CHART PACK

BIOPHARMACEUTICALS IN PERSPECTIVE SUMMER 2019

PhRMA
RESEARCH • PROGRESS • HOPE

Dr. Ryan

Ryan is a senior research scientist who works to discover potential treatments for autoimmune conditions like lupus. Ryan believes nothing is possible without innovation, which spurs his drive and passion to keep moving forward despite the numerous setbacks researchers in his field commonly face.

RESEARCHERS MAKING AN IMPACT

Mitra

Mitra is a school counselor living with an autoimmune disease she fights daily. Knowing that an army of researchers is working to develop the next treatment to improve her own and others' lives serves as a source of optimism for Mitra and helps her maintain the resilience needed to face the challenges caused by her disease.

TABLE OF CONTENTS

Cover photo: Dr. Ryan Moslin, Bristol-Myers Squibb researcher, and Mitra, autoimmune disease survivor

INTRODUCTION

This chart pack provides facts and figures about prescription medicines and their role in the health care system. Topics include medicines' impact on health and quality of life, the drug discovery and development process, health care spending and costs, the challenges of addressing treatment gaps and improving the use of prescribed therapies, the contributions of the biopharmaceutical sector, and costs and access in other developed countries.

Data and information in this publication were drawn from a wide range of sources, including government agency reports, peer-reviewed journals, and the Pharmaceutical Research and Manufacturers of America's (PhRMA's) own research and analysis. PhRMA hopes this publication provides useful context for discussions regarding the role of medicines and the US economy.

1 ADVANCES IN TREATMENT

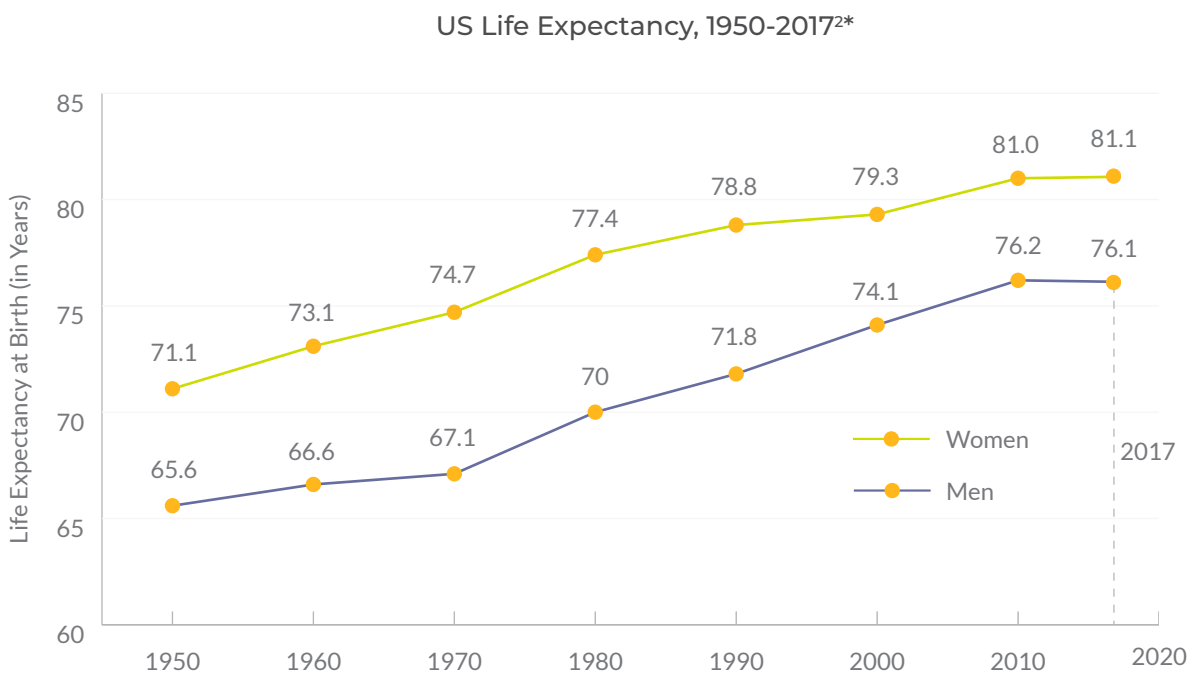
Medicines' Impact on Health and Quality of Life

Prescription medicines have yielded important advances, helping patients live longer and healthier lives. Over the past 25 years, prescription medicines have transformed the trajectory of many debilitating diseases and conditions, including heart disease, HIV/AIDS, cancer, and hepatitis C, resulting in decreased death rates, improved health outcomes, and better quality of life for patients.

Today, new drugs are targeting the underlying causes of disease in ways never seen before, and diseases previously regarded as deadly are now manageable and even curable. In this new era of medicine, breakthrough science and personalized therapies are revolutionizing the way we treat patients with a broad range of chronic and rare conditions. Looking forward, continued advances in biopharmaceutical innovation will be critical in addressing unmet needs, improving public health, and solving future health care challenges.

Increases in US Life Expectancy

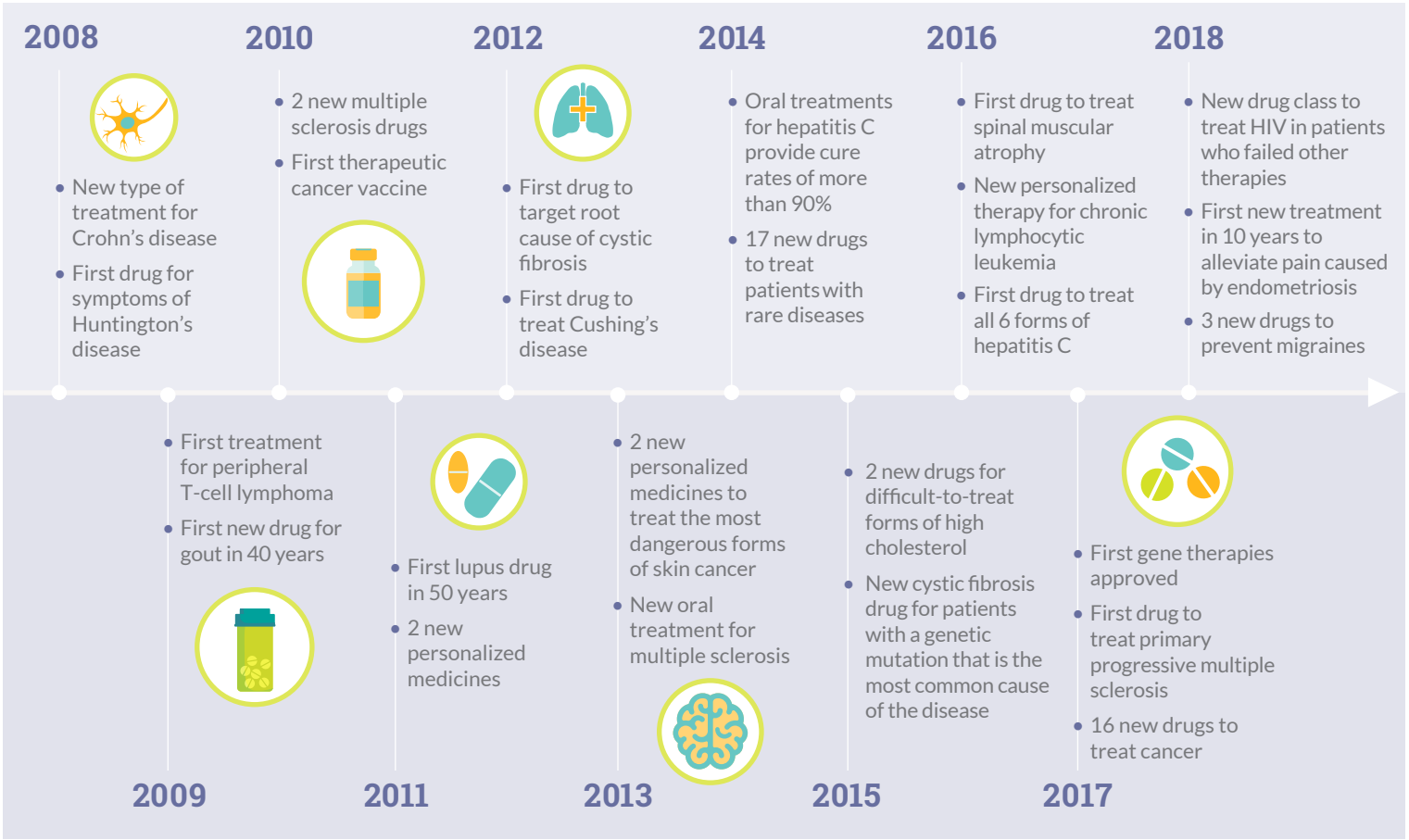
Innovative medicines have played an integral role in improving life expectancy over the last century.[1]



*Life expectancies before 1997 and those in and after 1997 were calculated using a slightly different methodology.

Sources: CDC[1,2]

A Decade of Advances



Source: FDA[3]

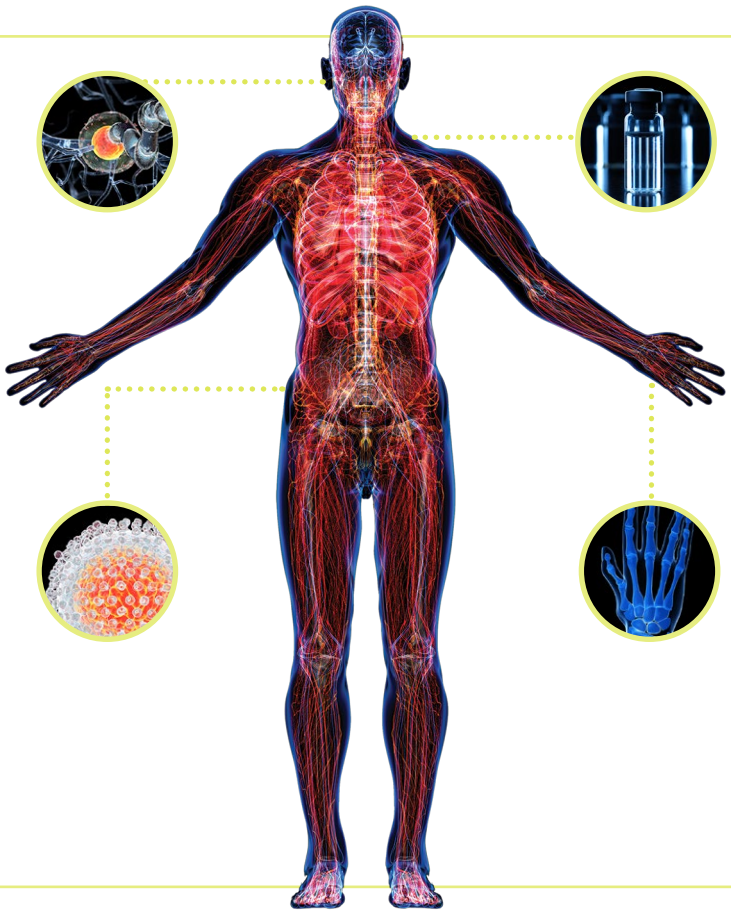
Medicines Are Transforming the Treatment of Many Diseases

Multiple Sclerosis (MS)

Advances in recent years, including convenient oral medicines and the first-ever treatment for progressive MS, offer patients greater opportunity to better manage MS and slow disease progression.[4]

Hepatitis C

Recent therapeutic advances can cure the disease and help patients avoid serious disease complications—including cirrhosis, advanced liver disease, liver cancer, and death.[5]



Cancer

New therapies have contributed to a 27% decline in cancer death rates since the 1990s.[6] The chance a cancer patient will live 5 years or more has increased 41% across all cancers since 1975.[7]

Rheumatoid Arthritis (RA)

Therapeutic advances have transformed the RA treatment paradigm, shifting from a focus on managing symptoms to aiming for slowed disease progression and even disease remission.[8]

Sources: PhRMA[4,5]; Siegel RL et al.[6]; ACS[7]; Boston Healthcare Associates[8]

Medicines Are Transforming Treatment of Many Rare Diseases

Collectively, rare diseases affect 30 million Americans. Treatments are available for only 5% of rare diseases, but recent advances are providing important new options to many patients for the first time.[9]

Fabry Disease[10]

Fabry disease is a genetic disorder that can cause fat buildup in blood vessels, nerves, and other organs and slowly progress to kidney disease, abnormal heart rhythm, stroke, and early death. The first treatment for adults was approved in 2018 and works by increasing the activity of a deficient enzyme.

Primary Hemophagocytic Lymphohistiocytosis (HLH)[11]

Primary HLH is an inherited and life-threatening immune disorder typically affecting children. The disorder causes damage to various organs, including the liver, brain, and bone marrow. The first treatment specifically for HLH was approved in 2018 for adults and children.

Hereditary Transthyretin-Mediated Amyloidosis (hATTR)[12]

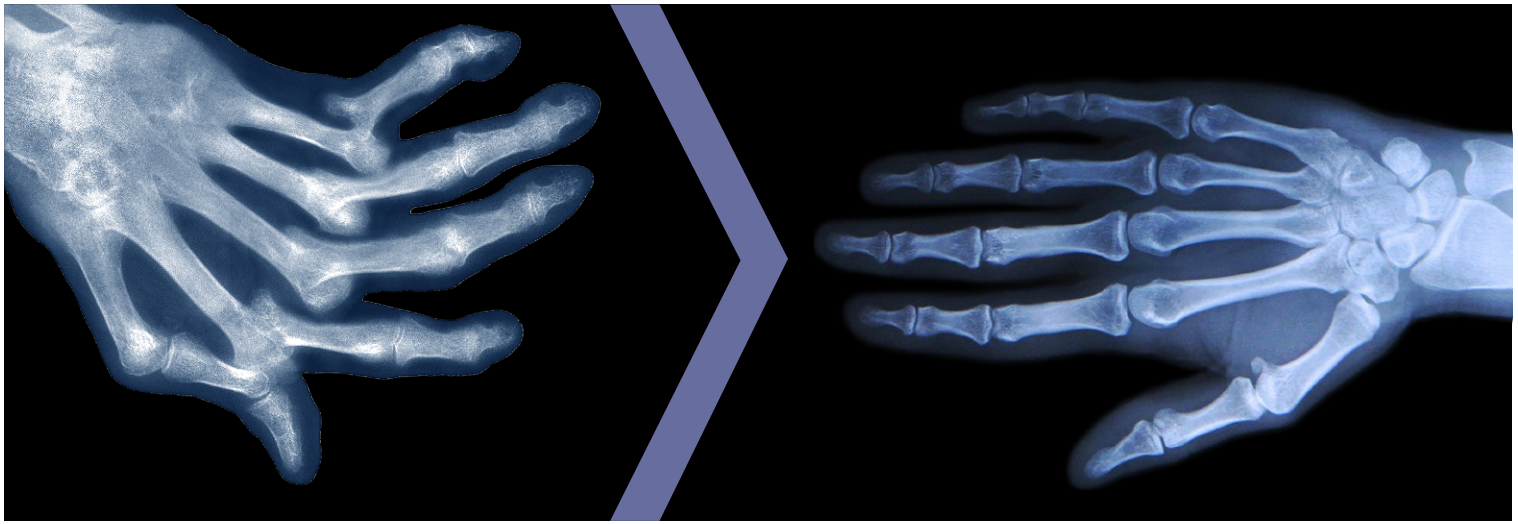
hATTR interferes with the normal functioning of nerves, heart, and other organs and can lead to loss of sensation, pain, or immobility in the limbs. The first treatment for this often fatal genetic disease was approved in 2018 and targets the root cause by interfering with abnormal RNA protein production.

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)[13]

BPDCN is an aggressive blood cancer affecting multiple organs, including the lymph nodes and skin. The first treatment specifically for BPDCN was approved in 2018 for adults and children. Prior to this treatment, intensive chemotherapy and bone marrow transplant had been the standard of care.

Sources: Global Genes[9]; FDA[10-13]

Rheumatoid Arthritis: Medicines Are Transforming the Lives of Patients



THEN:

Treatments for rheumatoid arthritis were generally effective at reducing joint inflammation but were limited to treating the symptoms of the disease, allowing for a steady, rapid progression from disease onset to disability.

NOW:

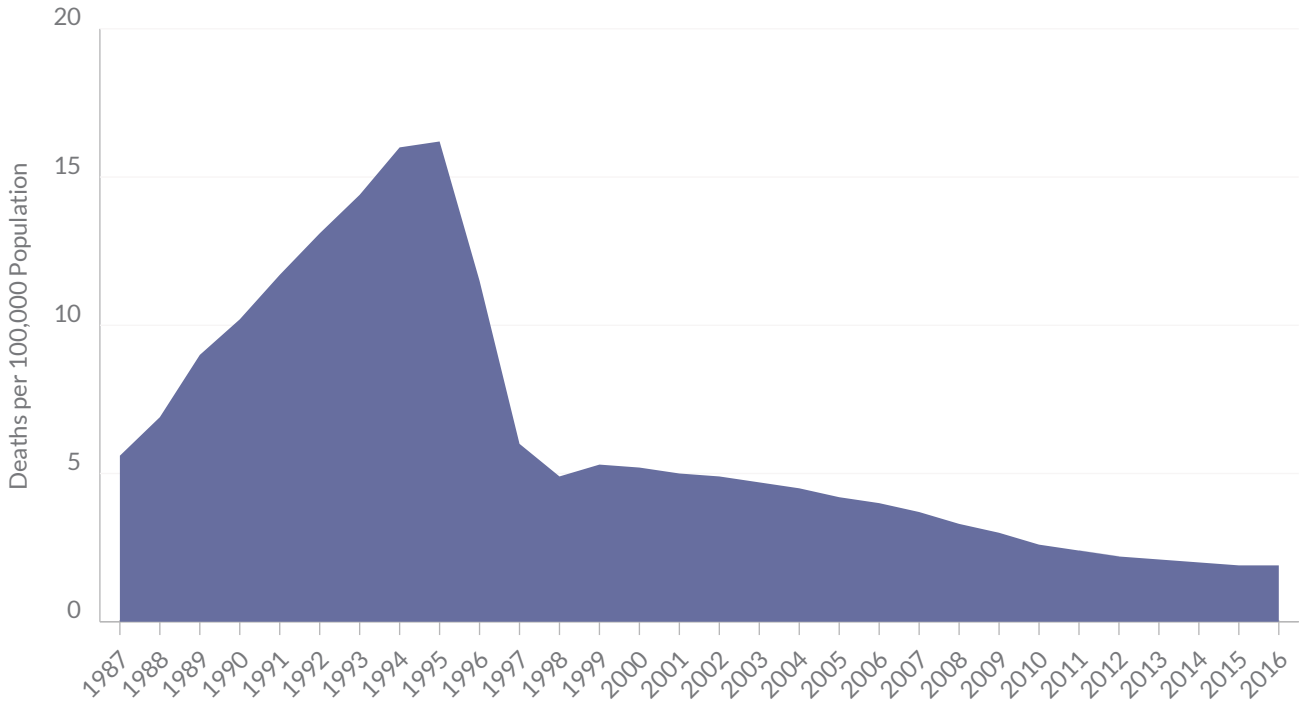
Biologic disease-modifying antirheumatic drugs target the underlying sources of inflammation, which improves physical functioning and prevents irreversible joint damage, making disease remission possible.

Source: Boston Healthcare Associates[14]

AIDS Mortality in the United States

The number of AIDS deaths in the US decreased dramatically following the introduction of highly active antiretroviral therapy (HAART) combinations in 1996. As a result of HAART and all the important medical innovations that followed, it is estimated that more than 862,000 premature deaths have been avoided in the United States alone.[15]

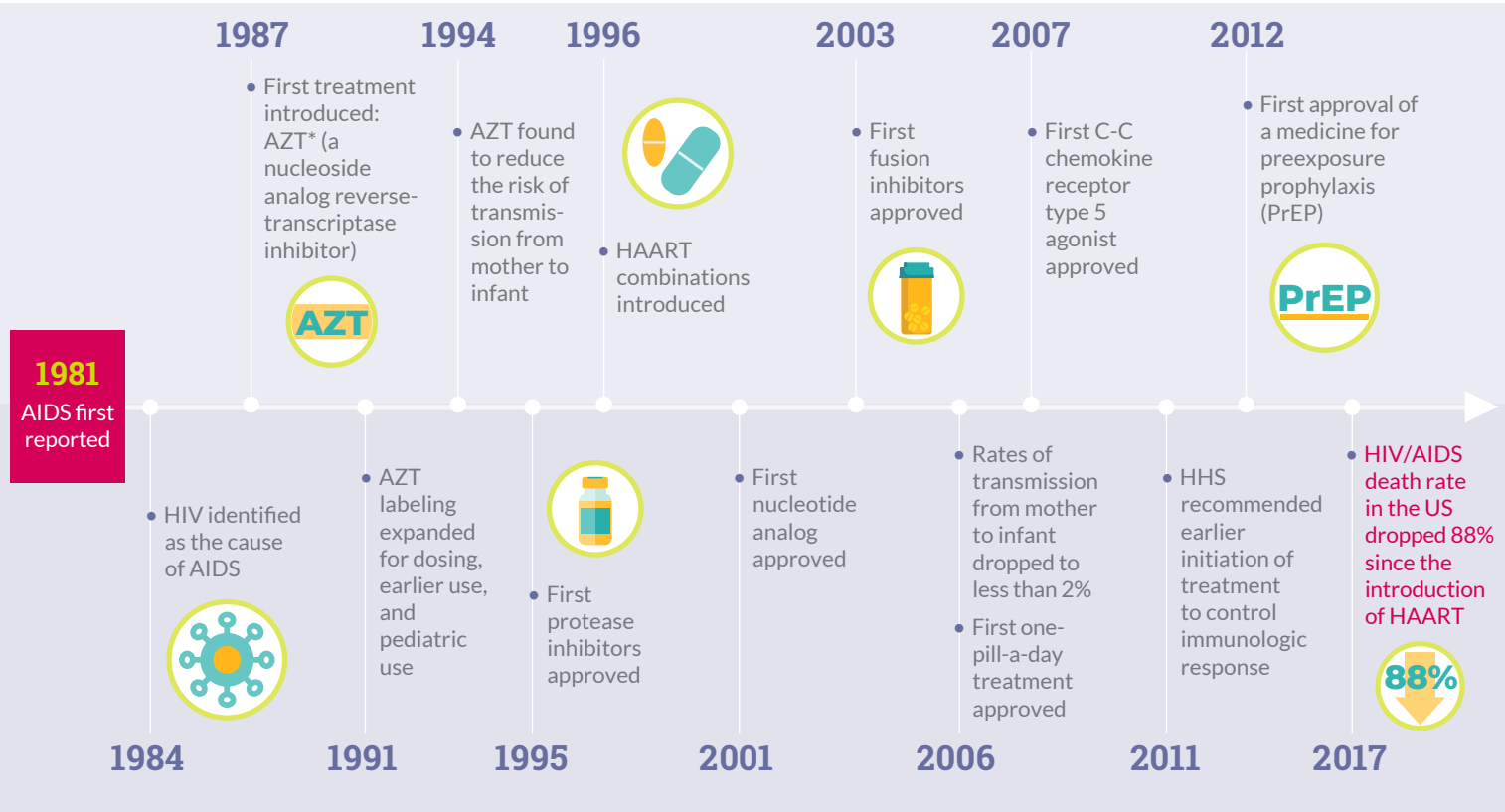
Annual Number of AIDS Deaths in the United States[16,17]



Sources: Truven Health Analytics[15]; CDC[16,17]

HIV/AIDS: Treatment Advances Build Over Time

Dramatic declines in death rates did not occur with one single breakthrough but rather through a series of advances providing important treatment options for patients over time.[18,19]



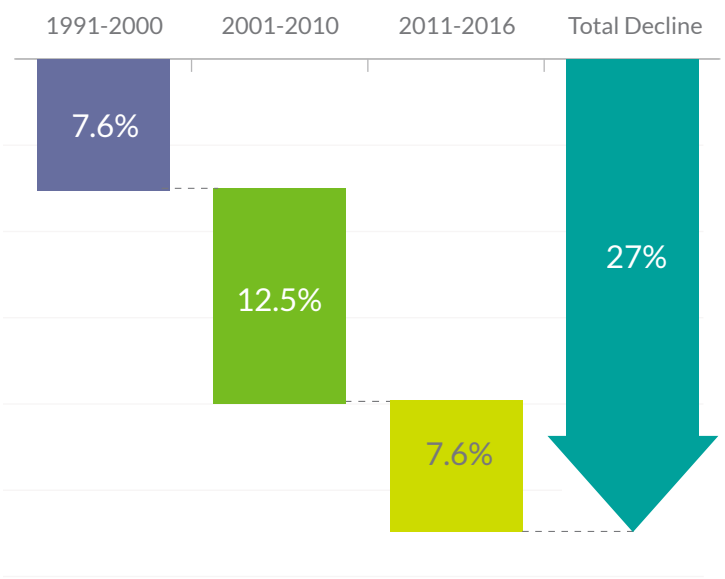
*AZT: Azidothymidine

Sources: Boston Healthcare Associates[18]; CDC[19,20]

Cancers: Decline in Death Rates

Since peaking in the 1990s, cancer death rates have declined 27%.[21] Approximately 73% of survival gains in cancer are attributable to new treatments, including medicines.[22]

Percent Change by Decade in US Death Rates From Cancer[21,23]



> I think some of the treatments that we have developed over the last half century or so are really starting to pay off and, honestly, [it] seems limitless as to what may pay off in the future."
>
> — William Nelson, MD, PhD, Director, Sidney Kimmel Comprehensive Cancer Center[24]

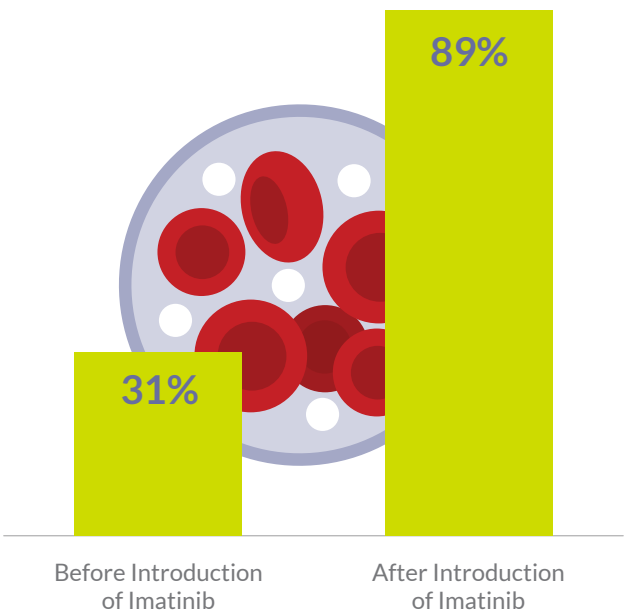
Sources: Siegel RL et al.[21]; Seabury SA et al.[22]; NCI[23]; Dunellari A[24]

Chronic Leukemia: Increased Survival Rates

When the first-in-class drug imatinib was approved in 2001 to treat chronic myeloid leukemia (CML), the transformative impact of this new class of medicines had not been completely realized.[25]

- After initial approval, continued research revealed that imatinib had a greater impact when initiated earlier in the progression of the disease.
- Further research revealed that imatinib was effective in combating other types of cancer.
- Additional drugs in this class have since been approved that target mutated forms of CML in patients who have become resistant or intolerant to imatinib.[26]
- Today, survival rates have improved dramatically, and **CML patients are living close to normal life spans.**[27]

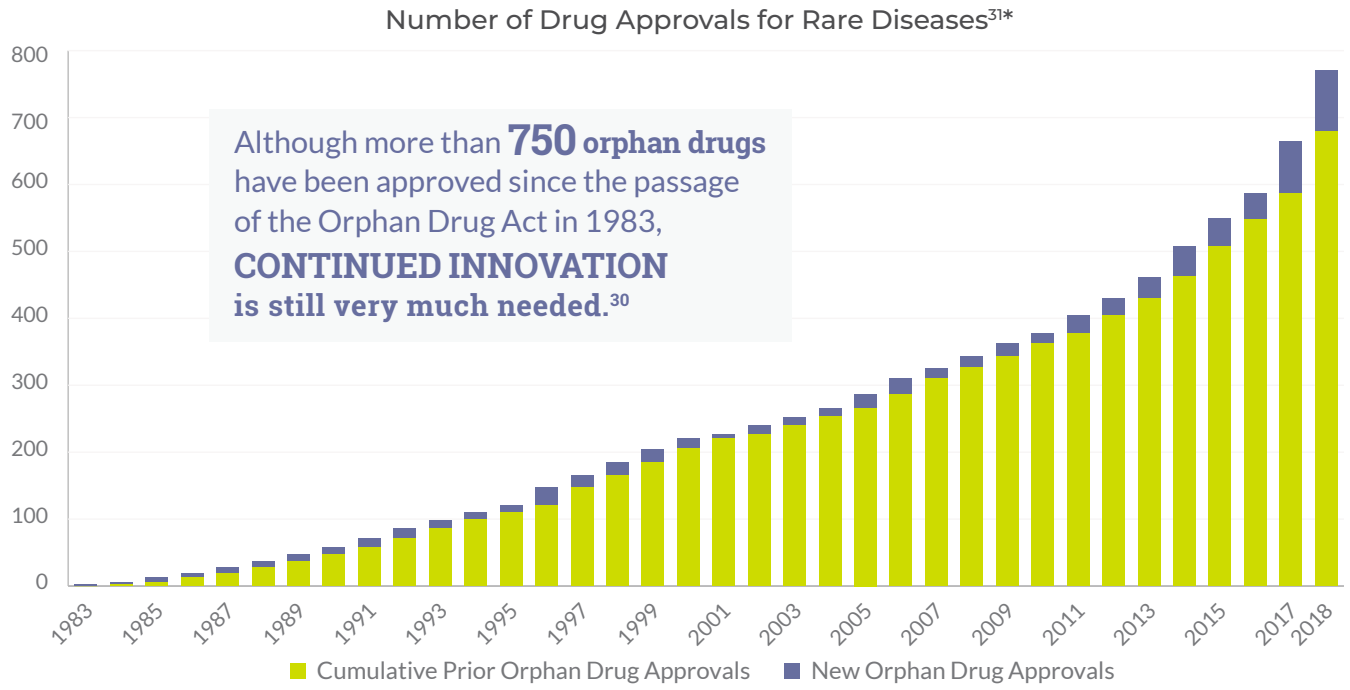
5-Year Survival Rates for CML Patients[28,29]



Sources: Boston Healthcare Associates[25]; PhRMA[26]; Gambacorti-Passerini C et al.[27]; ACS[28]; Druker BJ et al.[29]

Rare Diseases: Drug Approvals for Rare Diseases Have Increased

Rare diseases are those that affect 200,000 or fewer people in the United States.[30]

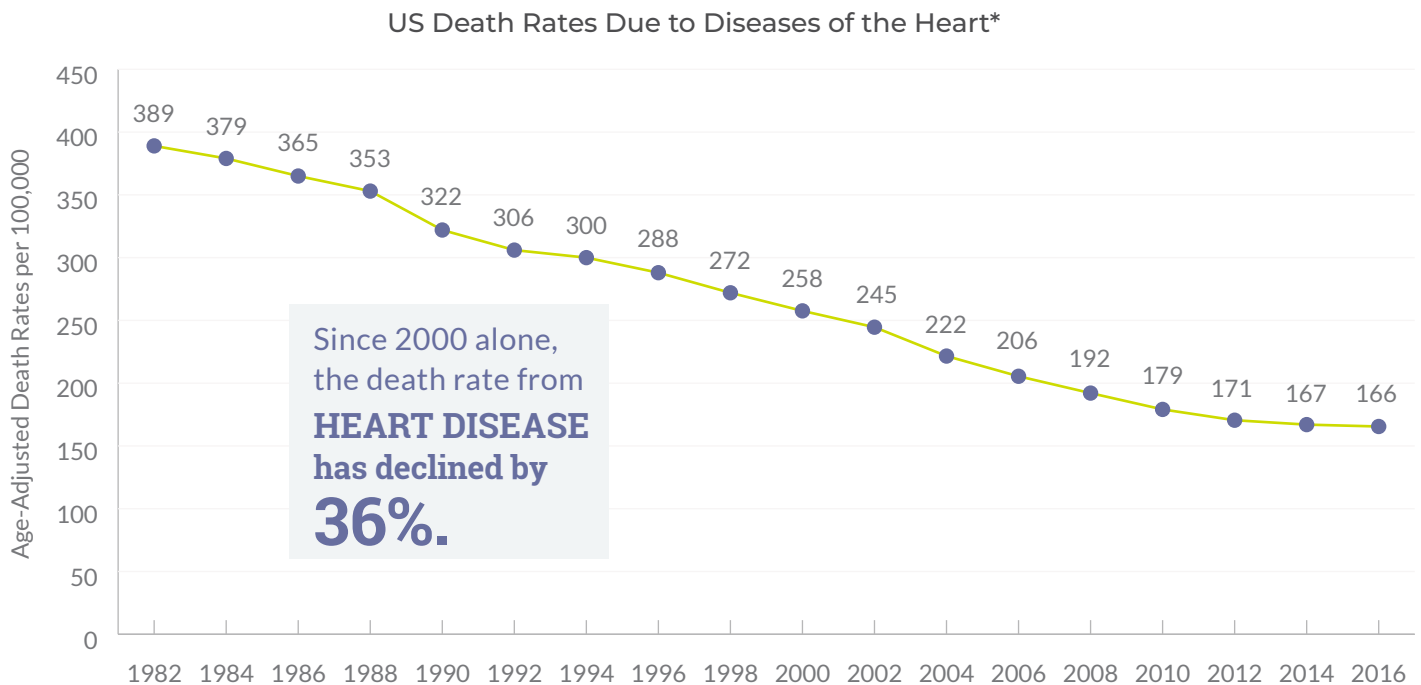


*Drug approvals for rare diseases include initial approvals of new medicines and subsequent approvals of existing medicines.

Sources: NIH[30]; FDA[31]

Cardiovascular Disease: Declining Rates of Death

Tremendous strides have been made in reducing cardiovascular disease morbidity and mortality, thanks in part to new medicines.

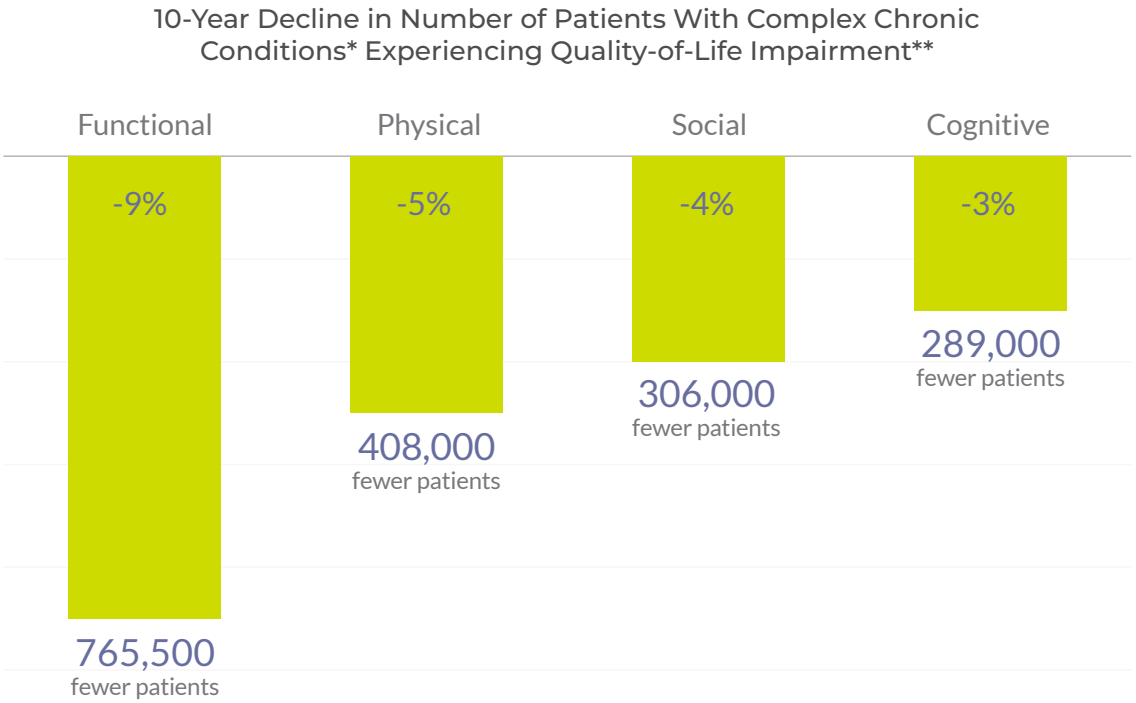


*Age-adjusted death rates based on year 2000 US standard population. 1980-1998 causes of death are classified by the International Classification of Diseases, Ninth Revision (ICD-9). Beginning in 1999, causes of death have been classified by the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10).

Sources: CDC[32,33]

Medicines Are Improving Patients' Quality of Life

Relative to medical technology available a decade ago, new treatments for complex chronic conditions are better tolerated, more efficacious, and more convenient, thereby improving not only life expectancy, but quality of life for patients.



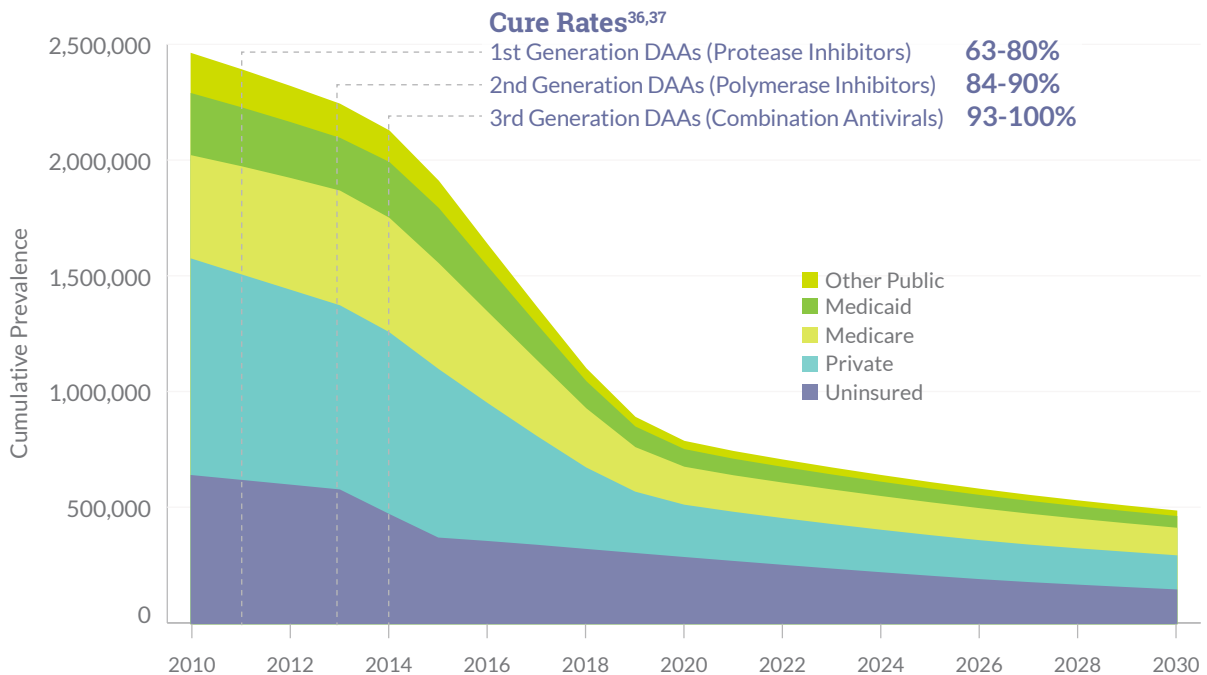
*HIV, rheumatoid arthritis, leukemias, non-Hodgkin's lymphoma, multiple sclerosis, and lupus
**Chart reflects unweighted estimates reported in study.

Source: Brien MJ et al.[34]

Hepatitis C: Advances Driving Down Prevalence of Disease

The introduction of direct-acting antivirals (DAAs) and subsequent improvements in cure rates revolutionized the treatment of hepatitis C (HCV), significantly driving down prevalence of disease.

Decreasing Number of HCV-Infected Patients, by Insurance Type, US 2010-2030[35]*

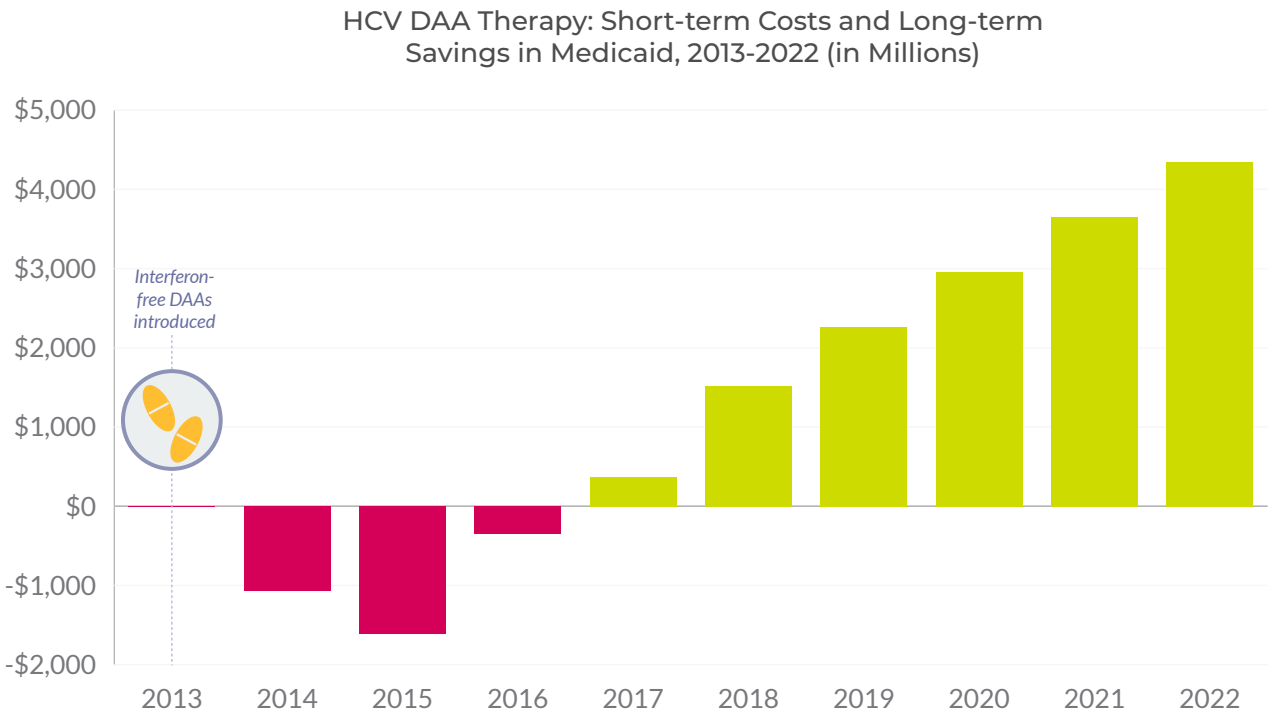


*Model takes into account launch of DAAs, change in HCV screening policies, and implementation of the Affordable Care Act.

Sources: Chhatwal J et al.[35]; PhRMA[36]; FDA[37]

Hepatitis C Medicines Produce Savings in Medicaid

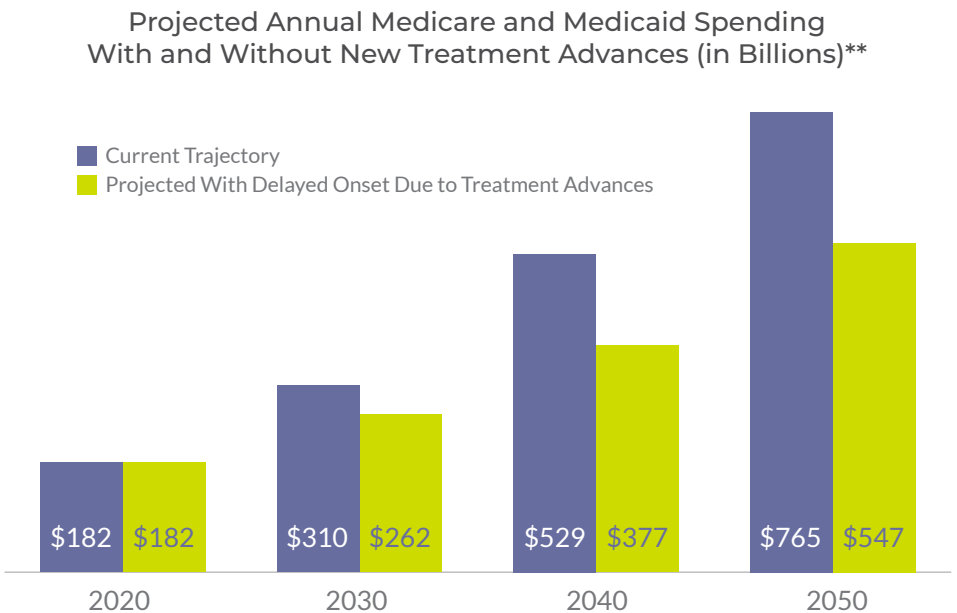
By 2019, total cumulative costs of HCV treatment since the introduction of highly effective interferon-free DAAs are expected to be fully offset by total cumulative health care costs associated with avoided costly disease complications in Medicaid. By 2020, these total cumulative savings are estimated to reach $12 billion.



