Treating Medicaid Patients With Hepatitis C: Clinical and Economic Impact

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ABSTRACT

OBJECTIVES: To estimate change in chronic hepatitis C virus (HCV) disease and the economic burden associated with comprehensive treatment of the chronic HCV–infected Medicaid population.

STUDY DESIGN: Decision-analytic Markov model.

METHODS: Treatment-naïve patients with genotype 1 chronic HCV were followed over a lifetime horizon from the third-party payer perspective. Patients entered the model insured under Medicaid and were treated under state-specific restrictions by Metavir fibrosis stage (base case) or all treated (all-patient strategy) with an approved all-oral regimen (ledipasvir/sofosbuvir [LDV/SOF] for 8 weeks or 12 weeks, depending on cirrhosis status, viral load, and state-specific LDV/SOF restrictions). Untreated patients were assumed to age into Medicare at 65 years, where they were treated with LDV/SOF without restriction by fibrotic stage.

RESULTS: The sustained virologic response (SVR) rate of the current Medicaid LDV/SOF restriction strategy was 75.2% versus 95.9% if all LDV/SOF-eligible patients were treated under Medicaid. Treating all eligible Medicaid patients with LDV/SOF, regardless of fibrotic stage, was projected to result in 36,752 fewer cases of cirrhosis; 1739 fewer liver transplants; 8169 fewer cases of hepatocellular carcinoma; 16,173 fewer HCV-related deaths; 0.84 additional life-years per patient; and 1.03 additional quality-adjusted life-years per patient. Treating all Medicaid patients with chronic HCV using LDV/SOF resulted in a 39.4% ($3.8 billion) savings and decreased the proportion of total costs attributable to downstream costs of care to 18.3%.

CONCLUSIONS: A "treat all" strategy in a Medicaid population resulted in superior SVRs, substantial reductions in downstream negative clinical outcomes, and considerable cost savings. Current restrictive state policies regarding HCV treatment in Medicaid populations must be reassessed in light of these data.

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Approximately 3.5 million Americans are infected with chronic hepatitis C virus (HCV),[1] with the majority born between 1945 and 1965 and considered part of the baby boomer generation. HCV is a systemic disease with both hepatic and extrahepatic clinical manifestations[2] that also has negative impacts on patient-reported outcomes (PROs),[3] such as fatigue and decreased work productivity.[4,5] These manifestations are associated with significant direct and indirect costs to individuals, their families, and society that increase in parallel with disease severity and the need for liver transplantation.[4,5]

Until recently, available treatments for HCV had limited efficacy and were often poorly tolerated; few patients received treatment and many remained uncured.[6,7] A number of barriers existed to curing HCV. First, conventional treatments were less tolerable than current regimes and had low effectiveness.[6] Second, risk-based screening for HCV failed to identify many patients with the disease.[7] Third, linking patients who are HCV-positive to care was suboptimal, with less than 40% of diagnosed patients receiving follow-up care.[8-10] Fourth, patients with HCV often lacked insurance coverage and frequently had psychiatric and clinical contraindications to interferon, leading to less than one-third being eligible for, and having access to, treatment.[11] These factors contributed to an epidemic of advanced liver disease, cirrhosis, and hepatocellular carcinoma (HCC) in the United States that led to increases in mortality, especially among men, blacks, and those aged 55 to 64 years.[12,13]

Between 1996 and 2006, the prevalence of cirrhosis and decompensated cirrhosis in patients with HCV more than doubled, and the prevalence of HCC increased more than 20-fold.[14] Further, the prevalence of HCV is disproportionally higher in inner cities in the United States and among those who are eligible for Medicaid.[15]

Data from 2012 suggest that 12.5% of liver transplant patients with HCV were covered by Medicaid. Considering that the average cost of a liver transplant due to HCV is $188,000,[16] Medicaid pays an estimated $147 million annually for liver transplantation, and there is additional significant cost for posttransplant immunosuppression and management of resulting complications. These costs

TAKEAWAY POINTS

A restrictive Medicaid policy in many states limits hepatitis C virus (HCV) treatment to patients with severe disease, leading to suboptimal treatment outcomes, high patient burden, and excess costs. This analysis estimated change in HCV disease and the economic burden associated with comprehensive treatment of eligible Medicaid patients with ledipasvir/sofosbuvir (LDV/SOF). A "treat all" strategy led to:

