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Broad Hepatitis C Treatment Scenarios Return Substantial Health Gains, But Capacity Is A Concern

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ABSTRACT Treatment of hepatitis C virus, the most common chronic viral infection in the United States, has historically suffered from challenges including serious side effects, low efficacy, and ongoing transmission and reinfection. Recent innovations have produced breakthrough therapies that are effective in more than 90 percent of patients. These treatments could dramatically reduce the virus's prevalence but are costly. To quantify the benefit of these treatments to society, including the value of reduced transmission, we estimated the effects of several hepatitis C treatment strategies on cost and population health. Treating patients at all disease stages could generate $610–$1,221 billion in additional quality-adjusted life-years, plus an additional $139 billion in saved medical expenditures over fifty years, and minimize the disease burden, but up-front treatment costs would exceed $150 billion. An intermediate scenario—treating 5 percent of the infected population annually, regardless of patients' disease stages—would also return substantial benefits and would be much more affordable under current financing schemes.

Assigning value to new breakthrough treatments for previously hard-to-treat diseases requires balancing patients' access to new treatments against innovators' incentives to develop them. Recently, this trade-off has come into sharp focus in the case of the hepatitis C virus—the most common chronic viral infection in the United States, where it affects approximately 2.7 million people.[1] The virus is the leading cause of liver disease and liver transplants. People infected with the virus are often asymptomatic in the early stages of the disease, but it can progress to serious liver complications such as cirrhosis and hepatocellular cancer over years or decades, with grave health consequences and high medical costs.[2] For further details, see the online Appendix.[3]

Until recently, standard hepatitis C therapy consisted of a difficult antiviral regimen that included interferon injections for up to a year with significant chronic side effects, including fatigue, malaise, apathy, and cognitive changes. Such regimens produced sustained virological responses in 30–80 percent of patients treated.[4] But recent innovation in hepatitis C treatment has produced breakthrough oral therapies of much shorter duration with minimal side effects and with sustained virological response rates of 93–99 percent in randomized clinical trials.[5–7] This introduces the possibility of dramatically reducing hepatitis C prevalence. However, these treatments are much more expensive than earlier therapies.[3]

The new hepatitis C treatments have generated intense scrutiny from legislators, payers, and the media, all of whom have raised concerns about whether price will limit access (even among pa-

tients with private insurance) and about the impact of hepatitis C treatment on insurance premiums and state and federal government budgets.[8–10] The new treatments, along with several other breakthrough therapies approved by the Food and Drug Administration since 2013,[11] are bringing the issues of value, innovation, and access to the forefront of the health care field.

To investigate the societywide implications of new hepatitis C treatments, we developed an economic and epidemiological model that evaluates the impact of treatment on disease progression, transmission, and spending across three distinct subpopulations, which were defined by the manner in which their members contracted the virus: in a health care setting, through injection drug use, or through sexual transmission. Together, these groups account for most new and existing hepatitis C cases in the United States.[1,12]

The health care exposure group is the largest group of people infected with hepatitis C because many people acquired the virus through transfusion of infected blood or blood products before 1992, when universal screening of the blood supply for the virus began. Today, transmission through health care exposure is very rare.[1,12,13] While this group represents the largest proportion of currently infected people, prevalence due to this mode of transmission will decline as the baby-boomer population ages.

Transmission through sexual exposure is also uncommon, but it occurs primarily among HIV-infected men who have sex with other men.[14] Infection through injection drug use poses the greatest risk of hepatitis C virus transmission in the United States today.[1,15] Some health care officials have argued that recent increases in injection drug use among young adults is driving a new wave of hepatitis C prevalence that will become increasingly important as prevalence due to health care exposure declines with the aging of the baby boomers.[15,16]

Our economic and epidemiological model of treatment impact differs from many existing hepatitis C burden models[17–23] in two important ways. First, we explicitly accounted for the three primary exposure groups and genotypes of the virus, which enabled us to consider the impact of different transmission and disease progression dynamics. While other researchers[24,25] have examined the transmission element, they did not include distinct dynamics for multiple genotypes and exposure groups.

Second, we modeled the impact of treatment not only on people already infected but also on those who are uninfected but susceptible, and who might be spared infection as a consequence of reduced disease prevalence. To our knowledge, this is the first economywide analysis of hepatitis C treatment to take into account both disease progression and transmission.

