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Cover photo: Jennifer O’Neil and Yingzi Yue, Merck cancer researchers
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 use of prescribed therapies, and the contributions of the biopharmaceutical sector.

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 about the role of medicines and the US economy.
Medicines’ Impact on Health and Quality of Life

Prescription medicines continue to yield 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 HIV/AIDS, cancer, and heart disease, resulting in decreased death rates, improved health outcomes, and better quality of life for patients. Recent advances continue to improve outcomes for patients and are slowing disease progression, preventing complications and the need for medical care across a broad range of chronic conditions—including, for example, asthma, diabetes, and hepatitis C. Today’s medicines are at the forefront of science, with many new drugs taking a targeted approach to attacking the underlying causes of disease. Advances such as these are opening up doors to the development of first-time treatments for many rare diseases and other unmet medical needs. Continued advances in biopharmaceutical innovation will be critical in addressing future health care challenges and improving health outcomes for patients.
Increases in US Life Expectancy

While nutrition, sanitation, other public health measures, and expanded access to care have been major sources of increasing human health, innovative medicines have also played a profound role in this progress.

— President’s Council of Advisors on Science and Technology

US Life Expectancy, 1950-2013*

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

Sources: President’s Council of Advisors on Science and Technology; Centers for Disease Control and Prevention (CDC)
A Decade of Advances

2005
• First new kidney cancer Rx in more than a decade
• 3 new therapies for diabetes

2006
• First vaccine for the prevention of cervical cancer
• First Rx for chronic chest pain in 20 years
• First once-a-day HIV medicine

2007
• New class of medicines to treat high blood pressure
• First treatment for fibromyalgia

2008
• A new type of treatment for Crohn’s disease
• The first Rx for symptoms of Huntington’s disease

2009
• First treatment for peripheral T-cell lymphoma
• First new Rx for gout in 40 years

2010
• 2 new multiple sclerosis drugs
• First therapeutic cancer vaccine

2011
• First lupus drug in 50 years
• 2 new personalized medicines

2012
• First drug to target root cause of cystic fibrosis
• First drug to treat Cushing’s disease

2014
• Oral treatments for hepatitis C provide cure rates of more than 90%
• 17 new drugs to treat patients with rare diseases

2015
• 2 new drugs for difficult-to-treat forms of high cholesterol
• New cystic fibrosis drug for patients with a genetic mutation that is the most common cause of the disease

Source: US Food and Drug Administration (FDA)
Medicines Are Transforming the Treatment of Many Diseases

**HIV/AIDS**
During the past 2 decades, advances in treatment have contributed to a nearly 87% decline in death rates and transformed the disease from an acute, fatal illness to a chronic condition.8

**Cystic Fibrosis (CF)**
Advances in understanding the genetic mutations that cause CF have led to the development of highly targeted treatments—including for patients with a mutation known to be the most common cause of the disease.4

**Cancer**
New therapies have contributed to a nearly 23% decline in cancer deaths since the 1990s. Today, 2 out of 3 people diagnosed with cancer survive at least 5 years.6,7

**Rheumatoid Arthritis (RA)**
Therapeutic advances have transformed the RA treatment paradigm over the past 20 years, shifting from a focus on managing symptoms to aiming for slowed disease progression and even disease remission.5

Sources: FDA4; Boston Healthcare Associates5; National Cancer Institute (NCI)6; American Cancer Society7; CDC8
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®
HIV/AIDS: Decline in Death Rates

The number of US AIDS deaths decreased dramatically following the introduction of highly active antiretroviral treatment (HAART). 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.

*Actual vs. Projected Death Rates for HIV/AIDS in the United States*

Sources: CDC, Truven Health Analytics
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.

1981
AIDS first reported

1984
HIV identified as the cause of AIDS

1987
First treatment (AZT) introduced (a nucleoside analog reverse-transcriptase inhibitor)

1991
AZT labeling expanded for dosing (IV), earlier use, and pediatric use

1994
AZT found to reduce the risk of transmission from mother to infant

1995
First protease inhibitors approved

1996
HAART combinations introduced

1998
First nucleotide analog approved

2001
First fusion inhibitors approved

2003
First fusion inhibitors approved

2006
First one-pill-once-a-day treatment approved

2007
First CCR-5 co-receptor agonist approved

2011
US HHS recommends earlier initiation of treatment to control immunologic response

2015
US death rate dropped 87% since the introduction of HAART

Sources: Boston Healthcare Associates12; CDC13
Cancers: Decline in Death Rates

Since peaking in the 1990s, cancer death rates have declined 23%.\textsuperscript{14} Approximately 83% of survival gains in cancer are attributable to new treatments, including medicines.\textsuperscript{15}

\textit{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 of Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University\textsuperscript{16}

\textbf{Percent Change by Decade in US Death Rates From Cancer}\textsuperscript{14}

Sources: NCI\textsuperscript{14}; Sun E, et al.\textsuperscript{15}; Dunellari A\textsuperscript{16}
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.17

• After initial approval, continued research revealed that imatinib had a greater impact when initiated earlier in the progression of the disease.

• Further research also 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.18

• Today, survival rates have improved dramatically, and CML patients are living close to normal life spans.19

Sources: Boston Healthcare Associates17; PhRMA18; Gambacorti-Passerini C, et al.19; American Cancer Society20; Druker BJ, et al.21
Rare Diseases: Drug Approvals for Rare Diseases Have Increased

Rare diseases are those that affect 200,000 or fewer people in the United States. The FDA has approved more than 500 orphan drugs since the passage of the Orphan Drug Act in 1983.

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

Source: FDA
Cardiovascular Disease: Declining Rates of Death

Tremendous strides have been made in reducing cardiovascular disease morbidity and mortality, thanks in part to new medicines. The death rate from heart disease has declined about 38% over the past decade alone.\textsuperscript{24}

\textit{US Death Rates Due to Diseases of the Heart*}

*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 Classification of Diseases, Tenth Revision (ICD-10).

Source: CDC\textsuperscript{24,25}
Hepatitis C (HCV): Cure Rates Are Rising

Sources: Armstrong GL, et al.26, PhRMA27
Projected Reductions in Hepatitis C–Related Complications

Increased screening and the availability of new treatments for hepatitis C are projected to dramatically reduce complications associated with the disease. Projections suggest that the number of liver-related deaths avoided will total 126,500 by 2050.28

![Avoided Cases of Hepatitis C–Related Complications by 2050](chart)

Source: Kabiri M, et al.28
Future Impact: Need for New Treatments for Alzheimer’s Disease

The development of a new treatment that delays the onset of Alzheimer’s could reduce Medicare and Medicaid spending on patients with Alzheimer’s 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*


Notes and Sources


Notes and Sources


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 7,000 medicines in development around the world. In 2015, PhRMA member companies invested an estimated $58.8 billion 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, and it has become more costly and complex over the past decade. Scientific complexities are creating new challenges in R&D, and biopharmaceutical companies are working to create efficiencies and are collaborating with others across the research ecosystem to navigate through the complexities.
More Than 7,000 Medicines in Development Globally

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

- **CANCERS**: 1,919
- **CARDIOVASCULAR DISEASE**: 563
- **INFECTIOUS DISEASES**: 1,261
- **IMMUNOLOGICAL DISORDERS**: 1,123
- **DIABETES**: 401
- **MENTAL HEALTH DISORDERS**: 510
- **HIV/AIDS**: 208
- **NEUROLOGICAL DISORDERS**: 1,308

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

Source: Adis R&D Insight Database¹
Potential First-in-Class Medicines in the Pipeline

An average of 70% of drugs across the pipeline are potential first-in-class medicines.

