

The Link Between Drug Prices and Research on the Next Generation of Cures

JOE KENNEDY | SEPTEMBER 2019

Academic studies consistently show that a reduction in current drug revenues leads to a fall in future research and the number of new drug discoveries.

KEY TAKEAWAYS

- The biopharmaceutical industry is one of America's leading sectors in terms of funding research and employing researchers. Public policy should try to encourage its growth and protect its competitiveness.
- Academic studies consistently show that a reduction in current drug revenues leads to a fall in future research and the number of new drug discoveries. Policymakers need to keep this cost in mind when setting any policies that affect drug revenues.
- Congress could lower drug prices by expanding access to affordable insurance, streamlining regulation, especially for the manufacture of approved drugs, encouraging other countries to pay their fair share of the cost of developing new drugs.

INTRODUCTION

Drug prices are once again a major focus of public policy in Washington D.C. President Trump has stated that reducing drug prices is one of his highest priorities.¹ The administration recently issued new regulations requiring manufactures to list the price of their drugs in television ads.² Congress has already passed the Know the Lowest Price Act and the Patient Right to Know Drug Prices Act, both of which try to promote transparency in prices.³ The Senate Special Committee on Aging recently conducted a series of hearings on drug pricing.⁴ And the Senate's bipartisan Prescription Drug Pricing Reduction Act would reduce government spending on drugs by an estimated \$100 billion over the next decade.⁵

This renewed attention is due to several factors. In a few cases, companies have dramatically raised the prices of specific drugs in order to generate more profits.⁶ Although these instances have been relatively rare, they have generated a great deal of publicity and comment. In other cases, new drugs have been introduced with large price tags. For instance, Novartis recently announced its new drug Zolgensma, which treats spinal muscular atrophy, will be priced at \$2.1 million for a one-time therapy.⁷ A large reason for the high cost is that relatively few people suffer from the disease and thus the cost of development must be spread over fewer patients. Finally, the rising cost of health care, including drugs, is placing greater pressure on individuals, insurers, and public budgets. A recent report by Accenture revealed a \$30 billion gap between the expected profits of drug companies from new drug launches and the projected drug spending of the public health programs in developed countries.⁸

Public policy demands a constant array of trade-offs whose difficulty only makes them more important. For prescription drugs these trade-offs occur on at least three levels. At the first level, policymakers must weigh the benefits of devoting more resources to health care as opposed to other important social needs such as infrastructure, education, and income support. Second, within health care they must balance spending on pharmaceuticals against other forms of health care, the prices of which have also been rising. These trade-offs may not be so stark, however, as in many cases the use of prescription drugs reduces the cost of other forms of health care.⁹ There is also the difficult question of whether to devote extensive resources to help a few people with severe conditions at the expense of slightly better care for the majority. Attempts to evaluate the worth of different treatments require that we assign a cost to human life. But this cost is extremely subjective and cannot be determined by economic considerations alone.¹⁰

Finally, policymakers must choose between the respective demands of current and future patients. Government price controls and other measures to reduce drug prices, such as weakened intellectual property protection will undoubtedly help current patients. But this will come at a cost. Money not consumed today can be invested for tomorrow. For the issue of pharmaceutical drugs, an overwhelming body of academic research shows that price controls will significantly restrict the number of new drugs in the future. The pharmaceutical industry is the epitome of a dynamic high-tech industry, wherein the profits from one generation of products go to pay the high development costs for the next generation. Artificially reducing drug revenues today will not only cause companies to cut back on their future research—meaning the next generation will benefit less from new drug discoveries—it will jeopardize U.S. leadership in an industry that punches above its weight in funding research and employing scientists.¹¹

An overwhelming body of academic research shows that price controls will significantly restrict the number of new drugs in the future.

All of these trade-offs are inevitable. Because there is no one right answer, many of these decisions should be subject to the political process, wherein policymakers can weigh the views and interests of different groups. This report does not presume to make these decisions for society. However, it is critical that when making these decisions, policymakers clearly understand the benefits and costs of each option. The purpose of this report is threefold. First, it reviews some of the data regarding drug spending. Second, it reviews the pharmaceutical industry's strong record in funding research and employing scientists. Finally, it summarizes the academic research showing a strong causal link between current drug prices and revenues on the one hand and future research and discoveries on the other.

ARE DRUG PRICES TOO HIGH?

In order to maximize social welfare with limited resources, policymakers need to appreciate the costs and benefits of each decision they make. In the context of drug prices, they need to clearly understand the strong link between current revenues (which may or may not be the same as consumer prices) and the generation of future drugs. Put simply, drug companies must make significant profits on their best-selling drugs in one generation in order to reinvest in the next generation. A large portion of these “profits” goes to three sources before they are available for distribution to shareholders. First, the revenues must cover the costs of the high number of failed research efforts, most of which generate no revenues. Second, they must pay for the long delays between initial research and product sales. These capital expenditures account for roughly half of the total costs of developing new drugs. Finally, a large portion of the remainder goes into new research on the next generation of drugs. Market investors quickly notice whenever companies do not have a group of promising drugs in their pipelines.

Put simply, drug companies must make significant profits on their best-selling drugs in one generation in order to reinvest in the next generation.

As figure 1 points out, change in total spending on retail pharmaceuticals varied dramatically between 2000 and 2017. Although spending rose in later years, the increases were mostly modest. The total number of pharmaceutical doses sold (the volume of drugs) also increased, in part because of the increase in the U.S. population (up an average of 0.84 percent per year since 2000) and the increase in the elderly population which on average consumes more drugs (the population of Americans older than 65 years of old has increased an average of 2.27 percent per year since 2000).¹²

Figure 1: Annual change in total U.S. retail pharmaceutical spending¹³

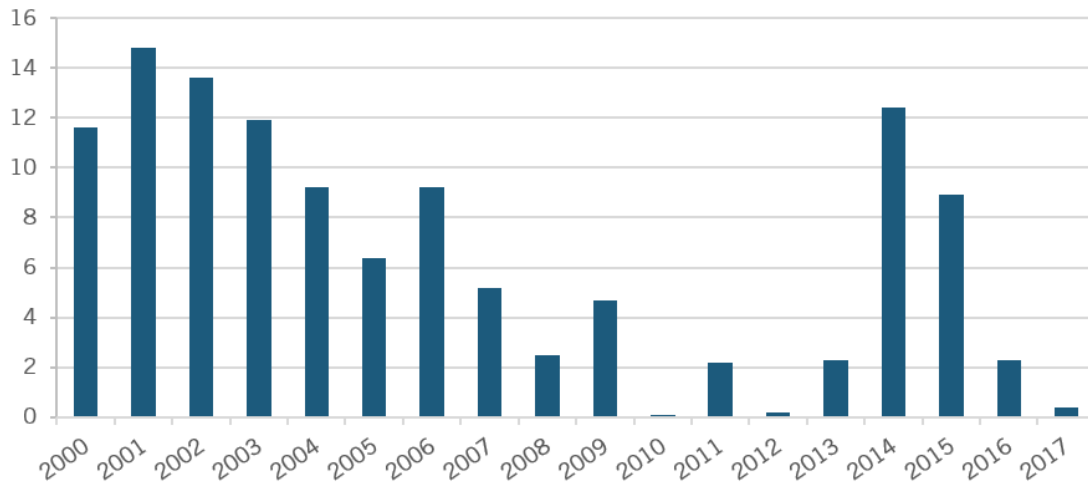


Figure 2, on the other hand, shows that the source of spending has changed dramatically. In 1960, fully 96 percent of all prescription drugs were paid for out of pocket. By 1980, this had fallen to 71.3 percent, and by 2000, it was 27.8 percent. In 2017, only 14 percent of prescription drugs were paid for out of pocket. Private insurance and Medicare/Medicaid paid for 42.0 percent and 40.2 percent, respectively. By 2027, the Centers for Medicare and Medicaid Services (CMS) expects the portion to decline to 12.8 percent. This trend has made many patients less sensitive to the cost of their medications.

Figure 2: Percentage of retail prescription drugs paid for out of pocket¹⁴

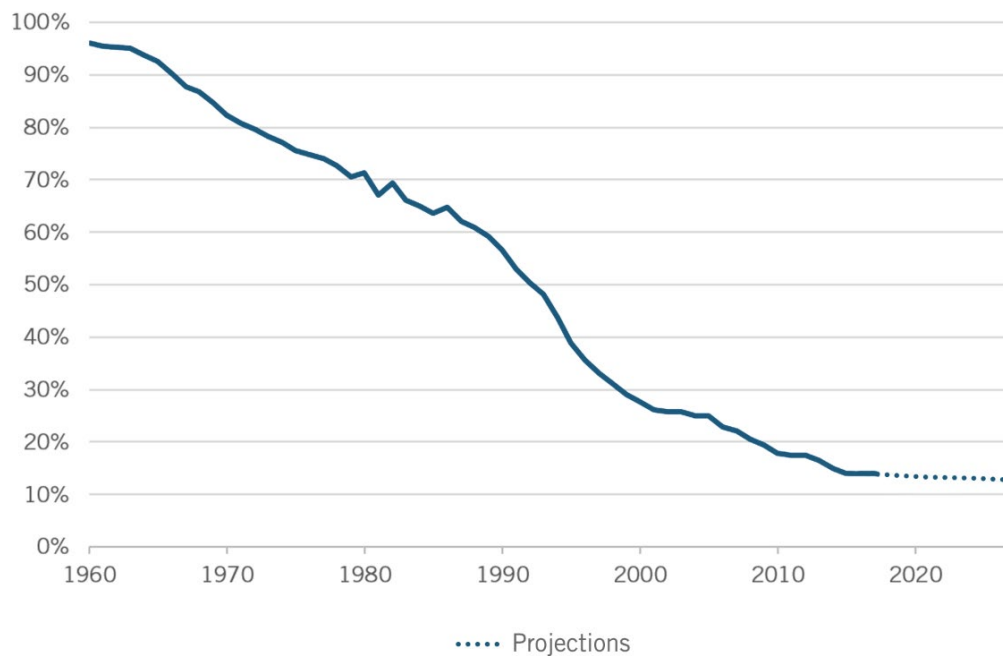
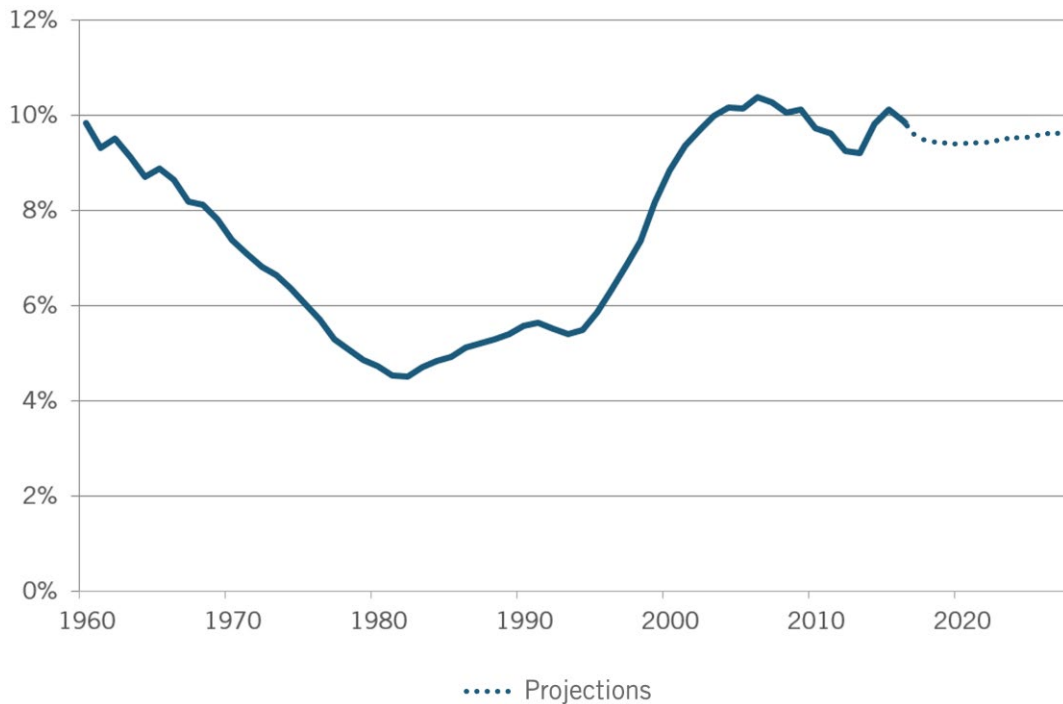


Figure 3 shows retail pharmaceutical sales as a percent of total health care spending. Although the fraction rose from 1980 to 2000, it has declined slightly since 2002 and is slightly lower than where it was in 1960. It is also projected to be relatively flat for the next decade.

Figure 3: Retail prescription drug spending and projections as a percentage of total health care spending: 1960–2027¹⁵



It should be no surprise that total health care spending is increasing, since the nation is getting richer and its population has grown. Nevertheless, total retail spending on drugs has increased almost sixfold, even after correcting for the Bureau of Labor Statistics' consumer price index for prescription drugs (see figure 4). However, so has gross domestic product (GDP). Figure 5 shows that, as a percentage of GDP, the rise was far less dramatic—with 2017 levels below 2009 levels—and only a small portion of total income.

Figure 4: Retail spending on prescriptions drugs adjusted for inflation (billions): 1970–2017¹⁶

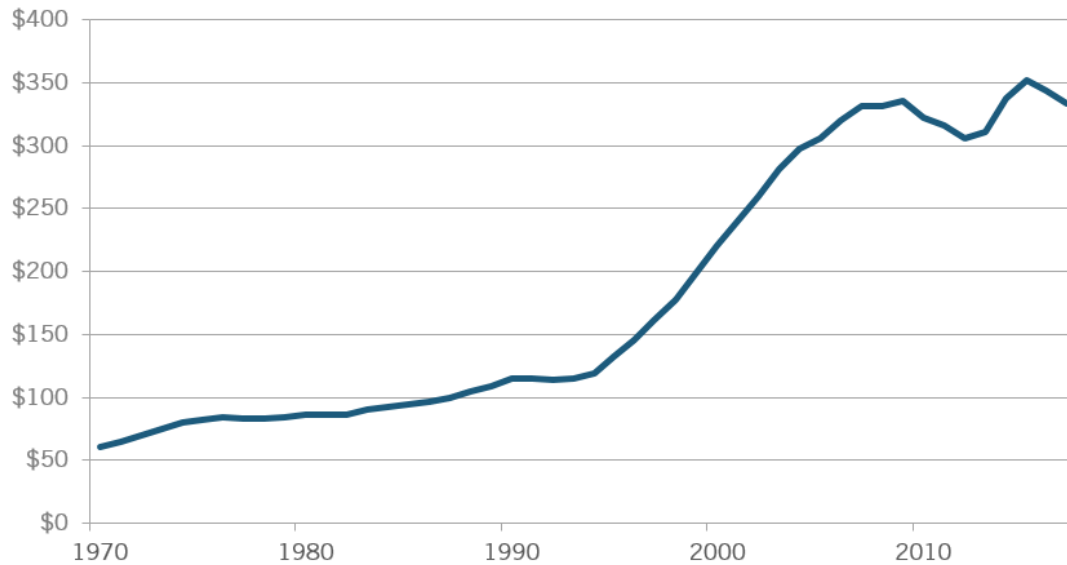
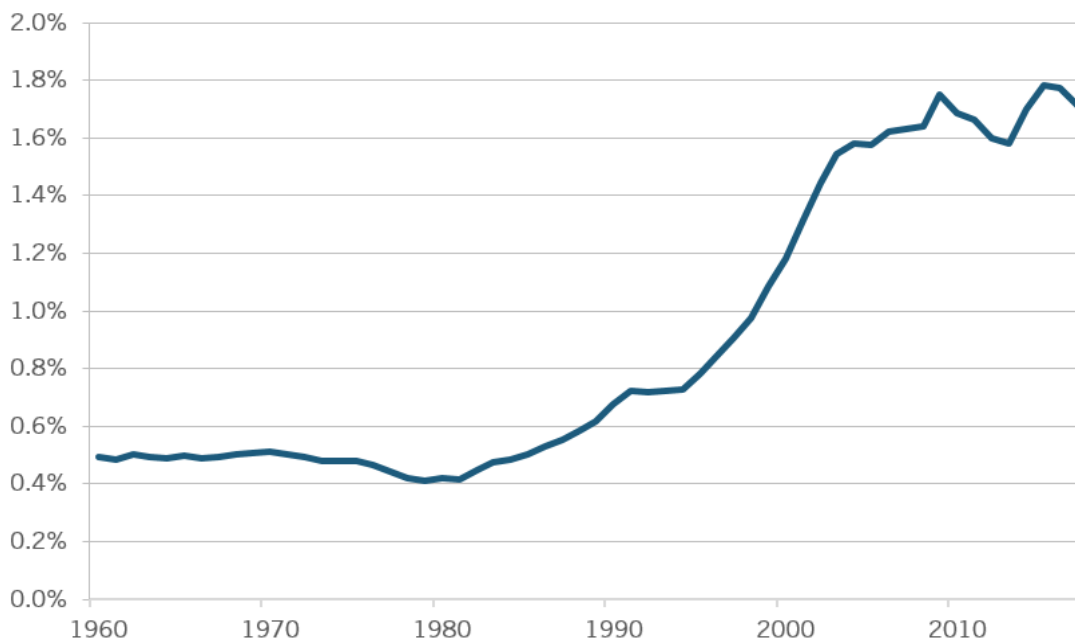
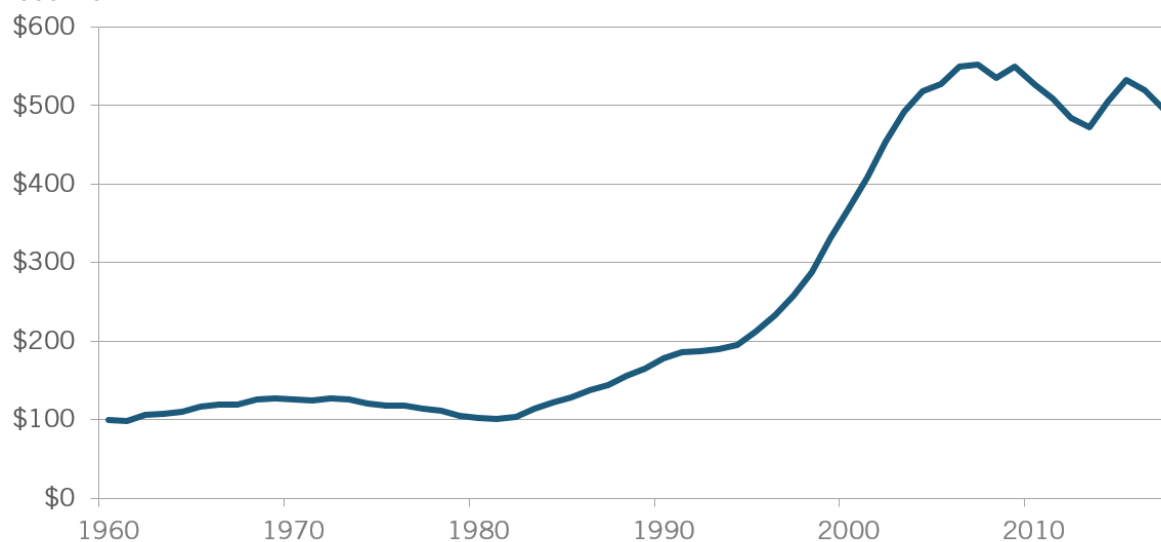


Figure 5: Retail prescription spending as a percentage of gross domestic product: 1960–2017¹⁷



Much of the increase has been driven by increased demand, in part as drugs have become more effective medical treatments. And much of the demand has been driven by those over the age of 65. Between 2002 and 2014, total retail spending on prescription drugs rose by \$140 billion. Spending on those over the age of 65 accounted for \$54 billion, or 38 percent of this rise. Yet the proportion of those over 65 in the population only rose from 12.3 percent to 14.3 percent of the total population. Figure 5 again shows total spending on retail prescription drugs, adjusted for inflation. It then adjusts this spending by the growth in the number of people ages 65 or older, revealing that when controlling for the growth of the elderly, real spending has declined 10.4 percent since 2007.

Figure 6: Real retail spending (billions) on prescription drugs indexed to the population over the age of 65: 1960–2017¹⁸



The Cost of Drug Development

Drug development is extremely costly for three main reasons. The first is the heavily regulated nature of the drug markets. Second, and partly due to this regulation, drug-development time is very lengthy, taking an average of 10 to 20 years. Because future revenues are worth less than those received today, a dollar of revenue in ten years will not come close to offsetting a dollar of research paid for today. Finally, drug development pushes at the boundaries of biological and chemical science, causing roughly 90 percent of all drug projects to fail.¹⁹ In order to survive, companies must recoup the costs of these failures in the revenues from the relatively rare successes. A recent study by the Congressional Budget Office (CBO) estimates pharmaceutical companies need to make a margin of 62.2 percent on their successful products in order to average a 4.8 percent rate of return on all of their assets. Based on past studies, the report assumes that 90 percent of all research spending results in no revenues, and that the approval process takes 12 years.²⁰

A recent CBO study estimates pharmaceutical companies need to make a margin of 62.2 percent on their successful products in order to average a 4.8 percent rate of return on all of their assets.

