Good overview of many issues.

Focus on data:
Table 1, Figure 1, Figure 2,
Table 4.

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# The Value of Sovaldi: Societal Cost Issues of New Interventions on Hepatitis C

A white paper on the Sovaldi pricing debate and a comprehensive analysis of the societal cost implications of Chronic Hepatitis C (HCV)

**By the Center for Healthcare Innovation**

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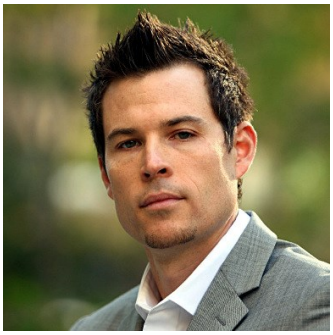
# Introduction



Joseph P. Gaspero
President & Co-Founder
Center for Healthcare Innovation

Welcome to this Center for Healthcare Innovation (CHI) white paper: *The Value of Sovaldi: Societal Cost Issues of New Interventions on Hepatitis C*.

In December 2013, the FDA approved a new drug, sofosbuvir, for the treatment of Chronic Hepatitis C. The drug, commonly known as Sovaldi, was developed by Gilead Sciences, a U.S. biotechnology company. The initial price tag of a 12-week treatment of Sovaldi was reported as approximately $84,000, or nearly $1,000 per pill. This resulted in considerable media attention and an ensuing pricing controversy. Editorials and op-eds sprung up around the country debating Sovaldi's price tag and the broader debate over fair drug pricing. Some politicians expressed outrage over the cost of new drugs, while others argued for free market pricing and rewards for the considerable R&D costs that biopharmaceutical companies incur when bringing a new drug to market. The often niche drug pricing debate had officially spilled over into the mainstream conversation. Payers, policymakers, pharma, patients, and providers all voiced strong— and sometimes contrasting— opinions.

At CHI, we aim to help these stakeholders increase their knowledge and understanding of healthcare value, which we view as a function of quality, access, and cost. Thus, we decided to further explore the value of Sovaldi and how the costs and benefits of the drug relate to the broader discussion of the treatment of Hepatitis C. Our goal is to offer a more informed and analytical approach to the discussion of the value of Sovaldi. One question that immediately arose was "How does the price of Sovaldi compare to the long term costs of the treatment of Chronic Hepatitis C?" Our goal was to analyze the complex interrelationships and broader macroeconomic principles relating to the costs and benefits of a drug, as well as the long term costs of treating Chronic Hepatitis C.

By analyzing the societal cost implications of Chronic Hepatitis C, we aim to help patients, providers, pharma, pharmacy, payers, and policymakers increase their knowledge and understanding of the value of this treatment—as well as the complex relationships between drug costs and the longer term costs of a disease. We hope that you find this white paper to be both thought-provoking and useful, and we welcome your feedback. We thank you for your interest, and we hope you enjoy our comprehensive analysis.

Joseph P. Gaspero
President & Co-Founder
Center for Healthcare Innovation

# PART 1: Hepatitis C Background

# THE SOVALDI PRICING DEBATE

The issue of fair drug pricing came to a head in December 2013 when Gilead's Sovaldi (sofosbuvir), a potent chronic hepatitis C (HCV) drug, hit the market. The twelve week treatment runs $1,000 per pill, or $84,000 for an entire regimen. These lofty costs immediately engendered a public debate about cost and value in healthcare, placing the pharmaceutical industry and health insurers in direct confrontation with state and federal agencies responsible for allocating financial resources.

Decision-makers in these organizations are tasked with determining who covers costs, the degree of financial resources for treatment, and whether the benefits of treatment outweigh economic costs to society. These decisions are central to the drug pricing conversation. At issue is the justification of drug pricing based on remuneration for millions of dollars in research costs and the criterion that delineates reasonable profit from outright extortion. Answers will shape the nexus of healthcare drug utilization and resource allocation for patients, pharmaceutical companies, hospitals, taxpayers, and insurance and regulatory agencies.

The figures surrounding Sovaldi's public debate are sobering. The Kaiser Family Foundation estimates that if the 3 million Americans infected with HCV were to be treated with Sovaldi at an average cost of $100,000 per treatment, the amount the U.S. spends on prescription drugs in one year would double from $300 billion to $600 billion (Appleby, 2014). The costs of specialty drugs like Sovaldi are expected to quadruple to $400 billion by 2020, which would account for 9.1% of national health spending (UnitedHealth Center for Health Reform & Modernization, 2014). The confluence of increasing drug costs and limited resources may elicit contentious topics such as determining who should receive treatment. Should those in taxpayer-funded programs have the same access as the sickest patients? Should severity of disease dictate allocation priorities? The American Association for the study of Liver Diseases and the Infectious Diseases of Society believe Sovaldi should be the preferred treatment for all who are viremic. The Department of Veterans Affairs, however, argues for a treatment reserved only for those with advanced liver disease, a complication from chronic HCV infection. Currently, 47 states provide limited coverage of Sovaldi for their Medicaid populations. Half these states implement policies of "prior authorization" that require a patient be in the worst stages of hepatitis C for eligibility. States practicing these policies are those with the largest Medicaid populations and the most patients who suffer from HCV. Evaluating the costs of HCV treatment equips policy makers with the knowledge to enact policies that engender the best health outcomes at the "right" price.