Source: Roebuck MC et al.[38]

Unmet Need: Future Impact of New Treatments for Alzheimer's Disease

The development of a new treatment that delays the onset of Alzheimer's disease could reduce Medicare and Medicaid spending on patients by $218 billion annually by 2050.*



*Assumes research advances that delay the average age of onset of Alzheimer's disease by 5 years beginning in 2025.
**Projected savings to Medicare and Medicaid assume research breakthroughs that slow the progression of Alzheimer's disease. This would dramatically reduce spending for comorbid conditions and expensive nursing home care.

Source: Alzheimer's Association[39]

Notes and Sources

1. Centers for Disease Control and Prevention (CDC). Ten great public health achievements—United States, 1900-1999. https://www.cdc.gov/mmwr/preview/mmwrhtml/00056796.htm. Accessed May 2017.
2. Murphy SL, Xu JQ, Kochanek KD, et al.; Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. Mortality in the United States, 2017. *NCHS Data Brief* 328. https://www.cdc.gov/nchs/data/databriefs/db328-h.pdf. Published November 2018. Accessed April 2019.
3. Food and Drug Administration (FDA), Center for Drug Evaluation and Research. Advancing health through innovation: 2018 new drug therapy approvals. https://www.fda.gov/media/120357/download. Published January 2019. Accessed April 2019.
4. Pharmaceutical Research and Manufacturers of America (PhRMA). Multiple sclerosis: expanded treatment options improve outcomes for a disabling chronic condition. In: *A Decade of Innovation in Chronic Diseases: 2006-2016*, 14-16. http://phrma-docs.phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf. Published February 2016. Accessed April 2018.
5. Pharmaceutical Research and Manufacturers of America (PhRMA). Hepatitis C: breakthroughs revolutionize treatment for patients. In: *A Decade of Innovation in Chronic Diseases: 2006-2016*, 25-28. http://phrma-docs.phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf. Published February 2016. Accessed April 2018.
6. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin.* 2019;69(1):7-34. https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21551. Accessed April 2019.
7. American Cancer Society (ACS). Cancer facts & figures 2018. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Published 2018. Accessed April 2018.
8. Augustyn C, Walker B, Goss TF; Boston Healthcare Associates. Recognizing the value of innovation in the treatment of rheumatoid arthritis. http://www.phrma.org/sites/default/files/pdf/BHARAWhitepaperMarch2013.pdf. Published March 2013. Accessed April 2018.
9. Global Genes. RARE facts. https://globalgenes.org/rare-facts. Accessed May 2019.
10. Food and Drug Administration (FDA). FDA approves new treatment for a rare genetic disorder, Fabry disease. https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-rare-genetic-disorder-fabry-disease. Published August 10, 2018. Accessed April 2019.
11. Food and Drug Administration (FDA). FDA approves first treatment specifically for patients with rare and life-threatening type of immune disease. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-specifically-patients-rare-and-life-threatening-type-immune-disease. Published November 20, 2018. Accessed April 2019.

Notes and Sources

12. Food and Drug Administration (FDA). FDA approves first-of-its kind targeted RNA-based therapy to treat a rare disease. https://www.fda.gov/news-events/press-announcements/fda-approves-first-its-kind-targeted-rna-based-therapy-treat-rare-disease. Published August 10, 2018. Accessed April 2019.
13. Food and Drug Administration (FDA). FDA approves first treatment for rare blood disease. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-rare-blood-disease-0. Published December 21, 2018. Accessed May 2019.
14. Augustyn C, Walker B, Goss TF; Boston Healthcare Associates. Recognizing the value of innovation in the treatment of rheumatoid arthritis. http://www.phrma.org/sites/default/files/pdf/BHARAWhitepaperMarch2013.pdf. Published March 2013. Accessed May 2017.
15. Lacey MJ, Hanna GJ, Miller JD, et al.; Truven Health Analytics. Impact of pharmaceutical innovation in HIV/AIDS treatment during the highly active antiretroviral therapy (HAART) era in the US, 1987-2010: an epidemiologic and cost-impact modeling case study. http://truvenhealth.com/Portals/0/Assets/Life-Sciences/White-Papers/pharma-innovation-hiv-aids-treatment.pdf. Published December 2014. Accessed March 2018.
16. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. *Health, United States, 2016: with chartbook on long-term trends in health*. https://www.cdc.gov/nchs/data/hus/hus16.pdf. Published 2017. Accessed June 2018.
17. Xu JQ, Murphy SL, Kochanek KD, et al.; Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, National Vital Statistics System. Deaths: final data for 2016. *Natl Vital Stat Rep*. 2018;67(5):1-76. https://www.cdc.gov/nchs/data/nvsr/nvsr67/nvsr67_05.pdf. Accessed April 2019.
18. Augustyn C, Walker B, Goss TF; Boston Healthcare Associates. Recognizing the value of innovation in the treatment of rheumatoid arthritis. http://www.phrma.org/sites/default/files/pdf/BHARAWhitepaperMarch2013.pdf. Published March 2013. Accessed May 2017.
19. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. *Health, United States, 2016: with chartbook on long-term trends in health*. https://www.cdc.gov/nchs/data/hus/hus16.pdf. Published 2017. Accessed June 2018.
20. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics. AIDS and HIV: mortality. https://www.cdc.gov/nchs/fastats/aids-hiv.htm. Accessed May 2019.
21. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7-34. https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21551. Accessed May 2019.
22. Seabury SA, Goldman DP, Gupta CN, et al. Quantifying gains in the war on cancer due to improved treatment and earlier detection. *Forum Health Econ Policy*. 2015;19(1):141-156.

Notes and Sources

23. National Cancer Institute (NCI), Surveillance, Epidemiology, and End Results Program. Cancer stats facts: Cancer of any site: number of new cases and deaths per 100,000 people (all races, males and females), age-adjusted. https://seer.cancer.gov/statfacts/html/all.html. Accessed May 2019.

24. Dunellari A. Researchers optimistic about future of cancer treatment. *VOA News*. https://www.voanews.com/science-health/researchers-optimistic-about-future-cancer-treatment. Published January 13, 2016. Accessed May 2017.

25. Goss TF, Picard EH, Tarab A; Boston Healthcare Associates. Recognizing value in oncology innovation. http://www.phrma.org/sites/default/files/flash/phrma_innovation_oncology.pdf. Published June 2012. Accessed May 2017.

26. Pharmaceutical Research and Manufacturers of America (PhRMA). A decade of innovation in rare diseases: 2005-2015. http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA-Decade-of-Innovation-Rare-Diseases.pdf. Published 2015. Accessed May 2017.

27. Gambacorti-Passerini C, Antolini L, Mahon F-X, et al. Multicenter independent assessment of outcomes in chronic myeloid leukemia patients treated with imatinib. *J Natl Cancer Inst*. 2011;103(7):553-561.

28. American Cancer Society (ACS). Cancer facts & figures 2012. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2012/cancer-facts-and-figures-2012.pdf. Published 2012. Accessed May 2019.

29. Druker BJ, Guilhot F, O'Brien SG, et al. Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. *N Engl J Med*. 2006;355(23):2408-2417.

30. National Institutes of Health (NIH), National Center for Advancing Translational Sciences. FAQs about rare diseases. https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases. Last updated November 30, 2017. Accessed April 2019.

31. Food and Drug Administration (FDA). Search orphan drug designations and approvals. http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm. Accessed April 2019.

32. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, National Vital Statistics System. Age-adjusted death rates for 72 selected causes by race and sex using year 2000 standard population: United States, 1979-98. http://www.cdc.gov/nchs/data/mortab/aadr7998s.pdf. Accessed May 2017.

33. Xu JQ, Murphy SL, Kochanek KD, et al.; Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, National Vital Statistics System. Deaths: final data for 2016. *Natl Vital Stat Rep*. 2018;67(5):1-76. https://www.cdc.gov/nchs/data/nvsr/nvsr67/nvsr67_05.pdf. Accessed April 2019.

34. Brien MJ, Carnow W, Dowdy MC, et al. Quantifying improvements in life quality of individuals with complex chronic medical conditions over the past decade. http://phrma-docs.phrma.org/files/dmfile/Study---Quality-of-Life-Improvements-Over-the-Past-Decade---March-2016.pdf. Published March 12, 2016. Accessed May 2017.

Notes and Sources

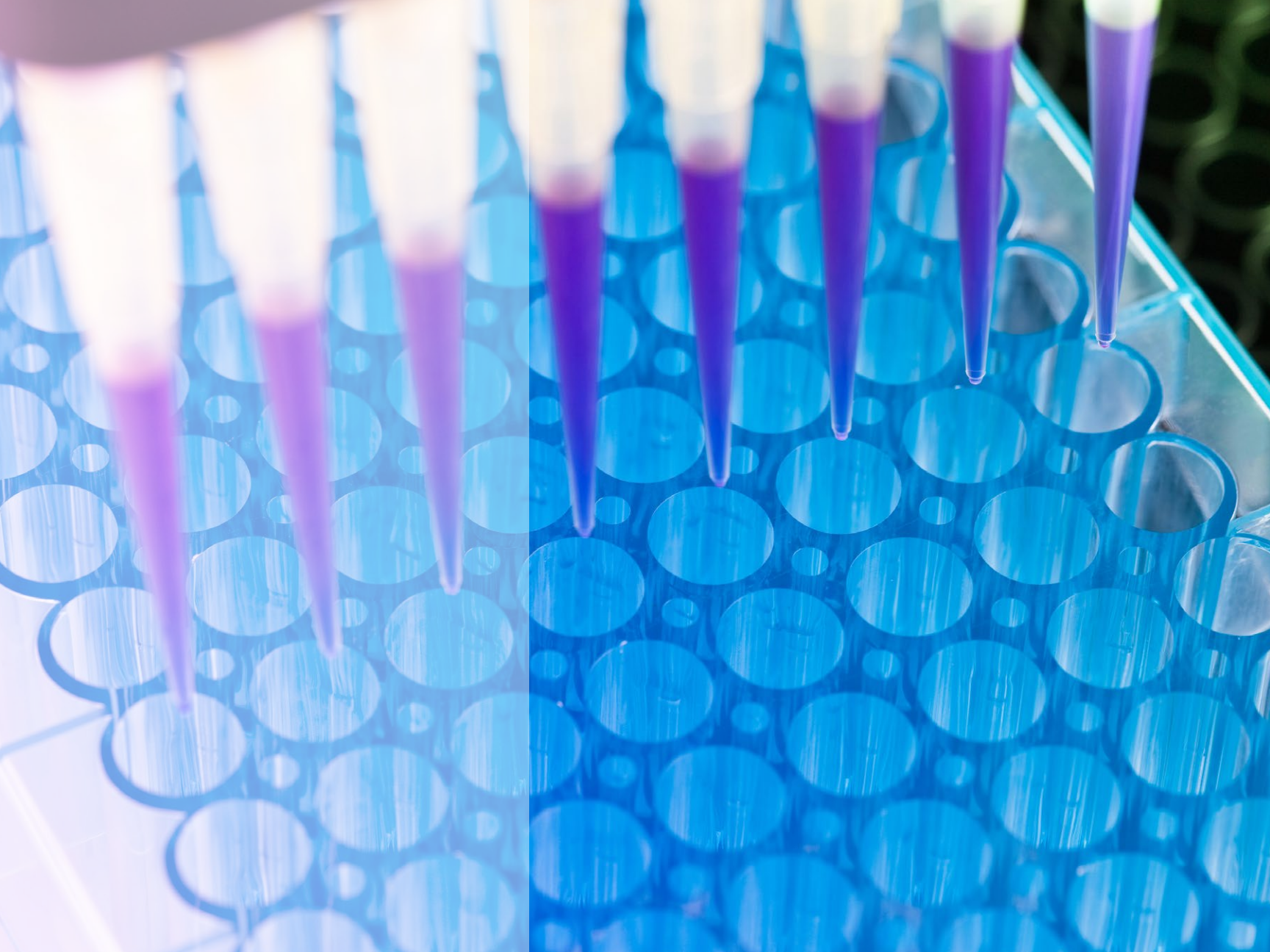
35. Chhatwal J, Wang X, Ayer T, et al. Hepatitis C disease burden in the United States in the era of oral direct-acting antivirals. *Hepatology*. 2016;64(5):1442-1450. doi:10.1002/hep.28571

36. Pharmaceutical Research and Manufacturers of America (PhRMA). A decade of innovation in chronic diseases: 2006-2016. http://phrma.org/sites/default/files/pdf/decade-of-innovation-chronic-disease.pdf. Published February 2016. Accessed May 2018.

37. Food and Drug Administration (FDA). Drugs@FDA: FDA approved drug products. http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed May 2018.

38. Roebuck MC, Liberman JN. Burden of Illness of chronic hepatitis c and impact of direct-acting antiviral use on healthcare costs in Medicaid. *Am J Manag Care*. In press.

39. Alzheimer's Association. Changing the trajectory of Alzheimer's disease: how a treatment by 2025 saves lives and dollars. https://www.alz.org/media/Documents/changing-the-trajectory-r.pdf. Published 2015. Accessed May 2017.



2 RESEARCH AND DEVELOPMENT

The Process of Drug Discovery and Development

The rapid pace of scientific advances is bringing tremendous hope to patients. The pipeline for new medicines has never been more promising, with more than 8,000 medicines in development around the world. Over the past decade, PhRMA member companies have invested more than half a trillion dollars in biopharmaceutical research and development (R&D), accounting for the majority of private biopharmaceutical R&D spending. Development of new medicines is a long and rigorous process, with many setbacks along the way. As scientific complexities create new challenges in R&D, biopharmaceutical companies are working to create efficiencies and enter new collaborations across the research ecosystem.

About 8,000 Medicines in Development Globally[1]

Biopharmaceutical researchers are pursuing many innovative scientific approaches that are driving therapeutic advances.

ALS (Amyotrophic Lateral Sclerosis)

Stem cell therapies aim to replace and/or protect damaged motor neurons and slow disease progression.

GENETIC DISORDERS

Gene therapies can halt the progression of many diseases by directly altering the genetic mutations that cause them.

RNAi technology can prevent disease from occurring by interfering with the expression of genes.

CANCER

Chimeric antigen receptor (CAR) T-cell immunotherapy involves the personalized modification of immune-boosting T-cells to target and kill blood cancer cells.

CRISPR/Cas9 technology edits gene sequences in T-cells, reprogramming them to seek and destroy tumor cells.

HEMOPHILIA

Adeno-associated viral (AAV) vector-mediated gene therapies enable patients to clot blood and can reduce the need for chronic treatment to prevent bleeding episodes.

Source: Adis R&D Insight Database[1]

About 4,500 Medicines in Development in the United States

Biopharmaceutical researchers are working on new medicines* for many diseases, including:

CANCERS
1,120

HEART DISEASE & STROKE
200

HIV
52

ASTHMA & ALLERGY
130

SKIN DISEASES
328

MENTAL DISORDERS
140

RARE DISEASES
566

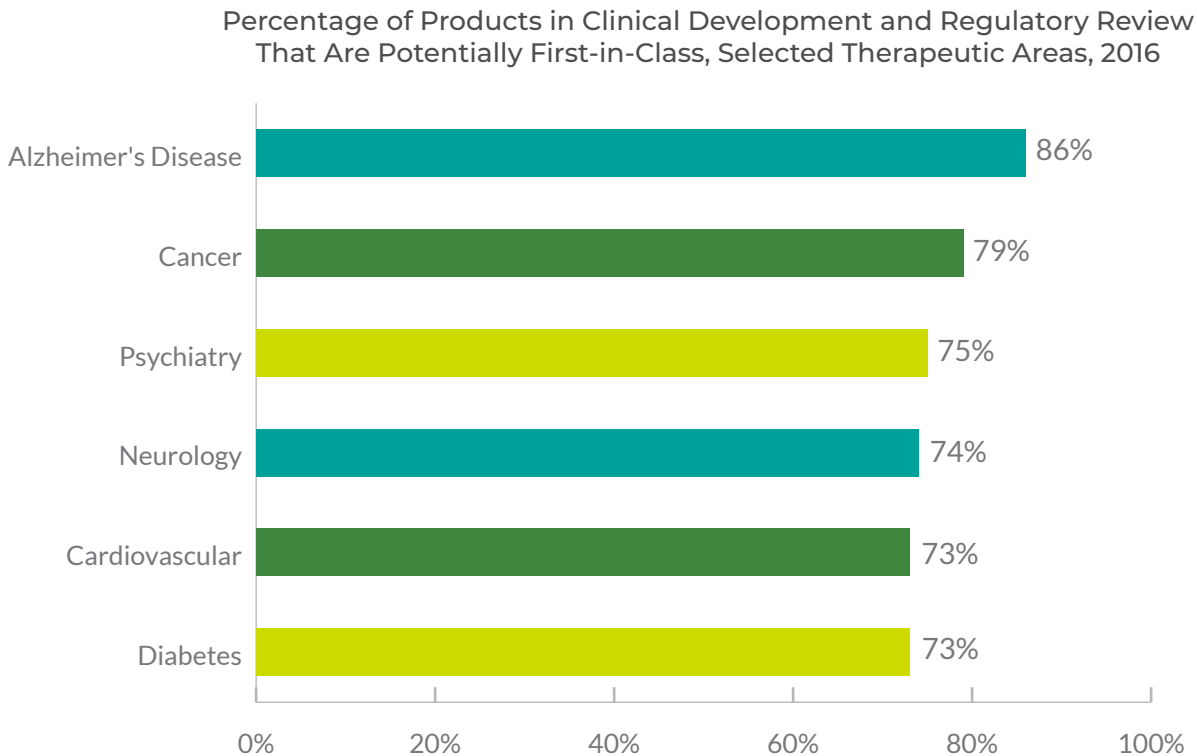
NEUROLOGICAL DISORDERS
537

*Defined as single products that are counted only once regardless of the number of indications pursued

Source: Adis R&D Insight Database[2]

Potential First-in-Class Medicines in the Pipeline

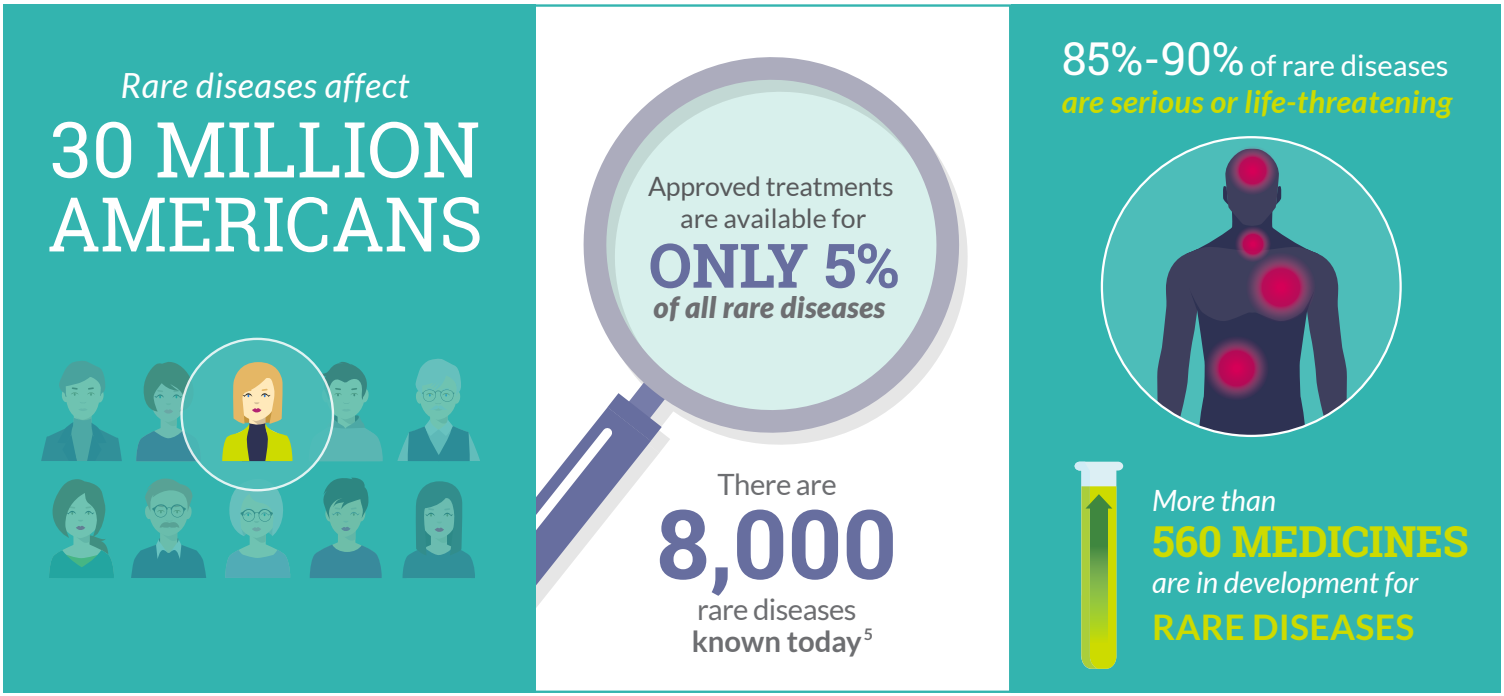
An average of 74% of drugs in the clinical pipeline are potential first-in-class medicines.



Source: Analysis Group[3]

Harnessing Innovation in Rare Diseases

Since the passage of the Orphan Drug Act in 1983, we have seen tremendous advances in treatments for rare diseases,* with more than 770 orphan drug approvals (compared with fewer than 10 in the decade before passage).[4]



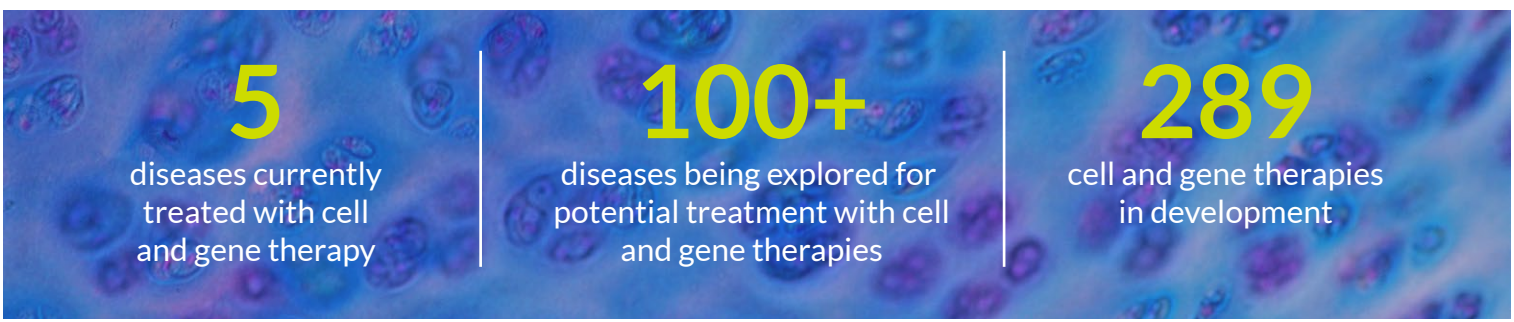
*Rare diseases are defined as conditions for which there are fewer than 200,000 patients diagnosed in the United States.

Sources: FDA[4]; Danese E et al.[5]; PhRMA[6]

Cell and Gene Therapies Offer to Transform the Treatment of Disease

An exciting field of medicine is emerging, offering the possibility of treating and even curing disease by directly altering genes and cells. At a basic level, these therapies entail genetic manipulation of cells either inside or outside the body so that cellular function is permanently changed within the body. These medicines are revolutionizing the way disease is treated, often offering profound and durable responses after a single dose or administration.

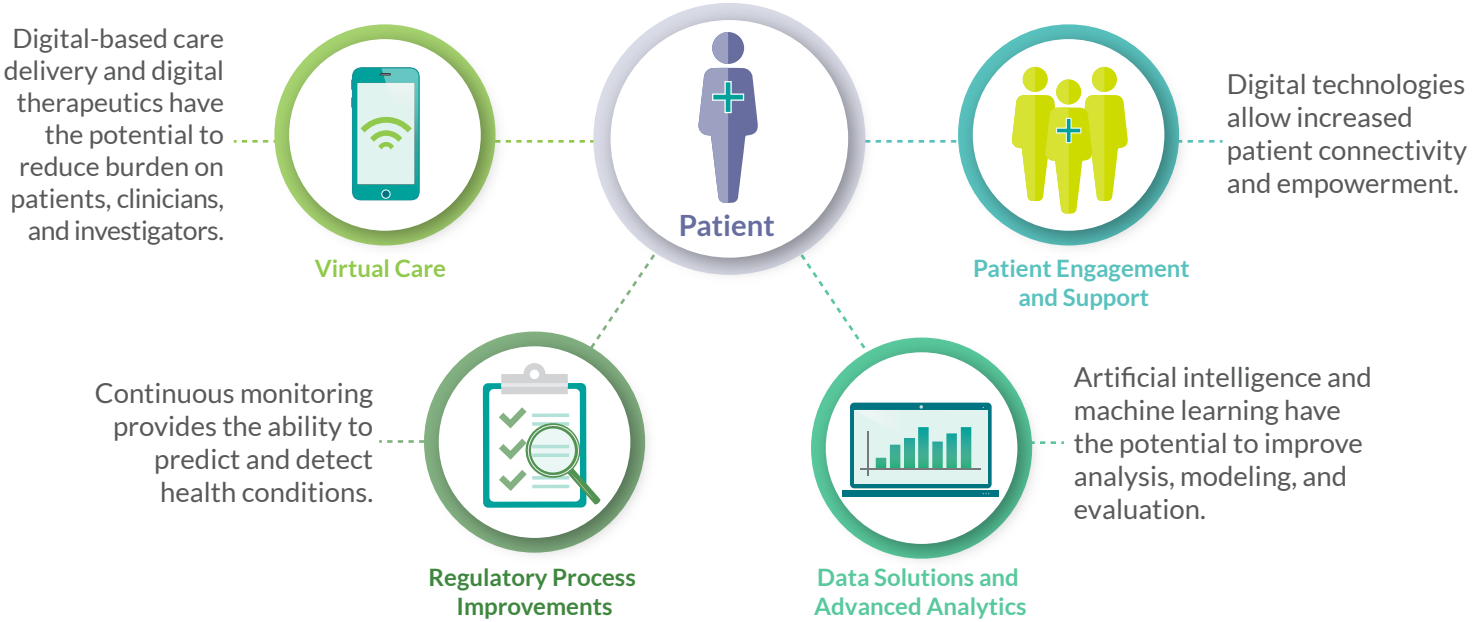
> Across multiple fields of science, we stand at an inflection point in medicine—where new technology is creating foundational opportunities to treat and cure disease in ways that weren't possible just a short time ago…. Over the next several years, we'll see this approach become a mainstay of treating, and probably curing, a lot of our most devastating and intractable illness."
>
> — Scott Gottlieb, MD[7]
> Commissioner, US Food and Drug Administration



Sources: FDA[7]; PhRMA[8]

The Potential for Digital Health Advances to Enhance Drug Development and Patient Care

Technological advances can increase access to clinical trials, enable efficient information exchange, speed drug development and delivery of new treatments, enhance clinical decision making, and engage patients.



Source: Adapted from Avalere Health[9]

Biopharmaceutical Companies Are Committed to Advancing Personalized Medicine

In recent years, we have seen remarkable advances in targeted therapy, and the R&D pipeline has never been more promising.

MORE THAN **42%**[10] of new medicines approved by the FDA in 2018 were

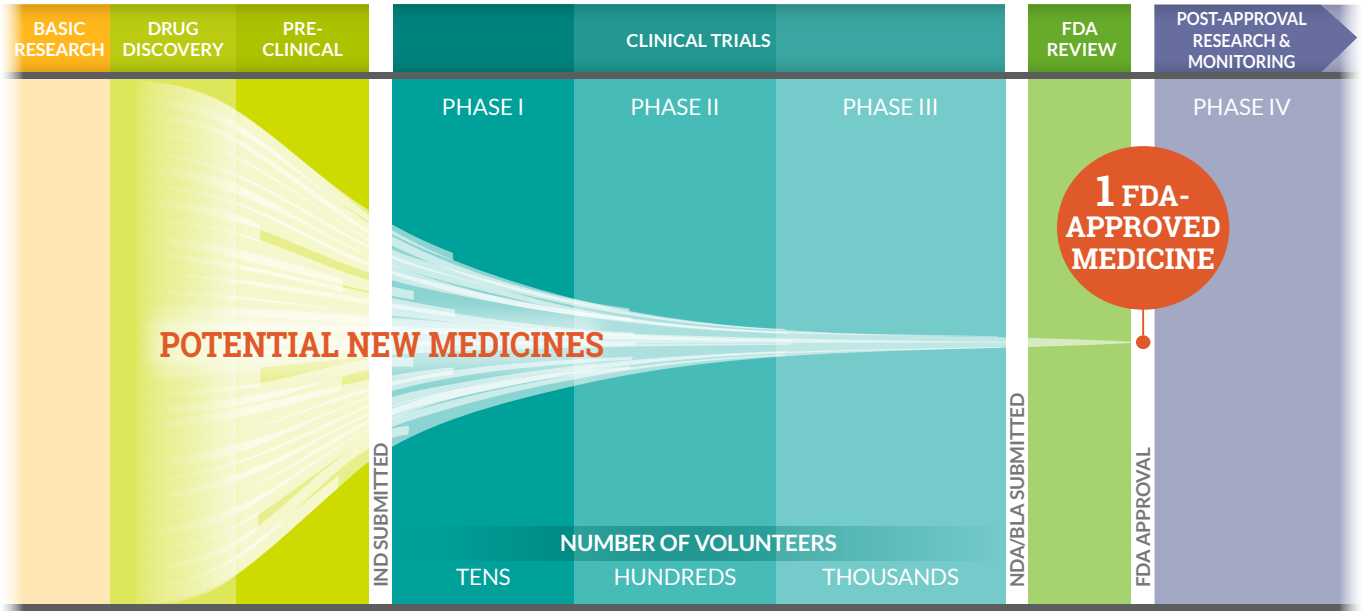
42%[11] of new medicines IN THE PIPELINE have the potential to be

PERSONALIZED MEDICINES

Sources: Personalized Medicine Coalition[10]; Tufts CSDD[11]

The R&D Process for New Drugs Is Lengthy and Costly, With High Risk of Failure

From drug discovery through FDA approval, developing a new medicine takes, on average, 10 to 15 years and costs $2.6 billion.* Less than 12% of the candidate medicines that make it into Phase I clinical trials are approved by the FDA.

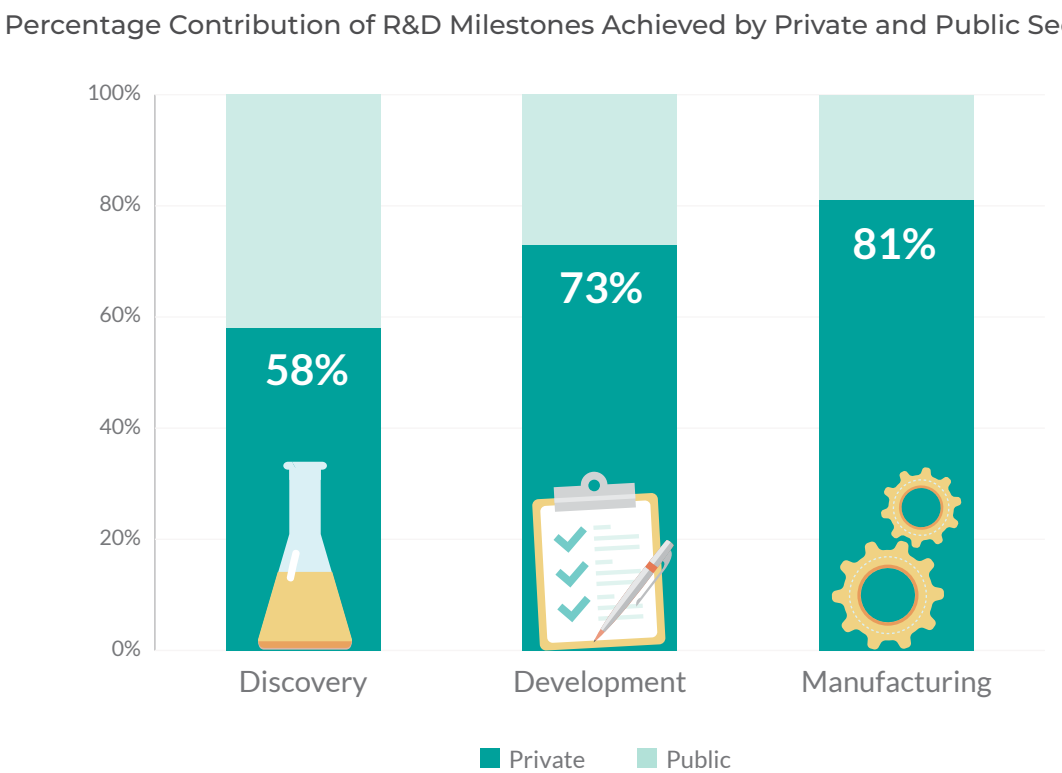


Key: IND=Investigational New Drug Application, NDA=New Drug Application, BLA=Biologics License Application

*The average R&D cost required to bring a new FDA-approved medicine to patients is estimated to be $2.6 billion over the past decade (in 2013 dollars), including the cost of the many potential medicines that do not make it through to FDA approval.

Sources: PhRMA adaptation of DiMasi JA et al.[12]; Tufts CSDD[13]; FDA[14]

The Private Sector Leads the Translation of Basic Research Findings Into New Medicines

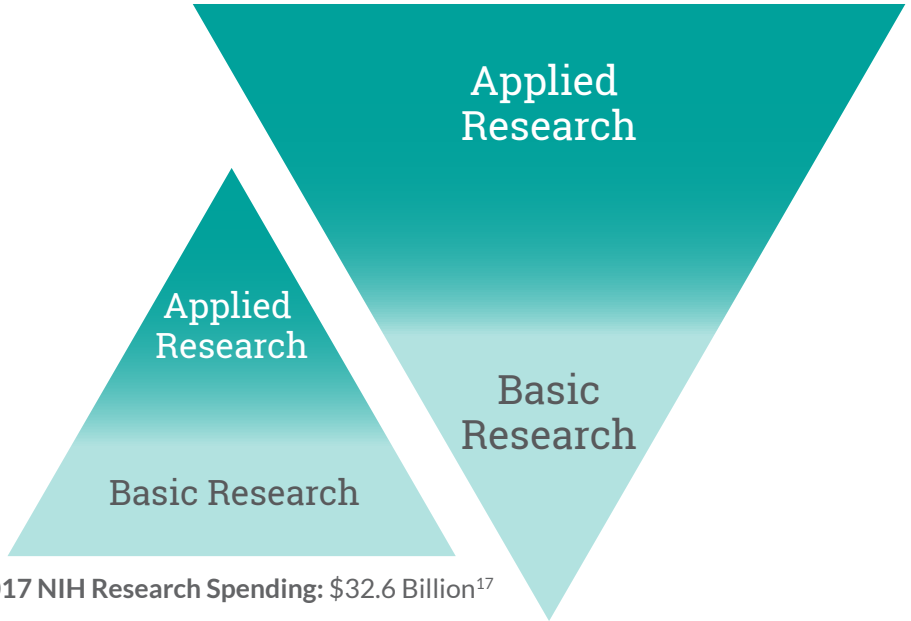


Source: Chakravarthy R et al.[15]

Biopharmaceutical Industry Does the Majority of Research to Translate Basic Science Into New Medicines

While basic science is often initiated in government and academia, it is biopharmaceutical firms that provide the necessary expertise and experience needed to develop new medicines.[16]

2017 Biopharmaceutical Industry R&D Investment: $97 Billion[17]



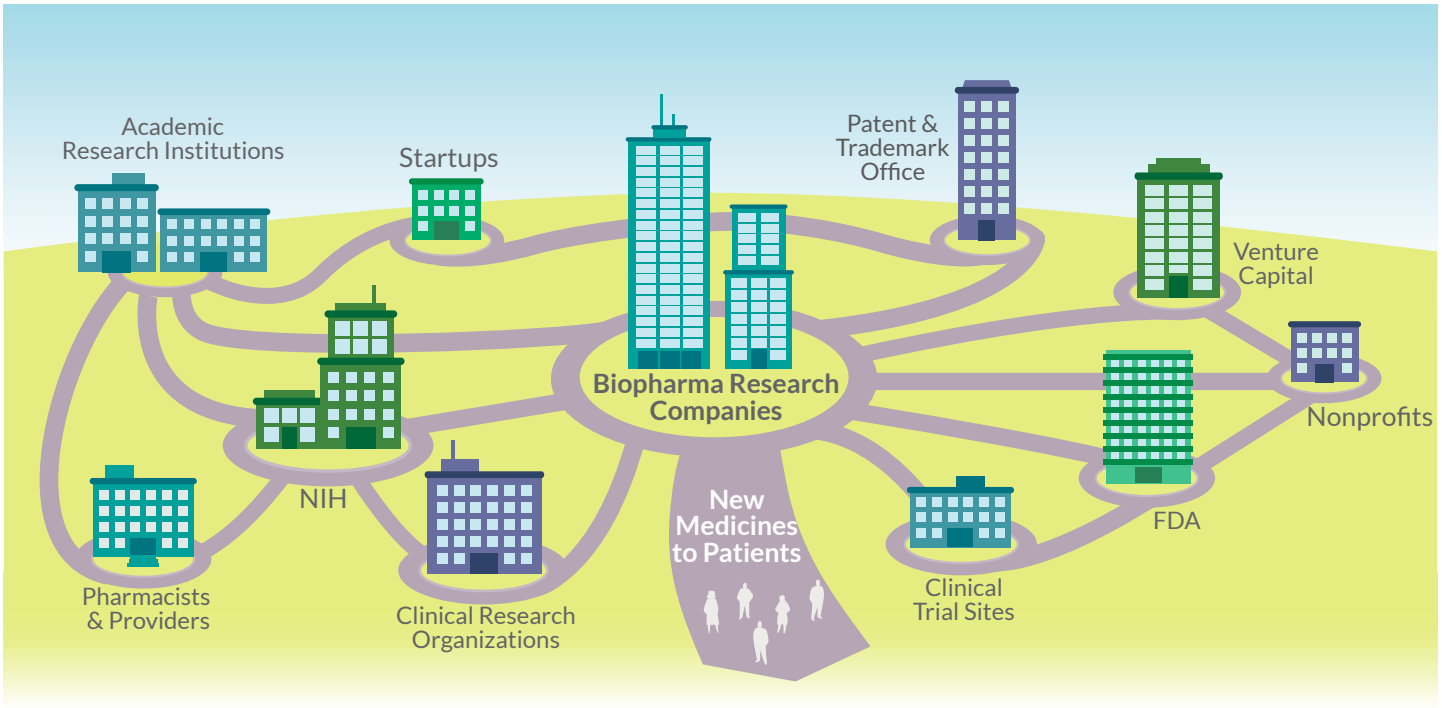
2017 NIH Research Spending: $32.6 Billion[17]

In addition to basic research and biopharmaceutical-related research, NIH supports applied research on medical devices, diagnostics, prevention, and other areas.[18]

Sources: Chakravarthy R et al.[16]; Research!America[17]; NIH[18]

Innovative Biopharmaceutical Companies Sit at the Heart of a Dynamic R&D Ecosystem in the United States

The vibrant US biomedical R&D ecosystem is critical in bringing new medicines to patients and maintaining US leadership in biopharmaceutical R&D.



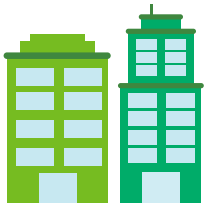
Technology Transfer Between Universities and Industry Has Resulted in Economic Growth and Continued Innovation

Enacted in 1980, the Bayh-Dole Act created a uniform framework for the sharing of technology between universities and the private sector that has facilitated timely and effective commercialization of federally funded research.

POSITIVE IMPACT OF BAYH-DOLE

Commercialization of federally funded research has increased dramatically.

In 2017:



MORE THAN 1,000
startup companies were formed[19]

NEARLY 800
commercial products stemming from university research were introduced[19]

From 1996 to 2015, licensing activity spurred by Bayh-Dole included:

Close to
$591 BILLION
contributed to US GDP[20]

ABOUT 4.2 MILLION
US jobs supported across all industries[20]

Sources: Association of University Technology Managers[19]; Pressman L et al.[20]

Collaboration Is Key in Researching and Developing New Medicines

The rapid pace of scientific and technological advances is propelling a new era in biopharmaceutical innovation in the United States. As the science becomes more complex, partnerships are crucial to advancing biomedical progress. Examples of key collaborative efforts across the R&D spectrum include:

Developing new diagnostics and biological targets for treatments in Alzheimer's disease, type 2 diabetes, rheumatoid arthritis, Parkinson's disease, and lupus[21]

THE PARTNERS
biopharmaceutical companies, NIH, patient and disease organizations

THE biomarkers CONSORTIUM

Combining expertise and resources to rapidly identify, develop, and qualify biomarkers, which will then advance new therapies and guide improvements in regulatory and clinical decision making[22]

THE PARTNERS
biopharmaceutical companies, NIH, CMS, FDA, FNIH, patient and disease organizations

LUNG-MAP

Using comprehensive genetic screening to identify mutations in lung cancer patients in order to direct them to a specific investigational treatment, while operating under a single clinical trial protocol[23]

THE PARTNERS
biopharmaceutical companies, NIH, FDA, patient and disease organizations

Bolstering research to improve prevention and treatment for opioid misuse and addiction and enhancing pain management by developing new biomarkers and a data sharing collaborative[24]

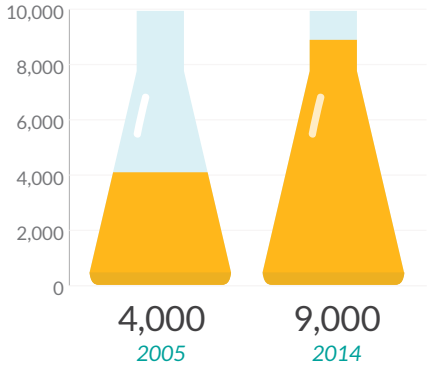
THE PARTNERS
biopharmaceutical companies, NIH, FNIH, patient and disease organizations

Sources: NIH[21]; FNIH[22]; Lung-MAP[23]; NIH[24]

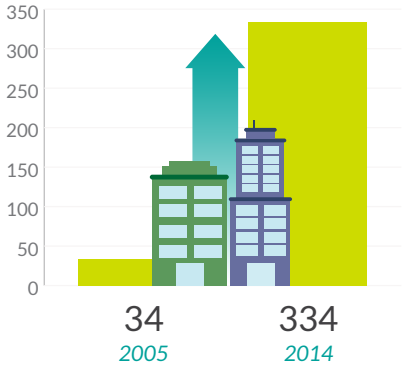
Researchers Are Harnessing Collaborations to Accelerate Innovation

In recent years, stakeholders across the biopharmaceutical research ecosystem have shifted to non-asset-based, precompetitive partnership models in order to leverage their strengths in creative ways, create efficiencies, and tackle scientific and technological challenges.