Study Data And Methods

CONCEPTUAL MODEL We developed a discrete-time Markov model to simulate the progression of a population susceptible to hepatitis C through infection and several stages of the disease, and to investigate the impact of new regimens and treatment strategies on population outcomes. The model accounts for the impact of treatment on disease transmission, because the probability of new infection depends on the number of people currently infected in the population. It also permits investigation of the impact of alternative treatment strategies on both infected and uninfected populations. In addition, it enables us to explore the possibility of minimizing hepatitis C prevalence through aggressive treatment strategies. The model updates the numbers in each disease state annually. More details on the model structure and disease transmission dynamics can be found in the Appendix.[3]

For model tractability, the three exposure groups were modeled independently. Our model accounts for the three hepatitis C virus genotypes most common in the United States—genotypes 1, 2, and 3—which affect 70 percent, 16 percent, and 12 percent of hepatitis C patients, respectively.[3] Patients can be infected with only one genotype at a time. However, once a patient is cured, he or she can be reinfected with any of the three genotypes. The Appendix provides more details on the differences modeled across genotypes and exposure groups.[3]

Once patients are infected, they enter an acute phase, and they have some chance of spontaneously clearing the infection without treatment. Those who do not clear the infection during the acute phase progress to chronic disease, which consists of seven stages of liver damage: scores of F0–F4 on the Metavir fibrosis scoring system,[26] decompensated cirrhosis, and hepatocellular carcinoma.

Patients in stage F0 or above may receive hepatitis C treatment during the simulation. If they are cured, they are no longer infectious and join the susceptible population. If they are not cured, treated patients progress at the same rate as infected and untreated patients. If hepatitis C is cured in stages F0–F2, liver damage is assumed to have been reversed,[27,28] and patients return to the susceptible population with healthy livers.

Patients cured of hepatitis C in stages F3 and higher may progress to additional liver damage, although more slowly than patients with active

hepatitis C, and the model does not assume that their liver damage is reversed.[27] These patients are also susceptible to reinfection at the same rate as patients without liver damage, but if the patients cured in stages F3 and higher are reinfected, they reenter the infected population with liver damage.

Patients with decompensated cirrhosis or hepatocellular carcinoma who are cured of the hepatitis C virus are eligible for liver transplant. If they receive a transplant and later become reinfected, they reenter the infected population with healthy livers. For more details on the progression dynamics, see the Appendix.[3]

We accounted for aging among the health care exposure group by increasing the background mortality rate as this cohort aged. In the other two exposure groups, we assumed a stable age distribution with a constant background mortality rate, based on the rationale that the exiting of older people from the exposure group is counterbalanced by the entry of younger people.

Model parameters were drawn from the published literature.When parameters specific to the exposure group and genotype were available, we used them. Otherwise, we used unstratified estimates. The Appendix details the parameter values and their sources.[3]

TREATMENT SCENARIOS Four treatment scenarios were modeled. In all scenarios, only diagnosed patients could be treated, and the diagnosis rate was assumed to be 50 percent.[29–31]

The baseline scenario represents the status quo before the introduction of direct-acting antiviral agents, in which the best available treatment for hepatitis C is pegylated interferon alpha plus ribavirin. Regimen duration, efficacy, and costs differ by genotype.[3] Treatment in the baseline scenario is provided annually to all infected and diagnosed individuals who have scores of F3 or higher, which amounts to 296,000 patients treated in the first year.

The "treat advanced" scenario treats the same patients as in the baseline scenario but uses the most effective regimen available for their genotype. Thus, this scenario has higher treatment costs than the baseline one.

The "treat all diagnosed" scenario treats all infected and diagnosed patients with a score of F0 or higher with new regimens, with 1.3 million patients treated in the first year. It represents a hypothetical scenario designed to minimize hepatitis C prevalence as rapidly as possible. Because this scenario treats the same proportion of infected patients annually, it assumes that ongoing screening efforts identify the same proportion of previously undiagnosed patients every year.

The "treat all diagnosed" scenario could be prohibitively expensive, particularly for public payers, and difficult to implement given limited screening and treatment capacity. Therefore, the fourth scenario is "treat 5 percent," in which 5 percent of patients who are infected with a score of F0 or higher are treated with new agents.[31–33] In this scenario, 125,000 patients are treated in the first year.

New hepatitis C treatments have generated intense scrutiny from legislators, payers, and the media.

