562	$7712	$1403	$5783	$2179	$9943	$1684	$8109**	$2420	$11,410^^

FFS indicates fee-for-service; HCV, hepatitis C virus; MAX, Medicaid Analytic eXtract files; peginterferon, pegylated interferon.
All costs have been inflated to 2017 dollars using the Consumer Price Index for Medical Care (Bureau of Labor Statistics; bls.gov).
Statistical significance of differences in variable means across liver disease severity groups, using the Kruskal-Wallis equality of populations test, are denoted as follows: $^{**}P < .001$; $^{*}P < .01$.
Statistical significance of differences in variable means across total chronic HCV and control groups, using the Kruskal-Wallis equality of populations test, are denoted as follows: $^{\wedge\wedge}P < .001$; $^{\wedge}P < .01$.

The nondisabled cohort had lower cost levels than the disabled cohort, but the incremental effect of chronic HCV was comparable in magnitude and significance ($P < .001$). For example, mean total healthcare costs were $26,788 for patients with chronic HCV versus $9610 for the control group; this difference is $17,178, strikingly similar to the $17,789 estimate derived for the disabled cohort (**Table 4**). Inpatient services accounted for just over one-third of this amount ($6263). Prescription drug spending was higher by $6658, of which $3177 was for boceprevir and telaprevir and $2265 was for the peginterferon and ribavirin treatment. Moreover, expenditures were greater for psychiatric services ($1242), outpatient hospital visits ($732), clinic visits ($726), laboratory and x-ray services ($697), and physician visits ($437). Total healthcare costs rose dramatically with liver disease severity, the most pronounced increase being for inpatient costs.

Simulated Impact of DAA Use on Healthcare Costs

The results of an analysis of the impact of the use of DAAs on healthcare costs in Medicaid revealed that in 2014, the first complete year following the release of interferon-free DAAs, 12,175 individuals were estimated to have been cured of HCV (see **Table 5**). Treatment rates increased over time, such that an estimated 157,519 individuals had been cured by the end of 2018. By the end of 2022, 10 years following the introduction of DAAs, we estimate that HCV will have been eliminated in approximately 331,967 Medicaid enrollees. On average, curing a patient with HCV saves an estimated $15,907 per

TABLE 4. Health Services Cost Means by MAX Type of Service by Liver Disease Severity for FFS Nondisabled Adults Cohort

	Noncirrhotic (n = 3638)		Cirrhosis (n = 231)		End-Stage Liver Disease (n = 393)		Total Chronic HCV (N = 4262)		Control Group (N = 4262)	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total healthcare costs	$23,411	$32,943	$30,497	$39,887	$55,873	$117,719	$26,788	$48,740**	$9610	$20,547^^
Total drug costs	$9066	$19,286	$13,946	$24,776	$10,509	$18,672	$9463	$19,596**	$2805	$7052^^
Peginterferon/ ribavirin costs	$2194	$6486	$3788	$8520	$2032	$6395	$2265	$6612	$0	$0^^
Percentage treated with peginterferon/ribavirin	14.18%	34.89%	22.51%	41.86%	11.96%	32.49%	14.43%	35.14%	0.00%	0.00%^^
Boceprevir, telaprevir costs	$3059	$12,103	$5067	$16,315	$3157	$11,113	$3177	$12,287	$0	$0^^
Total nondrug costs	$14,345	$26,822	$16,551	$30,251	$45,365	$116,018	$17,325	$44,518**	$6805	$18,197^^
Inpatient hospital	$6114	$22,064	$7211	$24,034	$30,720	$112,049	$8442	$40,648**	$2179	$12,666^^
Nursing facility services	$446	$6485	$922	$10,978	$1935	$10,624	$609	$7278	$481	$7504
Outpatient hospital	$1544	$4153	$1964	$3116	$3240	$5520	$1723	$4277**	$991	$3432^^
Physicians	$866	$2209	$1089	$1771	$2366	$2918	$1016	$2303**	$579	$2514^^
Lab and x-ray	$1183	$1515	$1623	$1781	$2404	$3042	$1319	$1764**	$622	$1477^^
Clinic	$1408	$2599	$1320	$2436	$1483	$3320	$1410	$2665	$684	$1878^^
Intermediate mental care facility	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Psychiatric services	$1794	$3173	$1636	$2714	$1419	$2429	$1751	$3089	$509	$1699^^
Personal care services	$30	$851	$0	$0	$0	$0	$26	$787	$7	$235
Home health	$71	$1277	$71	$459	$210	$919	$84	$1218*	$51	$1195^
Durable medical equipment	$271	$1601	$220	$413	$747	$2581	$312	$1682**	$195	$1273^^
Residential care	$1	$33	$0	$0	$0	$0	$1	$30	$84	$4166
Transportation services	$143	$604	$143	$374	$432	$956	$170	$641**	$53	$278^^
Other	$474	$1546	$353	$571	$408	$660	$461	$1449	$369	$1646^^

