



Medicine Markup

Americans pay a lot for prescription drugs. Does that mean we pay too much?

By Jessie Romero

Diabetics rationing their insulin because they can't afford the full dose. Senior citizens choosing between filling their prescriptions and buying groceries. Parents hoping an expired EpiPen will still work if their child has an allergic reaction.

Stories about Americans unable to pay the high cost of prescription drugs are not new. But in recent years, drug prices have drawn increased attention from policymakers on both sides of the aisle, prompted by the advent of expensive new treatments for Hepatitis C, cancer, and other illnesses, as well as steep price increases for existing treatments such as EpiPens and insulin. Prices look especially high when compared to those in many other developed countries, particularly in Europe.

In theory, the lack of drug price regulation in the United States stimulates innovation: The potential for high returns is why pharmaceutical manufacturers (and their investors) are willing to fund risky and expensive research. In practice, however, there are reasons to believe that the large revenues pharmaceutical companies earn from the U.S. market reflect not just the value of the innovations the companies have provided, but also the efforts those companies have expended to circumvent competition.

There are several reasons policymakers may want to ask to what extent drug pricing leads to an efficient distribution of resources. Prescription drug spending totaled nearly \$330 billion in 2016, 1.8 percent of GDP, and the government paid for more than 40 percent of it. More generally, drug spending and health expenditures overall affect both sides of the Fed mandate to support maximum employment and price stability. Health care spending totals 18 percent of GDP and health care is the third-largest employment sector. In addition, medical spending can alter the behavior and overall level of inflation. "The U.S. [pharmaceutical] system performs well when competitive forces are

strong,” wrote Fiona Scott Morton and Lysle Boller of Yale University in a 2017 paper. But when manufacturers can earn high profits by weakening or sidestepping competition, “the system no longer incentivizes the invention of valuable drugs. Rather, it incentivizes firms to locate regulatory niches where they are safe from competition on the merits with rivals.”

Americans Pay More for Drugs

“Price” is not a straightforward concept in the pharmaceutical industry. Manufacturers sell drugs to wholesalers, who distribute them to pharmacies and mail order prescription services, who then distribute them to patients according to the reimbursement plans established by insurers and pharmacy benefit managers. At each step along the way, buyers and sellers negotiate substantial — and confidential — rebates and discounts. As a result, the published list price is generally much higher than what patients actually pay, although that is less true for patients with a high-deductible insurance plan or no health insurance at all.

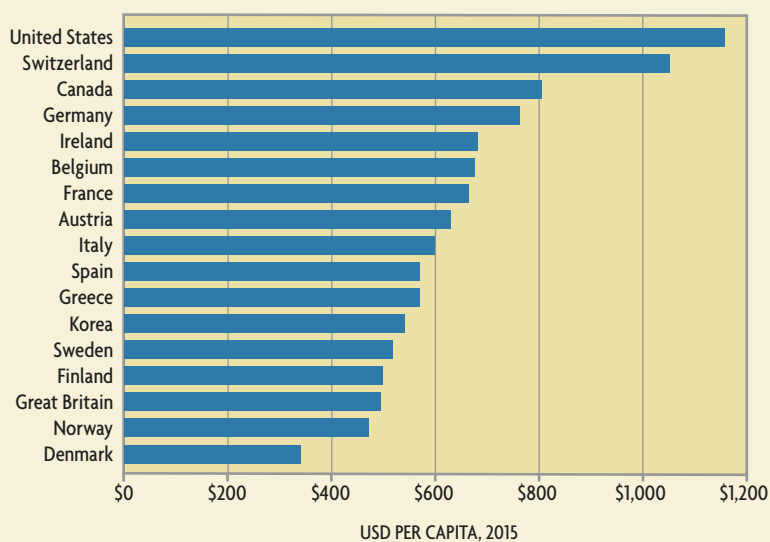
Even taking those discounts into account, which researchers can do by comparing sales data to list prices, Americans pay more for many prescription drugs. Net prices in the United States for the country’s 20 highest-selling drugs averaged more than twice the list prices in four other developed countries in 2015, according to research by Nancy Yu and Peter Bach of the Memorial Sloan Kettering Cancer Center and Zachary Helms, formerly a project coordinator at the center.