The most commonly accepted estimate of the cost of developing a new drug comes from the Tufts Center for the Study of Drug Development. Looking at drugs that began human testing between 1995 and 2007, it estimated that the average cost of developing and bringing to market a new compound had been \$2.6 billion (in 2013 dollars). Post-approval costs added another \$300 million. Out-of-pocket costs were \$1.4 billion. The rest was the cost of capital, using a discount rate of 10.5 percent. Costs had risen over the last decade due to a decline in clinical success rates and a rise in average research costs.²¹ The study also found that, although tax provisions such as the research and development (R&D) and the orphan-drug tax credits reduce the cost of development, their effect is relatively small compared to the total costs. While this study has been criticized, other estimates have produced comparable results.²²

The problem of rising drug costs is made worse by the fact that Americans must pay a large share of the costs of drug development. Since the United States accounts for roughly half of the global market (in terms of the amount of drugs consumed), one might normally expect it to pay for only about half of subsequent rounds of innovation.²³ But many countries, including high-income ones, pursue policies that keep the prices of their patented drugs artificially low.²⁴ Because manufacturers cannot recover much of their fixed costs overseas, they must charge higher prices in the United States in order to achieve a given rate of return. Somewhat surprisingly, some also raise the price of generic drugs in order to protect domestic manufacturers of those drugs. As a result, U.S. consumers pay approximately 70 percent of all global patented biopharmaceutical profits.²⁵

Many countries, including high-income ones, pursue policies that keep the prices of their patented drugs artificially low. As a result, U.S. consumers pay approximately 70 percent of all global patented biopharmaceutical profits.

This makes sense from the point of view of each country, particularly low-income countries. Because of their relatively small market size compared with the United States, raising drug prices would have little effect on either the amount or direction of global research. Collectively, however, price restrictions harm the global community.²⁶ They result in significantly less research, and fewer drugs. Everyone, including Americans, would benefit if all nations contributed their fair share to drug research. Solving this collective action problem has proven difficult, however.

It is interesting to note that efforts to fight climate change share the same dynamic. For most countries, especially smaller ones, the rational action would be to not pay the price premium required for clean energy because the cost of not doing so would be widely diffused to all nations, while the benefit of a higher living standard from cheaper energy would be accrued by the individual nation. Yet, most nations have decided that, when it comes to clean energy innovation and adoption, they will put the interests of the globe ahead of their own interest. Nations such as Canada, Japan, and much of Europe that prioritize fighting climate change think nothing of free-riding on U.S. expenditures when it comes to fighting global diseases, thereby slowing rates of new drug innovation.

Measuring Prices and Profits

Measurement problems complicate any analysis of the pharmaceutical industry. First, there are problems measuring drug prices. For one thing, it can be very difficult to determine the correct price of a given drug. Pharmaceutical pricing involves a number of different players and several levels of discounts. Very few buyers pay list price, discounts vary significantly depending upon the buyer, and manufacturers have become more reliant on rebates in order to sell products. A recent Accenture report found that 4 of 11 drug companies studied had issued rebates totaling more than half of their gross U.S. sales.²⁷ Two pills with identical ingredients but different names can vary in price by a factor of five.²⁸ Moreover, middlemen play an important role in drug distribution and pricing.

Even when a common price definition is used, price indexes of the real cost of pharmaceuticals tend to overestimate the amount of inflation.²⁹ First, The U.S. Bureau of Labor Statistics (BLS)

infrequently changes the market basket of drugs whose prices it monitors, so new generics are often not included in the sample for several years even though their entrance into the market quickly lowers prices. And when they are included, they are measured as new products, not as cheaper versions of the branded drugs.³⁰ According to an estimate from 1993, this resulted in an upward bias in the measured price of drugs of 1.2 percentage points a year.³¹ Making this adjustment would mean actual prices fell in 3 of the last 9 years (see figure 1).

Second, price increases tend to be more rapid for mature branded pharmaceuticals that have proven their worth, while the prices of new products increase more slowly and can even decline. However, because new products are not included in the index until several years after their market entry, this declining-price experience is underrepresented. Finally, BLS does not measure improvements in consumer benefits associated with new drugs. If a new version of a drug costs the same as an existing one but delivers better results, its real cost has fallen, although the index would not capture that. In contrast, the government does include quality improvements in its measures of inflation for most other products, such as cars and computers. Although the government has tried to address some of these problems, the indexes likely still overstate the rate of inflation.

A second problem concerns how profits are measured, and particularly the accounting treatment of research costs and marketing expenses. Because both of these costs have a useful life of more than one year, standard accounting practice would include them as assets and amortize them over a period of years (perhaps five to eight) beyond which they cease to have value. For example, the Bureau of Economic Analysis now counts research as an asset and depreciates the value of biopharmaceutical research by 10 percent each year.³² However, the convention in the pharmaceutical industry is to deduct research and marketing costs from revenues in the first year. Although expensing for tax purposes makes sense in order to reduce the after-tax cost of research, and to reflect actual cash flow within the company, the measurement of return on assets should reflect traditional accounting principles. The deduction of research costs temporarily lowers measured profits because it raises the amount of costs that are deducted from revenues. However, by ignoring the continued value of research assets, it significantly understates a company's assets and therefore overstates the rate of return on assets.³³ CBO has reported that, after properly adjusting for the asset value of research, the industry's profitability remains "somewhat" higher than the average for all industries, but not twice as large, as standard measures show.³⁴

When research was properly accounted for, the return on equities fell to 8.3 percent for pharmaceuticals and rose to 0.9 percent for biotechnology. The market average was 14.1 percent.

In recent years, industry returns have been even lower. New York University professor Aswath Damodaran calculated estimated returns on equity (ROE) for different industries going back several years. His calculations include estimates that treat research as both a standard expense and a capital expenditure. For 2018, the return on equity for pharmaceuticals and biotechnology was 12.6 percent and -1.6 percent, respectively, compared with an economy average of 15.6 percent.³⁵ However, when research was properly accounted for, the ROEs fell to 8.3 percent for pharmaceuticals and rose to 0.9 percent for biotechnology. The market average was 14.1 percent. This relative performance is reflected in stock prices. Over the past five years, the NYSE

ARCA Pharmaceutical Index experienced an annual return of 2.0 percent, compared to 7.6 percent for the broader S&P 500.³⁶

Finally, even a significant reduction in margins would not transform drug pricing. The Government Accountability Office estimated that pharmaceutical and biotechnology revenues were \$775 billion in 2015, with an industry profit margin of 17.1 percent (not taking into account capitalization of research).³⁷ Reducing this margin to 6.7 percent (the average for Fortune 500 companies) and assuming all savings were used to lower prices would have lowered prices by only 10 percent.

Measuring the Benefits

Any analysis of the cost of drugs needs to also consider the benefits from their use. There is ample evidence that the benefits substantially exceed the costs. Policies that restrict the flow of future drugs are therefore likely to harm society, particularly if the savings are consumed, rather than invested.

Any analysis of drug costs needs to consider the benefits from their use. Policies that restrict the flow of future drugs are therefore likely to harm society, particularly if the savings are consumed, rather than invested.

A 2008 study by CBO found that average returns to society from past drug R&D appeared to have been large.³⁸ A study of the use of other medical services and whether advances in pharmaceutical treatments had any effect on days lost to sickness found that conditions that had larger increases in post-1990 drugs per affected person also had larger declines in disability days and the use of almost all non-drug medical devices.³⁹ The total benefit was \$95 per person, or twice the cost of the additional drugs. All of this social benefit went to patients and health care providers. In another study, improved medication adherence in patients with four chronic diseases resulted in benefit-to-cost ratios of between 3.1:1 and 10.1:1 depending on the condition. Annual savings per patient varied from \$1,258 to \$7,823.⁴⁰

The creation of net benefits also extends to future drugs. Reduced biomedical innovation would increase future health care costs and slow improvements in health and longevity.⁴¹ The Alzheimer's Association recently evaluated the current cost of treating the disease.⁴² By 2050, 16 percent of Americans 65 or older will suffer from some stage of Alzheimer's, with 6.5 million individuals in the severe stage of needing round-the-clock care. The cost of treating Alzheimer's that year will be \$1.2 trillion in 2019 dollars. The report estimates that discovering a drug in 2025 that would delay the onset of Alzheimer's by 5 years would reduce the cost of treatment in 2050 by one-third. Savings in the first 10 years alone would total \$935 billion. The high cost of mental illness (roughly \$1.5 trillion annually) also offers a great opportunity for cost reduction through better drugs.⁴³

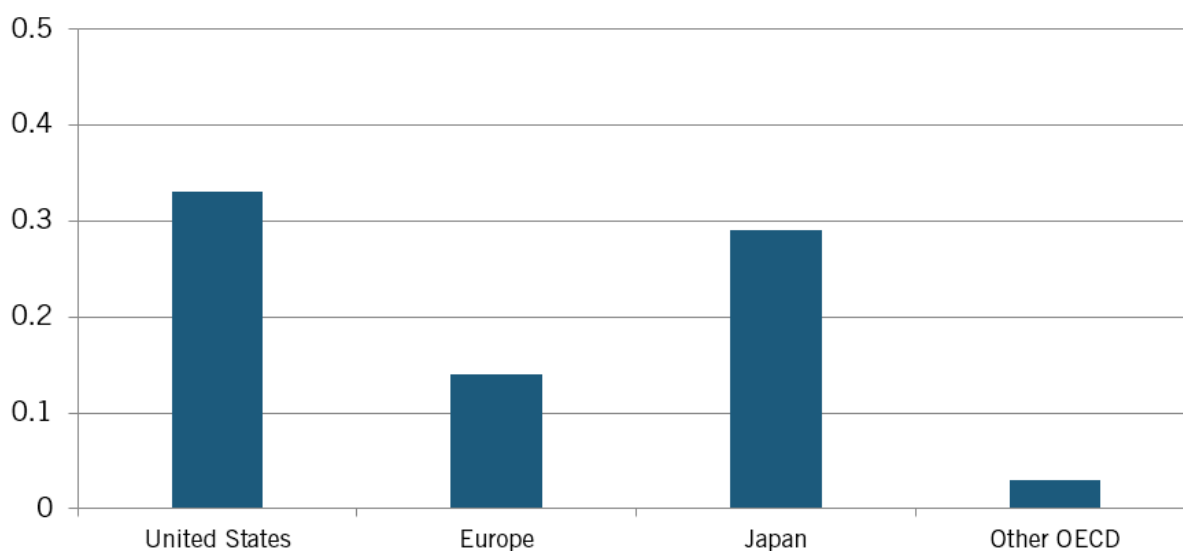
However, the presence of large social benefits is not enough. Companies must still be able to realize a profit on their drugs. A recent news article reports on the difficulty biotech firms face in developing new antibiotics.⁴⁴ Despite a growing need, a decline in market returns has caused larger firms to shift research over to other areas. For example, only three companies are currently conducting clinical research on antibiotics. The article speculates that part of the problem is few doctors know about the new antibiotics, which may be the result of a lack of marketing. Another

problem is new drugs, due to their high costs, are only used when other treatments do not work, meaning their overall sales are likely not enough to pay for new-drug development.

PHARMA'S ROLE IN PROMOTING RESEARCH

The pharmaceutical and biotechnology industries combined account for a large percentage of U.S. research, both as a fraction of their profits and as a fraction of total U.S. R&D. Figure 7 shows total business expenditures on pharmaceutical R&D in 2014 (the latest year for which data is available), with private research developing new drugs in the United States at a significantly higher percentage of GDP than in the rest of the world. Although Japan comes close in percentage terms, total private R&D spending was \$56.6 billion in the United States, compared with \$14.6 billion in Japan.

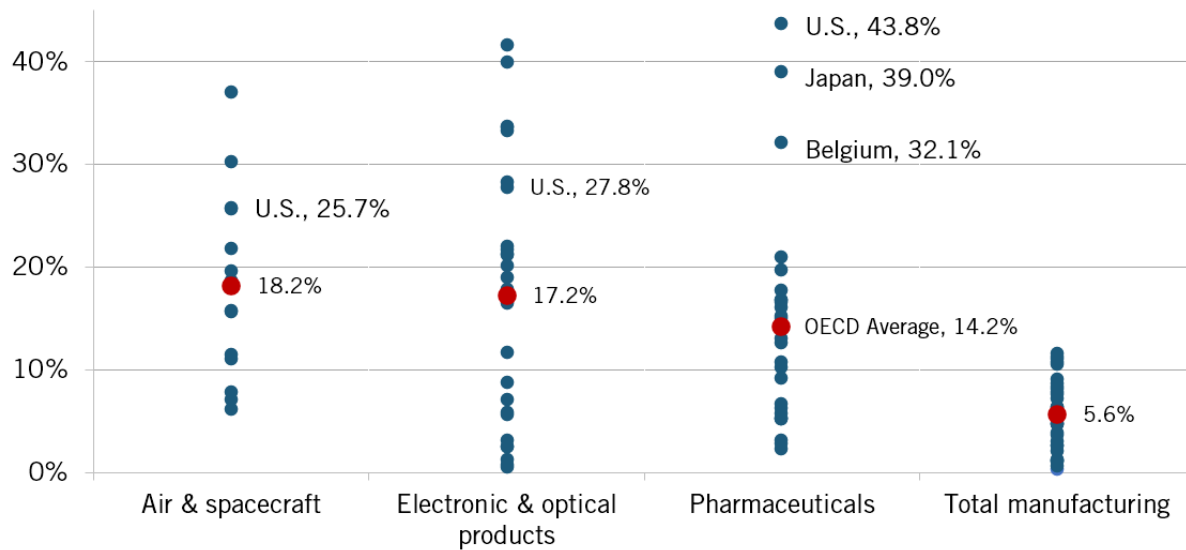
Figure 7: Business expenditure for pharmaceutical budgets for health-related R&D as a percentage of GDP, 2014⁴⁵



The U.S. pharmaceutical industry conducts far more pharma research than other countries, and more research overall than other U.S. industries.

This high level of investment also applies to the total value of the pharmaceutical industry. Figure 8 shows R&D intensity by industry, measured as business R&D spending as a percentage of the gross value added of an industry. Once again, the U.S. pharmaceutical industry conducts far more pharma research than other countries, and more research overall than other U.S. industries. U.S. pharmaceutical companies devoted 43.8 percent of their total value added in 2014 back into R&D, ahead of both air and spacecraft, and electronic and optical products.

Figure 8: R&D intensity by industry and country, 2014⁴⁶



Because of this research, Americans enjoy earlier access to new drugs. The European Federation of Pharmaceutical Industries and Associations recently found that, although the North American market accounted for only 48.9 percent of worldwide pharmaceutical sales, 65.2 percent of sales of new medicines launched between 2013 and 2018 were in the United States.⁴⁷ It also determined that, although the growth of drug research had stagnated from 2009 to 2013 (a period in which significant reforms to health care were being discussed), it grew at an 8.6-percent rate between 2014 and 2018. The European rate was only 3.8 percent.⁴⁸

Worldwide, the pharmaceuticals and biotechnology industry spent almost \$112 billion on R&D in 2013 (the latest year for which data is available).⁴⁹ The National Science Foundation regularly collects data on business research. According to its latest data, companies producing pharmaceuticals and medicines paid for \$65.8 billion of research in 2016.⁵⁰ This was almost 17 percent of all research funded by manufacturing companies in the United States. Biotechnology firms contributed another \$6.1 billion. Over 85 percent of this pharmaceutical research was conducted in the United States. Over 64 percent of this funding was devoted to development, while another 21 percent was spent on applied research.⁵¹ Companies devoted 16.5 percent of sales to domestic R&D.⁵² The only industries with higher ratios that year were semiconductor machinery and scientific R&D services (which include biotechnology). Biopharmaceutical companies accounted for 687,000 domestic employees, of which 144,000, or 21 percent worked in R&D.⁵³ This is over 9 percent of all R&D workers funded by industry.

THE EFFECT OF DRUG PRICES ON INNOVATION

The previous section discussed the strong contribution the pharmaceutical industry makes to U.S. research. The U.S. lead in life-sciences research delivers large benefits to the economy in the form of faster, more numerous breakthrough drugs and continued advances in existing therapies, as well as tens of thousands of high-paying jobs across the nation.⁵⁴

This section reviews the academic literature on the strong link between drug prices and the future introduction of new drugs. Like any industry, pharmaceutical manufacturers need to earn

an adequate rate of return on their assets in order to remain in business. However, the special nature of the pharmaceutical industry, in particular the heavy upfront investment in drug research and testing, and the long and uncertain delay between initial investments and drug revenues, means government price controls or other policies to reduce revenue (such as weakened intellectual property protection) will reduce drug innovation.

Numerous studies have shown a firm link between prices and profits on the one hand and higher levels of research and drug innovation on the other.

Numerous studies have shown a firm link between prices and profits on the one hand and higher levels of research and drug innovation on the other. Although this report will not attempt to define the proper balance in detail, policymakers need to be aware this link is well established. Lowering prices now will result in less future research and fewer new drugs. The decline in future drugs will in turn reduce patient welfare over the longer term. This is not to say the federal government should sit on the sidelines regarding the affordability of drugs, but rather that price controls will come at a cost to innovation and long-term patient well-being.

The Trade-Off Between Short-Term Affordability and Long-Term Innovation

The unique nature of the pharmaceutical industry complicates the task of setting prices. In many traditional industries with a competitive market, firms often set prices only slightly higher than the marginal cost of producing an additional unit. This is because in most traditional industries fixed costs (e.g., capital equipment, R&D, and other overhead) are relatively low compared with total costs of production.

However, setting prices close to marginal cost won't work for innovation industries—including biopharmaceuticals—wherein the marginal cost of producing another unit (e.g., a pill or dose) is usually relatively small in comparison with the overall fixed costs, especially research, development, and testing. As innovation companies, drug companies must be able to recover these high up-front costs. Like some other industries such as movies, wherein there is a risk of the product being a bust, biopharmaceutical companies must be able to price drugs to cover not just the fixed and marginal costs of the successful drug, but also the costs of the failures. High fixed costs (from both successes and failures) ensure companies will need to price drugs significantly above the marginal cost. Although short-term affordability of drugs may be increased if drug revenues are based on marginal cost, drug companies will not be able to recover their costs, which will make them stop investing in future research, lose money, and go out of business.

Ensuring prices remain high enough to allow drug manufacturers to recover their high fixed costs requires government intervention. In the United States, this is done mainly by giving drug companies patent protection for new discoveries. These policies give companies the ability to raise prices above marginal—and even average—cost, at least as long as there are few close substitutes to a particular treatment. Without patent protection, other companies would swoop into markets, thereby avoiding the hard and expensive work of developing and testing a drug and bearing only production and marketing costs. This is in fact what happens once the patent on a popular drug expires.

The granting of a monopoly through patents and other intellectual property protection has a positive effect on product development—which in the case of drug companies, is on research, development, and testing. While market power from intellectual property protection may reduce short-term welfare, it increases long-term welfare by encouraging more investment and innovation. This is why the Founding Fathers included patent protection in the Constitution.⁵⁵ Moreover, in many cases, a patent may not confer much effective pricing power. A company with a patent on a drug for a given disease may face strong competition from other drugs with similar effectiveness.⁵⁶ In such cases, the patents may not translate into effective pricing power.⁵⁷ In addition, the maker of a particular drug may face some limitations on market power from buyers, such as health care insurers and drug benefit plans, with their own market power. These restraints help ensure pharmaceutical prices will be roughly based on the value to patients and the broader health care system.⁵⁸ For example, although Zolgensma is priced at \$2.1 million for a one-time treatment, it treats spinal muscular atrophy (SMA). Infants born with SMA Type 1 typically die within 18 months or can only survive on life support. Roughly 30 new patients are born each month. The only existing therapy, Spinraza, costs \$750,000 for the first treatment and \$375,000 per year after that.⁵⁹

But even when companies set prices high, society can still benefit. When companies decide how much money to invest in research, they typically invest until the benefits to them stop exceeding their costs. Because companies do not benefit from the spillover benefits to society (the benefit competitors and consumers get from their innovation), they do not take them into account. In fact, research levels would be maximized by letting these companies capture all the social benefits.⁶⁰ A recent study by Tomas Philipson and Anupam Jena shows that drug companies typically capture only a small fraction of the total social benefit they produce.⁶¹ The study concentrated on therapies for HIV/AIDS introduced after the late 1980s. It estimated that these drugs increased social welfare by nearly \$1.4 trillion. However, the companies that produced these drugs increased their profits by only \$62.9 billion. They therefore captured less than 5 percent of the total welfare. The remainder went to the rest of society. Looking at over 200 previous studies of the cost efficiency of other drugs, the authors estimated that in 25 percent of the studies, companies captured less than 7 percent of the societal surplus. The appropriation of social welfare exceeded 25 percent in only one-quarter of the studies. Philipson and Jena also found that “dynamic efficiency only occurs when those undertaking the costs of R&D have incentives that are properly aligned with society, which is true when social surplus is entirely appropriated as profits.”⁶² Because firms capture only a small part of the total surplus, they do too little research. Although patent law, the R&D tax credit, and other policies can mitigate this effect, policymakers should remember that allowing firms to appropriate more of the surplus directly may promote dynamic efficiency (e.g., new drugs) and long-term societal benefits (e.g., health).