***"The Kaiser Family Foundation estimates that if the 3 million Americans infected with HCV were to be treated with Sovaldi at an average cost of $100,000 per treatment, the amount the U.S. spends on prescription drugs in one year would double from $300 billion to $600 billion."***

# METHODS OF EVALUATING SOCIETAL COST EFFECTIVENESS

The first step in answering these cost-benefit ethical and practical dilemmas is identifying the perspective from which costs and benefits are assessed. An individual suffering from a chronic illness weighs the costs and benefits of treatment differently from a policy maker who views costs from an aggregated perspective. An insurer may view the costs of treatment differently from a hospital that treats the disease and provides ancillary care. We take a societal perspective.

Costs are viewed as an aggregated sum to assess the cost burden of hepatitis C to the United States. Because states and local governments will have varied budget constraints when evaluating the costs of chronic illness, a cost analysis will vary at the community level. However, the following thought exercise illustrates the importance of cost analyses when allocating finite resources across populations and is not limited to a national level.

A second consideration is that cost-savings do not always equate to cost-effectiveness. A study published in October 2014 found that the use of sofosbuvir-based treatment in prison populations was cost-effective. Analysis showed, however, that treatment could cost as much as $30 billion for the Federal Bureau of Prisons and other entities (Goldhaber-Fiebert et. al., 2014). Thus, while the treatment may be cost-effective, it may not be affordable. Consequently, we will take a holistic approach to analyzing the costs of drug treatment with respect to drug pricing policies.

Lastly, the time horizon is significant in chronic disease cost analyses. Costs may surpass the benefits of cost-saving treatments in the short term, but large cost-savings opportunities may eclipse initial expenses. Policy makers must be forward-thinking when assessing resource utilization and distribution. The time of drug intervention may vary depending on the severity and prevalence of disease. Chronic HCV exhibits a protracted disease progression. In this evaluation, we choose a time horizon of ten years for analysis and discussion.

***"Policy makers must be forward-thinking when assessing resource utilization and distribution."***

# PREVALENCE AND CLINICAL PROGRESSION OF HCV INFECTION

Of the 4.1 million Americans who have been exposed to the hepatitis C (HCV) virus in the United States, 3.2 million Americans, or 1.3% of the population, suffer from chronic HCV infection (Armstrong et. al., 2006; Centers for Disease Control and Prevention, 2014). A blood-borne disease that infects the liver, HCV accounts for one-third of all liver transplantations in the United States. Currently, the viral infection is most often acquired by intravenous drug use. Prior to blood screenings in the early 1990's, the virus was commonly spread through blood transfusions and organ transplantations. Table 1 provides a glimpse of the prevalence of HCV infection in the United States by demographics.

The most recent National Health and Nutrition Examination Survey (NHANES) reveals HCV infection is more common in men than in women. The highest incidence of infection is among 40-49 year-olds and is owed to blood transfusions that predate universal screening of blood donors. Prevalence is twice as high for non-Hispanic blacks than for both non-Hispanic whites and Mexican Americans. The large variation is almost entirely attributable to differences in older age groups. Non-Hispanic blacks between the ages of 40 and 49 experience a prevalence of 9.4%. The demographic group with the highest prevalence is non-Hispanic black men in the age group 40-49 with an infection rate of 13.6%. Most individuals with HCV infection were born between 1945 and 1960.

The prevalence of infection is likely greater than the aforementioned statistics due to underrepresentation of high risk groups. One limitation of the

***"3.2 million Americans, or 1.3% of the population, suffer from chronic HCV infection."***

**Table 1** | Prevalence by Demographic

| Demographic | Rate of Infection |
|---|---|
| Total Men | 2.1% |
| Total Women | 1.1% |
| Non-Hispanic Blacks | 3.0% |
| Non-Hispanic Whites | 1.5% |
| Mexican Americans | 1.3% |

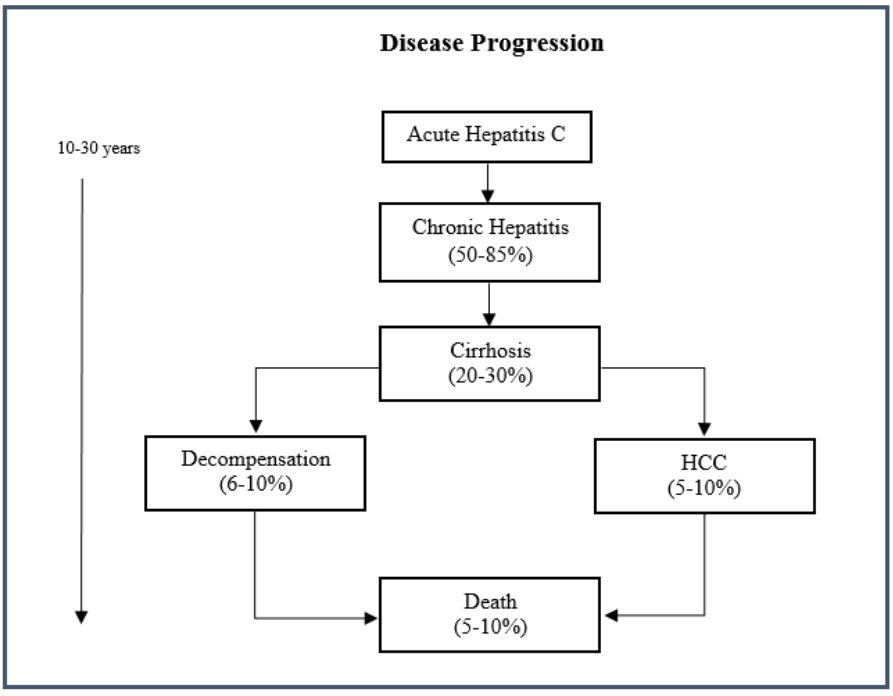
Adapted from Armstrong et al. (2006). Prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Annals of Internal Medicine, 144*, 705–714.