- Increased sustained virologic response rates were 95.9% if all LDV/SOF-eligible patients were treated under Medicaid versus 75.2% under the current Medicaid LDV/SOF restriction strategy.
- Improved clinical outcomes: 36,752 fewer cases of cirrhosis; 1739 fewer liver transplants; 8169 fewer cases of hepatocellular carcinoma; 16,173 fewer HCV-related deaths; 0.84 additional life-years per patient; and 1.03 additional quality-adjusted life-years per patient.
- A $3.8-billion overall savings in healthcare costs.

are likely underestimated because many patients never receive transplants and require repeated hospitalization for complications of cirrhosis and HCC.[14] Furthermore, premature death of patients with HCV leads to significant societal costs.[17,18]

Several highly effective, well-tolerated targeted treatments for HCV, such as sofosbuvir (SOF)-based regimens, have been developed over the last 5 years. The cost of these more effective regimens is higher than for older regimens; however, the cost per cure is lower and the regimens are generally considered to be highly cost-effective.[6,23,24] It has been well established that universal, immediate treatment with these all-oral, interferon-free highly effective targeted regimens is cost-effective and decreases downstream medical costs, due primarily to the avoidance of liver-related complications.[19-21] Furthermore, in the United States, marketplace competition has reduced the net cost of these drugs as manufacturers provide substantial discounts for Medicaid patients. Despite these factors, a recent study from the TRIO registry found that Medicaid was the least likely payer to cover HCV treatment[22]; states that do cover HCV treatment under Medicaid typically subject newer regimens to reimbursement restrictions by fibrotic stage, patient characteristic (eg, not reimbursed in intravenous drug users), or prescriber type (eg, hepatologist only).[23]

As patients with HCV reach Medicare age, the cost of care will be shifted to Medicare, where current drug discounts do not exist, but full coverage is possible. In this context, we used a decision-analytic model to estimate the reduction of disease and economic burden of immediate treatment of Medicaid patients with HCV with highly effective all-oral regimens versus delayed treatment in Medicare.

METHODS

Model Structure

We constructed a decision-analytic Markov model, described previously,[21] which followed a cohort of treatment-naïve (TN) patients with genotype 1 (GT1) mono-infected chronic HCV over a lifetime horizon from the third-party payer perspective. Patients entered the model insured under Medicaid and were treated or untreated with an approved all-oral regimen (ledipasvir/SOF [LDV/SOF] 8 weeks [W] or 12W, depending on cirrhotic status, viral load, and state-specific LDV/SOF restrictions). Untreated patients were assumed to age into Medicare at 65 years, after which they were treated with LDV/SOF without restriction by fibrotic stage. No retreatment of patients previously treated with an LDV/SOF regimen was permitted in Medicare.

Discounting of costs and outcomes was assumed at 3%. The model compared the health and cost consequences of treatment under current Medicaid state-specific restrictions by Metavir fibrosis stage (current situation) versus treatment in Medicaid without restriction by fibrotic stage (comparative situation).

Population Inputs

Medicaid patients were assumed to enter the model with a mean age of 43 years.[15,24] The number of patients with HCV covered under each state's Medicaid program was sourced from claims analyses[24] (and Gilead Sciences confidential data on file) and inflated to 2015 numbers based on the calculated growth rate of the national population (**eAppendix Table A** [eAppendices available at **ajmc.com**]).[25] According to sources and Gilead Sciences internal data on file, assumptions included 70% with GT1,[26] 100% were aware of their infection, 60% had a viral load under 6 million copies and thus were potentially eligible for LDV/SOF 8W,[27,28] 87% were TN,[29] 82% were monoinfected,[30,31] and 83% were noncirrhotic according to internal Ipsos data on file. These inputs were assumed to apply uniformly across all state Medicaid populations.

A recent Medicaid policy audit for SOF[23] was used to inform restrictions for LDV/SOF; restrictions for LDV/SOF were assumed to be identical to SOF restrictions. States without any data for SOF restrictions by Metavir fibrosis stage were excluded from the analysis (15.3% of state Medicaid patients) and not modeled.

Clinical Inputs

Transition probabilities and utilities have been described previously[21] and were obtained from the literature and hepatologist consensus. Transition probabilities and utilities were assumed to be identical for Medicaid and Medicare patients, although background mortality was age-adjusted as patients progressed through the model. These inputs are summarized in **eAppendix Tables B**, **C**, and **D**.

