Innovation in Hepatitis C Treatment: New Opportunities for Action

California Healthcare Institute

in collaboration with
The Boston Consulting Group

July 2014
Executive Summary

Hepatitis C (hep C) is a viral disease caused by the Hepatitis C virus (HCV) and transmitted by blood, primarily in health care settings. It can progressively damage the liver, and, if left untreated, cause liver cirrhosis, liver cancer, and death. Hep C is the leading cause of liver cancer and liver transplants. In addition, the virus is associated with a variety of conditions beyond liver disease, including diabetes and depression. The US Centers for Disease Control and Prevention (CDC) estimates that approximately 3.2 million people in the US are chronically infected with hep C, though only half of them are aware of their infection. Approximately 16,000 deaths related to hep C were recorded in the US in 2010, but a recent analysis published by CDC-affiliated authors suggests that true hep C-related mortality might be closer to 53,000 deaths annually.\(^1,2\)

Since 1989, when HCV was identified as the cause of hep C, discovering effective treatment for the disease has been an intense field of research by academic scientists and pharmaceutical companies. In the 1990s, the introduction of interferon and, shortly thereafter, pegylated interferon and ribavirin offered, for the first time, the potential to cure hep C patients. From the start, though, the limitations were obvious as many patients were ineligible for treatment with interferon, and in those suitable for the treatment, the regimen’s success rate was only 50 percent.\(^1\) Moreover, among patients who started treatment, a high percentage dropped out due to interferon’s harsh side effects, which include depression, nausea, severe anemia, and flu-like symptoms.\(^3\) Fortunately, in recent years, scientific advances have led to far better and safer treatments.

The ultimate goal in treating any disease is a safe, simple, and highly effective cure that is achieved rapidly with minimal eligibility constraints. All clinical evidence to date suggests that we are reaching that point in hep C: new anti-HCV medicines entering the market are expected to have cure rates exceeding 95 percent and very few side effects.\(^4\)

Over time, these new medicines can transform the face of hep C in the US by dramatically reducing the sickness and death associated with the disease. To illustrate the impact of HCV innovation on human health, we use an epidemiological model created by the Center for Disease Analysis and demonstrate that treating the US hep C population with these new drugs, as opposed to the previous standard of care, could save the lives of thousands of people.\(^2,5\)

\(^1\) For genotype 1, the most prevalent form of Hepatitis C in the U.S.
\(^2\) Assuming no increase in the percentage of patients diagnosed or treated
Background and Objective

Although the public-health burden of the disease received little public attention for decades, hep C has attracted intense media coverage over the past several months, much of it focused on the pricing of new anti-HCV drugs and the consequent impact on the budgets of public and private payors. Various stakeholders have weighed in on the debate about the prices of these new medicines, how to pay for them, and who should be treated. Although this public dialogue is important, we do not aim to address these questions here.

Rather, we seek to provide a broader understanding of the public-health impact of hep C and to highlight the significance of the breakthroughs that have brought us to a new era of treatment. We believe that the current discussion too often ignores revolutionary discoveries in hep C and their potential to save lives and prevent human suffering. This report is intended to elevate this perspective in the ongoing public debate.

Furthermore, we believe that similar debates will arise in the future as new breakthroughs for other devastating diseases come to market, and we hope that our collective approach to those discussions will include an appreciation for the impact of innovation on human life.

Glossary

**Incidence**: The number of new cases of a disease in a population; often expressed as number of new cases per 100,000 population

**Prevalence**: The percentage of a certain population with a disease

**Chronic HCV infection**: Established infection with the Hepatitis C virus that cannot be spontaneously cleared without targeted treatment

**Genotype**: A genetic variant (“form”) of a particular virus; three HCV genotypes are prevalent in the US

**Mortality rate**: The number of deaths caused by a disease in a population; often expressed as number of deaths per 100,000 population

**Morbidity**: All human suffering caused by a disease except death

**Liver cirrhosis**: Scarring of the liver, whereby hard scar tissue replaces soft healthy tissue and progressively renders the liver non-functional

** Decompensated cirrhosis**: The final, life-threatening stage of cirrhosis in which the liver stops functioning; symptoms include internal bleeding, brain toxicity, and confusion

**Cure of HCV**: The elimination of HCV from a patient’s body, which significantly lowers the probability of liver disease and other related sickness