FFS indicates fee-for-service; HCV, hepatitis C virus; MAX, Medicaid Analytic eXtract files; peginterferon, pegylated interferon.
All costs have been inflated to 2017 dollars using the Consumer Price Index for Medical Care (Bureau of Labor Statistics; bls.gov).
Statistical significance of differences in variable means across liver disease severity groups, using the Kruskal-Wallis equality of populations test, are denoted as follows: $^{**}P < .001$; $^{*}P < .01$.
Statistical significance of differences in variable means across total chronic HCV and control groups, using the Kruskal-Wallis equality of populations test, are denoted as follows: $^{\wedge\wedge}P < .001$; $^{\wedge}P < .01$.

year in healthcare costs associated with the disease (ie, an HCV burden-of-illness estimate of $17,674 multiplied by the 90% assumed reduction in disease-related spending). Importantly, these spending reductions persist every year post cure. In aggregate, we estimate that the total annual healthcare cost savings associated with alleviated HCV burden were $2.5 billion in 2018 and are expected to reach $5.3 billion in 2022.

To calculate the net impact of DAA use on healthcare spending in Medicaid, the costs of DAAs themselves were subtracted from the estimated savings in reduced HCV burden. As previously discussed, per-user DAA costs have steadily decreased since 2015 as multiple DAAs have entered the marketplace. For the Medicaid program, total estimated annual postrebate DAA costs peaked in 2015 at $2.1 billion and declined to less than $1 billion in 2018. In the years immediately following the approval of interferon-free DAA regimens (2013-2016), annual DAA costs exceeded annual savings from reduced HCV burden. However, in 2017 and beyond, the annual healthcare cost offsets generated by curing HCV in Medicaid patients eclipsed DAA costs. By 2018, the expected savings in annual healthcare expenditures exceeded the costs of DAAs by $1.5 billion, and this net impact is expected to reach more than $4.3 billion by 2022.

Table 5 depicts the cumulative impact of DAAs since their debut in 2013. Although accrued spending on DAAs was higher than the savings from reduced HCV burden between 2013 and 2018, beginning in 2019, Medicaid will have fully recouped all its investment

TABLE 5. Impact of DAA Use on Healthcare Costs in Medicaid, 2013-2022[a]

	YEAR									
	2013 ACT	2014 ACT	2015 ACT	2016 ACT	2017 ACT	2018 EST	2019 EST	2020 EST	2021 EST	2022 EST
DAA treatment costs										
Total amount reimbursed for DAAs ($M)	$4	$1505	$3021	$3666	$3149	$2001	$2001	$2001	$2001	$2001
Estimated average rebate rate	23.1%	23.1%	31.0%	59.5%	54.1%	50.6%	53.3%	53.3%	53.3%	53.3%
Estimated total net cost of DAAs ($M)	$3	$1157	$2084	$1485	$1445	$988	$934	$934	$934	$934
HCV healthcare cost savings										
Estimated number of patients cured	32	12,175	26,199	35,157	40,344	43,612	43,612	43,612	43,612	43,612
Estimated cumulative number of patients cured	32	12,207	38,406	73,563	113,907	157,519	201,131	244,743	288,355	331,967
Burden of illness of HCV ($PPPY)	$15,808	$16,186	$16,612	$17,241	$17,674	$17,674	$17,674	$17,674	$17,674	$17,674
Estimated percentage of burden saved if cured	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
Estimated healthcare cost savings ($PPPY)	$14,227	$14,567	$14,951	$15,517	$15,907	$15,907	$15,907	$15,907	$15,907	$15,907
Estimated total healthcare cost savings ($M)	$0.5	$178	$574	$1141	$1812	$2506	$3199	$3893	$4587	$5280
Net total healthcare cost savings from DAA use ($M, nominal)	–$3	–$979	–$1510	–$344	$367	$1517	$2265	$2959	$3653	$4346
Net total healthcare cost savings from DAA use ($M, 2017)	–$3	–$1070	–$1606	–$352	$367	$1517	$2265	$2959	$3653	$4346
Cumulative net total healthcare cost savings from DAA use ($M, 2017)	–$3	–$1072	–$2679	–$3031	–$2664	–$1147	$1118	$4077	$7729	$12,076

