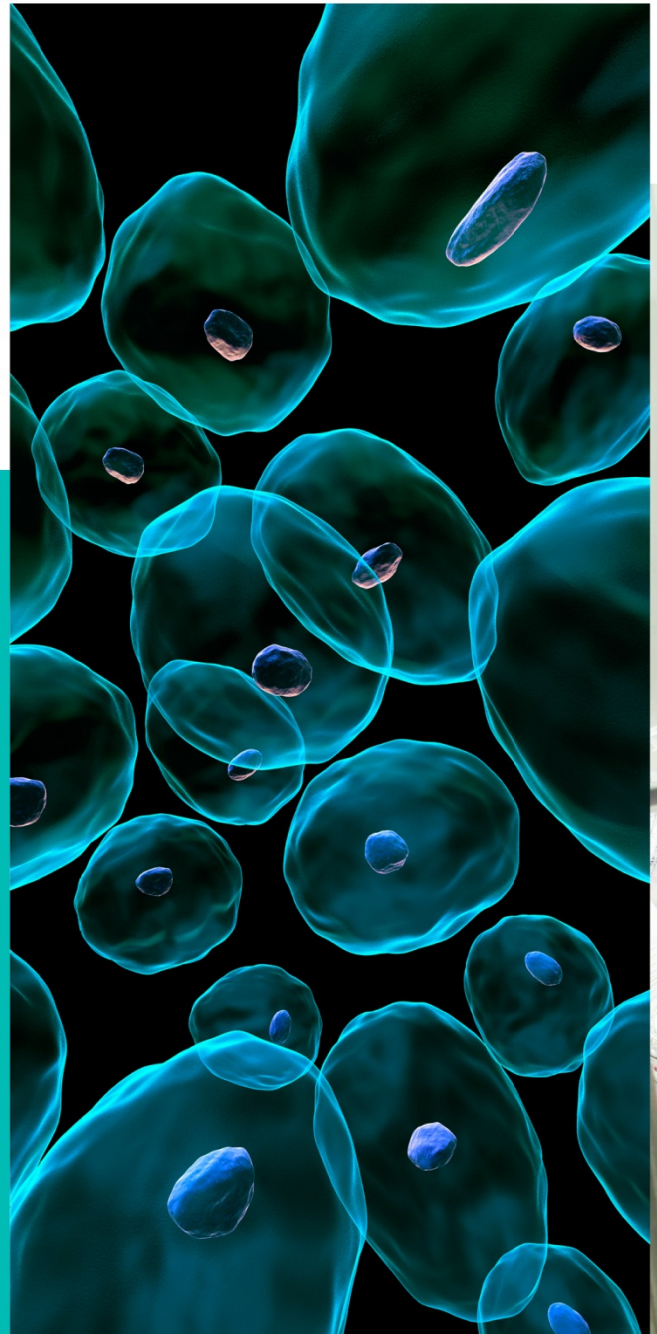
CHART PACK

Biopharmaceuticals In Perspective

SPRING 2015



PhRMA

RESEARCH • PROGRESS • HOPE

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Cover photo: Janet Buhlmann, Pfizer's Centers for Therapeutic Innovation

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 found 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.

1 ADVANCES IN TREATMENT

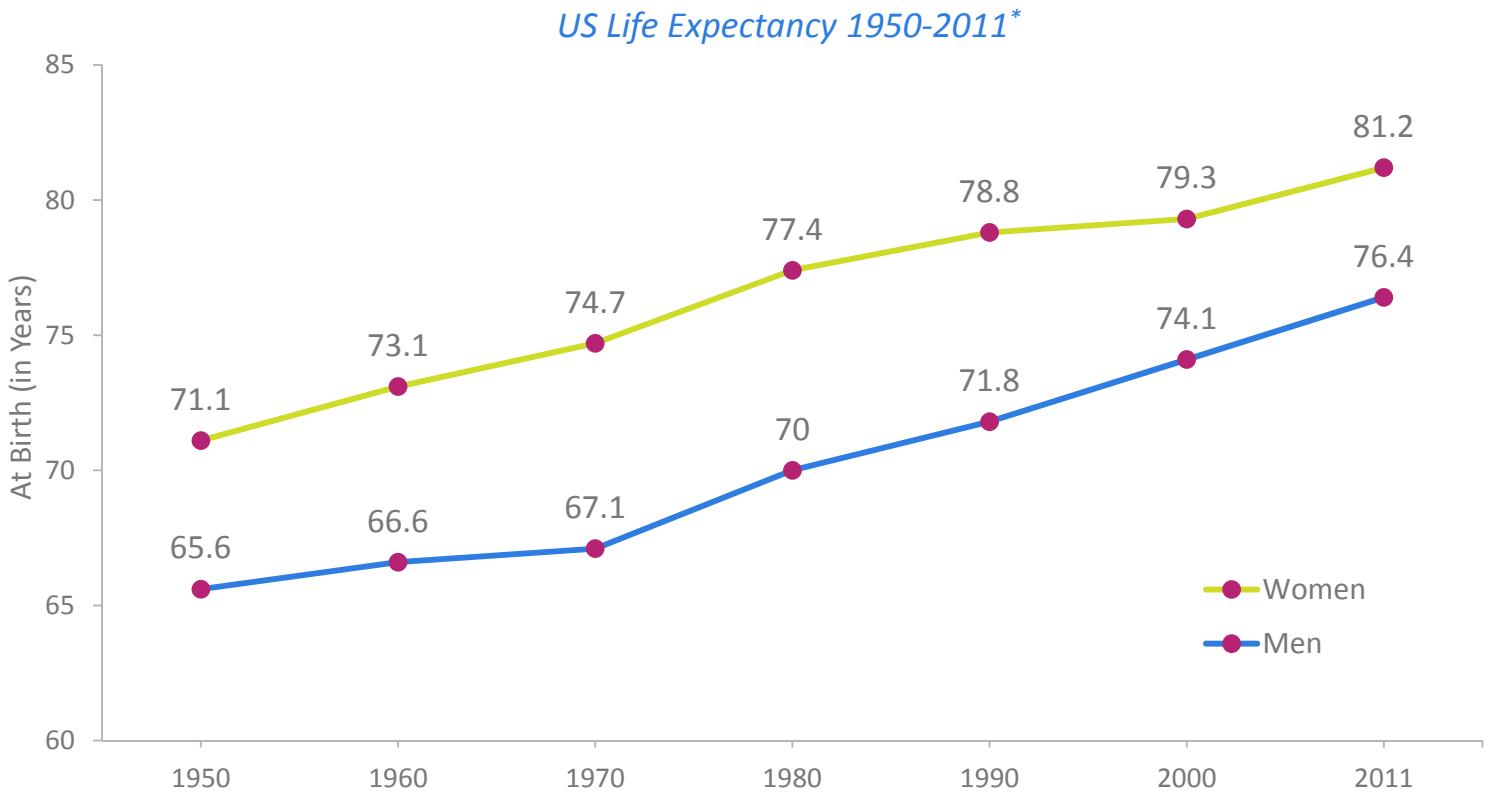
Medicines' Impact on Health and Quality of Life

Prescription medicines continue to yield important advances, helping patients live longer and healthier lives. Over the last 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 preventing the need for unnecessary hospital services 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 attack underlying causes of disease. Advances such as these are opening up doors to the development of the first new 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."

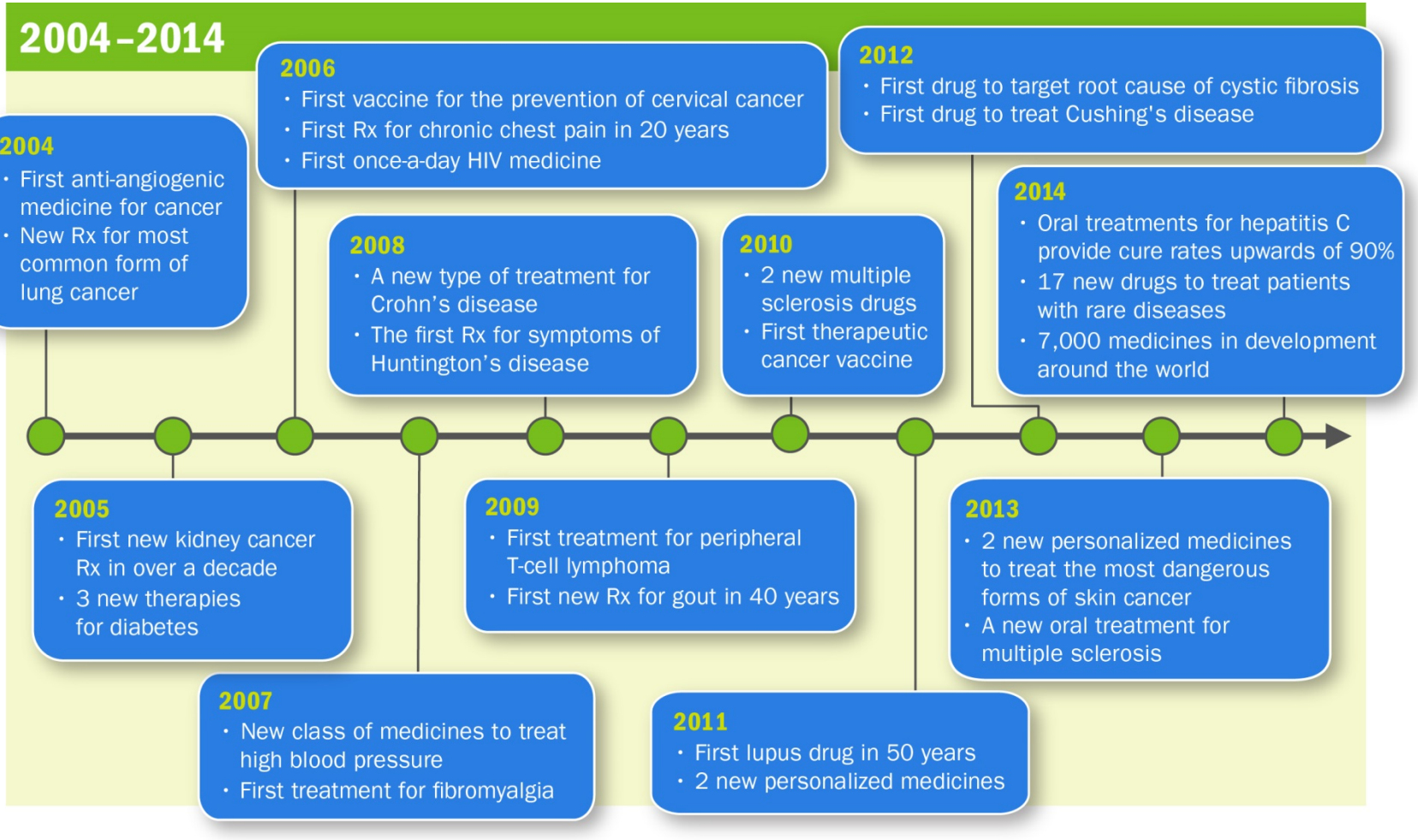
— The President's Council of Advisors on Science and Technology[1]