**Sustained viral response (SVR)**: A measure of the effective cure rate after drug treatment that signifies the percentage of patients whose blood contains no detectable virus 12 or 24 weeks after the end of treatment

**Treatment burden**: The number of pills, injections, or both required for a full course of treatment

**Interferon**: Class of proteins naturally made as part of the immune response that has anti-viral activity; a modified interferon protein, pegylated interferon, has been a key component of Hepatitis C treatment regimens

**Ribavirin**: A nucleoside inhibitor that has been given in combination with interferon for the treatment of Hepatitis C; nucleoside inhibitors interfere with viral replication
Hepatitis C and Its Impact in the US

The Hepatitis C Epidemic in the US

Hep C is a viral disease that infects the liver. Because the virus spreads throughout the body, it is also associated with a variety of disorders outside the liver. The disease is transmitted through contact with an infected person’s blood and is most often contracted in health care settings although some infections are spread through sexual contact or sharing of needles among intravenous-drug users. The majority of people in the US infected with the disease today contracted it through contaminated blood in the 1970s and 1980s, before routine blood screening for the virus became available in the early 1990s (Exhibit 1). It is estimated that 75 percent of the US hep C burden is carried by baby boomers. It is also thought that roughly 75 percent of all HCV infections in the US are genotype 1, the ‘form’ of the disease that is hardest to treat.

Exhibit 1: Prevalence and Incidence of Hep C in the US

The CDC estimates that today 4.1 million people in the US have been exposed to HCV and 3.2 million (more than the combined populations of Dallas, San Francisco, Boston, and Atlanta) are chronically infected, meaning that they will not be able to eliminate the virus in their bodies without targeted treatment.

3 People born between 1946 and 1964
Other researchers place their estimates at 5.2 million people in the US exposed to the virus, after including prison inmates and the homeless. In fact, a rising infection rate has recently been reported among young drug users, these reports are concerning, particularly given that many of these patients are not linked to the health care system.

Hep C does not affect all people to the same degree; its impact falls disproportionately on low-income communities, intravenous-drug users, prisoners, veterans, and other vulnerable populations. Those below the poverty line are three times more likely to have been exposed to HCV than those with higher incomes. People who have used injection drugs are 150 times more likely than those who have not to be infected with HCV. Worse yet, the poor are disproportionately unaware of their HCV infection status. As just one example, although data on prevalence rates in US prison populations is sparse, some studies suggest that up to 39 percent of all prisoners are infected with HCV, which is particularly disturbing given that there are currently no screening or treatment requirements for hep C in the US prison system. When it comes to health coverage, approximately 480,000 people in the US who are infected with HCV are uninsured, and an additional 430,000 are on Medicaid insurance, the government's program for low-income individuals and families. States that expand Medicaid under the Affordable Care Act (ACA) are expected to cover many thousands of additional patients.

The Impact of Hepatitis C

Hep C progresses slowly but can be fatal. The CDC estimates that for every 100 patients infected with HCV, 65 will develop chronic liver disease, 13 will develop cirrhosis, and 3 will die as a consequence of their infection (Exhibit 2). Academic studies have suggested much higher mortality rates, including one source that estimates that up to 30 percent of chronically infected patients will die a hep C–related death. In terms of absolute numbers, a report published by CDC-affiliated authors notes that 16,622 hep C–related deaths were recorded in 2010; however, after taking into account the underdiagnosis of the disease and inadequate record-keeping, they estimated that hep C-related mortality may be closer to 53,000 people annually in the US.
In addition to devastating mortality, hep C causes significant morbidity. Chronic liver disease and cirrhosis can lead to jaundice, anemia, type 2 diabetes, brain toxicity, and liver cancer. Importantly, if treatment is delayed until later in the disease progression, many of these debilitating symptoms persist even after a patient is cleared of the HCV infection, because the liver has already been permanently damaged. The disease is currently the nation’s leading cause of liver cancer. It is also the leading cause of liver transplants in the US; in many instances, liver transplant is the only treatment option for advanced cirrhosis or liver cancer. Unfortunately, the supply of livers available for transplant is inadequate, with more than 16,000 people in the US currently on slow-moving transplant waiting lists.