ACT indicates actual; DAA, direct-acting antiviral; EST, estimated; HCV, hepatitis C virus; M, millions; PPPY, per patient per year.
[a]Actual values from quarters 1 and 2 of 2018 used to forecast values for remainder of 2018 through 2022.

in these HCV cures. The cumulative impact of DAA use in Medicaid due to total healthcare expenditure reductions, net of cumulative DAA costs since 2013, is expected to grow from $1.1 billion at the end of the 2019 to more than $12 billion after 2022—just a decade after the debut of interferon-free DAAs. These financial savings will have been generated through the estimated avoidance of 1.5 million hospitalizations, 2.7 million ED visits, and 16.6 million prescription drug fills. (See the Appendix for more details.)

Discussion

The objectives of this study were to estimate the burden of HCV and quantify the impact of DAA use on healthcare costs in Medicaid. Few investigators have evaluated these specific topics using real-world evidence. Medicaid claims and DAA utilization data were employed to address this gap in the extant literature. Annual healthcare costs due to chronic HCV infection were estimated at $17,879 for the disabled cohort and $17,178 for the nondisabled cohort. The burden of illness increased with liver disease severity, from a low of $10,561 for noncirrhotic disabled individuals to a high of $46,263 for nondisabled individuals with ESLD. Among the disabled patients, inpatient hospitalizations accounted for nearly two-thirds of the costs of chronic HCV, yet they accounted for only one-third of the costs among nondisabled patients. Prescription drug costs were also substantially higher for patients with chronic HCV, the majority of which were attributed to older HCV treatment regimens.

In a privately insured cohort, McAdam-Marx et al[13] estimated the per-person per-year incremental impact of chronic HCV to be $9681 in 2009 ($12,251 inflated to 2017 dollars).[41] This estimate is about 30% lower than the $17,178 and $17,789 figures reported herein. Using the same underlying commercial claims database, Gordon et al[14] calculated the average annual total healthcare costs for a patient with HCV to be $24,176 in 2010 ($30,595 in 2017 dollars),[41] also about 30% lower than the blended (disabled and nondisabled adults) average of $45,347 derived in the present analysis. Gordon et al also concluded that individuals with HCV and cirrhosis had total healthcare costs that were about 30% greater than those of patients with HCV who were noncirrhotic, and those with ESLD had expenditures that were 2.6 times that of cirrhotic patients.[14]

Considered alongside these 2 published studies, the current findings suggest that the burden of illness of chronic HCV may be greater among patients with Medicaid compared with those with employer-sponsored or other commercial health insurance.

With both higher per-patient HCV burden and higher HCV prevalence rates, Medicaid program directors should be keenly interested in understanding the financial impact of DAA use. The cure rates offered by highly effective DAAs present the rare opportunity to substantially and permanently reduce overall healthcare costs. Findings from this study indicate that the cost of DAA treatment, at 2018 estimated net prices, can be expected to be fully offset by healthcare cost savings after only 16 months, on average, on a per-person basis. These savings are realized in several ways. First, patients who are cured of HCV require less medical care. The current results demonstrate that individuals who are HCV-free have fewer hospitalizations, ED visits, laboratory tests, and physician encounters. Importantly, these reductions in HSU and costs are not onetime events but instead occur annually for individuals who are HCV-free. Second, prior to the introduction of DAAs, the most common treatment for HCV infection involved interferon, which is associated with significant costs and harmful adverse effects. The morbidity issues and financial expenditures associated with older ineffective regimens can be avoided entirely. Third, costs for patients with HCV who are treated with DAAs are declining over time because of increased competition within the therapeutic class, which has led to estimated rebates as high as 60%.[22-24] This competitive landscape has also resulted in a decline in list prices, which have fallen by more than 70% since the launch of the first interferon-free DAAs.[22-24]