In all treatment scenarios that used new agents, the cost of treatment is assumed to drop by 46 percent in year 2 to account for market entry by other brand-name therapies, and by 79 percent in year 15 to account for patent expiration.[34,35]

MODEL OUTPUTS Using the approach described above, the model calculates the number of people in each disease state in each year. These populations are then multiplied by published estimates of annual disease state–specific per person values for quality-adjusted life-years (QALYs), hepatitis C treatment costs, and other nontreatment medical expenditures to generate populationwide estimates specific to each scenario.

To value QALYs, we used estimates derived from Richard Hirth and coauthors' analysis of forty-two QALY value estimates from the value-of-life literature.[36] Hirth and coauthors found that estimates varied by the methods used, with revealed-preference studies yielding intermediate values. In 2014 dollars the median value of a QALY from these types of analyses was $137,767 for studies of nonoccupational safety and $492,760 for studies of occupational safety. In baseline analyses we used a conservative estimate from this range, $150,000, but we considered values ranging from $100,000 to $200,000 in sensitivity analyses.[37]

Economic values were discounted at 3 percent per year. The hepatitis C transmission rate for each period was calculated from the size of the infected and uninfected populations in that period. The Appendix contains further details on how the transmission rate was calculated.[3]

LIMITATIONS Like any model, ours has several limitations related to assumptions made for tractability. Individuals are assumed to be treated only once per infection; those who do not respond to initial treatment are not treated again. Throughout, the model assumes that 50 percent of the population with hepatitis C infection is diagnosed—consistent with published estimates[29–31]—and that there is sufficient health care capacity to treat the infected at whatever rate is modeled.

In addition, the model does not account for behavioral changes that could result from the availability of a cure. For example, susceptible individuals might become more likely to engage in riskier behavior or to be screened.[38] Such behavioral changes could either increase or decrease infectivity overall. The model also does not account for the benefits associated with increased employment and reduced disability from hepatitis C treatment, because of uncertainty about the benefits' magnitudes. However, such benefits exist, and if they were included, they would tend to increase any estimate of the social value of treatment.[39–41]

Finally, all model parameters were derived from published literature, but some were uncertain. These included the size of the initial infected population, the value of a QALY, and the reduction in quality of life associated with various disease states. The impact of many of these limitations is explored in sensitivity analyses described below and in the Appendix.[3]

Study Results

Assuming a starting hepatitis C prevalence of 2.7 million, that number is reduced to 207,000 over fifty years in the baseline scenario (Exhibit 1). Treatment with newer agents reduces the prevalence more quickly in all of the other scenarios. After fifty years the prevalence is reduced to 103,000 in the "treat advanced" scenario, 39,000 in the "treat 5 percent" scenario, and 1,400 in the "treat all diagnosed" scenario.

Comparing just the scenarios that use newer agents, by year 7 the "treat 5 percent" scenario lowers prevalence by more than the "treat advanced" scenario in spite of treating fewer patients, though at earlier stages in the disease process. The "treat all diagnosed" scenario produces a very low disease burden by year 10, with fewer than 50,000 infected people.

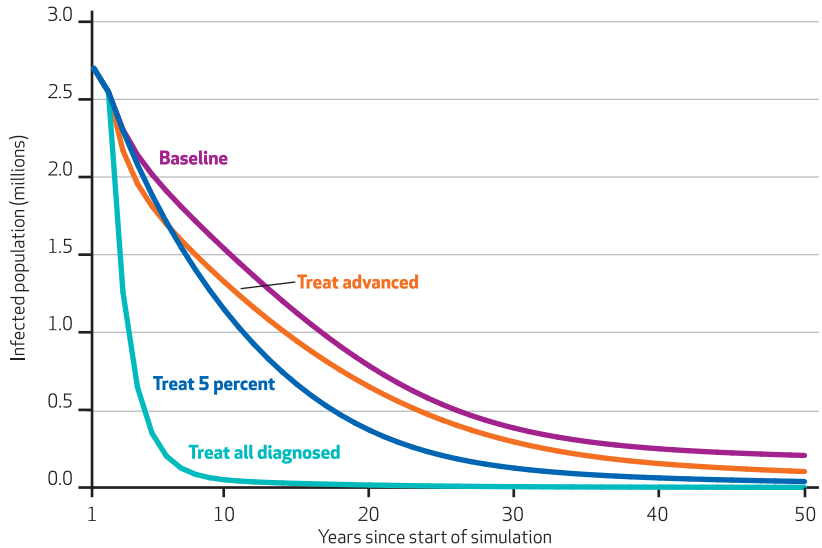
Compared to the baseline scenario, the "treat advanced" scenario costs more in every year of the simulation, amounting to an additional $105 billion in medical and treatment expenditures over fifty years (Exhibit 2). The "treat all diagnosed" scenario results in large expenditures within the first ten years to treat the initial diagnosed population. However, over time fewer patients require treatment relative to baseline as transmission of the disease falls, and cumulative expenditures over baseline decline quickly. Nontreatment medical expenditures also decline relative to baseline, which partially offsets the higher treatment costs. After thirteen years, the cumulative expenditures in this scenario are lower than those in the "treat advanced" scenario, and after fifty years they are $34 billion less than in the baseline scenario.