Drug pricing therefore requires a balance between short-term affordability and long-term innovation. Low prices (as well as public subsidies) allow more individuals to afford existing drugs now, but if they come at the expense of drug company revenues, they reduce the incentive to invest in new cures. Higher prices increase this incentive but can also make prices unaffordable for many patients. Subsidies for drugs, particularly for low- and moderate-income households, either through private insurance or government payments, is one way to balance this conflict. Unfortunately, there is no right answer for obtaining the proper balance, but those who try to strike it need to be aware of the trade-off.

The justification for high prices on any particular drug therefore depends on the assumption that they are needed to fund the subsequent round of innovation. This link has been established by numerous empirical studies over the last several decades. A recent survey summarized the scholarly literature this way: “The preponderance of evidence suggests that raising reimbursements for pharmaceuticals stimulates innovation, primarily because the expected rewards for innovation go up and secondarily because the cost of financing falls for cash-constrained pharmaceutical firms.”⁶³

“The preponderance of evidence suggests that raising reimbursements for pharmaceuticals stimulates innovation, primarily because the expected rewards for innovation go up and secondarily because the cost of financing falls for cash-constrained pharmaceutical firms.”

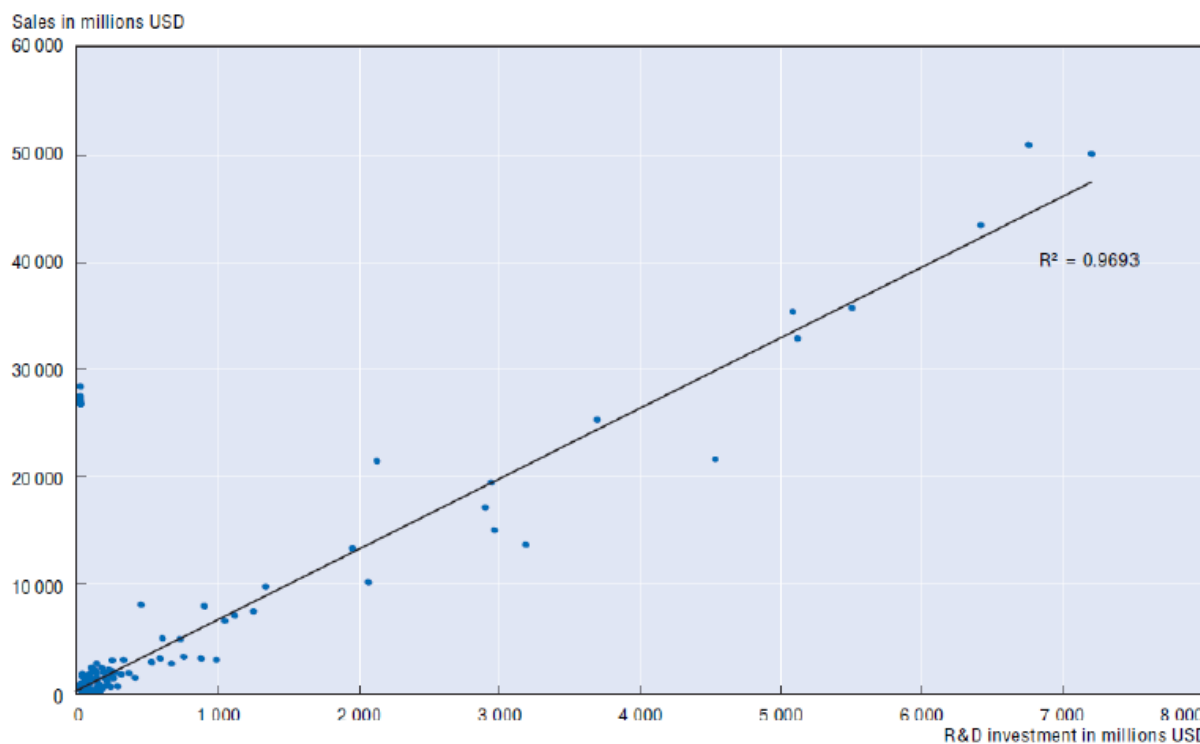
Previous Literature Reviews

Previous government reports have summarized the link between biopharmaceutical profits and innovation within the drug industry. CBO pointed to two underlying reasons why this link might be so strong.⁶⁴ First, as in most industries, the introduction of successful new drugs often leads to higher profits as companies are able to capture some of the social value created by their products. The profitability of current drugs also serves as a proxy for the profitability of future drugs. If biopharmaceutical firms are allowed to make reasonably large profits from their current products, they are likely to conclude that the same will be true in the future. This may cause them to increase both the speed and amount of their research activities. Conversely, they may view current attempts to hold down prices as likely to continue into the future, in which case they may decrease research funding.

The second reason CBO identified is adequate profits generate significant cash flow, which allows companies to finance the next round of innovation.⁶⁵ The availability of cash flow is important because raising significant amounts of money in the stock or bond markets is more costly. Biopharma companies have a much more detailed knowledge of disease models, the status of their current research, and the probabilities of success. Because investors cannot adequately assess these risks for themselves, they demand higher returns for investing. Assuming firms invest in R&D until their cost of capital exceeds the rate of return, financing through cash flow should allow them to justify more projects than if they have to raise the money from outside investors.

The Organization for Economic Cooperation and Development (OECD) conducted a detailed study of this issue in the pharmaceutical industry. It found that “[p]harmaceutical pricing and reimbursement policies stand to affect innovation through multiple channels, influencing both the *incentives* to invest in private R&D and the *costs of investment*. The main channel of prospective influence is the impact of pricing and reimbursement policies on the *expected return on investment* in R&D.”⁶⁶ In fact the generation of large revenues is closely related to the amount of research an individual company does. Figure 9 shows R&D expenditures and sales of the 151 largest pharmaceutical firms in the world in 2006. There was clearly a very strong correlation (0.97).

Figure 9: R&D expenditures and sales in the pharmaceutical industry, 2006⁶⁷



Note: The data were prepared on the basis of annual reports and consolidated accounts received up to and including 31 July 2006. Annual reports with a year-end older than 30 months from the cut-off date or a publication date older than 24 months from cut-off date are excluded.

Source: DIUS (2007).

Pricing policies affect not only the amount of research conducted (leading-edge or marginal improvements) but also the type and the decision of whether and when to introduce a new product to the market.

The Government Accountability Office recently completed its own review of trends in pharmaceutical profits and R&D.⁶⁸ It found that both experts and academic research has concluded that high revenue potential associated with a large number of patients, or the ability to charge a high price, is an important incentive for R&D investment.⁶⁹ Exclusivity periods and patent protection, tax incentives, and expedited review programs were also cited as influencing R&D. Of course, while biopharmaceutical companies, like other firms, would like to charge as high a price as possible, their ability to do so is limited by both buyers not being willing to pay more for a drug than the benefits it delivers in terms of longer, healthier lives, and the presence of at least some competition in the marketplace.

Experts and academic research have concluded that high revenue potential associated with a large number of patients, or the ability to charge a high price, is an important incentive for R&D investment.

Academic studies that explore the causal link between drug revenues and research face a common difficulty in finding good data. They also take different approaches to choosing the inputs, outputs, and econometric model to measure the relationship between prices and profits, and research and innovation. So it is somewhat remarkable that, collectively, they arrive at the

common answer that high prices for today's treatments are closely associated with more research and a larger number of future drugs. There appear to be no scholarly studies that show no relationship between current prices and future innovation. Given their common conclusion that short-term price declines will endanger future drug innovation, it is worthwhile to discuss some of the major studies individually.

Grabowski and Vernon (2000)

Two studies by Duke University's Henry Grabowski and John A. Vernon from the University of North Carolina at Chapel Hill looked at the relationship between expected returns and cash flows on the one hand, and company research on the other. The first study covered the period from 1962 to 1975.⁷⁰ This followed passage of the Kefauver-Harris Amendment to the Food, Drug, and Cosmetic Act, which required a showing of efficacy as well as safety in order to get FDA approval. This increased development times by several years and R&D costs per new drug by several-fold. The authors found that research productivity, defined as sales of recent new drug introductions divided by lagged R&D spending, declined rapidly during the period. This eventually influenced cash flows, the decline of which along with the fall in research productivity together had the effect of reducing R&D.

A later study looked at research spending between 1974 and 1994 in 11 firms specializing in prescription drugs.⁷¹ Together, these firms represented just over 40 percent of the U.S. market and half of the innovative output (defined as the first 3 years' sales of all new chemical entities introduced in a period of time). Unlike the previous period, research productivity rose over 50 percent. Grabowski and Vernon found that both expected productivity of R&D and available cash flow positively affect R&D spending. Again, the link between cash flow and research is due to the fact that internally generated funds, which are often the result of higher profits, cost less than either borrowed funds or new equity, and therefore lower the required rate of return for new research at the margin.⁷²

U.S. Department of Commerce (2004)

In 2004, Congress asked the U.S. Department of Commerce to study the effect of pharmaceutical price controls in OECD countries.⁷³ The department concluded that most OECD countries use a variety of controls to limit the price of patent-protected drugs in their countries. These restrictions reduced the revenue of drug companies by \$18 billion to \$27 billion per year. The department estimated that lower revenues reduced global R&D by \$5 billion to \$8 billion, or 3 to 4 new drug entities annually. This latter effect was based on outside estimates regarding the cost of developing a new drug. Note that using a lower cost of development would imply that the reduction in research spending resulted in a higher number of new drugs not being discovered. Access to these new drugs would benefit U.S. consumers by \$5 billion to \$7 billion a year. In contrast, OECD countries also used price floors on generic drugs in order to protect their domestic manufacturers. Eliminating these floors would save Europeans \$5 billion to \$30 billion annually, potentially paying for restoring a competitive market to patent drugs. The study also found that significantly more new active substances were available in the United States than in other countries, which it attributed to companies' increased ability to capture more of the social benefit from current drugs.⁷⁴

Acemoglu and Linn (2004)

One problem with modeling the relationship between prices and research is the causation may go both ways. It is possible that better research increases profits rather than the other way around. To get at this problem, economists Daron Acemoglu and Joshua Linn examined the pharmaceutical industry using the theory of induced innovation, which says that changes in the real prices of different goods or inputs should cause companies to change the direction of innovation.⁷⁵ Their 2004 study looked at changes in demographic trends between 1970 and 1990. Demographic changes affect the potential market size for a drug but they do not depend on the amount of research being done. If research spending and the size of the market move together, causation should run from prices to research.

Acemoglu and Linn divided specific drugs into categories depending on the age of the population that primarily used them. The results showed a strong relationship between market size and the entry of new drugs. As baby boomers aged over a 30-year period, the market for drugs mostly consumed by the young declined, while those used by older individuals increased. This produced a matching change in the number of new drugs in each category. A 1-percent increase in the potential market size led to a 6-percent increase in the number of new drugs entering that market. Although much of this increase came from generics, both the number of nongeneric drugs (those not identical or bioequivalent to an existing drug) and the number of new molecular compounds (drugs containing an active component that has never been approved by the FDA or marketed in the United States) increased by at least 4 percent. They also found that drug firms anticipated these demographic changes with a lead of 10 to 20 years.

Giaccotto, Santerre, and Vernon (2005)

A 10-percent increase in real prices caused firms to increase their R&D intensity by nearly 6 percent the following year.

Another study, by Giaccotto, Santerre, and Vernon, found a strong link between real drug prices and firm R&D.⁷⁶ Their 2005 study focused on R&D intensity (the ratio of R&D spending to product sales) rather than the level of research, and found that real drug prices, real GDP per capita, and the amount of foreign sales as a percentage of total sales all had a strong impact on R&D intensity the following year. Specifically, a 10-percent increase in real prices caused firms to increase their R&D intensity by nearly 6 percent the following year. Applying this result to the past, they estimated that if drug prices had not increased in real terms between 1980 and 2001, R&D spending would have been 30 percent below its actual level. The number of new drugs entering the market during this time would have fallen by between 330 and 365, or about one-third of the actual number.

Abbott and Vernon (2005)

Some studies have tried to estimate the impact of future price controls on research. In 2005, economists Thomas Abbott of Thomson-Medstat and John A. Vernon found a strong impact on future innovation.⁷⁷ They used the history of specific firms to look at the impact of prices on the initial decision whether to start Phase I trials on a perspective drug. With data on actual development costs, drug revenues, and a measure of the uncertainty facing firms, they found that minor price changes would have relatively little effect. A price decline of 5 to 10 percent

would reduce product development by about 5 percent. But larger price declines would have a more serious impact. For example, a price cut of 40 to 45 percent in real terms would reduce the number of new development projects by 50 to 60 percent.

Lichtenberg (2006)

A 2006 study by Frank Lichtenberg looks at relationships between expected market revenues on the one hand and both the number of chemotherapy regimens for treating a cancer site (i.e., skin, lungs) and the number of articles published in scientific journals pertaining to drug therapy for that cancer site.⁷⁸ As the importation of drugs would decrease the U.S. price and therefore the expected revenues, Lichtenberg hypothesized that importation would cause both the number of regimens and the number of publications to fall. He started by assuming that the responsiveness of innovation to a change in revenues is at least as great as its responsiveness to the number of patients. To estimate the latter, he looked at both changes in the number of patents with particular types of cancer in Canada and the United States, and the number of regimens and research papers devoted to that type of cancer. The results showed the elasticity of the number of cancer patients to the number of chemotherapy regimens available to treat a specific type of cancer is 0.53. The elasticity of journal citations is 0.60. Therefore, a 10-percent fall in drug prices is likely to cause a 5- to 6-percent decline in both cancer regimens and research articles.

A 10-percent fall in drug prices is likely to cause a 5- to 6-percent decline in both cancer regimens and research articles.

The study also looked at the relationship between the number of innovations within a company (defined as FDA-approved active ingredients contained in products sold by the company that are not contained in any other company's products) and the number of its employees. It finds an elasticity of 0.71 across 14 pharmaceutical companies; a 10-percent reduction in new approved active ingredients would cut the number of employees by 7 percent.

Civan and Maloney (2009)

In 2009, economists Abdulkadir Civan and Michael Maloney looked at both the existing drugs available to treat specific diseases and the number of new drugs in development for those same diseases.⁷⁹ After correcting for the number of existing treatments available for a specific condition, they found a positive relationship between the average price of available drugs and the number of new drugs being developed. A 30-percent increase in drug prices for a given condition would increase the number of drugs in development for that condition by 25 percent. Of course, as generics enter the market in response to favorable market conditions, prices usually fall.

Golec and Vernon (2010)

Economists Joseph Golec of the University of Connecticut and John A. Vernon looked at the relationship between an index of drug prices in both the United States and Europe and the profitability, research spending, and stock price of U.S. and EU pharmaceutical firms, respectively.⁸⁰ Between 1993 and 2004, European price controls prevented pharmaceutical prices from rising in inflation-adjusted terms, whereas real prices in the United States rose by 50 percent. However, the authors found a statistically significant positive correlation (0.64) between changes in the price increases and R&D spending.⁸¹

Market conditions not only affected the size of research spending, it also affected its location. Looking at other sets of data, they found biopharmaceutical research in the EU countries exceeded research conducted in the United States by 24 percent in 1986. But by 2004, U.S. levels were 15 percent greater than EU levels.⁸² This is mostly due to EU spending stalling between 1997 and 2001, roughly the same time the two price indexes diverged. Total U.S. biopharma research by foreign firms has been growing at a faster rate than foreign research by U.S. firms, largely because U.S. prices for on-patent drugs are higher than those in Europe. Higher prices have therefore caused foreign companies to divert their attention to the U.S. market, thereby strengthening the U.S. domestic industry.

Golec and Vernon also looked at the real annual growth rate in research spending. U.S. research consistently grew about 3.4 percentage points more than EU research each year. However, both rates have been trending down in recent years. Using regression analysis, the study shows firms that were more sensitive to European prices spent less on R&D, while the opposite was true of sensitivity to U.S. prices. By assuming the annual real increase in R&D spending would have maintained its rate of 6.6 percent had the Europeans not introduced price controls, the report estimates the present value of reduced R&D from regulations has been almost \$12 billion in current dollars and 1,680 R&D jobs.⁸³ Using an average cost per drug of \$260 million, this translates to 46 fewer medicines between 1986 and 2004. They noted that between 1987 and 1991, EU firms introduced 101 new medicines. This figure dropped to 57 new medicines between 2000 and 2004, the difference of which was roughly the number they attributed to the decline in R&D. Meanwhile, the number of U.S. new medicines increased from 54 to 70. Similar price controls in the United States would have reduced the present value of research by almost \$31 billion, resulting in a loss of 117 new medicines and 4,368 jobs.⁸⁴

Schwartz (2018)

In 2018, researchers at Precision Health Economics used a model of the over-50 population to simulate the elimination of price controls in non-U.S. OECD countries.⁸⁵ The study estimated that removing price controls would raise pharmaceutical revenues by 30 percent. The paper estimated that a 30-percent price increase in non-U.S. OECD countries would increase the size of the global pharmaceutical market by around 12 percent. This in turn would produce a 12 percent increase in research and 13 new drugs per year. The impact grows to 44 new molecules per year by 2060. Assuming these drugs would also be introduced into the United States, the expected longevity of American 45-year-olds would increase by 0.86 years, which the report values at \$1.54 trillion, or \$67,000 per individual. For 15-year-olds, the increase in longevity would be 1.6 years, worth \$115,000 per person. Although the net benefits to non-U.S. individuals would be partially offset by higher drug prices in the near term, these benefits would still be significant. Life expectancy for a 45-year-old European would increase by 0.81 years, and welfare gains would exceed \$80,000 per person.

POSSIBLE POLICY SOLUTIONS

Although the purpose of this report is not to promote one policy solution over others, a number of possible reforms could improve the situation. The first lesson is policymakers should exercise caution before pursuing any policies that would reduce the net revenues from the sale of current drugs. Efforts in this direction are likely to lower long-term welfare by reducing the number of future breakthroughs.

Policies that encourage other nations to raise the price of patented drug prices are likely to boost the funding of future research. If done collectively, all nations would benefit.

Policies that encourage other nations to raise the price of patented drug prices are likely to boost the funding of future research. If done collectively, all nations would benefit. These reforms could be accompanied by changes that make it easier to introduce generic drugs, likely resulting in net benefits to consumers. Taking full advantage of generics would lower drug revenues. But despite the link between revenues and research, the goal of public policy should not be to prop prices up as far as possible, but rather to structure a well-functioning market that adequately rewards innovation and links prices to social benefits. Once a fair patent period has expired, patients should benefit from heightened competition.

Other reforms could aim at reducing the cost of drug development, which would likely result in both lower prices and increased investment in R&D. Congress and the FDA should continue to improve and streamline, wherever possible, the drug approval process, keeping in place existing safety and efficacy standards. Another option is to encourage more innovation in drug manufacturing. A recent article argues that pharmaceutical manufacturing could be more efficient. It attributes much of this to high regulatory barriers and inefficient intellectual-property protection of manufacturing methods. Proposed changes, such as faster regulatory approvals for manufacturing innovations that do not affect quality, and preventing other companies from immediately copying improvements discovered by others either through process patents or by administratively denying other companies from copying the innovation for a certain period of time, could result in savings of \$50 billion each year.⁸⁶ As Congress reauthorizes the Manufacturing USA program, it should add funding for at least one center focused on biopharmaceutical manufacturing process technology to complement the existing BioFabUSA center, which focuses on the production process for large-molecule biotech drugs.

Congress could also ease drug discovery by appropriately loosening data restrictions in the health care market. Data-driven innovation promises to transform many aspects of medicine.⁸⁷ Within the pharmaceutical industry, better access to data can improve discovery, clinical review, testing, and post-market monitoring. However, these benefits require access to massive amounts of data from many people. Current federal policy makes the sharing of data difficult, even de-identified data individual patients are eager to share in order to help find a cure.

Finally, the federal government should significantly increase funding for basic medical research.⁸⁸ While the federal government is not well positioned to evaluate the most promising areas of applied research, it does play a large role in underwriting advances in the basic research on which these applications rest. Despite conservative worries that federal research displaces private research, the evidence shows that it clearly serves as a complement to it. Steady advances in the basic understanding of chemical and biological science reduce the risks and improve the returns from private efforts.

CONCLUSION

The U.S. biopharmaceutical industry is the most innovative and research-intensive industry in the world. Rather than channeling most current revenue into profits, companies pour a large portion of their revenues from each generation of drugs into research in the next round of development. As a result, the industry funds a large share of total U.S. R&D, employs a significant number of researchers, and continues to develop new drugs.

Some have argued high prices are not needed to maintain this virtuous cycle because, in the face of price controls or other measures to lower prices, companies can maintain high revenues for research by cutting marketing expenses.⁸⁹ However, Frosch et al. found that direct-to-consumer advertising was \$4.9 billion in 2007, or just 1.4 percent of total sales, hardly a honeypot of savings to be applied to lower drug pricing.⁹⁰ Moreover, while much advertising is designed to gain market share over competitors, some is about educating consumers and health care providers. Moreover, the drug industry is different than, say, the soap or car industry where it is relatively easy for consumers to find out on their own about new products and the differences between them. This is why Frosch et al. found that more than half of physicians agree that ads educate patients about health conditions and available treatments; and nearly 75 percent of patient respondents agree that advertisements improve their understanding of diseases and treatments.⁹¹ Moreover, absent some government restrictions on marketing, companies devote resources to marketing because they think that, even after accounting for its cost, it will increase demand and therefore revenues. Marketing and innovation are usually complements, because marketing makes it possible to sell new products.⁹²

The biopharmaceutical industry funds a large share of total U.S. R&D, employs a significant number of researchers, and continues to develop new drugs.