*Percentage of Projects in Development That Are Potentially First-in-Class Medicines in Selected Therapeutic Areas, 2011*

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurology</td>
<td>84%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>81%</td>
</tr>
<tr>
<td>Cancer</td>
<td>80%</td>
</tr>
<tr>
<td>Psychiatry</td>
<td>79%</td>
</tr>
<tr>
<td>Immunology</td>
<td>72%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>71%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>69%</td>
</tr>
<tr>
<td>Infections</td>
<td>57%</td>
</tr>
</tbody>
</table>

Source: Analysis Group²
Cutting-Edge Research Drives Development of Medicines

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

**MULTIPLE SCLEROSIS**

Anti-LINGO-1 Antibodies can protect the nerves damaged by multiple sclerosis by spurring myelin growth.

**CANCER**

Chimeric Antigen Receptor (CAR) T-Cell Immunotherapy involves the personalized modification of immune-boosting T-cells to target and kill blood cancer cells.

Cancer Metabolism-Targeting Drugs disrupt cancer cell metabolism and can impede cancer cell growth.

**RARE DISEASES**

Viral-Based Gene Therapies involve using a virus to insert a therapeutic gene into removed stem cells, then returning the cells to the patient.

Source: PhRMA³
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. The rapid pace of the science holds significant promise for the future.

Source: PhRMA®
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.

73% of cancer medicines
42% of new medicines

in the PIPELINE have the potential to be

MORE THAN 25% of new medicines approved by the FDA in 2015 were PERSONALIZED MEDICINES

Sources: Personalized Medicine Coalition5; Tufts Center for the Study of Drug Development (CSDD)6
Biopharmaceutical Firms Conduct the Largest Share of Biomedical Research in the United States

The biopharmaceutical industry was the source of nearly half of all US biomedical research funding in 2012, accounting for the largest share of funding, public or private.

*Share of US Biomedical Research Funding, 2012*

- **Biopharmaceutical Industry, 49%**
- **National Institutes of Health (NIH), 27%**
- **Medical Device Industry, 10%**
- **Foundations, Charities, Other Private Sector, 4%**
- **Other Federal Government Entities, 6%**
- **State and Local Government Entities, 5%**

*Total US biomedical research funding in 2012 estimated to be $116.5 billion. The biopharmaceutical industry’s total share of funding comprised funding from pharmaceutical firms (32%) and biotechnology firms (17%).*  

Source: Moses H III, et al.  

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2 • Research and Development
The Lengthy, Costly, and Uncertain Biopharmaceutical Research and Development Process

From drug discovery through FDA approval, developing a new medicine on average takes 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.

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*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.


Source: PhRMA adaptation based on DiMasi JA, et al.; Tufts CSDD; FDA®
Biopharmaceutical Research Companies Play a Pivotal Role in Drug Discovery and Development

The private sector makes the largest R&D contributions in translating basic research findings into therapeutic advances for patients.

*Share of Contributions to Key R&D Milestones for the Most Transformative Drugs of the Past 25 Years*

```
<table>
<thead>
<tr>
<th>Milestone</th>
<th>Discovery</th>
<th>Development</th>
<th>Manufacturing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public</td>
<td>42%</td>
<td>27%</td>
<td>19%</td>
</tr>
<tr>
<td>Private</td>
<td>58%</td>
<td>73%</td>
<td>81%</td>
</tr>
</tbody>
</table>
```

"Today, most important developments in medical science typically begin in laboratories, such as the discovery of specific new biological molecules, processes, or pathways, or innovative applications of existing knowledge. In most cases, these discoveries in and of themselves have limited effect beyond meeting a fairly narrow research goal. **Their real impact for public health generally comes after several more significant steps—including further R&D, testing, approval by appropriate regulatory bodies (such as the FDA), manufacturing, and distribution.**

— NIH, Office of Intramural Research (OIR), Office of Technology Transfer (OTT)\(^\text{10}\)

Sources: Tufts CSDD\(^\text{9}\); NIH OIR OTT\(^\text{10}\)
Biopharmaceutical Companies Do the Vast 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 critical mass, expertise, and experience needed to develop new medicines.12

2015 PhRMA Member Companies
Biopharmaceutical R&D Investment: $58.8 Billion (est.)11,13

2015 TOTAL NIH Budget: $30.3 Billion11,14

In addition to biopharmaceutical R&D, the NIH budget includes funding in support of medical devices, diagnostics, prevention, training, and other activities.

Sources: Tufts CSDD12; PhRMA13; NIH14
Innovative Biopharmaceutical Companies Sit at the Heart of a Dynamic R&D Ecosystem in the United States

While research-based biopharmaceutical companies are responsible for bringing new medicines to patients, they are part of an ecosystem marked increasingly by collaborations with academic institutions, government agencies, venture capital firms, nonprofit foundations, patients, and others.
Collaboration Is Key in Researching and Developing New Medicines

The rapid pace of science and technological advances is propelling a new era in biopharmaceutical innovation in the United States. Along with these advances come complexities in translating complex learnings into medical advances. Partnerships are crucial to address these challenges. Select examples of key collaborative efforts across the R&D spectrum include:

**AMP (ACCELERATING MEDICINES PARTNERSHIP)**

Developing new diagnostics and biological targets for treatments in Alzheimer’s disease, type 2 diabetes, rheumatoid arthritis, and lupus

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

**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

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

**LUNG-MAP (LUNG CANCER MASTER PROTOCOL)**

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

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

Sources: NIH\(^{16}\); Foundation for NIH\(^{17}\); Lung-MAP\(^{18}\)
PhRMA Member Company R&D Investment

The pharmaceutical industry is one of the most research-intensive industries in the United States. Pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm.

— Congressional Budget Office (CBO)¹⁹

PhRMA Member Company R&D Expenditures, 1995-2015

*Estimated fiscal year 2015

Sources: CBO¹⁹, PhRMA²⁰
The Costs of Drug Development Have More Than Doubled Over the Past Decade

Less than 12% of the candidate medicines that make it into phase I clinical trials are approved by the FDA, less than half the rate a decade ago.

*Previous research by the same author 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? *Managerial Decis Economics.* 2007;28:469-479). That estimate is based on the same underlying survey as the author’s 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.