*Life expectancies prior to 1997 were calculated using a slightly different methodology than for those after 1997.

Sources: President's Council of Advisors on Science and Technology[1]; Centers for Disease Control and Prevention (CDC)[2]

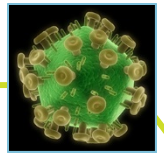
A Decade of Advances



Sources: US Food and Drug Administration (FDA)[3]; Adis R&D Insight Database[4]

Medicines Are Transforming the Treatment of Many Diseases

HIV/AIDS
In the last 2 decades, advances in treatment have contributed to a nearly 85% decline in death rates and transformed the disease from an acute, fatal illness to a chronic condition.[9]



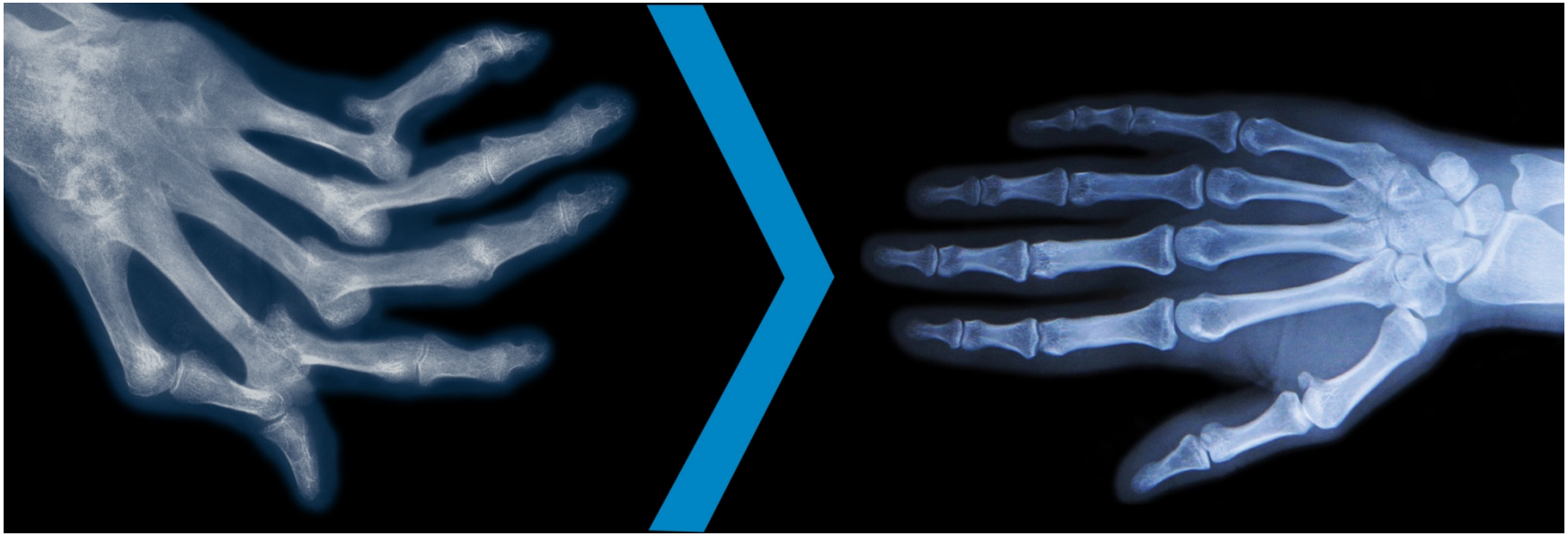
Cystic Fibrosis
New treatments targeting both the symptoms and root cause of the disease have contributed to improvements in quality of life for patients as well as increases in life expectancy.[5]

Cancer
New therapies have contributed to a nearly 22% decline in cancer deaths since the 1990s. Today, 2 out of 3 people diagnosed with cancer survive at least 5 years.[7,8]

Rheumatoid Arthritis (RA)
Therapeutic advances have transformed the RA treatment paradigm over the last 20 years, shifting from a focus on symptom management to now aiming for slowed disease progression and even disease remission.[6]

Sources: PhRMA[5]; Boston Healthcare[6]; National Cancer Institute (NCI)[7]; American Cancer Society[8]; CDC[9]

Rheumatoid Arthritis: Medicines Are Transforming the Lives of Patients



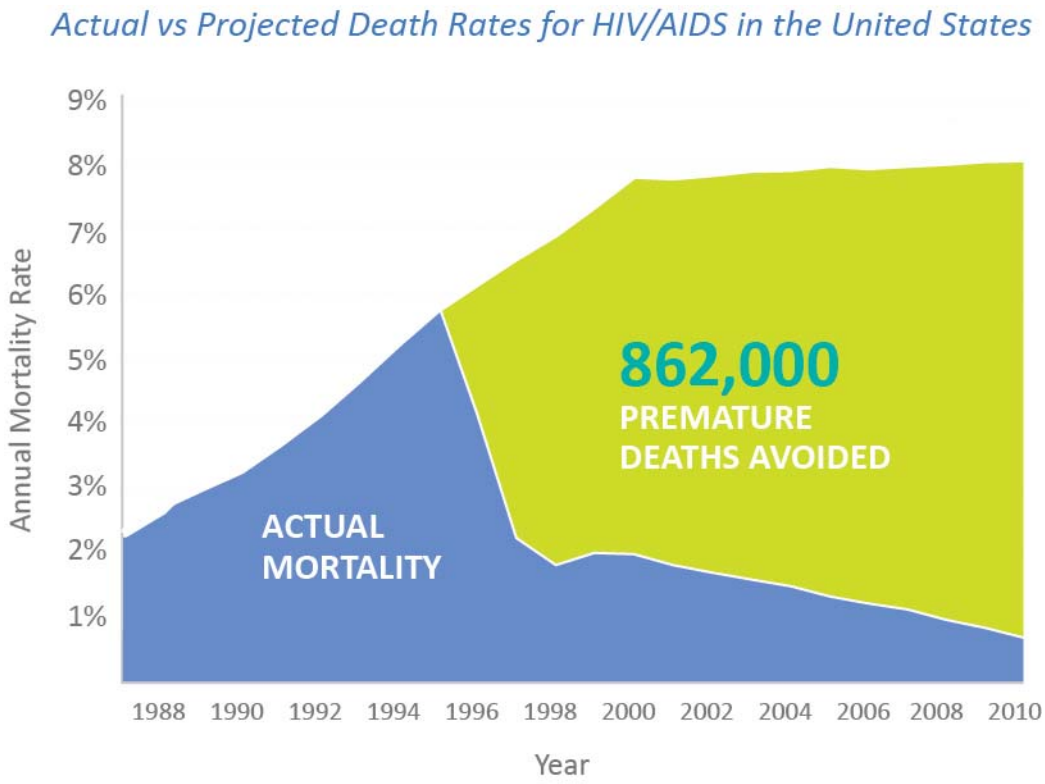
THEN:
Treatments for RA were effective at reducing joint inflammation but were limited to treating the symptoms of the disease, allowing for steady progression from disease onset to disability fairly rapidly.

