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THE FUTURE OF CURES: INVESTING IN VALUE, INNOVATION AND ACCESS

Work by researchers at the USC Leonard D. Schaeffer Center for Health Policy & Economics illustrates how game-changing medical innovations for prevalent diseases, including diabetes and Alzheimer's disease, could generate billions of dollars in value to society and more than justify high price tags. For example, they estimate a five-year delay in onset could reduce prevalence of Alzheimer's in 2050 by 3.7 million patients, or 40.6 percent, and save nearly $600 billion in total care costs by 2050. But when targeting which new therapies to develop, pharmaceutical manufacturers must choose between pursuing cures to be used for a short period and discontinued once the patient is well, or chronic therapies that manage but do not cure disease, to be taken for the patient's lifetime. The economics of this choice often favor the chronic treatment, unless a cure can be sold at a very high price. But high prices bring their own problems, from public outcry and political backlash to affordability barriers that keep the patients who need the cures or breakthrough treatments from getting them. Along with innovative financing methods, novel pricing models that better align the cost of all drugs—not just cures—to the value they provide may be ways to ensure the risk is not too high or the reward too little for drug makers to pursue cures that generate tremendous social value.

U.S. Life Expectancy Increases Dramatically

Over the last 100 years or so, the average American's lifespan has increased by nearly two-thirds—from 47.3 years in 1900 to 78.7 years in 2014.[1] Much of the increase in life expectancy during the first half of the 20th century resulted from improvements in infectious disease control, both through public health advances like safe drinking water and innovations in medical care including antibiotics that cured bacterial infections and vaccines that prevented small pox, polio and measles.[2]

As noncommunicable diseases like heart disease and stroke, cancer, Alzheimer's disease, and diabetes replaced infectious diseases as the leading killers of Americans in the second half of the 20th century, advances in medical care played an even larger role in driving longer U.S. lifespans. By one estimate, lower cardiovascular disease rates are responsible for 70 percent of the seven-year increase in life expectancy between 1960 and 2000, with the bulk of the decline in mortality—as much as two-thirds—attributable to advances in cardiovascular care.[3]

Across the globe, if medical innovations that essentially cure once-deadly diseases could eradicate hepatitis C and six other plausible targets—malaria, measles, mumps, rubella, filariasis and pork tapeworm—an estimated 1.2 million lives would be saved annually.[4]

Faster development of breakthrough therapies and cures is a U.S. priority. In recent years, legislative and regulatory actions have authorized the Food & Drug Administration (FDA) to expedite approvals of promising drugs. New FDA tools include designations for breakthrough therapies when preliminary clinical evidence indicates a drug to treat a serious or life-threatening condition offers "substantial improvement over existing therapies" and fast track approval for drugs that fill unmet treatment needs for serious conditions.[5]

Value of a Cure

Work by researchers at the USC Leonard D. Schaeffer Center for Health Policy & Economics illustrates what such game-changing innovations could mean for Americans in the 21st century. Among other tools, Schaeffer Center researchers use the Future Elderly Model (FEM)—a microsimulation model of health and economic outcomes for older Americans—to explore the impact on the U.S. population of changes in health technology or policy. The FEM follows Americans aged 51 years and older and projects their health and medical spending over time. Rather than following the average or aggregate characteristics of a cohort,[6] the FEM follows the evolution of individual-level health trajectories and economic outcomes.

Several published FEM studies show the possible impact of breakthrough therapies that cure, dramatically reduce the incidence or delay onset

of various diseases, including diabetes and Alzheimer's disease. One such study examined the implications of hypothetical treatment improvements for diabetes and hypertension, including a cure for both conditions.[7] Researchers estimated that a cure for diabetes would increase the average life expectancy of a person aged 51-52 in 2004 by 1.36 years and reduce per-capita lifetime medical spending by nearly $15,000. The total discounted value associated with a diabetes cure is more than $280,000 per person cured.[8] Similarly, a cure for hypertension would generate over $200,000 in value per person.

While cures may be thought of as the paragon of medical innovation, preventing or delaying onset of a disease also has immense value. One Schaeffer Center study looked at the impact of a hypothetical breakthrough technology that could delay the onset of Alzheimer's disease.[9] Although the scenarios studied fell significantly short of a "cure," the potential gains were enormous: For a one-year delay in onset, the number of patients with Alzheimer's in 2050 fell 14.3 percent—from 9.1 million to 7.8 million people—and the total cost of caring for patients with the disease fell by $219 billion. A five-year delay in onset was estimated to reduce 2050 prevalence of Alzheimer's by 3.7 million patients, or 40.6 percent, and save nearly $600 billion in total care costs by 2050 (see Figure 1).