Source: DiMasi JA, et al. 21
Setbacks in Alzheimer’s Disease Research Provide Stepping Stones for Future Innovation

Since 1998, 123 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.

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

Developing a new cancer medicine is a complex process, fraught with setbacks, but these so-called “failures” are not wasted efforts. Researchers learn from them to inform future study and direct 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
Chief, Breast Medicine Service, Memorial Sloan Kettering Cancer Center; Professor, Weill Cornell Medical College

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**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.23; PhRMA24
The Complexity of Clinical Trials Has Increased

During the past decade, clinical trial designs and procedures have become much more complex, demanding more staff time and effort and discouraging patient enrollment and retention.

*Trends in Clinical Trial Protocol Complexity*

<table>
<thead>
<tr>
<th></th>
<th>2000-2003</th>
<th>2008-2011</th>
<th>Increase in Complexity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Procedures per Trial Protocol (median) (eg, bloodwork, routine exams, x-rays)</td>
<td>105.9</td>
<td>166.6</td>
<td>57%</td>
</tr>
<tr>
<td>Total Investigative Site Work Burden (median units)</td>
<td>28.9</td>
<td>47.5</td>
<td>64%</td>
</tr>
<tr>
<td>Total Eligibility Criteria</td>
<td>31</td>
<td>46</td>
<td>48%</td>
</tr>
<tr>
<td>Clinical Trial Treatment Period (median days)*</td>
<td>140</td>
<td>175</td>
<td>25%</td>
</tr>
<tr>
<td>Number of Case Report Form Pages per Protocol (median)</td>
<td>55</td>
<td>171</td>
<td>211%</td>
</tr>
</tbody>
</table>

*These numbers reflect the “treatment duration” of the protocol only.

Source: Getz KA, et al.; Tufts CSDD25
Innovative Biopharmaceutical Companies Seek to Improve R&D Efficiency

Biopharmaceutical companies are using new approaches to increase R&D efficiency and effectiveness.

Select examples include:

• Improving target validation methods to allow for greater accuracy in identifying and selecting the most promising drug candidates

• Enhancing IT infrastructure to improve efficiencies in translating drug discovery and preclinical data into clinical research activity

• Using adaptive trial designs to improve late-stage success rates and optimize clinical trial performance and data quality

“Biopharmaceutical companies...are using a wide variety of innovative approaches to adapt the R&D and manufacturing process to the changing scientific landscape. These innovative approaches to drug discovery, development, and manufacturing shed light on a resilient enterprise making progress in improving the quality, performance, and efficiency of R&D and manufacturing.”

— Tufts Center for the Study of Drug Development

Source: Tufts CSDD
Modernizing the Drug Discovery and Development Process

The use of novel drug development tools will enable researchers to follow the trajectory of the science, which is creating new avenues of research, exploration, and discovery.

- **Increasing acceptance of innovative clinical trial designs**
  Create efficiencies in development through use of adaptive clinical trial designs as well as increased use of advanced data analytics.

- **Accelerating qualification and use of biomarkers**
  Speed development timelines by creating efficiencies in review of biomarkers in order to advance personalized medicines and companion diagnostics.

- **Integrating patient perspective**
  Advance patient-centered drug development at the FDA and throughout clinical trials process through appropriate use of real-world evidence and increased patient engagement.
Notes and Sources


Notes and Sources

11. Total National Institutes of Health (NIH) spending is for fiscal year 2015. In addition to funding for basic and applied research, the total NIH budget includes funding in support of prevention (e.g., suicide prevention), diagnostics and medical devices, Superfund Research Program activities, training and education (e.g., dental), program evaluation, management and support, buildings and facilities, and other activities. PhRMA member companies’ R&D spending is estimated for calendar year 2015. PhRMA member companies account for the majority of private biopharmaceutical R&D spending. Nonmember company data are not included.


Notes and Sources


Biopharmaceutical competition begins in the research and development (R&D) process, well before a medicine ever reaches a patient. Companies “race” to bring the first medicine in a therapeutic class to market, and once a medicine is approved, it typically faces swift competition from other brands in its class. The US prescription drug lifecycle promotes innovation while providing built-in cost containment because brands eventually lead to lower-cost generics—and soon many biosimilars—that bring long-term value to patients.

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. Recent research has found that average lifetime revenues from new drug launches have declined. Health plans have powerful tools, such as tiered formularies and step therapy, to manage the use of medicines, and negotiating power is increasingly concentrated among fewer pharmacy benefit managers, driving large rebates that reduce overall drug spending. Meanwhile, the market is rapidly evolving, increasingly linking payment to quality and value.
Illustrative Pharmaceutical Lifecycle

New pharmaceutical medicines face competition after a relatively short period on the market.

Average time to develop a new medicine = at least 10 yrs

Average time on market before generic entry = 12.5* yrs

*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: PhRMA¹; Grabowski H, et al.²; Tufts CSDD³
Increasing Competition Within Therapeutic Categories

The time a medicine is the only drug available in its pharmacologic class declined from a median of more than 10 years in the 1970s to close to 2 years in the 2000s.

*Time Between Approval of First and Second Medicines in a Pharmacologic Class*

Half of second medicines in a class were approved within 2.3 years of the first medicine’s approval. One-quarter were approved within just 4 months.

Source: Tufts CSDD⁴
Earlier and More Frequent Patent Challenges by Generic Companies

As early as 4 years after brand launch, a generic company may file with the FDA a Paragraph IV certification 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

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>14.3</td>
</tr>
<tr>
<td>2005</td>
<td>8.5</td>
</tr>
<tr>
<td>2014</td>
<td>5.2</td>
</tr>
</tbody>
</table>

*...and are more common*

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

<table>
<thead>
<tr>
<th>Year</th>
<th>25%</th>
<th>60%</th>
<th>94%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: 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.5
Newly Introduced Generics Are Adopted Rapidly

When a generic version of a medicine becomes available for the first time, it captures an average of three-quarters of the market within 3 months, and some generics capture as much as 90% by that time.

*Average Generic Share of Total Use Following Launch of a Brand Medicine’s First Generic, 2013-2014*

*Average monthly generic share of total standardized units of a unique molecule/form combination

Sources: Grabowski H, et al. 6; Express Scripts 7
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.

![Present Value of Lifetime Sales of Medicines Introduced 1991-2009](chart)

Just 2 in 10 Approved Medicines Produce Revenues That Exceed Average R&D Costs

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.

Sources: Berndt ER, et al.⁸; Vernon JA, et al.⁹
Average Lifetime Returns From Newly Introduced Medicines Have Declined in Recent Years

The R&D investments required to bring medicines to patients in the future rely on revenues from existing approved innovative medicines. Continued declines in average lifetime revenues from new medicines could reduce the ability of companies to maintain their historically high levels of innovation.