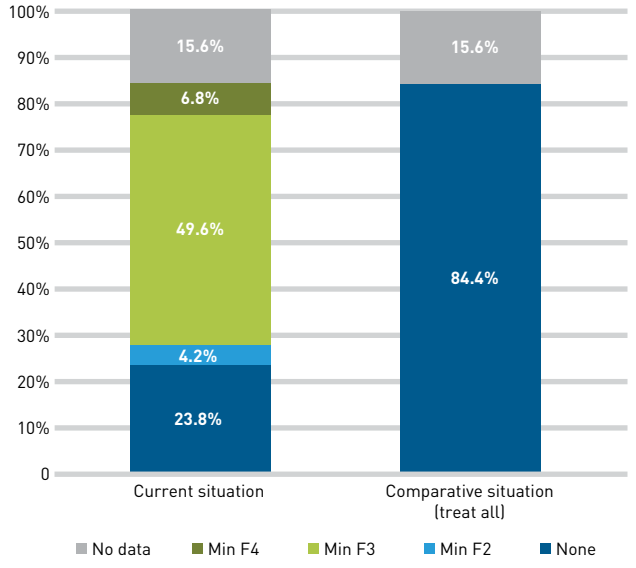
Costing Inputs

Wholesale acquisition costs (WAC) for LDV/SOF 8W and 12W were sourced from Red Book (Micromedex, Greenwood Village,

Colorado) and reported in 2014 US$. In the base case, no price increases for LDV/SOF were assumed over the time horizon of the model. A best price rebate to Medicaid of 50% of the WAC for LDV/SOF was assumed (Medicaid 8W price: $31,500; Medicaid 12W price: $47,250). To derive Medicare prices for LDV/SOF 22 years into the future, an LDV/SOF annual WAC price increase of 2.6% was assumed, which was derived from the rate of historical price increases for a market basket of 13 antivirals indicated for the treatment of HIV (5.6%), launched in the United States between 2005 and 2012, net of the annual rate of inflation over this time period (3%). Currently marketed HCV direct-acting antivirals (DAAs) have not been on the market enough time (<4 years) to robustly extrapolate price increases over a 22-year horizon. LDV/SOF's rebate in Medicare was assumed to be 25% (Medicare future 8W price: $83,108.18; Medicare future 12W price: $124,662.26). Rebate assumptions were based on the magnitude of the rebates currently offered for LDV/SOF to Medicare and Medicaid.[32]

Health state and monitoring costs for the Medicare population are reported in 2014 US$ and are summarized in **eAppendix Table E** based on our previously developed model.[21] An inflation factor was not applied for medical costs, as, unlike for pharmacy costs, these were not assumed to increase at a rate faster than that of inflation. These were adapted to a Medicaid population by applying the national Medicaid-to-Medicare fee ratio of 0.66, sourced from the Kaiser Family Foundation.[33]

FIGURE 1. Current LDV/SOF Medicaid Restrictions by Percentage of Patients



F2/F3/F4 indicates treatment of patients with Metavir fibrosis stages 2 through 4; LDV/SOF, ledipasvir/sofosbuvir; min, minimum.

RESULTS

Current Medicaid Restrictions

A total of 120,980 Medicaid patients with chronic HCV were included: 60,248 receiving LDV/SOF 8W; 40,165 noncirrhotic patients receiving LDV/SOF 12W; and 20,567 compensated cirrhosis patients receiving LDV/SOF 12W. Under current Medicaid restrictions, 4.2%, 49.6%, and 6.8% of Medicaid patients with HCV GT1 could access LDV/SOF treatment only at Metavir fibrosis stages F2, F3, or F4, respectively (**Figure 1**).

Health Outcomes

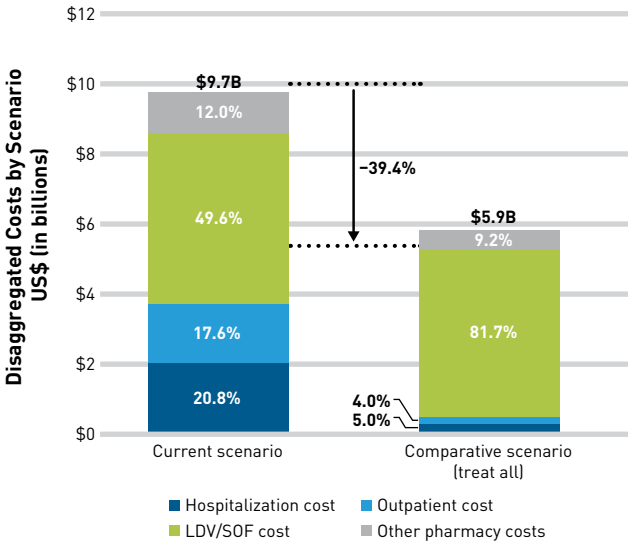
In the aggregate (ie, including treated and untreated patients to calculate a weighted average), the SVR rate of the current Medicaid LDV/SOF restriction strategy was 75.2% versus 95.9% if all potentially LDV/SOF-eligible patients were treated (**Table**). Under current restrictions, 9618 patients potentially eligible for LDV/SOF 8W were assumed to age into Medicare as compensated cirrhotics and become