Cumulative expenditures in the "treat 5 percent" scenario reach a maximum of $22 billion more than baseline after eight years and decline thereafter. After sixteen years, this scenario is less costly than the baseline one.

Compared to the baseline scenario, the other three treatment scenarios generate more value from QALYs, ranging from $87–$175 billion for the "treat advanced" scenario to $610–$1,221 billion for the "treat all diagnosed" scenario (stacked blue bars in Exhibit 3). All three scenarios result in increased discounted treatment costs, compared to the baseline scenario. The "treat advanced" scenario increases discounted nontreatment medical expenditures by $39 bil-

EXHIBIT 1

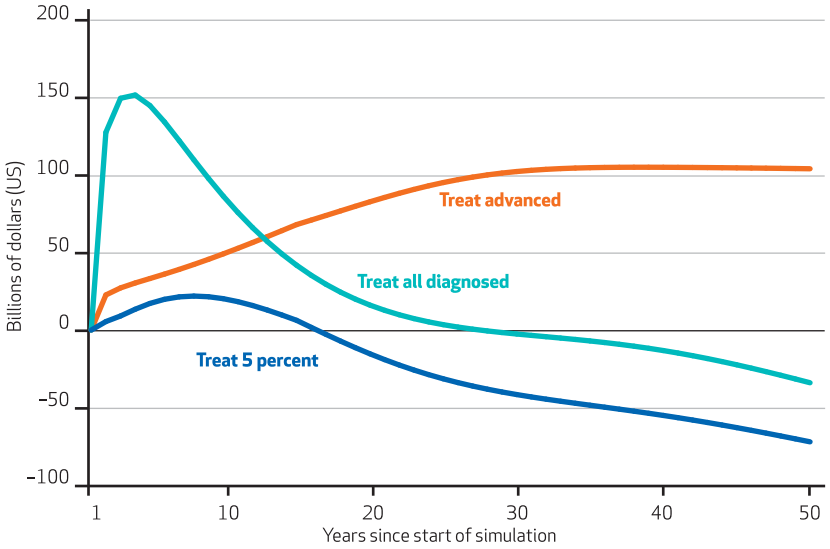
Size Of The US Population Infected With Hepatitis C In A 50-Year Simulation, By Treatment Scenario



SOURCE Authors' analysis of model results. **NOTES** The simulation starting year was 2014. The "baseline" treatment scenario treats all of the population infected and diagnosed with hepatitis C virus with advanced disease (a score of F3 or higher on the Metavir fibrosis scoring system, decompensated cirrhosis, or hepatocellular carcinoma) with old agents annually. The "treat advanced" scenario treats the same population with new agents annually. The "treat 5 percent" scenario treats 5 percent of the infected population with a score of F0 or higher with new agents annually. The "treat all diagnosed" scenario treats all of the population infected and diagnosed with a score of F0 or higher with new agents annually. For more details on the scenarios, see the text.