**Average Present Value of Lifetime Sales of Medicines by When They Were Introduced**

<table>
<thead>
<tr>
<th>Year of Launch</th>
<th>2005 Dollars, in Billions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991-1994</td>
<td>$3.4</td>
</tr>
<tr>
<td>1995-1999</td>
<td>$4.6</td>
</tr>
<tr>
<td>2000-2004</td>
<td>$5.1</td>
</tr>
<tr>
<td>2005-2009</td>
<td>$2.9</td>
</tr>
</tbody>
</table>

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.\(^\text{10}\)
The Economics of Biopharmaceuticals Has Changed Markedly in Recent Years

**THE SCIENCE IS MORE COMPLEX AND MORE COSTLY**

- Researchers targeting more complex diseases
- Higher regulatory hurdles
- Longer, more complex clinical trials
- Genomics/molecular medicine are complex new frontiers
- Increased cost of R&D

**THE MARKET IS MORE CHALLENGING**

- Slow uptake of new medicines/rapid adoption of generics
- Unprecedented scale of patent expiries and patent challenges
- Increased payer demand for evidence
- Increased patient cost sharing and access restrictions

Source: PhRMA¹¹
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

[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

Usual profit figures greatly overstate the industry’s economic profit rate.

— Joseph Newhouse, Harvard University

Sources: Scherer FM\textsuperscript{12}; CBO\textsuperscript{13}; Newhouse JP\textsuperscript{14}
The US Prescription Drug Lifecycle Promotes Innovation and Affordability

<table>
<thead>
<tr>
<th>MEDICINE</th>
<th>BRAND NAME THEN</th>
<th>VS. GENERIC NOW</th>
<th>% CHANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIOVAN HCT Hypertension</td>
<td>2010 $87</td>
<td>2010 $13</td>
<td>-85%</td>
</tr>
<tr>
<td>LIPITOR Cholesterol</td>
<td>2010 $85</td>
<td>2010 $4</td>
<td>-95%</td>
</tr>
<tr>
<td>PLAVIX Blood Thinner</td>
<td>2011 $166</td>
<td>2011 $5</td>
<td>-97%</td>
</tr>
<tr>
<td>SEROQUEL Schizophrenia</td>
<td>2010 $87</td>
<td>2010 $3</td>
<td>-97%</td>
</tr>
<tr>
<td>ZYPREXA Schizophrenia &amp; Bipolar Disorder</td>
<td>2010 $393</td>
<td>2010 $8</td>
<td>-98%</td>
</tr>
</tbody>
</table>

**THEN & NOW**

How Prescription Drug Prices Fall Significantly Over Time

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

Figures represent 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 CY 2014.

Source: IMS Health
Savings From the Prescription Drug Lifecycle Reduce Treatment Costs for the Most Common Conditions

Incredible advances by innovative pharmaceutical companies, resulting from pioneering scientific work and large-scale investments, eventually lead to lower-cost generics that bring long-term value to consumers.

*Daily Cost of Top 10 Therapeutic Classes* Most Commonly Used by Medicare Part D Enrollees

*Ten therapeutic classes most commonly used by Part D enrollees in 2006 were lipid regulators, angiotensin-converting-enzyme inhibitors, calcium channel blockers, beta blockers, proton pump inhibitors, thyroid hormone, angiotensin II, codeine and combination products, antidepressants, and seizure disorder medications.

Source: Kleinrock M16
Medicines Offer Built-in Cost Containment, Which Is Unique in Health Care

The price of a common medicine used to prevent cardiovascular disease dropped 92% between 2005 and 2013, while the average charge for a surgical procedure used to treat it increased 66% over the same period.

Source: PhRMA analysis of Healthcare Cost and Utilization Project Hospital Charge Database; IMS\textsuperscript{17}
Powerful Purchasers Negotiate on Behalf of Payers

Negotiating power is increasingly concentrated among fewer pharmacy benefit managers (PBMs), with the top 3 PBMs accounting for three-quarters of the market.

*OptumRx and Catamaran merged in 2015. Their 2014 shares are shown combined.

Source: Drug Channels Institute18
In the US System, Health Plans Have Powerful Tools to Reduce Spending on Medicines

**TIERED COPAYS**
Higher cost to patients for brands than for generics and preferred brands

**FORMULARIES**
List of covered drugs

**PRIOR AUTHORIZATION**
Requirement to justify medicine’s use before it is covered

**CONCENTRATED PURCHASING POWER**
Individual Pharmacy Benefit Managers buy medicines for more people than those who live in entire European countries

**FINANCIAL INCENTIVES**
Payments to physicians and/or pharmacies for generic prescribing or switching patients to preferred drugs

**STEP THERAPY**
Patients must try and fail on alternatives before certain medicines are covered

Plans drive nearly all use of medicines to generics and “preferred” brands.

Source: IMS Health\(^{19}\)
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.²⁰

<table>
<thead>
<tr>
<th>What Payers Claimed Would Happen</th>
<th>What Actually Happened</th>
</tr>
</thead>
</table>
| 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 2014²¹ | 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 2015²³ |
| 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 2014²² | We are receiving market-leading rates from both companies. Neither company wanted to be left off the formulary.  
  — Prime Therapeutics, January 2015²⁴ |
| 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 2015²⁵ | |

Sources: LaMattina J²⁰; Cortez MF²¹; Ignagni K²²; Silverman E²³; Langreth R²⁴; New York Times Editorial Board²⁵
Many Factors Affect Physicians’ Prescribing Decisions

Factors Influencing Prescribing Decisions in the United States in 2013

- Clinical knowledge and experience: 91% (A great deal), 8% (Some)
- Patient’s particular situation, including drug interactions, side effects, and contraindications: 89% (A great deal), 9% (Some)
- Articles in peer-reviewed medical journals: 50% (A great deal), 42% (Some)
- Clinical practice guidelines: 48% (A great deal), 44% (Some)
- Patient’s insurance coverage and formulary: 39% (A great deal), 44% (Some)
- Information from colleagues and peers: 38% (A great deal), 54% (Some)
- Pharmaceutical company–sponsored educational programs featuring physician speakers, not Continuing Medical Education: 11% (A great deal), 47% (Some)
- Information from pharmaceutical company representatives: 10% (A great deal), 53% (Some)
- Information from insurance and prescription benefits manager representatives: 10% (A great deal), 35% (Some)

Source: KRC Research26
Direct-to-Consumer Advertising Encourages Patient Engagement and Appropriate Use of Medicines

Advertising has promoted the appropriate use of oral breast cancer therapies consistent with medical practice guidelines.*

Medically Appropriate Population: Breast cancer patients age 60+

Doctor

Medically Inappropriate Population: Breast cancer patients younger than 60

Significant increase in prescribing of aromatase inhibitors to medically appropriate population

No increase in prescribing of aromatase inhibitors to medically inappropriate population

*Study measured the effect of DTCA on patients and doctors regarding the use of aromatase inhibitors (AIs) consistent with medical practice guidelines. The study found that DTCA spending on AIs was associated with an overall new AI prescription increase of 0.18% after 3 months (approximately 118 new AI prescriptions per million dollars spent). There was “no significant change associated with DTCA spending for AIs for those aged 40 years or less at any time from 0 to 6 months.”