TABLE. Base-Case Model Results: Health Outcomes, Current Restrictions Versus a "Treat All" Strategy

	Current Scenario	Comparative Scenario (treat all)	Delta (%)
Patients treated with LDV/SOF	95,206	120,980	+25,775 (+27.1%)
Medicaid	53,096	120,980	+67,885 (+127.9%)
Medicare	42,110	–	–42,110 (–100%)
Patients unable to be treated with 8W regimen in Medicare	9618	–	–9618 (–100%)
Patients unable to be treated with 12W regimen in Medicare	25,774	–	–25,774 (–100%)
Strategy aggregate SVR rate[a] (%)	75.2%	95.9%	+20.6% (+27.4%)
Number of cases of:			
CC	29,927	2796	–27,132 (–90.7%)
DCC	12,172	2551	–9621 (–79.0%)
HCC	11,214	3045	–8169 (–72.3%)
LT	2135	395	–1739 (–81.5%)
Deaths	116,263	115,251	–1011 (–0.87%)
HCV-related deaths	20,897	4723	–16,173 (–77.4%)
Non-HCV deaths	95,366	110,528	+15,162 (+15.9%)
Cumulative LYs per patient	20.08	20.92	+0.84 (+4.12%)
Cumulative QALYs per patient	16.42	17.45	+1.03 (+6.3%)

CC indicates compensated cirrhosis; DCC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; LT, liver transplant; LY, life-year; QALY, quality-adjusted life-year; SVR, sustained virologic response, W, week.
[a]Reflects the weighted average SVR of treated and untreated patients.

FIGURE 2. Base-Case Model Results: Cost Outcomes, Current Restrictions Versus a "Treat All" Strategy



B indicates billion; LDV/SOF, ledipasvir/sofosbuvir

ineligible for 8W treatment. An additional 25,774 patients would age into Medicare with decompensated cirrhosis or hepatocellular carcinoma or as liver transplant patients (or die due to liver-related mortality) and become ineligible for LDV/SOF 12W (Table).

Relative to current restrictions, treating all eligible Medicaid patients with LDV/SOF regardless of fibrotic stage would result in 36,752 fewer cases of cirrhosis (–87%); 1739 fewer liver transplants (–81%); 8169 fewer cases of hepatocellular carcinoma (–73%); 16,173 fewer HCV-related deaths (–77%); 0.84 additional life-years per patient (+4%); and 1.03 additional quality-adjusted life-years (QALYs) per patient (+6%), given that earlier treatment with LDV/SOF universally resulted in better health outcomes (**eAppendix Table F**).

Cost Outcomes

Under the current scenario of Medicaid LDV/SOF restrictions, the total costs of treating the HCV cohort totaled $9.7 billion, with the majority of costs (50.4%) attributable to downstream costs of care (ie, hospitalization costs, outpatient costs, and non-LDV/SOF pharmacy costs). Treating all Medicaid patients with chronic HCV using LDV/SOF led to a 39.4% ($3.8 billion) savings over the model time horizon (**Figure 2**) and decreased the relative proportion of total costs attributable to downstream costs of care to 18.3%.

Although the largest cost savings were attributable to downstream medical cost offsets, pharmacy costs attributable to LDV/SOF treatment decreased 2%, from $4.84 billion to $4.75 billion; this is due in part to the 9618 patients potentially eligible for LDV/SOF 8W treatment under Medicaid at the onset of the model who age into Medicare as compensated cirrhotics and can only receive treatment with the 12W regimen. Additional LDV/SOF cost savings result from treating a larger number of patients under Medicaid and the lower price for LDV/SOF under this scheme versus Medicare ($31,500 vs $83,108.18 [inflation-adjusted future price] for LDV/SOF 8W).

Under the current scenario of Medicaid LDV/SOF restrictions, the aggregate cost per SVR across the entire patient cohort—patients treated in Medicaid, patients treated in Medicare, and patients unable to be treated—was $51,809. Treating all Medicaid patients with LDV/SOF led to a 19.8% ($10,282) savings per SVR and was dominant from a cost-effectiveness (cost per life-year gained, cost per QALY gained) standpoint, given that earlier treatment with LDV/SOF resulted in better health and cost outcomes (**eAppendix Tables F** and **G**).