EXHIBIT 2

Cumulative Hepatitis C Treatment And Nontreatment Medical Expenditures Net Of Baseline Expenditures In A 50-Year Simulation, By Treatment Scenario



SOURCE Authors' analysis of model results. **NOTES** The simulation starting year was 2014. The scenarios are described in the notes to Exhibit 1. Per period treatment and nontreatment medical expenditures were taken from the literature, as discussed in the text. More details on parameter values and sources are available in the Appendix (see Note 3 in text).

lion over fifty years. The "treat 5 percent" and "treat all diagnosed" scenarios reduce them by $55 billion and $139 billion, respectively. If a ten-year horizon is used instead of a fifty-year one, treatment costs, nontreatment medical expenditures, and value from QALYs all have the same general shape as in the fifty-year case, but total benefits exceed treatment costs only in the "treat all diagnosed" scenario (for ten-year horizon results, see the Appendix).[3]

Exhibit 4 shows the total social value from treatment using different values for a QALY and the manufacturers' share of the social value. Part of this social value is the value of health gains, which includes the value of QALYs gained by patients and any savings in nontreatment medical expenditures, since those medical savings free up resources that can be deployed elsewhere. For example, Exhibit 3 shows that in the "treat all diagnosed" scenario with QALYs valued at $150,000 each, the value of the QALYs gained is $916 billion, and reduced medical spending frees up additional resources of $139 billion, for a total health gain of $1,055 billion.

In addition to health gains, social-value calculations typically also include any profits earned by manufacturers, and we considered two scenarios for calculating profits. First, we assumed that the costs of production for these oral agents were negligible and that manufacturers' profits were equal to their revenues. This assumption provides an upper bound on total social value.

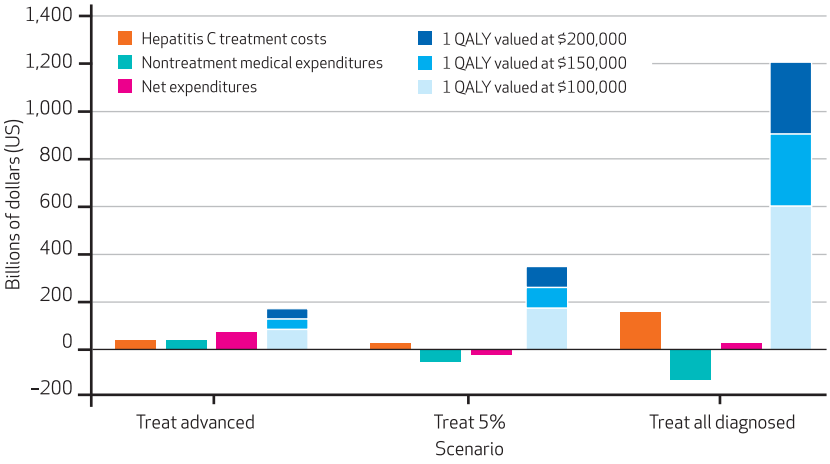
To put a lower bound on that value, we made a set of conservative assumptions about the costs of production. In particular, we assumed that the research and development costs were $2.6 billion, based on recent research.[42] This figure is well above the $0.3 billion that others have cited.[43] We then assumed that the cost of production of the drug was 21 percent of the treatment cost, a figure that is in line with the literature[34] and that should be conservative, given the relatively high price of the therapy. Thus, in the lower-bound scenario, the total social value in the "treat all diagnosed" scenario falls between $883 million (if each QALY is valued at $100,000) and $1,493 billion (if the value is $200,000), with manufacturers' profits representing 9–15 percent of that value (Exhibit 4). In the upper-bound scenario, total social value in the "treat all diagnosed" scenario ranges from $916 to $1,527 billion, depending on the value of each QALY used, with manufacturers' profits representing 11–18 percent of that value.

Depending on the value of each QALY, the "treat advanced" scenario generates $83–$170 billion in total value in the lower-bound scenario, with manufacturers' profits representing 20–42 percent of the total value. In the upper-bound scenario, the value is $87–$175 billion, with manufacturers' profits representing 22–45 percent, depending on each QALY's value.

Under the assumptions in the lower-bound scenario, the "treat 5 percent" scenario gener-

EXHIBIT 3

Cumulative Discounted Costs And Benefits Of Hepatitis C Treatment Strategies In A 50-Year Simulation Relative To Baseline, By Treatment Scenario



SOURCE Authors' analysis of model results. **NOTES** Benefits are expressed as quality-adjusted life-years (QALYs). The scenarios are described in the notes to Exhibit 1. All model parameters are taken from the literature, as discussed in the text. The discount rate is 3 percent. More details on parameter values and sources are available in the Appendix (see Note 3 in text).