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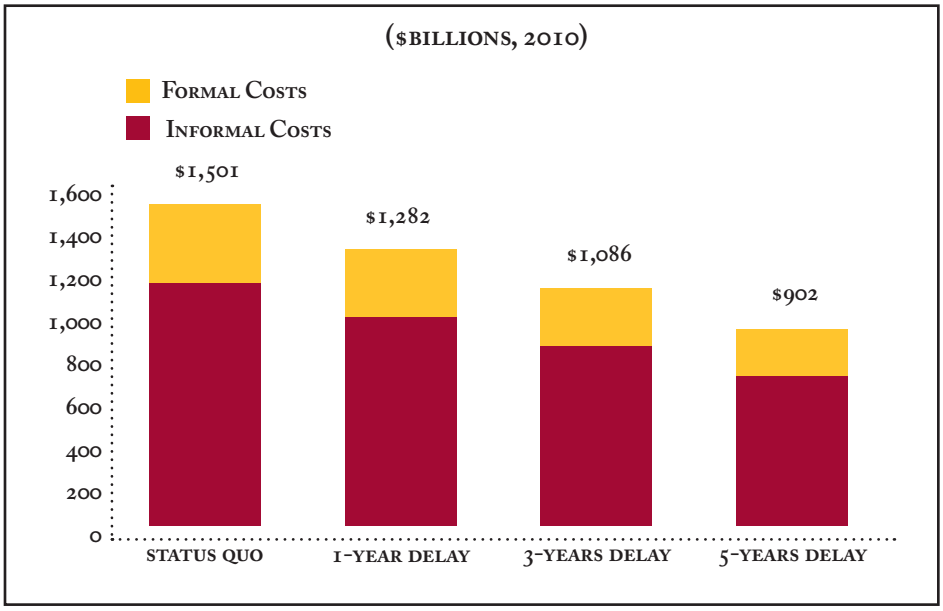
Figure 1

Total Costs of Care in 2050 for Persons Aged 70+ with Alzheimer's Disease delaying onset for 1, 3 and 5 years



Source: Zissimopoulos et al., "The Value of Delaying Alzheimer's Disease Onset," Forum for Health Economics and Policy *(2015).*

Potential Even Greater for Infectious Diseases

The population dynamics of a cure or treatment breakthrough are even more compelling for infectious diseases like hepatitis C and HIV/AIDS. Recently introduced therapies for hepatitis C are effective in upwards of 90 percent of patients, and combined antiretroviral therapy (cART) has rendered HIV/AIDS, once considered a death sentence, a chronic disease that has little impact on life expectancy when treated early.[10]

Because these diseases are transmissible, the benefits of curing one patient are not limited to the cured patient, who

benefits from longer life expectancy, lower medical expenditures and higher quality of life. Benefits also accrue to healthy people who avoid illness because the cured patient never infects them.

A 2015 study published in *Health Affairs* found that prevalence of hepatitis C in the United States could be reduced from 2.7 million people to less than 50,000 in 10 years if all U.S. patients diagnosed with hepatitis C were treated with the new generation of antiviral therapy.[11] Such a step could generate total social value of $1.2 trillion over the next 50 years.

Although cART does not cure HIV/AIDS, it dramatically reduces viral loads in infected patients and reduces the probability that a person under treatment will transmit the infection to others. According to another *Health Affairs* study, guidelines for initiating cART earlier in the course of the disease prevented 188,000 cases of HIV in the period from 1996 through 2009, and the life-years saved by early treatment with cART were worth $128 billion.[12]

Pay Now or Pay Later

While having more cures and breakthrough treatments would clearly be valuable to society, there is a real question of whether and how quickly such innovations will come to market, because the playing field is tilted away from them and toward therapies to manage long-term chronic disease. When considering what types of new therapies to search for and develop, pharmaceutical manufacturers face a stark calculus. A cure will be used by a sick patient once for a relatively short period and discontinued once the illness is resolved, eliminating a market.