A Bloomberg analysis found similar results. In 2015, the cholesterol pill Crestor cost \$86 per month after discounts in the United States versus list prices of \$41 in Germany, \$32 in Canada, and \$20 in France. Humira, which treats rheumatoid arthritis, cost \$2,505 per month after discounts in the United States but listed for just \$1,749 in Germany, \$1,164 in Canada, and \$982 in France. Partly as a result, per capita drug spending in the United States far exceeds per capita spending in other developed countries. (See chart.)

Prices are higher in the United States for many medical goods and services, not just prescription drugs, and by some measures drug spending has remained on par with overall medical spending. According to data from the Centers for Medicare and Medicaid Services (CMS), for example, drug spending has fluctuated around 10 percent of total health care spending since the early 2000s. Other measures paint a different picture, however. According to the Bureau of Economic Analysis (BEA), drug prices increased nearly 70 percent between 2002 and the end of 2017, while prices for health care services increased 43 percent. In contrast to the CMS, the BEA data suggest that drug spending has increased from about 16 percent of health care services spending to 20 percent of spending over the past 15 years.

Dollars for Drugs

Higher drug prices contribute to higher per capita drug spending in the United States



NOTE: Per capita spending refers in most countries to “net” spending, i.e., adjusted for possible rebates. Data include spending on over-the-counter drugs. Data exclude pharmaceuticals consumed in hospitals or other health care facilities.

SOURCE: Organisation for Economic Co-operation and Development

Do High Costs Justify the High Prices?

Developing new drugs is risky. Researchers may test thousands of molecules before they identify a compound with the potential to be a new drug. Of the few compounds that do proceed to the first phase of human clinical testing, only about 10 percent go on to gain Food and Drug Administration (FDA) approval.

It’s also expensive. Pharmaceutical companies spend about \$1.4 billion on average to research and test an entirely novel drug, or “new molecular entity,” according to a 2014 estimate by researchers at Tufts University’s Center for the Study of Drug Development (CSDD). Including the cost of capital and the costs of failed drugs, the total price tag rises to \$2.6 billion. The last estimate the CSDD released, in 2003, put the cost of a new drug at \$800 million; the authors attribute the difference largely to the increased cost and complexity of clinical trials.

The CSDD study, which was based on survey data from 10 multinational firms, might overstate the cost of developing the typical drug, as new molecular entities are only a small share of the drugs that come to market. Most new drugs are variations on existing molecules and thus far less costly to develop. Also, the study includes only drugs that were first developed in-house — but increasingly, large multinationals license drugs from the smaller biotech firms that conduct the initial research. Other research suggests new drugs can be developed for less than \$1 billion.

Whatever the actual cost of each new drug, there’s no doubt pharmaceutical companies spend a great deal of money on research and development. In 2015, U.S.-based manufacturers spent \$75 billion on R&D, according to the Pharmaceutical Research and Manufacturers of America, a trade group, and they had higher R&D intensity (the ratio

of R&D to revenues) than other sectors. The National Science Foundation calculated that R&D intensity among pharma companies was 12.9 percent in 2015, compared to 9.8 percent in computer products, 8.5 percent in aerospace, and 6.7 percent in chemical manufacturing.

While high R&D spending is often used to explain high drug prices, there is a flaw in that reasoning, says Margaret Kyle, an economist at MINES ParisTech and a visiting professor at Northwestern University. “The causality is reversed. Pharmaceutical companies expect high prices, which allows them to justify making very large investments — rather than giving them greater incentive to look for ways to lower their costs by, say, running clinical trials more efficiently.”

In addition, the revenues pharmaceutical companies earn from high U.S. prices far exceed their R&D investments, according to Yu, Bach, and Helms’ research. They contend this pokes holes in the argument that high prices are necessary to cover high costs. For the 20 top-selling drugs in the United States, they compared revenue earned in the United States to the revenue earned in several European countries and Canada. The premium earned in the United States by U.S. net prices being higher than other countries’ list prices totaled \$116 billion. Only about two-thirds of that “excess” revenue was spent on global R&D.