Advocates also argue price controls won't hurt drug innovation because companies must engage in continued research if they want to remain in business.⁹³ Revenues from current products play a large role in funding future research. Academic studies demonstrate a strong consensus that drug price controls limit revenues for biopharmaceutical companies, and that this in turns leads companies to invest less in research to develop new drugs. When countries intervene to set a cap on drug prices, as Europe did in the 1980s, research and innovation suffer. Moreover, firms are unlikely to invest in future research unless they believe doing so will be profitable.⁹⁴ Private firms routinely exit markets—and entire industries—once they lose profitability, even as they try to enter new, more promising markets. Price controls reduce industry R&D, which decreases the number of new drugs developed and thereby hurts patients in the future. It is simply not true that government can impose significant price controls without damaging the chances for future cures. Countries that allow higher drug prices experience more innovation. They also benefit from a more competitive domestic industry and more good jobs.

Finally, the reduction in research and new drug development will reduce overall societal welfare. Studies show that drugs create a large amount of social value. Yet even with current U.S. drug prices, firms usually capture only a small portion of this total value. The rest goes to patients, health care and insurance providers, and the rest of the population.

While the evidence does not dictate how policymakers should strike the proper balance between short-term availability and long-term health, it does show a trade-off exists. The close relationship between prices and research led one early study to conclude that:

[A] pell-mell march toward regulation of pharmaceutical industry pricing could seriously impair the industry's incentives for investment in new products.... If profits were held to "reasonable" levels on blockbuster drugs, aggregate profits would almost surely be insufficient to sustain a high rate of technological progress.... Should a tradeoff be required between modestly excessive prices and profits versus retarded technical progress, it would be better to err on the side of excessive profits.⁹⁵

ACKNOWLEDGMENTS

The author would like to thank Robert D. Atkinson and Stephen Ezell for helpful comments. All errors remain the author's responsibility.

ABOUT THE AUTHOR

Joe Kennedy is a senior fellow at ITIF. For almost 30 years, he has worked as an attorney and economist on a wide variety of public policy issues. His previous positions include chief economist with the U.S. Department of Commerce and general counsel for the U.S. Senate Permanent Subcommittee on Investigations. He is president of Kennedy Research, LLC, and the author of *Ending Poverty: Changing Behavior, Guaranteeing Income, and Transforming Government* (Rowman & Littlefield, 2008). Kennedy has a law degree and a master's degree in agricultural and applied economics from the University of Minnesota and a Ph.D. in economics from George Washington University.

ABOUT ITIF

The Information Technology and Innovation Foundation (ITIF) is a nonprofit, nonpartisan research and educational institute focusing on the intersection of technological innovation and public policy. Recognized as the world's leading science and technology think tank, ITIF's mission is to formulate and promote policy solutions that accelerate innovation and boost productivity to spur growth, opportunity, and progress.

For more information, visit us at www.itif.org.

ENDNOTES

1. See, Remarks by President Trump on Prescription Drug Prices, October 25, 2018, <https://www.whitehouse.gov/briefings-statements/remarks-president-trump-prescription-drug-prices/>.
2. The regulation was struck down by a judge after opponents challenged it in courts. Ricardo Alonzo Zaldivar, “Judge Strikes Down Rule Requiring Drug Ads To Reveal Prices,” *The Seattle Times*, July 19, 2019, <https://www.seattletimes.com/business/judge-strikes-down-rule-requiring-drug-ads-to-reveal-prices/>. The Administration is appealing.
3. P.L. 115-262 and P.L. 115-263, respectively.
4. United States Senate, Special Committee on Aging, <https://www.aging.senate.gov/press-releases/in-the-third-hearing-in-a-series-on-drug-pricing-administration-officials-detail-policies-focused-on-reducing-prescription-drug-costs>.
5. Congressional Budget Office, “Preliminary Estimate of the Prescription Drug Pricing Reduction Act of 2019,” https://www.cbo.gov/system/files/2019-07/PDPRA_preliminary_estimate.pdf.
6. Andrew Pollack, “Drug Goes From \$13.50 a Tablet to \$750, Overnight,” *The New York Times*, September 20, 2015, <https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html>.
7. Christopher Rowland, “The FDA Approves a Gene Therapy that is the Most Expensive Drug in the World,” *Washington Post*, May 24, 2019, https://www.washingtonpost.com/business/economy/the-fda-approves-a-gene-therapy-that-is-the-most-expensive-drug-in-the-world/2019/05/24/57c66500-7e4a-11e9-8ede-f4abf521ef17_story.html?utm_term=.02ada99c4378.
8. Accenture, *Time to Change: Bringing Outcomes to Market in a New Era of Breakthrough Science*, https://www.accenture.com/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Dualpub_26/Accenture-Pharma-High-Performance-Business-Research-2017.pdf#zoom=50.
9. Frank R. Lichtenberg, “The Impact of Pharmaceutical Innovation on Disability Days and the Use of Medical Services in the United States, 1997–2010,” *Journal of Human Capital*, Vol. 8(4), Winter 2014, https://www.jstor.org/stable/10.1086/679110?seq=1#page_scan_tab_contents.
10. An interesting approach is to ask how much the United States would have paid for a cure to HIV/AIDs 20 years ago, or how much it would pay for a cure for breast cancer delivered today.
11. Robert D. Atkinson, “China’s Biopharmaceutical Strategy: Challenge or Complement to U.S. Industry Competitiveness?” (Information Technology and Innovation Foundation, August 2019), <https://itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry>.
12. U.S. Census Bureau, (accessed August 9, 2019) <https://www2.census.gov/library/publications/decennial/2000/c2kprof00-us/c2kprof00-us.pdf>; <https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=CF>.
13. Centers for Medicare and Medicaid Services, National Health Expenditures, Retail Prescription Drugs Expenditures; Levels, Percent Change, and Percent Distribution, by Source of Funds: Selected Calendar Years 1970–2017, Table 16, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/Tables.zip>.
14. Centers for Medicare and Medicaid Services, National Health Expenditure Amounts by Type of Expenditure and Source of Funds: Calendar Years 1960–2017, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHE60-27.zip>.
15. Ibid.

16. Centers for Medicare and Medicaid Services, National Health Expenditures, Aggregate and Per Capita Amounts, Annual Percent Change and Percent Distribution: Calendar Years 1960–2017, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHEGDP17.zip>. GDP Deflator: Bureau of Labor Statistics, Consumer Price Index for Prescription Drugs, U.S. city average, [https://beta.bls.gov/dataQuery/find?fq=survey:\[cu\]&s=popularity:D](https://beta.bls.gov/dataQuery/find?fq=survey:[cu]&s=popularity:D); Population Data is from Federal Reserve Bank of St. Louis, FRED (POPTOTUSA647NWDB and SPPOP65UPTOZSUSA) (Accessed August 17, 2019).
17. Ibid; Centers for Medicare and Medicaid Services, National Health Expenditure Amounts by Type of Expenditure and Source of Funds: Calendar Years 1960–2017, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHE60-27.zip>.
18. The figure shows total retail spending on prescription drugs adjusted for inflation. This number is divided by the population ages 65 or more. The series is then indexed with 1960 equal to 100. Centers for Medicare and Medicaid Services, National Health Expenditures, Aggregate and Per Capita Amounts, Annual Percent Change and Percent Distribution: Calendar Years 1960–2017, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHEGDP17.zip>; GDP Deflator: Bureau of Labor Statistics, Consumer Price Index, All Urban Consumers, [https://beta.bls.gov/dataQuery/find?fq=survey:\[cu\]&s=popularity:D](https://beta.bls.gov/dataQuery/find?fq=survey:[cu]&s=popularity:D); Population Data is from Federal Reserve Bank of St. Louis, FRED (POPTOTUSA647NWDB and SPPOP65UPTOZSUSA), (accessed August 17, 2019).
19. Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs,” *Journal of Health Economics*, Vol 47, 2016, 23.
20. Congressional Budget Office, *How Taxes Affect the Incentive to Invest in New Intangible Assets*, November 2018, <https://www.cbo.gov/publication/54648>.
21. Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs.”
22. Donald W. Light and Rebecca Warburton, “Demythologizing the High Costs of Pharmaceutical Research,” *BioSocieties*, Vol. 6(1), March 2011, <https://link.springer.com/article/10.1057/biosoc.2010.40>; Jorge Mestre-Ferrandiz, Jon Sussex, and Adrian Towse, “The R&D Cost of a New Medicine” (December 2012), Office of Health Economics, <https://www.ohe.org/system/files/private/publications/380%20-%20R%26D%20Cost%20NME%20Mestre-Ferrandiz%202012.pdf?download=1>.
23. Statista, (accessed August 9, 2019), <https://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/>.
24. Department of Commerce, *Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Customers, Pricing, Research and Development, and Innovation*, December 2004, <https://2016.trade.gov/td/health/DrugPricingStudy.pdf>.
25. Council of Economic Advisors, *Reforming Biopharmaceutical Pricing at Home and Abroad*, February 2018, <https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf>.
26. Stephen J. Ezell, Adams B. Nager, and Robert D. Atkinson, “Contributors and Detractors: Ranking Countries’ Impact on Global Innovation” (Innovation Technology and Innovation Foundation, January 2016), <https://itif.org/publications/2016/01/20/contributors-and-detractors-ranking-countries-impact-global-innovation>.
27. Accenture, *Time to Change: Bringing Outcomes to Market in a New Era of Breakthrough Science*, 9, https://www.accenture.com/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Dualpub_26/Accenture-Pharma-High-Performance-Business-Research-2017.pdf#zoom=50.

28. Axene Health Partners, “US Pharmaceutical Pricing: An Overview,” <https://axenehp.com/us-pharmaceutical-pricing-overview/>.
29. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” *Journal of Economic Perspectives*, Vol. 7(3), Summer 1993, 102-03.
30. Ibid.
31. Ibid.
32. Bureau of Economic Analysis, *BEA Depreciation Estimates*, https://apps.bea.gov/national/pdf/BEA_depreciation_rates.pdf.
33. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” 104; Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 43–44, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drugr-d.pdf>.
34. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, 4.
35. Aswath Damodaran, [Data set 2018], accessed July 31, 2019, http://people.stern.nyu.edu/adamodar/New_Home_Page/data.html.
36. Yahoo! Finance, <https://finance.yahoo.com>, (accessed August 29, 2019).
37. Government Accountability Office, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, November 2017, <https://www.gao.gov/assets/690/688472.pdf>.
38. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 48, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drugr-d.pdf>.
39. Frank R. Lichtenberg, “The Impact of Pharmaceutical Innovation on Disability Days and the Use of Medical Services in the United States, 1997–2010,” *Journal of Human Capital*, Vol. 8(4), Winter 2014, 457, https://www.jstor.org/stable/10.1086/679110?seq=1#page_scan_tab_contents.
40. M. Christopher Roebuck, et al., “Medication Adherence Leads to Lower Health Care Use and Costs Despite Increased Drug Spending,” *Health Affairs*, 30(1) 2011, <https://doi.org/10.1377/hlthaff.2009.1087>.
41. Robert D. Atkinson, “Why Life-Sciences Innovation Is Politically ‘Purple’—and How Partisans Get It Wrong” (Information Technology and Innovation Foundation, February 2016), 2, <http://www2.itif.org/2016-life-sciences-purple.pdf>.
42. Alzheimer’s Association, *Changing the Trajectory of Alzheimer’s Disease: How a Treatment by 2025 Saves Lives and Dollars*, 2015, <https://www.alz.org/media/Documents/changing-the-trajectory-r.pdf>.
43. Adams B. Nager and Robert D. Atkinson, “A Trillion Dollar Opportunity: How Brain Research Can Drive Health and Prosperity” (Information Technology and Innovation Foundation, July 2016), <https://itif.org/publications/2016/07/11/trillion-dollar-opportunity-how-brain-research-can-drive-health-and>.
44. “Antibiotics biotech firms are struggling,” *The Economist*, May 4, 2019, <https://www.economist.com/business/2019/05/04/antibiotics-biotech-firms-are-struggling>.
45. Organization for Economic Cooperation and Development, *Health at a Glance 2017*, Table 10.12, https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2017_health_glance-2017-en. Data is for 2014 or latest year.
46. Ibid, Table 10.13, Business Enterprise R&D Expenditure as a Portion of Gross Value Added. Data is for 2014 or latest year.
47. European Federation of Pharmaceutical Industries and Associations, *The Pharmaceutical Industry in Figures, 2019*, 4, <https://www.efpia.eu/media/412931/the-pharmaceutical-industry-in-figures-2019.pdf>.

48. Ibid, 9.
49. International Federation of Pharmaceutical Manufacturers & Associations, *The Pharmaceutical Industry and Global Health: Fact and Figures 2015*, 14, <https://www.ifpma.org/resource-centre/facts-figures-2015/>.
50. National Science Foundation, *Business Research and Development and Innovation: 2016*, May 13, 2019, Table 2, <https://ncses.nsf.gov/pubs/nsf19318/#&>.
51. Ibid, Table 12.
52. Ibid, Table 18.
53. Ibid, Table 53.
54. Joe Kennedy, “How to Ensure That America’s Life-Sciences Sector Remains Globally Competitive” (Information Technology and Innovation Foundation, 2018), <https://itif.org/publications/2018/03/26/how-ensure-americas-life-sciences-sector-remains-globally-competitive>.
55. Richard A. Epstein, Review of *The Constitutional Foundations of Intellectual Property* by Randolph J. May and Seth L. Cooper, *The Federalist Society Review*, Vol. 17(1), February 2016, <https://fedsoc-cms-public.s3.amazonaws.com/update/pdf/sUvIjbOFb28cFAEch9SUERotlc2Ekcmo8mmzSQEh.pdf>.
56. Ernst R. Berndt, “Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price,” *Journal of Economic Perspectives*, Vol. 16(4), 2000, 55, 57.
57. Drug prices may be more resistant to price competition than other products. Limits on physician awareness of new treatments and drug prices, consumer insensitivity due to the presence of insurance, and the lack of transparency about prices can all limit the degree of competition. However, studies show the introduction of generics results in a rapid fall in prices. Council of Economic Advisors, *Reforming Biopharmaceutical Pricing at Home and Abroad*, February 2018, <https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf>. However, in some cases drug prices may clearly be too low. Severe shortages of BCG, the leading drug for bladder cancer, have been blamed on the fact that its price is too low to encourage an expansion of manufacturing capacity. Laurie McGinley, “Low Prices of Some Lifesaving Drugs Make Them Impossible to Get,” *Washington Post*, June 18, 2019, https://www.washingtonpost.com/national/health-science/low-prices-of-some-lifesaving-drugs-make-them-impossible-to-get/2019/06/18/abd03190-66bb-11e9-82ba-fcfeff232e8f_story.html?utm_term=.af6cdbf1b79f.
58. Ernst R. Berndt, “Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price,” 59. Berndt finds that “[o]ver the longer term, expectations of reduced freedom to price in the United States would undoubtedly have a very substantial negative impact on all phases of drug R&D, and therefore would reduce the future supply of new products, decreasing price competition among them.”; Ibid, 61.
59. Christopher Rowland, “The FDA Approves a Gene Therapy that is the Most Expensive Drug in the World.”
60. Robert D. Atkinson, “How the Biopharmaceutical Industry Contributes to Open Scientific Knowledge” (Information Technology and Innovation Foundation, November 2018), <https://itif.org/publications/2018/11/05/how-biopharmaceutical-industry-contributes-open-scientific-knowledge>.
61. Tomas J. Philipson and Anupam B. Jena, “Surplus Appropriation from R&D and Health Care Technology Assessment Procedures,” NBER Working Papers No. 12016, <https://www.nber.org/papers/w12016>.
62. Ibid, 5–6.

63. Darius N. Lakdawalla, "Economics of the Pharmaceutical Industry," *Journal of Economic Literature*, Vol. 56(2), 2018, 424, <https://doi.org/10.1257/jel.20161327>.
64. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 9, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drug-r-d.pdf>.
65. Ibid.
66. Organization for Economic Cooperation and Development, *Pharmaceutical Pricing Policies in a Global Market*, 192, <https://www.oecd.org/els/pharmaceutical-pricing-policies-in-a-global-market.htm>. Italics in original.
67. Ibid, 190, citing DIUS, *The R&D Scoreboard 2007: The Top 850 UK and 1250 Global Companies by R&D Investment – Main Tables*, Department of Innovation, Universities and Skills, London.
68. Government Accountability Office, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, November 2017, <https://www.gao.gov/assets/690/688472.pdf>.
69. Ibid.
70. Henry Grabowski and John Vernon, "The Determinants of R&D Expenditures," *Drugs and Health* (R.B. Helms ed.), Washington, D.C., AEI Press 1981.
71. Henry Grabowski and John Vernon, "The Determinants of Pharmaceutical Research and Development Expenditures," *Journal of Evolutionary Economics*, Vol. 10, 2000.
72. Ibid, 207.
73. Department of Commerce, *Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Customers, Pricing, Research and Development, and Innovation*, December 2004, <https://2016.trade.gov/td/health/DrugPricingStudy.pdf>.
74. New active substances are those that either contain a chemical active substance that is not previously authorized or that demonstrate the substance differs significantly in safety or efficacy from prior drugs.
75. Daron Acemoglu and Joshua Linn, "Market Size in Innovation: Theory and Evidence From the Pharmaceutical Industry," *Quarterly Journal of Economics*, Vol. 119(3), August 2004, <https://economics.mit.edu/files/4464>.
76. Carmelo Giaccotto, Rexford E. Santerre, and John A. Vernon, "Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry," *The Journal of Law & Economics*, Vol. 48(1) April 2005, https://www.jstor.org/stable/10.1086/426882?seq=1#page_scan_tab_contents.
77. Thomas A. Abbott and John A. Vernon, "The Cost of U.S. Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions," NBER Working Paper No. 11114, February 2005, <https://www.nber.org/papers/w11114>.
78. Frank R. Lichtenberg, "Importation and Innovation," NBER Working Paper No. 12539, September 2006, <https://www.nber.org/papers/w12539>.
79. Abdulkadir Civan and Michael T. Maloney, "The Effect of Price on Pharmaceutical R&D," *The B.E. Journal of Economic Analysis & Policy*, Vol. 9(1), January 2009, https://www.researchgate.net/publication/46556017_The_Effect_of_Price_on_Pharmaceutical_RD.
80. Joseph Golec and John A. Vernon, "Financial Effects of Pharmaceutical Price Regulation on R&D Spending by EU Versus US Firms," 625, *Pharmacoeconomics*, Vol. 28(8), 2010. All cost estimates have been converted to 2019 dollars using the consumer price index.
81. Ibid, 620.
82. Ibid, 621.
83. Ibid, 625.

84. Ibid.
85. Taylor T. Schwartz et al., “The Impact of Lifting Government Price Controls on Global Pharmaceutical Innovation and Population Health,” Poster Presented at the ISPOR 23rd Annual International Meeting, Baltimore, MD, May 22, 2018, https://tools.ispor.org/research_pdfs/58/pdffiles/PHP216.pdf
86. W. Nicholson Price II, “Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing,” *Boston College Law Review*, Vol. 55(2), 2014, <http://lawdigitalcommons.bc.edu/bclr/vol55/iss2/5>.
87. Joshua New, “The Promise of Data-Driven Drug Development,” (Center for Data Innovation, forthcoming), <https://www.datainnovation.org/2019/09/accelerating-data-driven-drug-development/>.
88. Robert D. Atkinson, “Healthy Funding: The Critical Role of Investing in NIH to Boost Health and Lower Costs,” (Information Technology and Innovation Foundation, March 2019), <https://itif.org/publications/2019/03/25/healthy-funding-critical-role-investing-nih-boost-health-and-lower-costs>.
89. Dean Baker, “Financing Drug Research: What Are the Issues?” (Center for Economic and Policy Research, Issue Brief, September 2004, 8–9, http://cepr.net/documents/publications/intellectual_property_2004_09.pdf.
90. D.L. Frosch, et al., “A Decade of Controversy: Balancing Policy with Evidence in the Regulation of Prescription Drug Advertising,” *American Journal of Public Health*, Vol. 100(1) (January 2010), 24–32.
91. Ibid.
92. Darius N. Lakdawalla, “Economics of the Pharmaceutical Industry,” *Journal of Economic Literature*, Vol. 56(2), 2018, 438, <https://doi.org/10.1257/jel.20161327>.
93. Hagop Kantarjian and S. Vincent Rajkumar, “Why are Cancer Drugs So Expensive in the United States, and What are the Solutions?” *Mayo Clinic Proceedings*, Vol. 90(4), 501, April 2015, [https://www.mayoclinicproceedings.org/article/S0025-6196\(15\)00101-9/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196(15)00101-9/fulltext); Donald W. Light and Rebecca Warburton, “Demythologizing the High Costs of Pharmaceutical Research,” *BioSocieties*, Vol. 6(1), March 2011, 2, <https://link.springer.com/article/10.1057/biosoc.2010.40>.
94. Megan McArdle, “There’s a High Cost to Making Drugs More Affordable for Americans,” *Washington Post*, May 7, 2019, https://www.washingtonpost.com/opinions/theres-a-high-cost-to-making-drugs-more-affordable-for-americans/2019/05/07/0a36ceba-7044-11e9-9f06-5fc2ee80027a_story.html.
95. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” *Journal of Economic Perspectives*, Vol. 7(3), Summer 1993, 113.