DISCUSSION

Access to HCV treatment under current state Medicaid programs is highly heterogeneous. Although HCV treatment qualification has become less stringent in some states, others refuse coverage, have instituted criteria for only treating patients with advanced fibrosis, or have not yet considered adding DAAs to their formularies.[23,34] This strategy is flawed: first, patients with advanced fibrosis are more difficult to treat;[35] second, fibrosis is a surrogate for liver-related mortality and fails to account for other negative impacts of HCV on patients and their well-being. In fact, evidence suggests that patients with early-stage fibrosis experience at least equivalent PROs and work productivity benefits from an HCV cure compared with those with more severe disease.[36]

The confluence of high HCV prevalence in the Medicaid population and lack of access to treatment may result in individual and societal harm and has cost implications beyond Medicaid. Although full coverage is possible as patients with HCV age in to Medicare, Medicaid-level drug discounts are not offered, thereby increasing the acquisition cost of HCV drugs for the population not treated earlier in their disease. Further, these policies disproportionately affect economic disadvantaged populations that rely on Medicaid, creating significant health disparities for aging and minority populations.

To our knowledge, this is the first study to estimate the HCV burden to both Medicare and Medicaid resulting from Medicaid HCV treatment restrictions. This study provides evidence that the current Medicaid strategy is flawed in providing treatment to different patients based on their state of residence. The current Medicaid strategy is estimated to result in 27,000 excess cases of cirrhosis and almost 10,000 excess cases of decompensated cirrhosis, leading to over 1700 liver transplants, over 8000 cases of HCC, and over 16,000 HCV-related deaths. This analysis likely underestimates the burden of HCV infection because it does not account for the negative impact of HCC-related extrahepatic diseases and PROs.[37]

Curing Medicaid patients with HCV using an extended "treat all" strategy could reduce the risk of complications, cirrhosis, HCC,

the need for liver transplantation, and liver-related deaths. Given the large number of patients with HCV, we acknowledge that such a strategy would require up-front investment in the context of state Medicaid budget constraints; however, this strategy would ultimately lead to cost savings for CMS by reducing the future burden to Medicare and the costs associated with HCV morbidity and mortality. Additionally, we believe that an HCV cure will lead to substantial improvement in PROs and work productivity. Most critically, a "treat all" strategy will reduce the health disparities caused by the current Medicaid strategy, which primarily affects minorities and baby boomers who are approaching Medicare age.

This analysis was conducted conservatively, excluding 15% of Medicaid patients for whom the restriction status of LDV/SOF was not publically available; this potentially underestimates the full impact of lifting Medicaid coverage restrictions. The restriction status of LDV/SOF was inferred from published restrictions of SOF, which may lead to uncertainty. This analysis used clinical trial data rather than real-world data as model inputs for SVR rates; however, recent studies (ie, HCV-TARGET38) have shown that real-world and clinical trial SVR rates with all-oral ribavirin-free regimens like LDV/SOF are similar. Our model structure only allowed for patients to receive treatment in Medicaid once as they entered the model and did not allow for potential treatment at subsequent time points in Medicaid as patients continued to be monitored and progress to more severe fibrosis stages; thus, the number of patients ineligible to receive treatment in Medicare may be overestimated. Finally, this analysis assumed that all chronic HCV Medicaid patients eligible for treatment were aged 43 years and aged into Medicare at 65 years, which may not reflect real-world demographics and coverage dynamics (eg, dual-eligible patients).

CONCLUSIONS

Institution of a less restrictive "treat all" strategy in Medicaid patients was associated with clinical outcome and cost benefits. Based on these data, we believe it is time to develop a national strategy to eradicate HCV from the United States regardless of payer status. Such a strategy requires collaboration among private payers, governmental payers (including Medicaid), healthcare providers, drug manufacturers, and patients. ■

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eAppendix Table A. Model Population Inputs

INPUT	VALUE	SOURCE
Number of Medicaid CHC patients, 2015	**287,074**	Kim, et. al., 2015[24] and confidential Gilead Sciences data on file
Percentage of chronic HCV patients who are GT1	70%	Nainan et al, 2006[26]
Percentage aware of infection	100%	Assumption
Percentage treatment-naive	87%	Denniston et al, 2014[29]
Percentage monoinfected	82%	Curry et. al., 2015,[30] Terrault et. al. 2015,[31] confidential Gilead Sciences data on file
Percentage of Medicaid population with published SOF restrictions	84.4%	Barua et al, 2015[23]
Total number of TN Medicaid CHC patients potentially eligible for treatment with LDV/SOF	**120,980**	Calculated
Percentage with VL <6 M copies	60%	Kowdley et. al. 2015,[28] Kowdley et al. 2014,[27] confidential Gilead Sciences data on file
Percentage NC	83%	Ipsos Healthcare 2012[32]
Number NC patients eligible for LDV/SOF 8W	**60,248**	Calculated
Number NC patients eligible for LDV/SOF 12W	**40,165**	Calculated
Number CC patients eligible for LDV/SOF 12W	**20,567**	Calculated