Source: Abel GA, et al.27
Notes and Sources


7. For example, a new generic version of an osteoporosis treatment launched in 2009 captured more than 90% of the mail order market in the first week and more than 90% of all prescriptions in the first 3 months. Express Scripts. 2009 drug trend report. https://www.express-scripts.com/research/research/dtr/archive/2009/dtrFinal.pdf. Published April 2010. Accessed April 2016.


Notes and Sources

15. IMS Health analysis for PhRMA. May 2015.
17. PhRMA analysis of average hospital charge data from Healthcare Cost and Utilization Project Hospital Charge Database 2005 and 2013; invoice price data for atorvastatin 10mg from IMS National Sales Perspective for 2005 (branded Lipitor), 2013 (generic), and 2014 (generic).
Notes and Sources


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 results in high cost sharing for some patients. High cost sharing for medications may limit patients’ access to needed treatments, reduce adherence, and lead to poor health outcomes. Out-of-pocket spending for prescription medications can represent a disproportionate share of total health care costs borne directly by patients, especially those who are low income or chronically ill.
Insurance Covers a Lower Share of Prescription Drug Costs Than the Costs of Other Medical Services

On average, patients pay out of pocket 17% of their total prescription drug costs compared with 4% of costs for hospital care.\(^1\)

*Average Share of Health Care Costs Patients Pay Out of Pocket, All Ages*

- **Hospital Care:** 4%
- **Prescription Drugs:** 17%

Average, All Health Care (14%)

Note: Prescription drug spending includes brand and generic ingredients, pharmacy, and distribution costs for retail prescriptions. Hospital care includes inpatient and outpatient.

Source: PhRMA analysis based on Medical Expenditure Panel Survey, 2013\(^1\)
More Plans Are Including Drugs in Combined Deductibles

The share of plans offered on the Health Insurance Exchanges including drugs in combined deductibles (a single deductible for medical services and drugs) has steadily increased over the 3 years the exchanges have been in operation. Plans that apply a large deductible to prescriptions can leave patients with high out-of-pocket costs from accessing needed medicines, like those that treat chronic conditions. About half of plans without a combined deductible have a separate drug deductible, and the remaining plans exempt drugs from the deductible.

In the Federally Facilitated Marketplace Individual Landscape File, plans note either a combined deductible, which reflects a single deductible for medical services and drugs, or separate deductibles that apply only to medical services or drugs.

Source: Avalere Health PlanScape®

Average Combined Deductible for Silver Plans
2015: $2,658
2016: $3,075
Subjecting Prescription Drugs to a Combined Deductible Results in Disproportionately High Cost Sharing

An analysis of the most common type of exchange plans under the Affordable Care Act found that drug coverage was generally less generous than coverage for other services—primarily because plans subjected drug spending to a large deductible.

Average Share of Costs Paid by the Plan
Among Silver Plans in 2014 With a Combined Medical/Drug Deductible*

- Pharmacy: 54%
- Hospital: 72%
- Professional/Other: 71%

*Silver Plans accounted for a majority of Health Insurance Exchange enrollment, and combined deductibles were the most common type of deductible arrangement among these plans. A deductible is the amount patients must pay annually with their own money (out of pocket) before a health plan will pay for any expenses. Figure shows the actuarial value for each service category listed (i.e., the percentage of covered costs paid by the plan).

Source: Milliman, Inc.3
Plans Often Charge Patients a Percentage of a Medicine’s Total Cost Rather Than Fixed-Dollar Copays

In the most frequently purchased type of Health Insurance Exchange plan, coinsurance for certain medicines is common: 74% of these plans require enrollees to pay a percentage of a specialty tier medicine’s total cost, with 36% of these plans requiring patients to pay coinsurance of more than 30% of the cost.

*Silver Plans are shown here because they account for a majority of Health Insurance Exchange enrollment. Plans subject different medicines to different levels of cost sharing, or “tiers.” Medicines assigned to a “specialty tier” typically require the highest level of cost sharing.

Source: Avalere Health PlanScape®
Plans Increasingly Subject Certain Medicines to Higher Cost Sharing

Patients taking medicines placed on higher cost sharing “tiers” commonly face serious and chronic health conditions. Increased use of 4 or more tiers by plans means that more patients are subject to what is commonly higher cost sharing in 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...

Share of Silver Plans by Number of Tiers6*

Share of Workers in Plans With 4 or More Tiers*

*Silver Plans account for a majority of Health Insurance Exchange enrollment. “Tiers” refer to the different levels of cost sharing that plans require patients to pay for different groupings of medicines.

Sources: Kaiser Family Foundation (KFF)5; Avalere Health PlanScape®6; KFF/Health Research & Educational Trust7
Insurers May Be Discouraging Enrollment Through Drug Benefit Design

By placing all drugs to treat certain high-cost conditions on the highest drug formulary cost sharing tier, a practice known as adverse tiering, some insurers may be trying to discourage patients with certain conditions from enrolling in their plans.

*There are no generic drugs available in this class. All products are single-source.

Source: Avalere Health PlanScape®
High Cost Sharing Reduces Adherence

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

*Percent Change in Adherence From Doubling Medicine Copays*

Source: Goldman DP, et al.
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 take twice as long to initiate treatment.

Percentage of Chronic Myeloid Leukemia Patients Initiating Treatment

- Patients facing high cost sharing
- Patients facing minimal cost sharing

<table>
<thead>
<tr>
<th>Time Following Diagnosis</th>
<th>Percentage of Patients Initiating Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>21%</td>
</tr>
<tr>
<td>3 months</td>
<td>36%</td>
</tr>
<tr>
<td>6 months</td>
<td>45%</td>
</tr>
</tbody>
</table>

Source: Doshi JA, et al.¹⁰
Formulary Restrictions Can Lead to Greater Medical Spending

Non-elderly Medicaid patients facing formulary restrictions* for antipsychotic medications were 7% to 13% more likely to be hospitalized and had higher medical costs than patients in states without formulary restrictions.

*Restrictions examined: prior authorization, step therapy, and quantity limits

Source: Seabury SA, et al.\textsuperscript{11}

![Medicaid Total Annual Medical Expenditures per Patient, 2008](chart)

- **Schizophrenia**
  - States Without Formulary Restrictions: $10,952
  - States With Formulary Restrictions: $13,299

- **Bipolar Disorder**
  - States Without Formulary Restrictions: $12,344
  - States With Formulary Restrictions: $13,735
Patient Assistance Programs Help Patients Access Needed Medicines

Despite more Americans having insurance, many are facing high cost sharing that puts their ability to stay on a needed therapy at risk. Patient assistance programs sponsored by US biopharmaceutical companies are one option to help patients maintain access to needed medicines.

Since 2005, the Partnership for Prescription Assistance (PPA) has helped connect

**NEARLY 10 MILLION uninsured or underinsured patients**
to assistance programs that may provide medicines they need for free or nearly free.