EXHIBIT 4

Discounted Social Value (In Billions Of Dollars), Net Of Baseline, From Treating Hepatitis C Over 50 Years, By Treatment Scenario

	Total social value and manufacturer share					
	QALY value = $100,000		QALY value = $150,000		QALY value = $200,000	
Scenario	Total	Manufacturer	Total	Manufacturer	Total	Manufacturer
LOWER-BOUND SCENARIO[a]						
Treat advanced	$ 83	42%	$ 126	27%	$ 170	20%
Treat 5 percent	258	10	347	8	435	6
Treat all diagnosed	883	15	1,188	11	1,493	9
UPPER-BOUND SCENARIO[b]						
Treat advanced	$ 87	45%	$ 131	30%	$ 175	22%
Treat 5 percent	260	11	349	8	437	6
Treat all diagnosed	916	18	1,222	14	1,527	11

SOURCE Authors' analysis of model results. **NOTES** All social-value amounts are in billions of dollars. Social-value calculations for alternative treatment scenarios are relative to the baseline scenario. All four scenarios are described in the notes to Exhibit 1. Social benefits include health benefits (quality-adjusted life-years, or QALYs, gained) and any savings (or loss) in nontreatment medical expenditures relative to the baseline scenario, as shown in Exhibit 3. All model parameters were taken from the literature, as discussed in the text. The calculation for adding the manufacturer's share in total social value is discussed in the text. The discount rate is 3 percent. More details on parameter values and sources are available in the Appendix (see Note 3 in text). [a]Assumes that the manufacturer's costs include $2.6 billion in research and development and unit manufacturing costs of 21 percent. [b]Assumes zero production costs—that is, the manufacturer's profits equal revenues.

ates $258–$435 billion in total value, with manufacturers' profits of 6–10 percent. Under the assumptions in the upper-bound scenario, the "treat 5 percent" scenario generates $260–$437 billion in total value, with manufacturers' profits of 6–11 percent.

We conducted sensitivity analyses along several dimensions, exploring the impact of changes in the following key variables: the initial size of the infected population, value of a QALY, retreatment for patients who fail initial baseline therapy, diagnosis rate among patients in the health care exposure group, treatment rate among those who are diagnosed, drug costs, and quality of life in early disease states. The analyses are detailed in the Appendix, and the results are presented in Tables A8 and A9.[3]

Importantly, the net social value of all three alternative treatment scenarios was positive compared to baseline for all of the parameter values tested. In the baseline scenario, the total infected population remained above 200,000 during the fifty-year simulation in all sensitivity analyses performed, except when retreatment with the baseline therapy was allowed. In this case, the infected population dropped below 200,000 in forty-eight years.

When we considered the results of all of the sensitivity analyses performed, we found that the "treat 5 percent," "treat advanced," and "treat all diagnosed" scenarios could reduce hepatitis C prevalence to under 200,000 within at most twenty-seven, thirty-eight, and eleven years, respectively.

Discussion

Most cost-effectiveness analyses of hepatitis C treatment have been based on models of populations of already infected individuals.[44–47] Such models do not account for the ongoing transmission of hepatitis C and hence the benefits of treatment to those currently uninfected. As a result, most models tend to undervalue treatments that reduce the number of infected individuals in the population. By explicitly incorporating this transmission dynamic, our model provides a more complete picture of the total social value of treatment over time.

Our results are broadly consistent with those of several other modeling studies of hepatitis C burden in the United States. Specifically, our study and three other modeling studies found that without the introduction of direct-acting antiviral agents, hepatitis C prevalence will decline to levels of 1.0–1.8 million by 2030.[22,32,48] Both our study and that of Mina Kabiri and coauthors[32] found that in the absence of direct-acting antiviral agents, hepatitis C prevalence would decline to about 400,000 by 2050 (compare our baseline scenario to the "Pre-DAA" scenario in Kabiri and coauthors' study).[32] Both our model and that of Kabiri and coauthors project that high coverage levels with the most effective new treatment regimens could further reduce hepatitis C prevalence to under 100,000 by 2050 (compare our "treat all diagnosed" and "treat 5 percent" scenarios with Kabiri and coauthors' "ideal" scenario).[32]

There are lessons here for reimbursement pol-

icy. Payers are debating how best to provide access to expensive new hepatitis C treatments within already tight budgets. Several payers have begun to implement policies that provide new treatments only to those with the most severe liver damage.[49] Our model shows that such a strategy increases social value: Despite their high costs, substituting new hepatitis C treatments for old ones could add $83–$175 billion in net social value, if the new treatments were administered to only the sickest patients.