CC indicates compensated cirrhotic; CHC, chronic hepatitis C; GT1, genotype 1; HCV, **hepatitis C virus**; LDV/SOF, ledipasvir/sofosbuvir; M, million; NC, noncirrhotic; SOF, **sofosbuvir**; TN, treatment naive; VL, viral load; W, week

eAppendix Table B. Model Transition Probabilities

Transition probabilities		
From–to	**Value**	**Source**
F0–F1	0.117	Thein, et al. 2008
F1–F2	0.085	Thein, et al. 2008
F2–F3	0.121	Thein, et al. 2008
F3–F4	0.115	Thein, et al. 2008
F3–DCC	0.012	Dienstag, et al. 2011
F3–HCC	0.011	Dienstag, et al. 2011
F3 SVR–DCC	0	Expert opinion
F3 SVR–HCC	"(RR=0.24)*0.011 = 0.00264"	Dienstag, et al. 2011 Morgan, et al. 2013
F4–DCC	0.039	Dienstag, et al. 2011
F4–HCC	0.024	Dienstag, et al. 2011
F4 SVR–DCC	"(RR=0.0857)*0.039 = 0.00334"	Dienstag, et al. 2011 Morgan, et al. 2013
F4 SVR–HCC	"(RR=0.24)* 0.024 = 0.00576"	Morgan, et al. 2013
DCC–HCC	0.014	Fattovich, et al. 1997
DCC–LT	0.031	Bennett, et al. 1997
DCC–EM	0.129	Fattovich, et al. 1997
HCC–EM	0.485	Liu, et al. 2012
LT–EM	0.107	Razavi, et al. 2013
PLT–EM	0.049	Razavi, et al. 2013
F4 SVR–F3 SVR	0.076	D'Ambrosio, et al. 2012
F4 SVR–F2 SVR	0.082	Maylin, et al. 2008
F3 SVR–F2 SVR	0.267	Maylin, et al. 2008

DCC indicates decompensated cirrhosis; EM, extra mortality; F0–F4, METAVIR liver fibrosis scores F0–F4; HCC, hepatocellular carcinoma; LT, liver transplant; PLT, post-liver transplant; RR, relative risk; SVR, sustained viral response.

eAppendix Table C. Model Clinical Inputs - SVRs

a) LDV/SOF 8-week regimen ION-3

Treatment-naïve (HCV viral load <6 million copies)					
HCV genotype 1a			**HCV genotype 1b**		
Fibrosis stage	**SVR, %**	**Source**	**Fibrosis stage**	**SVR, %**	**Source**
F0	90	ION-3[a]	F0	94	ION-3[a]
F1	96	ION-3[a]	F1	100[b]	ION-3[a]
F2	92	ION-3[a]	F2	96	ION-3[a]
F3	95	ION-3[a]	F3	100	ION-3[a]
F4	N/A	Not indicated	F4	N/A	Not indicated

[a]Indicated for treatment-naïve, NC, HIV-negative patients with an HCV viral load <6 million copies. Data are from LDV/SOF 8-week patients from ION-3 with an HCV viral load <6 million copies. Equivalent SVRs are assumed in the overall patient population and the <6 million copies population. RR assumptions from the <6 million copies population are then applied between fibrosis stages, and HCV genotype 1a/1b to the total SVRs.
[b]Any values over 100% were capped at 100%.
F0–F4 indicates METAVIR liver fibrosis score F0–F4; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; NC, non-cirrhotic; RR, relative rate; SVR, sustained virologic response.

b) LDV/SOF 12-week regimen ION-3 , ION-1

Treatment-naïve					
HVC genotype 1a			**HCV genotype 1b**		
Fibrosis stage	**SVR, %**	**Source**	**Fibrosis stage**	**SVR, %**	**Source**
F0	99	ION-3[a]	F0	100	ION-3[a]
F1	93	ION-3[a]	F1	97	ION-3[a]
F2	97	ION-3[a]	F2	100[b]	ION-3[a]
F3	96	ION-3[a]	F3	100[b]	ION-3[a]
F4	97	ION-1[b]	F4	97	ION-1[b]