**WHAT PPA OFFERS**

- Single point of access to information on **more than 475 public and private patient assistance programs**—including nearly 200 programs offered by biopharmaceutical companies

- A database of nearly 10,000 free or low-cost health care clinics across the country

Source: Partnership for Prescription Assistance
Notes and Sources

1. PhRMA analysis based on US Department of Health and Human Services, Agency for Healthcare Research and Quality, Medical Expenditure Panel Survey, 2013. http://www.meps.ahrq.gov/mepsweb. Accessed April 2016. Prescription drug spending includes brand and generic ingredients, pharmacy, and distribution costs. Hospital includes inpatient and outpatient. 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.

2. Avalere Health PlanScape®, a proprietary analysis of exchange plan features, December 2015. This analysis is based on data collected by Managed Markets Insight & Technology, LLC. Avalere Health PlanScape®, a proprietary analysis of exchange plan features, December 2014. Avalere Health analyzed data from the Federally Facilitated Marketplace Individual Landscape File released November 2014 and the California and New York state exchange Web sites.


4. Avalere Health PlanScape®, a proprietary analysis of exchange plan features, December 2015. This analysis is based on data collected by Managed Markets Insight & Technology LLC.


6. Avalere Health PlanScape®, a proprietary analysis of exchange plan features, December 2015. This analysis is based on data collected by Managed Markets Insight & Technology LLC.


8. Avalere Health PlanScape®, a proprietary analysis of exchange plan features, updated February 2015. This analysis is based on data collected by Managed Markets Insight & Technology, LLC. The sample includes Silver Plans in 6 states (Florida, Georgia, Illinois, North Carolina, Pennsylvania, and Texas), relying on HealthCare.gov and California and New York. Coverage is weighted according to unique plan-state combinations.

Notes and Sources


Prescription medicines represent a small share of national health spending, and government estimates project medicines to remain a stable share of health spending through the next decade. Overall drug price growth has been in line with overall medical price growth, in large part due to the cost containment built into the drug cost lifecycle; 9 of every 10 US prescriptions are filled with generics. Despite reported increases in list prices for brand medicines, average net brand price growth has declined in recent years, a result of increased rebates negotiated by payers.
Prescription Medicine Spending Growth: 2008-2024*

After spiking at 12.2% in 2014, government actuaries project prescription drug spending growth to moderate over the next few years to 5% to 7% through 2024, back in line with overall health care spending growth.¹

2014 saw a record 41 medicines approved by the FDA—including a number of transformative medicines for many debilitating diseases—as well as nearly 15.7 million Americans gaining coverage through the Affordable Care Act.²,³

*Total retail sales including brand medicines and generics

Sources: PhRMA analysis of Centers for Medicare & Medicaid Services (CMS) data¹; RAND Corporation²; FDA³
Medicines Are Expected to Account for a Stable Share of Total Health Care Expenditures Through the Next Decade

*Health Care Expenditures Attributable to Retail and Nonretail Prescription Medicines, 2008-2024*

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.

Source: Altarum Institute
Retail Spending on Prescription Medicines Is a Small Share of Total US Health Care Spending

Prescription medicines today account for about 10% of the $3 trillion of annual health care spending in the United States, the same percentage as in 1960.

2014 Health Care Dollar*

$0.08
Government Admin. and Net Cost of Private Health Insurance

$0.08
Home Health and Nursing Home Care

$0.10
**PRESCRIPTION DRUGS**

$0.20
Physicians and Clinical Services

$0.23
Other**

$0.32
Hospital Care

*Figures may not sum due to rounding.
**Other includes dental, home health, and other professional services as well as durable medical equipment costs.

Source: PhRMA analysis based on CMS data5
Growth in Prescription Medicine Prices Has Been in Line With Other Health Care Prices

*Consumer Price Index (2005 = 100)*

Source: PhRMA analysis based on Bureau of Labor Statistics data

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5 • Drug Spending Trends
Nine Out of Every 10 US Prescriptions Are Filled With Generics

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

Source: PhRMA analysis based on IMS Health data

Generic Share* of Prescriptions Filled, 1984-2015

- 1984: 19%
- 1990: 33%
- 1996: 43%
- 2002: 52%
- 2008: 72%
- 2014: 88%
- 2015: 91%
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, 2013

For example, medicines account for 6% of the difference in total health care spending between the United States and Canada and 9% between the United States and Germany.

Source: PhRMA analysis based on Organisation for Economic Co-operation and Development data®
Spending on Cancer Medicines Represents About 1% of Overall Health Care Spending

Cancer Medicines as a Portion of Total US Health Care Spending, 2014

Total Health Care Spending
$3.03 Trillion

Cancer Medicines
$32.6 Billion

Sources: IMS Institute for Healthcare Informatics9; CMS10
Forecasts of Specialty Drug Spending Have Been Routinely Overstated

A recent analysis of annual drug trend reports found that inconsistent and arbitrary definitions of “specialty medicines” can bias spending projections.

Forecasted vs. Actual Annual Growth in Specialty Drug Spending
From a Major Pharmacy Benefits Management Company*

*As reported in annual Drug Trend Reports from Express Scripts.

Source: Milliman, Inc.¹¹
Average Net Brand Price Growth Declined as a Result of Increased Rebates

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

**Table: Average Price Growth for Brand Medicines**

<table>
<thead>
<tr>
<th>Year</th>
<th>Invoice Price Growth</th>
<th>Estimated Net Price Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>8.7%</td>
<td>9.3%</td>
</tr>
<tr>
<td>2012</td>
<td>9.1%</td>
<td>10.0%</td>
</tr>
<tr>
<td>2013</td>
<td>4.9%</td>
<td>11.5%</td>
</tr>
<tr>
<td>2014</td>
<td>5.1%</td>
<td>14.3%</td>
</tr>
<tr>
<td>2015</td>
<td>2.8%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

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

Source: IMS Institute for Healthcare Informatics

Source: IMS Institute for Healthcare Informatics

89
$93 Billion of US Brand Sales Are Projected to Face Generic Competition From 2016 to 2020

The savings from patent expiries in the coming years are expected to match the large-scale savings observed in recent years.

*Pre-expiry Value of Small Molecule Products at Risk (in Billions), 2011-2020*

2011-2015: $101 Billion

2016-2020: $93 Billion

Pre-expiry sales of products are calculated for products facing loss of exclusivity (LOE) in each year; the sales in the prior year for each product are aggregated to represent the collective industry exposure to LOE. LOE does not indicate generic market entry. Only small molecule LOEs are included.

Source: IMS Institute for Healthcare Informatics\(^{13}\)
Notes and Sources


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

AMERICANS
191 million have at least one
75 million have multiple

Costs of CHRONIC DISEASE in 2015

ANNUAL COSTS
$2.8 trillion
in medical costs and lost productivity

5% of the population accounts for
50% of US health care spending

Sources: Agency for Healthcare Research and Quality1; IHS Life Sciences2
Diabetes: An Example of Underdiagnosis and Undertreatment

Uncontrolled diabetes can lead to kidney failure, amputation, blindness, and stroke.