But revenue earned today is the result of past investments, and there is no guarantee that today’s investments will yield the same returns. In fact, after increasing 290 percent between 2010 and mid-2015, the S&P pharmaceutical stock index fell nearly 30 percent over the subsequent two and a half years. (In comparison, the S&P 500 index increased 111 percent between 2010 and mid-2015 and has risen an additional 32 percent since then.)

Research suggests that the returns from pharmaceutical R&D are declining. In a 2015 article, Ernst Berndt of the Massachusetts Institute of Technology and several co-authors from the IMS Institute for Healthcare Informatics calculated net economic returns for drugs launched between 1991 and 2009. They found that the average present value for lifetime sales for drugs launched between 2005 and 2009, the most recent cohort studied, had declined to less than \$3 billion from more than \$5 billion for the 2000-2004 cohort. “If this level of diminished returns persists,” the authors concluded, “we believe that the rewards for innovation will not be sufficient for pharmaceutical manufacturers to maintain the historical rates of investments needed to sustain biomedical innovation.”

The Government’s Role in Prices

France made headlines in 2014 when its government negotiated a price of about \$51,000 for a 12-week course of Sovaldi, a breakthrough drug that cures Hepatitis C, by threatening to tax drug makers if the health ministry’s costs exceeded a certain level. In the United States, the list price for the same treatment was \$84,000, a difference that many

attributed in part to the increased negotiating power that comes from having a single-payer health care system.

The U.S. government does pay a significant portion — roughly 42 percent — of the country’s prescription drug costs through Medicare, Medicaid, the Department of Veterans Affairs, and other insurance programs. But the market is still highly fragmented: In 2018, there will be nearly 800 stand-alone prescription drug plans available to seniors through Medicare Part D, for example. (In previous years, there have been more than 1,000 available plans.) The insurers who provide these plans can negotiate with drug manufacturers, but the 2003 law that created Part D also barred Medicare itself from doing the same.

In some circumstances the government does intervene in pricing. The federal 340B program requires drug manufacturers to give discounted prices to certain hospitals and other facilities with a high proportion of low-income patients. In addition, Medicaid, the Veterans Administration, and the Department of Defense receive mandatory discounts and rebates and are allowed to negotiate for further reductions. Because these organizations’ discounts are based on the prices charged elsewhere in the market, however, some research suggests these rules have actually led drug manufacturers to raise prices overall.

At a national level, the United States is the only developed country that does not regulate drug prices in some manner. The primary objection to enacting such regulations, or to allowing Medicare to negotiate lower prices, is that such policies would reduce pharmaceutical companies’ incentive to innovate. “Without doubt, government-imposed price controls in the largest market in the world would seriously harm investment in the next generation of medical breakthroughs,” according to the Biotechnology Innovation Organization, a Washington, D.C.-based trade group.

The group cites research by Joseph Golec of the University of Connecticut and the late John Vernon of the University of North Carolina at Chapel Hill. In a 2010 article, they concluded that if the United States had price controls similar to those in Europe, 117 fewer medicines would have been developed between 1986 and 2004. Other research has found a link between increases in market size and the number of new drugs targeted toward that market.

From that perspective, it’s possible U.S. consumers are funding innovation that benefits the rest of the world. “Particularly in smaller markets, it is tempting and individually rational for a government to free ride on high prices elsewhere,” says Kyle. “If you’re a small country, you know you’re too small to affect global innovation incentives, even if you double or triple your spending. Pharmaceutical companies are going to make the investment no matter what you do. So why incur the cost?”

It’s also possible, however, that Americans are paying for innovation that isn’t actually all that innovative. Many new drugs — as many as 70 percent, according to some estimates — are what detractors call “me-too” drugs.

These are treatments that have a different chemical mechanism but offer little or no clinical benefit over what's already on the market. If a decrease in expected revenue would mostly affect the development of me-too drugs, the effect on health outcomes might not be large.