[a]Indicated for treatment-naïve, NC, HIV-negative patients with an HCV viral load >6 million copies. Data are from LDV/SOF 12-week patients in ION-3 with an HCV viral load >6 million copies. RR assumption applied between fibrosis stages, HCV genotype 1a/1b and the total population.
[b]Indicated for treatment-naïve, CC, HIV-negative patients with an HCV viral load >6 million or <6 million copies.
F0–F4 indicates METAVIR liver fibrosis score F0–F4; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; NC, non-cirrhotic; RR, relative rate; SVR, sustained virologic response.

eAppendix Table D. Model Utilities

Utilities		
Health state: mono-infected	**Utility value**	**Source**
F0	0.790	McLernon, et al. 2008
F1	0.790	McLernon, et al. 2008
F2	0.790	McLernon, et al. 2008
F3	0.790	McLernon, et al. 2008
F4	0.748	McLernon, et al. 2008
F0 SVR	0.840	Wright and Tompkins 2006
F1 SVR	0.840	Wright and Tompkins 2006
F2 SVR	0.840	Wright and Tompkins 2006
F3 SVR	0.840	Wright and Tompkins 2006
F4 SVR	0.799	Wright and Tompkins 2006
DCC	0.672	McLernon, et al. 2008
HCC	0.610	Hsu, et al. 2012
Liver transplant	0.650	Hsu, et al. 2012
Post-liver transplant	0.709	McLernon, et al. 2008
Utility change on treatment	**Value,%**	**Source**
LDV/SOF 8 weeks	+4.5	Younossi, et al. 2014
LDV/SOF 12 weeks	+4.5	Younossi, et al. 2014

DCC indicates decompensated cirrhosis; F0–F4, METAVIR liver fibrosis scores F0–F4; HCC, hepatocellular carcinoma; LDV, ledipasvir; PLT, post-liver transplant; SOF, sofosbuvir; SVR, sustained viral response

eAppendix Table E. Model Health State Costs

Health state costs			
Model state	**Annual Cost (Medicaid[a], USD 2014)**	**Annual Cost (Medicare, USD 2014)**	**Source**
F0	$3,347.26	$5,071.61	Mean of McAdam-Marx 2011 and Gordon 2012, inflated to USD 2014
F1	$3,347.26	$5,071.61	
F2	$3,347.26	$5,071.61	
F3	$3,347.26	$5,071.61	
F4	$3,850.36	$5,833.88	
DCC	$26,479.25	$40,120.08	
HCC	$70,224.00	$70,224.00	
LT	$118,632.56	$179,746.30	
PLT	$29,190.35	$44,227.80	McAdam-Marx 2011, inflated to USD 2014

[a]Medicaid health state costs were calculated by adjusting the annual Medicare costs by the 2014 Kaiser Family Foundation National Medicaid:Medicare Fee Index of 0.66, available at http://kff.org/medicaid/state-indicator/medicaid-to-medicare-fee-index/.
DCC indicates decompensated cirrhosis; F0–F4, METAVIR liver fibrosis scores F0–F4; HCC, hepatocellular carcinoma; LT, liver transplant; PLT, post-liver transplant.

eAppendix Table F. Health Outcomes Results by Treatment at Different Metavir Stages for a 10,000 Patient Cohort

LDV/SOF 8W: NC patients with VL <6 M copies	**No Restriction**	**Minimum F2**	**Minimum F3**	**Minimum F4**
# TREATED PATIENTS	10000	8730	7083	5602
Medicaid	10000	5500	2200	0
Medicare	0	3230	4883	5602
UNABLE TO BE TREATED 8W	0	836	1849	2448
UNABLE TO BE TREATED AT ALL	0	1270	2917	4398
NUM. CASES CIRRHOSIS	493	2090	4582	7033
NUM. CASES COMPENSATED CIRRHOSIS	323	1541	3357	5062
NUM. CASES DECOMPENSATED CIRRHOSIS	170	549	1226	1971
NUM. CASES HCC	150	488	1054	1621
NUM. CASES LIVER TRANSPLANTS	26	94	217	348
NUM. DEATHS	9520	9564	9632	9700
NUM. HCV-RELATED DEATHS	260	911	2046	3220
NUM. NON-HCV DEATHS	9261	8653	7587	6481
CUM LYs PER PATIENT	21.10	20.56	20.53	18.29
CUM QALYs PER PATIENT	17.66	16.83	17.00	14.36
AGGREGATE SVR*	95.1%	82.3%	67.2%	52.8%
LDV/SOF 12W: NC patients with VL >6 M copies	**No Restriction**	**Minimum F2**	**Minimum F3**	**Minimum F4**
# TREATED PATIENTS	10000	8730	7083	5602
Medicaid	10000	5500	2200	0
Medicare	0	3230	4883	5602
UNABLE TO BE TREATED	0	1270	2917	4398
NUM. CASES CIRRHOSIS	321	1834	4527	6992
NUM. CASES COMPENSATED CIRRHOSIS	212	1374	3318	5032
NUM. CASES DECOMPENSATED CIRRHOSIS	109	460	1209	1959
NUM. CASES HCC	104	422	1042	1613
NUM. CASES LIVER TRANSPLANTS	16	81	215	346
NUM. DEATHS	9514	9554	9630	9699
NUM. HCV-RELATED DEATHS	171	786	2024	3205
NUM. NON-HCV DEATHS	9342	8768	7606	6493
CUM LYs PER PATIENT	21.16	20.64	19.53	18.30