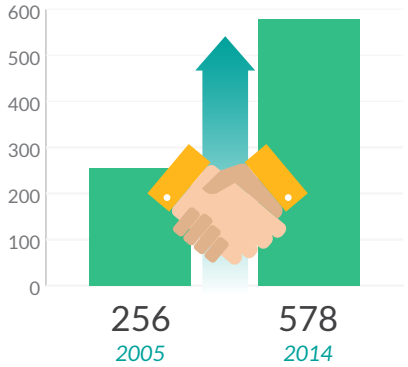
New R&D
PARTNERSHIPS
more than doubled



The number of
CONSORTIA
increased 9x

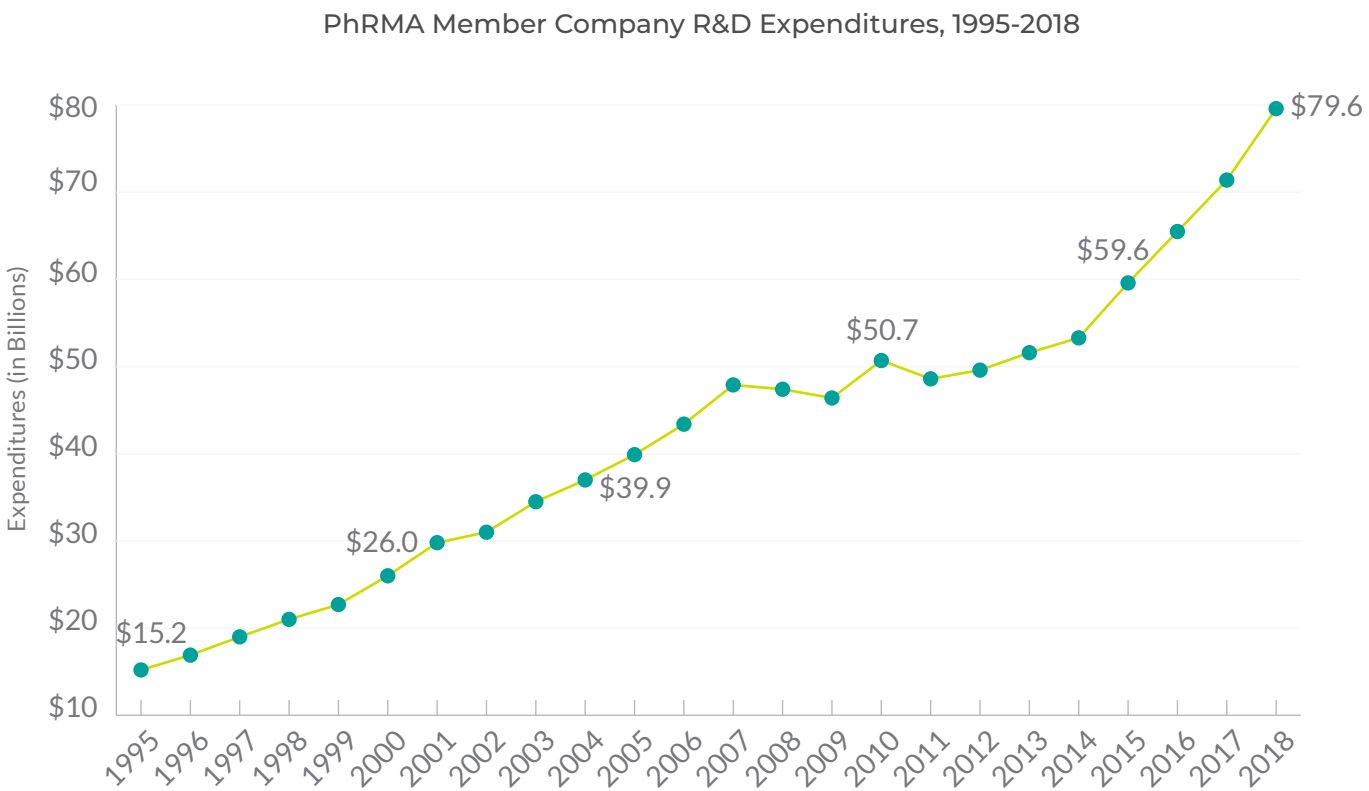


Early-stage
PARTNERSHIPS
more than doubled



Source: Deloitte[25]

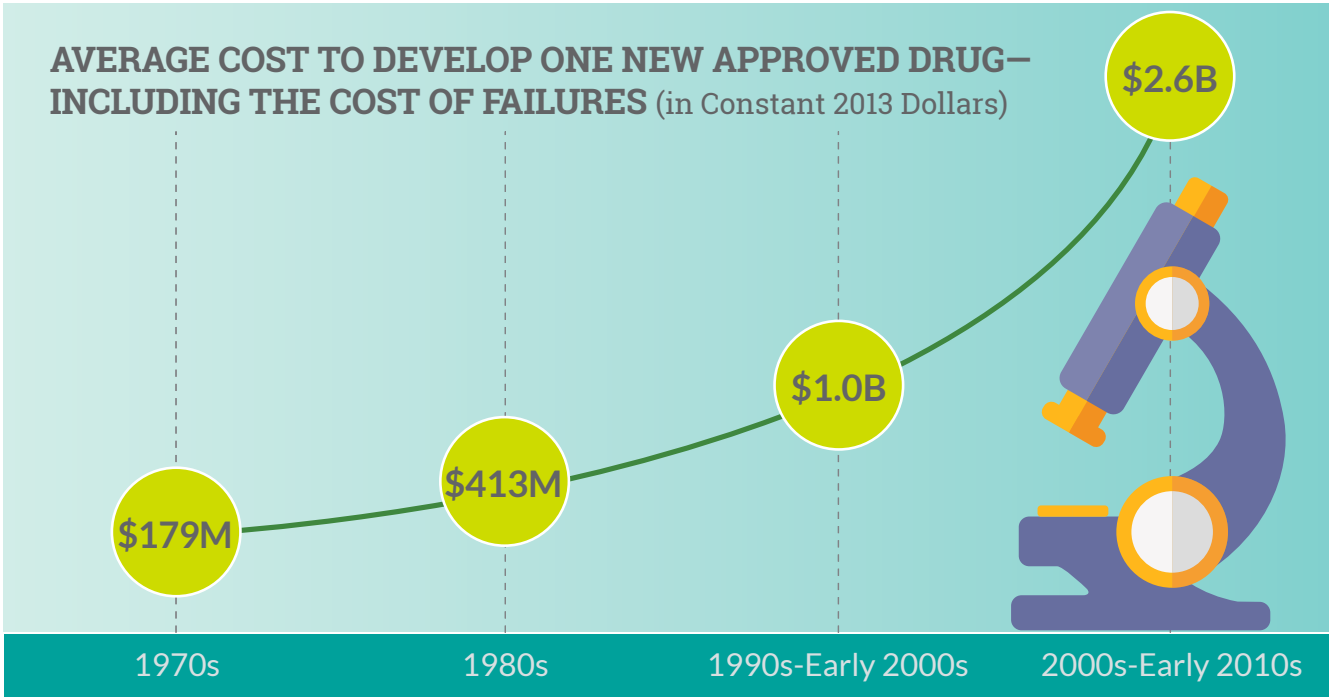
PhRMA Member Company R&D Investment



Source: PhRMA[26]

The Costs of Drug Development Have More Than Doubled Over the Past Decade

Many factors are driving increasing costs of biopharmaceutical R&D, including increased clinical trial complexity, larger clinical trial sizes, greater focus on targeting chronic and degenerative diseases, and higher failure rates for drugs tested in earlier-phase clinical studies.



Source: DiMasi JA et al.[27]

The Complexity of Clinical Trials Has Increased

During the past decade, clinical trial designs and procedures have become much more complex, reducing trial participation and retention rates.

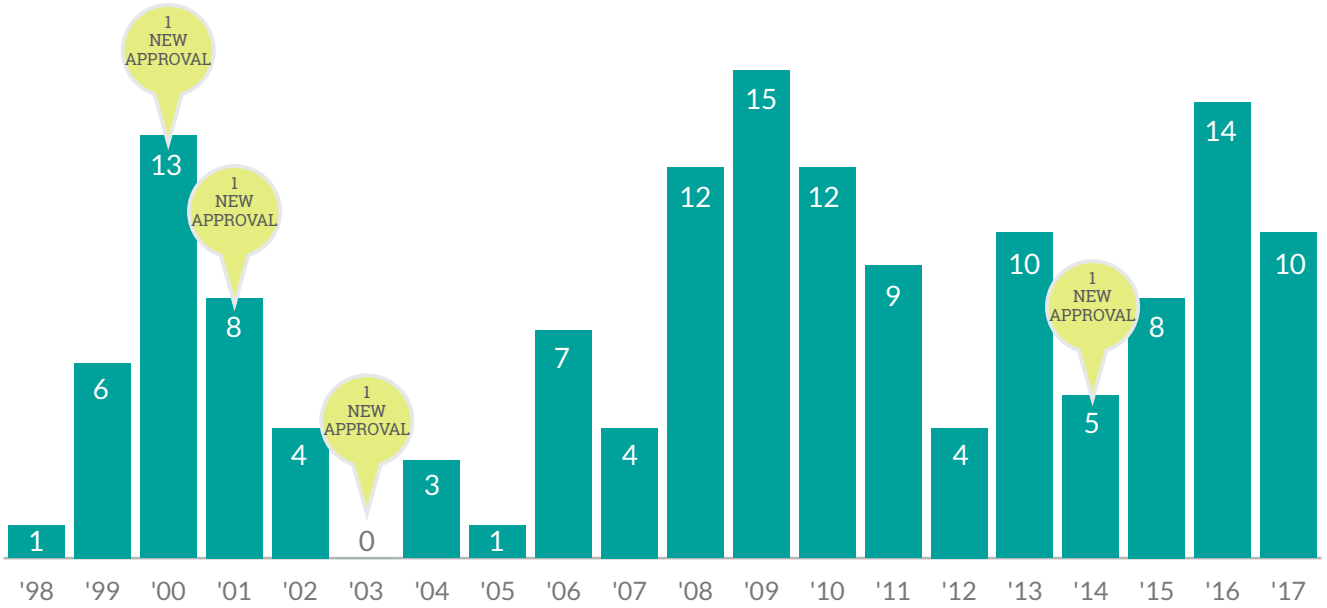
Typical Phase III Protocol (Mean of Total Numbers)	2001-2005 **THEN**	2011-2015 **NOW**	**Increase in COMPLEXITY**
Endpoints	7	13	+86%
Procedures	110	187	+70%
Eligibility Criteria	31	50	+61%
Investigative Sites	40	65	+63%
Data Points Collected	494,236	929,203	+88%

Source: Getz KA et al.[28]

Setbacks in Alzheimer's Disease Research Provide Stepping Stones for Future Innovation

Since 1998, 146 medicines in development for the treatment of Alzheimer's disease have not made it through clinical trials, with only 4 gaining FDA approval. These setbacks highlight the complexity of the R&D process. Though disappointing, they provide important knowledge to fuel future research.

Unsuccessful Investigational Drugs for Alzheimer's Disease, 1998-2017



146 Total Unsuccessful Drugs | **4** Total Approved Medicines

Source: PhRMA[29]

Cancer Researchers Build on Knowledge Gained From Setbacks to Inform Future Advances

Developing a new cancer medicine is a complex process and can take, on average, 1.5 years longer than the development of other medicines. Although the process is fraught with setbacks, some "failures" can inform future study and help guide research efforts.

> The scientific process is thoughtful, deliberate, and sometimes slow, but each advance, while helping patients, now also points toward new research questions and unexplored opportunities."

— Clifford A. Hudis, MD, FACP[30]
Chief Executive Officer, American Society of Clinical Oncology
Chief, Breast Medicine Service, Memorial Sloan Kettering Cancer Center
Professor, Weill Cornell Medical College

MELANOMA*

96 unsuccessful attempts
7 new drugs

BRAIN CANCER*

75 unsuccessful attempts
3 new drugs

LUNG CANCER*

167 unsuccessful attempts
10 new drugs

*Setbacks and advances from 1998 to 2014

Sources: Patel JD et al.[30]; PhRMA[31]

Pediatric Clinical Research: Overcoming Challenges

The Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act (PREA) establish requirements and provide important incentives that help increase the number of clinical studies in pediatric populations. These laws spur pediatric research for this vulnerable population.

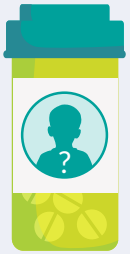
BPCA/PREA Success

Since 1998,
more than 770 pediatric labeling changes[32]

Since 2007,
more than 680 pediatric studies have been completed[33,34]

Before 1997

>80%
of medicines used to treat children did not have pediatric dosing information[35]

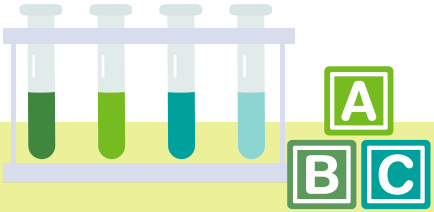


By 2012

That number had been reduced to nearly
50%[36]

Unique Challenges in PEDIATRIC RESEARCH[37]

- Small patient populations
- Distinct dosage and formulation requirements
- Unique ethical, scientific, and medical considerations
- Difficult to enroll patients in trials



Sources: FDA[32-36]; ACS[37]

Enhancing the Drug Discovery, Development, and Review Process

The 21st Century Cures Act and Prescription Drug User Fee Act help ensure the FDA has the tools and resources needed to better manage the significant emerging science and innovation of today to meet the challenges of tomorrow.

INTEGRATING PATIENT PERSPECTIVE

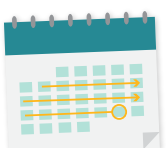
Advance patient-focused drug development at the FDA and throughout the clinical trials process through appropriate incorporation of patient input, patient-reported outcomes, and increased patient engagement.

ADVANCING USE OF REAL-WORLD EVIDENCE

Keep pace with latest technological advances by enabling use of real-world evidence and real-world data in regulatory decision making.

INCREASING ACCEPTANCE OF INNOVATIVE CLINICAL TRIAL DESIGNS

Create efficiencies in drug development through use of adaptive clinical trial designs and pragmatic clinical trials as well as increased use of advanced data analytics.



ACCELERATING QUALIFICATION AND USE OF BIOMARKERS

Adapt biomarker qualification development and other regulatory pathways to support the development of emerging cell and gene therapies, personalized medicines, and companion diagnostics.

Learning From Patients to Develop Better Treatments

As important stakeholders in the drug development process, patients, family members, and caregivers can provide unique and valuable perspectives on the disease and available treatment options. These perspectives can inform evaluation of a medicine's benefits and risks and provide the context for FDA regulatory decision making.

WHO CAN PROVIDE PATIENT PERSPECTIVES?

Patients | Family Members | Caregivers

BENEFITS OF PATIENT PERSPECTIVES

RESEARCHERS
include patient perspective throughout drug development process.

THE FDA
incorporates patient perspective into its regulatory decision making.

NEW MEDICINES
reflect patient and caregiver needs.

Source: PhRMA[38]

Notes and Sources

1. Adis R&D Insight Database. https://adis.springer.com. Accessed May 2019.
2. Adis R&D Insight Database. https://adis.springer.com. Accessed April 2019. Disease-specific numbers are available in PhRMA's Medicines in Development reports. http://www.phrma.org/science/in-the-pipeline/medicines-in-development.
3. Long G; Analysis Group. The biopharmaceutical pipeline: innovative therapies in clinical development. http://phrma-docs.phrma.org/files/dmfile/Biopharmaceutical-Pipeline-Full-Report.pdf. Published July 2017. Accessed May 2018.
4. Food and Drug Administration (FDA). Search orphan drug designations and approvals. http://www.accessdata.fda.gov/scripts/opdlisting/oopd. Accessed February 2019.
5. Danese E, Lippi G. Rare diseases: the paradox of an emerging challenge. *Ann Transl Med*. 2018;6(17):329. doi:10.21037/atm.2018.09.04
6. Pharmaceutical Research and Manufacturers of America (PhRMA). Spurring innovation in rare diseases. http://phrma-docs.phrma.org/files/dmfile/RareDisease_Backgrounder.pdf. 2018 update. Accessed April 2018.
7. Food and Drug Administration (FDA). FDA news release. Remarks from FDA Commissioner Scott Gottlieb, M.D., as prepared for oral testimony before the U.S. Senate Committee on Health, Education, Labor & Pensions Hearing, "Implementation of the 21st Century Cures Act: Progress and the Path Forward for Medical Innovation." https://www.fda.gov/news-events/press-announcements/remarks-fda-commissioner-scott-gottlieb-md-prepared-oral-testimony-us-senate-committee-health. Published December 7, 2017. Accessed May 2019.
8. Pharmaceutical Research and Manufacturers of America (PhRMA). Medicines in development for cell therapy and gene therapy. http://phrma-docs.phrma.org/files/dmfile/MID_Cell_and_Gene_Therapy_2018_FINAL.pdf. Accessed April 2019.
9. Avalere Health. A conversation on digital health [webinar]. https://avalere.com/webinars/a-conversation-on-digital-health. Published April 2019. Accessed April 2019.
10. Personalized Medicine Coalition. Personalized medicine at FDA: a progress and outlook report 2018. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_A_Progress_and_Outlook_Report.pdf. Accessed April 2019.
11. Tufts Center for the Study of Drug Development (CSDD). Personalized medicine gains traction but still faces multiple challenges. *Tufts CSDD Impact Rep*. 2015;17(3).
12. PhRMA adaptation of DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*. 2016;47:20-33.
13. Tufts Center for the Study of Drug Development (CSDD). Cost of developing a new drug [briefing]. https://csdd.tufts.edu/csddnews/2018/3/9/march-2016-tufts-csdd-rd-cost-study. Published November 18, 2014. Accessed May 2018.

Notes and Sources

14. Food and Drug Administration (FDA). U.S. Food and Drug Administration drug approval process. http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf. Accessed May 2017.
15. Chakravarthy R, Cotter K, DiMasi J, et al. Public- and private-sector contributions to the research and development of the most transformational drugs in the past 25 years: from theory to therapy. *Ther Innov Regul Sci.* 2016;50(6):759-768.
16. Chakravarthy R, Cotter K, DiMasi J, et al. Public- and private-sector contributions to the research and development of the most transformational drugs in the past 25 years: from theory to therapy. *Ther Innov Regul Sci.* 2016;50(6):759-768.
17. Research!America. U.S. investments in medical and health research and development, 2013-2017. https://www.researchamerica.org/sites/default/files/Policy_Advocacy/2013-2017InvestmentReportFall2018.pdf. Published 2018. Accessed April 2019.
18. National Institutes of Health (NIH). Overall appropriations. https://officeofbudget.od.nih.gov/pdfs/FY18/Overall%20Appropriations.pdf. Accessed April 2019.
19. Association of University Technology Managers. AUTM US licensing activity survey: 2017. https://autm.net/AUTM/media/SurveyReportsPDF/AUTM_2017_US_Licensing_Survey_no_appendix.pdf. Accessed April 2019.
20. Pressman L, Planting M, Yuskavage R, et al. The economic contribution of university/nonprofit inventions in the United States: 1996-2015. https://www.autm.net/AUTMMain/media/Partner-Events/Documents/Economic-_Contribution_University-Nonprofit_Inventions_US_1996-2015_BIO_AUTM.pdf. Published June 2017. Accessed April 2018.
21. National Institutes of Health (NIH). Accelerating Medicines Partnership (AMP). https://www.nih.gov/research-training/accelerating-medicines-partnership-amp. Accessed April 2019.
22. Foundation for the National Institutes of Health (FNIH). Biomarkers Consortium. https://fnih.org/what-we-do/biomarkers-consortium. Accessed April 2019.
23. Lung-MAP. About Lung-MAP. http://www.lung-map.org/about-lung-map. Accessed April 2019.
24. National Institutes of Health (NIH). NIH HEAL Initiative. https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative. Accessed April 2019.
25. Lesser N, Hefner M; Deloitte. Partnering for progress: how collaborations are fueling biomedical advances. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-lshc-partnering-for-progress-how-collaborations-are-fueling-biomedical-advances.pdf. Published 2017. Accessed June 2017.
26. Pharmaceutical Research and Manufacturers of America (PhRMA). *PhRMA Annual Membership Survey, 1996-2018*. Washington, DC: PhRMA; 2019.

Notes and Sources

27. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*. 2016;47:20-33. Previous research by DiMasi and Grabowski estimated the average R&D costs in the early 2000s at $1.2 billion in constant 2000 dollars (see DiMasi JA, Grabowski HG. The cost of biopharmaceutical R&D: is biotech different? *MDE Manage Decis Econ*. 2007;28:469-479). That estimate is based on the same underlying survey as estimates for the 1990s to early 2000s reported here ($800 million in constant 2000 dollars) but is updated for changes in the cost of capital.
28. Getz KA, Campo RA. New benchmarks characterizing growth in protocol design complexity. *Ther Innov Regul Sci*. 2018;52(1):22-28.
29. Pharmaceutical Research and Manufacturers of America (PhRMA). Researching Alzheimer's medicines: setbacks and stepping stones. http://phrma-docs.phrma.org/files/dmfile/AlzheimersSetbacksSteppingStones_FINAL_digital.pdf. Published 2018. Accessed April 2019.
30. Patel JD, Krilov L, Adams S, et al. Clinical cancer advances 2013: annual report on progress against cancer from the American Society of Clinical Oncology. *J Clin Oncol*. 2014;32(2):129-160. http://jco.ascopubs.org/content/early/2013/12/09/JCO.2013.53.7076.full.pdf+html. Accessed May 2017.
31. Pharmaceutical Research and Manufacturers of America (PhRMA). Researching cancer medicines: setbacks and stepping stones. http://www.phrma.org/sites/default/files/pdf/2014-cancer-setbacks-report.pdf. Published 2014. Accessed May 2017.
32. Food and Drug Administration (FDA). New pediatric labeling information database. https://www.accessdata.fda.gov/scripts/sda/sdnavigation.cfm?filter=&sortColumn=1a&sd=labelingdatabase&page=1. Current as of March 31, 2019. Accessed May 2019.
33. Food and Drug Administration (FDA). Pediatric studies characteristics. https://www.accessdata.fda.gov/scripts/SDA/sdNavigation.cfm?filter=&sortColumn=1a&sd=fdaaadescriptorssortablewebdatabase&displayAll=false&page=8. Accessed May 2019.
34. Food and Drug Administration (FDA). Number of pediatric studies completed (under both PREA and BPCA). https://www.accessdata.fda.gov/scripts/fdatrack/view/track.cfm?program=cder&status=public&id=CDER-RRDS-Number-of-pediatric-studies-completed&fy=All. Current as of December 31, 2017. Accessed April 2018.
35. Food and Drug Administration (FDA). Drug research and children. https://www.fda.gov/drugs/drug-information-consumers/drug-research-and-children. Current as of May 4, 2016. Accessed May 2019.
36. Karesh A; Food and Drug Administration (FDA). Pediatric drug development: regulatory expectations basic. https://www.fda.gov/media/91673/download. Accessed May 2019.
37. American Cancer Society (ACS). Translating discovery into cures for children with cancer: childhood cancer research landscape report. https://www.cancer.org/content/dam/cancer-org/research/translating-discovery-into-cures-for-children-with-cancer-landscape-report.pdf. Published 2016. Accessed May 2017.
38. Pharmaceutical Research and Manufacturers of America (PhRMA). Patient-focused drug development. https://www.phrma.org/fact-sheet/patient-focused-drug-development. Published June 2016. Accessed May 2019.

3 MARKET DYNAMICS

The Economics of Drug Development and the Market Forces That Shape Spending on Medicines

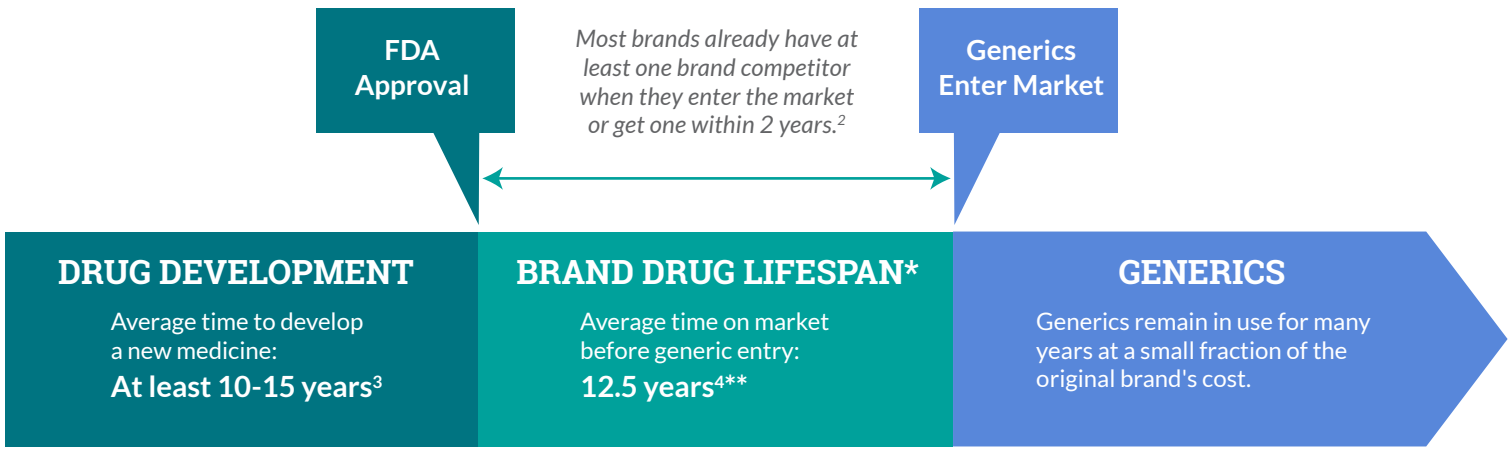
Competition is a hallmark of the US prescription medicines market. Negotiating power is concentrated among a few pharmacy benefit managers (PBMs), which forces new medicines to compete for coverage and increases the likelihood of excluding medicines from coverage altogether. The built-in cost containment of the prescription drug lifecycle remains unique in health care, where new medicines eventually lead to lower-cost generics—and soon many biosimilars—that bring long-term value to patients.

Ongoing investment in research and development (R&D) depends on the commercial success of a few products that must make up for all the rest, including those that never reach the market. Average returns on R&D investments have been declining. Accounting for uncertainty and risk, biopharmaceutical industry profits are in the middle range among all industries.

The market is rapidly evolving, increasingly linking payment to results and affecting how drugs are prescribed. Value-based contracts and other market-based arrangements show promise for improving outcomes and reducing costs.

Illustrative Pharmaceutical Lifecycle

New pharmaceutical medicines typically face competition after a relatively short time on the market, first from brand competitors, and eventually from generics.

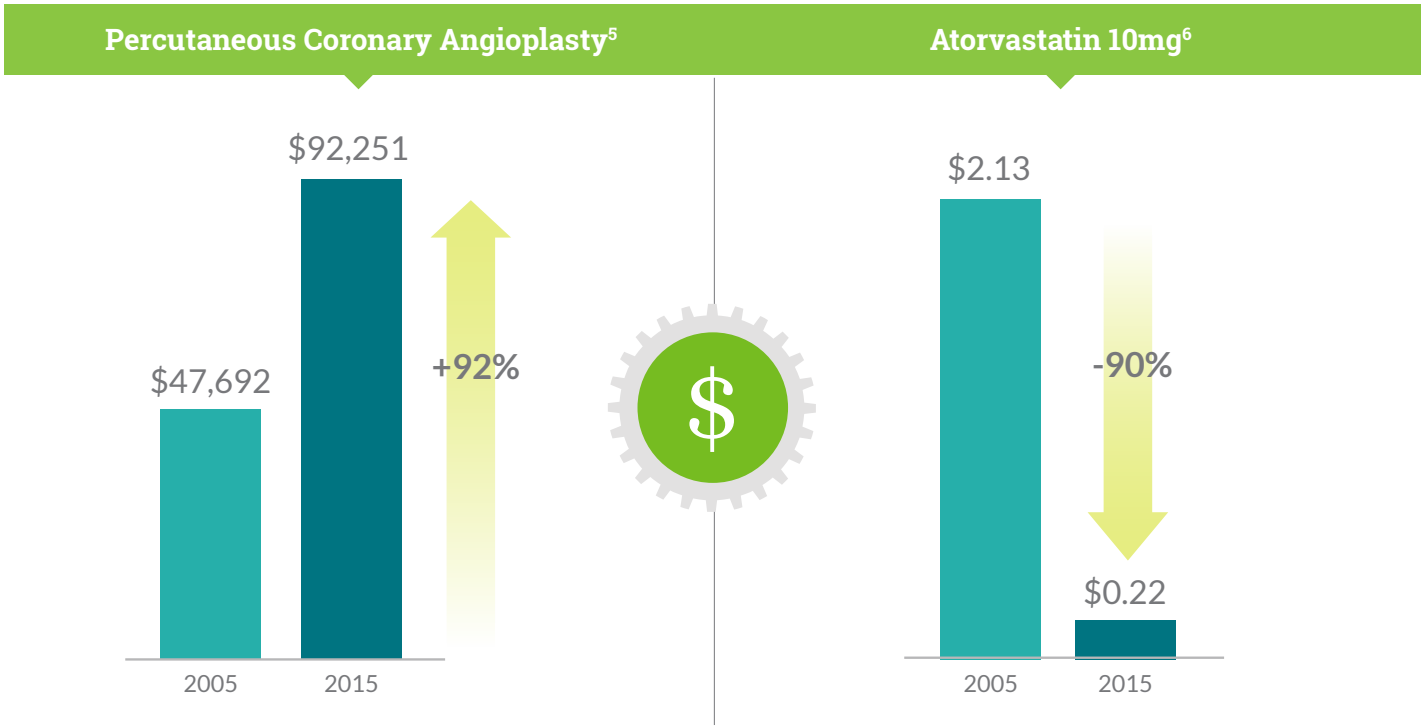


*Brand drug market share generally declines rapidly after generic entry.
**For brand medicines with more than $250 million in annual sales in 2008 dollars, which account for 92% of sales of the brand medicines analyzed

Sources: PhRMA[1]; DiMasi JA et al.[2,3]; Grabowski H et al.[4]

Medicines Offer Built-in Cost Containment, Which Is Unique in Health Care

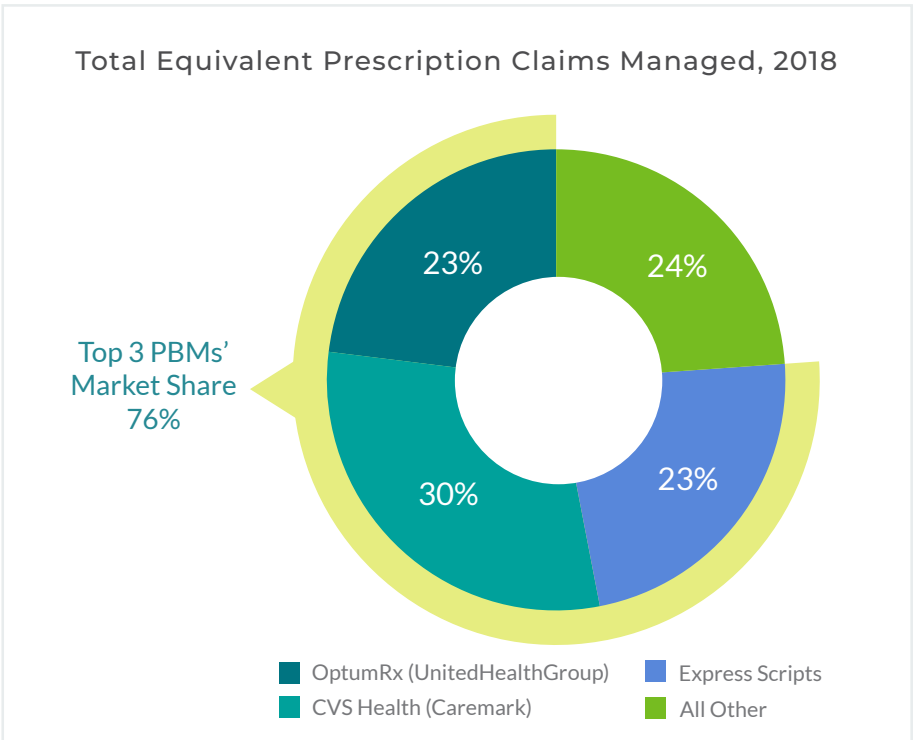
The price of a medicine commonly used to prevent cardiovascular disease dropped 90% between 2005 and 2015, while the average charge for a surgical procedure to treat it increased 92% over the same period.



Sources: PhRMA analysis of HCUP Hospital Charge data[5]; IQVIA[6]

Powerful Purchasers Negotiate on Behalf of Payers

Negotiating power is increasingly concentrated among fewer pharmacy benefit managers (PBMs), each purchasing medicines for more people than the populations of entire European countries.



PBMs and insurers determine:

FORMULARY
if a medicine is covered

TIER PLACEMENT
patient cost sharing

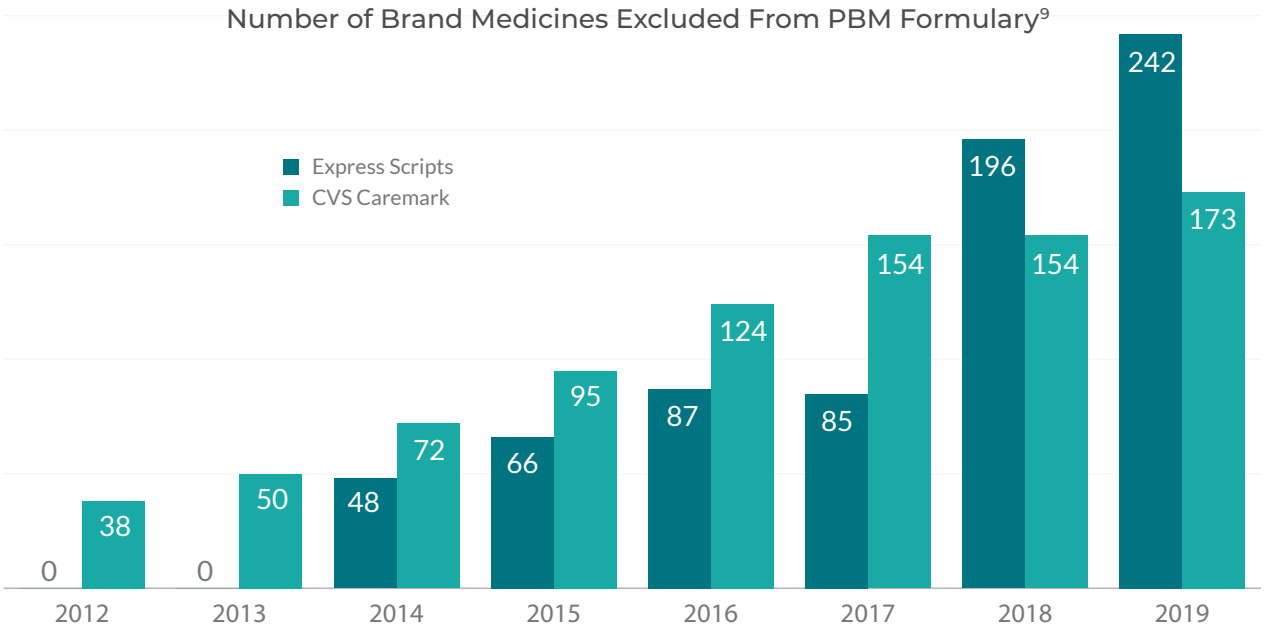
ACCESSIBILITY
utilization management through prior authorization or fail first

PROVIDER INCENTIVES
preferred treatment guidelines and pathways

Source: Drug Channels Institute[7]

Number of Brand Medicines Excluded From PBM Formularies Has Increased Over Time

When a medicine is excluded from a pharmacy benefit manager's (PBM's) formulary, patients cannot access it without paying the list price. This can interrupt the continuity of a patient's treatment as well as their doctor's ability to make prescribing decisions that best meet their patients' needs.[8]



Sources: Tufts CSDD[8]; Drug Channels Institute[9]

Case Study in Manufacturer-Payer Negotiations: Hepatitis C Medicines

Leveraging increased competition in the hepatitis C market, payers negotiated deep discounts off list prices for new medicines with manufacturers, reducing prices below those in many Western European countries.[10]

What Payers Claimed Would Happen

"What they have done with this particular drug will break the country.... It will make pharmacy benefits no longer sustainable. Companies just aren't going to be able to handle paying for this drug."

— Express Scripts, April 2014[11]

"This pricing, which Gilead attempts to justify as the cost of medical advancement, will have a tsunami effect across our entire health care system."

— America's Health Insurance Plans, July 2014[12]

What Actually Happened

"The price is sufficiently low that we can go to our clients and say that they can treat every patient with hepatitis C."

— Express Scripts, January 2015[13]

"We are receiving market-leading rates from both companies. Neither company wanted to be left off the formulary."

— Prime Therapeutics, January 2015[14]

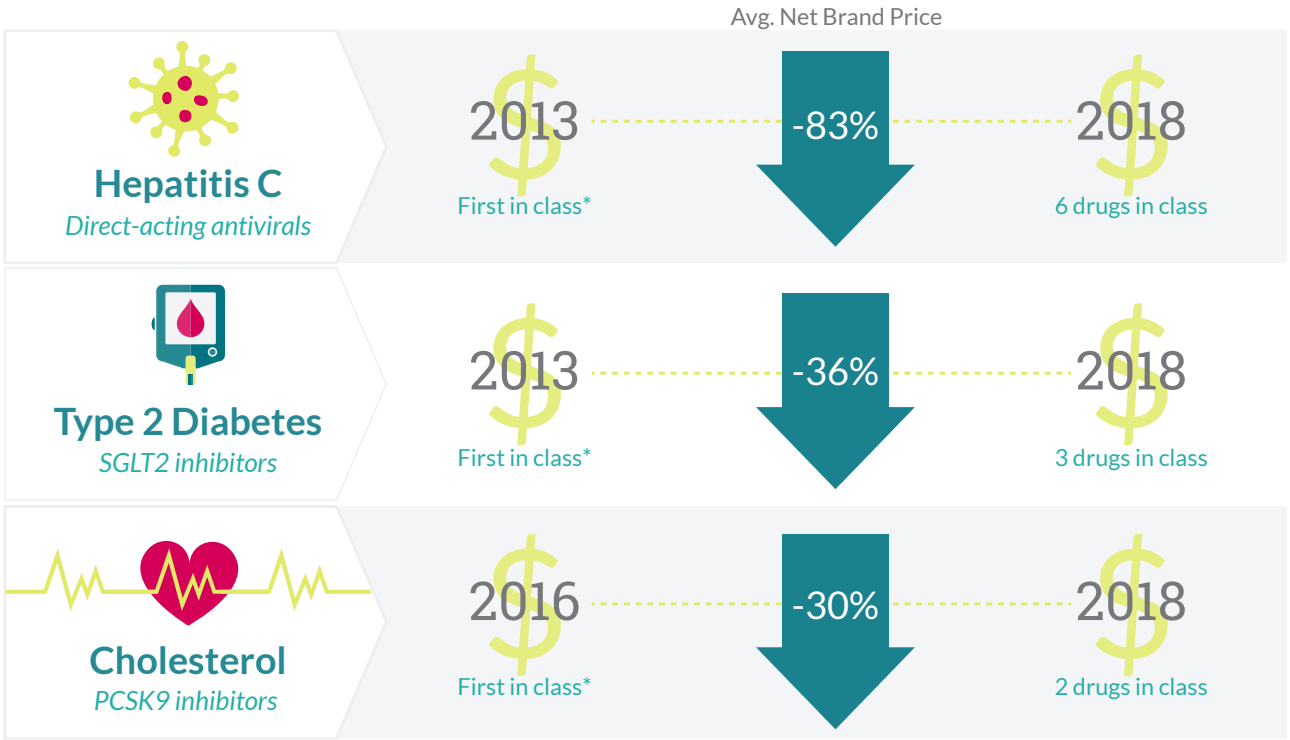
"Competitive market forces and hard-nosed bargaining make 'tremendously effective' new hepatitis C medicines not just more accessible to ailing patients—but also offer good value to the U.S. health care system."

— The New York Times Editorial Board, September 2015[15]

Sources: LaMattina J[10]; Cortez MF[11]; Ignagni K[12]; Silverman E[13]; Langreth R[14]; New York Times Editorial Board[15]

Brand-to-Brand Competition Drives Savings in US Market-Based System

Payers leverage purchasing power and competition among brand medicines to negotiate substantial discounts on medicines.

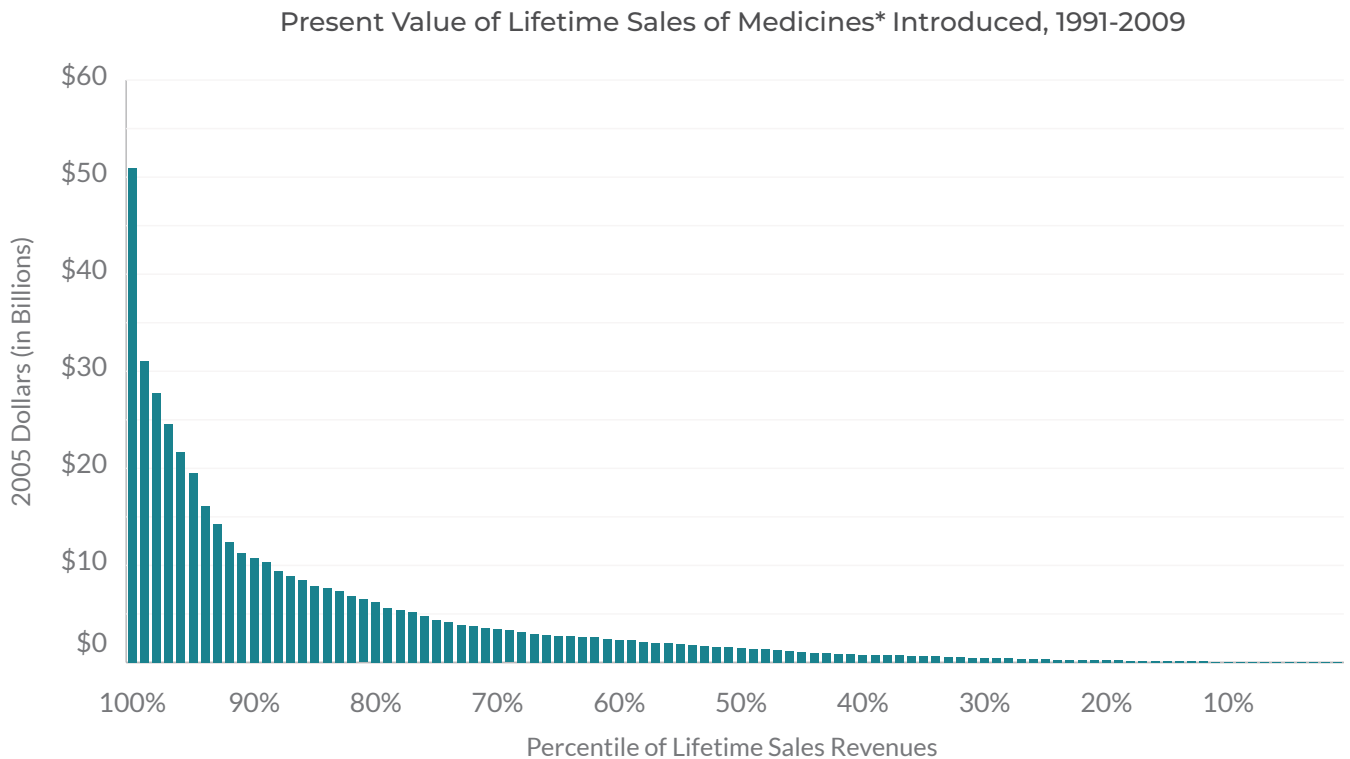


*Indicates launch year of the first drug in this pharmacologic class.

Source: PhRMA analysis of SSR health data[16]

Few Approved Medicines Are Commercially Successful

Ongoing investment in R&D depends on the commercial success of a few products that must make up for all the rest, including those that never reach the market.



*A "medicine" is defined as a novel active substance (ie, a molecular or biologic entity or combination product in which at least one element had not been previously approved by the FDA). Sales are global sales, net of rebates and discounts.

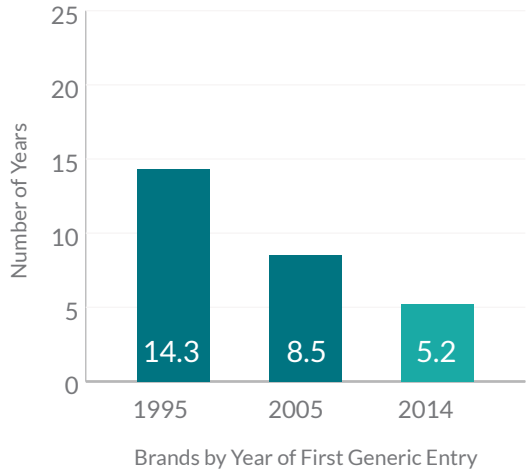
Source: Berndt ER et al.[17]

Earlier and More Frequent Patent Challenges by Generic Companies

As early as 4 years after brand launch, a generic company may file a Paragraph IV certification with the FDA to challenge patents associated with the brand medicine, often allowing generic market entry before the patent expiration date.

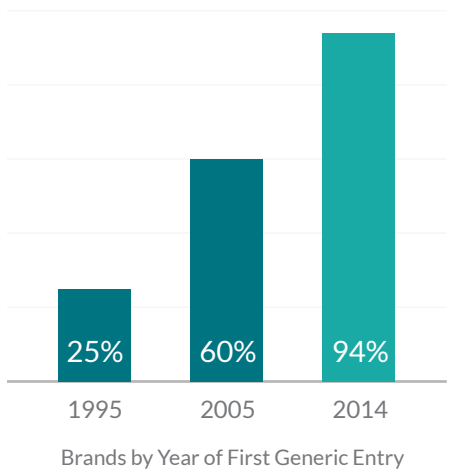
Patent challenges are occurring earlier...