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

Source: Boston Healthcare[10]

HIV/AIDS: Decline in Death Rates

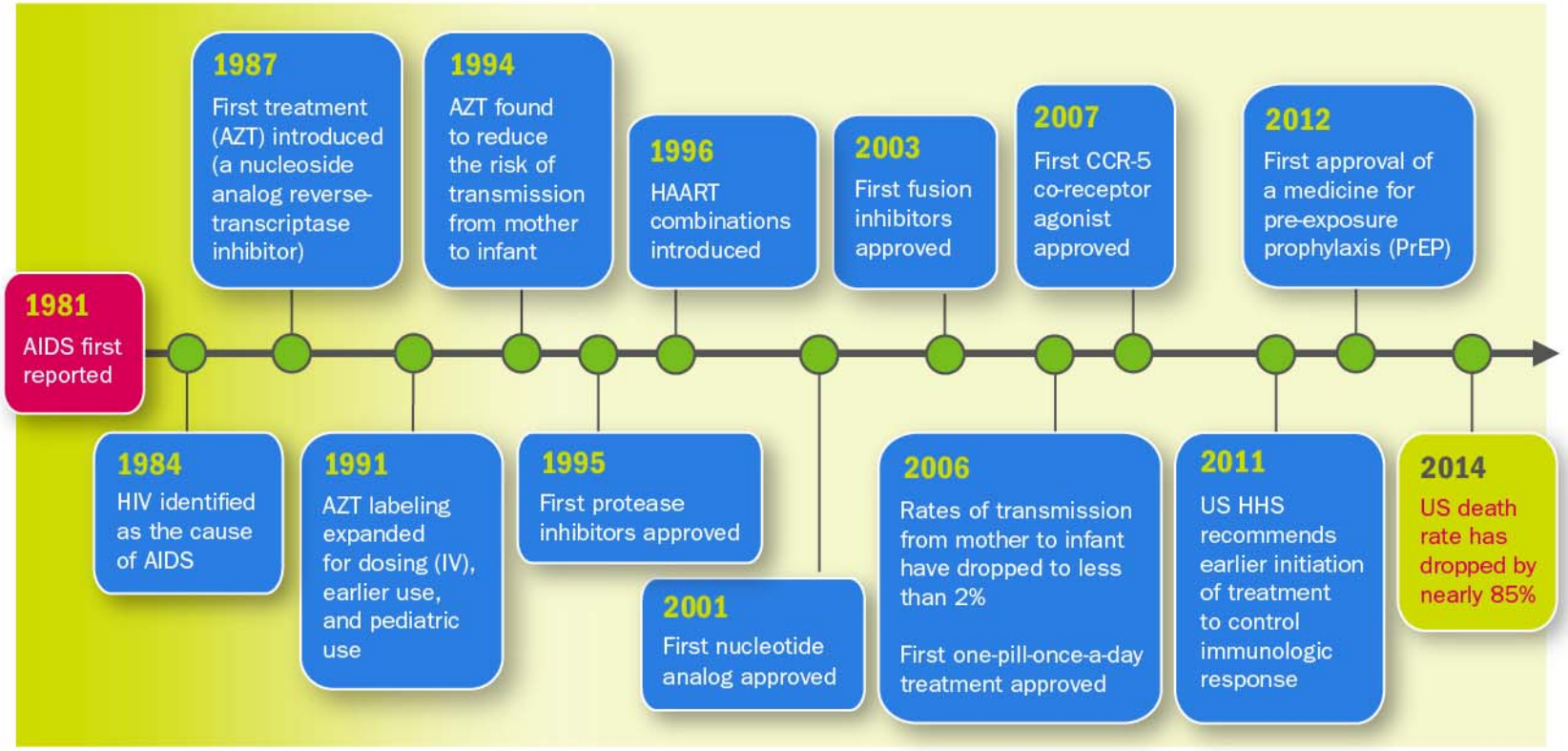
The number of US AIDS deaths decreased dramatically following the introduction of highly active antiretroviral treatment (HAART).[11] As a result of HAART and all the important medical innovations that followed, it is estimated that over 862,000 premature deaths have been avoided in the United States alone.[12]



Sources: CDC[11]; Truven Health Analytics[12]

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.

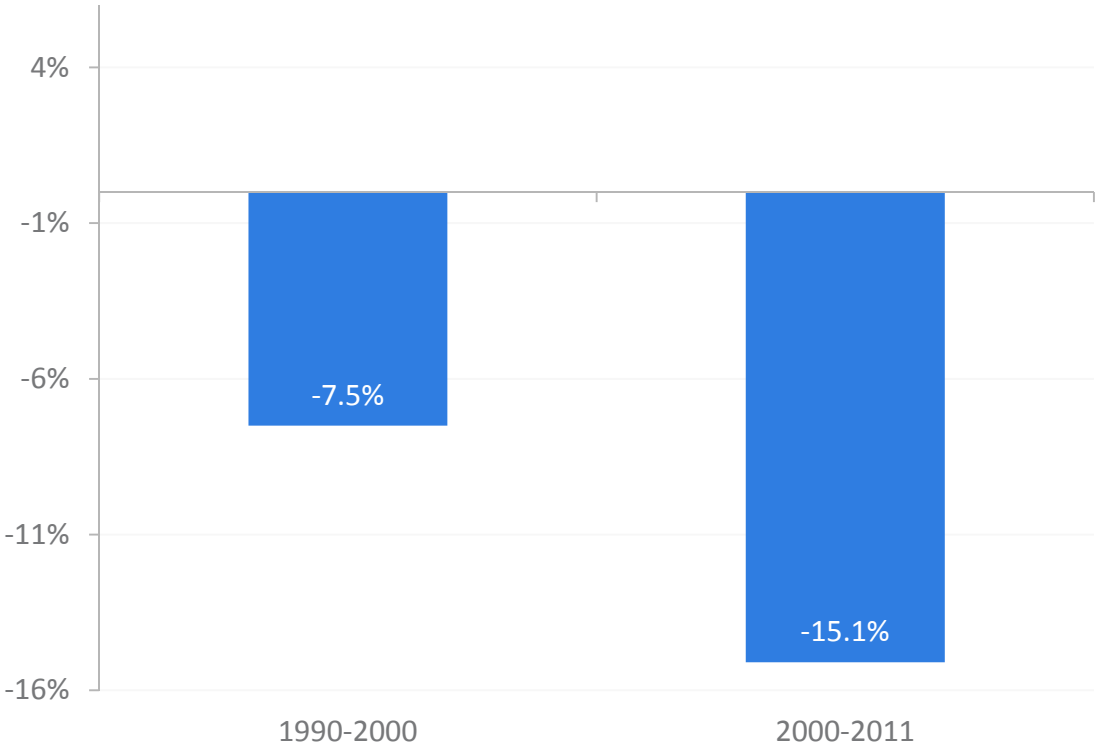


Source: Boston Healthcare[13]

Cancers: Decline in Death Rates

Since peaking in the 1990s, cancer death rates have declined nearly 22 percent.[14] Approximately 83% of survival gains in cancer are attributable to new treatments, including medicines.[15]

Percent Change by Decade in US Death Rates From Cancer[14]



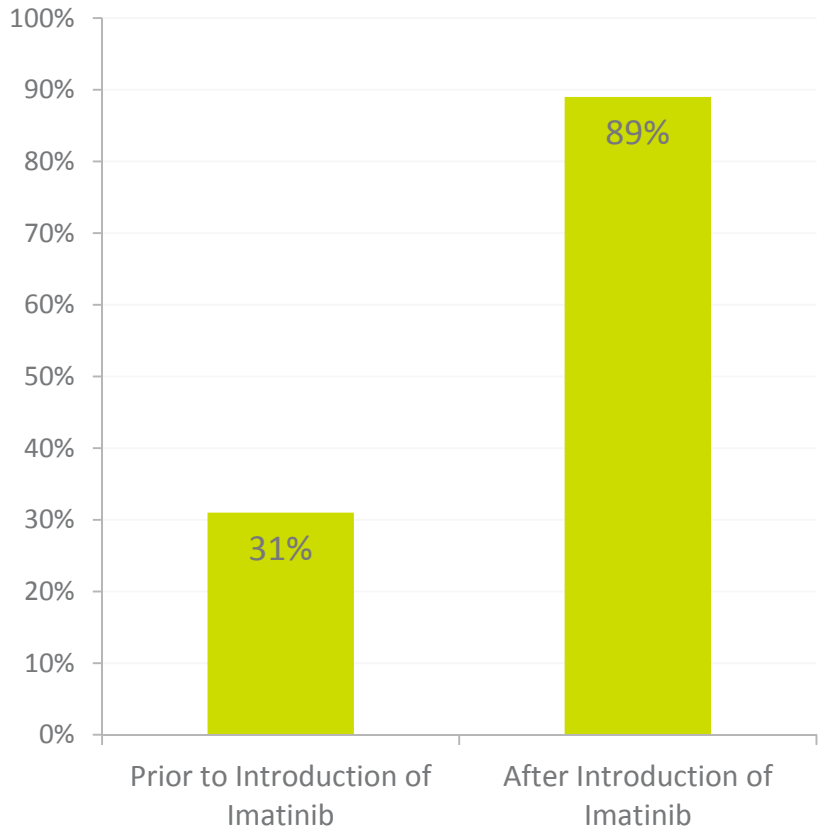
Sources: NCI[14]; Sun E, et al.[15]

Chronic Leukemias: Increased Survival Rates

When the first tyrosine kinase inhibitor (TKI)—imatinib—was approved in 2001 to treat chronic myeloid leukemia (CML), the transformative impact of this class of medicines had not been completely realized.[16]

- 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 TKIs have since been approved that target mutated forms of CML in patients who have become resistant or intolerant to imatinib.[17]
- Today, survival rates have improved dramatically, and **CML patients are living close to normal life spans.**[18]

5-Year Survival Rates for CML Patients[19,20]