NHANES study is that it does not include homeless or incarcerated individuals. In one study, researchers detected HCV antibodies, an indicator for viral infection, in 41.7% of homeless veterans (Cheung et. al., 2002). The incarcerated population in the U.S. has a similarly high HCV exposure rate. One study estimates that 12% to 45% of the prison population has been exposed to the HCV virus (Weinbaum et al., 2005). Related studies estimate a prevalence of 30% to 40% for inmates (Gough et. al., 2010; Vescio et. al., 2008). This means that of the 6,899,000 reported incarcerated individuals in the United States (Bureau of Justice Statistics, 2014), between 2,070,000 and 2,760,000 may have been exposed to HCV. The estimate of 3.2 million with chronic HCV is taken from the National Health and Nutrition Examination Survey between 1999 and 2002 and is still the most cited estimate of the prevalence of HCV in the U.S. The most accurate estimate of those with chronic HCV may in fact be much higher.

The most ominous aspect of HCV is its ability to cause severe liver damage years before symptoms appear. A 2013 report by the New England Journal of Medicine estimates that of the 3.2 million Americans living with the virus, only about half have been diagnosed. Moreover, fewer than 40% of those infected receive medical care for the condition. In 2009, there were an estimated 16,000 cases of acute hepatitis C in the United States (Centers for Disease Control and Prevention, 2014). A short-term illness lasting up to 6 months, acute infection is typically asymptomatic. However, 70% to 90% of those with HCV infection will develop chronic infection (Jakate, 2013). Those with chronic HCV may exhibit nonspecific symptoms of fatigue, nausea, weight loss, arthralgi-

***"A 2013 report by the New England Journal of Medicine estimates that of the 3.2 million Americans living with the virus, only about half have been diagnosed."***

**Figure 1** | HCV Disease Progression




Source: Jenkins, E. & Aronsohn, A. (2013). *Natural History of Hepatitis C*. In Oxford American Infectious Disease Library: Hepatits C. Oxford University Press.

as, or weakness. Of these, 20% to 40% will develop cirrhosis and related complications over a 10 to 20 year horizon (Jenkins & Aronsohn, 2013). Hepatic failure occurs in one-third of patients with HCV cirrhosis after 10 years (Planas et. al., 2004). Figure 1 illustrates hepatitis C progression from acute infection to death and corresponding percentages of individuals who advance into each stage.

Chronic HCV begins six months after infection and continues for decades. Chronic infection causes inflammation of the liver, resulting in liver fibrosis and ultimately cirrhosis. Approximately 20% to 40% of patients will develop cirrhosis 20 years post infection, and 41% by 30 years (Thein et. al., 2008). Hepatic failure occurs in one-third of individuals with HCV cirrhosis for over 10 years. Five-year survival for those who experience hepatic failure is 50% (Planas et. al., 2004). The rate of liver degeneration from HCV varies by individual. The slow progression and asymptomatic nature of the disease leaves many individuals unaware of their condition. For this reason, most cases are undiagnosed until after the onset of liver disease when costs for treatment are highest.

# PART 2: Comparison of Treatment Costs and Analysis

# COSTS OF HCV UNTREATED

Chronic diseases such as hepatitis C are costly in many ways. Direct costs include payments for treatment and side effects, physician visits, and drug costs. Indirect costs, while not explicitly measured, are incurred by lost time from work, reduced productivity, and decreased quality of life. Chronic diseases are especially costly as both direct and indirect costs compound over one's lifetime. Consideration of both direct and indirect costs of disease and medical treatment is essential for determining the true value of resource allocation in health systems.

Chronic diseases account for about $3 of every $4 dollars spent on healthcare, or about $7,900 per American with at least one chronic illness (Centers for Disease Control and Prevention, 2007). Direct and indirect costs in the U.S. for HCV were an estimated $5.46 billion in 1997. Direct medical costs are predicted to increase to $10.7 billion for the period 2010 through 2019, mostly due to the increasing number of HCV patients with advanced liver disease (Wong et. al., 2000). Estimated health care costs for managed care organization enrollees with HCV were $20,961 per patient per year (PPPY) from 2002 through 2006 (Davis et. al., 2011). One retrospective analysis, estimated that all-cause health care costs to commercial insurers for individuals with HCV were $14,915, or twice as high as costs for non-HCV enrollees with similar health statuses (McAdam-Marx et al., 2011). They found all-cause PPPY incremental costs were more than $27,000 in patients with decompensated cirrhosis and $93,000 for those requiring liver transplant.