Average Time From Brand Launch to Paragraph IV Patent Challenge*



...and are more common

Share of Brand Products Experiencing at Least 1 Paragraph IV Patent Challenge Prior to Generic Entry*

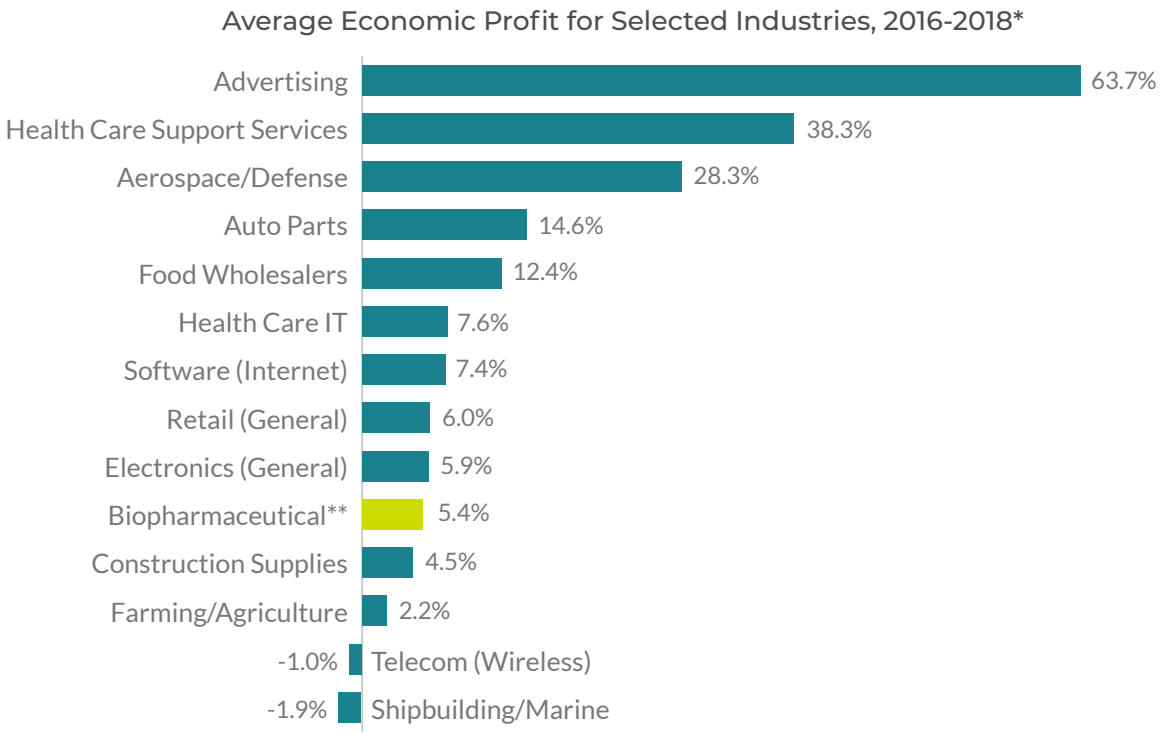


*All numbers are 3-year moving averages for brand medicines with more than $250 million in annual sales in 2008 dollars, which account for 92% of sales of the brand medicines analyzed.

Source: Grabowski H et al.[18]

Biopharmaceutical Profits Are in Line With Those of Other Industries

Adjusted for the significant risk and capital investments required to develop medicines, biopharmaceutical industry profits are average among industries.

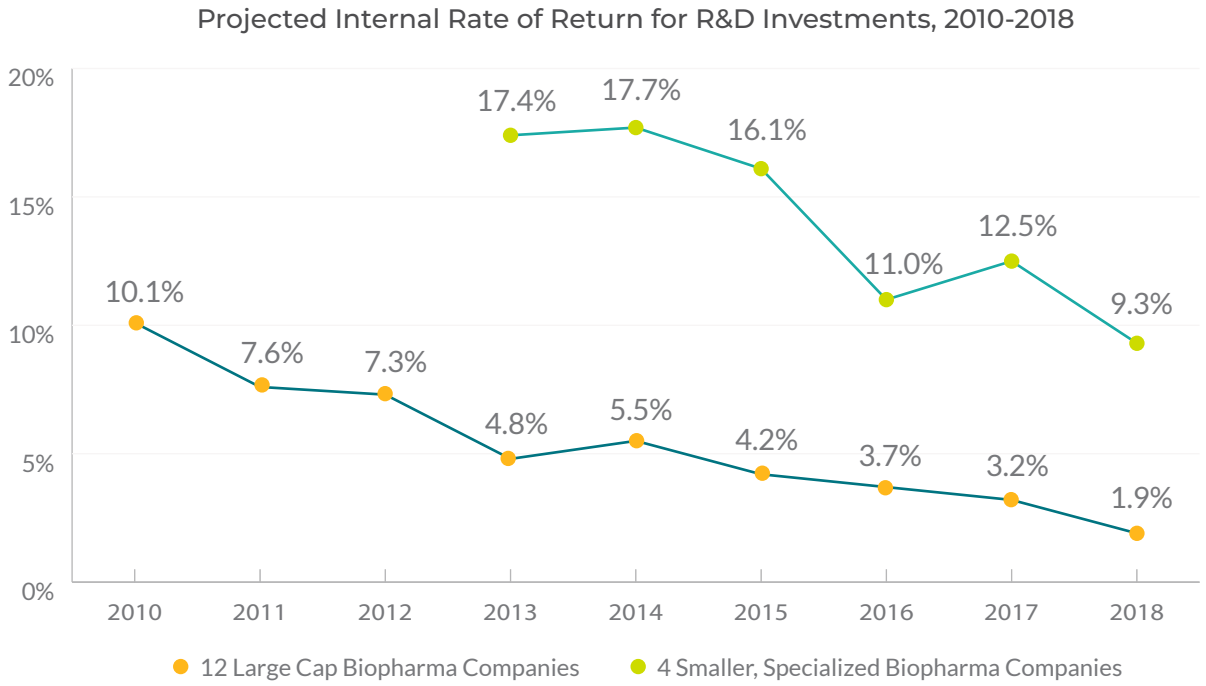


*Economic profits are accounting profits minus capital expenses.
**Represents the weighted average of pharmaceuticals (8.2%) and biotechnology (2.2%), which are listed as separate industries in the source data.

Source: Adapted from Bates White[19]

Increasingly Complex Science and Challenging Markets Have Led to Diminishing Returns on Research Investments

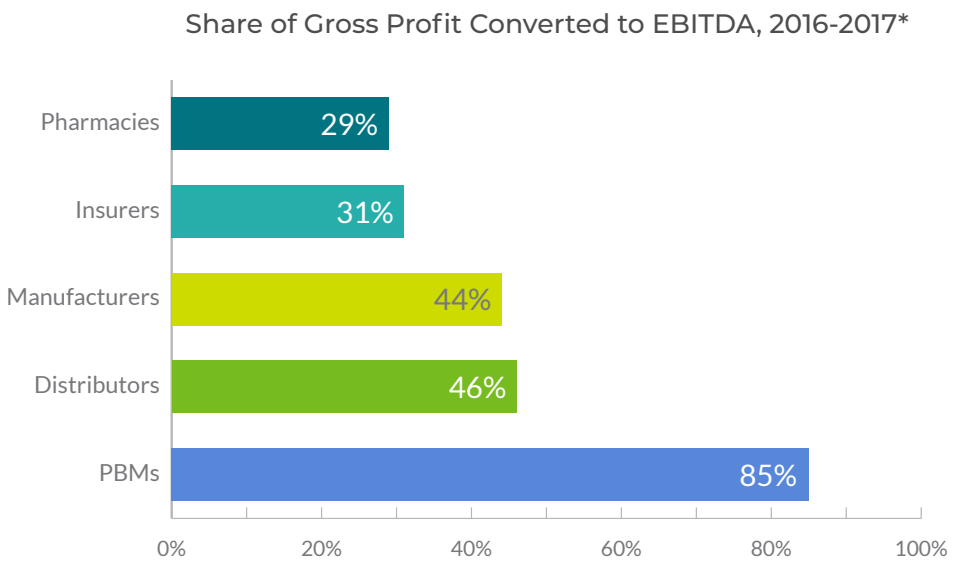
Despite headlines about large revenues from new drug launches, biopharmaceutical companies have faced declining financial returns on their R&D investments.



Source: Deloitte[20]

PBM Profit Margins Are Well Above Others in the Drug Distribution and Supply Chain

Pharmacy benefit managers (PBMs) do not take possession of the medicines they manage, keeping their spending on fixed assets and other expenses very low. Their resulting profits are even higher than manufacturers' profits, despite bearing very little risk.



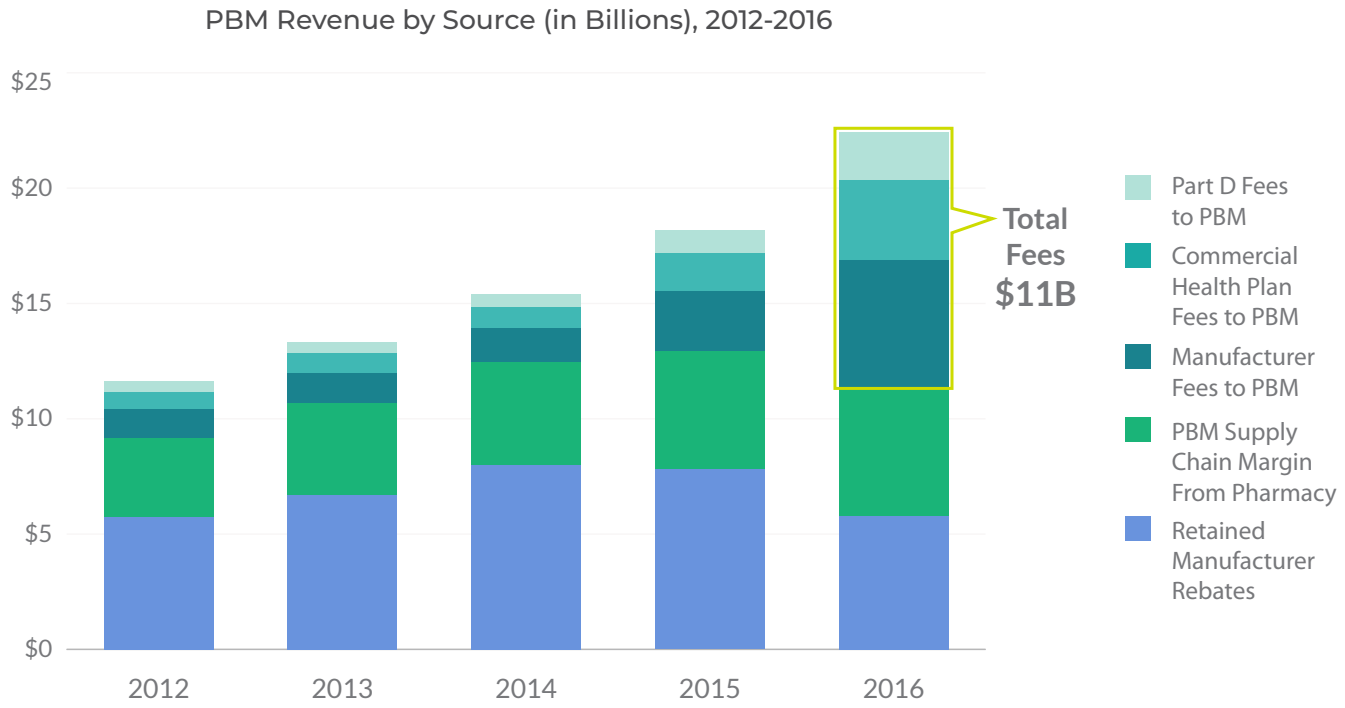
> Analysts at Bernstein tried to get a better picture of how profitable these [supply chain] companies are by excluding the cost of the drugs that are included in their revenue... By this analysis, pharmacy-benefit managers are exceptionally profitable."
>
> — Charley Grant, *Wall Street Journal*[23]

*Calculated as EBITDA (Earnings Before Interest, Taxes, Depreciation, and Amortization) margin divided by gross margin

Sources: Bernstein Research[21]; NDP Analytics[22]; Grant C[23]

Fees Paid to PBMs Have Increased Significantly

While pharmacy benefit managers (PBMs) have retained a smaller share of total rebates, they have offset lost profit from rebates with increased fees. In 2016, PBM revenue surpassed $22 billion, nearly twice the 2012 PBM revenue of $11.6 billion. Fees paid to PBMs quadrupled between 2014 and 2016 alone.



Source: Pew Charitable Trusts[24]

Accounting Treatment of R&D Overstates Biopharmaceutical Profits

> Correctly accounting for R&D as a long-lived investment tends to reduce substantially, if not to eliminate altogether, the inference that pharmaceutical companies are on average achieving supranormal profit returns."
>
> — Frederic Scherer, AEI-Brookings Joint Center for Regulatory Studies[25]

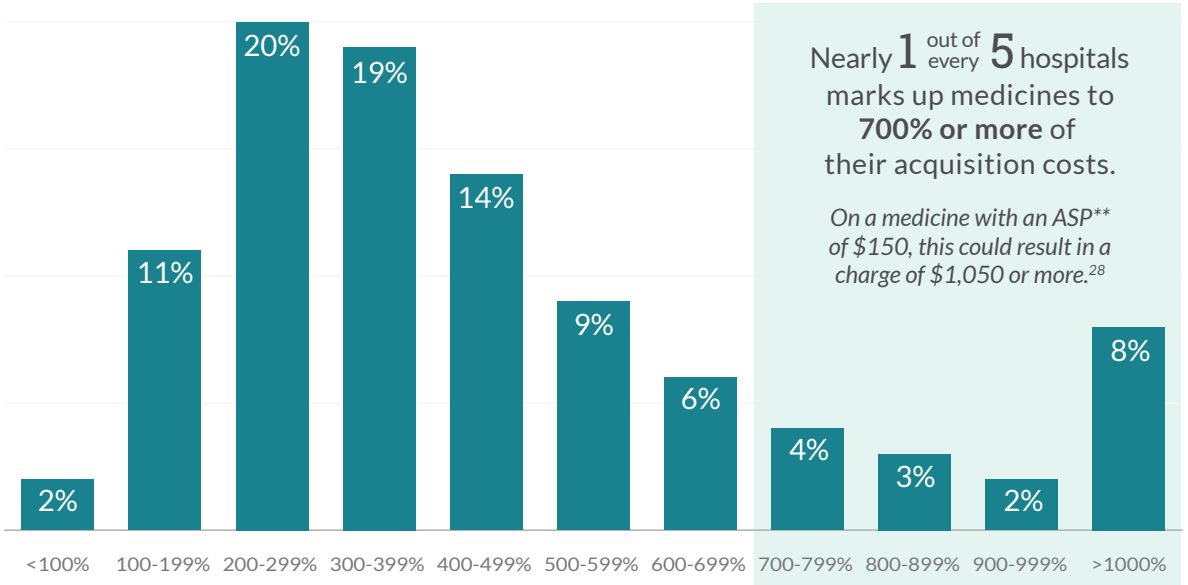
> [T]he standard accounting measure of profits overstates true returns to R&D-intensive industries, such as pharmaceuticals, and makes it difficult to meaningfully compare profit levels among industries. Accounting measures treat most R&D spending (except for capital equipment) as a deductible business expense rather than as a capitalized investment. But the intangible assets that research and development generate—such as accumulated knowledge, new research capabilities, and patents—increase the value of a company's asset base. Not accounting for that value overstates a firm's true return on its assets."
>
> — Congressional Budget Office[26]

Sources: Scherer FM[25]; CBO[26]

Hospitals Mark Up Medicines in the Outpatient Setting, Driving Up Costs to Patients and the Health System

Hospitals mark up medicine prices, on average, nearly 500%. The amount hospitals receive after negotiations with commercial payers is, on average, more than 250% what they paid to acquire the medicine.[27]

Percentage of Hospitals by Average Level of Markup for Medicines* (3,792 Hospitals)



*Percentages in chart may not add up to 100% due to rounding.
**ASP: Average Sales Price

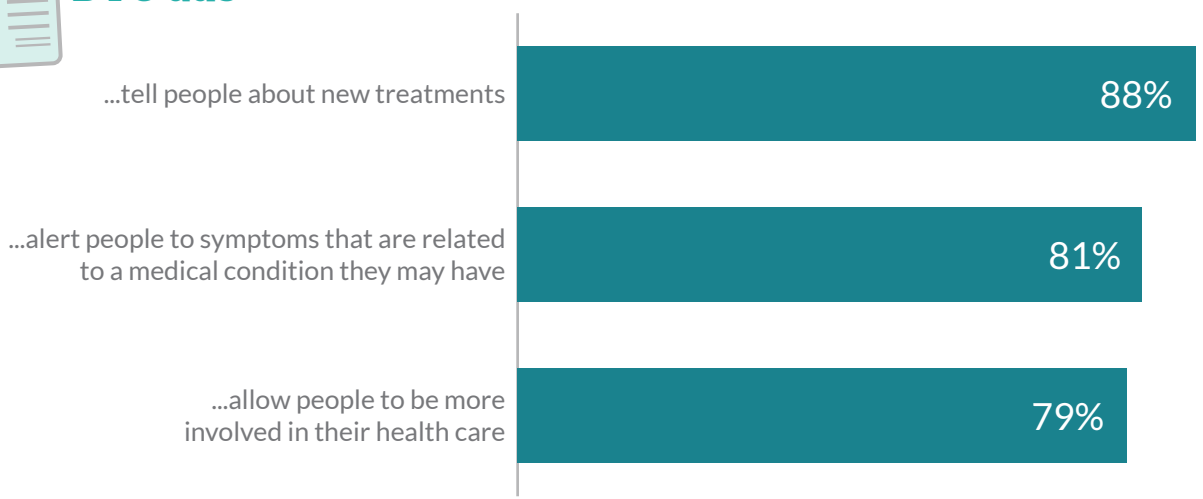
Sources: The Moran Company[27,28]

Direct-to-Consumer Advertising Increases Awareness of Conditions and Treatments

A recent survey of consumers demonstrated the positive contribution of direct-to-consumer (DTC) advertising to patients' knowledge.

How strongly do you agree or disagree with each statement?
Percentage who AGREE with each statement
(Survey of 1,564 consumers, April 2017)

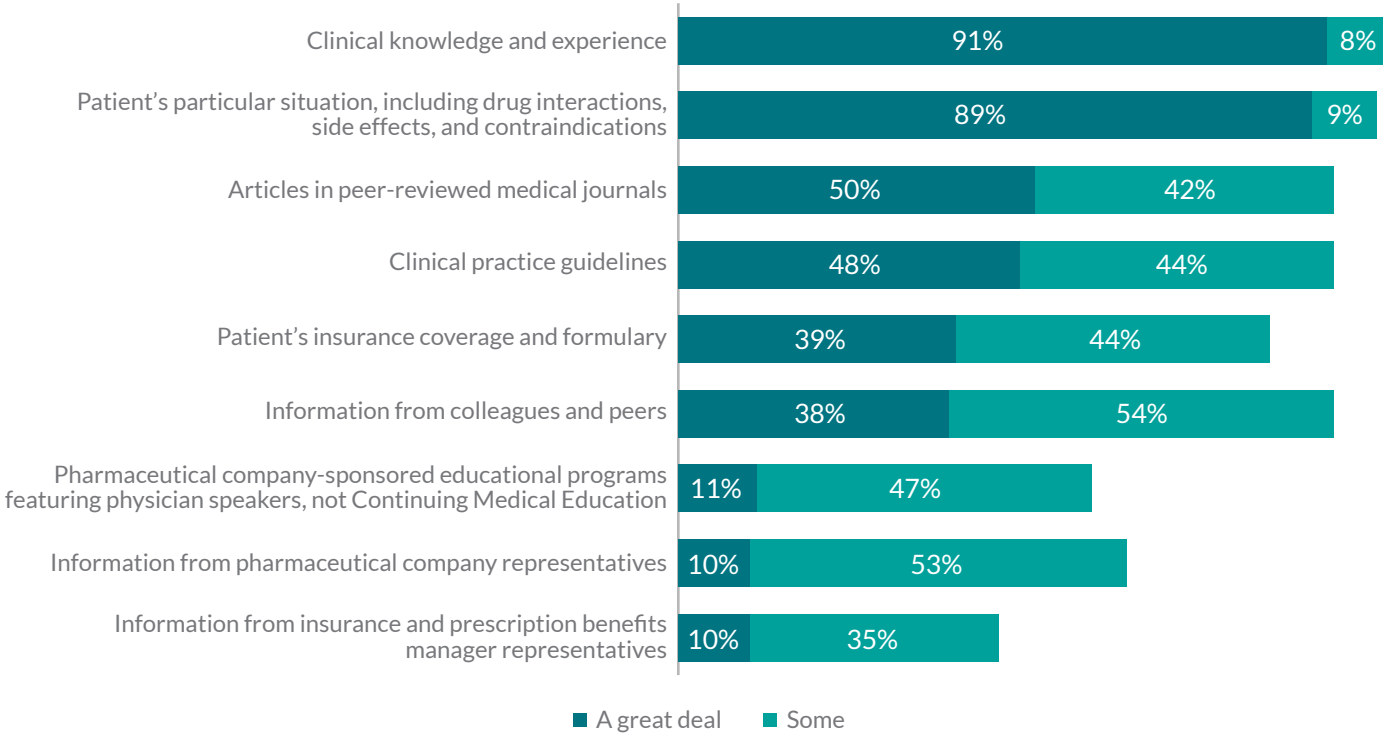
DTC ads



Source: Princeton Survey Research Associates International[29]

Clinical Factors Are the Biggest Driver of Physicians' Prescribing Decisions

Factors Influencing Physicians' Prescribing Decisions in the United States, 2013

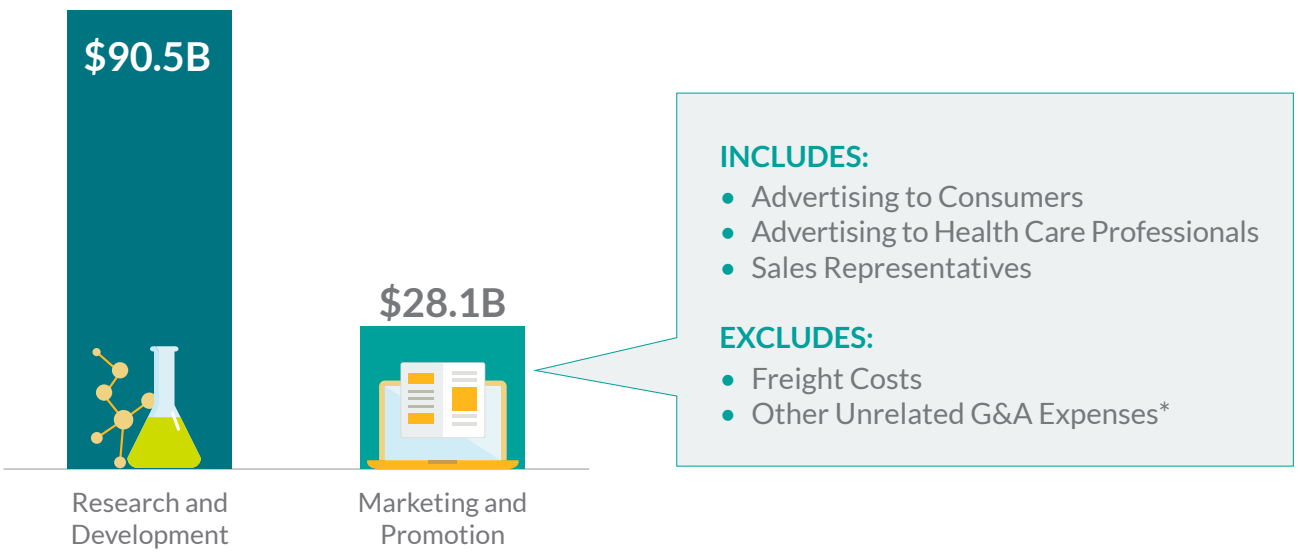


Source: KRC Research[30]

Biopharmaceutical Company Marketing and Promotion Spending in Context

Use of inflated estimates of marketing and promotion spending has created the false impression that the biopharmaceutical industry spends more on marketing than on R&D. More precise estimates show the opposite to be true.

Select US Biopharmaceutical Industry Expenses, 2016



*Indicates general and administrative (G&A) expenses unrelated to marketing and promotion, such as finance and office staffs, rent, utilities, and supplies. Some have inaccurately used sales and G&A expenses as a proxy for industry marketing and promotion expenses.

Sources: Schwartz L et al.[31]; Research!America[32]

Increasing Provider Accountability for Cost of Care and Pathway Implementation Is Influencing Prescribing Decisions

	THEN	NOW
Health plan clinical pathway programs fully implemented with network oncologists[33]	34% 2015	57% 2018
Hospital participation in accountable care organizations responsible for cost of care[34,35]	6% 2011	42% 2017
Medicare payments tied to alternative payment models, which include cost or quality incentives[36,37]	0% 2009	38%* 2017
Commercial market payments in which provider is at risk for cost of care[37,38]	6% 2013	28% 2017

*Only represents fee-for-service and is a conservative estimate

Sources: Health Strategies Insights by EVERSANA[33]; American Hospital Association[34,35]; HHS[36]; HCP LAN[37]; Catalyst for Payment Reform[38]

Value-Based Contracts Deliver Results for Patients

Value-based contracts have the potential to benefit patients and the health care system by improving patient outcomes, reducing medical costs, and reducing the costs of medicines.

Outcomes-Based Contracts are associated with

28% lower

patient copayments.

Value-Based Contracts could generate more than

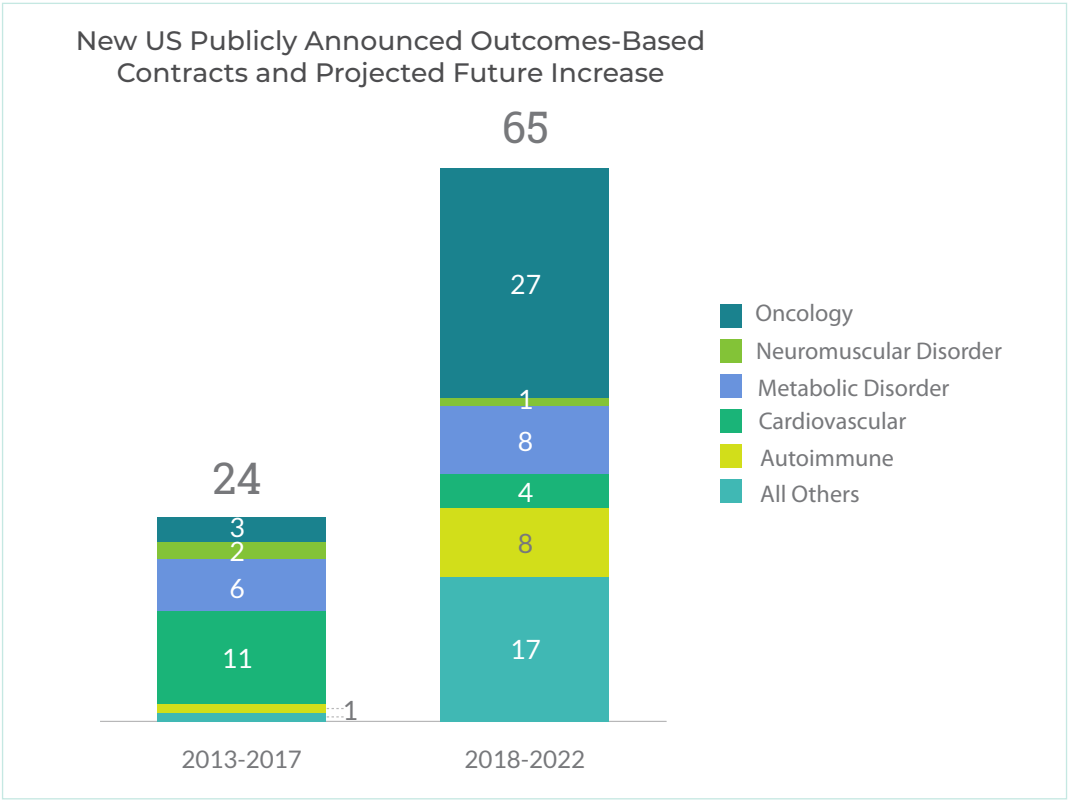
$12 Billion

if they reduced the diabetes burden in the United States by only 5%.

> We've been able to get the best of both worlds. The insurer gets competitive guaranteed discounts on prescriptions, and the manufacturer is aligned and accountable when something doesn't work."
>
> — Chris Bradbury, Cigna[40]

Sources: PhRMA[39]; Hopkins JS et al.[40]

Innovative Market-Based Arrangements That Link Payment for Medicines to Outcomes Are on the Rise



The number of publicly announced outcomes-based contracts is expected to more than double by **2022.**

Source: IQVIA Institute[41]

Notes and Sources

1. Pharmaceutical Research and Manufacturers of America (PhRMA). *Drug Discovery and Development: Understanding the R&D Process*. Washington, DC: PhRMA; 2014.
2. DiMasi JA, Chakravarthy R. Competitive development in pharmacologic classes: market entry and the timing of development. *Clin Pharmacol Ther*. 2016;100(6):754-760
3. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*. 2016;47:20-33.
4. Grabowksi H, Long G, Mortimer R, et al. Updated trends in US brand-name and generic drug competition. *J Med Econ*. 2016;19(9):836-844.
5. Average hospital charge data from Healthcare Cost and Utilization Project (HCUP) Hospital Charge Database 2005, 2013, and 2015. https://www.ahrq.gov/research/data/hcup/index.html. Accessed May 2018.
6. Invoice price data for atorvastatin 10mg from IQVIA National Sales Perspectives data for 2005 (branded Lipitor) and 2015 (generic). https://www.iqvia.com/locations/united-states/commercial-operations/essential-information/sales-information. Accessed May 2018.
7. Fein AJ; Drug Channels Institute. The 2019 economic report on U.S. pharmacies and pharmacy benefit managers. https://www.drugchannels.net/2019/03/new-2019-economic-report-on-us.html. Published March 2019. Accessed March 2019.
8. Tufts Center for the Study of Drug Development (CSDD). Rapid growth in PBM exclusion lists poses challenge to drug developers. *Tufts CSDD Impact Rep*. 2016;18(3). https://csdd.tufts.edu/s/Summary-MayJunIR2016.pdf. Accessed May 2019.
9. Fein AJ; Drug Channels Institute. The 2019 economic report on U.S. pharmacies and pharmacy benefit managers. https://www.drugchannels.net/2019/03/new-2019-economic-report-on-us.html. Published March 2019. Accessed March 2019.
10. LaMattina J. For hepatitis C drugs, U.S. prices are cheaper than in Europe. *Forbes*. http://www.forbes.com/sites/johnlamattina/2015/12/04/for-hepatitis-c-drugs-u-s-prices-are-cheaper-than-in-europe/#7ced43f564bb. Published December 4, 2015. Accessed May 2017. Citing comments made at Forbes Healthcare Summit 2015.
11. Cortez MF. Express Scripts raises pressure on Gilead for drug price. *Bloomberg*. https://www.bloomberg.com/news/articles/2014-04-08/express-scripts-raises-pressure-on-gilead-for-drug-price. Published April 8, 2014. Accessed May 2018.
12. Ignagni K. We all pay for $1,000 a pill drug. CNN. http://edition.cnn.com/2014/07/07/opinion/ignagni-hepatitis-c-drug. Published July 24, 2014. Accessed May 2017.
13. Silverman E. 'The big issue has not been choice, but access:' Express Scripts' Miller explains. *Wall Street Journal*. http://blogs.wsj.com/pharmalot/2015/01/06/the-big-issue-has-not-been-choice-but-access-express-scripts-miller-explains. Published January 6, 2015. Accessed May 2017.

Notes and Sources

14. Langreth R. Hepatitis drug prices fall so low, no exclusives needed. *Bloomberg*. https://www.bloomberg.com/news/articles/2015-01-12/prime-covers-both-gilead-and-abbvie-liver-drugs-as-prices-plunge. Published January 12, 2015. Accessed May 2018.
15. New York Times Editorial Board. Costly hepatitis C drugs for everyone? *New York Times*. https://www.nytimes.com/2015/09/02/opinion/costly-hepatitis-c-drugs-for-everyone.html?_r=0. Published September 2, 2015. Accessed May 2017.
16. SSR health data. http://www.ssrhealth.com/research-archive. April 2019.
17. Berndt ER, Nass D, Kleinrock M, et al. Decline in economic returns from new drugs raises questions about sustaining innovations. *Health Aff.* 2015;34(2):245-252.
18. Grabowksi H, Long G, Mortimer R, et al. Updated trends in US brand-name and generic drug competition. *J Med Econ.* 2016;19(9):836-844.
19. Adapted by PhRMA from Bates White. Economic profitability of the biopharmaceutical industry. Report for PhRMA, June 2018. Updated data tables April 2019. Economic profit for each industry is calculated as: (net operating profit less adjusted taxes) - (invested capital x weighted average cost of capital).
20. Deloitte Centre for Health Solutions. Unlocking R&D productivity: measuring the return from pharmaceutical innovation 2018. https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/deloitte-uk-measuring-return-on-pharma-innovation-report-2018.pdf. Published December 2018. Accessed May 2019.
21. Wilkes L; Bernstein Research. US healthcare services: Amazon—dual threats to healthcare services and their implications to the sector including ESRX [subscription analyst report]. February 22, 2018.
22. Pham ND; NDP Analytics. Prescription drug supply chain profitability. http://www.ndpanalytics.com/s/Prescription-Drug-Supply-Chain-Profitability-102518-Final-ykak.pdf. Published October 2018. Accessed April 2019.
23. Grant C. Hidden profits in the prescription drug supply chain. *Wall Street Journal*. https://www.wsj.com/articles/hidden-profits-in-the-prescription-drug-supply-chain-1519484401. Published February 24, 2018. Accessed May 2018.
24. Pew Charitable Trusts. The prescription drug landscape, explored. https://www.pewtrusts.org/en/research-and-analysis/reports/2019/03/08/the-prescription-drug-landscape-explored. Published March 2019. Accessed May 2019.
25. Scherer FM. Pharmaceutical innovation. AEI-Brookings Joint Center for Regulatory Studies Working Paper 07-13. July 2007. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=902395##. Published July 2007. Accessed May 2018.
26. Congressional Budget Office (CBO). Research and development in the pharmaceutical industry. http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/76xx/doc7615/10-02-drugr-d.pdf. Published October 2006. Accessed May 2017.

Notes and Sources

27. The Moran Company; for PhRMA. Hospital charges and reimbursement for drugs: analysis of markups relative to acquisition cost. http://www.themorancompany.com/wp-content/uploads/2017/10/Hospital-Charges-Report-2017_FINAL.pdf. Published October 2017. Accessed May 2018.
28. The Moran Company; for PhRMA. Hospital charges and reimbursement for medicines: analysis of cost-to-charge ratios. http://www.themorancompany.com/wp-content/uploads/2018/09/Hospital-Charges-Reimbursement-for-Medicines-August-2018.pdf. Published September 2018. Accessed April 2019.
29. Survey conducted by Princeton Survey Research Associates International for PhRMA. April 2017.
30. KRC Research; for PhRMA. *Survey of Physicians About Pharmaceutical and Biotech Research Company Activities and Information: Nationally Representative Survey of 502 Physicians*. Washington, DC: KRC Research; February 2014.
31. Schwartz LM, Woloshin S. Medical marketing in the United States, 1997-2016. *JAMA*. 2019;321(1):80-96.
32. Research!America. U.S. investments in medical and health research and development, 2013-2017. https://www.researchamerica.org/sites/default/files/Policy_Advocacy/2013-2017InvestmentReportFall2018.pdf. Published 2018. Accessed May 2019.
33. Health Strategies Insights by EVERSANA. Health plan oncology pathways insight and evolution. May 2018.
34. American Hospital Association. *AHA Hospital Statistics*. 2016 ed. Chicago, IL: Health Forum; 2016.
35. American Hospital Association. Accountable care organizations. https://www.aha.org/accountable-care-organizations-acos. Accessed May 2019.
36. US Department of Health and Human Services (HHS). HHS reaches goal of tying 30 percent of Medicare payments to quality ahead of schedule [press release]. https://mountsinaihealth.me/file/2016/05/HHS-reaches-goal-of-tying-30-percent-of-Medicare-payment-to-quality-ahead-of-schedule.pdf. Published March 3, 2016. Accessed May 2019.
37. Health Care Payment Learning & Action Network (HCP LAN). Measuring progress: adoption of alternative payment models in commercial, Medicaid, Medicare Advantage, and Fee-for-Service Medicare programs. https://hcp-lan.org/2018-apm-measurement. Published October 22, 2018. Accessed May 2019.
38. Catalyst for Payment Reform. 2014 national scorecard on payment reform. https://www.catalyze.org/product/2014-national-scorecard. Published 2014. Accessed May 2019.
39. Pharmaceutical Research and Manufacturers of America (PhRMA). Delivering results for patients: the value of value-based contracts. https://www.phrma.org/report/delivering-results-for-patients-the-value-of-value-based-contracts. Published February 26, 2018. Accessed May 2018.

Notes and Sources

40. Hopkins JS, Langreth R, Paton J. Big pharma's offer to Trump: discounts when drugs don't work. *Bloomberg*. https://www.bloomberg.com/news/articles/2017-02-06/big-pharma-s-offer-to-trump-discounts-when-drugs-don-t-work. Published February 6, 2017. Accessed June 2018.

41. IQVIA Institute for Human Data Science. Medicine use and spending in the U.S.: a review of 2017 and outlook to 2022. https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-review-of-2017-outlook-to-2022. Published April 19, 2018. Accessed April 2018.

4 COST SHARING TRENDS

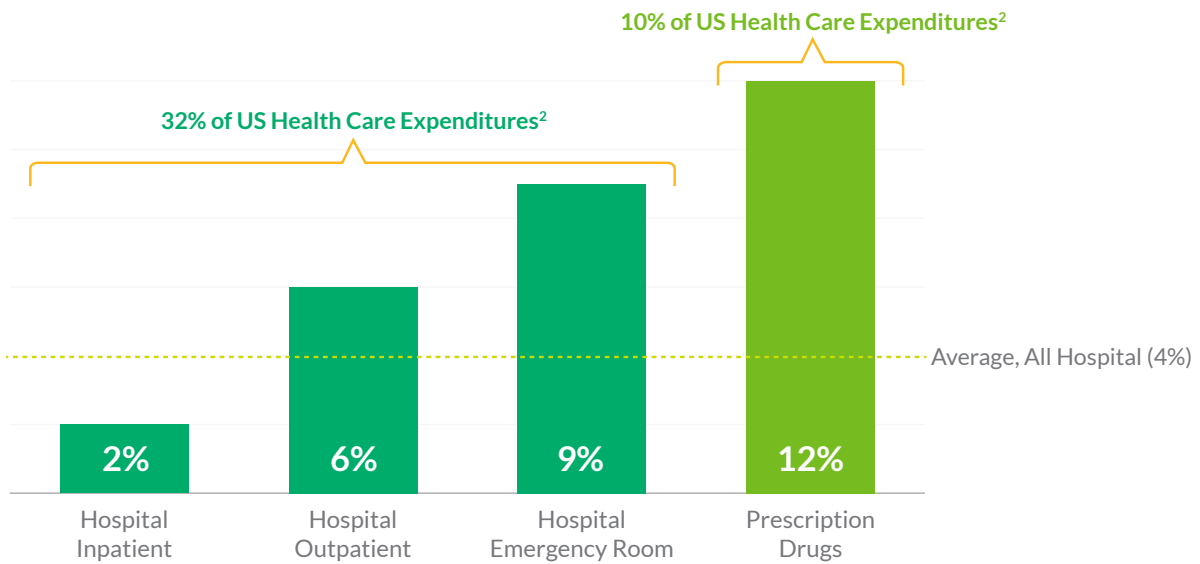
Evaluating the Impact of Insurance Benefit Design on Patients

Insurers are increasingly using high deductibles, coinsurance, and multiple cost sharing tiers, which push more costs to some patients. Out-of-pocket spending for prescription medicines can represent a disproportionate share of total health care costs borne directly by patients, especially those who are low income or chronically ill. High cost sharing for medicines may limit patients' access to needed treatments, reduce adherence, and lead to poor health outcomes. Manufacturer cost sharing assistance can help patients afford their medicines and lower abandonment rates.

Insurance Covers a Lower Share of Prescription Drug Costs Than Hospital Care Costs

On average, patients pay out of pocket 12% of their prescription drug costs compared with 4% of costs for hospital care. Meanwhile, hospital care as a percentage of US health care expenditures is significantly larger than outlays on medicines.

Average Share of Health Care Costs Patients Pay Out of Pocket, All Ages[1]

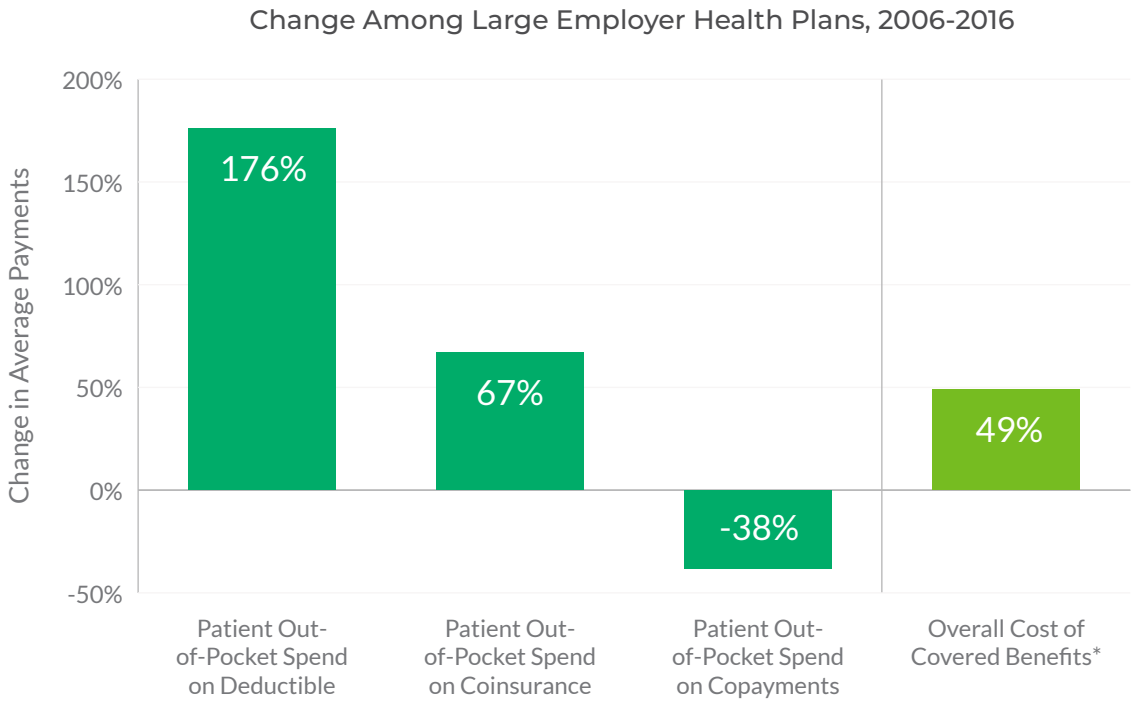


Analysis includes individuals with any source of health care coverage, public or private; this includes individuals who had health coverage without coverage for prescription drugs, which can be expected to account for less than 2% of those with health coverage. Prescription drug spending includes spending on brand and generic drugs, pharmacy, and distribution costs for retail prescriptions. Note: Prescription drug out-of-pocket costs are based on gross medicine price, not the net price after rebates.

Sources: Avalere analysis of Medical Expenditure Panel Survey, 2016[1]; CMS[2]

Patient Spending Rises as Plans Use More Deductibles and Coinsurance

Trends in health plan design—toward higher deductibles, coinsurance, and decreased use of copayments—have shifted costs to patients at a higher rate than overall health plan costs.

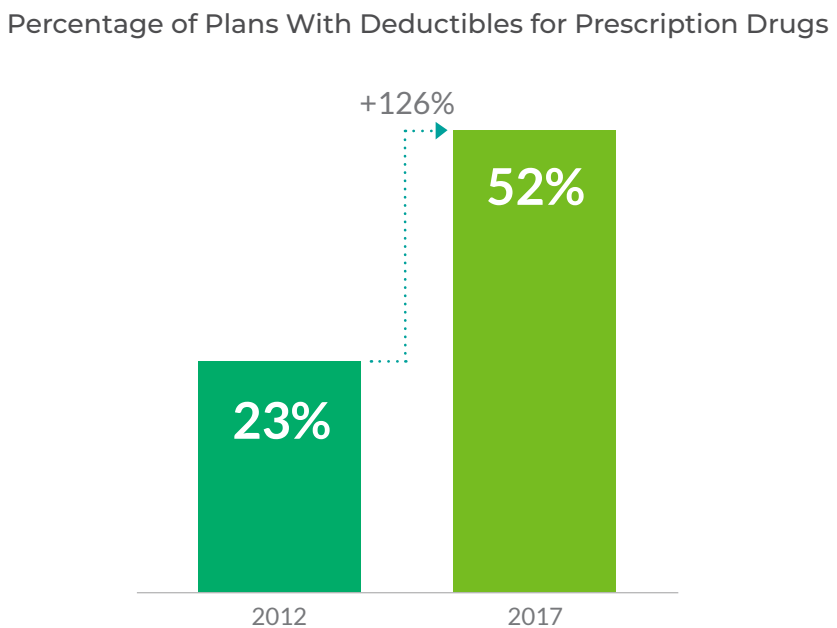


*Patient out-of-pocket costs are growing faster than overall costs of benefits.