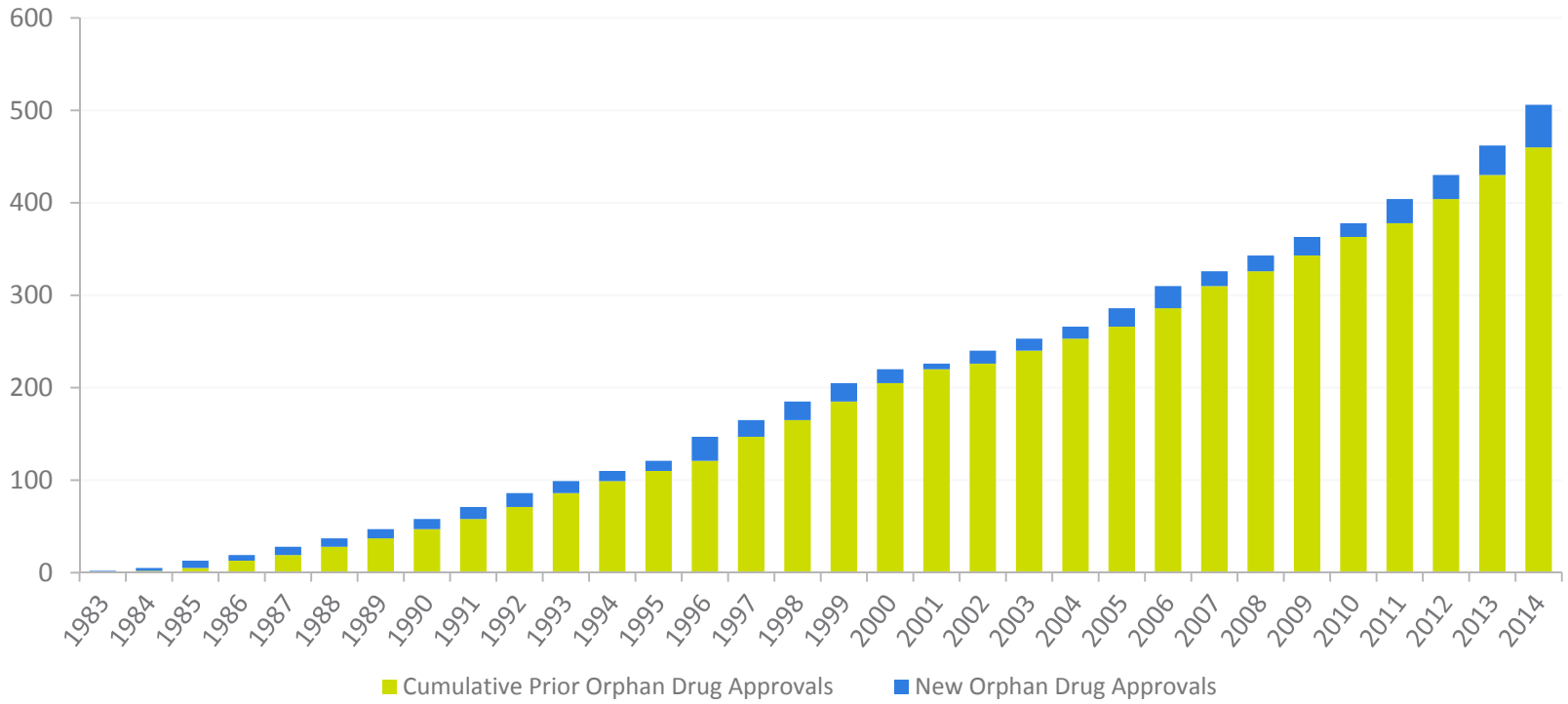


Sources: Boston Healthcare[16]; PhRMA[17]; Gambacorti-Passerini C, et al.[18]; American Cancer Society[19]; Druker B, et al.[20]

Rare Diseases: Drug Approvals for Rare Diseases Have Increased

Rare diseases are those that affect 200,000 or fewer people in the United States. There are nearly 7,000 rare diseases affecting a combined 30 million Americans.[21]

*Number of Drug Approvals for Rare Diseases**



*Approvals for rare diseases include initial approvals of new medicines and subsequent approvals of existing medicines for rare disease areas.

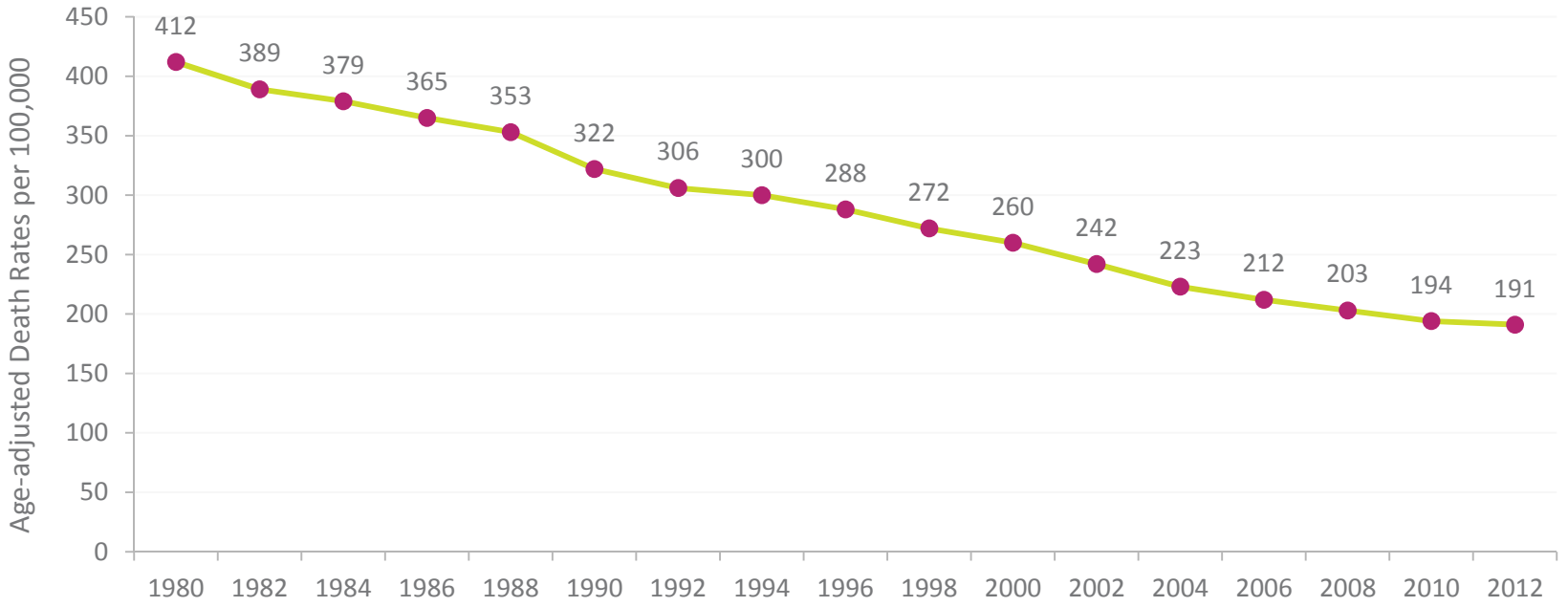
Source: FDA[21,22]

Cardiovascular Disease: Declining Rates of Death

> *"Factors contributing to the decline in heart disease and stroke mortality include better control of risk factors, improved access to early detection, and better treatment and care, **including new drugs and expanded uses for existing drugs**."*

— CDC[23]

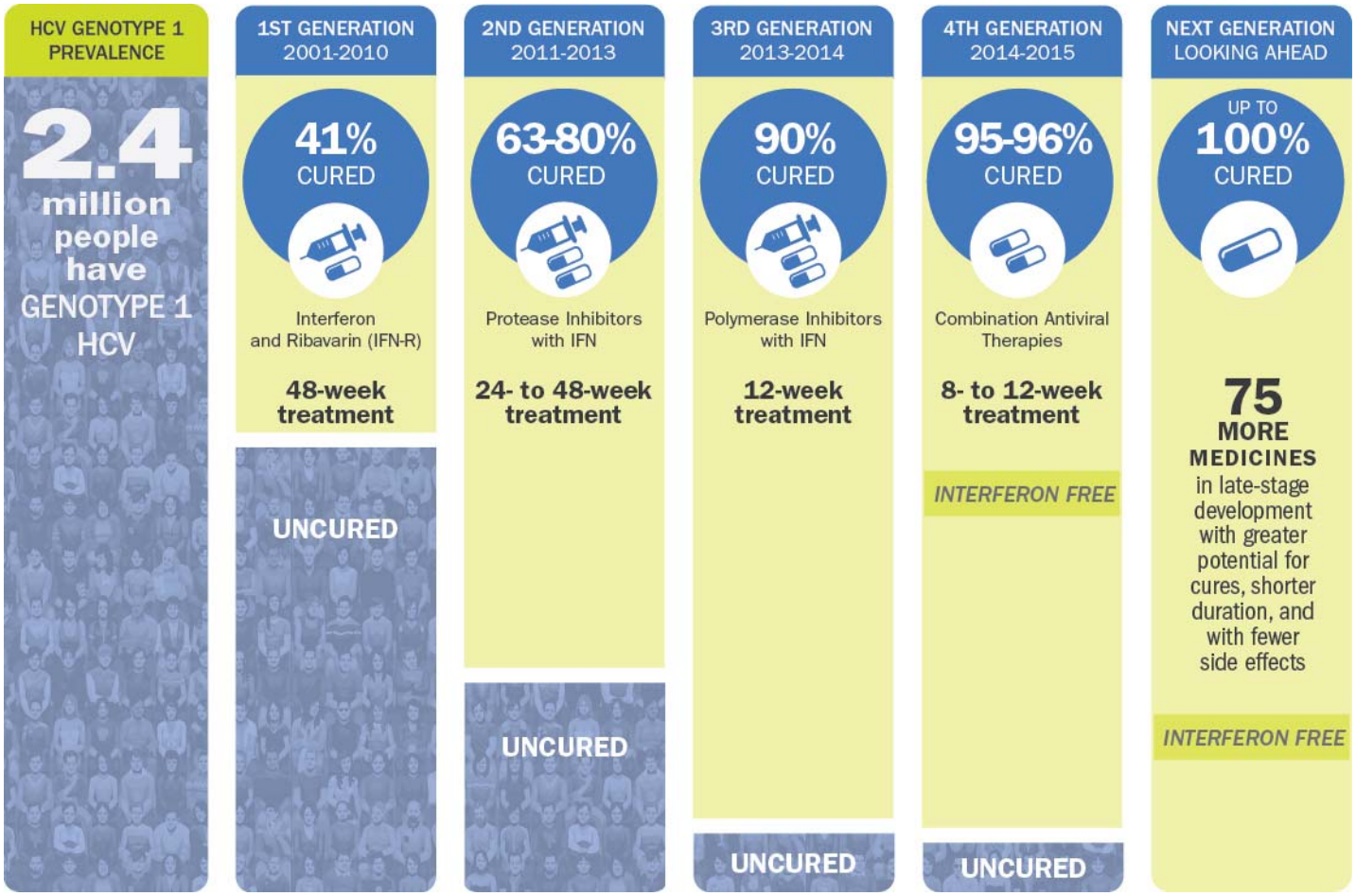
*US Death Rates Due to Diseases of the Heart**



*Age-adjusted death rates based on Year 2000 US Standard Population. 1980-1998 causes of death are classified by the Ninth Revision International Classification of Diseases (ICD-9). Beginning in 1999, causes of death are classified by the Tenth Revision International Classification of Diseases (ICD-10).