A key finding of this study is that, since 2017, annual Medicaid healthcare savings for patients cured of HCV have exceeded DAA treatment costs. We estimate annual savings of $1.5 billion resulting from curative treatment; that figure is expected to grow to more than $4.3 billion in 2022. Thus, on a cumulative basis, Medicaid will have fully recouped all its investment in these HCV cures by mid-2019 with cumulative savings of $1.1 billion, growing to more than $12 billion after 2022, just a decade after the debut of interferon-free HCV drugs. Improvements in patient quality of life and enhanced productivity can also be expected to accompany these healthcare cost savings.

Limitations

This study is not without limitations. First, despite the large sample size, Medicaid claims data used to estimate burden of HCV on all 50 states were not received. Therefore, results might not be generalizable to the entire adult Medicaid population. Second, the control group was constructed by matching on demographic and plan characteristics, as well as on HIV/AIDS status; positive HIV/AIDS status is a high-cost comorbidity that is not caused by, but is otherwise correlated with, HCV infection. The omission of control variables for other conditions could give rise to biased estimates if they are correlated with HCV, but inclusion of them could also lead to bias if they are causally linked to HCV.[42] For example, injection drug use—one cause of infection—may persist post HCV cure. In such cases, the HSU and costs associated with injection drug use would not be averted by DAAs. Without a reliable claims-based algorithm for identifying persons who inject drugs, this potential confounding remains a limitation of the present study. Third, the construction of chronic HCV and liver severity cohorts was based on diagnosis and procedure codes from claims data and encounter records. Although this case-finding definition was highly detailed and had been published previously,[14] the possibility for misclassification remains. More recent work by Gordon et al[43] demonstrates the limitations of relying on claims data alone to define levels of liver disease severity. It is also worth noting that since HCV infection often goes undiagnosed, the control group may contain individuals who are infected with HCV, which would result in downward-biased burden-of-illness estimates.

Additionally, the projected savings to Medicaid are calculated based on DAA spending and utilization from 2013 to 2018; however, the burden of illness of HCV, used to approximate cost savings following cure, is estimated using 2012 claims data. It is possible that patterns of healthcare spending and utilization have evolved since 2012. Similarly, the distribution of liver disease severity among individuals infected with HCV may be changing over time, particularly since interferon-free DAAs were initially focused on patients with cirrhosis. Finally, although the impact of DAA use was assessed from the perspective of Medicaid, it is possible, or even probable, that much of the healthcare cost savings resulting from DAAs may be enjoyed by other payers—most notably Medicare, because of the aging of the population infected with HCV.

Conclusions

Given the considerable burden of HCV in Medicaid and the tremendous value delivered by DAAs, Medicaid policies that restrict access to them—such as requirements for liver biopsy, advanced disease stage, sobriety, and specialist prescribers—would seem to be shortsighted. Although many barriers to treatment remain, positive efforts to improve access are under way. A 2017 report on the status of access to DAAs in Medicaid found that many states have decreased restrictions based on severity of liver damage, and fewer states require prescriptions by specialists relative to policies in place in 2014. However, the report also found that more states have implemented sobriety requirements.[27] In recognition of the findings presented herein, the elimination of access restrictions on interferon-free DAAs for patients with HCV would not only drive down prevalence of the disease and associated healthcare costs but also produce substantial savings for state Medicaid programs. ■

Author Affiliations: RxEconomics, LLC

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Address correspondence to: M. Christopher Roebuck, PhD, President & CEO; RxEconomics, LLC, 11350 McCormick Rd, EPII Ste 705; Hunt Valley, MD 21031. Email: mcr@rxeconomics.com.

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