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

Source: IHS Life Sciences analysis based on CDC data³
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.

Avoidable Annual US Health Care Costs (in Billions, 2012)

- Nonadherence: $105
- Medication Errors*: $21
- Suboptimal Prescribing**: $87
- Total Avoidable Costs: $213

*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

$0 $50 $100 $150 $200 $250

*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
Failure to Prescribe the Indicated Treatment Is the Most Common Prescribing Quality Problem

RAND researchers report that failure to prescribe an indicated treatment is a far more common quality problem than inappropriate medicine use.

![Quality Problems Among Vulnerable Older Patients](image)

*Quality indicators were developed and implemented based on systematic literature reviews and multiple layers of expert judgment.*

*Source: RAND Health*
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

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.7

**MEDICAID**

Increased use of medicines is associated with reductions in Medicaid expenditures from avoided use of inpatient and outpatient services.8

Sources: CBO6; Roebuck MC7; Roebuck MC, et al.9
Mounting Evidence Demonstrates the Potential for Savings and Improved Outcomes

**HYPERTENSION**
Better treatment and adherence to antihypertensive medications could save nearly 200,000 lives and avert more than 1 million hospitalizations.\(^9\)

**DIABETES**
Improved medication adherence among diabetes patients could result in more than 1 million avoided emergency department visits and hospitalizations annually, for potential savings of $8.3 billion each year.\(^10\)

**MENTAL HEALTH**
The use of atypical antipsychotics reduced the risk of hospitalization by 27% and health care costs by $27,664.\(^11\)

**CONGESTIVE HEART FAILURE**
Improving adherence to congestive heart failure medicines could result in federal savings of $22.4 billion over 10 years.\(^12\)

Nonadherence has also been linked to excess hospitalizations for conditions such as osteoporosis, chronic obstructive pulmonary disease, and other chronic conditions with costs of more than $200 billion per year.\(^19\)

Recent Studies Show Significant Value From Better Use of Medicines

Patients with less common diseases are able to offset health care spending by exercising better adherence.

**PARKINSON’S DISEASE**
Health care savings of **up to $6,300** can be achieved among patients with Parkinson’s who continually stay on therapy.20

**MULTIPLE SCLEROSIS**
Improved persistence to medications reduces the likelihood of a patient’s hospital admission by **up to 50%**.21

**CYSTIC FIBROSIS**
Among children with cystic fibrosis, poor medication adherence is associated with more hospitalizations and emergency department visits and **more than $14,000** in higher same-year medical costs compared with children who are highly adherent.22

**LUPUS**
Nonadherence among children in Medicaid who are diagnosed with lupus is associated with a **55%** increased rate of emergency department use and a nearly **40%** increased rate of hospitalizations.23

Sources: Wei YJ, et al.20; Thomas NP, et al.21; Quittner AL, et al.22; Feldman CH, et al.23
Improving Adherence Increases Worker Productivity

For workers with asthma/chronic obstructive pulmonary disease (COPD), better medication adherence results in more than $3,100 in savings on average per worker annually.

Source: Carls GS, et al.24
Gaining Drug Coverage Reduced Other Medical Spending

The Medicare drug benefit increased access to medicines for those previously without drug coverage, resulting in reduced medical spending\(^\text{25}\) and an overall savings of $13.4 billion in 2007, the first full year of the benefit.\(^\text{26}\)

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### Average Reduction in Medical Spending in 2006 and 2007 for Beneficiaries Who Gained Drug Coverage Through Medicare Part D

<table>
<thead>
<tr>
<th>Category</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part A</td>
<td>-$816</td>
</tr>
<tr>
<td>Part B</td>
<td>-$268</td>
</tr>
<tr>
<td>Other Nondrug*</td>
<td>-$140</td>
</tr>
<tr>
<td>Total Nondrug</td>
<td>-$1,224</td>
</tr>
</tbody>
</table>

*Home health, durable medical equipment, hospice, and outpatient institutional services

---

**PART D**

Since the implementation of Part D in 2006, nearly 200,000 Medicare beneficiaries **have lived at least 1 year longer**, with an average increase in longevity of **3.3 years.**\(^\text{27}\)

Sources: McWilliams JM, et al.\(^\text{25}\); Afendulis CC, Chernew ME\(^\text{26}\); Semilla AP, et al.\(^\text{27}\)
Notes and Sources


Notes and Sources


Notes and Sources


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 supply chain supports high-quality jobs in communities across the United States.
The Biopharmaceutical Sector Is the Single Largest Funder of Business R&D in the United States

The biopharmaceutical industry accounts for the single largest share of all US business R&D, representing 1 out of every 6 dollars (17%) spent on domestic R&D by US businesses.

*The remaining 57% share of business R&D spending is conducted by other industries, including subsectors of the machinery sector, the electrical equipment sector, and the professional, scientific, and technical services sector.

Source: PhRMA analysis of National Science Foundation data

Share of Total US Business R&D by Industry, 2013*
The biopharmaceutical sector invests more in R&D relative to sales than any other manufacturing industry, investing more than 6 times the average for all manufacturing industries.

### R&D as a Percentage of Sales by Industry, 2000-2012

<table>
<thead>
<tr>
<th>Industry</th>
<th>R&amp;D as % of Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceuticals &amp; Medicines</td>
<td>18.3%</td>
</tr>
<tr>
<td>Semiconductor</td>
<td>14.6%</td>
</tr>
<tr>
<td>Computer &amp; Electronic</td>
<td>11.9%</td>
</tr>
<tr>
<td>Medical Equipment &amp; Supplies</td>
<td>7.3%</td>
</tr>
<tr>
<td>Chemical</td>
<td>6.5%</td>
</tr>
<tr>
<td>Aerospace</td>
<td>6.2%</td>
</tr>
<tr>
<td>Transportation</td>
<td>3.9%</td>
</tr>
<tr>
<td>All Manufacturing</td>
<td>3.0%</td>
</tr>
<tr>
<td>Petroleum &amp; Coal</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

Source: NDP Analytics²
The Biopharmaceutical Industry Invests More R&D Dollars per Employee Than Any Other Industry

Biopharmaceutical companies invest more than 12 times the amount of R&D dollars per employee than manufacturing industries overall.