INTRODUCTION

Drug prices are once again a major focus of public policy in Washington D.C. President Trump has stated that reducing drug prices is one of his highest priorities.¹ The administration recently issued new regulations requiring manufactures to list the price of their drugs in television ads.² Congress has already passed the Know the Lowest Price Act and the Patient Right to Know Drug Prices Act, both of which try to promote transparency in prices.³ The Senate Special Committee on Aging recently conducted a series of hearings on drug pricing.⁴ And the Senate's bipartisan Prescription Drug Pricing Reduction Act would reduce government spending on drugs by an estimated \$100 billion over the next decade.⁵

This renewed attention is due to several factors. In a few cases, companies have dramatically raised the prices of specific drugs in order to generate more profits.⁶ Although these instances have been relatively rare, they have generated a great deal of publicity and comment. In other cases, new drugs have been introduced with large price tags. For instance, Novartis recently announced its new drug Zolgensma, which treats spinal muscular atrophy, will be priced at \$2.1 million for a one-time therapy.⁷ A large reason for the high cost is that relatively few people suffer from the disease and thus the cost of development must be spread over fewer patients. Finally, the rising cost of health care, including drugs, is placing greater pressure on individuals, insurers, and public budgets. A recent report by Accenture revealed a \$30 billion gap between the expected profits of drug companies from new drug launches and the projected drug spending of the public health programs in developed countries.⁸

Public policy demands a constant array of trade-offs whose difficulty only makes them more important. For prescription drugs these trade-offs occur on at least three levels. At the first level, policymakers must weigh the benefits of devoting more resources to health care as opposed to other important social needs such as infrastructure, education, and income support. Second, within health care they must balance spending on pharmaceuticals against other forms of health care, the prices of which have also been rising. These trade-offs may not be so stark, however, as in many cases the use of prescription drugs reduces the cost of other forms of health care.⁹ There is also the difficult question of whether to devote extensive resources to help a few people with severe conditions at the expense of slightly better care for the majority. Attempts to evaluate the worth of different treatments require that we assign a cost to human life. But this cost is extremely subjective and cannot be determined by economic considerations alone.¹⁰

Finally, policymakers must choose between the respective demands of current and future patients. Government price controls and other measures to reduce drug prices, such as weakened intellectual property protection will undoubtedly help current patients. But this will come at a cost. Money not consumed today can be invested for tomorrow. For the issue of pharmaceutical drugs, an overwhelming body of academic research shows that price controls will significantly restrict the number of new drugs in the future. The pharmaceutical industry is the epitome of a dynamic high-tech industry, wherein the profits from one generation of products go to pay the high development costs for the next generation. Artificially reducing drug revenues today will not only cause companies to cut back on their future research—meaning the next generation will benefit less from new drug discoveries—it will jeopardize U.S. leadership in an industry that punches above its weight in funding research and employing scientists.¹¹

An overwhelming body of academic research shows that price controls will significantly restrict the number of new drugs in the future.

All of these trade-offs are inevitable. Because there is no one right answer, many of these decisions should be subject to the political process, wherein policymakers can weigh the views and interests of different groups. This report does not presume to make these decisions for society. However, it is critical that when making these decisions, policymakers clearly understand the benefits and costs of each option. The purpose of this report is threefold. First, it reviews some of the data regarding drug spending. Second, it reviews the pharmaceutical industry's strong record in funding research and employing scientists. Finally, it summarizes the academic research showing a strong causal link between current drug prices and revenues on the one hand and future research and discoveries on the other.

ARE DRUG PRICES TOO HIGH?

In order to maximize social welfare with limited resources, policymakers need to appreciate the costs and benefits of each decision they make. In the context of drug prices, they need to clearly understand the strong link between current revenues (which may or may not be the same as consumer prices) and the generation of future drugs. Put simply, drug companies must make significant profits on their best-selling drugs in one generation in order to reinvest in the next generation. A large portion of these “profits” goes to three sources before they are available for distribution to shareholders. First, the revenues must cover the costs of the high number of failed research efforts, most of which generate no revenues. Second, they must pay for the long delays between initial research and product sales. These capital expenditures account for roughly half of the total costs of developing new drugs. Finally, a large portion of the remainder goes into new research on the next generation of drugs. Market investors quickly notice whenever companies do not have a group of promising drugs in their pipelines.

Put simply, drug companies must make significant profits on their best-selling drugs in one generation in order to reinvest in the next generation.

As figure 1 points out, change in total spending on retail pharmaceuticals varied dramatically between 2000 and 2017. Although spending rose in later years, the increases were mostly modest. The total number of pharmaceutical doses sold (the volume of drugs) also increased, in part because of the increase in the U.S. population (up an average of 0.84 percent per year since 2000) and the increase in the elderly population which on average consumes more drugs (the population of Americans older than 65 years of old has increased an average of 2.27 percent per year since 2000).¹²

Figure 1: Annual change in total U.S. retail pharmaceutical spending¹³

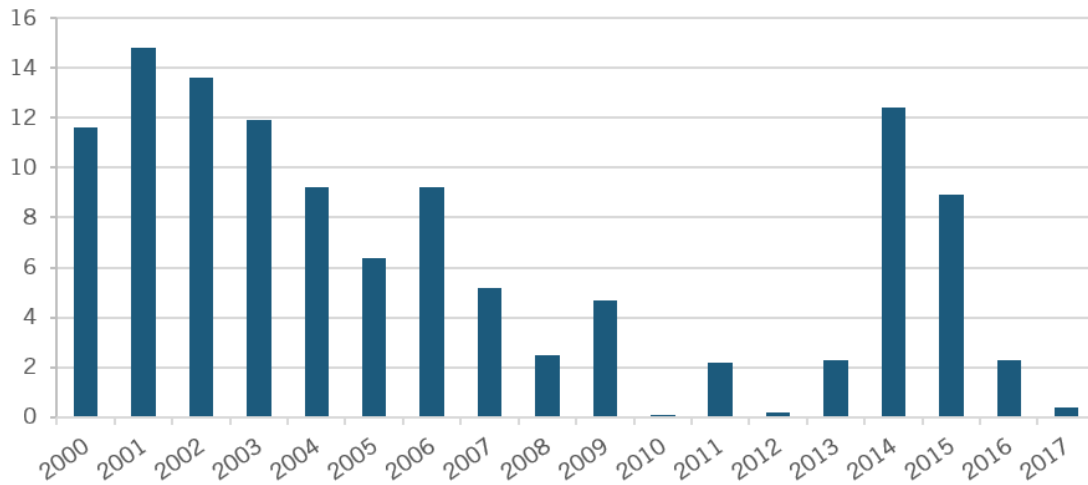


Figure 2, on the other hand, shows that the source of spending has changed dramatically. In 1960, fully 96 percent of all prescription drugs were paid for out of pocket. By 1980, this had fallen to 71.3 percent, and by 2000, it was 27.8 percent. In 2017, only 14 percent of prescription drugs were paid for out of pocket. Private insurance and Medicare/Medicaid paid for 42.0 percent and 40.2 percent, respectively. By 2027, the Centers for Medicare and Medicaid Services (CMS) expects the portion to decline to 12.8 percent. This trend has made many patients less sensitive to the cost of their medications.

Figure 2: Percentage of retail prescription drugs paid for out of pocket¹⁴

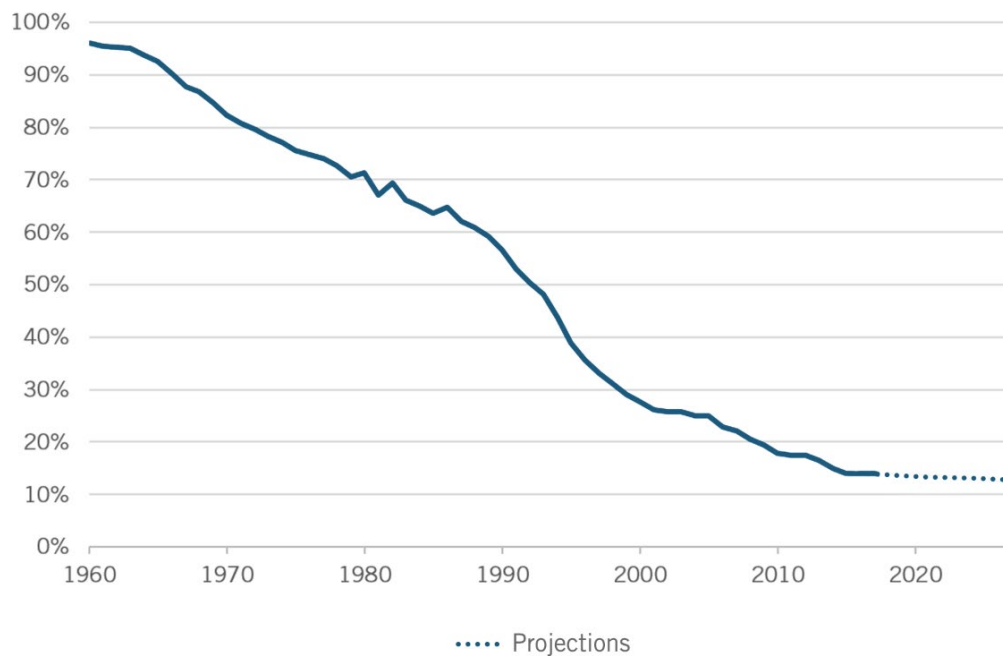
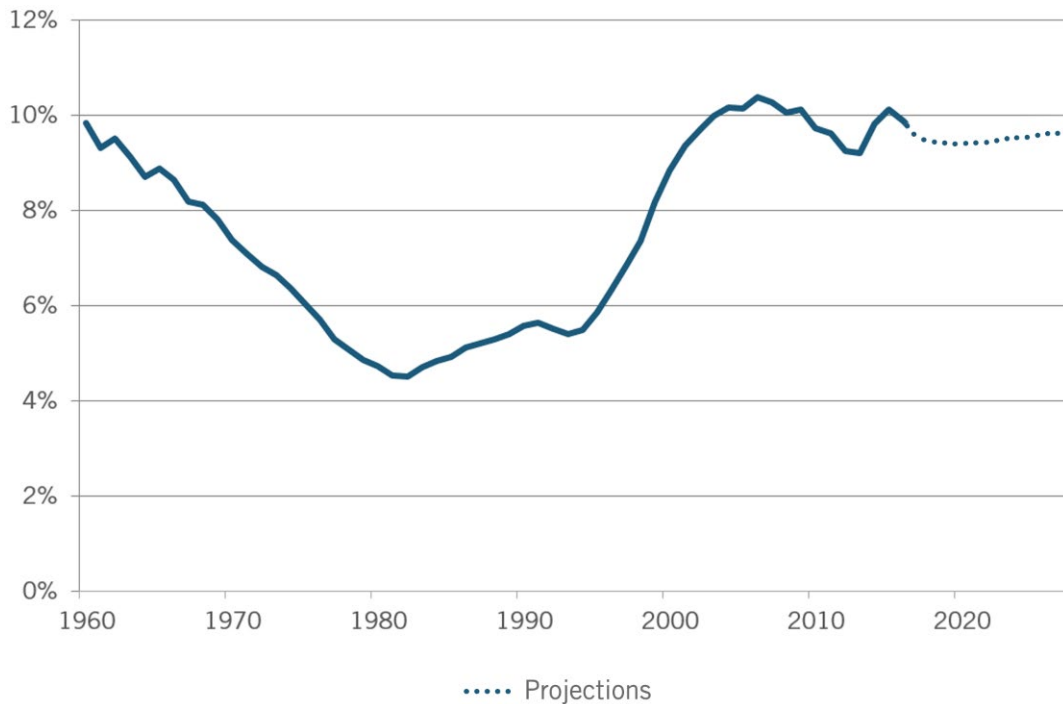


Figure 3 shows retail pharmaceutical sales as a percent of total health care spending. Although the fraction rose from 1980 to 2000, it has declined slightly since 2002 and is slightly lower than where it was in 1960. It is also projected to be relatively flat for the next decade.

Figure 3: Retail prescription drug spending and projections as a percentage of total health care spending: 1960–2027¹⁵



It should be no surprise that total health care spending is increasing, since the nation is getting richer and its population has grown. Nevertheless, total retail spending on drugs has increased almost sixfold, even after correcting for the Bureau of Labor Statistics' consumer price index for prescription drugs (see figure 4). However, so has gross domestic product (GDP). Figure 5 shows that, as a percentage of GDP, the rise was far less dramatic—with 2017 levels below 2009 levels—and only a small portion of total income.

Figure 4: Retail spending on prescriptions drugs adjusted for inflation (billions): 1970–2017¹⁶

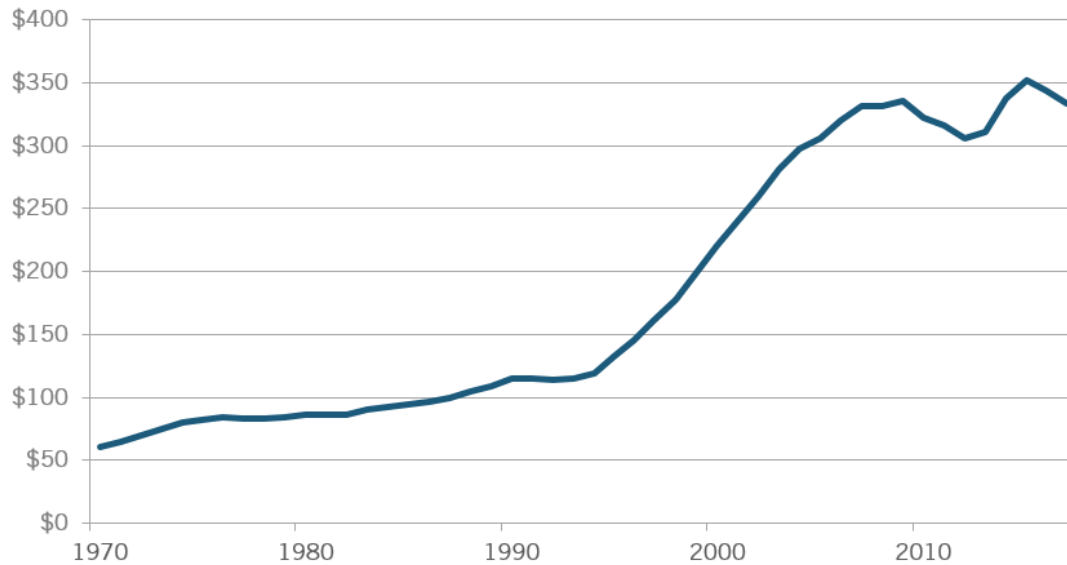
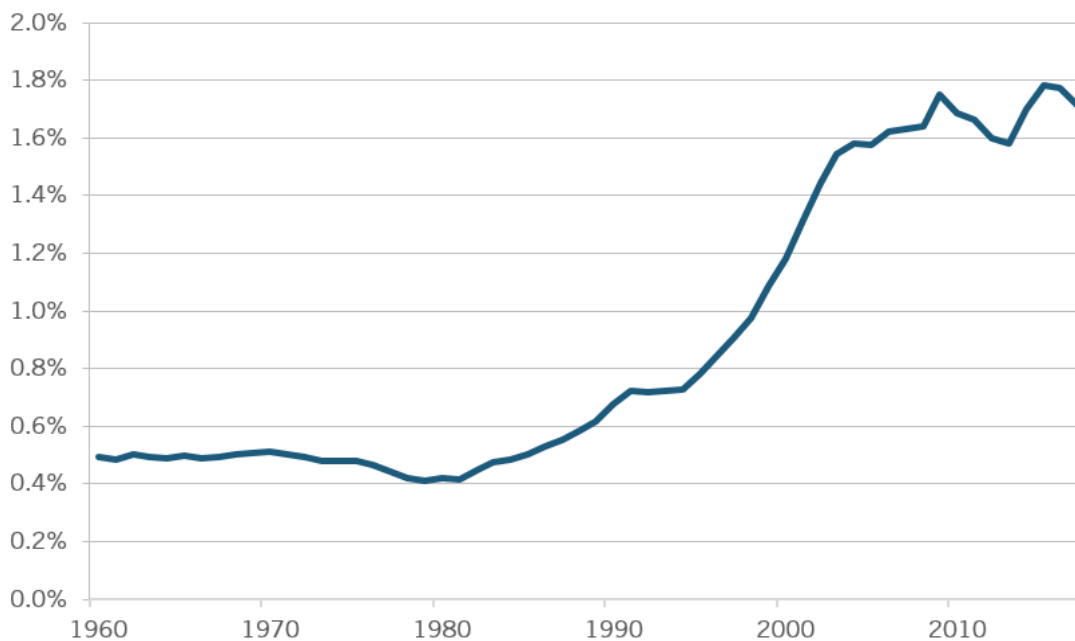
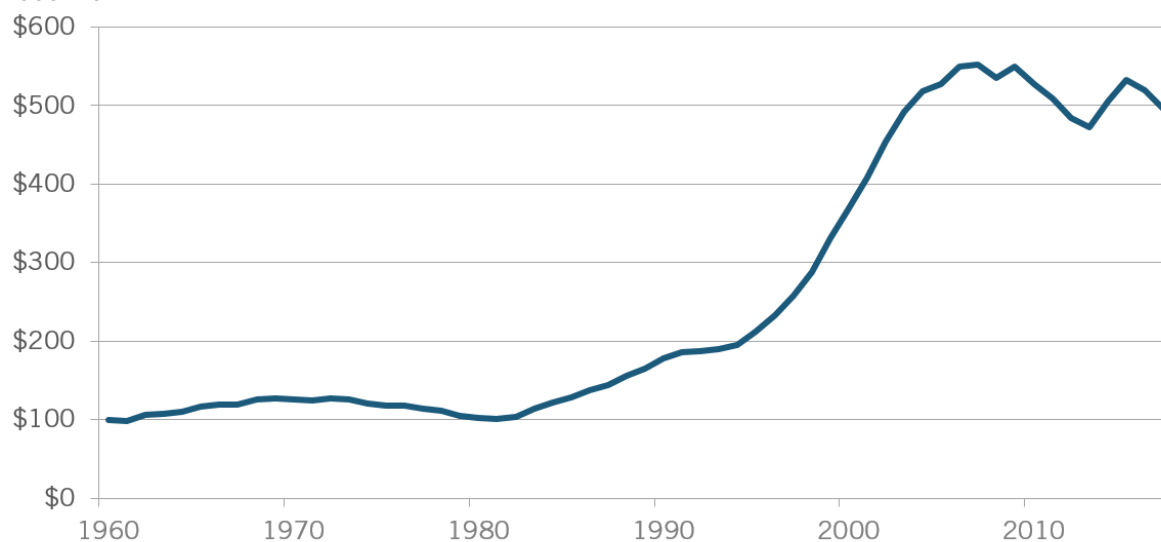


Figure 5: Retail prescription spending as a percentage of gross domestic product: 1960–2017¹⁷



Much of the increase has been driven by increased demand, in part as drugs have become more effective medical treatments. And much of the demand has been driven by those over the age of 65. Between 2002 and 2014, total retail spending on prescription drugs rose by \$140 billion. Spending on those over the age of 65 accounted for \$54 billion, or 38 percent of this rise. Yet the proportion of those over 65 in the population only rose from 12.3 percent to 14.3 percent of the total population. Figure 5 again shows total spending on retail prescription drugs, adjusted for inflation. It then adjusts this spending by the growth in the number of people ages 65 or older, revealing that when controlling for the growth of the elderly, real spending has declined 10.4 percent since 2007.

Figure 6: Real retail spending (billions) on prescription drugs indexed to the population over the age of 65: 1960–2017¹⁸



The Cost of Drug Development

Drug development is extremely costly for three main reasons. The first is the heavily regulated nature of the drug markets. Second, and partly due to this regulation, drug-development time is very lengthy, taking an average of 10 to 20 years. Because future revenues are worth less than those received today, a dollar of revenue in ten years will not come close to offsetting a dollar of research paid for today. Finally, drug development pushes at the boundaries of biological and chemical science, causing roughly 90 percent of all drug projects to fail.¹⁹ In order to survive, companies must recoup the costs of these failures in the revenues from the relatively rare successes. A recent study by the Congressional Budget Office (CBO) estimates pharmaceutical companies need to make a margin of 62.2 percent on their successful products in order to average a 4.8 percent rate of return on all of their assets. Based on past studies, the report assumes that 90 percent of all research spending results in no revenues, and that the approval process takes 12 years.²⁰

A recent CBO study estimates pharmaceutical companies need to make a margin of 62.2 percent on their successful products in order to average a 4.8 percent rate of return on all of their assets.

The most commonly accepted estimate of the cost of developing a new drug comes from the Tufts Center for the Study of Drug Development. Looking at drugs that began human testing between 1995 and 2007, it estimated that the average cost of developing and bringing to market a new compound had been \$2.6 billion (in 2013 dollars). Post-approval costs added another \$300 million. Out-of-pocket costs were \$1.4 billion. The rest was the cost of capital, using a discount rate of 10.5 percent. Costs had risen over the last decade due to a decline in clinical success rates and a rise in average research costs.²¹ The study also found that, although tax provisions such as the research and development (R&D) and the orphan-drug tax credits reduce the cost of development, their effect is relatively small compared to the total costs. While this study has been criticized, other estimates have produced comparable results.²²

The problem of rising drug costs is made worse by the fact that Americans must pay a large share of the costs of drug development. Since the United States accounts for roughly half of the global market (in terms of the amount of drugs consumed), one might normally expect it to pay for only about half of subsequent rounds of innovation.²³ But many countries, including high-income ones, pursue policies that keep the prices of their patented drugs artificially low.²⁴ Because manufacturers cannot recover much of their fixed costs overseas, they must charge higher prices in the United States in order to achieve a given rate of return. Somewhat surprisingly, some also raise the price of generic drugs in order to protect domestic manufacturers of those drugs. As a result, U.S. consumers pay approximately 70 percent of all global patented biopharmaceutical profits.²⁵

Many countries, including high-income ones, pursue policies that keep the prices of their patented drugs artificially low. As a result, U.S. consumers pay approximately 70 percent of all global patented biopharmaceutical profits.