A similar study (Gordon et. al., 2012) segmented the costs of HCV to the U.S. health system by severity of disease. They found annual all-cause healthcare costs to be $24,176 for patients with chronic HCV infection. They derived average annual cost estimates of $17,277 for patients with noncirrhotic liver disease, $22,752 for patients with compensated cirrhosis, and $59,995 for patients with end-stage renal disease. Pharmacy, ambulatory, and inpatient care accounted for 90% of costs for noncirrhotic liver disease and 93% for compensated cirrhosis and endstage renal disease. Khoury et. al. (2012) estimated total direct costs between $694 and $1,660 million per year. Accounting for severity of disease, they approximated the cost of hepatocellular carcinoma as $140 million per year and chronic liver disease and cirrhosis at $1,421 million per year.

Indirect costs include forgone earnings or production due to hospitalization, ambulatory care, premature death, and work loss. Some studies estimated indirect costs of $490 per year per diagnosed individual (Everheart & Ruhl, 2010). Khoury et. al. (2012) found indirect costs for HCV per individual per year totaled $10,316. Of this, $2,107 was lost to absenteeism and $8,209 was lost to presenteeism. They found average total costs were $27,000 per untreated HCV infected patient per year. Variation in indirect costs are due to definitions of direct and indirect costs in

***"Chronic diseases account for about $3 of every $4 dollars spent on healthcare, or about $7,900 per American with at least one chronic illness."***

empirical studies and the time at which the study is conducted.

As chronic HCV progresses, costs associated with its treatment increase. The only treatment for end stage liver disease is orthotopic liver transplantation (replacing the liver of the recipient with a donor liver). It is estimated that HCV is responsible for one-third of all liver transplants in the United States. The average cost of liver transplantation was an estimated $201,110 in 2010 U.S. dollars (Hilst et. al., 2009). Estimates from the C. Everett Koop Institute at Dartmouth University approximate that at a cost of $280,000 per liver transplant, the costs from liver transplantation for hepatitis C alone total $300 million each year. Moreover, the Institute estimates the average lifetime cost for hepatitis C, excluding liver transplantation, to be $100,000 per individual. Thus, if 80% of the 4.5 million Americans who may be infected develop chronic liver disease, the collective lifetime cost would be $360 billion. Assuming a 40-year survival rate, the annual health care costs for the U.S. population with chronic hepatitis C reaches $9 billion (C. Everett Koop Institute, 2015), which is compounded by the fact that recurrence of the HCV virus is nearly universal in transplant patients (Tsoulfas et. al., 2009). In a study by the University of California Los Angeles of 500 patients evaluated over ten years, researchers found a median reoccurrence of HCV infection of three years (Ghobrial et. al., 2001).

***"Thus, if 80% of the 4.5 million Americans who may be infected develop chronic liver disease, the collective lifetime cost would be $360 billion."***

# COSTS OF USUAL CARE

Aside from physician visits for diagnosing, treating, and monitoring disease complications from chronic illness, costs are incurred from the drug itself. Successful treatment for HCV may prevent or slow disease progression, curtailing future costly outcomes such as liver transplantation. Drug therapies yield sunk costs if the treatment drug proves ineffective, produces intolerable adverse side effects, or causes death.

The criterion for success of any HCV treatment is a sustained viral response (SVR), defined as a negative HCV ribonucleic acid level as measured by a polymerase chain reaction 24 weeks after final treatment (Dawravoo & Martin Cohen, 2013). Standard treatment for hepatitis C includes a combination of pegylated interferon and ribavirin (PEG-RBV) for 48 weeks, taken twice daily. The genotype of the patient is a significant determinant of success. Of the 6 major genotypes, genotype 1 is the most common in the United States and represents 70% of Americans. Patients with genotype 1 exhibit the lowest response rate, around 40%, to PEG-RBV. In addition to its low success rate, PEG-RBV produces universal side effects that include fatigue, flu-like symptoms, anxiety, skin rash, anemia, depression, and gastrointestinal symptoms like nausea and diarrhea (U.S. Department of Veterans Affairs). A comprehensive listing of negative symptoms and frequencies follows. Side effects reduce adherence to therapy and induce suboptimal dos-

**Table 2 | PEG-RBV Therapy Side Effects and Estimated Frequencies**

| *Side Effect* | *Frequency (%)* |
|---|---|
| Fatigue | 54-64 |
| Headache | 47-62 |
| Myalgias (muscle pain) | 42-56 |
| Pyrexia (fever) | 43-46 |
| Rigors (chills) | 24-48 |
| Insomnia | 37-40 |
| Nausea | 29-43 |
| Alopecia | 28-36 |
| Irritability | 24-35 |
| Arthralgias (joint pain) | 27-34 |
| Anorexia | 21-32 |
| Depression | 22-31 |
| Dermatitis | 21-24 |