Source: CDC[23,24]

Hepatitis C (HCV): Cure Rates Are Rising

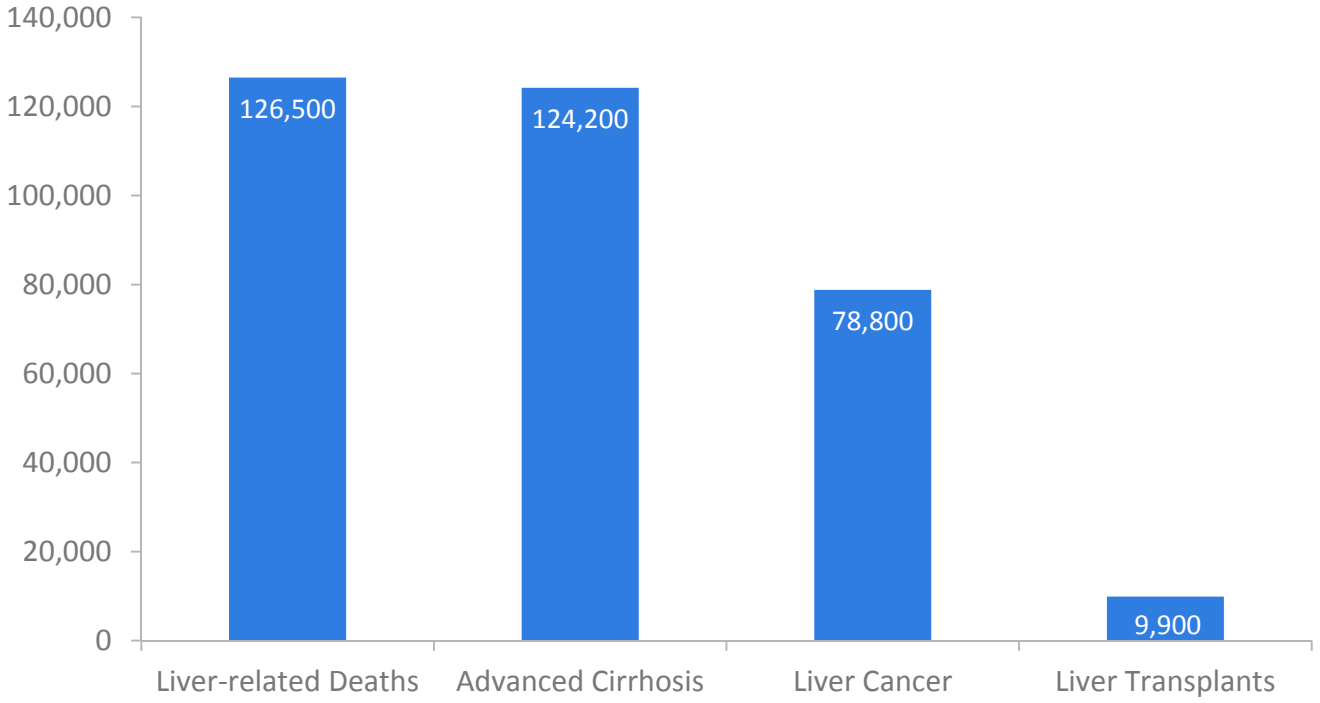


Sources: Armstrong GL, et al.[25]; FDA[26]; PhRMA[27]

Projected Reductions in Hepatitis C-Related Complications

Increased screening and the availability of new treatments for HCV are projected to dramatically reduce complications associated with the disease. Projections suggest the number of liver-related deaths avoided will total 126,500 by 2050.[28]

Avoided Cases of HCV-Related Complications by 2050

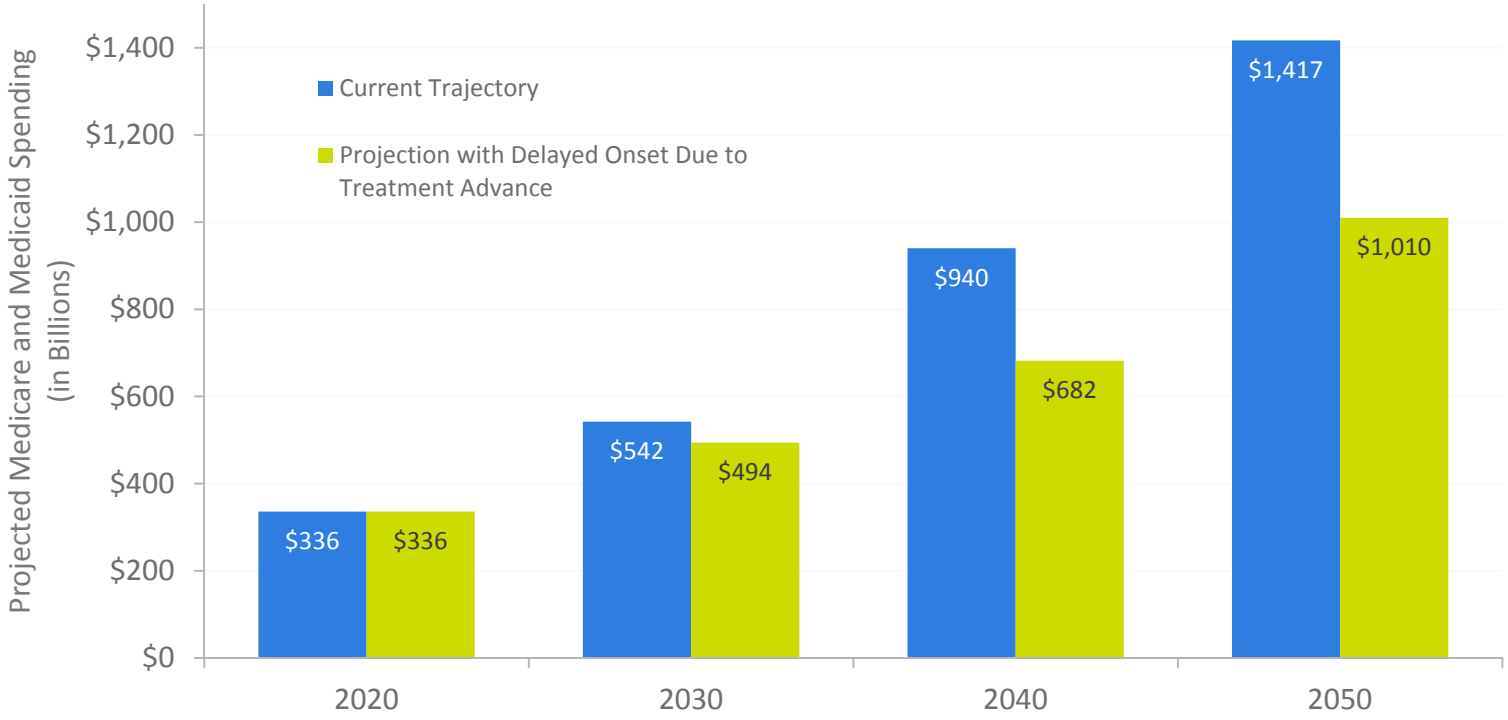


Sources: Kabiri M, et al.[28]

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 more than $400 billion annually by 2050.*

*Projected Annual Medicare and Medicaid Spending, With and Without New Treatment Advances (Billions)***



*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[29]

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2 RESEARCH AND DEVELOPMENT

The Process of Drug Discovery and Development

More than 7,000 medicines are in development globally and the pipeline has never been more promising. PhRMA member companies invested an estimated $51.2 billion in biopharmaceutical research and development (R&D) in 2014, accounting for the majority of private biopharmaceutical R&D spending. Development of new medicines is a rigorous and long process, and it has become more costly and complex over the last decade. Less than 12% of the candidate medicines that make it into phase I clinical trials will be approved by the FDA. Companies “race” to bring the first medicine in a class to market, and just 2 in 10 approved drugs are ultimately commercial successes. Recent biopharmaceutical advances—driven by scientific research and creative ingenuity—would not have been possible without a system of laws, including intellectual property (IP) protections, that provide the structure, stability, and opportunity for the needed investment.

More Than 7,000 Medicines in Development Globally

Biopharmaceutical researchers are working on new medicines for many diseases.