This makes sense from the point of view of each country, particularly low-income countries. Because of their relatively small market size compared with the United States, raising drug prices would have little effect on either the amount or direction of global research. Collectively, however, price restrictions harm the global community.²⁶ They result in significantly less research, and fewer drugs. Everyone, including Americans, would benefit if all nations contributed their fair share to drug research. Solving this collective action problem has proven difficult, however.

It is interesting to note that efforts to fight climate change share the same dynamic. For most countries, especially smaller ones, the rational action would be to not pay the price premium required for clean energy because the cost of not doing so would be widely diffused to all nations, while the benefit of a higher living standard from cheaper energy would be accrued by the individual nation. Yet, most nations have decided that, when it comes to clean energy innovation and adoption, they will put the interests of the globe ahead of their own interest. Nations such as Canada, Japan, and much of Europe that prioritize fighting climate change think nothing of free-riding on U.S. expenditures when it comes to fighting global diseases, thereby slowing rates of new drug innovation.

Measuring Prices and Profits

Measurement problems complicate any analysis of the pharmaceutical industry. First, there are problems measuring drug prices. For one thing, it can be very difficult to determine the correct price of a given drug. Pharmaceutical pricing involves a number of different players and several levels of discounts. Very few buyers pay list price, discounts vary significantly depending upon the buyer, and manufacturers have become more reliant on rebates in order to sell products. A recent Accenture report found that 4 of 11 drug companies studied had issued rebates totaling more than half of their gross U.S. sales.²⁷ Two pills with identical ingredients but different names can vary in price by a factor of five.²⁸ Moreover, middlemen play an important role in drug distribution and pricing.

Even when a common price definition is used, price indexes of the real cost of pharmaceuticals tend to overestimate the amount of inflation.²⁹ First, The U.S. Bureau of Labor Statistics (BLS)

infrequently changes the market basket of drugs whose prices it monitors, so new generics are often not included in the sample for several years even though their entrance into the market quickly lowers prices. And when they are included, they are measured as new products, not as cheaper versions of the branded drugs.³⁰ According to an estimate from 1993, this resulted in an upward bias in the measured price of drugs of 1.2 percentage points a year.³¹ Making this adjustment would mean actual prices fell in 3 of the last 9 years (see figure 1).

Second, price increases tend to be more rapid for mature branded pharmaceuticals that have proven their worth, while the prices of new products increase more slowly and can even decline. However, because new products are not included in the index until several years after their market entry, this declining-price experience is underrepresented. Finally, BLS does not measure improvements in consumer benefits associated with new drugs. If a new version of a drug costs the same as an existing one but delivers better results, its real cost has fallen, although the index would not capture that. In contrast, the government does include quality improvements in its measures of inflation for most other products, such as cars and computers. Although the government has tried to address some of these problems, the indexes likely still overstate the rate of inflation.

A second problem concerns how profits are measured, and particularly the accounting treatment of research costs and marketing expenses. Because both of these costs have a useful life of more than one year, standard accounting practice would include them as assets and amortize them over a period of years (perhaps five to eight) beyond which they cease to have value. For example, the Bureau of Economic Analysis now counts research as an asset and depreciates the value of biopharmaceutical research by 10 percent each year.³² However, the convention in the pharmaceutical industry is to deduct research and marketing costs from revenues in the first year. Although expensing for tax purposes makes sense in order to reduce the after-tax cost of research, and to reflect actual cash flow within the company, the measurement of return on assets should reflect traditional accounting principles. The deduction of research costs temporarily lowers measured profits because it raises the amount of costs that are deducted from revenues. However, by ignoring the continued value of research assets, it significantly understates a company's assets and therefore overstates the rate of return on assets.³³ CBO has reported that, after properly adjusting for the asset value of research, the industry's profitability remains "somewhat" higher than the average for all industries, but not twice as large, as standard measures show.³⁴

When research was properly accounted for, the return on equities fell to 8.3 percent for pharmaceuticals and rose to 0.9 percent for biotechnology. The market average was 14.1 percent.

In recent years, industry returns have been even lower. New York University professor Aswath Damodaran calculated estimated returns on equity (ROE) for different industries going back several years. His calculations include estimates that treat research as both a standard expense and a capital expenditure. For 2018, the return on equity for pharmaceuticals and biotechnology was 12.6 percent and -1.6 percent, respectively, compared with an economy average of 15.6 percent.³⁵ However, when research was properly accounted for, the ROEs fell to 8.3 percent for pharmaceuticals and rose to 0.9 percent for biotechnology. The market average was 14.1 percent. This relative performance is reflected in stock prices. Over the past five years, the NYSE

ARCA Pharmaceutical Index experienced an annual return of 2.0 percent, compared to 7.6 percent for the broader S&P 500.³⁶

Finally, even a significant reduction in margins would not transform drug pricing. The Government Accountability Office estimated that pharmaceutical and biotechnology revenues were \$775 billion in 2015, with an industry profit margin of 17.1 percent (not taking into account capitalization of research).³⁷ Reducing this margin to 6.7 percent (the average for Fortune 500 companies) and assuming all savings were used to lower prices would have lowered prices by only 10 percent.

Measuring the Benefits

Any analysis of the cost of drugs needs to also consider the benefits from their use. There is ample evidence that the benefits substantially exceed the costs. Policies that restrict the flow of future drugs are therefore likely to harm society, particularly if the savings are consumed, rather than invested.

Any analysis of drug costs needs to consider the benefits from their use. Policies that restrict the flow of future drugs are therefore likely to harm society, particularly if the savings are consumed, rather than invested.

A 2008 study by CBO found that average returns to society from past drug R&D appeared to have been large.³⁸ A study of the use of other medical services and whether advances in pharmaceutical treatments had any effect on days lost to sickness found that conditions that had larger increases in post-1990 drugs per affected person also had larger declines in disability days and the use of almost all non-drug medical devices.³⁹ The total benefit was \$95 per person, or twice the cost of the additional drugs. All of this social benefit went to patients and health care providers. In another study, improved medication adherence in patients with four chronic diseases resulted in benefit-to-cost ratios of between 3.1:1 and 10.1:1 depending on the condition. Annual savings per patient varied from \$1,258 to \$7,823.⁴⁰

The creation of net benefits also extends to future drugs. Reduced biomedical innovation would increase future health care costs and slow improvements in health and longevity.⁴¹ The Alzheimer's Association recently evaluated the current cost of treating the disease.⁴² By 2050, 16 percent of Americans 65 or older will suffer from some stage of Alzheimer's, with 6.5 million individuals in the severe stage of needing round-the-clock care. The cost of treating Alzheimer's that year will be \$1.2 trillion in 2019 dollars. The report estimates that discovering a drug in 2025 that would delay the onset of Alzheimer's by 5 years would reduce the cost of treatment in 2050 by one-third. Savings in the first 10 years alone would total \$935 billion. The high cost of mental illness (roughly \$1.5 trillion annually) also offers a great opportunity for cost reduction through better drugs.⁴³

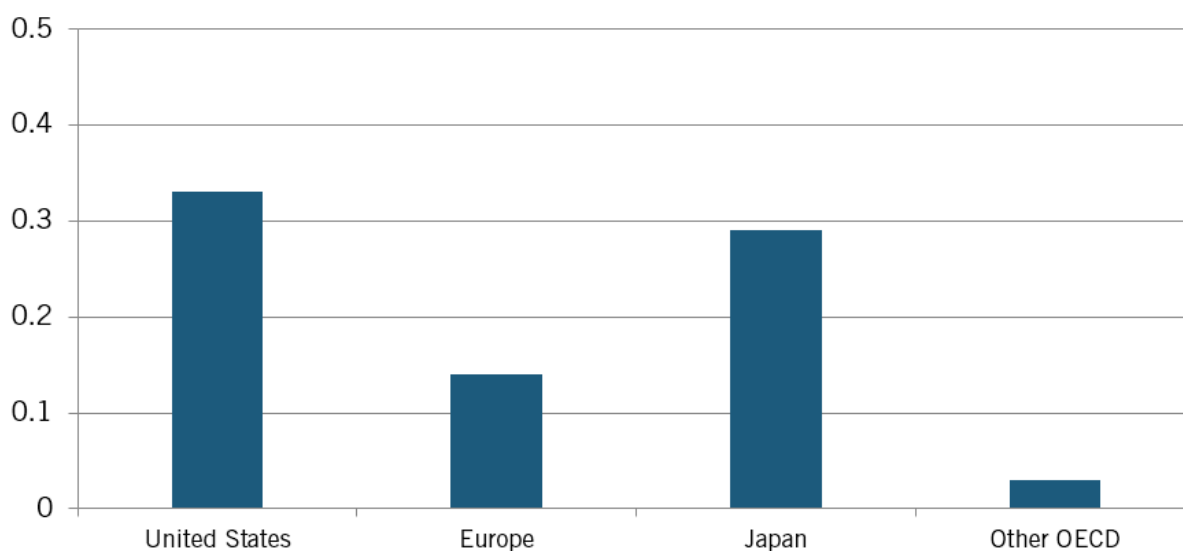
However, the presence of large social benefits is not enough. Companies must still be able to realize a profit on their drugs. A recent news article reports on the difficulty biotech firms face in developing new antibiotics.⁴⁴ Despite a growing need, a decline in market returns has caused larger firms to shift research over to other areas. For example, only three companies are currently conducting clinical research on antibiotics. The article speculates that part of the problem is few doctors know about the new antibiotics, which may be the result of a lack of marketing. Another

problem is new drugs, due to their high costs, are only used when other treatments do not work, meaning their overall sales are likely not enough to pay for new-drug development.

PHARMA'S ROLE IN PROMOTING RESEARCH

The pharmaceutical and biotechnology industries combined account for a large percentage of U.S. research, both as a fraction of their profits and as a fraction of total U.S. R&D. Figure 7 shows total business expenditures on pharmaceutical R&D in 2014 (the latest year for which data is available), with private research developing new drugs in the United States at a significantly higher percentage of GDP than in the rest of the world. Although Japan comes close in percentage terms, total private R&D spending was \$56.6 billion in the United States, compared with \$14.6 billion in Japan.

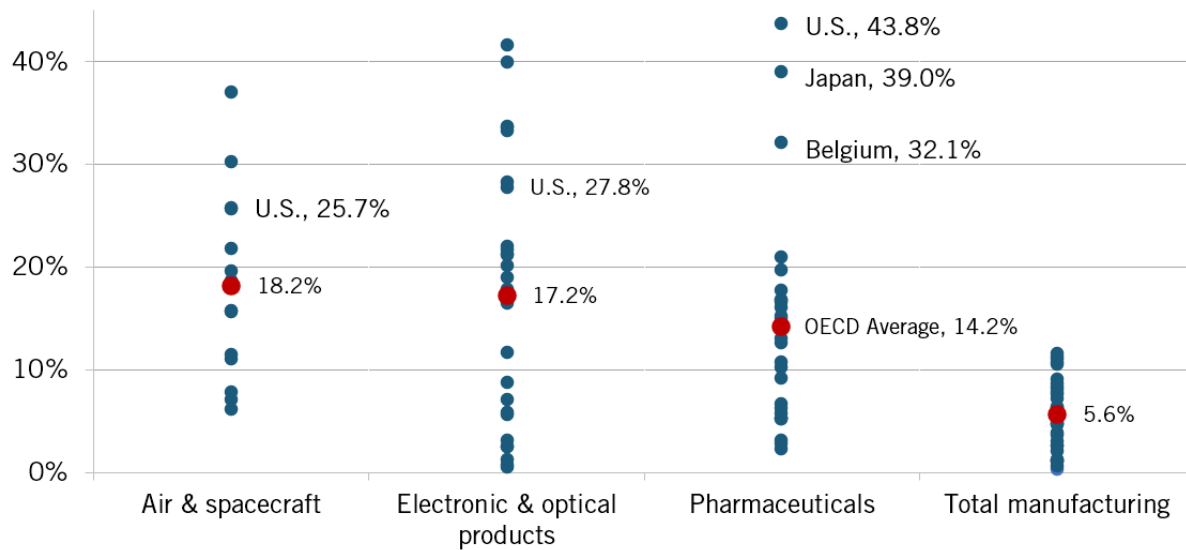
Figure 7: Business expenditure for pharmaceutical budgets for health-related R&D as a percentage of GDP, 2014⁴⁵



The U.S. pharmaceutical industry conducts far more pharma research than other countries, and more research overall than other U.S. industries.

This high level of investment also applies to the total value of the pharmaceutical industry. Figure 8 shows R&D intensity by industry, measured as business R&D spending as a percentage of the gross value added of an industry. Once again, the U.S. pharmaceutical industry conducts far more pharma research than other countries, and more research overall than other U.S. industries. U.S. pharmaceutical companies devoted 43.8 percent of their total value added in 2014 back into R&D, ahead of both air and spacecraft, and electronic and optical products.

Figure 8: R&D intensity by industry and country, 2014⁴⁶



Because of this research, Americans enjoy earlier access to new drugs. The European Federation of Pharmaceutical Industries and Associations recently found that, although the North American market accounted for only 48.9 percent of worldwide pharmaceutical sales, 65.2 percent of sales of new medicines launched between 2013 and 2018 were in the United States.⁴⁷ It also determined that, although the growth of drug research had stagnated from 2009 to 2013 (a period in which significant reforms to health care were being discussed), it grew at an 8.6-percent rate between 2014 and 2018. The European rate was only 3.8 percent.⁴⁸

Worldwide, the pharmaceuticals and biotechnology industry spent almost \$112 billion on R&D in 2013 (the latest year for which data is available).⁴⁹ The National Science Foundation regularly collects data on business research. According to its latest data, companies producing pharmaceuticals and medicines paid for \$65.8 billion of research in 2016.⁵⁰ This was almost 17 percent of all research funded by manufacturing companies in the United States. Biotechnology firms contributed another \$6.1 billion. Over 85 percent of this pharmaceutical research was conducted in the United States. Over 64 percent of this funding was devoted to development, while another 21 percent was spent on applied research.⁵¹ Companies devoted 16.5 percent of sales to domestic R&D.⁵² The only industries with higher ratios that year were semiconductor machinery and scientific R&D services (which include biotechnology). Biopharmaceutical companies accounted for 687,000 domestic employees, of which 144,000, or 21 percent worked in R&D.⁵³ This is over 9 percent of all R&D workers funded by industry.

THE EFFECT OF DRUG PRICES ON INNOVATION

The previous section discussed the strong contribution the pharmaceutical industry makes to U.S. research. The U.S. lead in life-sciences research delivers large benefits to the economy in the form of faster, more numerous breakthrough drugs and continued advances in existing therapies, as well as tens of thousands of high-paying jobs across the nation.⁵⁴

This section reviews the academic literature on the strong link between drug prices and the future introduction of new drugs. Like any industry, pharmaceutical manufacturers need to earn

an adequate rate of return on their assets in order to remain in business. However, the special nature of the pharmaceutical industry, in particular the heavy upfront investment in drug research and testing, and the long and uncertain delay between initial investments and drug revenues, means government price controls or other policies to reduce revenue (such as weakened intellectual property protection) will reduce drug innovation.

Numerous studies have shown a firm link between prices and profits on the one hand and higher levels of research and drug innovation on the other.

Numerous studies have shown a firm link between prices and profits on the one hand and higher levels of research and drug innovation on the other. Although this report will not attempt to define the proper balance in detail, policymakers need to be aware this link is well established. Lowering prices now will result in less future research and fewer new drugs. The decline in future drugs will in turn reduce patient welfare over the longer term. This is not to say the federal government should sit on the sidelines regarding the affordability of drugs, but rather that price controls will come at a cost to innovation and long-term patient well-being.

The Trade-Off Between Short-Term Affordability and Long-Term Innovation

The unique nature of the pharmaceutical industry complicates the task of setting prices. In many traditional industries with a competitive market, firms often set prices only slightly higher than the marginal cost of producing an additional unit. This is because in most traditional industries fixed costs (e.g., capital equipment, R&D, and other overhead) are relatively low compared with total costs of production.

However, setting prices close to marginal cost won't work for innovation industries—including biopharmaceuticals—wherein the marginal cost of producing another unit (e.g., a pill or dose) is usually relatively small in comparison with the overall fixed costs, especially research, development, and testing. As innovation companies, drug companies must be able to recover these high up-front costs. Like some other industries such as movies, wherein there is a risk of the product being a bust, biopharmaceutical companies must be able to price drugs to cover not just the fixed and marginal costs of the successful drug, but also the costs of the failures. High fixed costs (from both successes and failures) ensure companies will need to price drugs significantly above the marginal cost. Although short-term affordability of drugs may be increased if drug revenues are based on marginal cost, drug companies will not be able to recover their costs, which will make them stop investing in future research, lose money, and go out of business.

Ensuring prices remain high enough to allow drug manufacturers to recover their high fixed costs requires government intervention. In the United States, this is done mainly by giving drug companies patent protection for new discoveries. These policies give companies the ability to raise prices above marginal—and even average—cost, at least as long as there are few close substitutes to a particular treatment. Without patent protection, other companies would swoop into markets, thereby avoiding the hard and expensive work of developing and testing a drug and bearing only production and marketing costs. This is in fact what happens once the patent on a popular drug expires.

The granting of a monopoly through patents and other intellectual property protection has a positive effect on product development—which in the case of drug companies, is on research, development, and testing. While market power from intellectual property protection may reduce short-term welfare, it increases long-term welfare by encouraging more investment and innovation. This is why the Founding Fathers included patent protection in the Constitution.⁵⁵ Moreover, in many cases, a patent may not confer much effective pricing power. A company with a patent on a drug for a given disease may face strong competition from other drugs with similar effectiveness.⁵⁶ In such cases, the patents may not translate into effective pricing power.⁵⁷ In addition, the maker of a particular drug may face some limitations on market power from buyers, such as health care insurers and drug benefit plans, with their own market power. These restraints help ensure pharmaceutical prices will be roughly based on the value to patients and the broader health care system.⁵⁸ For example, although Zolgensma is priced at \$2.1 million for a one-time treatment, it treats spinal muscular atrophy (SMA). Infants born with SMA Type 1 typically die within 18 months or can only survive on life support. Roughly 30 new patients are born each month. The only existing therapy, Spinraza, costs \$750,000 for the first treatment and \$375,000 per year after that.⁵⁹

But even when companies set prices high, society can still benefit. When companies decide how much money to invest in research, they typically invest until the benefits to them stop exceeding their costs. Because companies do not benefit from the spillover benefits to society (the benefit competitors and consumers get from their innovation), they do not take them into account. In fact, research levels would be maximized by letting these companies capture all the social benefits.⁶⁰ A recent study by Tomas Philipson and Anupam Jena shows that drug companies typically capture only a small fraction of the total social benefit they produce.⁶¹ The study concentrated on therapies for HIV/AIDS introduced after the late 1980s. It estimated that these drugs increased social welfare by nearly \$1.4 trillion. However, the companies that produced these drugs increased their profits by only \$62.9 billion. They therefore captured less than 5 percent of the total welfare. The remainder went to the rest of society. Looking at over 200 previous studies of the cost efficiency of other drugs, the authors estimated that in 25 percent of the studies, companies captured less than 7 percent of the societal surplus. The appropriation of social welfare exceeded 25 percent in only one-quarter of the studies. Philipson and Jena also found that “dynamic efficiency only occurs when those undertaking the costs of R&D have incentives that are properly aligned with society, which is true when social surplus is entirely appropriated as profits.”⁶² Because firms capture only a small part of the total surplus, they do too little research. Although patent law, the R&D tax credit, and other policies can mitigate this effect, policymakers should remember that allowing firms to appropriate more of the surplus directly may promote dynamic efficiency (e.g., new drugs) and long-term societal benefits (e.g., health).

Drug pricing therefore requires a balance between short-term affordability and long-term innovation. Low prices (as well as public subsidies) allow more individuals to afford existing drugs now, but if they come at the expense of drug company revenues, they reduce the incentive to invest in new cures. Higher prices increase this incentive but can also make prices unaffordable for many patients. Subsidies for drugs, particularly for low- and moderate-income households, either through private insurance or government payments, is one way to balance this conflict. Unfortunately, there is no right answer for obtaining the proper balance, but those who try to strike it need to be aware of the trade-off.

The justification for high prices on any particular drug therefore depends on the assumption that they are needed to fund the subsequent round of innovation. This link has been established by numerous empirical studies over the last several decades. A recent survey summarized the scholarly literature this way: “The preponderance of evidence suggests that raising reimbursements for pharmaceuticals stimulates innovation, primarily because the expected rewards for innovation go up and secondarily because the cost of financing falls for cash-constrained pharmaceutical firms.”⁶³

“The preponderance of evidence suggests that raising reimbursements for pharmaceuticals stimulates innovation, primarily because the expected rewards for innovation go up and secondarily because the cost of financing falls for cash-constrained pharmaceutical firms.”