Adapted from McGowan, C., & Fried, M. (2013). Side Effect Management of Peginterferon and Ribavirin. In Hepatitis C (pp. 99-107). New York, New York: Oxford University Press.

ing, all of which generate substantial costs and reduced desired health outcomes. In some trials 10% to 14% of patients discontinued treatment due to adverse effects. Furthermore, dose reductions, which strongly correlate to reduced success rates, occurred in 32% to 42% of patients (Fried et. al., 2002; Manns et. al., 2001). Due to adverse treatment-related events, it is recommended that patients taking PEG-RBV receive routine laboratory testing at weeks 2, 4, and every 4 to 8 weeks thereafter, increasing direct medical costs in physician visits and testing.

Few studies have evaluated the direct economic cost of PEG-RBV treatment. One such study uses a medical claims database of 20,002 individuals to evaluate direct economic costs of treatment over a five -year period. Solomon et. al. (2011), found that HCV-treated patients had higher overall costs relative to HCV-untreated patients which were driven mainly by pharmaceutical drugs of PEG-RBV drug therapy. Treated patients had fewer hospitalizations and lower average length-of-stay, but more outpatient physician visits due to active treatment monitoring requirements. For HCV-treated patients, total direct medical costs were $28,547 versus $21,752 for non-treated HCV patients. For untreated-HCV patients, costs were $17,419 for outpatient pharmacy expenditures, $894 for outpatient physician visits, $3,942 inpatient costs, and $366 in emergency room costs.

# ESTIMATING THE VALUE OF SOVALDI

At $84,000 per treatment, Sovaldi is expensive. Traditional drug treatments are less expensive but exhibit low success rates and many side effects. Conversely, Sovaldi exhibits high success rates, effectively curbing complications from HCV infection and repressing continued liver damage. As a result, long term costs decrease. Patients using Sovaldi also experience fewer side effects, which increases adherence and reduces wasteful spending on discontinued treatment and unforeseen adverse events.

With 16,000 cases of HCV infection reported each year (Centers for Disease Control and Prevention, 2009), HCV will remain a significant burden on health systems without appropriate intervention. Less than one-third of patients with chronic HCV have been referred for disease management, and of those only 3% to 6% are treated (North et. al., 2013). As noted earlier, the high prevalence of HCV in the Baby Boomer generation will only add to the economic burden of HCV as the cohort ages. Current estimates find that the Baby Boomer generation accounts for 75% of those with chronic HCV in the United States (Younossi, 2014). It has been estimated that by 2020, the proportion of patients with cirrhosis will increase from 16% to 20%, hepatocellular carcinoma will increase by 81%, and liver-related deaths will increase by 180% (Davis et. Al., 2003). Although HCV-related complications and costs are expected to rise, breakthrough drugs like Sovaldi present a viable solution. Sovaldi's high SVR is expected to decrease long-term outcomes associated with HCV progression. Patients taking Sovaldi experience SVR rates between 87% and 93% (Lawitz et. al., 2014). Further, SVR is associated with a decrease in all-cause mortality, liver-related mortality, and hepatocellular carcinoma in HCV-infected patients (van der Meer, 2012). The most common side effects of Sovaldi are fatigue, headache, and nausea. In Phase III trials of Sovaldi, 2% of patients discontinued treatment compared to 4% in the placebo group. 5% of patients in the treatment group experienced serious side effects compared to 3% in the placebo group (Lam et. al., 2014). Clinical trials report a 95% success rate for Sovaldi treatment.

***"Although HCV-related complications and costs are expected to rise, breakthrough drugs like Sovaldi present a viable solution."***

# RESULTS

The costs of untreated HCV as well as associated treatments are detailed in the literature. Cost-effectiveness analyses of HCV treatment commonly evaluate treatments in QALYs (quality-adjusted life years), providing a composite measure of overall health and well being in response to a treatment intervention. Incremental cost effectiveness ratios (ICERs) are also utilized to determine the comparative advantages of various treatments. Many HCV analyses have compared the relative costs of untreated HCV patients with those who experience drug intervention. As noted previously, many studies focus on the costs of each stage of HCV. The framework for this empirical investigation is a simple cost analysis. Using published data, costs of annual per-patient usual care treatment are compared to the annual per-patient costs of treatment with Sovaldi over a ten year period.