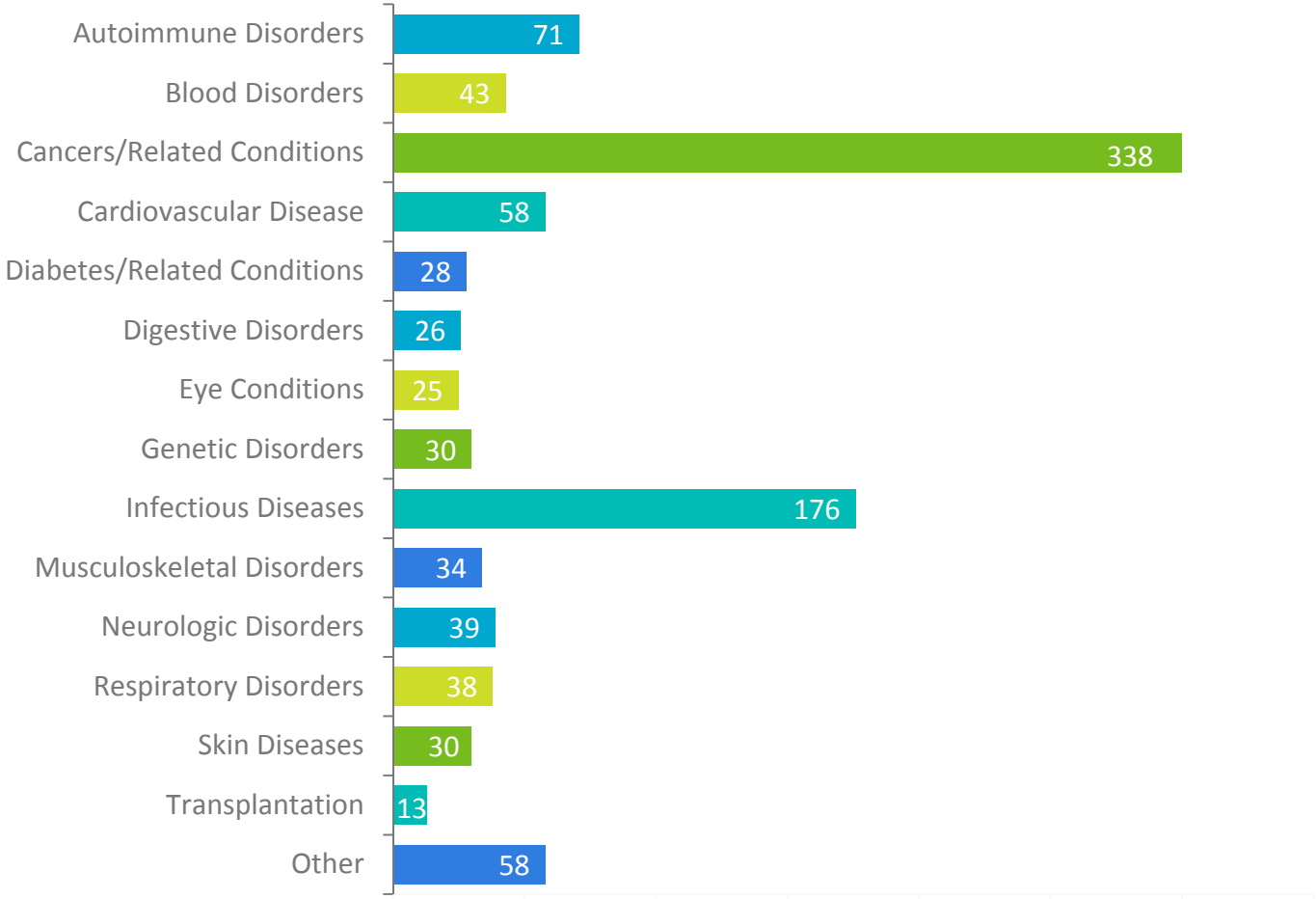
Selected Diseases	Medicines in Development*
Cancers	1,813
Cardiovascular disorders	599
Diabetes	475
HIV/AIDS	159
Immunological disorders	1,120
Infectious diseases	1,256
Mental health disorders	511
Neurological disorders	1,329

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

Source: Adis R&D Insight Database[1]

More than 900 Biologic Medicines in Development in 2013

Biologic medicines—large, complex molecules derived from living cells—frequently represent novel strategies that have the potential to transform the clinical treatment of disease.

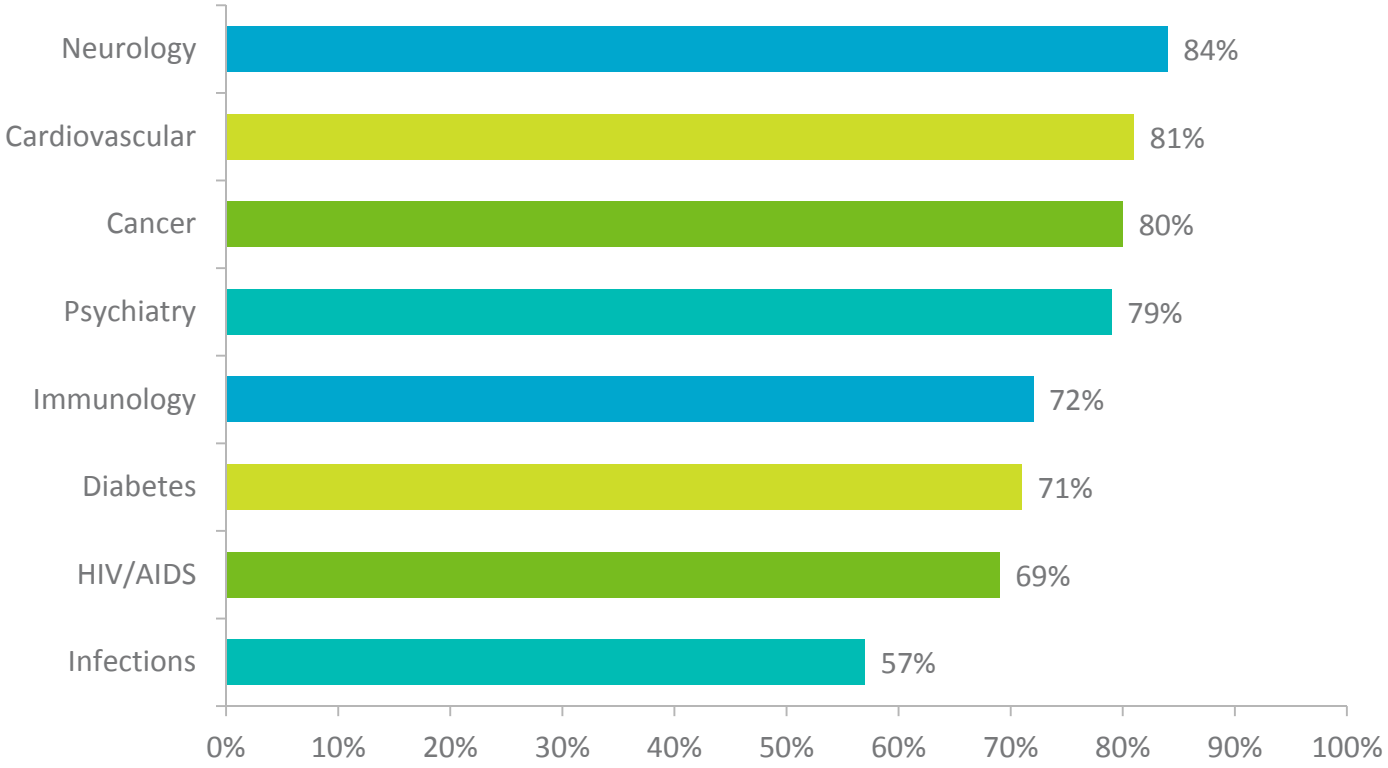


Source: PhRMA[2]

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



Source: Analysis Group[3]

Biopharmaceutical Companies Are Advancing Personalized Medicine

Biopharmaceutical research companies increased R&D investment in personalized medicine by 75% between 2005 and 2010.

UP TO 50%

of new medicines in the pipeline are reportedly **personalized medicines** (across all diseases)

"The last couple of years have seen some dramatic examples of how things are changing in terms of applications of personalized medicine…we now have noninvasive prenatal diagnosis, treatments for melanoma where before there was nothing people could do, and immune therapies for cancer that just a few years ago were a dream.

There is an opportunity to develop targeted therapies for many, many disorders because of the genetic knowledge we're gaining about them."

— Raju Kucherlapati,
Harvard Medical School, Brigham and Women's Hospital

Sources: Tufts Center for the Study of Drug Development (CSDD)[4]; Harvard[5]

Cutting-Edge Research Drives Development of Medicines

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

CANCER

Conjugated Monoclonal Antibodies target and kill tumors while sparing nearby healthy cells.

Immunotherapies enable the immune system to recognize and fight cancers in the same way it does infectious agents.

CARDIOVASCULAR DISEASE

PCSK9 Inhibitors lower LDL cholesterol levels by mimicking a natural mutation in a gene that regulates this "bad" cholesterol in the body.

Angiotensin-receptor Neprilysin Inhibitors reduce blood pressure and treat heart failure through 2 separate pathways.