CUM QALYs PER PATIENT	17.74	16.92	15.65	14.37
AGGREGATE SVR*	96.6%	84.6%	67.8%	53.3%

LDV/SOF 12W: CC patients

	No Restriction	**Not available**
# TREATED PATIENTS	10000	2188
Medicaid	10000	0
Medicare	0	2188
UNABLE TO BE TREATED	0	7812
NUM. CASES CIRRHOSIS	528	5367
NUM. CASES COMPENSATED CIRRHOSIS	0	0
NUM. CASES DECOMPENSATED CIRRHOSIS	528	5367
NUM. CASES HCC	839	3764
NUM. CASES LIVER TRANSPLANTS	85	892
NUM. DEATHS	9570	12049
NUM. HCV-RELATED DEATHS	1201	7917
NUM. NON-HCV DEATHS	8368	4132
CUM LYs PER PATIENT	19.91	13.43
CUM QALYs PER PATIENT	16.28	9.93
AGGREGATE SVR*	96.8%	20.8%

CC indicates compensated cirrhotic; CUM, cumulative; F2-F4, Metavir fibrosis stages 2 to 4; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; LY, life-years; M, million; NC, noncirrhotic; NUM, number; QALY, quality-adjusted life-year; SVR, sustained virologic response; VL, viral load; W, week

*Note: this reflects the weighted average SVR of treated and untreated patients

eAppendix Table G. Cost Outcomes Results by Treatment at Different Metavir Stages (Per Patient)

LDV/SOF 8W: NC patients with VL <6M copies	**No Restriction**	**Minimum F2**	**Minimum F3**	**Minimum F4**
Cumulative cost per patient	$39,049.36	$44,735.29	$76,914.20	$115,316.30
Attributable to hospitalization	6.2%	23.1%	20.9%	32.1%
Attributable to outpatient costs	5.2%	20.4%	17.9%	27.1%
Attributable to non-HCV pharmacy costs	7.9%	8.4%	11.5%	15.2%
Attributable to HCV pharmacy costs	80.7%	48.1%	49.7%	25.7%
Cost per SVR	$35,141.54	$41,608.57	$48,462.05	$56,172.77
LDV/SOF 12W: NC patients with VL >6M copies	**No Restriction**	**Minimum F2**	**Minimum F3**	**Minimum F4**
Cumulative cost per patient	$53,044.62	$52,671.00	$104,441.97	$121,685.21
Attributable to hospitalization	3.1%	18.5%	26.3%	30.3%
Attributable to outpatient costs	2.6%	16.4%	22.7%	25.6%
Attributable to non-HCV pharmacy costs	5.7%	6.6%	10.8%	14.3%
Attributable to HCV pharmacy costs	88.6%	58.5%	40.3%	29.9%
Cost per SVR	$50,955.81	$56,653.27	$62,573.28	$68,089.90
LDV/SOF 12W: CC patients	**No Restriction**	**Not available**		
Cumulative cost per patient	$67,279.69	$139,334.92		
Attributable to hospitalization	6.2%	35.0%		
Attributable to outpatient costs	4.2%	27.2%		
Attributable to non-HCV pharmacy costs	17.2%	35.6%		
Attributable to HCV pharmacy costs	72.4%	2.2%		
Cost per SVR	$51,572.74	$77,237.11		

CC indicates compensated cirrhotic; F2-F4, Metavir fibrosis stages 2 to 4; HCV, hepatitis C virus; LDV/SOF, ledipasvir/sofosbuvir; M, million; NC, noncirrhotic; SVR, sustained viral response; VL, viral load; W, week.

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