To begin, it is assumed that 3.2 million people are currently infected with chronic HCV in the United States. Of these, it is assumed that only half are aware of their infection and only 20% are referred for treatment. This translates to 10% of the 3.2 million infected individuals who potentially begin treatment. Furthermore, we assume that 100% of this cohort elect to begin treatment with Sovaldi at a 95% success rate. Thus, if each year 16,000 new infections are documented, 1,600 new individuals will begin a treatment regimen annually in this model. Because the costs of death are difficult to quantify over an aggregated population, the number of deaths per year are omitted from the analysis. In the case of Sovaldi treatment, 5% will fail at achieving a successful SVR. Once an individual fails treatment it is assumed he will not elect additional treatment and incur the annual direct and indirect costs of untreated HCV. Costs are calculated over a ten year period and indexed to 2010 US dollars. Treatment with Sovaldi costs $79,000 in 2010 US dollars. The same

**Table 3** | Cost Per Patient Per Year, Selected Studies

| Research | Untreated Mean (SD) | | | Usual Care Mean (SD) | | |
|---|---|---|---|---|---|---|
| | Direct | Indirect | Total | Direct | Indirect | Total |
| Rosenberg et. al. (2000) *Costs in 1997 US dollars | - | - | - | - | - | $19,692 (not reported) |
| Armstrong & Charland (2004) *Costs in 2004 US dollars | - | - | - | - | - | $17,768 (not reported) |
| McCombs et. al. (2011) *Costs in 2010 US dollars | - | - | - | - | - | $37,390 ($72,154) |
| Solomon et. al (2011) *Costs in 2007 US dollars | - | - | $21,752 ($56,060) | - | - | $28,547 ($36,769) |
| El Khoury et. al. (2012) *Costs in 2010 US dollars | $22,818 ($34,373) | $10,316 ($14,582) | $26,897 ($36,410) | - | - | - |

methodology is used to determine the costs of a hypothetical cohort in which 100% elect usual care treatment. Based on the literature, 50% of those who elect usual care treatment will achieve a successful SVR. Costs for untreated HCV and usual care treatments are taken from published literature. Values used in the analysis are derived from averaging costs from selected sources. Table 3 exhibits findings from selected empirical studies. (A summary table of costs indexed to 2010 US dollars is located in the Appendix.)

Only studies that demarcate untreated costs of HCV and costs of usual care are included for analysis. Additionally, only studies that exclude HIV coinfection are included to provide a more robust representation of HCV-related costs. Of note is the work by McAdam-Marx et. al. (2011), who retrospectively evaluate claims data to determine per patient per year (PPPY) costs for HCV disease states. They find PPPY costs range from more than $27,000 PPPY in patients with decompensated cirrhosis to more than $93,000 in patients in need of liver transplantation. Rosenberg et. al. (2000) is omitted from empirical analysis as their data includes cases of HIV coinfection.

***"They find PPPY (per patient per year) costs range from more than $27,000 PPPY in patients with decompensated cirrhosis to more than $93,000 in patients in need of liver transplantation"***

Following the assumptions listed, the calculated costs for Sovaldi and usual care treatment are noted accordingly:

Year 1: (320,000*cost of Sovaldi) = *Total costs in Year 1*
Year 2: (5% unsuccessful in Year 1*costs untreated) + (# of new entrants*cost of Sovaldi)= *Total costs in Year 2*
Year 3: (% unsuccessful from Years 1 & 2*costs untreated) + (# of new entrants* cost of Sovaldi)= *Total costs in Year 3*

The same logic is applied in years four through ten. Similarly, the equation for annual Usual Care (UC) costs is:

Year1: (320,000*cost of UC) = *Total costs in Year 1*
Year 2: (50% unsuccessful patients*cost untreated) + (# of new entrants*cost of UC) = *Total costs in Year 2*
Year 3: (% unsuccessful patients from Years 1 and 2*cost untreated) + (# of new entrants* cost of UC) = *Total costs in Year 3*

The same logic is applied in years four through ten. Completing the calculations through ten years yields results shown in Figure 2.