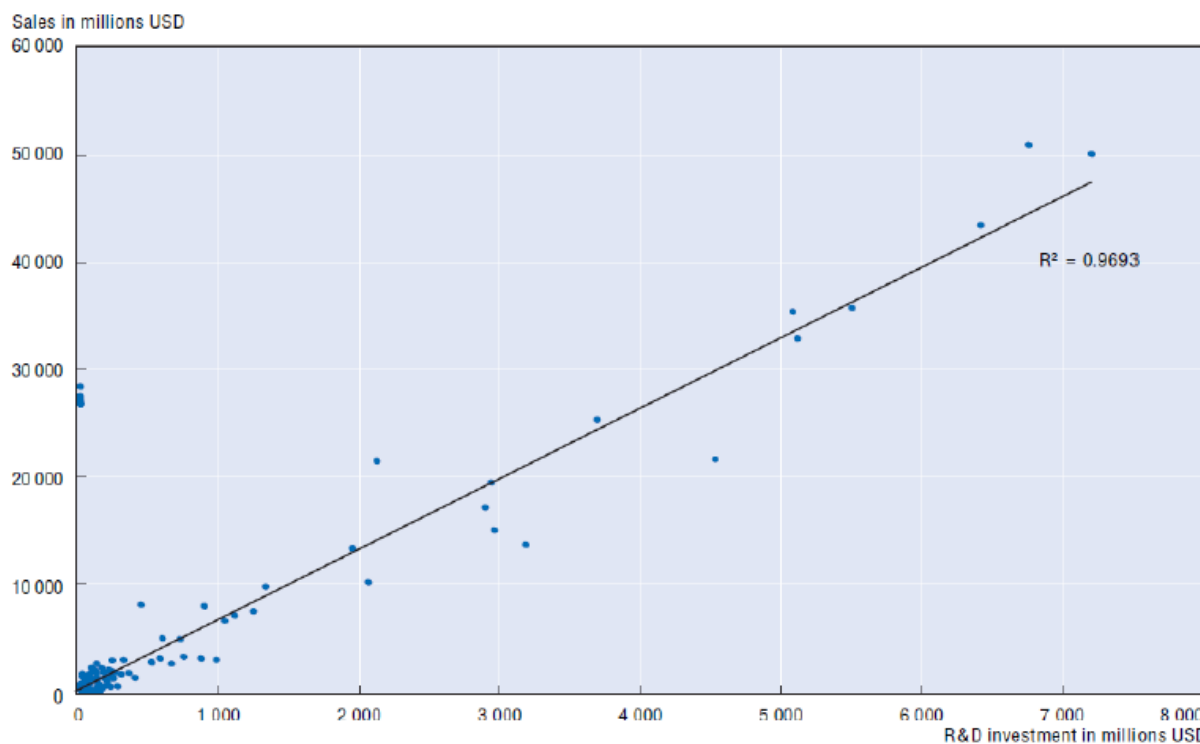
Previous Literature Reviews

Previous government reports have summarized the link between biopharmaceutical profits and innovation within the drug industry. CBO pointed to two underlying reasons why this link might be so strong.⁶⁴ First, as in most industries, the introduction of successful new drugs often leads to higher profits as companies are able to capture some of the social value created by their products. The profitability of current drugs also serves as a proxy for the profitability of future drugs. If biopharmaceutical firms are allowed to make reasonably large profits from their current products, they are likely to conclude that the same will be true in the future. This may cause them to increase both the speed and amount of their research activities. Conversely, they may view current attempts to hold down prices as likely to continue into the future, in which case they may decrease research funding.

The second reason CBO identified is adequate profits generate significant cash flow, which allows companies to finance the next round of innovation.⁶⁵ The availability of cash flow is important because raising significant amounts of money in the stock or bond markets is more costly. Biopharma companies have a much more detailed knowledge of disease models, the status of their current research, and the probabilities of success. Because investors cannot adequately assess these risks for themselves, they demand higher returns for investing. Assuming firms invest in R&D until their cost of capital exceeds the rate of return, financing through cash flow should allow them to justify more projects than if they have to raise the money from outside investors.

The Organization for Economic Cooperation and Development (OECD) conducted a detailed study of this issue in the pharmaceutical industry. It found that “[p]harmaceutical pricing and reimbursement policies stand to affect innovation through multiple channels, influencing both the *incentives* to invest in private R&D and the *costs of investment*. The main channel of prospective influence is the impact of pricing and reimbursement policies on the *expected return on investment* in R&D.”⁶⁶ In fact the generation of large revenues is closely related to the amount of research an individual company does. Figure 9 shows R&D expenditures and sales of the 151 largest pharmaceutical firms in the world in 2006. There was clearly a very strong correlation (0.97).

Figure 9: R&D expenditures and sales in the pharmaceutical industry, 2006⁶⁷



Note: The data were prepared on the basis of annual reports and consolidated accounts received up to and including 31 July 2006. Annual reports with a year-end older than 30 months from the cut-off date or a publication date older than 24 months from cut-off date are excluded.

Source: DIUS (2007).

Pricing policies affect not only the amount of research conducted (leading-edge or marginal improvements) but also the type and the decision of whether and when to introduce a new product to the market.

The Government Accountability Office recently completed its own review of trends in pharmaceutical profits and R&D.⁶⁸ It found that both experts and academic research has concluded that high revenue potential associated with a large number of patients, or the ability to charge a high price, is an important incentive for R&D investment.⁶⁹ Exclusivity periods and patent protection, tax incentives, and expedited review programs were also cited as influencing R&D. Of course, while biopharmaceutical companies, like other firms, would like to charge as high a price as possible, their ability to do so is limited by both buyers not being willing to pay more for a drug than the benefits it delivers in terms of longer, healthier lives, and the presence of at least some competition in the marketplace.

Experts and academic research have concluded that high revenue potential associated with a large number of patients, or the ability to charge a high price, is an important incentive for R&D investment.

Academic studies that explore the causal link between drug revenues and research face a common difficulty in finding good data. They also take different approaches to choosing the inputs, outputs, and econometric model to measure the relationship between prices and profits, and research and innovation. So it is somewhat remarkable that, collectively, they arrive at the

common answer that high prices for today's treatments are closely associated with more research and a larger number of future drugs. There appear to be no scholarly studies that show no relationship between current prices and future innovation. Given their common conclusion that short-term price declines will endanger future drug innovation, it is worthwhile to discuss some of the major studies individually.

Grabowski and Vernon (2000)

Two studies by Duke University's Henry Grabowski and John A. Vernon from the University of North Carolina at Chapel Hill looked at the relationship between expected returns and cash flows on the one hand, and company research on the other. The first study covered the period from 1962 to 1975.⁷⁰ This followed passage of the Kefauver-Harris Amendment to the Food, Drug, and Cosmetic Act, which required a showing of efficacy as well as safety in order to get FDA approval. This increased development times by several years and R&D costs per new drug by several-fold. The authors found that research productivity, defined as sales of recent new drug introductions divided by lagged R&D spending, declined rapidly during the period. This eventually influenced cash flows, the decline of which along with the fall in research productivity together had the effect of reducing R&D.

A later study looked at research spending between 1974 and 1994 in 11 firms specializing in prescription drugs.⁷¹ Together, these firms represented just over 40 percent of the U.S. market and half of the innovative output (defined as the first 3 years' sales of all new chemical entities introduced in a period of time). Unlike the previous period, research productivity rose over 50 percent. Grabowski and Vernon found that both expected productivity of R&D and available cash flow positively affect R&D spending. Again, the link between cash flow and research is due to the fact that internally generated funds, which are often the result of higher profits, cost less than either borrowed funds or new equity, and therefore lower the required rate of return for new research at the margin.⁷²

U.S. Department of Commerce (2004)

In 2004, Congress asked the U.S. Department of Commerce to study the effect of pharmaceutical price controls in OECD countries.⁷³ The department concluded that most OECD countries use a variety of controls to limit the price of patent-protected drugs in their countries. These restrictions reduced the revenue of drug companies by \$18 billion to \$27 billion per year. The department estimated that lower revenues reduced global R&D by \$5 billion to \$8 billion, or 3 to 4 new drug entities annually. This latter effect was based on outside estimates regarding the cost of developing a new drug. Note that using a lower cost of development would imply that the reduction in research spending resulted in a higher number of new drugs not being discovered. Access to these new drugs would benefit U.S. consumers by \$5 billion to \$7 billion a year. In contrast, OECD countries also used price floors on generic drugs in order to protect their domestic manufacturers. Eliminating these floors would save Europeans \$5 billion to \$30 billion annually, potentially paying for restoring a competitive market to patent drugs. The study also found that significantly more new active substances were available in the United States than in other countries, which it attributed to companies' increased ability to capture more of the social benefit from current drugs.⁷⁴

Acemoglu and Linn (2004)

One problem with modeling the relationship between prices and research is the causation may go both ways. It is possible that better research increases profits rather than the other way around. To get at this problem, economists Daron Acemoglu and Joshua Linn examined the pharmaceutical industry using the theory of induced innovation, which says that changes in the real prices of different goods or inputs should cause companies to change the direction of innovation.⁷⁵ Their 2004 study looked at changes in demographic trends between 1970 and 1990. Demographic changes affect the potential market size for a drug but they do not depend on the amount of research being done. If research spending and the size of the market move together, causation should run from prices to research.

Acemoglu and Linn divided specific drugs into categories depending on the age of the population that primarily used them. The results showed a strong relationship between market size and the entry of new drugs. As baby boomers aged over a 30-year period, the market for drugs mostly consumed by the young declined, while those used by older individuals increased. This produced a matching change in the number of new drugs in each category. A 1-percent increase in the potential market size led to a 6-percent increase in the number of new drugs entering that market. Although much of this increase came from generics, both the number of nongeneric drugs (those not identical or bioequivalent to an existing drug) and the number of new molecular compounds (drugs containing an active component that has never been approved by the FDA or marketed in the United States) increased by at least 4 percent. They also found that drug firms anticipated these demographic changes with a lead of 10 to 20 years.

Giaccotto, Santerre, and Vernon (2005)

A 10-percent increase in real prices caused firms to increase their R&D intensity by nearly 6 percent the following year.

Another study, by Giaccotto, Santerre, and Vernon, found a strong link between real drug prices and firm R&D.⁷⁶ Their 2005 study focused on R&D intensity (the ratio of R&D spending to product sales) rather than the level of research, and found that real drug prices, real GDP per capita, and the amount of foreign sales as a percentage of total sales all had a strong impact on R&D intensity the following year. Specifically, a 10-percent increase in real prices caused firms to increase their R&D intensity by nearly 6 percent the following year. Applying this result to the past, they estimated that if drug prices had not increased in real terms between 1980 and 2001, R&D spending would have been 30 percent below its actual level. The number of new drugs entering the market during this time would have fallen by between 330 and 365, or about one-third of the actual number.

Abbott and Vernon (2005)

Some studies have tried to estimate the impact of future price controls on research. In 2005, economists Thomas Abbott of Thomson-Medstat and John A. Vernon found a strong impact on future innovation.⁷⁷ They used the history of specific firms to look at the impact of prices on the initial decision whether to start Phase I trials on a perspective drug. With data on actual development costs, drug revenues, and a measure of the uncertainty facing firms, they found that minor price changes would have relatively little effect. A price decline of 5 to 10 percent

would reduce product development by about 5 percent. But larger price declines would have a more serious impact. For example, a price cut of 40 to 45 percent in real terms would reduce the number of new development projects by 50 to 60 percent.

Lichtenberg (2006)

A 2006 study by Frank Lichtenberg looks at relationships between expected market revenues on the one hand and both the number of chemotherapy regimens for treating a cancer site (i.e., skin, lungs) and the number of articles published in scientific journals pertaining to drug therapy for that cancer site.⁷⁸ As the importation of drugs would decrease the U.S. price and therefore the expected revenues, Lichtenberg hypothesized that importation would cause both the number of regimens and the number of publications to fall. He started by assuming that the responsiveness of innovation to a change in revenues is at least as great as its responsiveness to the number of patients. To estimate the latter, he looked at both changes in the number of patents with particular types of cancer in Canada and the United States, and the number of regimens and research papers devoted to that type of cancer. The results showed the elasticity of the number of cancer patients to the number of chemotherapy regimens available to treat a specific type of cancer is 0.53. The elasticity of journal citations is 0.60. Therefore, a 10-percent fall in drug prices is likely to cause a 5- to 6-percent decline in both cancer regimens and research articles.

A 10-percent fall in drug prices is likely to cause a 5- to 6-percent decline in both cancer regimens and research articles.

The study also looked at the relationship between the number of innovations within a company (defined as FDA-approved active ingredients contained in products sold by the company that are not contained in any other company's products) and the number of its employees. It finds an elasticity of 0.71 across 14 pharmaceutical companies; a 10-percent reduction in new approved active ingredients would cut the number of employees by 7 percent.

Civan and Maloney (2009)

In 2009, economists Abdulkadir Civan and Michael Maloney looked at both the existing drugs available to treat specific diseases and the number of new drugs in development for those same diseases.⁷⁹ After correcting for the number of existing treatments available for a specific condition, they found a positive relationship between the average price of available drugs and the number of new drugs being developed. A 30-percent increase in drug prices for a given condition would increase the number of drugs in development for that condition by 25 percent. Of course, as generics enter the market in response to favorable market conditions, prices usually fall.

Golec and Vernon (2010)

Economists Joseph Golec of the University of Connecticut and John A. Vernon looked at the relationship between an index of drug prices in both the United States and Europe and the profitability, research spending, and stock price of U.S. and EU pharmaceutical firms, respectively.⁸⁰ Between 1993 and 2004, European price controls prevented pharmaceutical prices from rising in inflation-adjusted terms, whereas real prices in the United States rose by 50 percent. However, the authors found a statistically significant positive correlation (0.64) between changes in the price increases and R&D spending.⁸¹

Market conditions not only affected the size of research spending, it also affected its location. Looking at other sets of data, they found biopharmaceutical research in the EU countries exceeded research conducted in the United States by 24 percent in 1986. But by 2004, U.S. levels were 15 percent greater than EU levels.⁸² This is mostly due to EU spending stalling between 1997 and 2001, roughly the same time the two price indexes diverged. Total U.S. biopharma research by foreign firms has been growing at a faster rate than foreign research by U.S. firms, largely because U.S. prices for on-patent drugs are higher than those in Europe. Higher prices have therefore caused foreign companies to divert their attention to the U.S. market, thereby strengthening the U.S. domestic industry.

Golec and Vernon also looked at the real annual growth rate in research spending. U.S. research consistently grew about 3.4 percentage points more than EU research each year. However, both rates have been trending down in recent years. Using regression analysis, the study shows firms that were more sensitive to European prices spent less on R&D, while the opposite was true of sensitivity to U.S. prices. By assuming the annual real increase in R&D spending would have maintained its rate of 6.6 percent had the Europeans not introduced price controls, the report estimates the present value of reduced R&D from regulations has been almost \$12 billion in current dollars and 1,680 R&D jobs.⁸³ Using an average cost per drug of \$260 million, this translates to 46 fewer medicines between 1986 and 2004. They noted that between 1987 and 1991, EU firms introduced 101 new medicines. This figure dropped to 57 new medicines between 2000 and 2004, the difference of which was roughly the number they attributed to the decline in R&D. Meanwhile, the number of U.S. new medicines increased from 54 to 70. Similar price controls in the United States would have reduced the present value of research by almost \$31 billion, resulting in a loss of 117 new medicines and 4,368 jobs.⁸⁴

Schwartz (2018)

In 2018, researchers at Precision Health Economics used a model of the over-50 population to simulate the elimination of price controls in non-U.S. OECD countries.⁸⁵ The study estimated that removing price controls would raise pharmaceutical revenues by 30 percent. The paper estimated that a 30-percent price increase in non-U.S. OECD countries would increase the size of the global pharmaceutical market by around 12 percent. This in turn would produce a 12 percent increase in research and 13 new drugs per year. The impact grows to 44 new molecules per year by 2060. Assuming these drugs would also be introduced into the United States, the expected longevity of American 45-year-olds would increase by 0.86 years, which the report values at \$1.54 trillion, or \$67,000 per individual. For 15-year-olds, the increase in longevity would be 1.6 years, worth \$115,000 per person. Although the net benefits to non-U.S. individuals would be partially offset by higher drug prices in the near term, these benefits would still be significant. Life expectancy for a 45-year-old European would increase by 0.81 years, and welfare gains would exceed \$80,000 per person.

POSSIBLE POLICY SOLUTIONS

Although the purpose of this report is not to promote one policy solution over others, a number of possible reforms could improve the situation. The first lesson is policymakers should exercise caution before pursuing any policies that would reduce the net revenues from the sale of current drugs. Efforts in this direction are likely to lower long-term welfare by reducing the number of future breakthroughs.

Policies that encourage other nations to raise the price of patented drug prices are likely to boost the funding of future research. If done collectively, all nations would benefit.

Policies that encourage other nations to raise the price of patented drug prices are likely to boost the funding of future research. If done collectively, all nations would benefit. These reforms could be accompanied by changes that make it easier to introduce generic drugs, likely resulting in net benefits to consumers. Taking full advantage of generics would lower drug revenues. But despite the link between revenues and research, the goal of public policy should not be to prop prices up as far as possible, but rather to structure a well-functioning market that adequately rewards innovation and links prices to social benefits. Once a fair patent period has expired, patients should benefit from heightened competition.

Other reforms could aim at reducing the cost of drug development, which would likely result in both lower prices and increased investment in R&D. Congress and the FDA should continue to improve and streamline, wherever possible, the drug approval process, keeping in place existing safety and efficacy standards. Another option is to encourage more innovation in drug manufacturing. A recent article argues that pharmaceutical manufacturing could be more efficient. It attributes much of this to high regulatory barriers and inefficient intellectual-property protection of manufacturing methods. Proposed changes, such as faster regulatory approvals for manufacturing innovations that do not affect quality, and preventing other companies from immediately copying improvements discovered by others either through process patents or by administratively denying other companies from copying the innovation for a certain period of time, could result in savings of \$50 billion each year.⁸⁶ As Congress reauthorizes the Manufacturing USA program, it should ensure that the two existing biopharma centers—BioFabUSA and the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)—are adequately funded.⁸⁷ Lawmakers also should consider establishing additional centers in areas such as synthetic biology (e.g., applying engineering principles to biology).

Congress could also ease drug discovery by appropriately loosening data restrictions in the health care market. Data-driven innovation promises to transform many aspects of medicine.⁸⁸ Within the pharmaceutical industry, better access to data can improve discovery, clinical review, testing, and post-market monitoring. However, these benefits require access to massive amounts of data from many people. Current federal policy makes the sharing of data difficult, even de-identified data individual patients are eager to share in order to help find a cure.

Finally, the federal government should significantly increase funding for basic medical research.⁸⁹ While the federal government is not well positioned to evaluate the most promising areas of applied research, it does play a large role in underwriting advances in the basic research on which these applications rest. Despite conservative worries that federal research displaces private research, the evidence shows that it clearly serves as a complement to it. Steady advances in the basic understanding of chemical and biological science reduce the risks and improve the returns from private efforts.

CONCLUSION

The U.S. biopharmaceutical industry is the most innovative and research-intensive industry in the world. Rather than channeling most current revenue into profits, companies pour a large portion of their revenues from each generation of drugs into research in the next round of development. As a result, the industry funds a large share of total U.S. R&D, employs a significant number of researchers, and continues to develop new drugs.

Some have argued high prices are not needed to maintain this virtuous cycle because, in the face of price controls or other measures to lower prices, companies can maintain high revenues for research by cutting marketing expenses.⁹⁰ However, Frosch et al. found that direct-to-consumer advertising was \$4.9 billion in 2007, or just 1.4 percent of total sales, hardly a honeypot of savings to be applied to lower drug pricing.⁹¹ Moreover, while much advertising is designed to gain market share over competitors, some is about educating consumers and health care providers. Moreover, the drug industry is different than, say, the soap or car industry where it is relatively easy for consumers to find out on their own about new products and the differences between them. This is why Frosch et al. found that more than half of physicians agree that ads educate patients about health conditions and available treatments; and nearly 75 percent of patient respondents agree that advertisements improve their understanding of diseases and treatments.⁹² Moreover, absent some government restrictions on marketing, companies devote resources to marketing because they think that, even after accounting for its cost, it will increase demand and therefore revenues. Marketing and innovation are usually complements, because marketing makes it possible to sell new products.⁹³

The biopharmaceutical industry funds a large share of total U.S. R&D, employs a significant number of researchers, and continues to develop new drugs.

Advocates also argue price controls won't hurt drug innovation because companies must engage in continued research if they want to remain in business.⁹⁴ Revenues from current products play a large role in funding future research. Academic studies demonstrate a strong consensus that drug price controls limit revenues for biopharmaceutical companies, and that this in turns leads companies to invest less in research to develop new drugs. When countries intervene to set a cap on drug prices, as Europe did in the 1980s, research and innovation suffer. Moreover, firms are unlikely to invest in future research unless they believe doing so will be profitable.⁹⁵ Private firms routinely exit markets—and entire industries—once they lose profitability, even as they try to enter new, more promising markets. Price controls reduce industry R&D, which decreases the number of new drugs developed and thereby hurts patients in the future. It is simply not true that government can impose significant price controls without damaging the chances for future cures. Countries that allow higher drug prices experience more innovation. They also benefit from a more competitive domestic industry and more good jobs.