Finally, hep C has considerable economic costs, largely because of its high prevalence in the US. A 2013 study estimated that US commercial payers spend five times as much on hep C–positive patients as they do on their average members. Partly due to the defects of earlier drug regimens, in the past, only 20 percent of the money spent for the care of hep C patients paid for prescription drugs; the rest went to inpatient and outpatient facility costs and professional fees associated not only with direct hep C care but also with related conditions and sicknesses. Treatment for late stage complications of hep C can be quite
expensive; for example, the estimated cost of a liver transplant is $577,000.\textsuperscript{6} In the future, the introduction of new drug regimens into the market and the coverage expansion under the ACA are expected to cause substantial shifts in the economics of hep C treatment.

**The Public-Health Response to Hepatitis C**

Despite the high prevalence and mortality rates of hep C in the US, the public response to the disease has been muted, especially compared with the national commitment to tackling other serious public health crises such as HIV/AIDS. For example, an analysis published in 2011 in the journal *Nature* noted that the CDC spent $728 million in 2010 on prevention and surveillance activities against HIV/AIDS versus $9 million against hep C.\textsuperscript{xv} Similarly, the US Health Resources and Services Administration\textsuperscript{7} reported spending $2.3 billion on HIV care and treatment and $70 million on hep C (Exhibit 3).

The contrast between HIV and hep C becomes particularly compelling when one considers the impact that these disproportionate public-health responses have had on the epidemiology of the diseases. In the past

---

\textsuperscript{6} Estimated US average 2011 billed charges per transplant  
\textsuperscript{7} The HRSA is a federal agency that provides supplemental funding to health care providers that care for uninsured patients and other vulnerable groups.
two decades, scientific research and innovation coupled with the public commitment to the fight against HIV/AIDS have brought the HIV-related mortality rate down to very low levels.\(^8\) In contrast, the hep C mortality rate has risen continuously and in 2007 actually surpassed that of HIV (Exhibit 3).\(^{xvi}\) Because HCV is often a contributing factor to a variety of disorders, a report published by CDC-affiliated authors recently estimated that more than two-thirds of hep C-related deaths are not reported as such, meaning that the mortality rate should, in fact, be significantly higher.\(^{ii}\) This comparison offers a glimpse into the magnitude of the public and private investment that was necessary to effectively tackle the HIV epidemic; a similar response to hep C might be not only warranted but overdue. It is worth noting that co-infection among HIV and hep C patients is substantial (25 percent of HIV patients are also hep C–positive\(^{xvii}\)); hence, responses to the two diseases will need to be coordinated closely.

**The Challenge of Treating Hep C**

Historically, the fight against hep C has been hampered in the US by four interconnected and mutually reinforcing factors: 1) Medicines with low cure rates and significant side effect profiles, 2) low diagnosis rates that leave perhaps 2 million hep C-infected people unaware of their status, 3) low treatment rates even among those aware of their status, and 4) socio-economic forces limiting access to health care for patient populations especially vulnerable to hep C.

In this report, we examine in detail the remarkable progress in addressing the first factor (imperfect medicines) and explore the impact that breakthrough innovation is having and will continue to have on the hep C epidemic in the US. We briefly touch upon the second (low diagnosis rates) and third (low treatment rates) factors, recognizing that designing the optimal public-health strategy to tackle hep C by targeting the right treatment to the right patients is a complex endeavor beyond the scope of this report.

**The Rise of Hepatitis C Treatments**

In the early 1980s, reports of a progressive, infectious liver disease that could not be classified as hepatitis A or B led researchers to create a new non-A/non-B (NANB) hepatitis disease category. Initially, NANB hepatitis was thought to be harmless, but its silent progression to cirrhosis or liver cancer soon came to light. In 1989, a researcher at Chiron identified the causative agent of NANB hepatitis and called it Hepatitis C virus.\(^{xviii}\) Since then, treatment of the disease has been the subject of intense research by

\(^8\) Importantly, the increases in investments in HIV and AIDS coincided with the discovery of improved medicines that could change the course of the disease for thousands of people. The Ryan White CARE Act, which funds HIV and AIDS treatment for patients with no other resources, was passed by Congress in 1990, the same year that the U.S. FDA approved AZT, the first anti-HIV medication. The act was reauthorized in 1996, just one year after saquinavir was approved by the FDA, marking a new era of improved treatments against HIV and AIDS.
academic scientists and pharmaceutical companies alike. The search for medicines has been focused on finding compounds that can produce a sustained viral response (SVR), an effective measure of a cure, meaning that no detectable virus is present in the patient’s blood after completion of treatment. Numerous studies have demonstrated that patients who achieve a SVR face very low probabilities of disease progression and death due to hep C.