**Figure 2** | Costs of Sovaldi vs. Usual Care Treatment

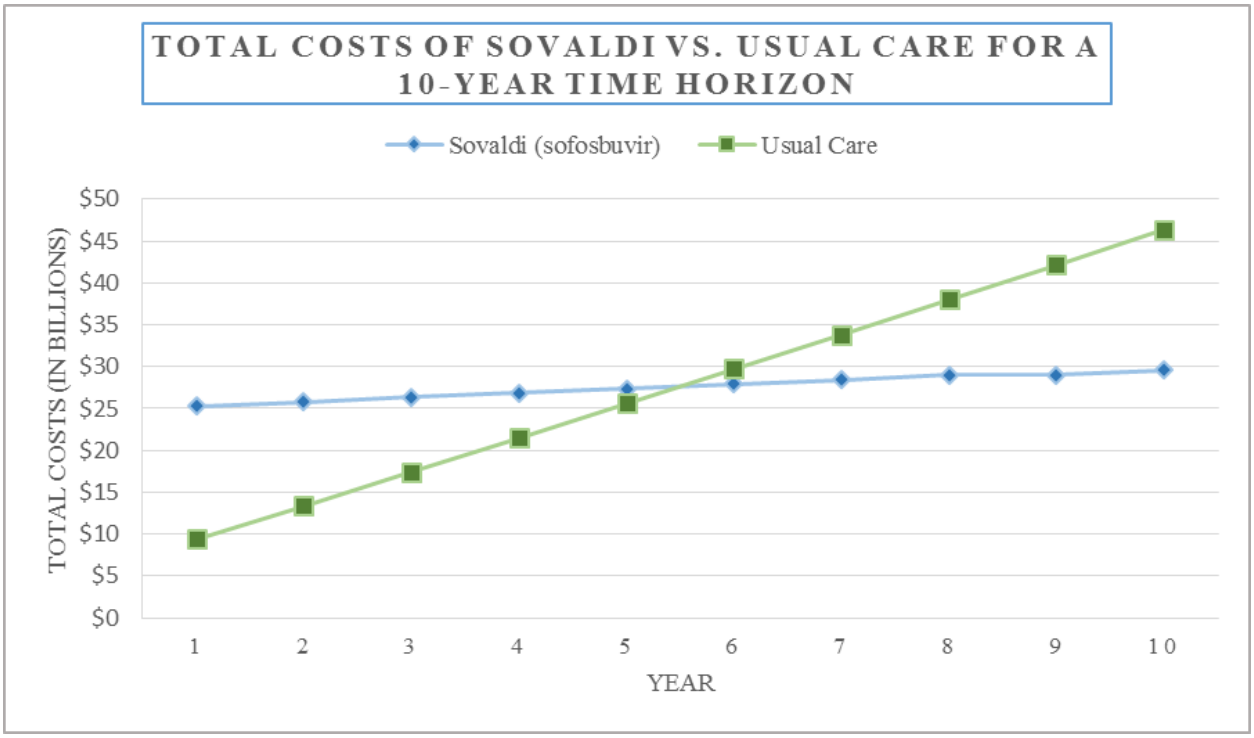



**Table 4** | Costs Per Year by Treatment

| Year | Sovaldi | Usual Care |
|---|---|---|
| 1 | $25,280,000,000 | $9,378,560,000 |
| 2 | $524,592,000 | $4,028,812,800 |
| 3 | $526,582,960 | $4,048,722,400 |
| 4 | $528,572,920 | $4,068,632,000 |
| 5 | $530,564,880 | $4,088,541,600 |
| 6 | $532,555,840 | $4,108,451,200 |
| 7 | $534,546,800 | $4,128,360,800 |
| 8 | $536,537,760 | $4,148,270,400 |
| 9 | $538,528,720 | $4,168,180,000 |
| 10 | $540,519,680 | $4,188,089,600 |

# ANALYSIS

Compounding ten years of costs, we found that costs from treating HCV with Sovaldi are greater than usual care treatment in the short run. However, by year six, the costs for usual care treatment outweigh the costs for treatment with Sovaldi. Yearly costs for usual care are much higher than those for Sovaldi due to lower success rates. Although the cost of Sovaldi treatment is initially high, the opportunity to avoid costs from HCV-related complications in the future outweighs the initial financial burden.

As with all cost analyses, limitations should be considered. Average costs per patient per year are taken from a number of published studies that employ different empirical methods with differing population sizes. The number of individuals who die each year due to HCV were omitted due to the difficulty in ascribing a monetary value to the loss of life. However, given that three-fourths of those with chronic infection are ages 40-49, the absence of work-life productivity lost may not be significant. This analysis assumes a constant number of newly infected individuals and costs for each treatment, resulting in linearly projected costs. As Baby-Boomers' complications from HCV become more pronounced with disease progression, costs may actually be greater in the future without drug intervention. It is also important to note that costs used in this analysis are aggregated across all HCV-infected individuals. HCV-related costs become increasingly greater with disease progression. Average costs are sensitive to the number of people in each disease state. For example, if more people advance to the costliest stages of HCV than there are people in the earlier stages, average costs per individual will increase substantially. Moreover, HCV exhibits significant variation in prevalence among racial groups. As a societal lens was adopted for this paper, costs in this analysis do not account for racial variability. One topic excluded from the analysis is that of HIV coinfection. HIV coinfection occurs in 25% of those infected with HCV and triples the risk for liver disease, liver failure, and liver-related death from HCV (Centers for Disease Control and Prevention, March 2014). An important consideration is that this analysis also does not account for the benefit of reducing the number of individuals with the potential to spread disease. The benefit of reducing the number of viral individuals may negate short-run costs. It is difficult, however, to quantify material benefits of preventing future infections. In reviewing the literature, no studies were found that address this topic. Future empirical analyses would benefit from computing these intangibles for the purpose of supporting a more comprehensive understanding of the HCV cost burden.

***"By year six, the costs for usual care treatment outweigh the costs for treatment with Sovaldi."***

# EXPANDING THE CONVERSATION

While the comparative effectiveness of two treatments was omitted from this analysis, the subject of drug costs was explored. Developing a cohort of individuals infected with chronic HCV in the U.S., costs per patient were ascribed to two treatments. Building on a framework of assumptions from published literature, costs of two treatments were projected ten years into the future. While Sovaldi was more costly in the first five years, it becomes cost-saving in the years thereafter.

Policy makers must be forward-thinking when enacting policy. While upfront costs of new drug therapies appear excessive, the potential future savings may be worth the price. Drugs with promising success rates reduce the number of future infections by diminishing the number of infected individuals. This is especially important for diseases that are initially asymptomatic such as HCV. Since 50% of individuals with HCV are unaware of their infection, any drug therapy, policy prescription, or combination that limits future infection must be considered. Developing sound policy prescriptions for select HCV drug treatments should consider the following: How many individuals are in the treatment population? What is the distribution of disease severity in the population? What is the racial composition of the population? What is the time horizon for treatment? What are the aggregated direct and indirect costs of competing treatments? And lastly, who will pay for cost-saving treatment?