HIV/AIDS

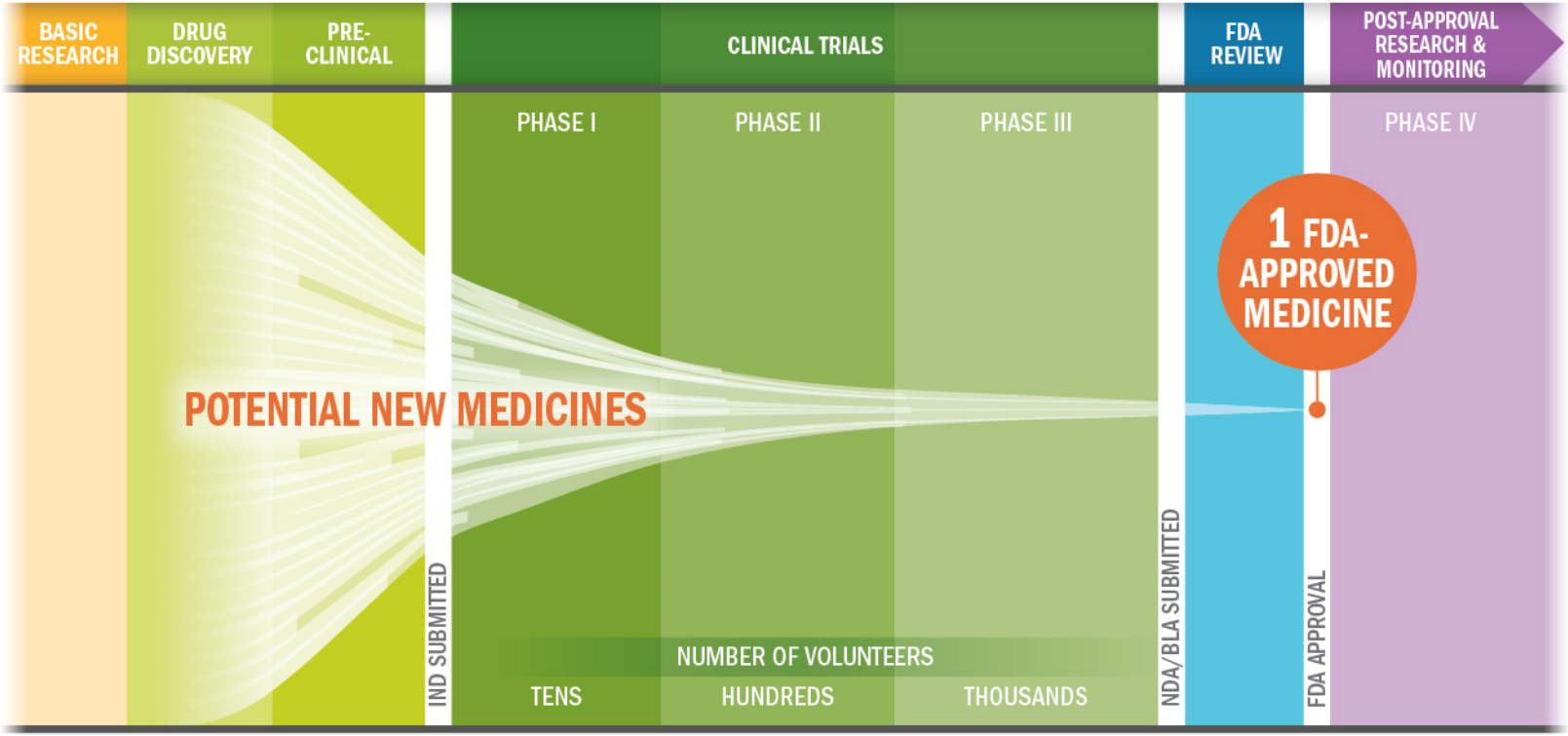
Attachment Inhibitors stop the virus from attaching to new cells, thus preventing infections.

Therapeutic Vaccines induce crucial immune responses and strengthen the body's natural anti-HIV immune response.

Source: 2015 PhRMA Profile[6]

The Biopharmaceutical Research and Development Process

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



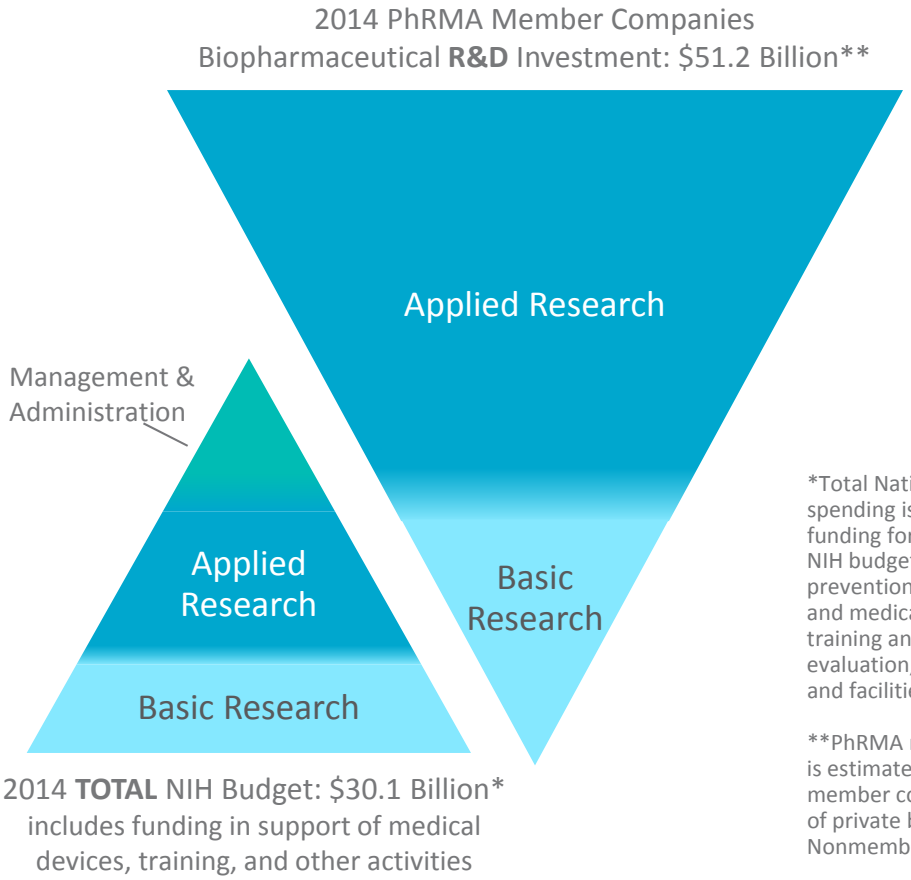
Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

*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.

Source: PhRMA[7]

Biopharmaceutical Companies Do the Vast Majority of Research to Translate Basic Science into New Medicines

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



*Total National Institutes of Health (NIH) spending is for fiscal year 2014. In addition to funding for basic and applied research, the total NIH budget includes funding in support of prevention (eg, suicide prevention), diagnostics and medical devices, superfund activities, training and education (eg, dental), program evaluation, management and support, buildings and facilities, and other activities.

**PhRMA member companies' R&D spending is estimated for calendar year 2014. PhRMA member companies account for the majority of private biopharmaceutical R&D spending. Nonmember company data are not included.

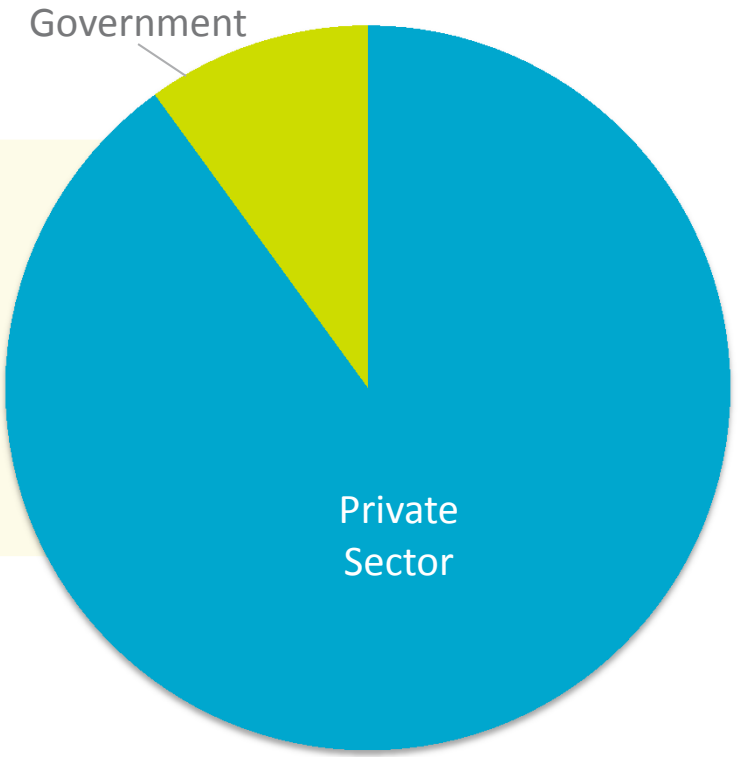
Sources: Tufts CSDD[8]; PhRMA[9]; NIH Office of Budget[10]

Biopharmaceutical Research Companies Play a Pivotal Role in Drug Discovery and Development

Recent studies show that biopharmaceutical companies perform the vast majority of development work to bring new medicines to patients.