Profit Maximizing ...

A key assumption of microeconomics is that firms seek to maximize profit. But many people appear to find it distasteful for a company in the health sector to do so. For example, a Senate investigation after the introduction of the infamous \$84,000 Sovaldi criticized its maker, Gilead Sciences, for employing a pricing strategy

that "it believed would maximize revenue" rather than "fostering broad affordable access." (Despite the uproar, some health care economists believe Sovaldi represented a genuine breakthrough that could justify the high price.)

Pharmaceutical companies also have been criticized for what they do with their revenue. Much of it goes toward stock buybacks, according to research by William Lazonick of the University of Massachusetts Lowell and several co-authors. Between 2006 and 2015, the 18 pharma companies in the S&P 500 stock index spent \$261 billion to repurchase shares, more than half of what they spent on R&D. In Lazonick and his co-authors' view, these buybacks were a means to artificially boost the companies' earnings per share

What About Generics?

Brand-name drugs typically get about 13 years of market exclusivity before they face competition from generic drugs. (Some of the initial 20-year patent term is taken up by clinical testing.) That competition has increased substantially in recent decades: Since 1994, the share of prescriptions filled with generic drugs has climbed from 36 percent to nearly 90 percent.

The generic industry got its first shot in the arm in 1984, when Congress passed the Drug Price Competition and Patent Term Restoration Act, commonly known as the Hatch-Waxman Act. Among other provisions, the law simplified the Food and Drug Administration (FDA) approval process for generic drugs. As generics became easier to manufacture and the quality improved, most states passed laws allowing pharmacists to automatically substitute generic for brand-name drugs unless the doctor specifies otherwise. Insurance companies promote generic drugs by charging lower co-pays for them or sometimes by not covering brand-name drugs if an equivalent is available.

Once multiple competitors have entered the market, the generic version of a drug sells for about 85 percent less than the brand-name version. Within a year of a generic entry, the branded drug's market share declines from 100 percent to 16 percent or less, according to research by Henry Grabowski, professor emeritus at Duke University, and Genia Long and Richard Mortimer of Analysis Group, an economic consulting firm. The IMS Health Institute estimates that generic drugs saved the U.S. health care system \$1.67 trillion between 2007 and 2016.

Brand-name manufacturers can employ a variety of strategies to try to retain their market share. For example, it's common for pharmaceutical companies to file additional patents for new versions of existing drugs by asserting the new version is clinically superior in some way, such as requiring fewer doses or having fewer side effects. Firms also can seek "orphan drug" status for an existing drug if it can be used to treat a rare disease,

which creates an additional period of market exclusivity. Critics view these follow-on drugs and orphan drug applications as attempts to curtail competition by gaming the system.

Sometimes, branded drug manufacturers just pay generic manufacturers to stay out of the market. These "pay-for-delay" agreements aren't necessarily illegal, although in 2013 the U.S. Supreme Court upheld the Federal Trade Commission's (FTC) ability to challenge them on antitrust terms. (In 2009, the FTC had filed a complaint against Solvay Pharmaceuticals for paying generic manufacturers as much as \$40 million per year to delay launching a testosterone treatment for nine years.) Pay-for-delay has become less common since the court decision, but it hasn't gone away. In 2015, the last year for which the FTC has released data, manufacturers struck 14 agreements affecting drugs worth about \$4.6 billion in sales.

The FDA allows citizens to file petitions when they have concerns about a product's safety. In recent years, more than 90 percent of the "citizen petitions" related to generic drugs actually have been filed by competitor companies. Even if the FDA ultimately denies the petition — which it usually does — the investigation can delay a generic drug's approval for several months. In the case of a blockbuster drug, those few months can be worth hundreds of millions of dollars to the brand-name manufacturer. Last year, the FDA implemented new rules designed to limit the potential abuse of the citizen petition system.

Generic drug manufacturers may have engaged in questionable business practices themselves. At the end of 2016, the attorneys general of 45 states and the District of Columbia filed a lawsuit against six generic drug manufacturers, alleging they had colluded to divide customers and fix prices. In October 2017, the AGs named 12 more companies and two individuals in the suit.