The number of individuals within a treatment population is positively correlated with costs. If the number of patients is so high that costs become unwieldy, the decision to strategically allocate pecuniary resources becomes necessary. The severity of disease and degree of liver degeneration increases the direct and indirect costs of treatment. It may benefit a community more in the long-run to subsidize a costly treatment like Sovaldi if many young adults are infected. By spending more in the short-run and reducing HCV complications for young adults, costly future indirect costs stemming from work-loss, increased hospitalizations, and liver transplantation may be avoided. The disproportionate effects of HCV infection on race may warrant specialized policy action. For example, a population that is significantly non-Hispanic Black, due to its high infection rate and disease prevalence, may warrant a policy that targets those at-risk populations. Preventive screenings may present an appropriate mechanism to defray HCV costs to these populations. Additionally, the time frame for implementation provides a lens from which to assess costs, as cost-savings and cost-effectiveness are not always concordant. Usual care treatment presents significant cost-savings in the short term, but Sovaldi may be more cost-effective in the long run.

As the majority of those with chronic HCV are aging, they will experience costly HCV complications and increase the economic burden of HCV. Taxpayer funded programs like Medicare and Medicaid will pay for expensive HCV-related complications for infected individuals. In summary, the total HCV-related costs to society are substantial and will only increase in the near future. With state and federal government entering the drug pricing discussion, conversations should consider cost not as a fixed price tag, but as an investment to reduce future costly health outcomes.

***"In summary, the total HCV-related costs to society are substantial and will only increase in the near future. With state and federal government entering the drug pricing discussion, conversations should consider cost not as a fixed price tag, but as an investment to reduce future costly health outcomes."***

# CONCLUSION

Value plays a pivotal role in policy prescriptions regarding the allocation of financial resources to medical care. Costs and benefits from treatment must be considered to accurately assess the true value of drug interventions to society.

Evaluating the costs of untreated HCV disease progression, standard pegylated interferon and ribavirin treatment, and treatment with Sovaldi provides a comprehensive understanding of potential societal cost-savings. We find that Sovaldi's current pricing is justified from a societal value perspective. While Sovaldi's price is more costly than alternate treatments in the short term, its high success rate drives increased value in the long term. Due to its high success rate, Sovaldi may reduce future infections and costly treatments for advanced liver degeneration, defraying even larger future costs.

Drug prices are not simple one-off costs. They reflect both immediate and future benefits in the way of increasing quality of life, reducing costly operations, and hindering the spread of future disease. To the contrary, they reflect additional costs by adverse effects from treatment or reduced adherence. Evaluating direct and indirect costs over an appropriate time horizon reveals the true value of any drug intervention. Sovaldi, at $84,000 per treatment, exhibits justifiable societal value.

***"Sovaldi, at $84,000 per treatment, exhibits justifiable societal value."***

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# APPENDIX

| Cost Per Patient Per Year (PPPY) Indexed to 2010 US Dollars | | | | | | |
|---|---|---|---|---|---|---|
| Research | Untreated Mean (SD) | | | Usual Care Mean (SD) | | |
| | Direct | Indirect | Total | Direct | Indirect | Total |
| Rosenberg et. al. (2000) *Costs in 1997 US dollars | - | - | - | - | - | $26,753.64 (not reported) |
| Armstrong & Charland (2004) *Costs in 2004 US dollars | - | - | - | - | - | $20,510.42 (not reported) |
| McCombs et. al. (2011) *Costs in 2010 US dollars | - | - | - | - | - | $37,390 ($72,154) |
| Solomon et. al (2011) *Costs in 2007 US dollars | - | - | $22,875.99 ($58,956.79) | - | - | $30,022.11 ($38,668.97) |
| El Khoury et. al. (2012) *Costs in 2010 US dollars | $22,818.48 ($34,372.73) | $10,316.00 ($14,582.01) | $26,897.69 ($36,410.05) | - | - | - |

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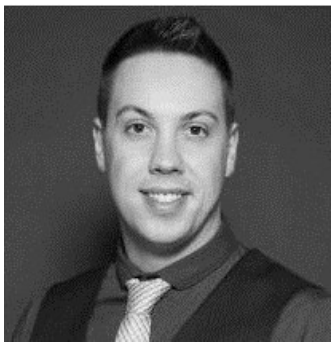

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The Center for Healthcare Innovation (CHI) is an independent, 501(c)(3) research and educational institute that helps patients and providers increase their knowledge and understanding of the opportunities and challenges of maximizing healthcare value to improve health and quality of life. We aim to make the world a healthier place. CHI encourages and enables meaningful and executable innovation that aims to address existing and ensuing healthcare dynamics through communication, education, training, symposia, reports, and research. By bringing the best and brightest healthcare leaders from all over the world together to share their ideas and expertise, CHI creates a unique opportunity to address and improve healthcare value, which we view as a function of quality, access, and cost. For more information, please visit **www.chisite.org**.

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