Exhibit 4 provides an overview of the remarkable progression of technological innovations in the treatment of hep C. In the early 1960s, all hepatitis disease was treated with strict bed rest and a nutritious diet. No chronically infected patients were cured with this approach.
In 1986, inspired by the success of interferon in the treatment of hep B, the National Institutes of Health encouraged a study of interferon’s efficacy in what was then known as NANB hepatitis (hep C). The results were disappointing: although many patients responded to treatment initially, most of them relapsed. Still, six percent achieved an SVR. Soon, however, ribavirin was added to the treatment regimen and interferon was chemically modified to persist longer in the patient’s body through a process called pegylation. The new pegylated-interferon-and-ribavirin regimens were an important breakthrough in the treatment of hep C. For the first time, the SVR for genotype 1 patients approached 50 percent, and the SVRs for genotypes 2 and 3 were even more promising (78 percent and 62 percent, respectively).9, iv, xviii

The trouble was that these regimens offered no hope for more than half of genotype 1 patients and, even when they worked, the treatment came with distressing side effects, including depression, nausea, severe reductions of certain blood cells, and flu-like symptoms.iii Beyond suffering and sickness from these side effects, patients required additional health-care services (including, sometimes, hospitalization) for their management. From a patient’s standpoint, these interferon-based treatments posed a large and difficult treatment burden: weekly interferon injections for 48 weeks and twice-daily ribavirin pills.iv The side effects, the daunting treatment burden, as well as the suboptimal efficacy of interferon-based therapy caused many patients to discontinue treatment before completion, thus all but eliminating their chances of achieving SVR. In a study among US veterans, as many as 54 percent of patients initiating interferon-based treatment failed to complete their course of treatment.xxi

The search for better medicines continued and, in 2011, two new drugs were approved by the US FDA. The new drugs, telaprevir and boceprevir, are protease inhibitors (PIs); they work by inactivating a critical piece of the Hepatitis C virus machinery called the protease. The improved regimen still required 24 to 48 weeks of weekly injections combined with eight oral tablets daily. Although PIs substantially improved the rate of SVR attainment for genotype 1 patients, they had to be taken together with interferon and ribavirin, which meant that they worsened the side effects and treatment burden of those regimens.iv

The ultimate goal of hep C drug research has been the discovery of a treatment that can be taken orally, has minimal side effects, and cures all patients of the virus. In 2013, the US FDA approved the first of an expected series of new drugs that align with these desired characteristics. Sofosbuvir, the first of these new compounds to reach the market, gives patients a 12-week, all-oral regimen, achieving SVRs of 97 percent and 93 percent in genotype 2 and genotype 3 patients, respectively, when taken together with ribavirin (without interferon).iv Soon, additional drug launches by AbbVie, Bristol-Myers Squibb, Gilead

---

9 The SVRs cited in this report come from highly controlled clinical trials. The real-world SVRs of these regimens have been found to be substantially lower because of differences in the clinical and behavioral characteristics of hep C patients who are not treated and followed in a clinical trial.
Sciences, and Merck & Co. will offer various interferon-free regimens, which are expected to have SVRs above 95 percent for all genotypes\textsuperscript{10}, including genotype 1, the most prevalent form of the disease in the US. In addition, they are expected to be administered orally only (one to five pills per day for 12-24 weeks) with limited side effects.

**The Opportunity to Act**

Scientific advances over the years have had a profound impact on the US hep C epidemic, in terms of both health outcomes (reduced morbidity and mortality) and economics (for example, fewer physician visits, reduced hospital care, increased productivity), and will continue to do so. The economic debate over the prices of new treatments has dominated the public sphere. To balance that debate with an accurate understanding of the human impact of treatment innovation, we asked the question: How much better off today and tomorrow are people in the US as a result of the breakthroughs in treating hep C?