Source: Kaiser Family Foundation[3]

Share of Employer-Sponsored Health Plans With a Prescription Drug Deductible Is Increasing

The percentage of employer-sponsored plans requiring deductibles for pharmacy benefits continues to increase.



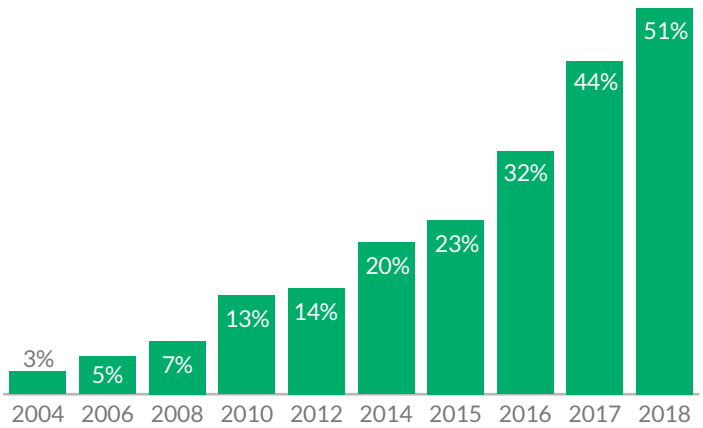
Source: PwC[4]

Plans Increasingly Subject Certain Medicines to Higher Cost Sharing

Increased use of 4 or more tiers by plans means that more patients are subject to what is commonly higher cost sharing on the specialty tier. Medicines on the specialty tier are also more likely to be subject to coinsurance than products placed on lower cost sharing tiers.[5]

The use of 4 or more cost sharing tiers is becoming more common in employer plans.

Share of Workers in Plans With 4 or More Tiers[6]



*For fourth tier[6]**

Average coinsurance
31%

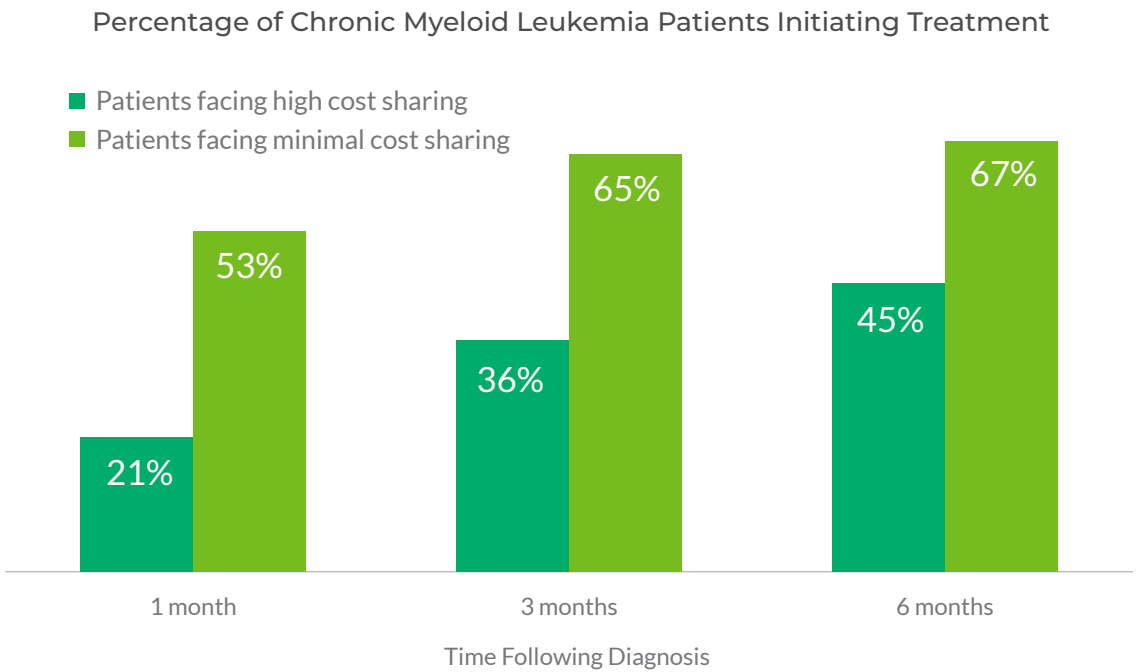
Average copay
$105

*52% of plans with coinsurance for the fourth tier have a maximum amount.

Sources: Kaiser Family Foundation[5,6]

Patients Facing High Cost Sharing Commonly Do Not Initiate Treatment

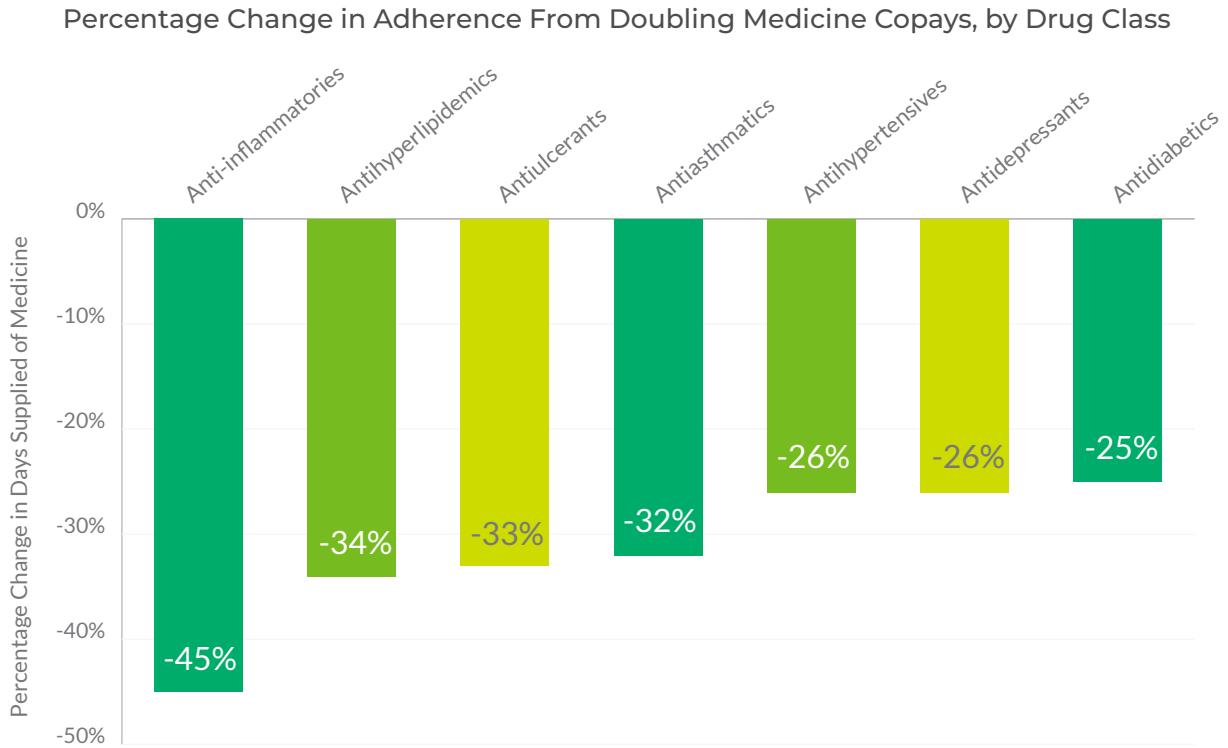
Chronic myeloid leukemia patients facing high out-of-pocket costs for medicines on a specialty tier are less likely to initiate drug therapy than patients receiving a cost sharing subsidy, and these patients take twice as long to initiate treatment.



Source: Doshi JA et al.[7]

High Cost Sharing Reduces Adherence

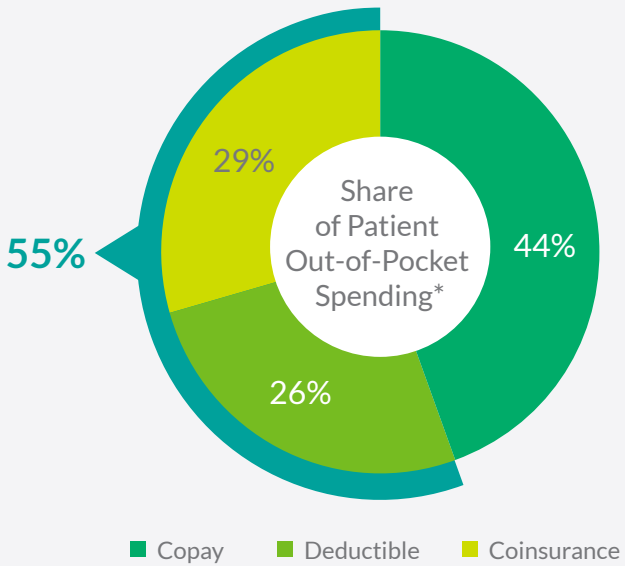
RAND researchers found that doubling copays reduced patients' adherence to prescribed medicines by 25%-45% and increased emergency room visits and hospitalizations.



Source: Goldman DP et al.[8]

Cost Sharing Is Based on the Undiscounted List Price When Patients Pay for Brand Drugs With Coinsurance or in a Deductible

In 2017, more than half of commercially insured patients' out-of-pocket spending for brand medicines was based on list price.

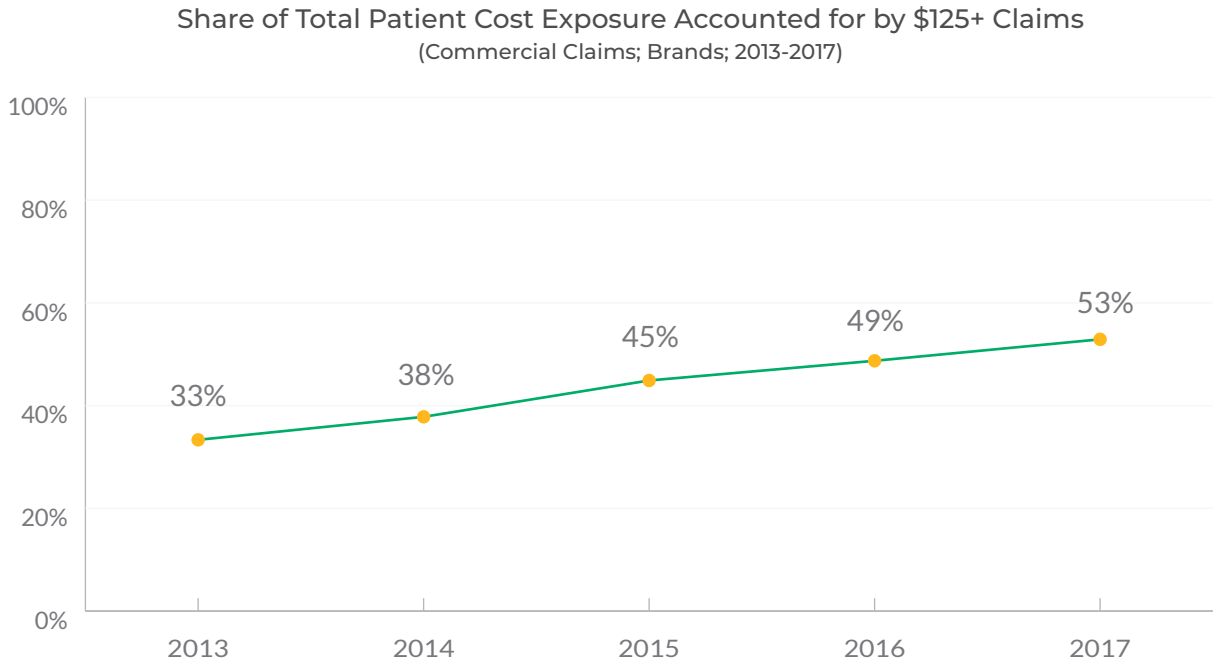


*Percentages may not add up to 100% due to rounding.

Source: IQVIA[9]

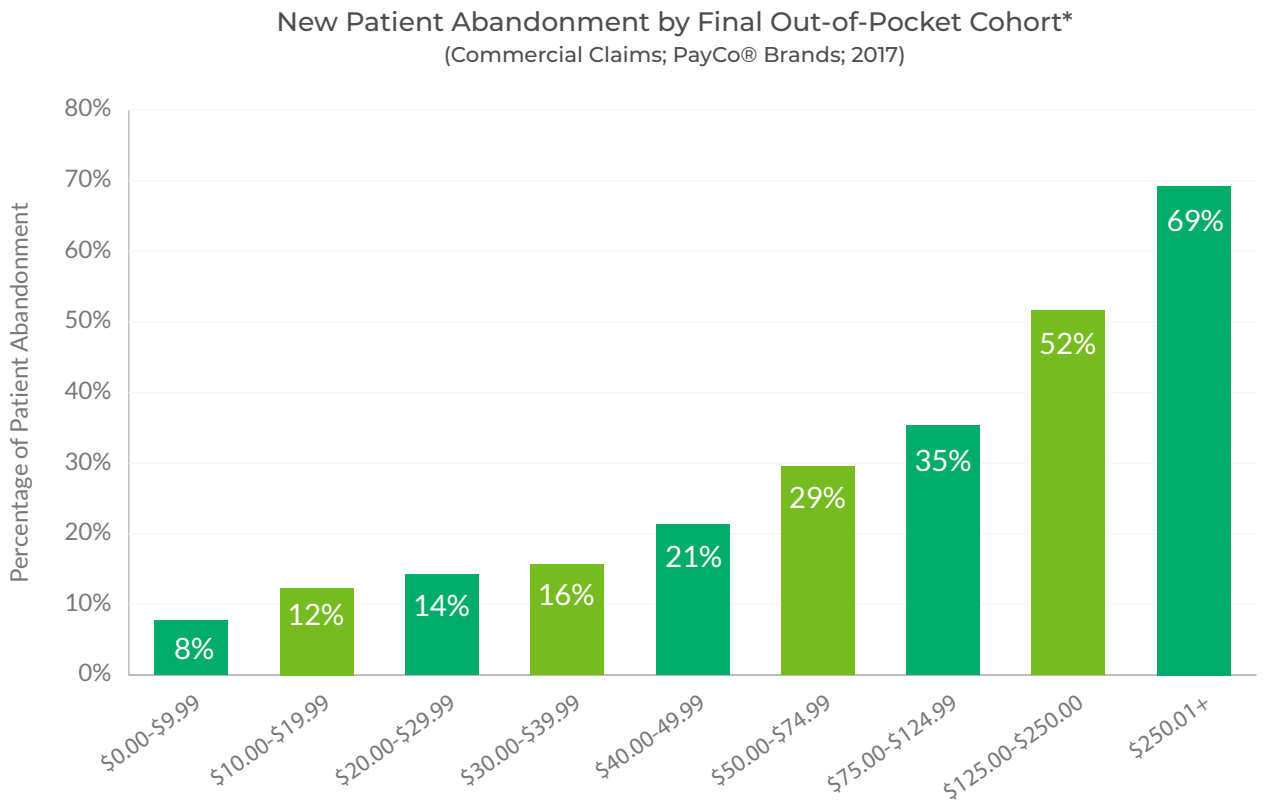
Cost Exposure for Brand Medicines Is Becoming More Prevalent Over Time

In 2017, 7% of claims for brand medicines had cost sharing of $125 or more, and these claims now represent more than half of total patient cost exposure.



Source: IQVIA[10]

As Cost Sharing Rises, Patients Are More Likely to Abandon Their New Medicines

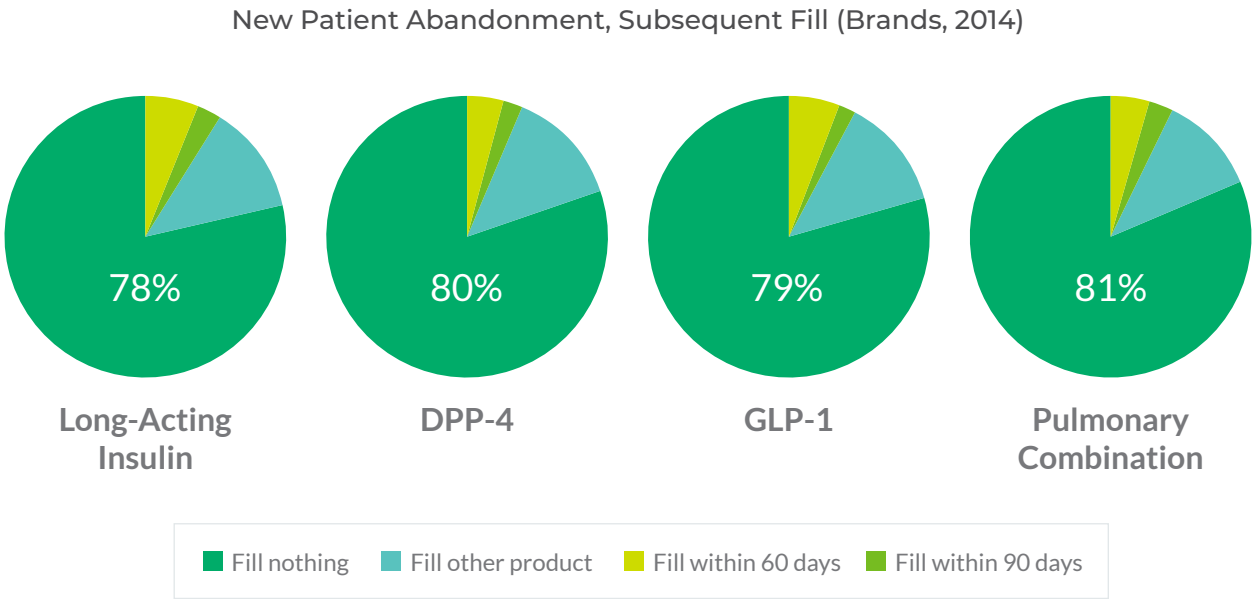


*Sample is limited to new patient approvals across top brands, which span over 25 traditional and specialty therapeutic areas.

Source: IQVIA[11]

Patients Who Abandon Prescriptions Often Do Not Initiate Another Therapy

Most patients who abandon a brand drug do not fill another drug prescription within 90 days, indicating that they may not be receiving any treatment for their condition.

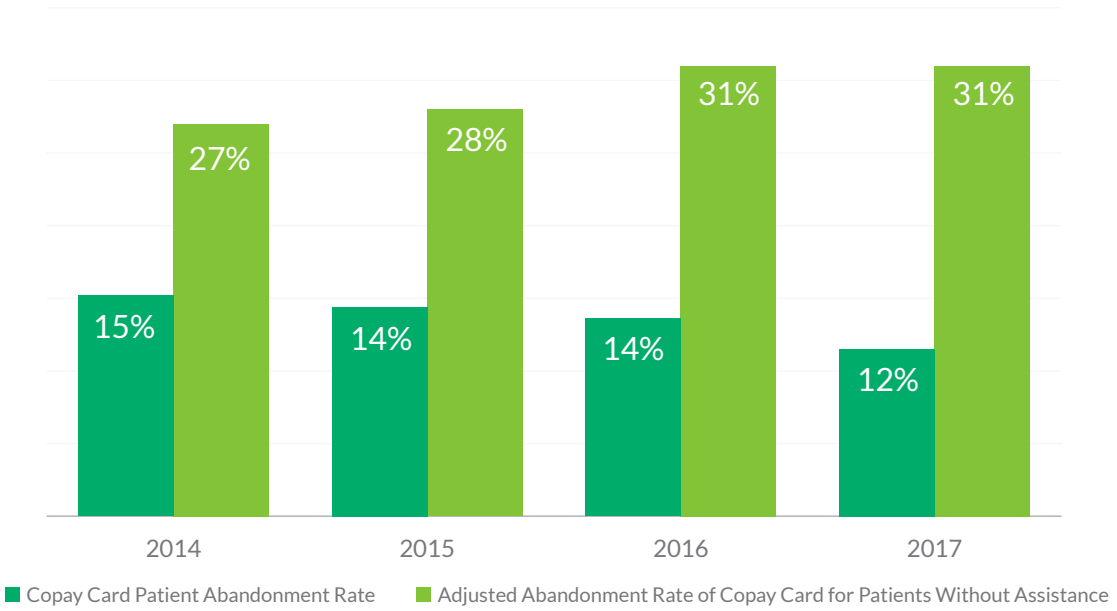


Source: IMS Institute for Healthcare Informatics[12]

Manufacturer Cost Sharing Assistance Cards Can Help Offset Patient Abandonment

Patient abandonment rates increase with out-of-pocket costs, but manufacturer cost sharing assistance, like copay cards, reduces patient out-of-pocket costs, which lowers abandonment rates.

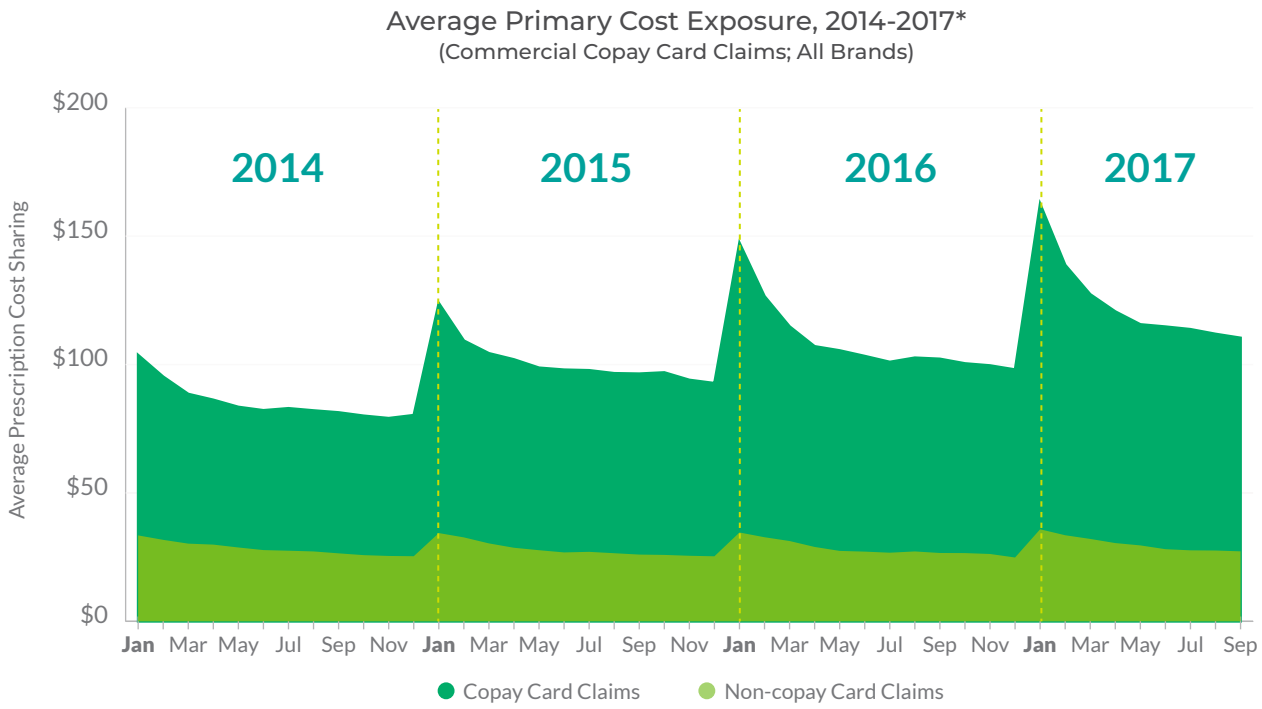
New Patient Abandonment Trend Comparing Current and Adjusted Copay Card for Patients (Commercial Claims; PayCo® Brands)



Source: IQVIA[13]

Without Coupons, Patients Would Face Higher Average Out-of-Pocket Costs per Prescription

Each January, patients in the commercial market with deductibles face steep increases in out-of-pocket costs for brand drugs.



*Averages are calculated among paid claims where a copay card is used as the secondary payer and normalized to 30 days.

Source: IQVIA[14]

Manufacturer Cost Sharing Assistance Can Help Ease Patients' Out-of-Pocket Costs

In 2017, just **0.4%** of commercial claims were filled with a coupon for a **brand medicine** that had a generic equivalent.

Programs that do not count manufacturer cost sharing assistance toward a patient's deductible or out-of-pocket maximum hurt the sickest patients, leaving them vulnerable to unexpected out-of-pocket costs as high as **several thousands of dollars** to continue taking their medicine.

Source: IQVIA[15]

Biopharmaceutical Company Assistance Resources Help Patients With Much-Needed Financial Support

Despite more Americans having insurance, many are facing high cost sharing that puts their ability to stay on a needed therapy at risk. Because of this, biopharmaceutical companies provide patient assistance in a variety of ways.

Building off the work of the Partnership for Prescription Assistance, PhRMA built the

Medicine Assistance Tool (MAT)

in 2019 to provide patients, caregivers, and providers with a streamlined point of access for information that can help them make more informed health care decisions.

MAT INCLUDES:

- A search engine to connect patients with **medicine-specific financial assistance programs**
- Resources to **help patients navigate** their insurance coverage
- Links to websites **providing cost information** referenced in PhRMA member company direct-to-consumer television advertising

Source: PhRMA[16]

Notes and Sources

1. Avalere Health analysis of the US Department of Health and Human Services, Agency for Healthcare Research and Quality's Medical Expenditure Panel Survey, 2016. https://meps.ahrq.gov/mepsweb. Accessed April 2019.
2. Centers for Medicare and Medicaid Services (CMS), Office of the Actuary, National Health Statistics Group. National health care spending in 2016. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/NHE-Presentation-Slides.pdf. Accessed May 2019.
3. Claxton G, Levitt L, Rae M, et al.; Kaiser Family Foundation. Increases in cost-sharing payments continue to outpace wage growth. Peterson-Kaiser Health System Tracker. https://www.healthsystemtracker.org/brief/increases-in-cost-sharing-payments-have-far-outpaced-wage-growth. Published June 15, 2018. Accessed April 2019.
4. PwC. Health & Well-being Touchstone Survey results. https://www.pwc.com/us/en/hr-management/publications/assets/pwc-touchstone-2017.pdf. Published June 2017. Accessed May 2019.
5. Rae M, Levitt L, Claxton G, et al.; Kaiser Family Foundation. Patient cost-sharing in marketplace plans, 2016. http://kff.org/health-costs/issue-brief/patient-cost-sharing-in-marketplace-plans-2016. Published November 13, 2015. Accessed May 2019.
6. Kaiser Family Foundation. 2018 Employer Health Benefits Survey. https://www.kff.org/health-costs/report/2018-employer-health-benefits-survey. Published October 2018. Accessed April 2019.
7. Doshi JA, Li P, Ladage VP, et al. Impact of cost sharing on specialty drug utilization and outcomes: a review of the evidence and future directions. *Am J Manag Care.* 2016;22(3):188-197. http://www.ajmc.com/journals/issue/2016/2016-vol22-n3/Impact-of-Cost-Sharing-on-Specialty-Drug-Utilization-and-Outcomes-A-Review-of-the-Evidence-and-Future-Directions. Accessed May 2019.
8. Goldman DP, Joyce GF, Escarce JJ, et al. Pharmacy benefits and the use of drugs by the chronically ill. *JAMA.* 2004;291(19):2344-2350.
9. IQVIA. Patient affordability part one: the implications of changing benefit designs and high cost-sharing. https://www.iqvia.com/locations/united-states/patient-affordability-part-one. Published May 18, 2018. Accessed May 2019.
10. IQVIA. Patient affordability part one: the implications of changing benefit designs and high cost-sharing. https://www.iqvia.com/locations/united-states/patient-affordability-part-one. Published May 18, 2018. Accessed May 2019.
11. IQVIA. Patient affordability part two: implications for patient behavior and therapy consumption. https://www.iqvia.com/locations/united-states/patient-affordability-part-two. Published May 18, 2018. Accessed May 2019.
12. IMS Institute for Healthcare Informatics. Emergence and impact of pharmacy deductibles: implications for patients in commercial health plans. https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/emergence-and-impact-of-pharmacy-deductibles.pdf. Published September 2015. Accessed May 2019.

Notes and Sources

13. IQVIA. Patient affordability part two: implications for patient behavior and therapy consumption. https://www.iqvia.com/locations/united-states/patient-affordability-part-two. Published May 18, 2018. Accessed May 2019.
14. IQVIA. Patient affordability part three: the implications of co-pay cards. https://www.iqvia.com/locations/united-states/patient-affordability-part-three. Published May 18, 2018. Accessed May 2019.
15. IQVIA. An evaluation of co-pay card utilization in brands after generic launch. https://www.iqvia.com/-/media/iqvia/pdfs/us-location-site/market-access/fact-sheet-evaluation-of-copay-card-utilization-post-loe.pdf. Published February 2018. Accessed May 2019.
16. Pharmaceutical Research and Manufacturers of America (PhRMA). Medicine Assistance Tool website. https://www.mat.org. Accessed May 2019.

5 SPENDING ON MEDICINES

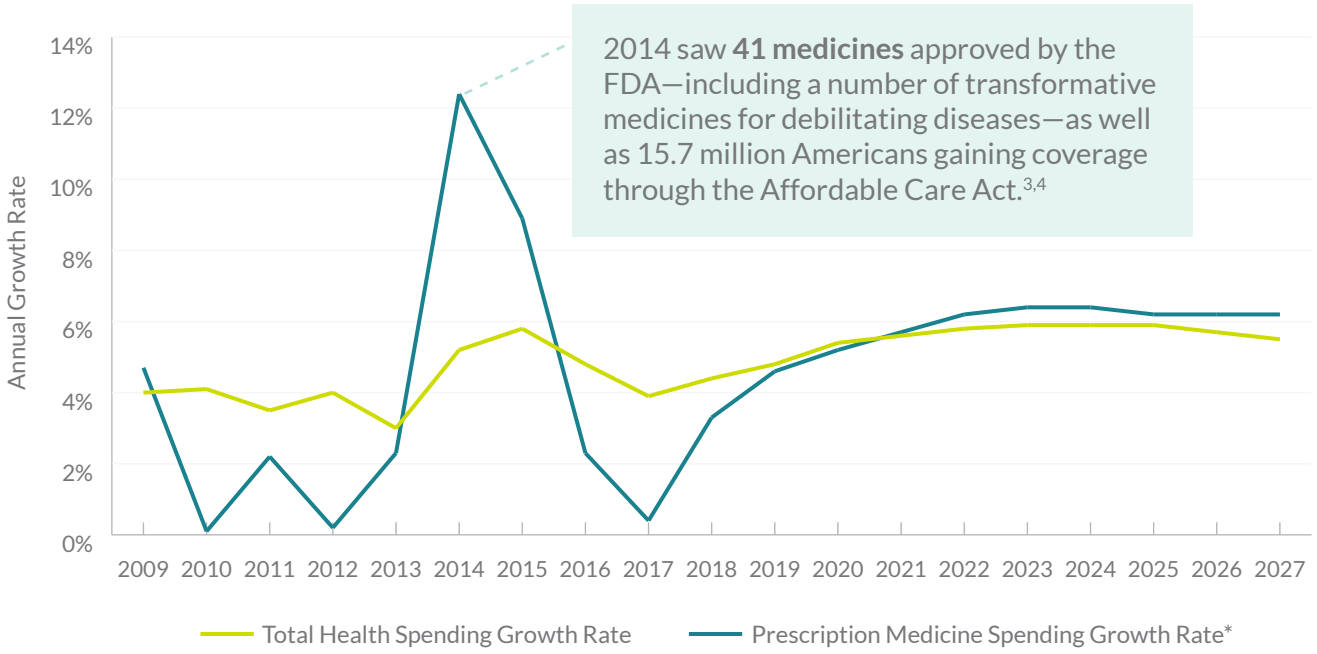
Understanding Medicine Costs in Context

Prescription medicines represent a small share of national health spending, and government estimates project that medicines will remain a stable share of health spending through the next decade. In 7 of the past 10 years, spending on retail prescription medicines grew more slowly than total health care costs and is projected to grow just 3 percent to 6 percent annually over the next decade, in line with total health care spending. Rebates, discounts, and fees paid by brand manufacturers to the government, private payers, and supply chain entities increased to $166 billion in 2018. Brand medicine net price growth, which reflects these rebates and discounts, was less than inflation for the second year in a row.

In 7 of the Last 10 Years, Retail Prescription Medicine Costs Grew More Slowly Than Total Health Care Costs

Government actuaries project prescription medicine spending growth to remain between 3% and 6% annually through 2027, in line with overall health care spending growth.[1]

Prescription Medicine Spending Growth: 2009-2027[2]

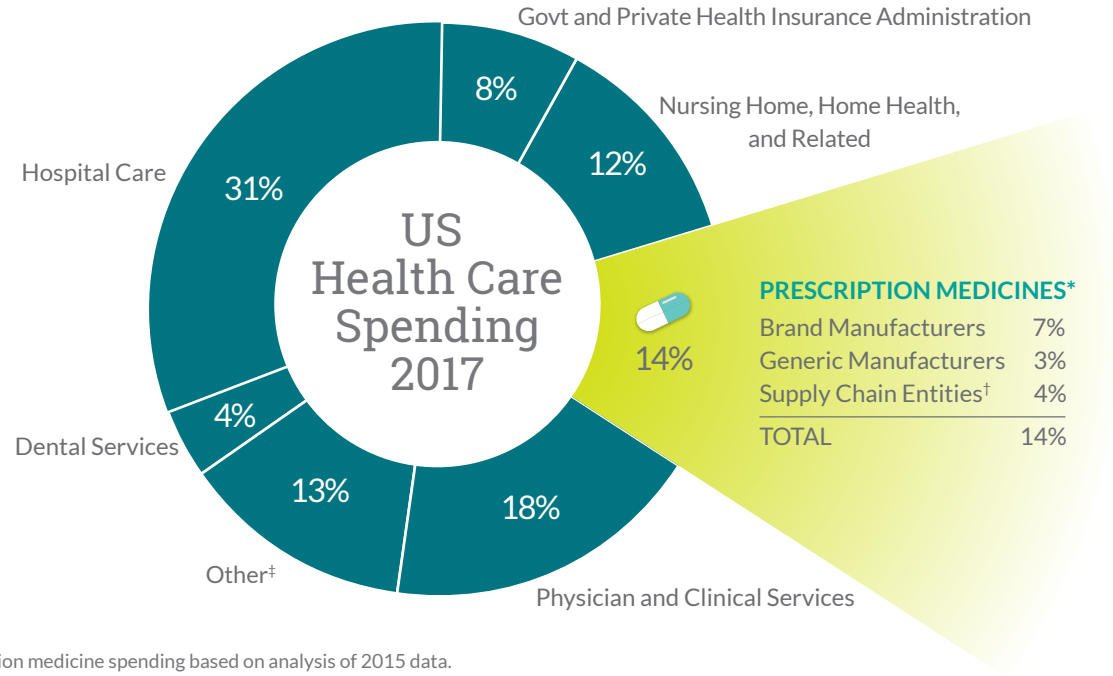


*Total net retail sales including brand medicines and generics

Sources: PhRMA analysis of CMS data[1,2]; RAND Corporation[3]; FDA[4]

Spending on All Prescription Medicines Is a Small Share of Total US Health Care Spending

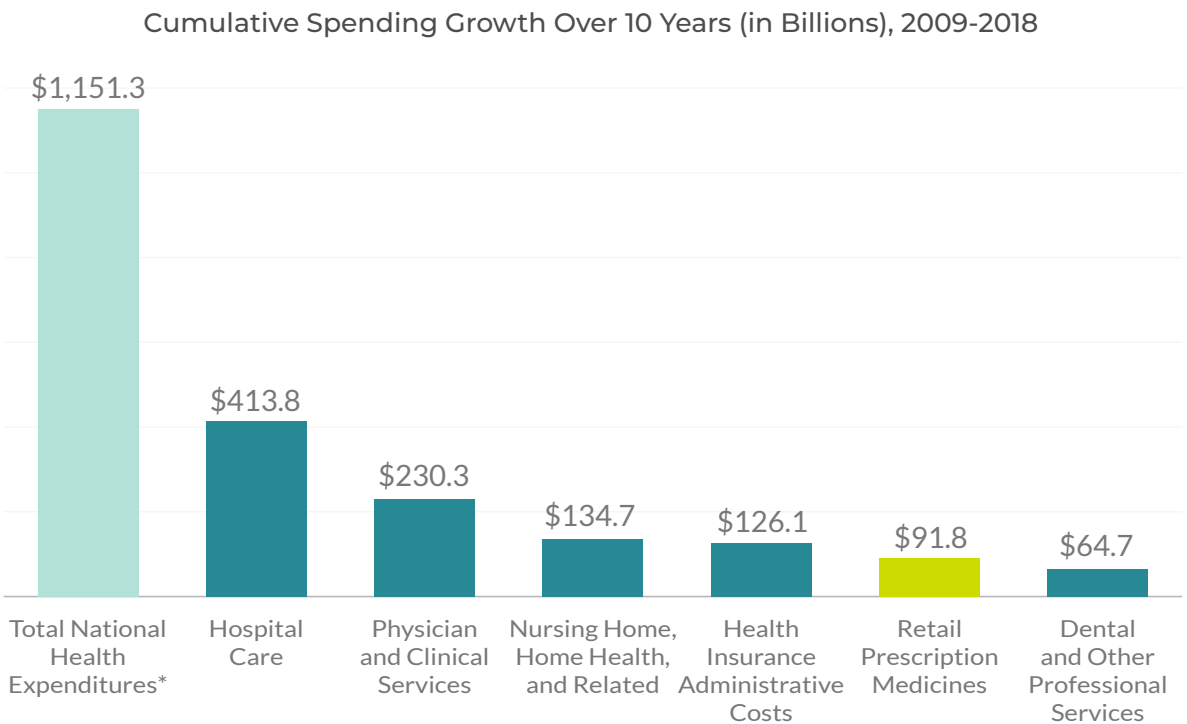
Prescription medicines, whether picked up at a retail pharmacy or administered in a physician's office or hospital, account for about 14% of total annual health care spending. Half of this total goes to brand manufacturers, with the rest going to generic manufacturers and the supply chain.



*Breakout of prescription medicine spending based on analysis of 2015 data.
†Supply chain entities include wholesalers, pharmacies, pharmacy benefit managers, and health care providers.
‡Other includes expenditures for Other Professional Services, Nondurable Medical Products, Durable Medical Equipment, Public Health Activity, Research, Structures, and Equipment.

Sources: PhRMA analysis of CMS data[5]; Altarum Institute[6]; Berkeley Research Group[7]

Prescription Medicine Spending Contributed Less Than One-Tenth of Total Health Care Spending Growth in the Past Decade

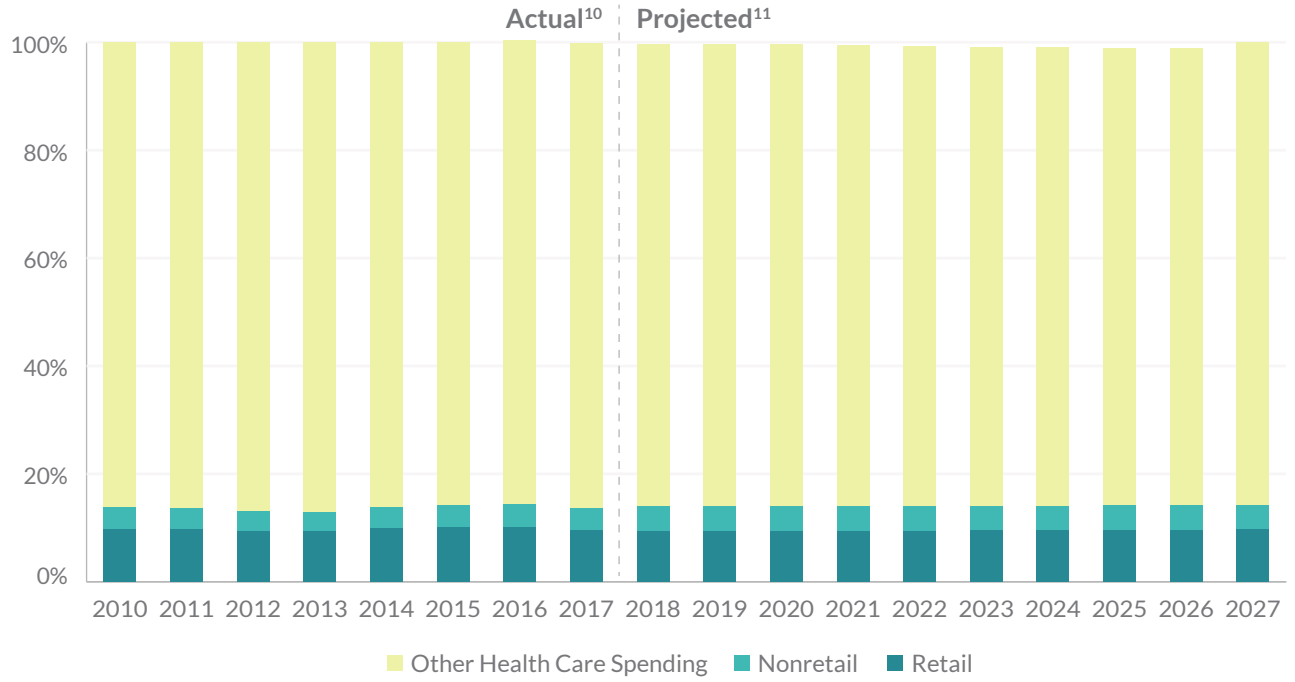


*Total National Health Expenditures amount does not reflect listed categories. Not all categories are shown.

Sources: PhRMA analysis of CMS data[8,9]

Prescription Medicines Are Expected to Account for a Stable Share of Total Health Care Expenditures Through the Next Decade

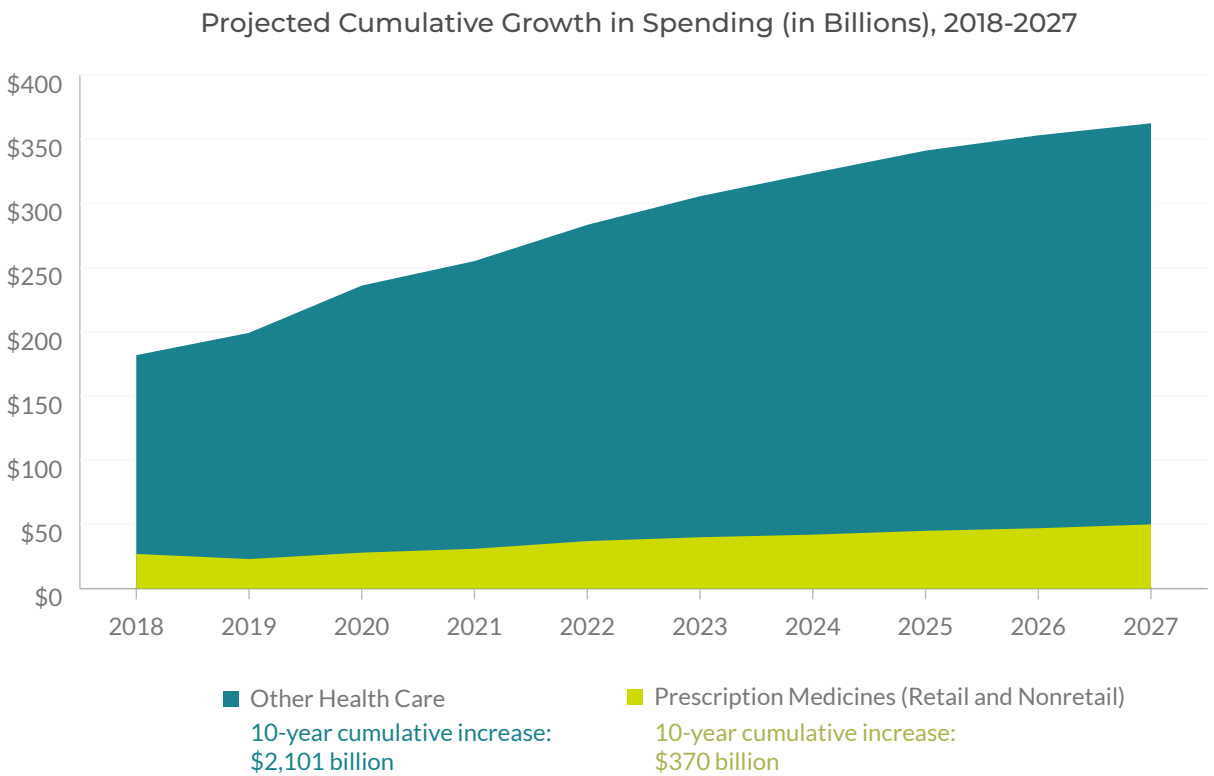
US Health Care Expenditures Attributable to Retail and Nonretail Prescription Medicines, 2010-2027*



*Retail prescription medicines are those filled at retail pharmacies or through mail service. Nonretail prescription medicines are those purchased through physicians' offices, clinics, and hospitals and are typically administered to the patient by the provider.