Finally, the reduction in research and new drug development will reduce overall societal welfare. Studies show that drugs create a large amount of social value. Yet even with current U.S. drug prices, firms usually capture only a small portion of this total value. The rest goes to patients, health care and insurance providers, and the rest of the population.

While the evidence does not dictate how policymakers should strike the proper balance between short-term availability and long-term health, it does show a trade-off exists. The close relationship between prices and research led one early study to conclude that:

[A] pell-mell march toward regulation of pharmaceutical industry pricing could seriously impair the industry's incentives for investment in new products.... If profits were held to "reasonable" levels on blockbuster drugs, aggregate profits would almost surely be insufficient to sustain a high rate of technological progress.... Should a tradeoff be required between modestly excessive prices and profits versus retarded technical progress, it would be better to err on the side of excessive profits.⁹⁶

ACKNOWLEDGMENTS

The author would like to thank Robert D. Atkinson and Stephen Ezell for helpful comments. All errors remain the author's responsibility.

ABOUT THE AUTHOR

Joe Kennedy is a senior fellow at ITIF. For almost 30 years, he has worked as an attorney and economist on a wide variety of public policy issues. His previous positions include chief economist with the U.S. Department of Commerce and general counsel for the U.S. Senate Permanent Subcommittee on Investigations. He is president of Kennedy Research, LLC, and the author of *Ending Poverty: Changing Behavior, Guaranteeing Income, and Transforming Government* (Rowman & Littlefield, 2008). Kennedy has a law degree and a master's degree in agricultural and applied economics from the University of Minnesota and a Ph.D. in economics from George Washington University.

ABOUT ITIF

The Information Technology and Innovation Foundation (ITIF) is a nonprofit, nonpartisan research and educational institute focusing on the intersection of technological innovation and public policy. Recognized as the world's leading science and technology think tank, ITIF's mission is to formulate and promote policy solutions that accelerate innovation and boost productivity to spur growth, opportunity, and progress.

For more information, visit us at www.itif.org.

ENDNOTES

1. See, Remarks by President Trump on Prescription Drug Prices, October 25, 2018, <https://www.whitehouse.gov/briefings-statements/remarks-president-trump-prescription-drug-prices/>.
2. The regulation was struck down by a judge after opponents challenged it in courts. Ricardo Alonzo Zaldivar, “Judge Strikes Down Rule Requiring Drug Ads To Reveal Prices,” *The Seattle Times*, July 19, 2019, <https://www.seattletimes.com/business/judge-strikes-down-rule-requiring-drug-ads-to-reveal-prices/>. The Administration is appealing.
3. P.L. 115-262 and P.L. 115-263, respectively.
4. United States Senate, Special Committee on Aging, <https://www.aging.senate.gov/press-releases/in-the-third-hearing-in-a-series-on-drug-pricing-administration-officials-detail-policies-focused-on-reducing-prescription-drug-costs>.
5. Congressional Budget Office, “Preliminary Estimate of the Prescription Drug Pricing Reduction Act of 2019,” https://www.cbo.gov/system/files/2019-07/PDPRA_preliminary_estimate.pdf.
6. Andrew Pollack, “Drug Goes From \$13.50 a Tablet to \$750, Overnight,” *The New York Times*, September 20, 2015, <https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html>.
7. Christopher Rowland, “The FDA Approves a Gene Therapy that is the Most Expensive Drug in the World,” *Washington Post*, May 24, 2019, https://www.washingtonpost.com/business/economy/the-fda-approves-a-gene-therapy-that-is-the-most-expensive-drug-in-the-world/2019/05/24/57c66500-7e4a-11e9-8ede-f4abf521ef17_story.html?utm_term=.02ada99c4378.
8. Accenture, *Time to Change: Bringing Outcomes to Market in a New Era of Breakthrough Science*, https://www.accenture.com/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Dualpub_26/Accenture-Pharma-High-Performance-Business-Research-2017.pdf#zoom=50.
9. Frank R. Lichtenberg, “The Impact of Pharmaceutical Innovation on Disability Days and the Use of Medical Services in the United States, 1997–2010,” *Journal of Human Capital*, Vol. 8(4), Winter 2014, https://www.jstor.org/stable/10.1086/679110?seq=1#page_scan_tab_contents.
10. An interesting approach is to ask how much the United States would have paid for a cure to HIV/AIDs 20 years ago, or how much it would pay for a cure for breast cancer delivered today.
11. Robert D. Atkinson, “China’s Biopharmaceutical Strategy: Challenge or Complement to U.S. Industry Competitiveness?” (Information Technology and Innovation Foundation, August 2019), <https://itif.org/publications/2019/08/12/chinas-biopharmaceutical-strategy-challenge-or-complement-us-industry>.
12. U.S. Census Bureau, (accessed August 9, 2019) <https://www2.census.gov/library/publications/decennial/2000/c2kprof00-us/c2kprof00-us.pdf>; <https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=CF>.
13. Centers for Medicare and Medicaid Services, National Health Expenditures, Retail Prescription Drugs Expenditures; Levels, Percent Change, and Percent Distribution, by Source of Funds: Selected Calendar Years 1970–2017, Table 16, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/Tables.zip>.
14. Centers for Medicare and Medicaid Services, National Health Expenditure Amounts by Type of Expenditure and Source of Funds: Calendar Years 1960–2017, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHE60-27.zip>.
15. Ibid.

16. Centers for Medicare and Medicaid Services, National Health Expenditures, Aggregate and Per Capita Amounts, Annual Percent Change and Percent Distribution: Calendar Years 1960–2017, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHEGDP17.zip>. GDP Deflator: Bureau of Labor Statistics, Consumer Price Index for Prescription Drugs, U.S. city average, [https://beta.bls.gov/dataQuery/find?fq=survey:\[cu\]&s=popularity:D](https://beta.bls.gov/dataQuery/find?fq=survey:[cu]&s=popularity:D); Population Data is from Federal Reserve Bank of St. Louis, FRED (POPTOTUSA647NWDB and SPPOP65UPTOZSUSA) (Accessed August 17, 2019).
17. Ibid; Centers for Medicare and Medicaid Services, National Health Expenditure Amounts by Type of Expenditure and Source of Funds: Calendar Years 1960–2017, <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHE60-27.zip>.
18. The figure shows total retail spending on prescription drugs adjusted for inflation. This number is divided by the population ages 65 or more. The series is then indexed with 1960 equal to 100. Centers for Medicare and Medicaid Services, National Health Expenditures, Aggregate and Per Capita Amounts, Annual Percent Change and Percent Distribution: Calendar Years 1960–2017, (accessed August 8, 2019), <https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHEGDP17.zip>; GDP Deflator: Bureau of Labor Statistics, Consumer Price Index, All Urban Consumers, [https://beta.bls.gov/dataQuery/find?fq=survey:\[cu\]&s=popularity:D](https://beta.bls.gov/dataQuery/find?fq=survey:[cu]&s=popularity:D); Population Data is from Federal Reserve Bank of St. Louis, FRED (POPTOTUSA647NWDB and SPPOP65UPTOZSUSA), (accessed August 17, 2019).
19. Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs,” *Journal of Health Economics*, Vol 47, 2016, 23.
20. Congressional Budget Office, *How Taxes Affect the Incentive to Invest in New Intangible Assets*, November 2018, <https://www.cbo.gov/publication/54648>.
21. Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, “Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs.”
22. Donald W. Light and Rebecca Warburton, “Demythologizing the High Costs of Pharmaceutical Research,” *BioSocieties*, Vol. 6(1), March 2011, <https://link.springer.com/article/10.1057/biosoc.2010.40>; Jorge Mestre-Ferrandiz, Jon Sussex, and Adrian Towse, “The R&D Cost of a New Medicine” (December 2012), Office of Health Economics, <https://www.ohe.org/system/files/private/publications/380%20-%20R%26D%20Cost%20NME%20Mestre-Ferrandiz%202012.pdf?download=1>.
23. Statista, (accessed August 9, 2019), <https://www.statista.com/statistics/272181/world-pharmaceutical-sales-by-region/>.
24. Department of Commerce, *Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Customers, Pricing, Research and Development, and Innovation*, December 2004, <https://2016.trade.gov/td/health/DrugPricingStudy.pdf>.
25. Council of Economic Advisors, *Reforming Biopharmaceutical Pricing at Home and Abroad*, February 2018, <https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf>.
26. Stephen J. Ezell, Adams B. Nager, and Robert D. Atkinson, “Contributors and Detractors: Ranking Countries’ Impact on Global Innovation” (Innovation Technology and Innovation Foundation, January 2016), <https://itif.org/publications/2016/01/20/contributors-and-detractors-ranking-countries-impact-global-innovation>.
27. Accenture, *Time to Change: Bringing Outcomes to Market in a New Era of Breakthrough Science*, 9, https://www.accenture.com/_acnmedia/Accenture/Conversion-Assets/DotCom/Documents/Global/PDF/Dualpub_26/Accenture-Pharma-High-Performance-Business-Research-2017.pdf#zoom=50.

28. Axene Health Partners, “US Pharmaceutical Pricing: An Overview,” <https://axenehp.com/us-pharmaceutical-pricing-overview/>.
29. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” *Journal of Economic Perspectives*, Vol. 7(3), Summer 1993, 102-03.
30. Ibid.
31. Ibid.
32. Bureau of Economic Analysis, *BEA Depreciation Estimates*, https://apps.bea.gov/national/pdf/BEA_depreciation_rates.pdf.
33. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” 104; Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 43–44, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drugr-d.pdf>.
34. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, 4.
35. Aswath Damodaran, [Data set 2018], accessed July 31, 2019, http://people.stern.nyu.edu/adamodar/New_Home_Page/data.html.
36. Yahoo! Finance, <https://finance.yahoo.com>, (accessed August 29, 2019).
37. Government Accountability Office, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, November 2017, <https://www.gao.gov/assets/690/688472.pdf>.
38. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 48, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drugr-d.pdf>.
39. Frank R. Lichtenberg, “The Impact of Pharmaceutical Innovation on Disability Days and the Use of Medical Services in the United States, 1997–2010,” *Journal of Human Capital*, Vol. 8(4), Winter 2014, 457, https://www.jstor.org/stable/10.1086/679110?seq=1#page_scan_tab_contents.
40. M. Christopher Roebuck, et al., “Medication Adherence Leads to Lower Health Care Use and Costs Despite Increased Drug Spending,” *Health Affairs*, 30(1) 2011, <https://doi.org/10.1377/hlthaff.2009.1087>.
41. Robert D. Atkinson, “Why Life-Sciences Innovation Is Politically ‘Purple’—and How Partisans Get It Wrong” (Information Technology and Innovation Foundation, February 2016), 2, <http://www2.itif.org/2016-life-sciences-purple.pdf>.
42. Alzheimer’s Association, *Changing the Trajectory of Alzheimer’s Disease: How a Treatment by 2025 Saves Lives and Dollars*, 2015, <https://www.alz.org/media/Documents/changing-the-trajectory-r.pdf>.
43. Adams B. Nager and Robert D. Atkinson, “A Trillion Dollar Opportunity: How Brain Research Can Drive Health and Prosperity” (Information Technology and Innovation Foundation, July 2016), <https://itif.org/publications/2016/07/11/trillion-dollar-opportunity-how-brain-research-can-drive-health-and>.
44. “Antibiotics biotech firms are struggling,” *The Economist*, May 4, 2019, <https://www.economist.com/business/2019/05/04/antibiotics-biotech-firms-are-struggling>.
45. Organization for Economic Cooperation and Development, *Health at a Glance 2017*, Table 10.12, https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2017_health_glance-2017-en. Data is for 2014 or latest year.
46. Ibid, Table 10.13, Business Enterprise R&D Expenditure as a Portion of Gross Value Added. Data is for 2014 or latest year.
47. European Federation of Pharmaceutical Industries and Associations, *The Pharmaceutical Industry in Figures, 2019*, 4, <https://www.efpia.eu/media/412931/the-pharmaceutical-industry-in-figures-2019.pdf>.

48. Ibid, 9.
49. International Federation of Pharmaceutical Manufacturers & Associations, *The Pharmaceutical Industry and Global Health: Fact and Figures 2015*, 14, <https://www.ifpma.org/resource-centre/facts-figures-2015/>.
50. National Science Foundation, *Business Research and Development and Innovation: 2016*, May 13, 2019, Table 2, <https://ncses.nsf.gov/pubs/nsf19318/#&>.
51. Ibid, Table 12.
52. Ibid, Table 18.
53. Ibid, Table 53.
54. Joe Kennedy, “How to Ensure That America’s Life-Sciences Sector Remains Globally Competitive” (Information Technology and Innovation Foundation, 2018), <https://itif.org/publications/2018/03/26/how-ensure-americas-life-sciences-sector-remains-globally-competitive>.
55. Richard A. Epstein, Review of *The Constitutional Foundations of Intellectual Property* by Randolph J. May and Seth L. Cooper, *The Federalist Society Review*, Vol. 17(1), February 2016, <https://fedsoc-cms-public.s3.amazonaws.com/update/pdf/sUvljbOFb28cFAEch9SUERotlc2Ekcmo8mmzSQEh.pdf>.
56. Ernst R. Berndt, “Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price,” *Journal of Economic Perspectives*, Vol. 16(4), 2000, 55, 57.
57. Drug prices may be more resistant to price competition than other products. Limits on physician awareness of new treatments and drug prices, consumer insensitivity due to the presence of insurance, and the lack of transparency about prices can all limit the degree of competition. However, studies show the introduction of generics results in a rapid fall in prices. Council of Economic Advisors, *Reforming Biopharmaceutical Pricing at Home and Abroad*, February 2018, <https://www.whitehouse.gov/wp-content/uploads/2017/11/CEA-Rx-White-Paper-Final2.pdf>. However, in some cases drug prices may clearly be too low. Severe shortages of BCG, the leading drug for bladder cancer, have been blamed on the fact that its price is too low to encourage an expansion of manufacturing capacity. Laurie McGinley, “Low Prices of Some Lifesaving Drugs Make Them Impossible to Get,” *Washington Post*, June 18, 2019, https://www.washingtonpost.com/national/health-science/low-prices-of-some-lifesaving-drugs-make-them-impossible-to-get/2019/06/18/abd03190-66bb-11e9-82ba-fcfeff232e8f_story.html?utm_term=.af6cdbf1b79f.
58. Ernst R. Berndt, “Pharmaceuticals in U.S. Health Care: Determinants of Quantity and Price,” 59. Berndt finds that “[o]ver the longer term, expectations of reduced freedom to price in the United States would undoubtedly have a very substantial negative impact on all phases of drug R&D, and therefore would reduce the future supply of new products, decreasing price competition among them.”; Ibid, 61.
59. Christopher Rowland, “The FDA Approves a Gene Therapy that is the Most Expensive Drug in the World.”
60. Robert D. Atkinson, “How the Biopharmaceutical Industry Contributes to Open Scientific Knowledge” (Information Technology and Innovation Foundation, November 2018), <https://itif.org/publications/2018/11/05/how-biopharmaceutical-industry-contributes-open-scientific-knowledge>.
61. Tomas J. Philipson and Anupam B. Jena, “Surplus Appropriation from R&D and Health Care Technology Assessment Procedures,” NBER Working Papers No. 12016, <https://www.nber.org/papers/w12016>.
62. Ibid, 5–6.

63. Darius N. Lakdawalla, "Economics of the Pharmaceutical Industry," *Journal of Economic Literature*, Vol. 56(2), 2018, 424, <https://doi.org/10.1257/jel.20161327>.
64. Congressional Budget Office, *Research and Development in the Pharmaceutical Industry*, October 2006, 9, <https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/10-02-drug-r-d.pdf>.
65. Ibid.
66. Organization for Economic Cooperation and Development, *Pharmaceutical Pricing Policies in a Global Market*, 192, <https://www.oecd.org/els/pharmaceutical-pricing-policies-in-a-global-market.htm>. Italics in original.
67. Ibid, 190, citing DIUS, *The R&D Scoreboard 2007: The Top 850 UK and 1250 Global Companies by R&D Investment – Main Tables*, Department of Innovation, Universities and Skills, London.
68. Government Accountability Office, *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, November 2017, <https://www.gao.gov/assets/690/688472.pdf>.
69. Ibid.
70. Henry Grabowski and John Vernon, "The Determinants of R&D Expenditures," *Drugs and Health* (R.B. Helms ed.), Washington, D.C., AEI Press 1981.
71. Henry Grabowski and John Vernon, "The Determinants of Pharmaceutical Research and Development Expenditures," *Journal of Evolutionary Economics*, Vol. 10, 2000.
72. Ibid, 207.
73. Department of Commerce, *Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Customers, Pricing, Research and Development, and Innovation*, December 2004, <https://2016.trade.gov/td/health/DrugPricingStudy.pdf>.
74. New active substances are those that either contain a chemical active substance that is not previously authorized or that demonstrate the substance differs significantly in safety or efficacy from prior drugs.
75. Daron Acemoglu and Joshua Linn, "Market Size in Innovation: Theory and Evidence From the Pharmaceutical Industry," *Quarterly Journal of Economics*, Vol. 119(3), August 2004, <https://economics.mit.edu/files/4464>.
76. Carmelo Giaccotto, Rexford E. Santerre, and John A. Vernon, "Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry," *The Journal of Law & Economics*, Vol. 48(1) April 2005, https://www.jstor.org/stable/10.1086/426882?seq=1#page_scan_tab_contents.
77. Thomas A. Abbott and John A. Vernon, "The Cost of U.S. Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions," NBER Working Paper No. 11114, February 2005, <https://www.nber.org/papers/w11114>.
78. Frank R. Lichtenberg, "Importation and Innovation," NBER Working Paper No. 12539, September 2006, <https://www.nber.org/papers/w12539>.
79. Abdulkadir Civan and Michael T. Maloney, "The Effect of Price on Pharmaceutical R&D," *The B.E. Journal of Economic Analysis & Policy*, Vol. 9(1), January 2009, https://www.researchgate.net/publication/46556017_The_Effect_of_Price_on_Pharmaceutical_RD.
80. Joseph Golec and John A. Vernon, "Financial Effects of Pharmaceutical Price Regulation on R&D Spending by EU Versus US Firms," 625, *Pharmacoeconomics*, Vol. 28(8), 2010. All cost estimates have been converted to 2019 dollars using the consumer price index.
81. Ibid, 620.
82. Ibid, 621.
83. Ibid, 625.

84. Ibid.
85. Taylor T. Schwartz et al., “The Impact of Lifting Government Price Controls on Global Pharmaceutical Innovation and Population Health,” Poster Presented at the ISPOR 23rd Annual International Meeting, Baltimore, MD, May 22, 2018, https://tools.ispor.org/research_pdfs/58/pdf/PHP216.pdf
86. W. Nicholson Price II, “Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing,” *Boston College Law Review*, Vol. 55(2), 2014, <http://lawdigitalcommons.bc.edu/bclr/vol55/iss2/5>.
87. Erratum: This report was amended shortly after its initial publication to add clarity in light of the fact that two of the 14 existing Manufacturing USA institutes—BioFabUSA and the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)—are highly complementary and well connected.
88. Joshua New, “The Promise of Data-Driven Drug Development,” (Center for Data Innovation, forthcoming), <https://www.datainnovation.org/2019/09/accelerating-data-driven-drug-development/>.
89. Robert D. Atkinson, “Healthy Funding: The Critical Role of Investing in NIH to Boost Health and Lower Costs,” (Information Technology and Innovation Foundation, March 2019), <https://itif.org/publications/2019/03/25/healthy-funding-critical-role-investing-nih-boost-health-and-lower-costs>.
90. Dean Baker, “Financing Drug Research: What Are the Issues?” (Center for Economic and Policy Research, Issue Brief, September 2004, 8–9, http://cepr.net/documents/publications/intellectual_property_2004_09.pdf.
91. D.L. Frosch, et al., “A Decade of Controversy: Balancing Policy with Evidence in the Regulation of Prescription Drug Advertising,” *American Journal of Public Health*, Vol. 100(1) (January 2010), 24–32.
92. Ibid.
93. Darius N. Lakdawalla, “Economics of the Pharmaceutical Industry,” *Journal of Economic Literature*, Vol. 56(2), 2018, 438, <https://doi.org/10.1257/jel.20161327>.
94. Hagop Kantarjian and S. Vincent Rajkumar, “Why are Cancer Drugs So Expensive in the United States, and What are the Solutions?” *Mayo Clinic Proceedings*, Vol. 90(4), 501, April 2015, [https://www.mayoclinicproceedings.org/article/S0025-6196\(15\)00101-9/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196(15)00101-9/fulltext); Donald W. Light and Rebecca Warburton, “Demythologizing the High Costs of Pharmaceutical Research,” *BioSocieties*, Vol. 6(1), March 2011, 2, <https://link.springer.com/article/10.1057/biosoc.2010.40>.
95. Megan McArdle, “There’s a High Cost to Making Drugs More Affordable for Americans,” *Washington Post*, May 7, 2019, https://www.washingtonpost.com/opinions/theres-a-high-cost-to-making-drugs-more-affordable-for-americans/2019/05/07/0a36ceba-7044-11e9-9f06-5fc2ee80027a_story.html.
96. F.M. Scherer, “Pricing, Profits, and Technological Progress in the Pharmaceutical Industry,” *Journal of Economic Perspectives*, Vol. 7(3), Summer 1993, 113.