However, treating patients at earlier stages of disease would have even greater benefits to society. A policy of treating every patient with new agents, regardless of the extent of his or her liver damage, would generate $0.8–$1.5 trillion in total social value, compared to the baseline scenario, or roughly ten times the social value of treating only patients with advanced disease. Over fifty years, this would break down into about $0.6–$1.2 trillion from improved health, $139 billion from reduced medical spending by preventing costly liver damage, and $0.1–$0.2 trillion in manufacturers' profits (Exhibit 3).

However, treating all diagnosed patients would cost nearly $167 billion more than baseline treatment, discounted over fifty years (Exhibit 3) and, with 1.3 million patients treated in the first year alone, would require much greater treatment capacity than is currently available.[31] The introduction of new hepatitis C therapies has generated great interest in expanding treatment capacity because they can be administered by primary care physicians, whereas older therapies using interferon and ribavirin had to be administered by specialists.[33,50] Pilot efforts using teleconferences to train primary care physicians to manage and treat hepatitis C have been promising. However, they are still nascent, and widespread expansion of capacity will take time. Although immediately treating all patients diagnosed with hepatitis C might generate more social value than other strategies, it would likely be impossible to implement that policy in the near term.

Thus, the "treat 5 percent" scenario, which treats 125,000 patients in the first year, represents a more realistic scenario given current treatment capacity. This scenario generates more value than the "treat advanced" scenario from all three sources (the number of QALYs, medical spending, and disease transmission). Compared to that scenario, the "treat 5 percent" scenario leaves more individuals infected in the first six years of the simulation, but it leaves fewer infected in year 7 and beyond. Over fifty years, the "treat 5 percent" scenario generates roughly $175–$260 billion more in social benefits than the "treat advanced" scenario, and by curing people at earlier disease stages, it prevents progression to cirrhosis and hepatocellular carcinoma.

Treating patients at earlier stages of liver disease generated more value than waiting to treat them until liver damage had progressed.

We conducted several sensitivity analyses to explore alternative values for various model parameters (for details about those analyses and their results, see the Appendix).[3] The overall conclusions from the model remained largely unchanged: Under a wide range of parameter values, treatment with new agents, while expensive, generated more social value than treatment with less expensive older agents, and treating patients at earlier stages of liver disease generated more value than waiting to treat them until liver damage had progressed.

Since recent recommendations for universal screening among baby boomers may increase the hepatitis C diagnosis rate among the health care exposure group, we also conducted sensitivity analyses in which we increased the proportion of baby boomers diagnosed with the virus. Social value changed somewhat, but it remained at a similar magnitude in all of the treatment scenarios.

We also tested a reduction in the proportion of diagnosed patients who were treated, with similar results. Allowing for retreatment of infection—an issue that is being debated by payers and policy makers—did not change the results appreciably because efficacy is already so high. In a few cases, it raised costs modestly, but it also increased social value.

Conclusion

The treatment of hepatitis C poses many challenging questions for the US health care system. Innovative treatments for the virus can generate tremendous value, and treating all diagnosed patients immediately reduces the disease burden from hepatitis C infection most rapidly and gen-

erates the greatest social benefits, compared to other scenarios. But tightening US health care budgets and limited treatment capacity render the strategy of treating everyone at once infeasible. Thus, new treatments must instead be meted out over time.

Limiting access to new therapies to a subset of diagnosed patients prolongs disease transmission and generates less value, but it is more realistic given system capacity constraints. It also requires a difficult trade-off between patients who will and those who will not get the new treatments. Many state Medicaid programs limit access to newer treatments by requiring patients to meet clinical criteria—often requiring a diagnosis of advanced disease (a score of F3 or higher on the Metavir fibrosis scoring system)—to gain prior authorization.[49] For more details about prior authorization requirements, see the Appendix.[3]

But we have shown that a strategy that treats patients earlier in the disease progression can cost less, increase total QALYs more, and reduce future medical expenditures further than a strategy that treats them later. In fact, the cumulative expenditures over fifty years under a strategy of earlier treatment are $105 billion lower than those under a strategy of treating only the sickest patients (Exhibit 3, net expenditures of the "treat 5 percent" scenario compared to those of the "treat advanced" scenario). Identifying the optimal treatment strategy—given limited public and private payer budgets now and health benefits that accrue much later—may be one of the most vexing health policy challenges facing the United States. ■

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3 To access the Appendix, click on the Appendix link in the box to the right of the article online.

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