Sources: Altarum Institute[10,11]

Cumulative Spending Growth for Other Health Care Will Be More Than Five Times That of Medicines Through the Next Decade

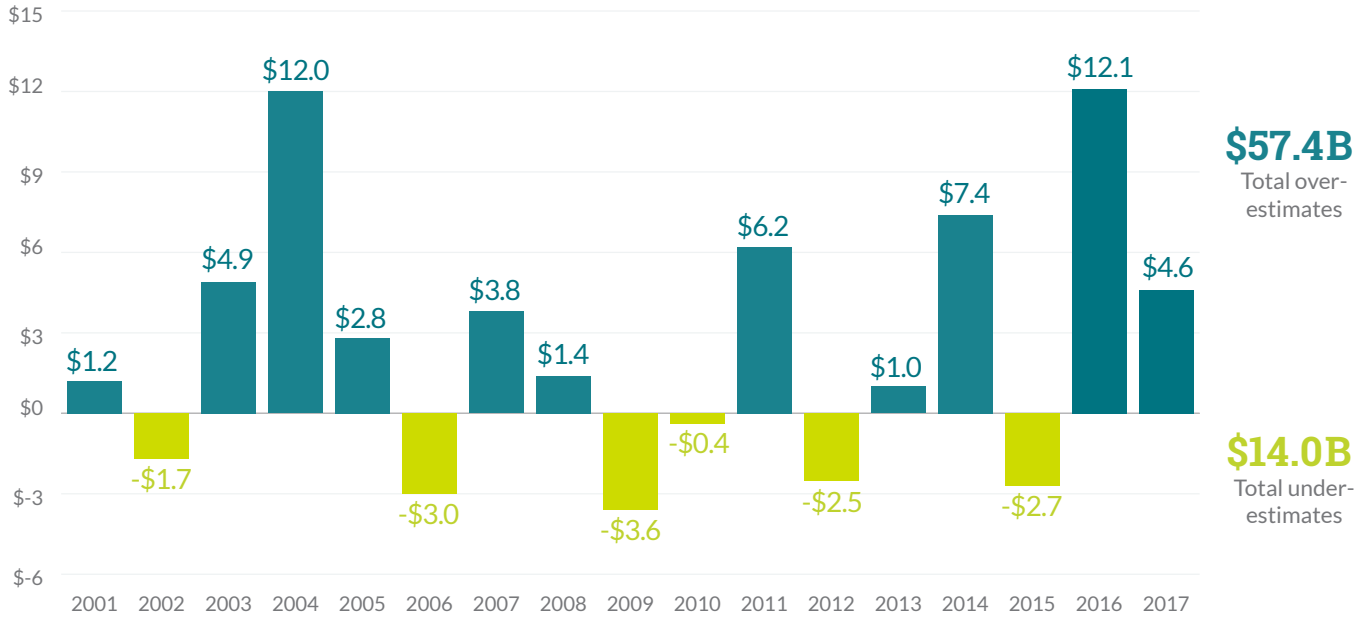


Sources: PhRMA analysis of CMS data[12]; PhRMA analysis of Altarum Institute data[13]

Projections of Future Medicine Spending Often Overestimate Actual Spending

Actuaries at the Centers for Medicare and Medicaid Services (CMS) annually publish estimates of retail prescription medicine spending for the next 10 years. Looking back at projections made since 2000, estimates made 1 year prior to the publication of actual spending amounts overestimated retail medicine spending two-thirds of the time.

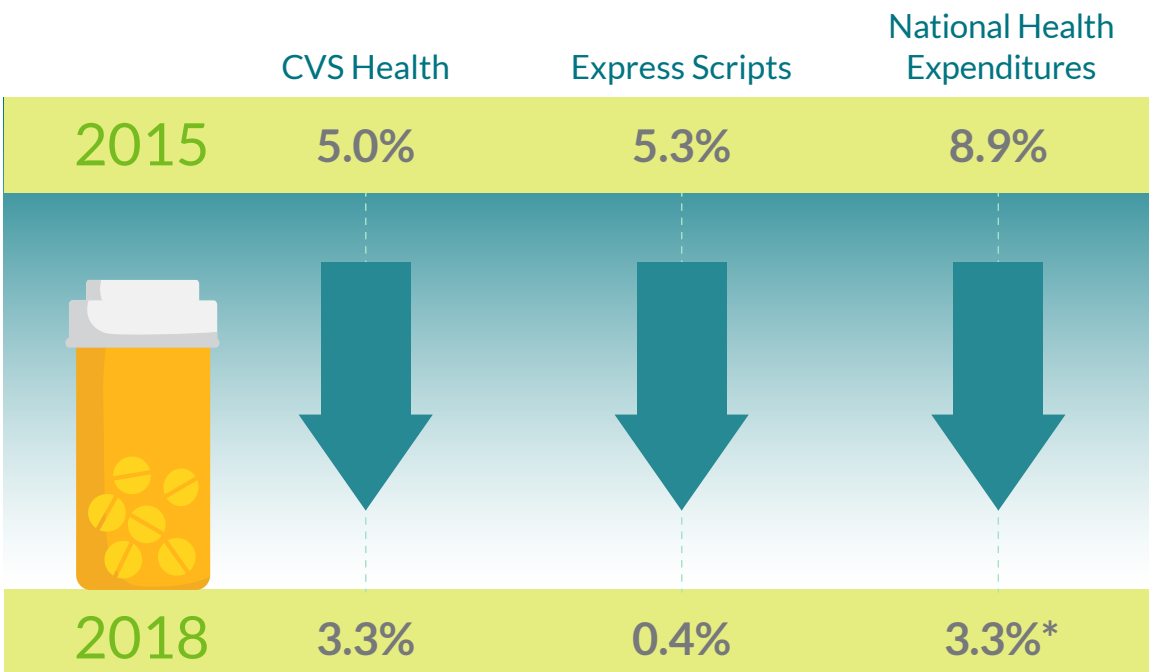
Difference Between Projected and Actual Retail Medicine Spending (in Billions), 2001-2017



Sources: PhRMA analysis of CMS data[14,15]

Pharmacy Benefit Managers (PBMs) and Government Actuaries Report Slowing Growth in Medicine Spending

Annual Growth in Net Retail Prescription Medicine Spending

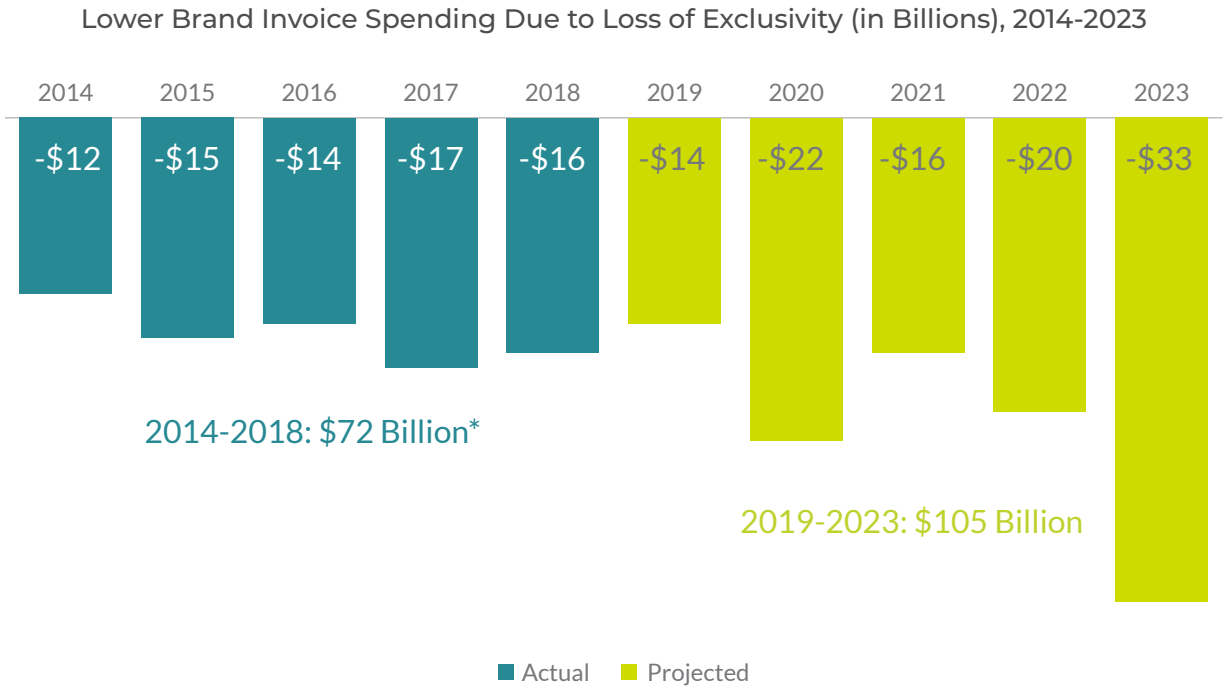


*Projected

Sources: CVS Health[16,17]; Express Scripts[18,19]; CMS[20,21]

Competition From Generics and Biosimilars Is Expected to Reduce US Brand Sales by $105 Billion From 2019 to 2023

The savings from new generics and biosimilars in the coming years are expected to match the large-scale savings observed in recent years.

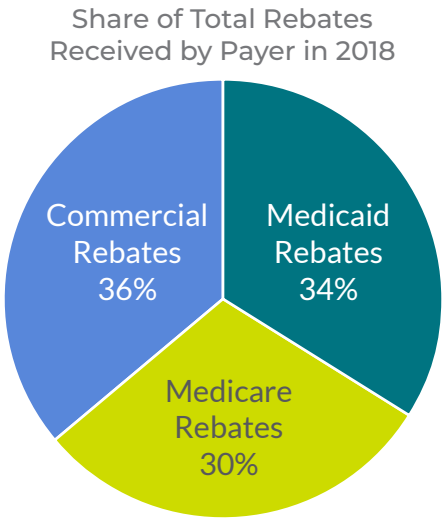


*Figures may not sum due to rounding.

Source: IQVIA Institute[22]

One-Third of Gross Spending for Medicines Is Rebated Back to Payers or Retained by the Supply Chain

Manufacturers received $66 for every $100 of gross spending on medicines in 2018.



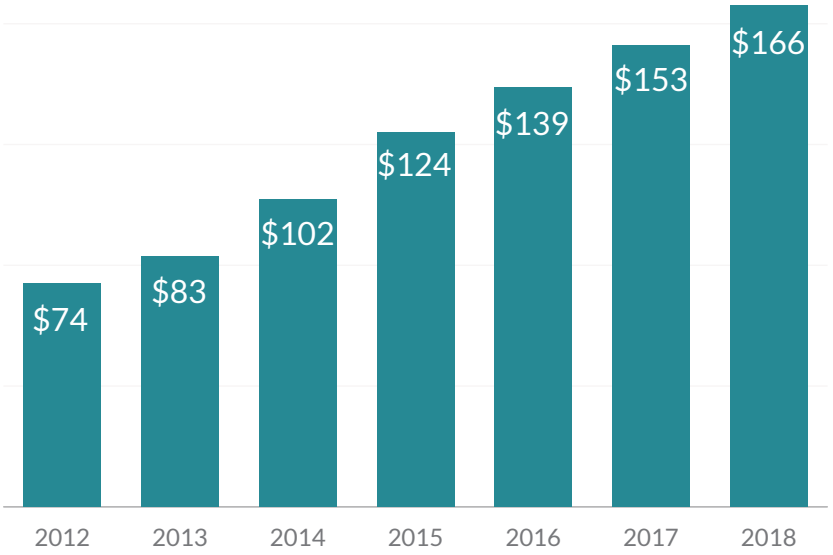
*Supply chain entities include pharmacies, providers, wholesalers, and group purchasing organizations.
**Includes FDA user fees, coverage gap discounts, 340B program discounts, and patient assistance.

Source: PhRMA analysis of Nephron Research data[23]

Manufacturers' Gross-to-Net Reductions Have More Than Doubled Since 2012

Rebates and discounts provided by manufacturers to government, private payers, and distributors totaled over $166 billion in 2018.

Total Value of Pharmaceutical Manufacturers' Gross-to-Net Reductions (in Billions), 2012-2018



GROSS-TO-NET REDUCTIONS are defined as "rebates, off-invoice discounts, copay assistance, price concessions, and other reductions like distribution fees, product returns, the 340B Drug Pricing Program, and more."

Source: Drug Channels Institute[24]

Patients Often Do Not Directly Benefit From Negotiated Rebates and Discounts Paid by Manufacturers

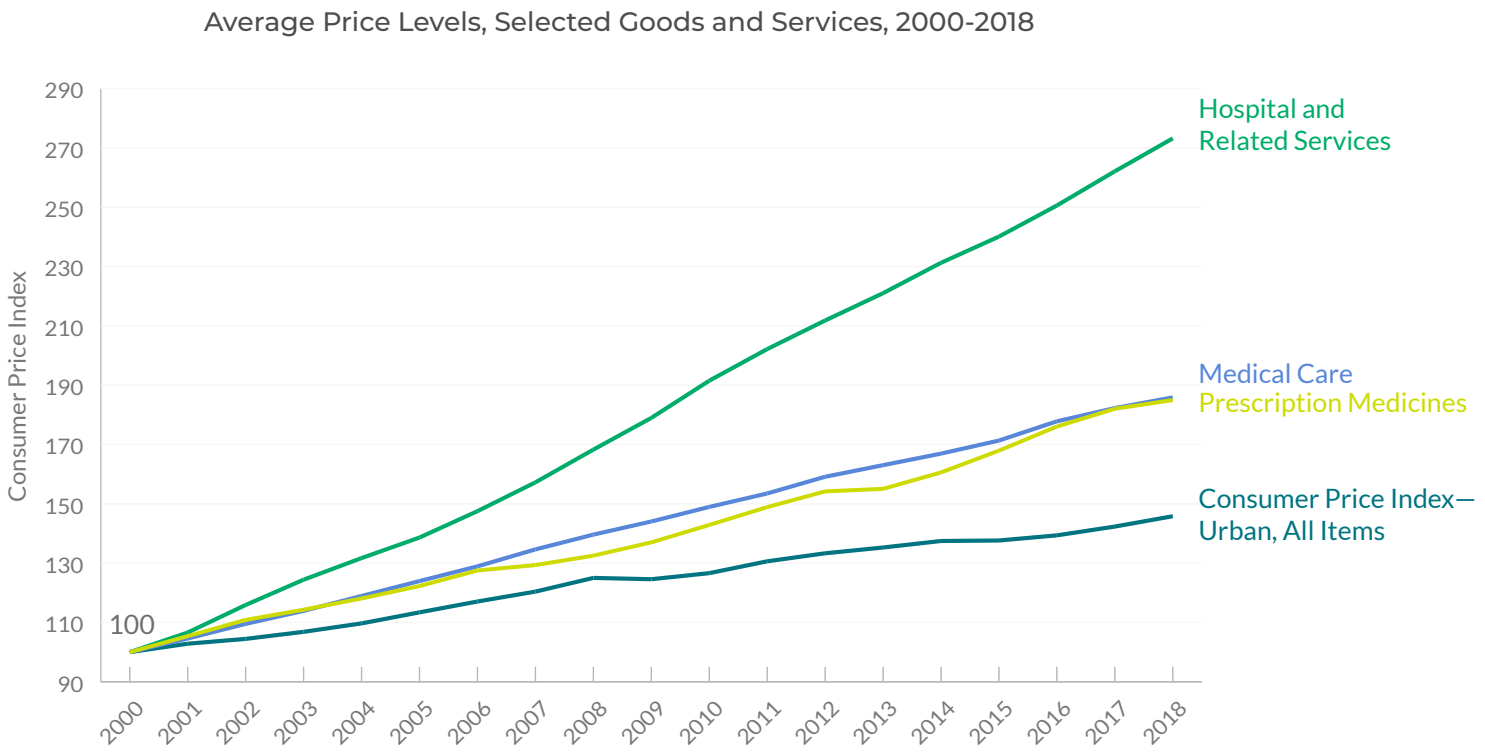
Prices paid by wholesalers, pharmacies, pharmacy benefit managers (PBMs), and health plan sponsors all vary and are determined by negotiations between stakeholders, each with varying degrees of negotiating power.

Flow of Payment for a $400 Insulin Prescription (Patient is in Deductible Phase)

This graphic is illustrative of a hypothetical product with a wholesale acquisition cost (WAC) of $400 and an average wholesale price (AWP) of $480. It is not intended to represent every financial relationship in the marketplace. The payment amounts do not add up to $400 due to markups and discounts along the supply chain.

Source: PhRMA[25]

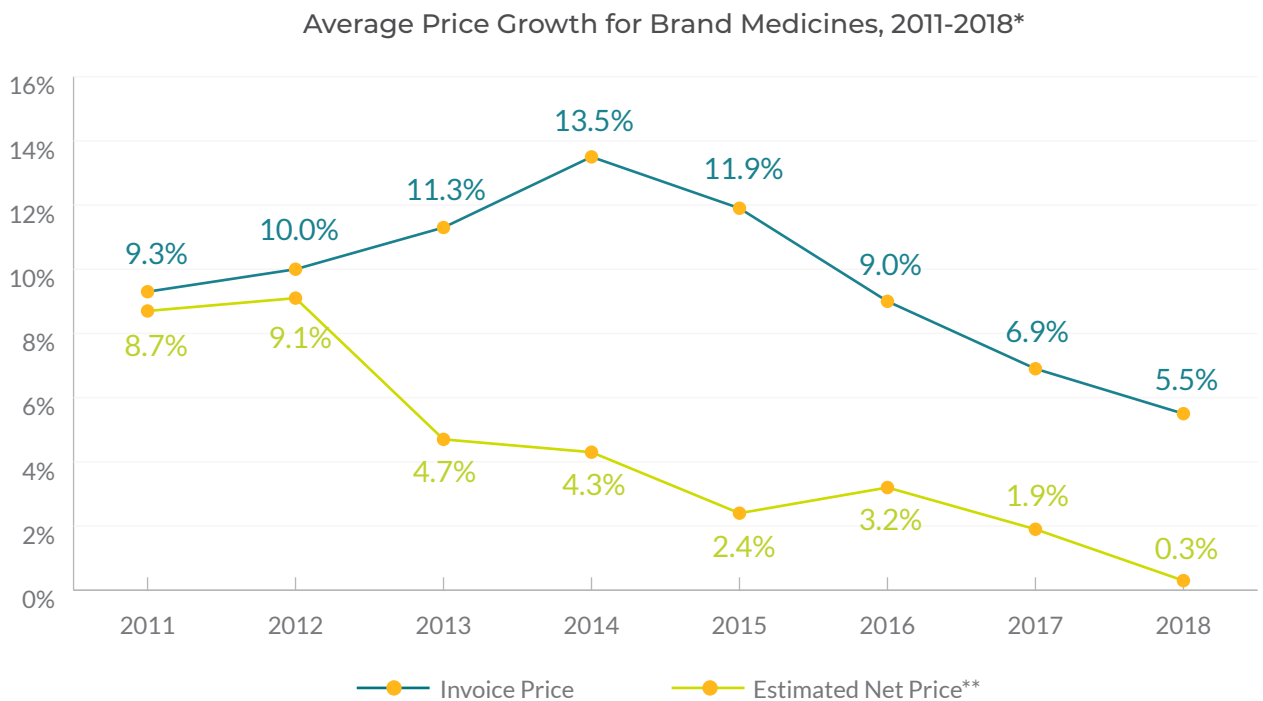
Growth in Prescription Medicine Prices Has Been in Line With Other Health Care Prices



Source: PhRMA analysis of Bureau of Labor Statistics data[26]

Rebates and Other Discounts Offset Virtually All Growth in Medicine Prices in 2018

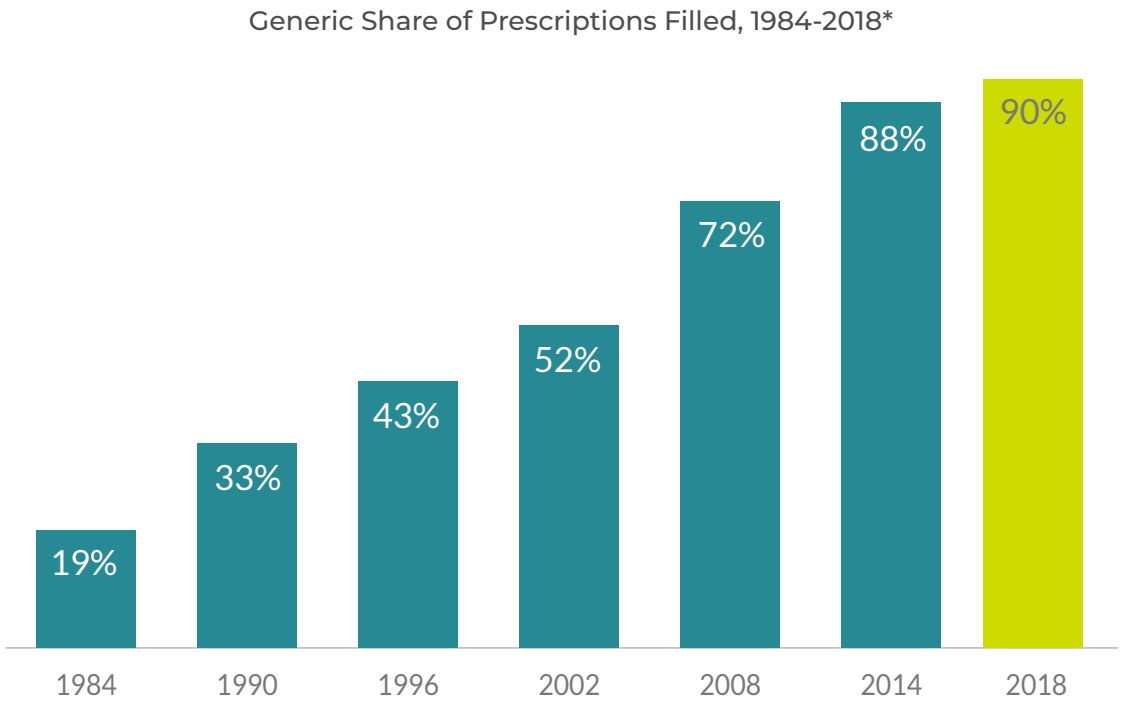
Commonly reported invoice (or list) prices are higher than what payers ultimately pay for medicines.



*Includes protected brand medicines only (ie, brand medicines without generic versions available in the year indicated).
**Estimated net price growth reflects impact of off-invoice rebates and discounts provided by manufacturers.

Source: IQVIA Institute[27]

Nine out of Every Ten US Prescriptions Are Filled With Generics



*Generic share includes generics and branded generics. "Other" category from IMS National Prescription Audit™ not included in calculation.

Sources: IQVIA Institute[28]; Drug Channels Institute[29]

The US Prescription Medicine Lifecycle Promotes Innovation and Affordability

Biopharmaceutical companies invest in pioneering research to bring new medicines to patients, and over time those medicines become available as lower-cost generic copies.

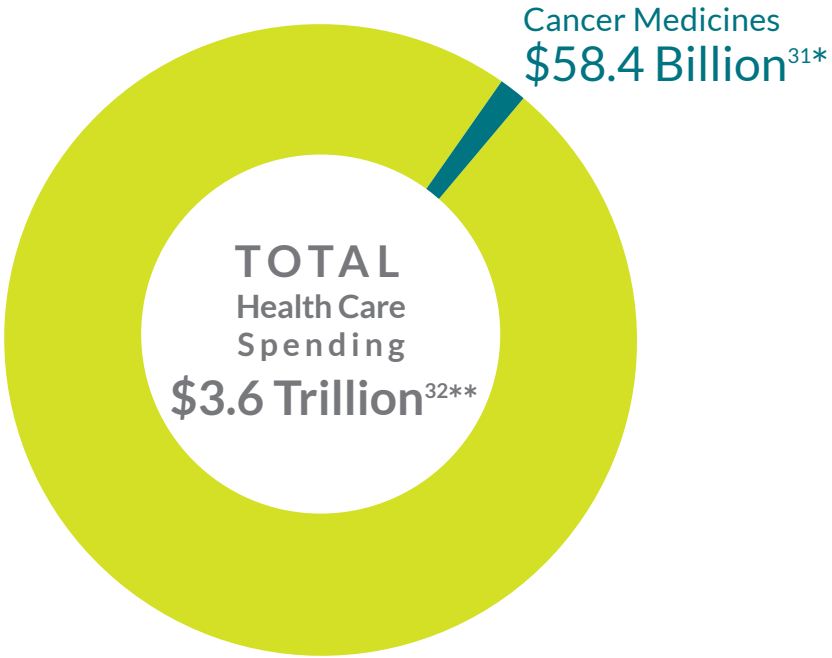
MEDICINE*		BRAND NAME THEN	VS.	GENERIC NOW	% CHANGE
DIOVAN HCT Hypertension	2010	$87		$7	-92%
LIPITOR Cholesterol	2010	$85		$6	-93%
PLAVIX Blood Thinner	2011	$166		$4	-98%
SEROQUEL Schizophrenia	2010	$87		$2	-98%
ZYPREXA Schizophrenia & Bipolar Disorder	2010	$393		$17	-96%

*Each price represents the average annual price for 30 pills of the most commonly dispensed form and strength. "Then" price represents the average price in the year prior to generic entry. "Now" price represents the average price in December 2017.

Source: IQVIA Institute[30]

Spending on Cancer Medicines Represents Less Than 2% of Overall Health Care Spending

Cancer Medicines as a Portion of Total US Health Care Spending, 2018



*Cancer medicine spending reflects invoice spending, which does not account for rebates and discounts.
**Projected

Sources: IQVIA Institute[31]; CMS[32]

Notes and Sources

1. Centers for Medicare & Medicaid Services (CMS). National health expenditure projections 2018-2027: forecast summary. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/ForecastSummary.pdf. Published February 2019. Accessed May 2019.
2. Centers for Medicare & Medicaid Services (CMS). National health expenditure data. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html. Accessed May 2019.
3. Carman KG; RAND Corporation. Health coverage grows under Affordable Care Act. http://www.rand.org/news/press/2015/05/06.html. Published May 6, 2015. Accessed May 2017.
4. Food and Drug Administration (FDA). New drugs at FDA: CDER's new molecular entities and new therapeutic biological products. https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products. Last updated February 2, 2018. Accessed May 2018.
5. Centers for Medicare & Medicaid Services (CMS). National health expenditures 2017 highlights. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf. Accessed May 2019.
6. Roehrig C; Altarum Institute. A ten year projection of the prescription drug share of national health expenditures, including non-retail. https://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief%20with%20Addendum%20May%202017.pdf. Published October 2014. Updated May 2017. Accessed May 2018.
7. Vandervelde A, Blalock E; Berkeley Research Group. The pharmaceutical supply chain: gross drug expenditures realized by stakeholders. http://www.thinkbrg.com/media/publication/863_Vandervelde_PhRMA-January-2017_WEB-FINAL.pdf. Published 2017. Accessed May 2017.
8. Centers for Medicare & Medicaid Services (CMS). National health expenditure data. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html. Accessed May 2019.
9. Centers for Medicare & Medicaid Services (CMS). National health expenditure projections 2018-2027: forecast summary. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/ForecastSummary.pdf. Published February 2019. Accessed May 2019.
10. Roehrig C; Altarum Institute. Projections of the prescription drug share of national health expenditures including non-retail. https://altarum.org/sites/all/libraries/documents/Projections_of_the_Prescription_Drug_Share_of_National_Health_Expenditures_June_2018.pdf. Published May 2018. Accessed June 2018.
11. Roehrig C; Altarum Institute. Projections of the prescription drug share of national health expenditures including non-retail. https://altarum.org/publications/projections-prescription-drug-share-national-health-expenditures-including-non-retail-0. Published June 2019. Accessed June 2019.

Notes and Sources

12. Centers for Medicare & Medicaid Services (CMS). National health expenditure data. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html. Accessed May 2019.
13. Roehrig C; Altarum Institute. Projections of the prescription drug share of national health expenditures including non-retail. https://altarum.org/publications/projections-prescription-drug-share-national-health-expenditures-including-non-retail-0. Published June 2019. Accessed June 2019.
14. Centers for Medicare & Medicaid Services (CMS). National health expenditure data. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html. Accessed May 2019.
15. Centers for Medicare & Medicaid Services (CMS). National health expenditure projections 2018-2027: forecast summary. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/ForecastSummary.pdf. Published February 2019. Accessed May 2019.
16. CVS Health. 2015 drug trend: tackling rising drug costs. https://cvshealth.com/thought-leadership/cvs-health-research-institute/2015-drug-trend-tackling-rising-drug-costs. Published February 22, 2016. Accessed April 2019.
17. CVS Health. 2018 drug trend report. https://payorsolutions.cvshealth.com/insights/2018-drug-trend-report. Published April 11, 2019. Accessed April 2019.
18. Express Scripts. 2015 drug trend report. http://lab.express-scripts.com/lab/drug-trend-report/previous-reports. Published March 2016. Accessed April 2019.
19. Express Scripts. 2018 drug trend report. http://lab.express-scripts.com/lab/drug-trend-report/2018-drug-trend-report. Accessed April 2019.
20. Centers for Medicare & Medicaid Services (CMS). National health expenditure data. Historical. NHE tables. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical.html. Accessed April 2019.
21. Centers for Medicare & Medicaid Services (CMS). National health expenditure projections 2018-2027: forecast summary. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/ForecastSummary.pdf. Published February 2019. Accessed May 2019.
22. IQVIA Institute for Human Data Science. Medicine use and spending in the U.S.: a review of 2018 and outlook to 2023. https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-a-review-of-2018-and-outlook-to-2023. Published May 2019. Accessed May 2019.
23. Nephron Research. Presentation at the Operationalizing a World Without Rebates Forum; March 21, 2019; Washington, DC.

Notes and Sources

24. Fein AJ; Drug Channels Institute. The 2019 economic report on U.S. pharmacies and pharmacy benefit managers. https://www.drugchannels.net/2019/03/new-2019-economic-report-on-us.html. Published March 2019. Accessed March 2019.
25. Pharmaceutical Research and Manufacturers of America (PhRMA). Follow the dollar: understanding how the pharmaceutical distribution and payment system shapes the prices of brand medicines. http://phrma-docs.phrma.org/files/dmfile/Follow-the-Dollar-Report.pdf. Published November 2017. Accessed May 2017.
26. US Bureau of Labor Statistics. CPI-all urban consumers (current series). https://data.bls.gov/PDQWeb/cu. Accessed May 2019.
27. IQVIA Institute for Human Data Science. Medicine use and spending in the U.S.: a review of 2018 and outlook to 2023. https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-a-review-of-2018-and-outlook-to-2023. Published May 2019. Accessed May 2019.
28. IQVIA Institute for Human Data Science. Medicine use and spending in the U.S.: a review of 2017 and outlook to 2022. https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-review-of-2017-outlook-to-2022. Published April 2018. Accessed April 2018.
29. Fein AJ; Drug Channels Institute. The 2019 economic report on U.S. pharmacies and pharmacy benefit managers. https://www.drugchannels.net/2019/03/new-2019-economic-report-on-us.html. Published March 2019. Accessed March 2019.
30. IQVIA Institute for Human Data Science analysis for PhRMA. May 2018.
31. IQVIA Institute for Human Data Science. Medicine use and spending in the U.S.: a review of 2018 and outlook to 2023. https://www.iqvia.com/institute/reports/medicine-use-and-spending-in-the-us-a-review-of-2018-and-outlook-to-2023. Published May 2019. Accessed May 2019.
32. Centers for Medicare & Medicaid Services (CMS). National health expenditure projections 2018-2027: forecast summary. https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/ForecastSummary.pdf. Published February 2019. Accessed May 2019.

6 OUTCOMES AND SAVINGS

Overcoming Gaps in Treatment, Improving Outcomes, and Reducing Costs Through Better Use of Medicines

Undertreatment of complex and chronic conditions as well as suboptimal use of prescribed medicines are significant public health problems, costing the US economy hundreds of billions of dollars each year. Medicines help patients live healthier lives and reduce the need for costly health care services such as emergency department visits, hospital stays, surgeries, and long-term care. An ever-growing body of evidence demonstrates that improved use of prescribed medicines can result in better health outcomes, lower costs for other health care services, and increased worker productivity.

The Human and Economic Costs of Chronic Disease

More than 1 million lives could be saved annually through better treatment and prevention of chronic disease.

$8,600
mean annual cost per person in the US

$42 trillion
estimated cost 2016-2030

Costs of CHRONIC DISEASE

AMERICANS

191 million have at least **one**

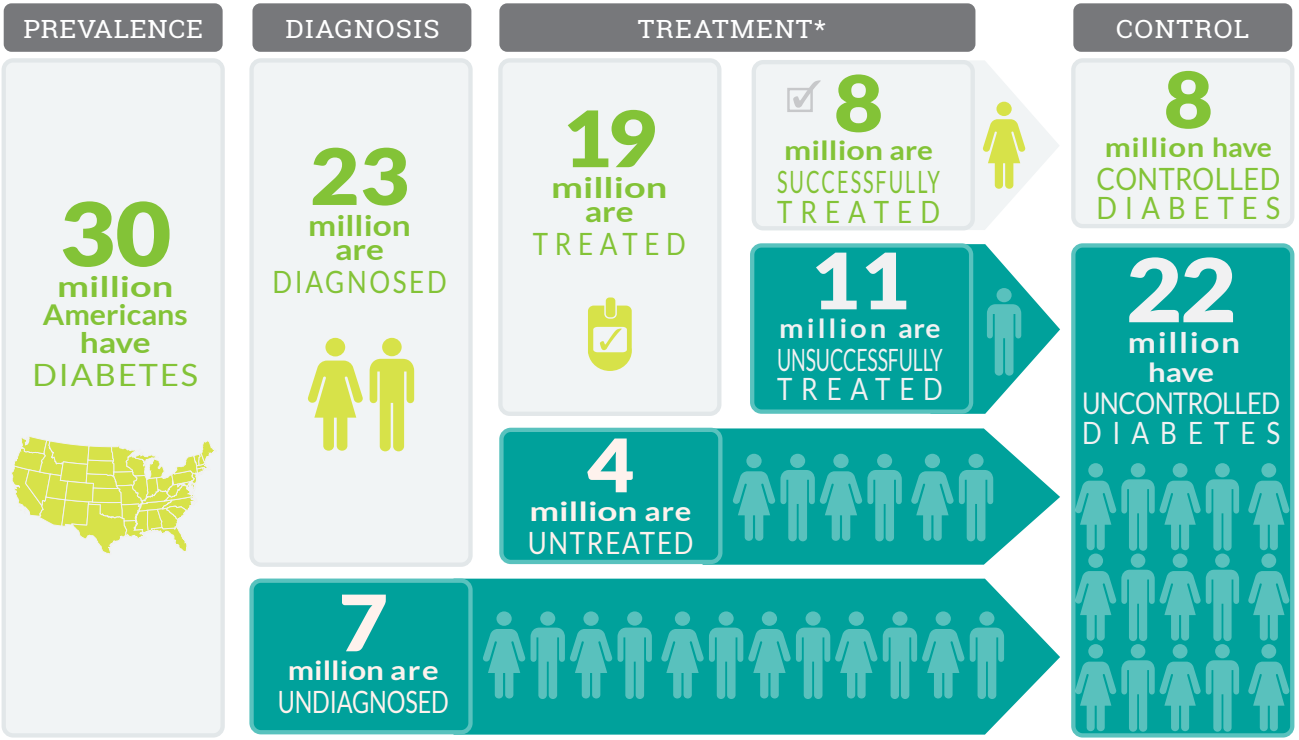
75 million have **multiple**

5% of the population accounts for **50%** of US health care spending[2]

Sources: IHS[1]; Agency for Healthcare Research and Quality[2]

Diabetes: An Example of Underdiagnosis and Undertreatment

Uncontrolled diabetes can lead to kidney failure, amputation, blindness, and stroke. Care for people with diagnosed diabetes accounts for 1 in 4 health care dollars in the United States.[3]

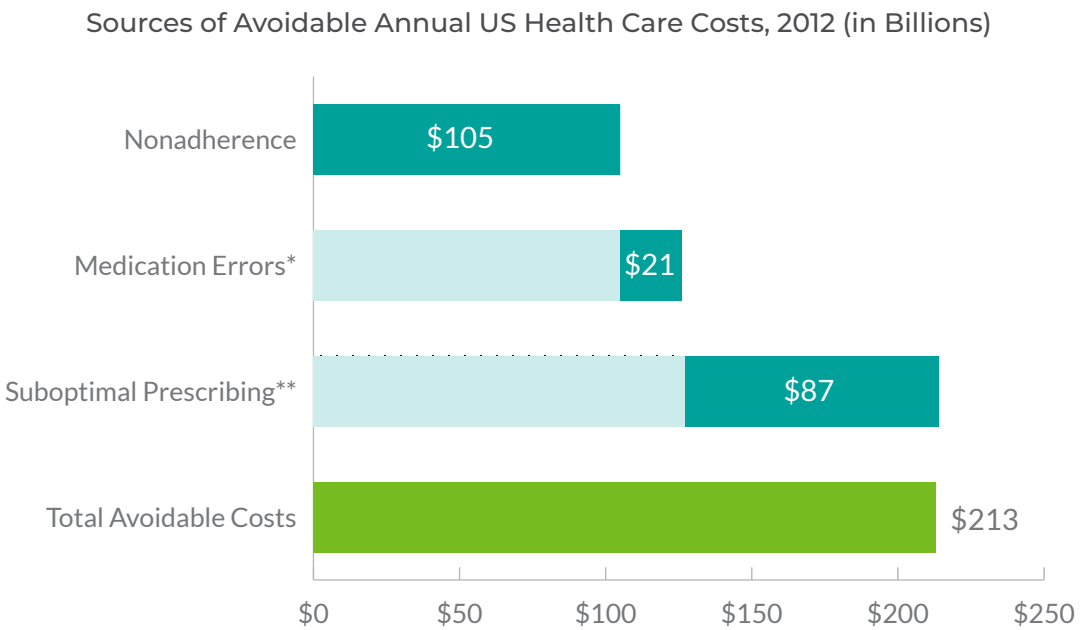


*Treatment includes blood sugar control (medicines, diet, and exercise) and testing to prevent complications.

Sources: American Diabetes Association[3]; IHS Life Sciences analysis of CDC data[4]

Potential Savings From Better Use of Medicines

Better use of medicines could eliminate up to $213 billion in US health care costs annually, which represents 8% of the nation's health care spending.



*Category includes medication errors ($20 billion) and mismanaged polypharmacy ($1 billion).
**Category includes untimely medicine use ($40 billion), inappropriate antibiotic use ($35 billion), and suboptimal generic use ($12 billion).

Source: IMS Institute for Healthcare Informatics[5]

Lowering Cost Sharing for Seniors at the Pharmacy Counter Can Generate Medicare Savings

Sharing a portion of negotiated manufacturer rebates directly with patients could improve medicine adherence and result in savings for seniors and Medicare in Part D.

BENEFITS OF SHARING NEGOTIATED REBATES:

Lower beneficiary out-of-pocket spend by
$350 per year

Save Medicare nearly
$1,000 per year
for every senior taking diabetes medicine

Reduce total health care spending by approximately
$20B over 10 years

Source: IHS Markit[6]

Better Use of Medicines Yields Significant Health Gains by Avoiding the Need for Other Medical Services

Due to a growing body of evidence, in 2012 the Congressional Budget Office (CBO) began recognizing reductions in other medical expenditures associated with an increased use of prescription medicines in Medicare.

> Pharmaceuticals have the effect of improving or maintaining an individual's health . . . adhering to a drug regimen for a chronic condition such as diabetes or high blood pressure may prevent complications . . . taking the medication may also avert hospital admissions and thus **reduce the use of medical services.**"
>
> — CBO[7]

Since the CBO announcement, the evidence has continued to develop, broadening the potential for cost offsets in the health care system.

CHRONIC DISEASES

Medicare savings due to better use of medicines may be 3 to 6 times greater than estimated by the CBO for seniors with common chronic conditions, including heart failure, diabetes, and hypertension.[8]

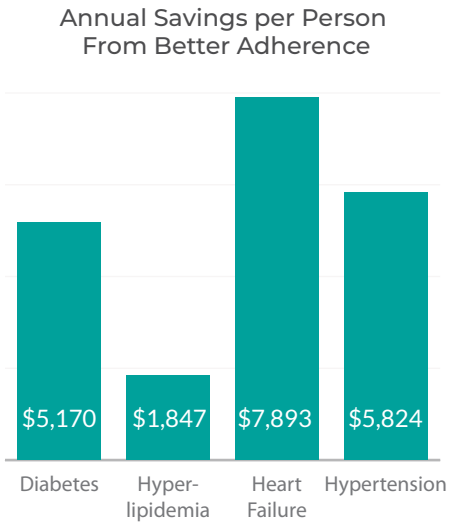
MEDICAID

Increased use of medicines is associated with reductions in Medicaid expenditures from avoided use of inpatient and outpatient services.[9,10]

Sources: CBO[7]; Roebuck MC[8]; Roebuck MC et al.[9,10]

Improved Medicine Use Can Lead to Savings in Medicare

Between 20% and 40% of Medicare beneficiaries with common chronic diseases are not adherent to their medicines. Billions of dollars in cost savings from avoided hospital stays can result from improved adherence.



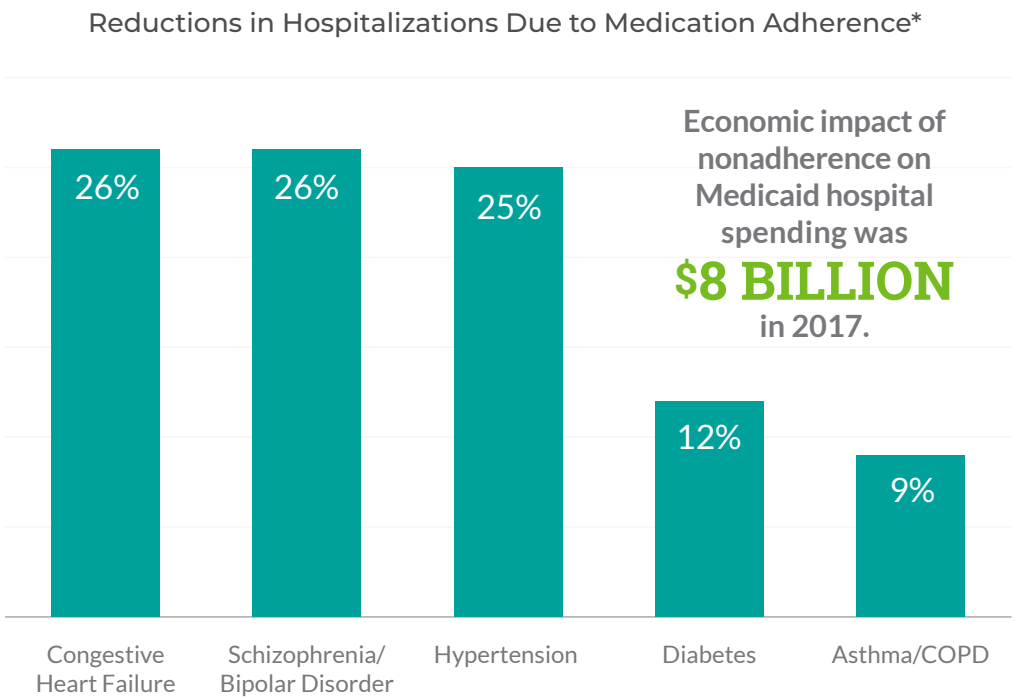
Outcomes With Improved Adherence

$4.5B cost savings	DIABETES	2.9M avoidable hospital inpatient days
$5.1B cost savings	HYPERLIPIDEMIA	5.2M avoidable hospital inpatient days
$5.6B cost savings	HEART FAILURE	4.2M avoidable hospital inpatient days
$13.7B cost savings	HYPERTENSION	7.3M avoidable hospital inpatient days

Source: Lloyd JT et al.[11]

Better Adherence Generates Savings in Medicaid

Optimal adherence to medicines for a range of chronic conditions leads to reductions in hospitalizations for many patients enrolled in Medicaid.



*Results apply to Medicaid populations that are not blind or disabled.