To answer this question, we collaborated with the Center for Disease Analysis (CDA), an independent research organization based in Colorado that conducts epidemiological analyses to assist governments and organizations with policy decisions. CDA constructed an epidemiological model to simulate the US hep C epidemic, in which people enter the system with new infections, progress through the various stages of the disease, and exit the system either when they are cured through drug treatment or when they die. To assess the impact of treatment innovation on the hep C epidemic in the US, we started with today’s HCV-infected population and modeled different treatment regimens from 2013 through 2030. To simplify the analysis, we held the diagnosis and treatment rates constant and altered only the SVR and compliance rates based on different, hypothetical treatment regimens.\textsuperscript{11} A detailed overview of our methodology and assumptions can be found in the appendix.

The results are a powerful demonstration of the impact that treatment innovation can have on human life. As seen in Exhibit 5, if no hep C drugs were available today (the “no drug treatment” scenario), hep C mortality would rise steadily, cumulatively claiming nearly half a million US lives from 2013 through 2030. Assuming a switch to the new “interferon-free regimens,” the model shows deaths from hep C beginning a sharp decline around 2025, such that 67,000 US lives that would have been lost with no treatment would be saved over the 2013-2030 period. Importantly, even a switch from today’s standard of care (“protease inhibitors”) to the new “interferon-free regimens” yields a substantial difference of more than 30,000 lives saved by 2030. While the exact figures are, of course, dependent on numerous assumptions (described in

\textsuperscript{10} Based on clinical trials; not yet approved by the FDA

\textsuperscript{11} Because the real-world compliance rates for interferon-free agents are not yet known, we used clinical-trial compliance rates for all regimens in our analysis (detailed in the appendix). These compliance rates are likely to be overestimates
detail in the appendix), the shape of the mortality curves over time clearly illustrates the difference improved medicines can make in saving lives.

As a proxy for morbidity, we modeled the number of new liver-cancer cases (Exhibit 5). In the “no drug treatment” scenario, 230,000 people in the US would have newly developed liver cancer by 2030. A switch from “no drug treatment” to “interferon-free regimens” could prevent 40,000 of those cases. A switch from “protease inhibitors” to “interferon-free regimens” could prevent 16,000 new liver-cancer cases.

At the same time that these new high-impact drugs are entering the market, changes in the US health-care system increase the likelihood that more infected people will be diagnosed and treated for hep C. The recently issued CDC recommendation to screen all baby boomers for hep C, as well as the expansion in
health care coverage under the ACA, should increase diagnosis and treatment rates. Exhibit 6 illustrates the potential impact that treatment and diagnosis scale-up will have on the suffering caused by hep C. Even a 5 percent annual increase in the number of patients treated with the new interferon-free agents could save 27,000 additional lives by 2030, on top of the 30,000 lives saved by switching to the new drugs, as described above.

Exhibit 6: Impact of treatment scale-up on human life

<table>
<thead>
<tr>
<th>Methodology</th>
<th>Using a model created by the Center for Disease Analysis (CDA), we applied different treatment regimens on today’s American Hep C positive population. Here we apply Interferon-free treatment to all patients vary the annual increases in treatment coverage.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% annual scale up</td>
<td>1.0M patients cured by 2030</td>
</tr>
<tr>
<td>5% annual scale up</td>
<td>1.1M patients cured by 2030</td>
</tr>
<tr>
<td>10% annual scale-up</td>
<td>1.6M patients cured by 2030</td>
</tr>
<tr>
<td>15% annual scale-up</td>
<td>2.2M patients cured by 2030</td>
</tr>
</tbody>
</table>

A 5% treatment scale up would save 27,000 additional lives

Source: Center for Disease Analysis Hepatitis C model.
*Cumulative number of patients cured between 2013 and 2030. Assumptions on medical eligibility, SVR, and compliance rates can be found in the Appendix.

Of course, scale-ups in treatment require significant financial investments, and detailed cost-benefit analyses will be necessary to determine how expanding treatment should be optimally timed and deployed. Ensuring that not only more patients but also the right patients have access to appropriate medications will be crucial to realizing the potential of the new treatments. This is a complex challenge that will require the collaboration and coordination of pharmaceutical companies, governments, payers, physicians, and patients.