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— and thus boost executive compensation that depended on share price. But firms repurchase shares for many reasons, and the practice is not unique to pharmaceutical companies; Lazonick and his co-authors also found that the vast majority of the companies in the S&P 500 spent a similar share of their net income on stock repurchases.

The fact that marketing expenses at the largest firms typically exceed R&D budgets by billions of dollars is often cited as proof that “Big Pharma” has its priorities misaligned. But “economic theory does not tell you that the amount spent on pharmaceutical R&D should exceed that spent on marketing,” says Joseph DiMasi, director of economic analysis at Tufts’ CSDD and one of the authors of the cost study. “Few if any other industries spend more on R&D than on marketing.” In addition, notes Kyle, “the value of an innovation is higher the more people are aware of and purchase the innovation. There’s no point spending money to develop a drug if no one knows about it and no one takes it.”

... or Profiteering?

Pharmaceutical prices in the United States might reflect the high costs of drug development and provide necessary incentives for innovation. But they might also reflect pharmaceutical companies’ attempts to avoid competition — for which the U.S. legal and regulatory framework provides multiple opportunities.

One such opportunity lies in the opacity of the distribution system. Pharmacy benefit managers typically negotiate large rebates for drugs and keep an undisclosed portion of those rebates for themselves. That might give manufacturers an incentive to raise their list prices in order to offer benefit managers more attractive rebates and earn a preferential space in their formularies. That’s what the three makers of insulin — Sanofi, Novo Nordisk, and Eli Lilly — are alleged to have done in a class action lawsuit filed at the beginning of 2017. Insulin prices increased nearly 300 percent between 2002 and 2013, despite the fact that the drug has been produced commercially since 1923.

Pharmaceutical companies also have been accused of exploiting the Orphan Drug Act, a 1983 law that encourages drug manufacturers to develop treatments for rare diseases by offering tax credits and extended market exclusivity. An investigation by Kaiser Health News published in January 2017 found that one-third of the 450 orphan drug approvals granted by the FDA since 1983

were for previously approved mass-market drugs that had been reclassified with a new use, or for drugs that had received multiple orphan designations — and thus multiple incentive packages. Drug makers may also use orphan drug status to delay the entry of generic competitors. (See sidebar.) Since Kaiser published its report, the Government Accountability Office has announced it will investigate the orphan drug system, and the FDA and Congress have begun closing some loopholes.

Taking advantage of existing laws or spending money on politics may not be inherently problematic. But economists tend to be especially wary of the latter when it takes the form of rent seeking, the economic term for attempting to acquire excess profits through political means. Not only is such behavior likely to result in inefficient policies, the money spent on lobbying or campaign donations to influence regulation is money that could have been spent on productive uses — such as developing new drugs.

Between 1990 and 2016, the pharmaceutical industry donated \$185 million to political candidates, political action committees, and other political groups, according to data compiled by the Center for Responsive Politics. Contributions increased from \$9.1 million in the 1998 cycle to \$19 million in 2000 and \$21.3 million in 2002. Many observers believe the pharmaceutical industry was instrumental in adding the ban on Medicare negotiations with drug companies in the 2003 law.

Campaign contributions are dwarfed by the amount spent on lobbying, on which there are no spending restrictions. Since 2007, the pharmaceutical industry has spent about \$240 million annually on lobbying; in 2009, a year of intense debate about changes to the health care system, lobbying totaled more than \$270 million.

At least when it comes to politicians’ rhetoric, political spending might not be having much of an effect recently; lawmakers across the political spectrum have declared their intention to lower drug prices. But while that might sound desirable from the consumer’s perspective, it’s far from clear that lower prices across the board would be an efficient outcome, either. “We pay too much attention to the average price level and not enough to variation across drugs,” says Kyle. “Big breakthrough drugs don’t get the prices that are justified, but then we pay too much for drugs with only marginal benefits. Aligning pricing with clinical benefits would create better incentives for innovation and make better use of our health care resources.” **EF**

READINGS

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