Source: Roebuck MC et al.[12]

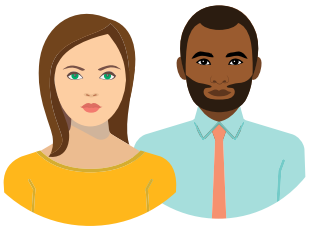
Improving Access to Treatment Could Reduce the Clinical and Economic Impact of Addiction

The economic impact of the opioid crisis in the United States was estimated to be $504 billion in 2015.[13] Medication-assisted treatment (MAT) is an evidence-based approach for the treatment of opioid use disorder that pairs behavioral therapy with medicines that block the effects of opioids and/or mitigate the symptoms of opioid withdrawal.

Doubling access to MAT in the commercial market alone over the next 15 years could[14]:

Prevent up to
6.1M
OVERDOSES

Save as many as
805K LIVES



Save the health care system as much as
$645B

Sources: Hagemeier, NE[13]; IHS Markit[14]

Recent Studies Show Significant Value From Better Use of Medicines

Patients with a range of diseases could offset health care spending by exercising better adherence.

PARKINSON'S DISEASE

Health care savings of **up to $6,300** in fewer than 2 years can be achieved among patients with Parkinson's who continually stay on therapy.[15]

MULTIPLE SCLEROSIS

Initiation of therapy is associated with **reductions of up to $5,700** in medical costs, driven by decreased use of outpatient services and inpatient hospital stays.[16]

CYSTIC FIBROSIS

Among children with cystic fibrosis, poor medication adherence is associated with more hospitalizations and emergency department visits and an increase of **more than $14,000** in same-year medical costs compared with children who are highly adherent.[17]

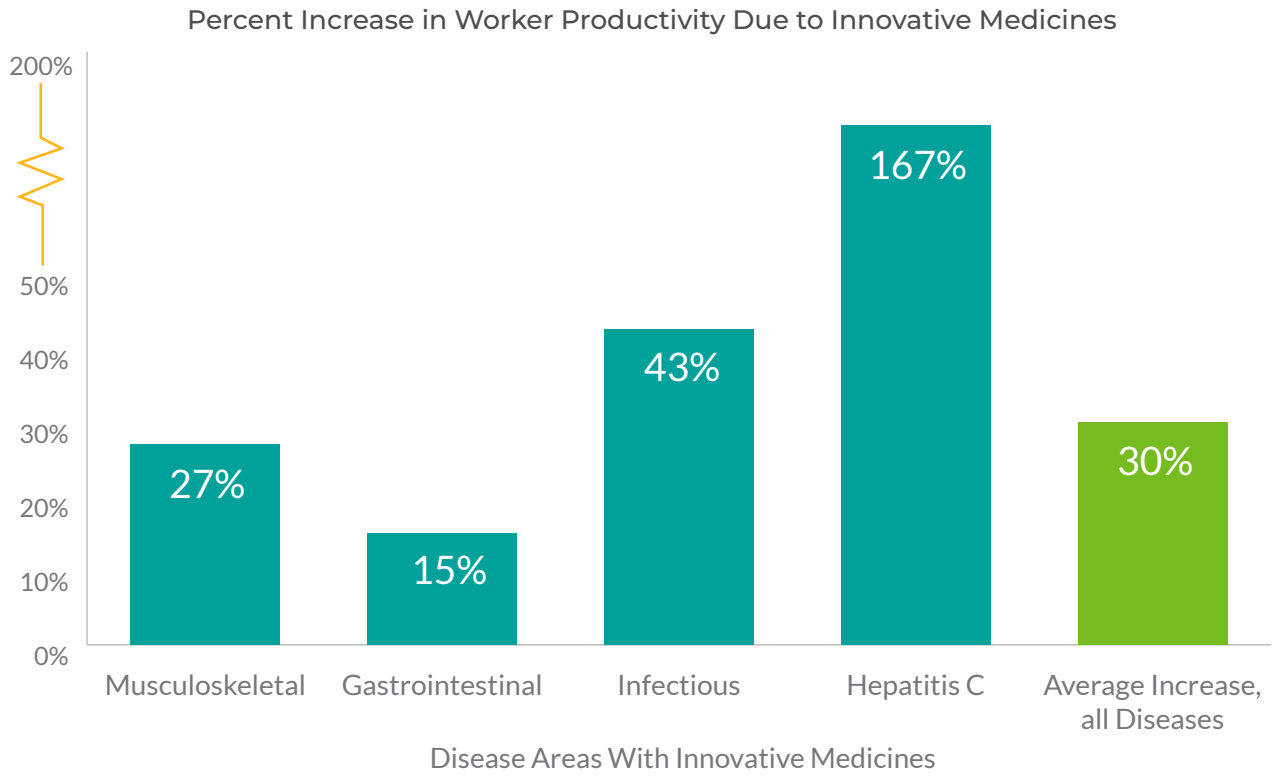
LUPUS

Nonadherence among children on Medicaid who are diagnosed with lupus is associated with a **55% increase** in emergency department use and a **nearly 40% increase** in hospitalizations.[18]

Sources: Wei YJ et al.[15]; Nicholas J et al.[16]; Quittner AL et al.[17]; Feldman CH et al.[18]

Innovative Medicines Improve Patients' Ability to Work

New drugs increase worker productivity by 4.8 million work days and add $221 billion in wages per year.



Source: Chen AJ et al.[19]

Notes and Sources

1. IHS. Burden of chronic illnesses in the US: technical overview. http://www.fightchronicdisease.org/sites/default/files/IHS_Technical_Report.pdf. Published May 2016. Accessed May 2017.
2. Cohen SB; Agency for Healthcare Research and Quality. The concentration and persistence in the level of health expenditures over time: estimates for the U.S. population, 2012-2013. *Statistical Brief* 481. http://meps.ahrq.gov/mepsweb/data_files/publications/st481/stat481.pdf. Published September 2015. Accessed May 2017.
3. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. http://care.diabetesjournals.org/content/early/2018/03/20/dci18-0007. Published March 2018. Accessed May 2018.
4. IHS Life Sciences analysis of Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, data. National Health and Nutrition Examination Survey, 2013-2014. https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/Default.aspx?BeginYear=2013. Accessed May 2017.
5. IMS Institute for Healthcare Informatics. Avoidable costs in U.S. healthcare: the $200 billion opportunity from using medicines more responsibly. https://www.drugstorenews.com/wp-content/uploads/2013/06/Avoidable-Costs-in-Healthcare.pdf. Published June 2013. Accessed May 2017.
6. Su W, Dall T; IHS Markit. Passing a portion of negotiated rebates through to seniors with diabetes can improve adherence and generate savings in Medicare. https://cdn.ihs.com/www/pdf/IHSM-RebateSharingReport-10May2018.pdf. Published May 2018. Accessed May 2019.
7. Congressional Budget Office (CBO). Offsetting effects of prescription drug use on Medicare's spending for medical services. https://www.cbo.gov/publication/43741. Published November 2012. Accessed May 2017.
8. Roebuck MC. Medical cost offsets from prescription drug utilization among Medicare beneficiaries [commentary]. *J Manag Care Spec Pharm*. 2014;20(10):994-995.
9. Roebuck MC, Dougherty JS, Kaestner R, et al. Increased use of prescription drugs reduces medical costs in Medicaid populations. *Health Aff* (Millwood). 2015;34(9):1586-1593.
10. Roebuck MC, Kaestner RJ, Dougherty JS. Impact of medication adherence on health services utilization in Medicaid. *Med Care*. 2018;56(3): 266-273.
11. Lloyd JT, Maresh S, Powers CA, et al. How much does medication nonadherence cost the Medicare fee-for-service program? *Med Care*. 2019; 57(3):218-224.
12. Roebuck MC, Kaestner RJ, Dougherty JS. Impact of medication adherence on health services utilization in Medicaid. *Med Care*. 2018;56(3): 266-273.

Notes and Sources

13. Hagemeier NE. Introduction to the opioid epidemic: the economic burden on the healthcare system and impact on quality of life. *Am J Manag Care.* 2018;24(suppl 10):S200-S206.

14. Chen F, Semilla A, Su W; IHS Markit. Improving access to medication-assisted treatment for opioid use disorder among the commercially-insured US population. https://cdn.ihs.com/www/pdf/1218/IHSMarkit-Impact-Improving-Access-Opioid-Addiction.pdf. Published November 2018. Accessed April 2019.

15. Wei YJ, Palumbo FB, Simoni-Wastila L, et al. Antiparkinson drug adherence and its association with health care utilization and economic outcomes in a Medicare Part D population. *Value Health.* 2014;17(2):196-204.

16. Nicholas J, Boster A, Wu N, et al. Comparison of disease-modifying therapies for the management of multiple sclerosis: analysis of healthcare resource utilization and relapse rates from US insurance claims data. *Pharmacoecon Open.* 2018;2(1):31-41.

17. Quittner AL, Zhang J, Marynchenko M, et al. Pulmonary medication adherence and health-care use in cystic fibrosis. *Chest.* 2014;146(1):142-151.

18. Feldman CH, Yazdany J, Guan H, et al. Medication nonadherence is associated with increased subsequent acute care utilization among Medicaid beneficiaries with systemic lupus erythematosus. *Arthritis Care Res.* (Hoboken). 2015;67(12):1712-1721.

19. Chen AJ, Goldman DP. Productivity benefits of medical care: evidence from US-based randomized clinical trials [published online March 9, 2018]. *Value Health.* 2018;21(8):905-910. doi:10.1016/j.jval.2018.01.009

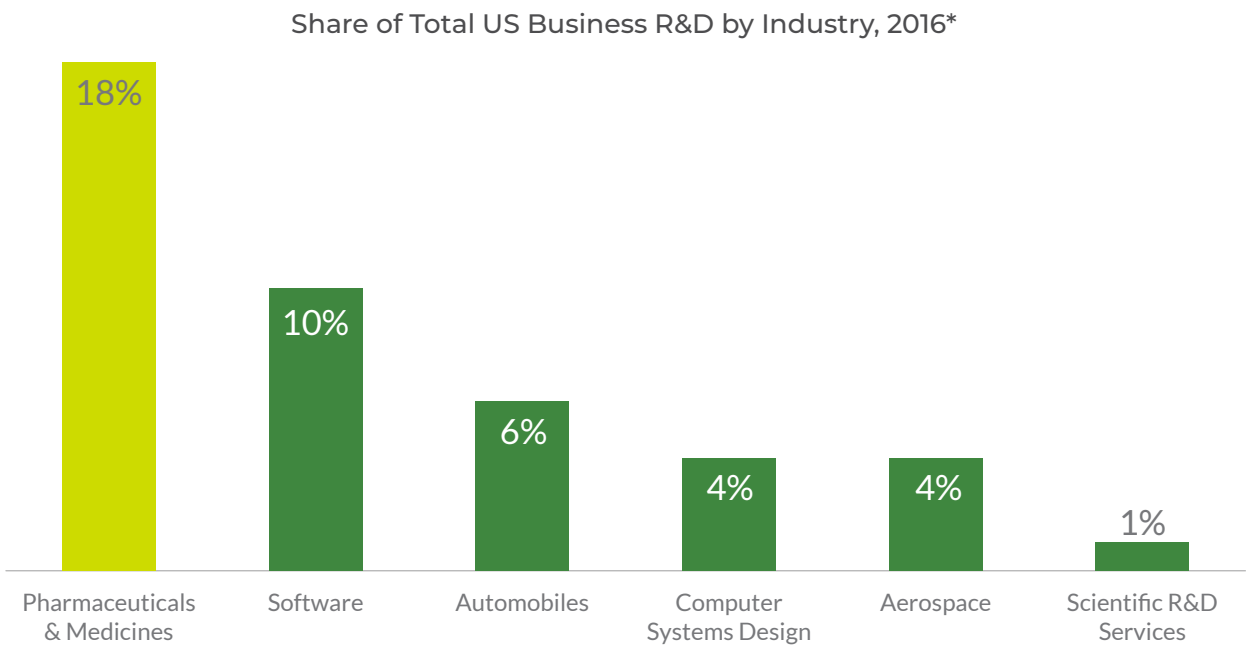
7 ECONOMIC IMPACT

Sustaining and Growing State and Local Economies

America's biopharmaceutical industry is the foundation for one of the country's most dynamic innovation and business ecosystems. The industry is among the most research and development (R&D)-intensive in the United States, accounting for 1 out of every 6 dollars spent on domestic R&D by US businesses. The industry's large-scale research and manufacturing footprint, along with its attendant supply chain, supports high-quality jobs in communities across the United States. More biopharmaceutical venture capital is invested in startups in the United States than anywhere else in the world, providing an ongoing source of highly skilled jobs aimed at making advances in biopharmaceutical science. However, US leadership in innovation is facing increasing challenges from emerging global competitors seeking to attract and grow a biopharmaceutical presence in their own countries.

The Biopharmaceutical Industry Is the Single Largest Funder of Business R&D in the United States

The biopharmaceutical industry accounts for the single largest share of all self-funded R&D, representing 1 out of every 6 dollars (18%) spent on domestic R&D by US businesses. Furthermore, US industry is also the largest global funder of biopharmaceutical R&D, accounting for about half of all R&D investments worldwide.

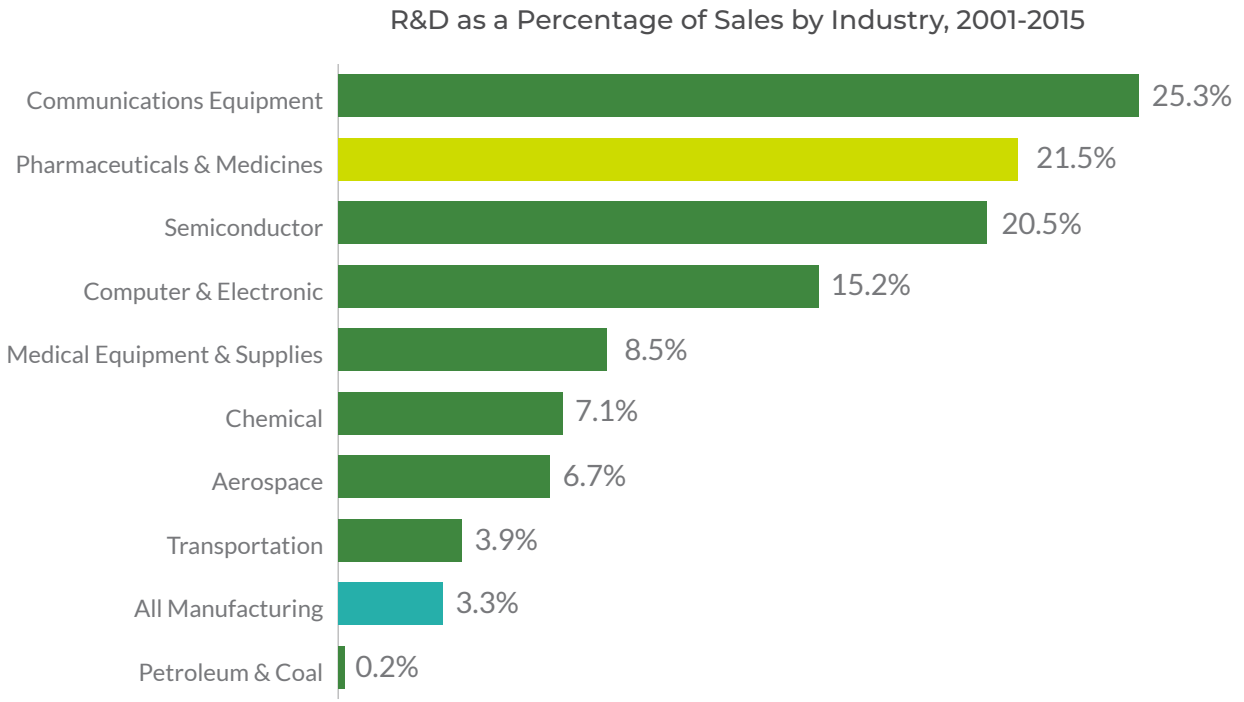


*The remaining 57% share of business R&D spending is conducted by other industries, including subsectors of the machinery sector, the computer and electronic products sector, and the electrical equipment, appliance, and components sector.

Source: PhRMA analysis of National Science Foundation data[1]

The US Biopharmaceutical Sector Is Among the Biggest Investors in R&D Relative to Sales

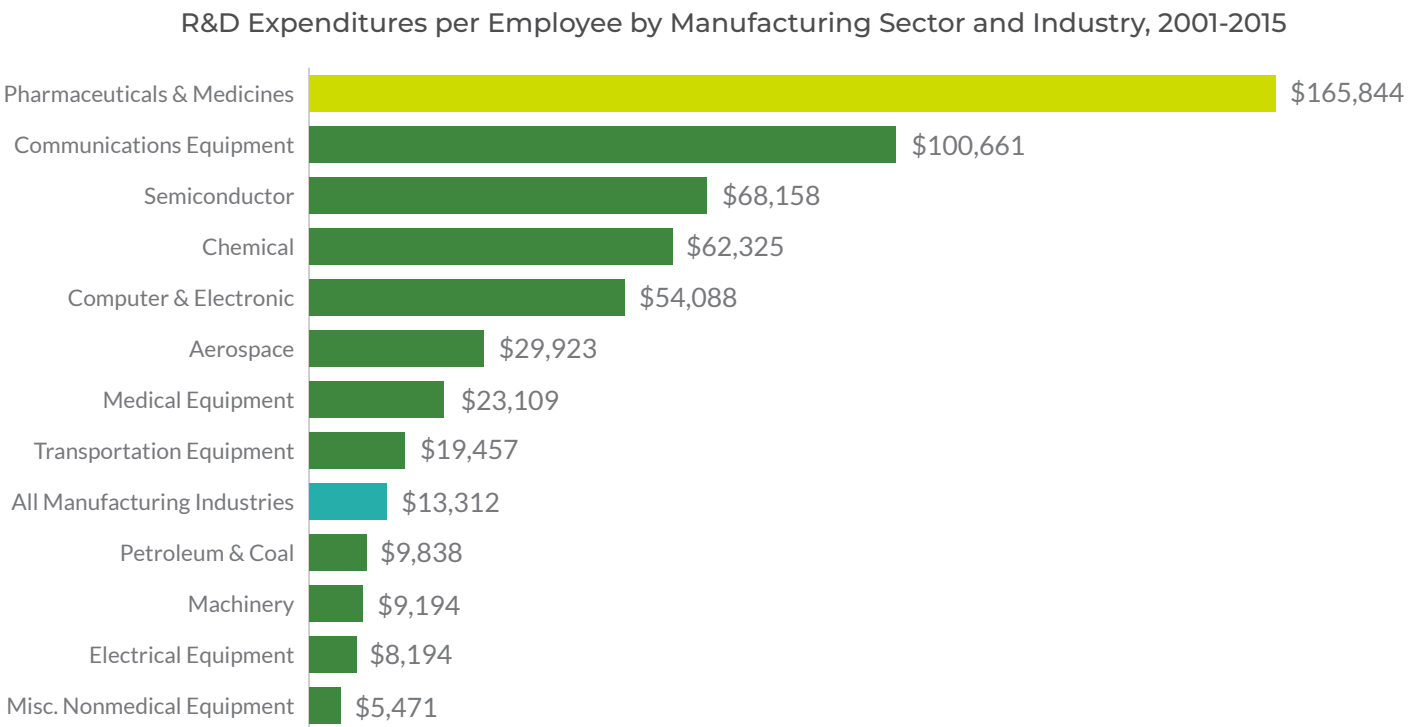
Biopharmaceutical investments in R&D, as a percentage of sales, are more than 6 times the average for all manufacturing industries, making the sector one of the most R&D-intensive industries.



Source: NDP Analytics[2]

The Biopharmaceutical Industry Invests More R&D Dollars per Employee Than Any Other Industry

On a per employee basis, biopharmaceutical companies invest 12 times more in R&D than the average for manufacturing industries overall.

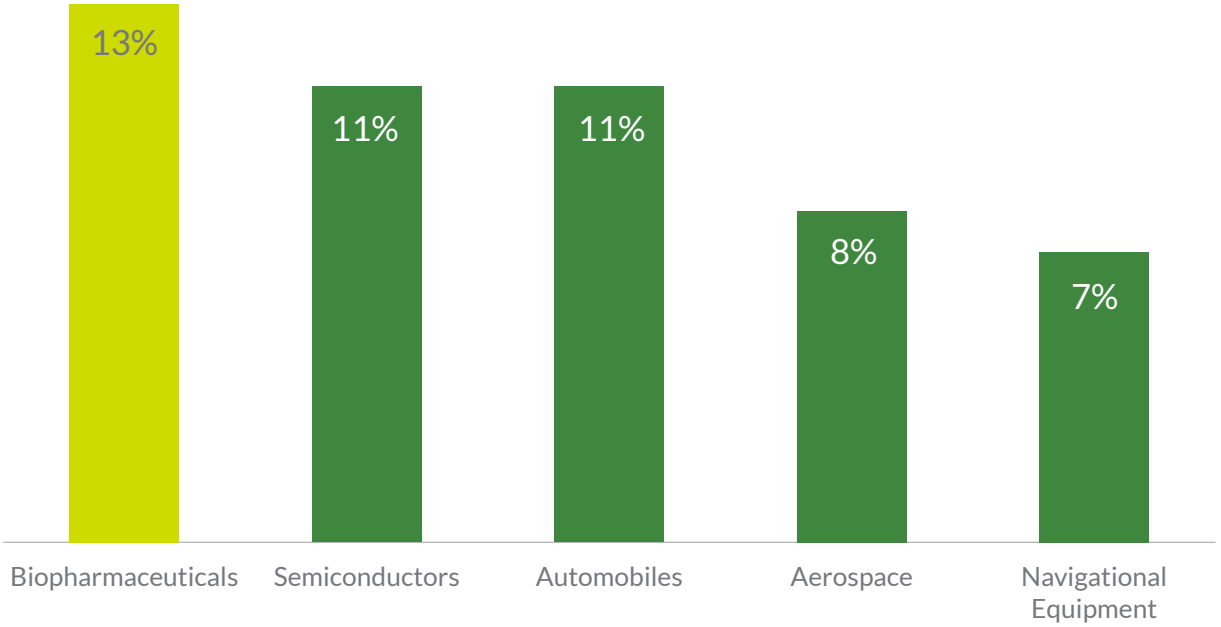


Source: NDP Analytics[3]

The Biopharmaceutical Industry Employs the Largest Share of All Manufacturing R&D Workers

One out of every eight R&D workers in the nation's manufacturing industries is employed by the biopharmaceutical industry.

Selected Manufacturing Industries' Share of Total R&D Workers, 2015*



*All other manufacturing sectors account for the remaining 50% of the R&D workforce.

Source: PhRMA analysis of National Science Foundation data[4]

The Economic Reach of the US Biopharmaceutical Industry

Every biopharmaceutical sector job supports a total of five jobs across the economy.

811,000 direct jobs
(Innovative Biopharmaceutical Industry)

1,422,000 indirect jobs
(Vendors and Suppliers)

\+ 1,806,000 induced jobs
(Additional Private Economic Activity)

4,039,000 TOTAL JOBS

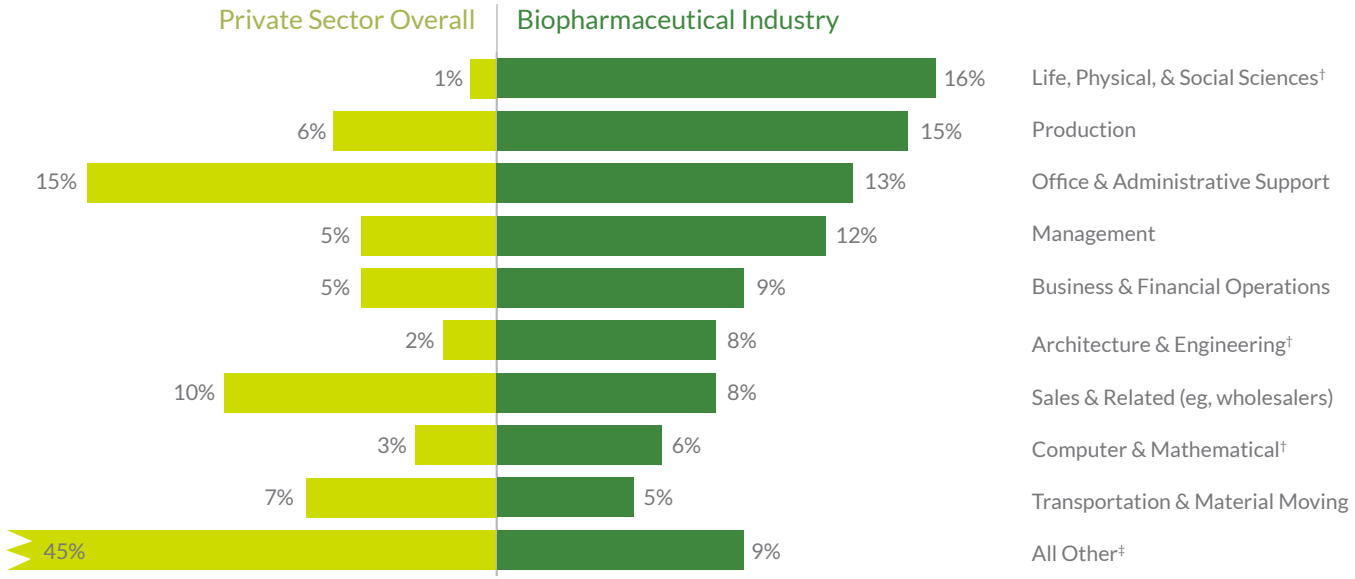
The biopharmaceutical industry supported more than 4 million jobs across the US economy in 2017.

Source: TEConomy Partners[5]

The US Biopharmaceutical Sector Produces High-Quality Jobs Across an Array of Fields

One-third of the jobs in the biopharmaceutical sector are in key STEM (Science, Technology, Engineering, and Mathematics) occupations, a far higher share than in the private sector as a whole.

Percentage of Jobs in Sector by Occupation, 2017*



*Column percentages may not add up to 100% due to rounding.
†Indicates a STEM occupation.
‡Other occupations include health care practitioners/techs (2.8% of biopharma industry jobs); installation/maintenance/repair (2.5%); arts/design/entertainment/sports/media (0.9%); building & grounds cleaning/maint (0.6%); legal (0.4%); health care support (0.4%); construction/extraction (0.3%); educ/training/library science (0.3%); protective services (0.2%); community/social services (0.2%); personal care & service (0.1%); farming/fishing/forestry (0.1%); and food prep/serving (0.1%).

Source: TEConomy Partners[6]

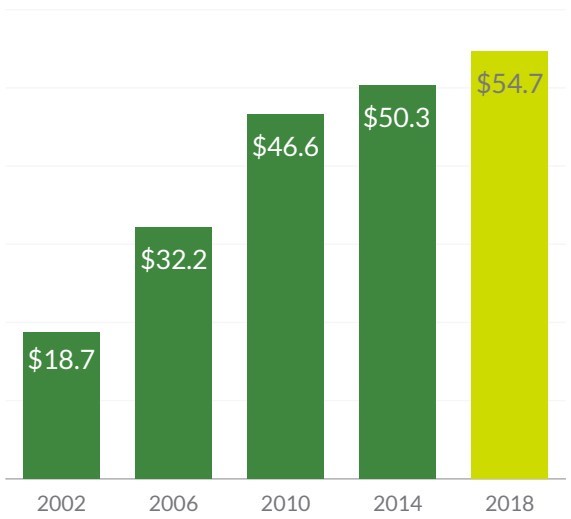
US Biopharmaceutical Exports Have Grown

Biopharmaceutical exports have nearly tripled since 2002, accounting for about 4% of all US exports in 2018.

Pharmaceuticals rank as one of the top exporting sectors for IP-intensive industries in the United States."

— International Trade Administration[7]

US Biopharmaceutical Goods Exports (in Billions)[8]

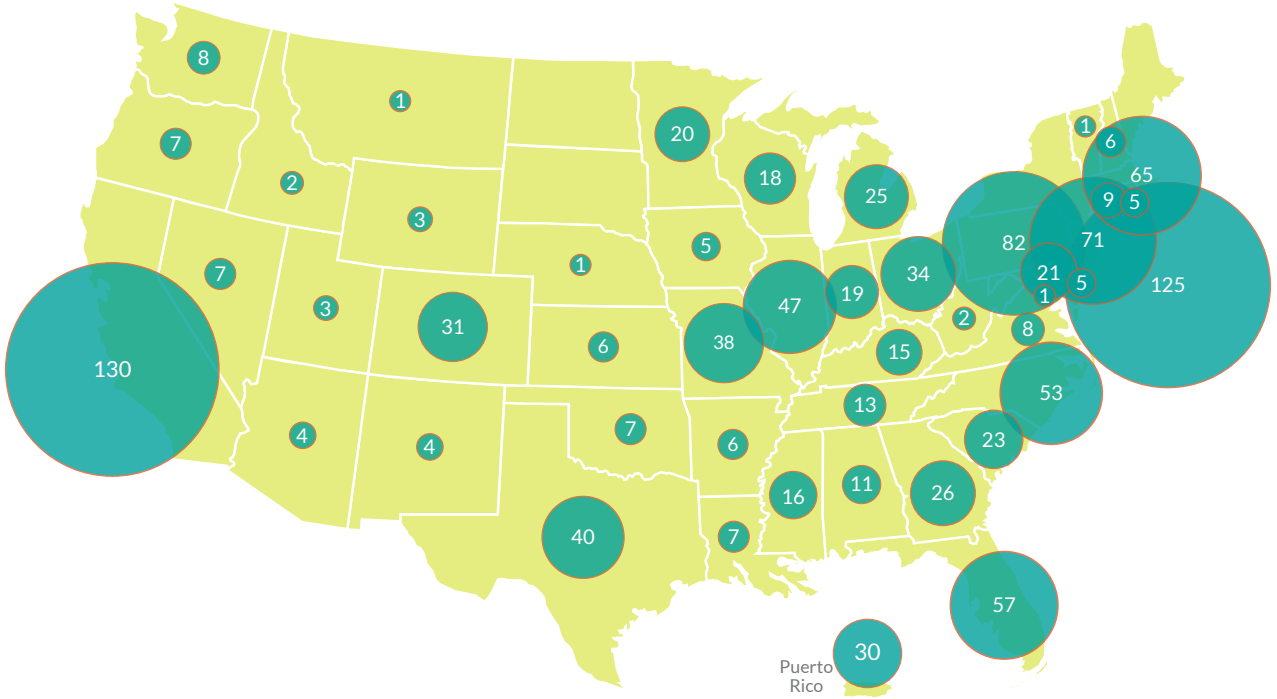


Sources: ITA[7]; PhRMA analysis of US Census Bureau data[8]

The Biopharmaceutical Sector's Extensive US Manufacturing Footprint

Approximately 1,100 manufacturing plants involved in the production of human-use medicines are located in 45 US states and Puerto Rico. Biopharmaceutical companies are building the plants to make cutting-edge therapies of the future in the United States.

Biopharmaceutical Manufacturing Facilities by State/Territory (January 2019)[9,10]

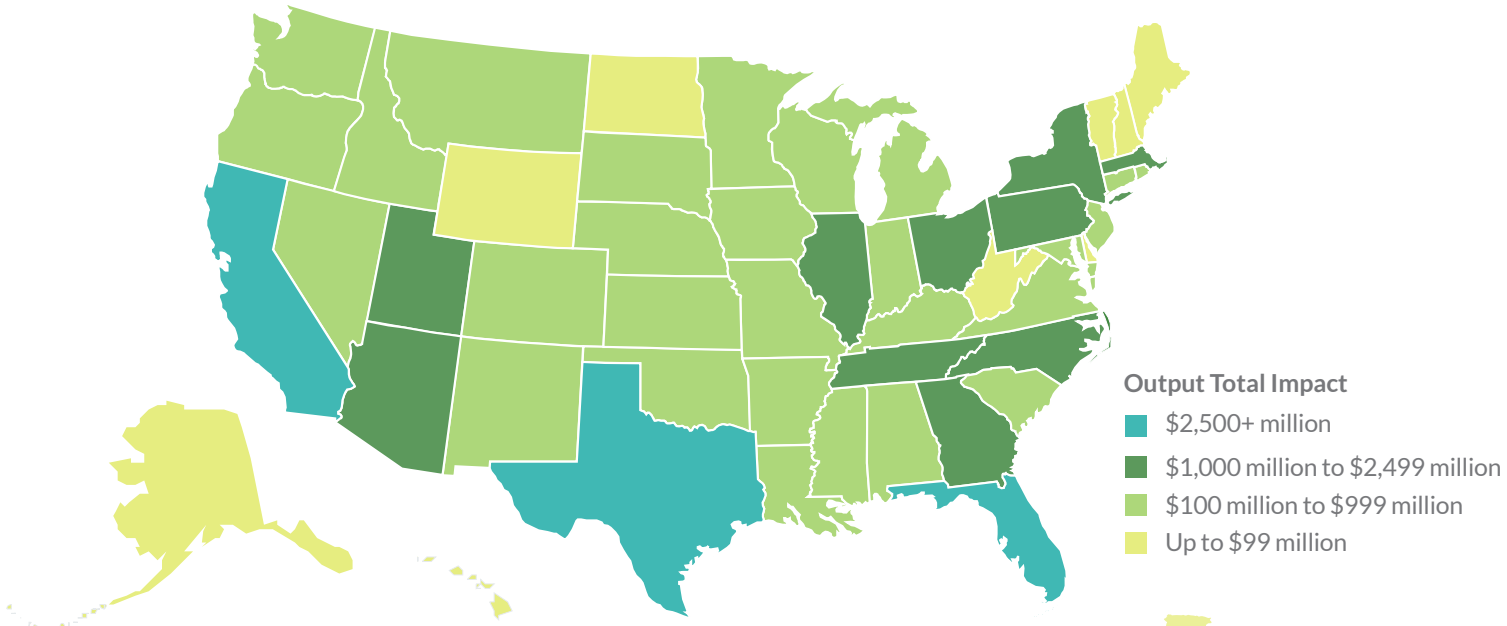


Sources: NDP Analytics[9]; Hargreaves B[10]

Industry-Sponsored Clinical Trials Contribute Significant Value to the Communities in Which They Are Located

In 2017, the biopharmaceutical industry sponsored more than 4,500 clinical trials of medicines in the United States, involving 920,000 participants and supporting $42 billion in economic activity across all 50 states, the District of Columbia, and Puerto Rico.*

Estimated Total Economic Impact of Industry-Sponsored Clinical Trials Activity Across the US, 2017



*Estimates reflect only those activities occurring at clinical trial sites and exclude more centralized cross-site functions such as coordination and data analysis. Also excluded are nonclinical R&D activities such as basic and preclinical research and the significant economic contribution from non-R&D activities of the industry such as manufacturing and distribution.

Source: TEConomy Partners[11]

States Are Increasingly Targeting the Biopharmaceutical Industry in Their Economic Development Plans

Recognizing the broad economic impact of the biopharmaceutical industry, states across the country are adopting a range of policies and programs to attract and grow the industry within their borders.

Common policies and programs that states are pursuing include:

Adopting comprehensive, targeted strategies for life science industry development

Building research capacity and infrastructure

Building advanced manufacturing capabilities

Advancing the STEM talent pipeline

Accelerating innovation through entrepreneurial development programs

Increasing the availability of financial capital for life science development

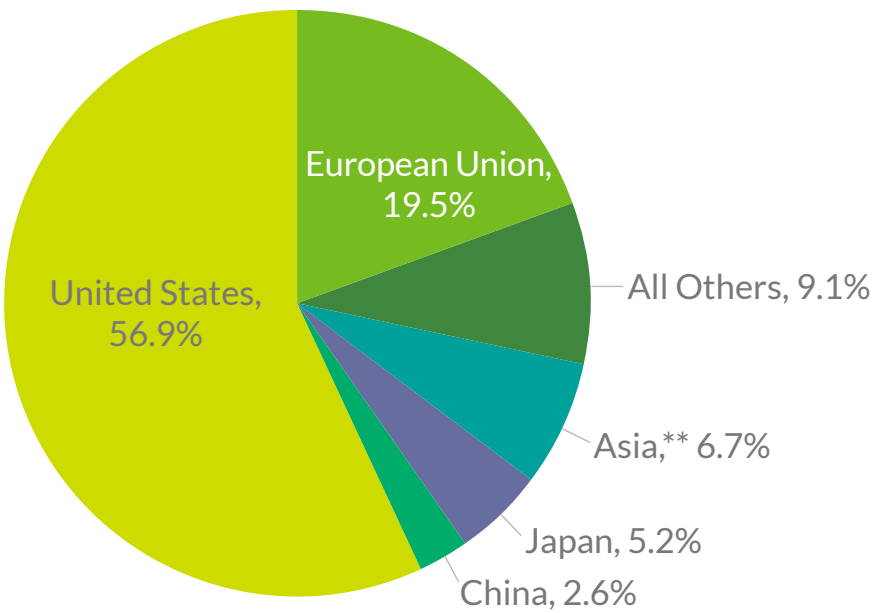
Establishing economic incentives for life science innovation

Source: TEConomy Partners[12]

The United States Leads in Biopharmaceutical Intellectual Property

More than half of the intellectual property related to new medicines was created in the United States.

US Patents Granted in Pharmaceuticals by Region/Country of Inventor, 2016*



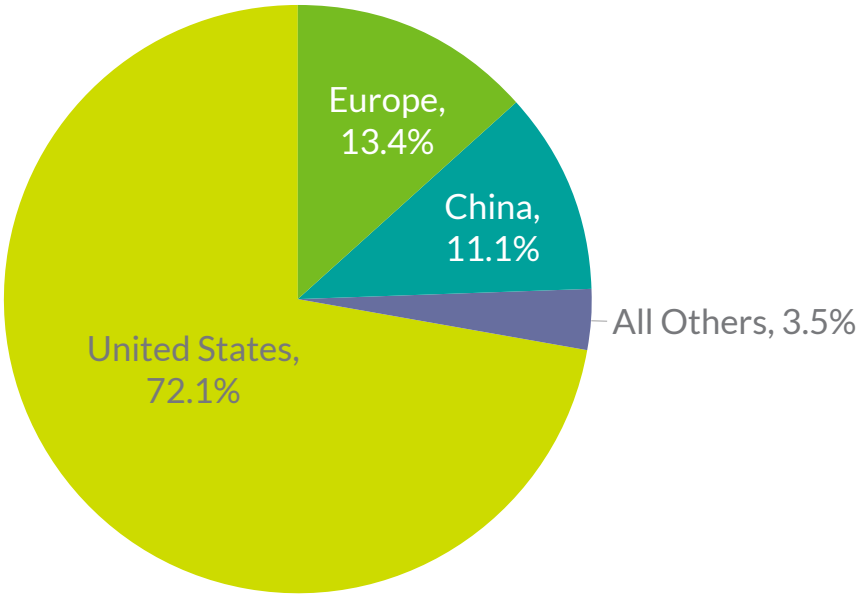
*Percentages may not add up to 100% due to rounding.
**Asia includes India, Malaysia, South Korea, and others.

Source: PhRMA analysis of National Science Foundation data[13]

The United States Leads in Biopharmaceutical Venture Capital Investment

Almost three-quarters of worldwide venture capital investments in biopharmaceutical startups are made in the United States.

Biopharmaceutical Venture Capital Investment by Region/Country, 2018*

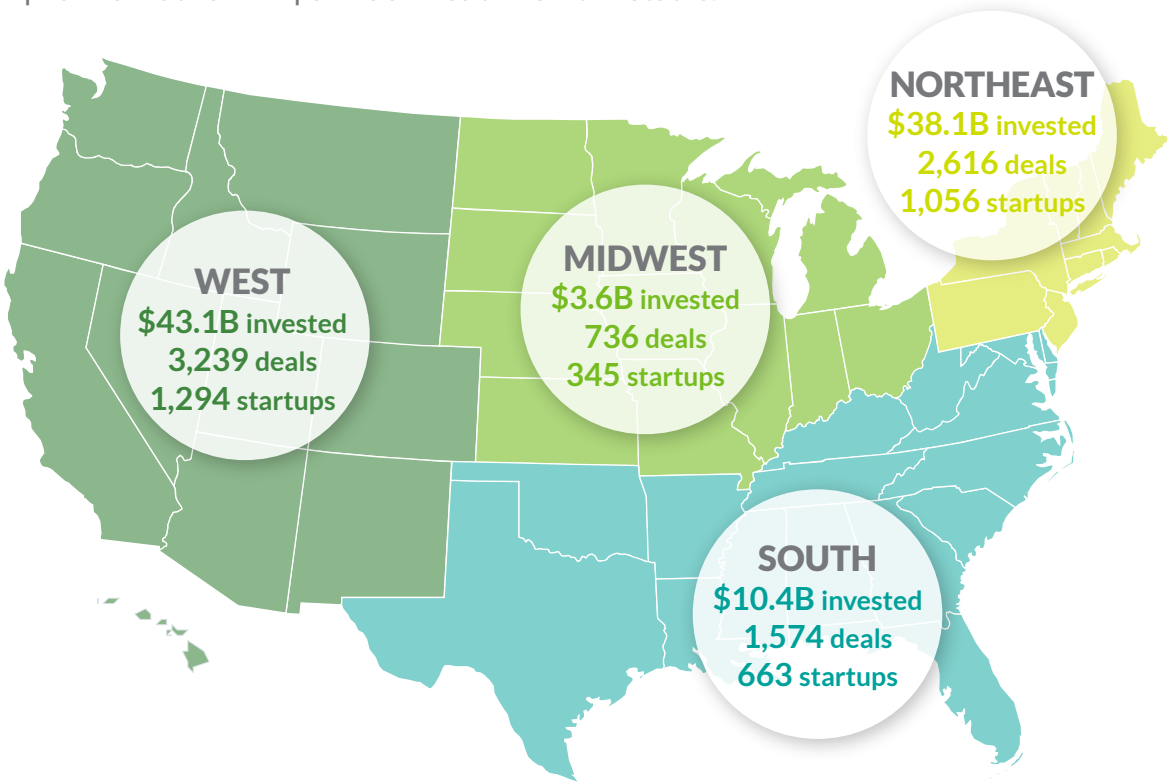


*Percentages may not add up to 100% due to rounding.

Source: TEConomy analysis for PhRMA[14]

Biopharmaceutical Venture Capital Provides Tremendous Resources for Startup Company Financing

Between 2000 and 2017, venture capitalists invested over $95 billion in more than 8,000 deals helping to start up over 3,300 biopharmaceutical companies across the United States.

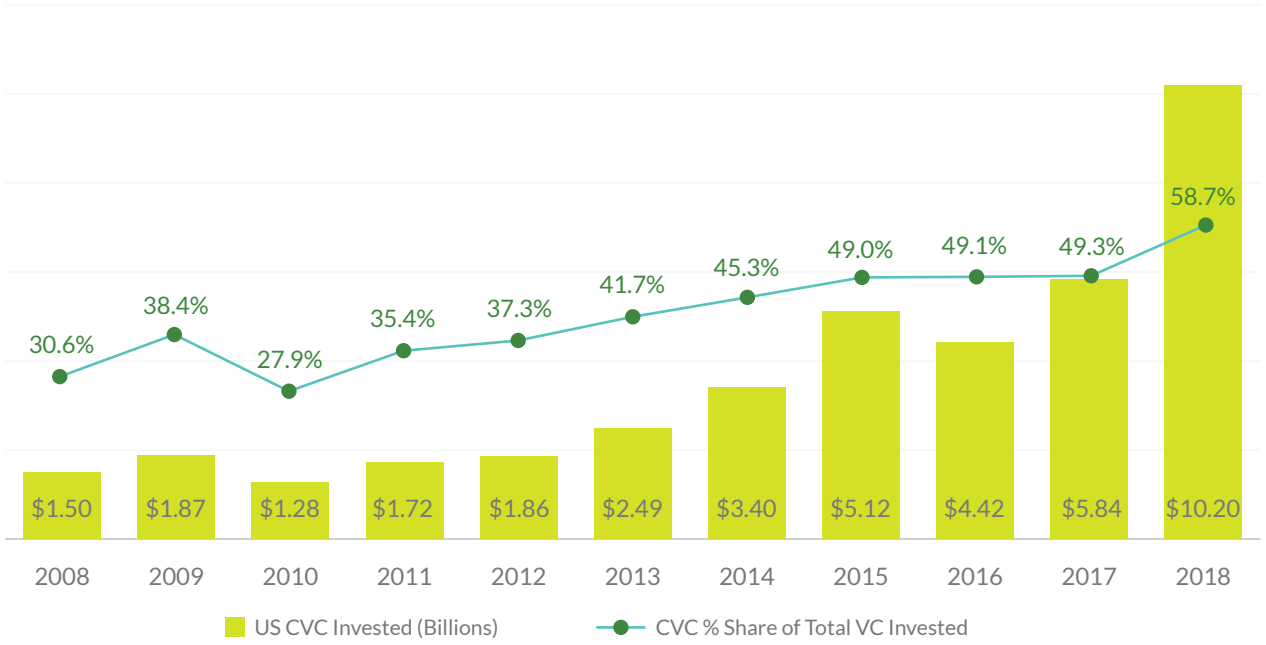


Source: PhRMA analysis of PitchBook Venture Investment database[15]

The Biopharmaceutical Industry Supports a Broader Ecosystem Through Corporate Venture Capital

Corporate venture capital (CVC) from biopharmaceutical companies and others plays an increasingly important role in financing emerging biopharmaceutical companies, now accounting for over half of VC investment in the sector.