Conclusion

Over the past two decades, extraordinary progress has been made in the ability to treat and cure hep C, and today we are at a critical juncture. New medicines are available that can transform hep C treatment, curing more people than ever before, reducing morbidity and saving thousands of lives. Much of the discussion around these technologies so far has been focused on the price and volume of these new drugs.
and whether the health care system can afford them. Interestingly, previous treatment regimens for hep C cost the same or more (depending on the length of treatment), take at least twice as long to administer, are less effective and can often require other health care services.\textsuperscript{12,xxii}

The debate over access to highly innovative, game changing drugs will continue, specifically: how does one reward and pay for innovation? In this report, we highlight the undeniable success in science and innovation in the hep C field along with the consequences if, as a society, we fail to act. At the same time we recognize that scientific innovation alone is not enough to save the lives of all US patients with hep C. The creation of policies and mechanisms that will place the right patients on the right treatments is necessary and urgent. To succeed, we will need the close and productive cooperation of all stakeholders.

As the world awaits cures for other devastating diseases (Alzheimer’s, HIV, methicillin-resistant Staphylococcus aureus infections, and more) and expects pharmaceutical companies to invest billions in R&D for these and other conditions, public health will be best served by understanding and appreciating the value of innovation in addition to its costs. Medical innovation can transform human life, but it requires significant investments. While economic arguments about the value of new medicines are certainly warranted, it is also critical to appreciate the unique opportunity to save and improve lives that these treatments represent.

\textsuperscript{12} Brennan and Shrank (2014) published that a 12-week course of sofosbuvir plus pegylated interferon and ribavirin costs $116,910.72; a 24-week course of telaprevir plus pegylated interferon and ribavirin is $111,606.48 or $143,827.92 for 48 weeks.
Appendix: Methodology  
Center for Disease Analysis Hepatitis C Model

The Center for Disease Analysis (CDA) is a research firm focused on providing independent research and analyses for poorly understood diseases. It uses a multi-discipline approach that combines epidemiology research, expert interviews, advanced modeling, forecasting, and decision science to provide predictive analyses. The organization has studied and modeled Hepatitis C for the last six years and published numerous papers in the peer reviewed journals on the subject.

The CDA Hepatitis C Model is a disease progression model that simulates the US hep C epidemic. The model tracks chronic HCV disease progression by five-year age and gender cohort and liver disease stage from 1950 through 2100. New infections enter the model at any year, progress through the disease stages using published transition probabilities, and exit upon spontaneous clearance of HCV, cure (through drug treatment), or mortality (all-cause or liver-related). Appendix Exhibit 1 shows the different stages of the disease (boxes) and the possible movements of a patient through the model (arrows).

Appendix Exhibit 1: Schematic of CDA Hepatitis C disease progression model

The full description of the CDA model, as well as results of its application to six countries, were published in the *Journal of Viral Hepatitis* earlier this year. The US model that was used for the production of this
publication has not yet been published in a peer-reviewed journal but was created by CDA in close collaboration with academic experts in the field of hepatitis.

To model different treatment scenarios in the US, CDA primed the model with current US population data (including incidence, prevalence, and distribution of patients across age-groups and stages of the disease). This dynamic model included an algorithm for patient aging and new Hepatitis C incidence. Data sources included the US CDC, academic publications, as well as interviews with leading Hepatitis C researchers. A full description of such sources will be made available in the coming months, when CDA publishes the US model results.

Different treatment scenarios were applied to the US population starting in 2013. Our assumptions on the SVRs of different treatment regimens and the risk of discontinuation are shown in Appendix Exhibit 2. To calculate the number of people progressing to decompensated cirrhosis, we summed the incident cases of diuretic sensitive ascites, variceal hemorrhage, and hepatic encephalopathy from 2013 to 2030. Lastly, to calculate liver-related deaths, we summed the annual liver-related mortality from 2013 to 2030.

### Appendix Exhibit 2: Treatment regimens assumptions used

<table>
<thead>
<tr>
<th>Drug regimen (Duration in weeks)</th>
<th>SVR (%)</th>
<th>Risk of discontinuation (clinical trial)</th>
<th>SVR if discontinued (assumption)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No drug treatment, Bed rest</td>
<td>G1: 0</td>
<td>G2: 0</td>
<td>G3: 0</td>
</tr>
<tr>
<td>Interferon only, Peg-IFN &amp; RBV</td>
<td>G1: 47</td>
<td>G2: 78</td>
<td>G3: 62</td>
</tr>
<tr>
<td>Peg-IFN &amp; RBV (48 for G1, 24 for G2/3/4)</td>
<td>8.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protease Inhibitors, PR (24) for G1, PR (24) for G2/3/4</td>
<td>G1: 74</td>
<td>G2: 78</td>
<td>G3: 62</td>
</tr>
<tr>
<td>IFN-free agents, NSSA inh. (12) for G1, NSSA inh. + R (12 for G2, 24 for G3) for G2/3/4 or other similar combination including PIs</td>
<td>G1: 95</td>
<td>G2: 97</td>
<td>G3: 84</td>
</tr>
</tbody>
</table>