In contrast, a therapy that treats—but does not cure—a chronic disease will be taken for the remainder of a patient's lifetime. To earn enough revenue to recover considerable development expenses, manufacturers of a cure must charge a high price—in some eyes, too high a price—for a short time. And while the one-time cost of a cure seems formidable, manufacturers of a chronic treatment often can charge a much lower price per dose over a much longer period of time to essentially earn the same amount—or even more—per patient.

Where Have All the Antibiotics Gone?

At a time when the U.S. and the world face a growing public health crisis of drug-resistant superbugs, the dearth of new antibiotics coming to market provides another example of the disincentives drug makers face in developing cures. Between 1940 and 1962, more than 20 new classes of antibiotics were developed and brought to market. In contrast, only two new classes of antibiotics were marketed between 1962 and 2011.[13] And, by one count, more than 35 large U.S. and European drug makers were researching antibiotics in 1980, while now there are four.[14]

Explaining this decline more than a decade ago, Steve Projan, then an executive with Wyeth Pharmaceuticals, wrote that "[t]he cost and complexities of drug discovery and development have shifted the investment equation away from the development of drugs targeting short course therapies for acute diseases and towards long-term treatment of chronic conditions."[15] In sum, the economic incentives manufacturers face to develop short course therapies, including cures like antibiotics, are less compelling than incentives to develop long-term therapies for chronic disease.

In the case of antibiotics, the FDA has implemented programs specifically to jumpstart more research and development. Under authority granted by the 2012 federal Generating Antibiotic Incentives Now Act, the FDA can now grant special status—qualified infectious disease product (QIDP)—to antibacterial drugs targeting serious or life-threatening infections. QIDPs receive expedited approval and five years of market exclusivity beyond existing patent protections.

There is some evidence that these programs may be working. As of early 2015, the FDA had approved six new QIDP-designated antibiotics, but all were modifications of known classes of antibiotics.[16] A truly new class of antibiotic— teixobactin—was reported in January 2015 but is still years away from human trials, let alone clinical use. The renewed interest in antibiotic development indicates targeted FDA incentive programs like QIDP and other regulatory mechanisms may help overcome the weak economic incentives manufacturers face when developing short-course therapies, including cures.

Miracles Don't Come Cheap

For drug makers interested in pursuing cures, charging high prices for a cure or breakthrough therapy—even for a short time—poses challenges, including potential access problems and public backlash. When the latest generation of hepatitis C cures was first introduced, many state Medicaid programs and other payers essentially rationed the treatment, providing it only to the sickest patients, despite its proven value to all patients, because their budgets couldn't handle large-scale treatment expenses over a short time.[17] And even when new drugs are genuine miracle cures that generate enormous value, setting a high price for them invites public outrage. When Gilead set the list price of Sovaldi at $84,000 for a 12-week course of treatment, public backlash was swift and strong, with protesters picketing outside Gilead meetings, a U.S. Senate investigation, and lawsuits alleging price gouging.[18]

Policy Implications

Even if regulatory changes can help strengthen incentives and diminish the uncertainty companies face when pursuing cures, breakthrough therapies will still command steep launch prices to provide innovators adequate return on investment. Therefore, the biggest hurdle to new cures may be how society is going

to afford breakthrough therapies.

Again, new hepatitis C treatments clearly illustrate the problem. In the U.S. alone, an estimated 3.5 million people have the disease, while worldwide the estimate is 130 million to 150 million people.[19] Even though the price of new treatments has been declining rapidly, the short-term costs of eradicating hepatitis C remain daunting. For example, the cost of treating hepatitis C to Medicare alone exceeded $4.7 billion in 2014.[20]

At its introduction, any new cure for a prevalent condition will generate a large number of patients needing immediate access, and payers may struggle to fund access to such a large volume of patients all at once. New approaches to financing access to cures—such as installment plans or bond issues in the case of public payers—that spread the cost of a cure over a longer horizon may be needed, particularly when the cure is first introduced. And novel pricing models that better align the cost of all drugs—not just cures—to the value they provide will simultaneously reward the development of breakthroughs and cures while improving system-wide affordability.

Just as public and private investments built the water and sewer systems that delivered safe drinking water and contributed to longer U.S. lifespans in the early 20th century, devising ways to finance cures may be the key to longer and healthier lives in the 21st century. Without changes to current pharmaceutical industry incentives to develop cures, the alternative will likely be far fewer future cures and continued incremental innovation targeted at keeping chronic disease sufferers filling prescriptions. ■

Notes

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