*R&D Expenditures per Employee by Manufacturing Industry, 2000-2010*

<table>
<thead>
<tr>
<th>Industry</th>
<th>Expenditures (2000-2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceuticals &amp; Medicines</td>
<td>$130,086</td>
</tr>
<tr>
<td>Chemical</td>
<td>$49,489</td>
</tr>
<tr>
<td>Semiconductor</td>
<td>$46,438</td>
</tr>
<tr>
<td>Computer &amp; Electronic</td>
<td>$40,848</td>
</tr>
<tr>
<td>Aerospace</td>
<td>$23,372</td>
</tr>
<tr>
<td>Medical Equipment</td>
<td>$16,981</td>
</tr>
<tr>
<td>Transportation Equipment</td>
<td>$16,404</td>
</tr>
<tr>
<td>Petroleum &amp; Coal</td>
<td>$14,268</td>
</tr>
<tr>
<td>All Manufacturing Industries</td>
<td>$10,529</td>
</tr>
<tr>
<td>Machinery</td>
<td>$7,212</td>
</tr>
<tr>
<td>Electrical Equipment</td>
<td>$6,516</td>
</tr>
<tr>
<td>Misc. Nonmedical Equipment</td>
<td>$2,791</td>
</tr>
</tbody>
</table>

Source: NDP Analytics
The Biopharmaceutical Industry Employs the Largest Share of R&D Workers Across All Manufacturing Industries

One out of every 8 R&D workers in the nation’s manufacturing industries is employed by the biopharmaceutical industry.

*Selected Manufacturing Industries’ Share of Total R&D Workers, 2012*

<table>
<thead>
<tr>
<th>Industry</th>
<th>Share of Total R&amp;D Workers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceuticals &amp; Medicines</td>
<td>13%</td>
</tr>
<tr>
<td>Semiconductors</td>
<td>11%</td>
</tr>
<tr>
<td>Navigational Equipment</td>
<td>9%</td>
</tr>
<tr>
<td>Aerospace</td>
<td>8%</td>
</tr>
<tr>
<td>Automobiles</td>
<td>7%</td>
</tr>
<tr>
<td>Communications Equipment</td>
<td>6%</td>
</tr>
<tr>
<td>Medical Equipment</td>
<td>5%</td>
</tr>
</tbody>
</table>

*The manufacturing industries that employ the remaining 41% of the R&D workforce each account for less than 5% of the total R&D workforce.

Source: PhRMA analysis of National Science Foundation data"
The Economic Reach of the US Biopharmaceutical Industry

Every biopharmaceutical sector job supports more than 4 additional jobs outside the industry.

854,000 direct jobs

1,710,000 indirect jobs

1,882,000 induced jobs

4,446,000 TOTAL JOBS

The biopharmaceutical industry supported more than 4.4 million jobs across the US economy in 2014.

Source: TEConomy Partners5
The Biopharmaceutical Sector Produces Jobs in a Wide Array of Fields

One-third of the jobs in the biopharmaceutical sector are in key STEM (Science, Technology, Engineering, and Math) occupations.

*Indicates a STEM occupation
**Occupations include health practitioners and persons in installation, maintenance, and repair; arts, design, and media; and building and grounds maintenance.

Source: TEConomy Partners®
US Biopharmaceutical Exports Have Grown

Biopharmaceutical exports have nearly tripled over the 13-year period from 2003 through 2015, accounting for 3.1% of all US exports by 2015.

Source: PhRMA analysis of data from US Department of Commerce, International Trade Administration
Industry-Sponsored Clinical Trials Contribute Significant Value to the Communities in Which They Are Located

In 2013, the biopharmaceutical industry sponsored 6,199 clinical trials of medicines in the United States, involving a total of 1.1 million volunteer participants and supporting a total of $25 billion in economic activity across all 50 states and the District of Columbia.*

*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 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: Battelle Technology Partnership Practice®
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®
The United States Leads in Biopharmaceutical Intellectual Property

The intellectual property related to more than half of new medicines was invented in the United States.

*US Patents Granted in Pharmaceutical Technology by Region/Country of Inventor, 2014*

- United States, 55.2%
- European Union, 21.6%
- Japan, 6.4%
- China, 1.8%
- Asia, * 5.4%
- All Others, 9.5%

*Asia includes India, Malaysia, Singapore, South Korea, Taiwan, and others.*

Source: PhRMA analysis of National Science Foundation data

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The United States Leads in Biopharmaceutical Venture Capital Investment

Nearly three-quarters of worldwide venture capital investments in high-growth potential biopharmaceutical startups are made in the United States.

Source: Evaluate Pharma

Biopharmaceutical Venture Capital Investment by Country, 2015

- United States, 73%
- European Union, 23%
- All Others, 4%
The Biopharmaceutical Industry Supports a Broader Ecosystem Through Corporate Venture Capital

The corporate venture arms of established biopharmaceutical companies have helped fuel the next generation of medical innovations by investing more than $6 billion in startups over the past decade. Much of this investment has been directed toward early-stage innovation and support for the formation of new startups.

*Biopharmaceutical Corporate Venture Capital Investment, 2006-2015*

Source: PricewaterhouseCoopers/National Venture Capital Association
Biopharmaceutical Companies Lead Corporate Giving

Biopharmaceutical companies led worldwide corporate giving* in 2013. Ninety percent of these contributions were in the form of in-kind product donations.

<table>
<thead>
<tr>
<th>Average Corporate Giving by Sector</th>
<th>Total Giving as % of Pretax Profit</th>
<th>Total Giving per Employee</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Companies</td>
<td>1.0%</td>
<td>$644</td>
</tr>
<tr>
<td>Biopharmaceuticals</td>
<td>19.4%</td>
<td>$24,453</td>
</tr>
<tr>
<td>Energy</td>
<td>0.8%</td>
<td>$2,912</td>
</tr>
<tr>
<td>Utilities</td>
<td>1.2%</td>
<td>$1,092</td>
</tr>
<tr>
<td>Information Technology</td>
<td>1.1%</td>
<td>$666</td>
</tr>
<tr>
<td>Consumer Staples</td>
<td>1.1%</td>
<td>$608</td>
</tr>
<tr>
<td>Industrials</td>
<td>0.8%</td>
<td>$244</td>
</tr>
</tbody>
</table>

*Domestic giving makes up the largest portion of total corporate giving across all sectors surveyed. Domestic giving made up 78% of total giving in 2013.

Source: CECP13
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:

- Number of employee volunteers: 4,500
- Number of employee hours volunteered: 27,000
- Percentage of industry-sponsored STEM programs focused on K-12: 85%
- Number of individual STEM-related grants awarded: 600
- Total STEM education program funding provided: $100M

Source: Battelle Technology Partnership Practice14
The Biopharmaceutical Industry is Increasingly Focused on Sustainability

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
- Expanding focus on setting and achieving environmental goals to reduce environmental impact at the company level

Source: Deloitte
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:

- **Strong INTELLECTUAL PROPERTY** protections, including patent and data protection
- **A well-functioning, science-based REGULATORY SYSTEM**
- **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\(^{16}\)

Sources: Battelle Technology Partnership Practice\(^{16}\), Deloitte\(^{17}\)
Notes and Sources


5. TEConomy Partners; for PhRMA. The Economic Impact of the US Biopharmaceutical Industry. Columbus, OH: TEConomy Partners; April 2016.

6. TEConomy Partners; for PhRMA. The Economic Impact of the US Biopharmaceutical Industry. Columbus, OH: TEConomy Partners; April 2016.


Notes and Sources