**Note:** SVRs presented here are a combination of published SVRs from multiple clinical studies and have been summarized in the CTAIF report on Sofosbuvir and Daclatasvir. Discontinuation risks denote the probability of a patient stopping treatment before the completion of a full course due to adverse events or other factors in the context of clinical trials. These are likely underestimates of real-world discontinuation risks. For simplicity, it is assumed that the likelihood of achieving SVR upon interruption of treatment is zero.
In Exhibit 5, diagnosis rates were held constant at approximately 50 percent of total hep C patients. Treatment rates were held constant at 59,000 patients per year regardless of treatment regimen. Treatment was allocated randomly to patients across medically eligible stages of the disease. For interferon-based treatments, patients with decompensated cirrhosis, liver transplants, and liver cancer were considered non-eligible based on clinical studies demonstrating that interferon can exacerbate cirrhosis. In addition, patients younger than 15 years and older than 65 years were considered ineligible for interferon-based treatments based on expert interviews with physicians, who noted that the side effects of interferon therapy are likely too severe for these patients. No stage restrictions were placed on interferon-free regimens, while patients as old as 74 years were considered eligible for the treatment, based on a significantly more favorable side-effect profile.

In Exhibit 6, treatment rates were scaled up annually at 1, 5, or 10 percent annually using the same medical eligibility criteria discussed above. For the 10 percent annual scale-up scenario, all medically eligible patients had been treated (or had died) by 2029 and, hence, no further scale-up was applied.
References

i United States Centers for Disease Control, Department of Viral Hepatitis. Viral Hepatitis Surveillance, United States, 2011 (accessed online at:
i Mahajan R, et al., “Chronic Hepatitis Cohort Study (CHeCS) Investigators. Mortality Among Persons in Care with Hepatitis C Virus Infection: the Chronic Hepatitis Cohort Study (CHeCS), 2006-2010,” Clinical Infectious Diseases, 2014.
iv Epidemiological modeling by the Center for Disease Analysis (unpublished).

xx American Liver Foundation website (http://hepc.liverfoundation.org/, accessed on 7/3/2014)
xxv Transplant living (http://www.transplantliving.org/before-the-transplant/financing-a-transplant/the-costs/, accessed on 7/14/2014)

xxviii U.S. CDC HIV and Viral Hepatitis Fact Sheet (http://www.cdc.gov/hepatitis/Populations/PDFs/HIVandHepFactSheet.pdf, accessed on 7/3/2014)


Report Authors

Todd E. Gillenwater, President and CEO, CHI-California Healthcare Institute
Dirk Calcoen, MD, Partner and Managing Director, The Boston Consulting Group
Laura Elias, PhD, Principal, The Boston Consulting Group

The authors would like to acknowledge Homie Razavi, PhD, the founder and managing director of the Center for Disease Analysis for extensive contributions to this report.

***

California Healthcare Institute (CHI)
CHI represents more than 275 leading biotechnology, medical device, diagnostics and pharmaceutical companies, and public and private academic biomedical research organizations. CHI’s mission is to advance biomedical research, investment, and innovation through effective advocacy of policies to improve public health and ensure the continued vitality of the life sciences sector. CHI’s website is www.chi.org. Follow us on Twitter @calhealthcare, Facebook, LinkedIn and YouTube.

Contact: gillenwater@chi.org

The Boston Consulting Group
The Boston Consulting Group (BCG) is a global management consulting firm and the world’s leading advisor on business strategy. We partner with clients from the private, public, and not-for-profit sectors in all regions to identify their highest-value opportunities, address their most critical challenges, and transform their enterprises. Our customized approach combines deep insight into the dynamics of companies and markets with close collaboration at all levels of the client organization. This ensures that our clients achieve sustainable competitive advantage, build more capable organizations, and secure lasting results. Founded in 1963, BCG is a private company with 81 offices in 45 countries.

Contact: calcoen.dirk@bcg.com