US CVC Investment in Biopharmaceutical Startups, 2008-2018



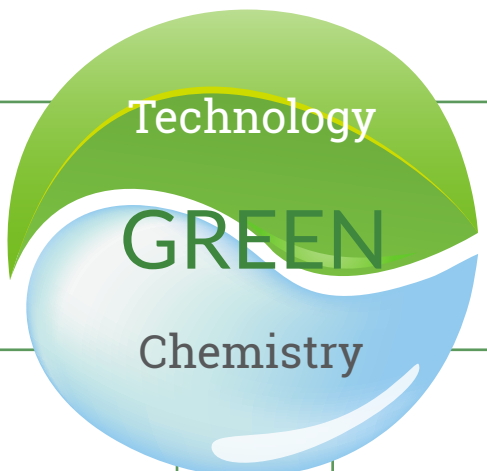
Source: 4Q 2018 Pitchbook-NVCA Venture Monitor[16]

The Biopharmaceutical Industry Is Reducing Its Impact on the Environment

Biopharmaceutical companies are pioneers in green chemistry and are committed to finding creative and innovative ways, including the following, to reduce waste, conserve energy, and adopt other more environmentally friendly processes.

Implementing manufacturing methods that **replace many solvents** with safer alternatives

Adopting new manufacturing processes to **reduce emissions and energy use**



Constructing facilities that are **LEED-certified** (Leadership in Energy and Environmental Design)

Adapting **single-use production systems** to minimize environmental impact

Expanding use of **biocatalyzed processes,** which are shorter, produce less waste, and reduce environmental impact

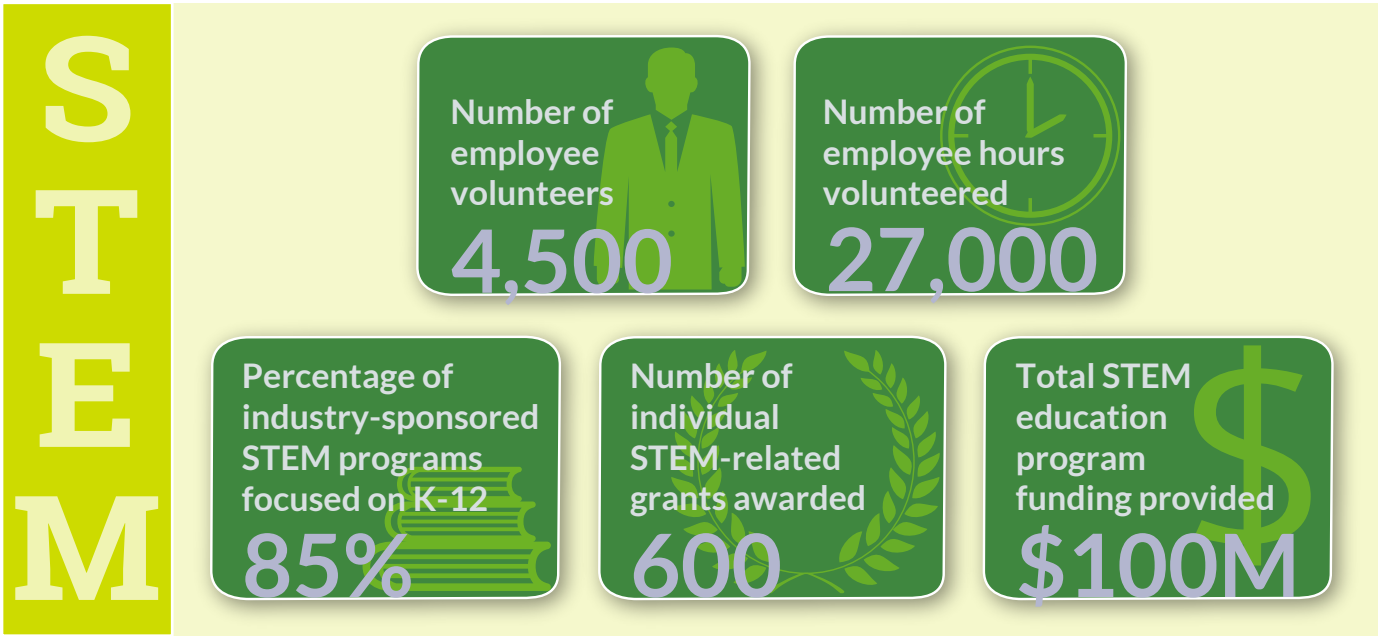
Setting **limits on wastewater discharges** to reduce environmental impact of manufacturing discharges[18]

Sources: Deloitte[17]; IFPMA[18]

The Biopharmaceutical Industry Is Advancing STEM Education in the United States

The STEM workforce accounts for more than 50% of the nation's sustained economic growth. From 2008 to 2012, PhRMA member companies and their foundations supported more than 90 STEM education programs across the United States, impacting more than 1.6 million students and 17,500 teachers.

PhRMA member company and foundation contributions to STEM education in the United States include:

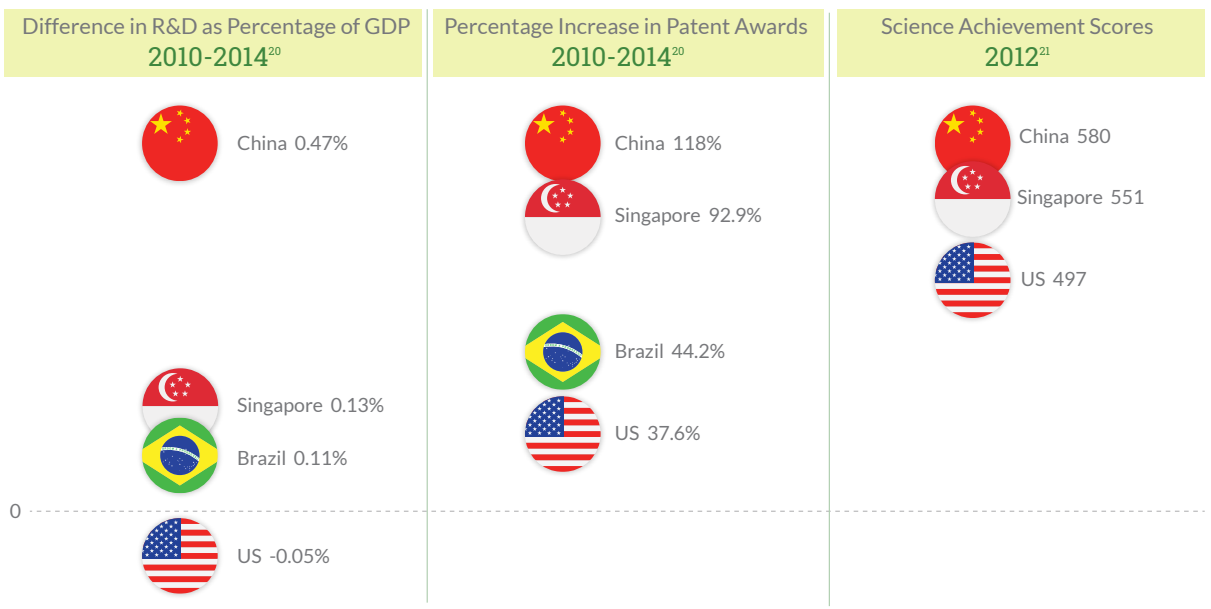


Source: Battelle Technology Partnership Practice[19]

Other Nations Are Challenging US Leadership in Biopharmaceutical Innovation

Emerging economies are exceeding US performance on key measures related to a robust biopharmaceutical environment.

> The United States is now facing increasing competition to attract and grow a biopharmaceutical presence, not just from developed countries, but also from emerging nations, such as Brazil, China, and Singapore, that are laying the groundwork for future growth."
>
> — TEConomy Partners[20]



Sources: TEConomy Partners[20,21]

Fostering Growth of the US Biopharmaceutical Industry Depends on Policies That Support R&D Investment

Industry analysts have consistently identified 3 policy areas as critical for the US biopharmaceutical industry to remain an engine of economic growth and innovation:

1

Strong
INTELLECTUAL PROPERTY
protections, including patent and regulatory data protection

2

A well-functioning, science-based
REGULATORY SYSTEM

3

COVERAGE AND PAYMENT POLICIES
that support and encourage medical innovation

> The capability to innovate is fast becoming the most important determinant of economic growth and a nation's ability to compete and prosper in the 21st century global knowledge-based economy."
>
> — Battelle Technology Partnership Practice[22]

Sources: Battelle Technology Partnership Practice, PhRMA[22]; Deloitte[23]

Notes and Sources

1. Wolfe RM; National Science Foundation, National Center for Science and Engineering Statistics. Businesses spent $375 billion on R&D performance in the United States in 2016. *InfoBriefs*. NSF 18-312. https://www.nsf.gov/statistics/2018/nsf18312/nsf18312.pdf. Published September 2018. Accessed April 2019.
2. NDP Analytics. IP-intensive manufacturing industries: driving US economic growth. http://www.ndpanalytics.com/s/IP-Report-2017.pdf. Published September 2017. Accessed April 2019.
3. NDP Analytics. IP-intensive manufacturing industries: driving US economic growth. http://www.ndpanalytics.com/s/IP-Report-2017.pdf. Published September 2017. Accessed April 2019.
4. National Science Foundation, National Center for Science and Engineering Statistics. Table 50: worldwide, domestic, and foreign total and R&D employment, by industry and company size: 2015. https://ncses.nsf.gov/pubs/nsf18313/#data-tables&. Published August 30, 2018. Accessed April 2019.
5. TEConomy Partners; for PhRMA. *The Economic Impact of the US Biopharmaceutical Industry 2017: National and State Estimates.* Columbus, OH: TEConomy Partners. In press.
6. TEConomy Partners; for PhRMA. *The Economic Impact of the US Biopharmaceutical Industry 2017: National and State Estimates.* Columbus, OH: TEConomy Partners. In press.
7. US Department of Commerce, International Trade Administration (ITA). *2016 Top Markets Report: Pharmaceuticals.* Executive summary. http://trade.gov/topmarkets/pdf/Pharmaceuticals_Executive_Summary.pdf. Published May 2016. Accessed June 2017.
8. US Census Bureau. U.S. international trade data. US Census Bureau website. https://www.census.gov/foreign-trade/data/index.html. Accessed March 2019.
9. NDP Analytics; for PhRMA. Analysis of the US Food and Drug Administration's Drug Establishments Current Registration Site. April 2019.
10. Hargreaves B. GSK ramps up Shingrix production with $100m investment. InPharma Technologist website. https://www.in-pharmatechnologist.com/Article/2019/04/25/GSK-ramps-up-investment-into-Shingrix-production. Published April 25, 2019. Accessed April 2019.
11. TEConomy Partners; for PhRMA. Biopharmaceutical industry-sponsored clinical trials: growing state economies. http://phrma-docs.phrma.org/files/dmfile/TEConomy_PhRMA-Clinical-Trials-Impacts.pdf. Published April 2019. Accessed May 2019.
12. TEConomy Partners; for PhRMA. *Driving Innovation and Economic Growth for the 21st Century: State Efforts to Attract and Grow the Biopharmaceutical Industry.* Columbus, OH: TEConomy Partners; December 2016.

Notes and Sources

13. National Science Foundation, National Science Board. *Science and Engineering Indicators 2018*. Chapter 8 Appendix Table 8-13: USPTO patents granted in pharmaceuticals, by region, country, or economy: 2000–16. https://www.nsf.gov/statistics/2018/nsb20181/data/appendix. Published 2018. Accessed April 2019.
14. TEConomy; for PhRMA. Analysis of Pitchbook data. https://pitchbook.com. April 2019.
15. Pharmaceutical Research and Manufacturers of America (PhRMA) analysis of PitchBook Venture Investment database. https://pitchbook.com. Accessed December 2018.
16. 4Q 2018 Pitchbook-NVCA Venture Monitor. https://pitchbook.com/news/reports/4q-2018-pitchbook-nvca-venture-monitor. Published January 2019. Accessed April 2019.
17. Jacoby R, Pernenkil L, Harutunian S, et al.; Deloitte. Advanced biopharmaceutical manufacturing: an evolution underway. https://www2.deloitte.com/content/dam/Deloitte/us/Documents/life-sciences-health-care/us-lshc-advanced-biopharmaceutical-manufacturing-white-paper-051515.pdf. Published 2015. Accessed May 2017.
18. International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). Industry roadmap for progress on combating antimicrobial resistance. https://www.ifpma.org/resource-centre/industry-roadmap-for-progress-on-combating-antimicrobial-resistance. Published September 20, 2016. Accessed April 2018.
19. Battelle Technology Partnership Practice; for PhRMA. STEM: building a 21st century workforce to develop tomorrow's new medicines. http://phrma-docs.phrma.org/sites/default/files/pdf/stem-education-report-2014.pdf. Published January 2014. Accessed May 2017.
20. TEConomy Partners; for PhRMA. Closing the gap: increasing global competition to attract and grow the biopharmaceutical sector. http://phrma-docs.phrma.org/files/dmfile/PhRMA-InternationalReport-vfinal.pdf. Published June 2017. Accessed June 2017.
21. TEConomy Partners; for PhRMA. Enhancing today's STEM workforce to ensure tomorrow's new medicines: biopharmaceutical industry partnerships with U.S. colleges and universities. http://phrma-docs.phrma.org/files/dmfile/TEConomy-PhRMA-STEM-Report-Final.pdf. Published June 2017. Accessed June 2017.
22. Battelle Technology Partnership Practice, Pharmaceutical Research and Manufacturers of America (PhRMA). The US biopharmaceutical industry: perspectives on future growth and the factors that will drive it. http://www.phrma.org/sites/default/files/pdf/2014-economic-futures-report.pdf. Accessed May 2017.
23. Lesser N, Terry C, Wu J, et al.; Deloitte. In the face of uncertainty: a challenging future for biopharmaceutical innovation. http://www2.deloitte.com/content/dam/Deloitte/lu/Documents/life-sciences-health-care/us_consulting_Inthefaceofuncertainty_040614.pdf. Published 2014. Accessed May 2017.

8 INTERNATIONAL COSTS AND ACCESS

Prescription Medicines in Other Developed Countries

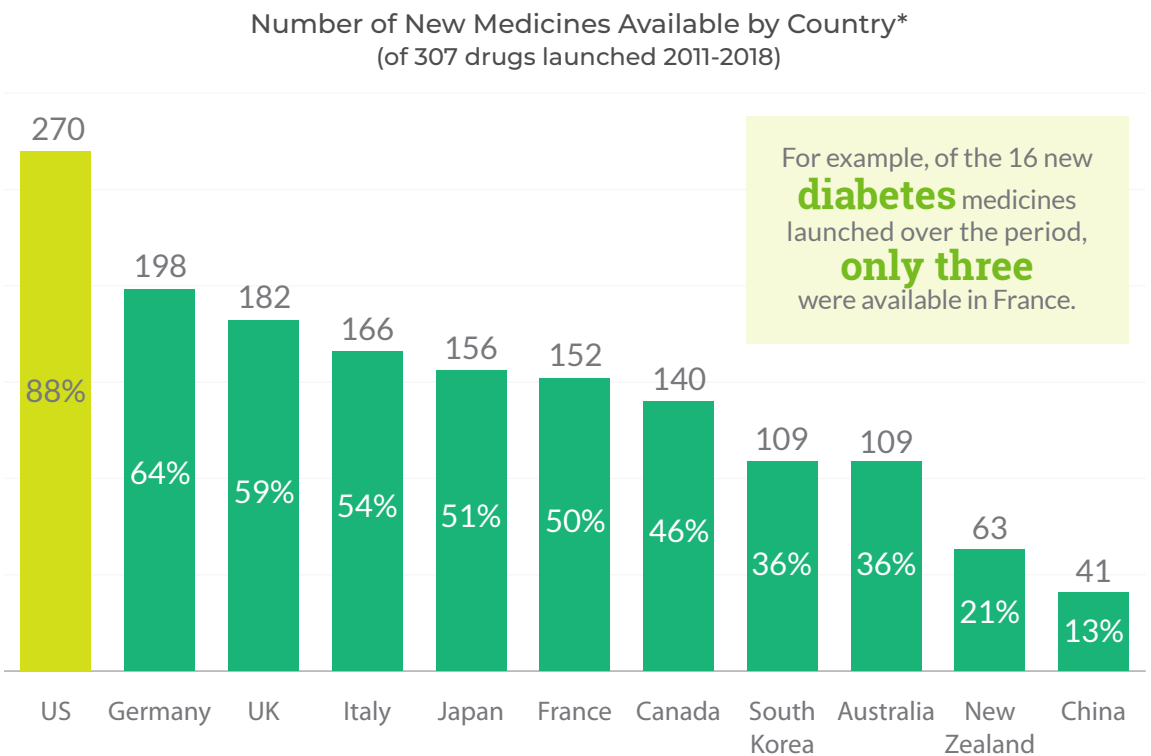
Of the new medicines launched globally each year, far more are available in the United States than in other developed countries. As a result, US patients have better outcomes for conditions where new medicines are most critical.

Spending on prescription medicines is a similarly small percentage of total health care spending in the United States as in other developed countries. Consequently, medicines account for a small share of the overall difference in per capita health spending between the US and these other countries.

US market-based prices for new medicines incentivize the large and uncertain investments required to bring new medicines to market. While the US system makes efficient use of cost saving generics and competition among brand medicines, other wealthy countries use a variety of government mandates or controls to set artificially low prices for new medicines. Emulating those practices in the United States would lead to reduced R&D and innovation, harming patients with unmet medical needs.

More Medicines Are Available to US Patients

Nearly 90% of newly launched medicines from 2011 to 2018 were available in the United States, compared to just two-thirds in Germany, half in France, and even less in Canada and Australia.



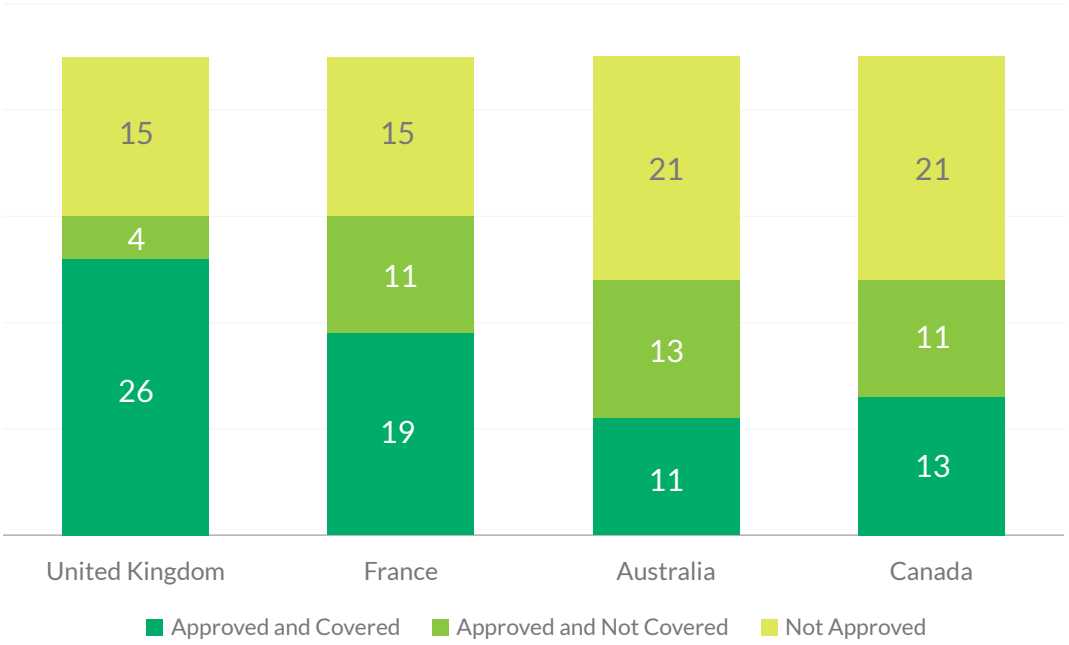
*New Molecular Entities (NMEs) approved by the FDA, European Medicines Agency (EMA), and/or Japan's Pharmaceuticals and Medical Devices Agency (PMDA), and launched in any country between 2011 and 2018.

Source: PhRMA analysis of IQVIA Analytics Link and FDA, EMA, and PMDA data[1]

US Patients Have Significantly Greater Access to New Cancer Medicines

Other developed countries use centralized government price setting and coverage decisions to manage drug spending. As a result, patients in those countries have fewer cancer medicines available to them than US patients.

International Approval and Coverage Decisions of 45 Oncology Drugs Approved in the US and Covered by Medicare, 2009-2013

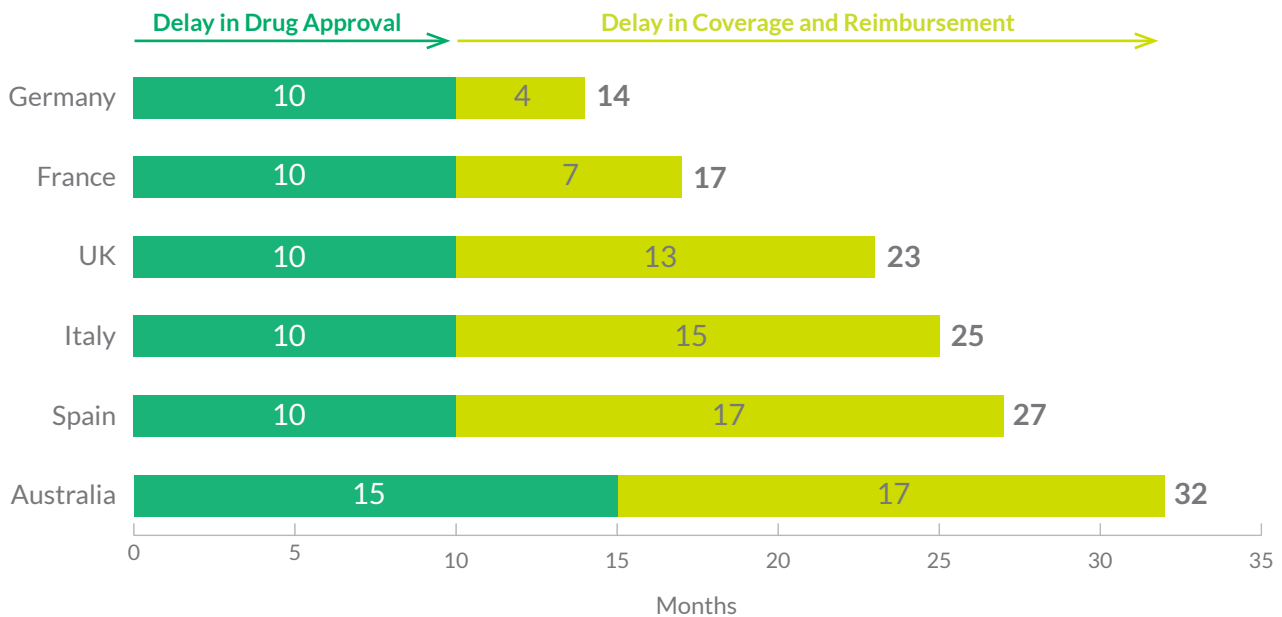


Source: Zhang Y et al.[2]

US Patients Have Access to Cancer Medicines on Average 2 Years Earlier

To the extent that patients in other developed countries have access to cancer medicines, they have to wait longer to access those medicines compared to patients in the United States.

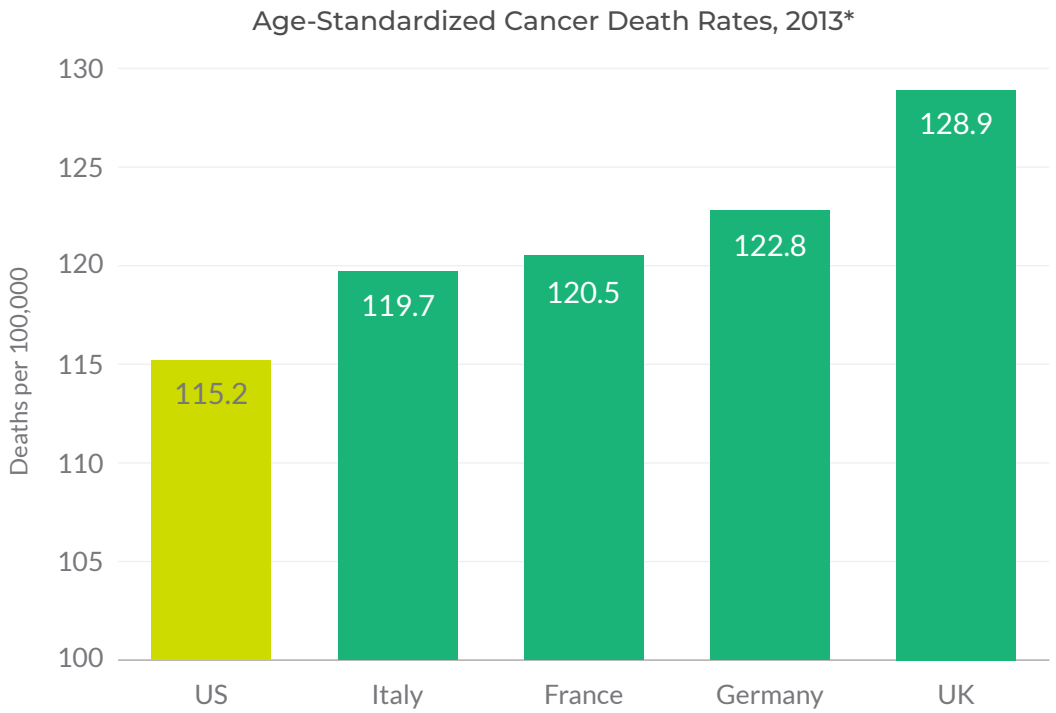
Average Delays in Oncology Medicine Approval and Reimbursement in Other Countries Following US Approval, 2010-2014



Source: IMS Consulting Group[3]

US Patients Have Better Outcomes for Conditions Where New Drugs Are Most Critical

Cancer death rates are lower in the United States, where patients have greater and more timely access to cancer medicines than in other developed countries.

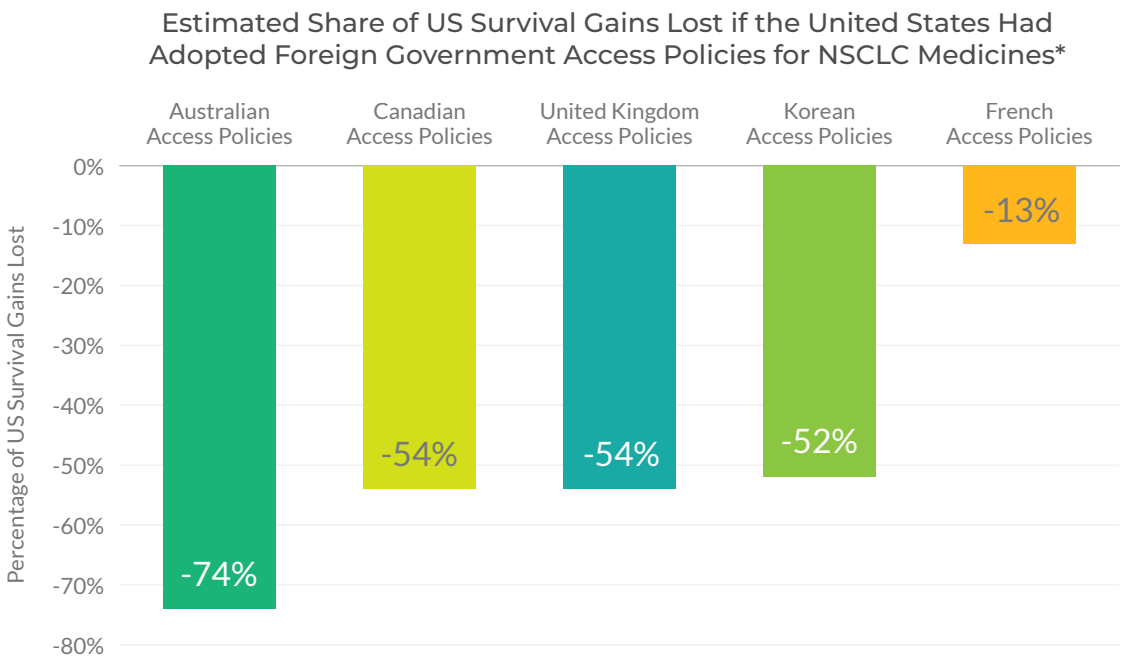


*2013 is the latest year for which data are available for all listed countries.

Source: PhRMA analysis of WHO data[4]

Lung Cancer Patients Experience Better Survival Under the Market Access Policies in the United States

American patients diagnosed with locally advanced and metastatic non-small cell lung cancer (NSCLC) gained an estimated 201,700 life-years in total due to innovative medicines being made available with little to no delay after regulatory approval. Half of these survival gains would have been lost if the United States had adopted health technology assessment frameworks like those used by foreign governments to determine access to care.

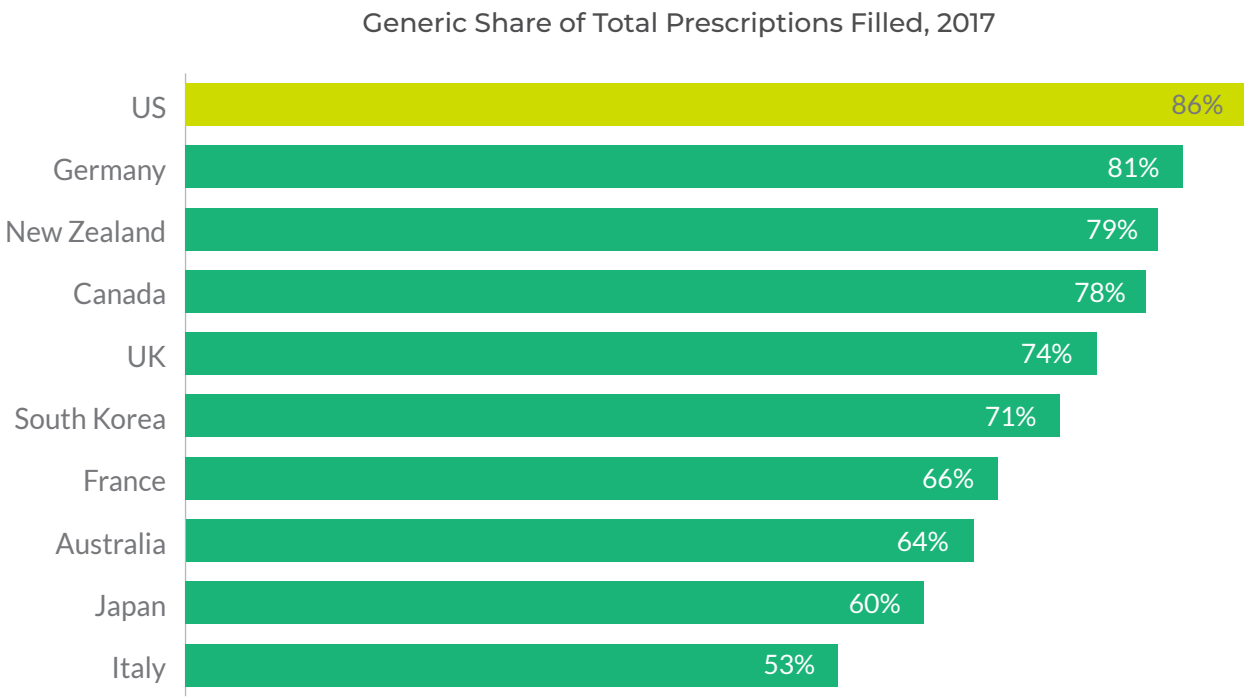


*US NSCLC patients diagnosed between 2006 and 2017

Source: IHS Markit[5]

Use of Generic Medicines Is Highest in the United States

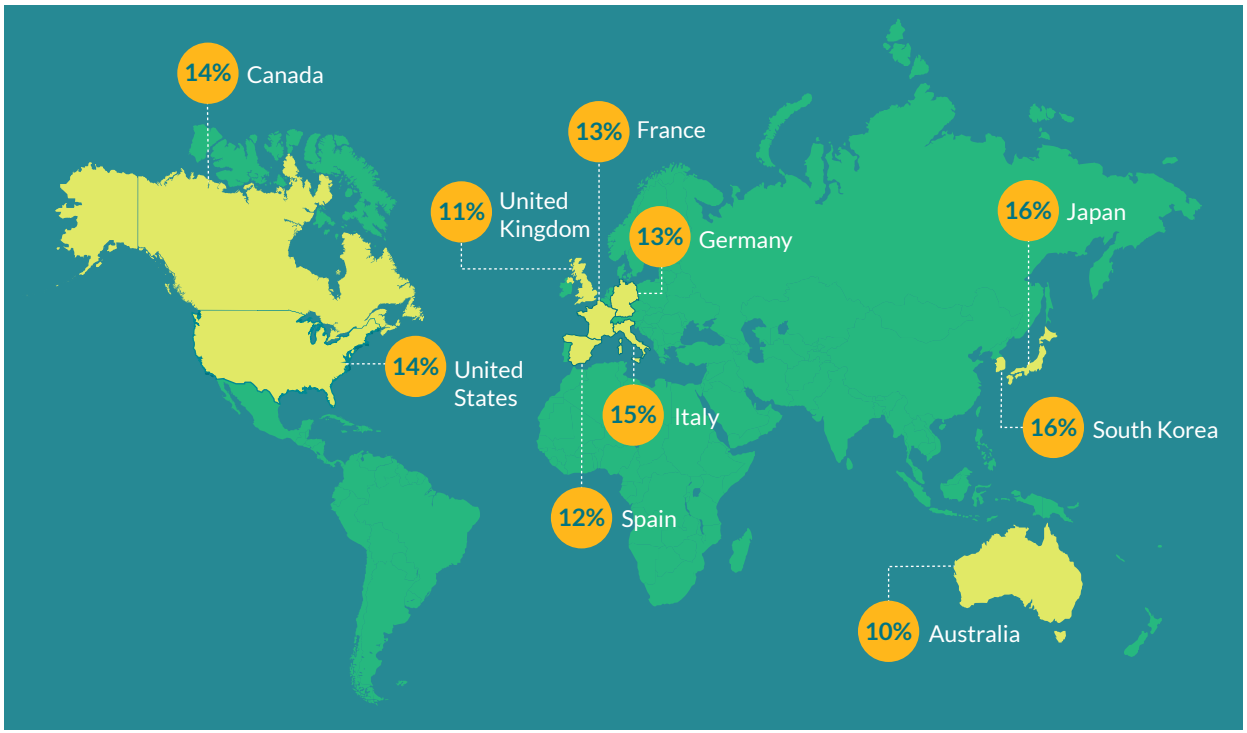
Payers in the United States drive rapid and widespread adoption of generic medicines, allowing them to devote more resources toward covering and reimbursing innovative medicines than payers in other developed countries.



Source: PhRMA analysis of IQVIA MIDAS® data[6]

Spending on Prescription Medicines Is a Small Percentage of Total Health Care Spending Around the World

Prescription Medicines as a Percentage of Total Health Care Spending,* 2015

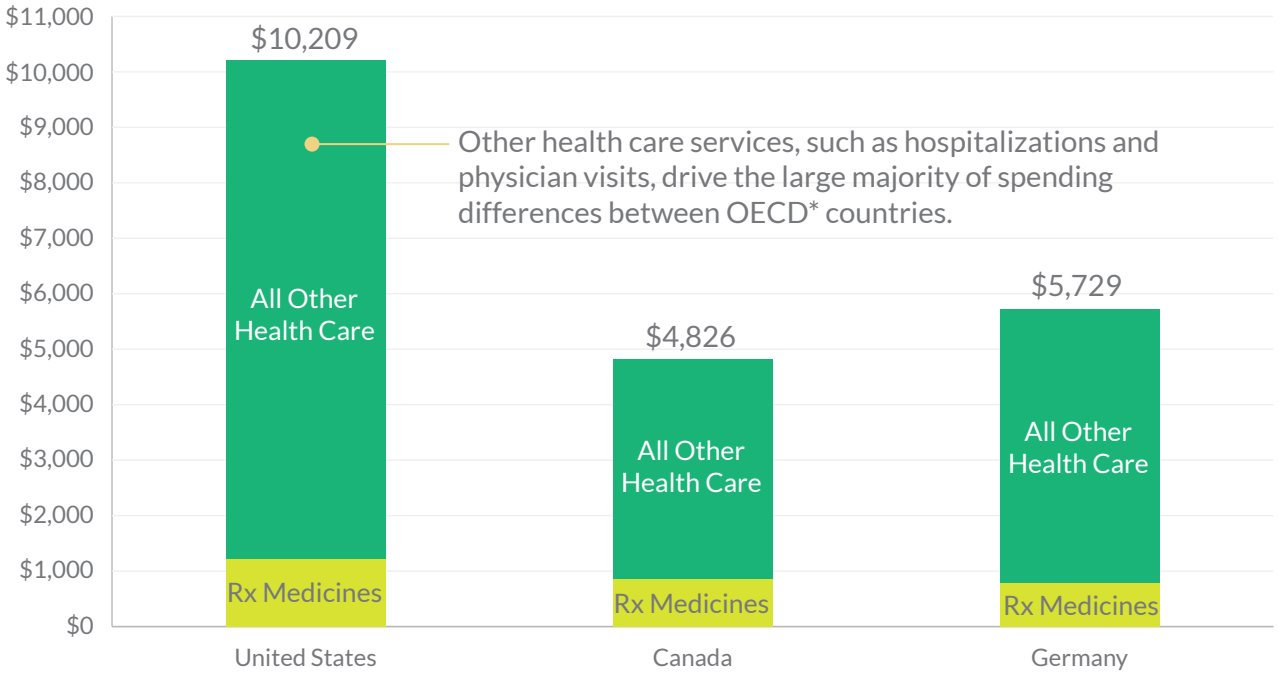


*Total health care spending includes hospital care, physician and clinical services, home health and nursing home care, government administration and net cost of private health insurance, dental and other professional services, as well as durable medical equipment.

Source: Altarum Institute[7]

Medicines Account for a Small Share of Health Spending Differences Between the United States and Other Countries

Per Capita Health Care Spending in the United States, Canada, and Germany, 2017



*Organisation for Economic Co-operation and Development

Source: PhRMA analysis of OECD data[8]

If Governments of Other Wealthy Countries Valued Medicines Fairly, Patients Globally Would Benefit

If prices for medicines in other OECD countries were just 20% higher, the resulting increase in R&D would benefit patients around the world, including those in the United States.

A shift toward market-based drug prices in other wealthy countries would result in:

1.1 years
of increased life expectancy for an American who is 15 years old today[9]

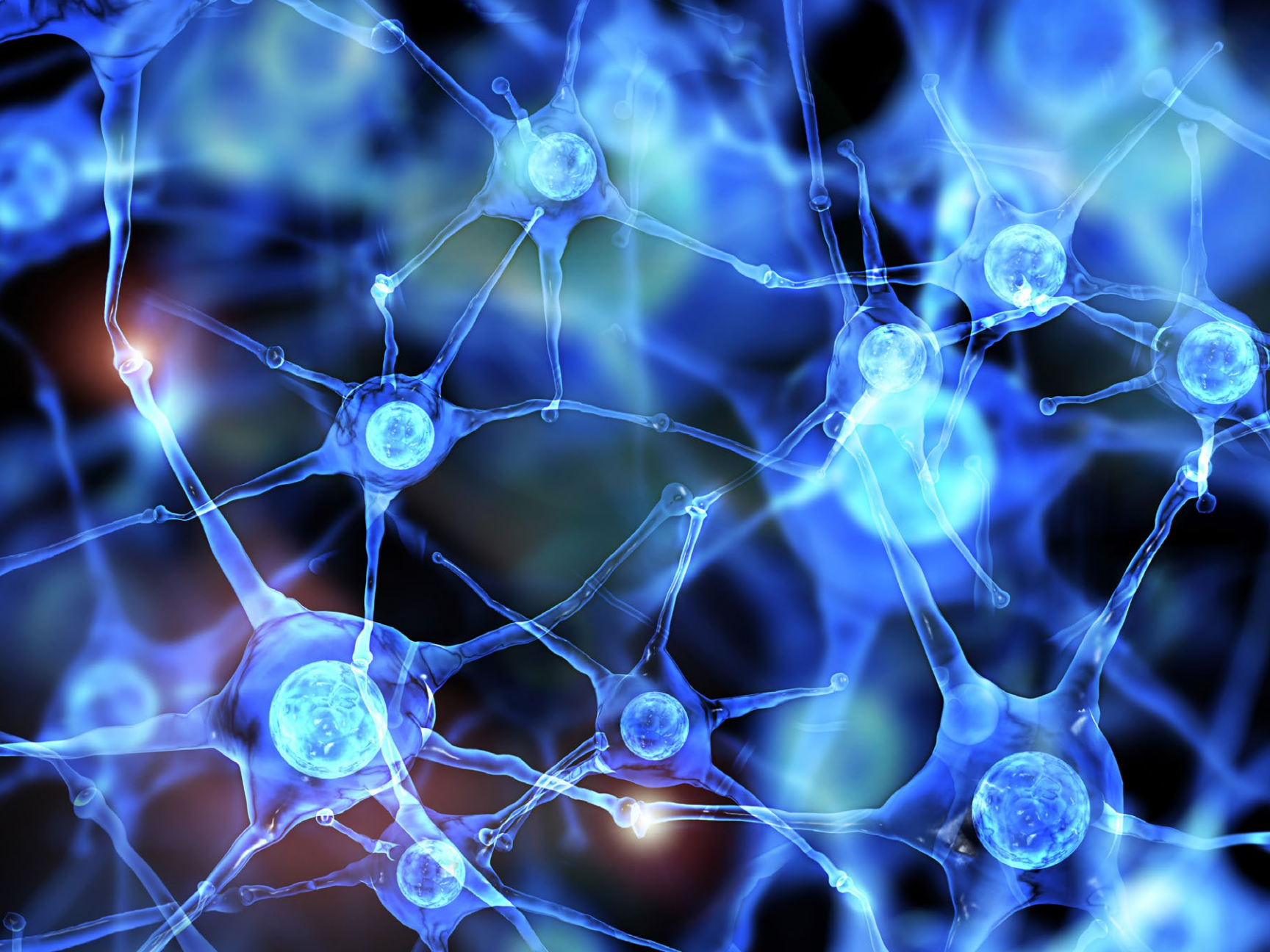
9% more
new treatments available annually by 2030—equivalent to 8 more new drugs launched in 2030 alone[9]

Welfare gains of
$10 trillion
for Americans and
$7 trillion
in other OECD countries over the next 50 years[10]

Sources: Schwartz TT et al.[9]; USC Schaeffer Center[10]

Notes and Sources

1. IQVIA Analytics Link. https://www.iqvia.com/solutions/commercialization/market-analysis/analytics-link. Accessed May 2019.
2. Zhang Y, Hueser HC, Hernandez I. Comparing the approval and coverage decisions of new oncology drugs in the United States and other selected countries. *J Manag Care Spec Pharm.* 2017;23(2):247-254.
3. IMS Consulting Group report for PhRMA. Patient access to innovative oncology medicines across developed markets. June 2016.
4. World Health Organization (WHO). WHO mortality database. http://www.who.int/healthinfo/mortality_data/en. Accessed May 2019. PhRMA analysis of data, using age-specific death rates.
5. Su W, Lockwood C; IHS Markit. Comparing health outcome differences due to drug access: a model in non-small cell lung cancer. https://cdn.ihs.com/www/prot/pdf/0119/IHSM_NSCLC%20HTA%20model%20white%20paper_18Jan2019r.pdf. Published December 13, 2018. Accessed April 2019.
6. IQVIA MIDAS® audited data. April 2019.
7. Altarum Institute; for PhRMA. A ten year projection of the prescription drug share of national health expenditures including non-retail. https://altarum.org/sites/default/files/uploaded-publication-files/Non-Retail%20Rx%20Forecast%20Data%20Brief%20with%20Addendum%20May%202017.pdf. Published October 2014. Updated May 2017. Accessed June 2018.
8. Organisation for Economic Co-operation and Development (OECD). Health resources. Health spending and pharmaceutical spending indicators. https://www.oecd-ilibrary.org/social-issues-migration-health/health-resources/indicator-group/english_777a9575-en
9. Schwartz TT, Ward AS, Xu XM, et al. The impact of lifting government price controls on global pharmaceutical innovation and population health. *Value Health.* 2018;21(suppl 1):S119.
10. Goldman D, Lakdawalla D; Leonard D. Schaeffer Center for Health Policy & Economics (USC Schaeffer Center). The global burden of medical innovation. http://healthpolicy.usc.edu/Global_Burden_of_Medical_Innovation.aspx. Published January 2018. Accessed May 2018.



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