91% OF DRUGS

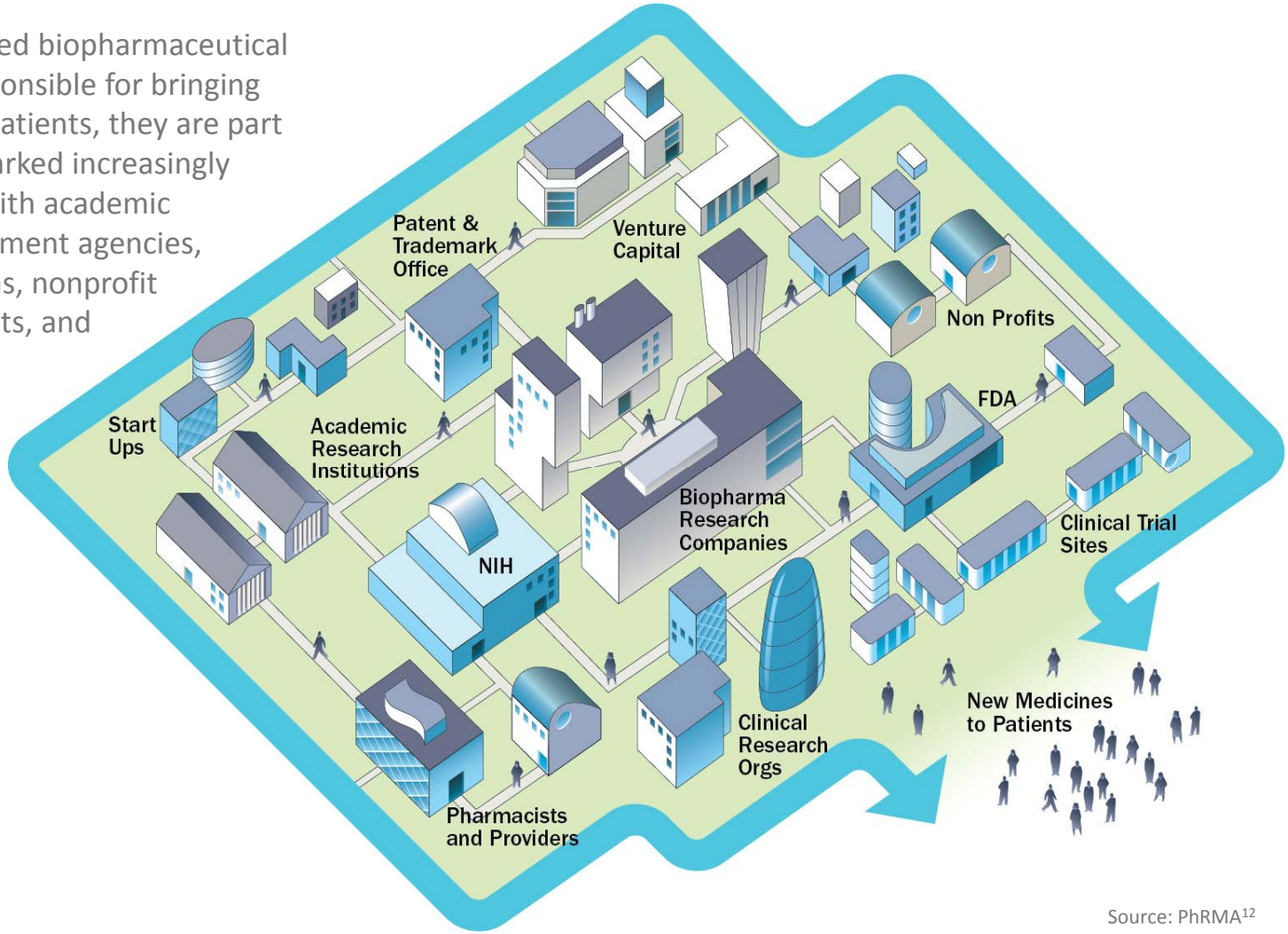
are developed by the **private sector** with no direct government role according to an article from *Health Affairs*.



Source: Health Affairs[11]

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.

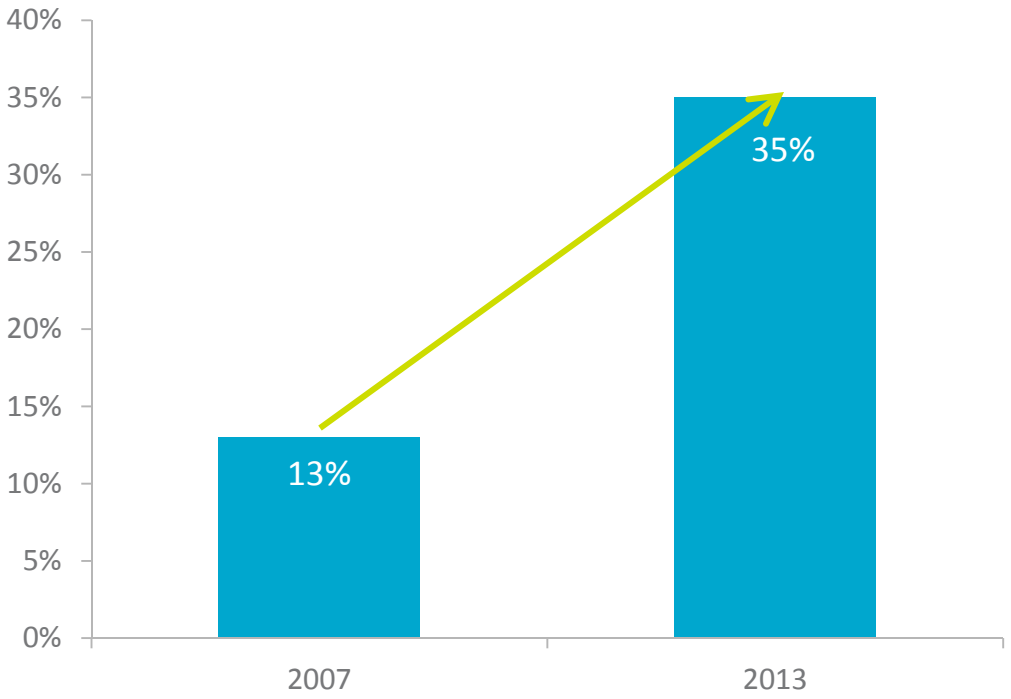


Source: PhRMA[12]

Biopharmaceutical Companies' Corporate Venture Capital Increasingly Fostering Early-Stage Innovation

As first-round venture capital (VC) investments have dropped nearly 40% since 2007, the corporate venture capital (CVC) arms of established biopharmaceutical companies are helping fill this growing funding gap for early-stage innovation.

Share of First-Round Biopharmaceutical VC Deals Involving CVC Funds, 2007-2013



Sources: Silicon Valley Bank[13]; PwC and National Venture Capital Association[14]

Collaboration Is Key in Researching and Developing New Medicines

Partnerships are crucial to maintaining robust biopharmaceutical innovation in the United States. Collaborations come in many different shapes and sizes. Here are some selected examples of key collaborative efforts across the R&D spectrum.

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 decisionmaking

The Partners: biopharmaceutical companies, NIH, CMS, FDA, patient and disease organizations

THE biomarkers CONSORTIUM

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

LUNG-MAP

Sources: Accelerating Medicines Partnership[15]; Biomarkers Consortium[16]; Lung-MAP[17]

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[18]

PhRMA Member Company R&D Expenditures: 1995-2014

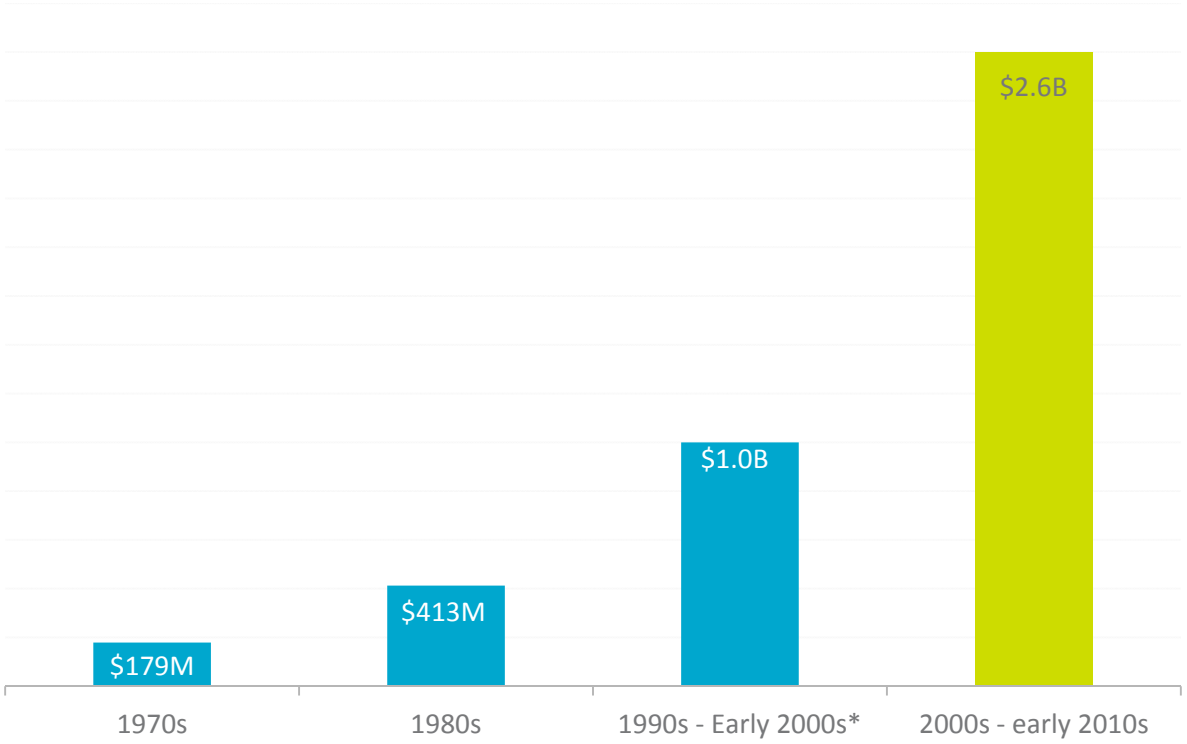
*Estimated FY 2014

Sources: Congressional Budget Office[18]; PhRMA[19]

Drug Development Costs Have Increased

According to a 2014 study, it costs an average of $2.6 billion to develop one new drug. Less than 12% of the candidate medicines that make it into phase I clinical trials will be approved by the FDA.

The Average Cost to Develop One New Approved Drug—Including the Cost of Failures (Constant 2013 Dollars)



*Previous research by same author estimated 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 and Decision Economics. 2007;28: 469-479). That estimate was 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 updated for changes in the cost of capital.

Source: Tufts CSDD[20]

Complexity of Clinical Trials Has Increased

During the last 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

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

*These numbers reflect only the "treatment duration" of the protocol.

Source: Getz KA, et al. and Tufts CSDD[21]

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:

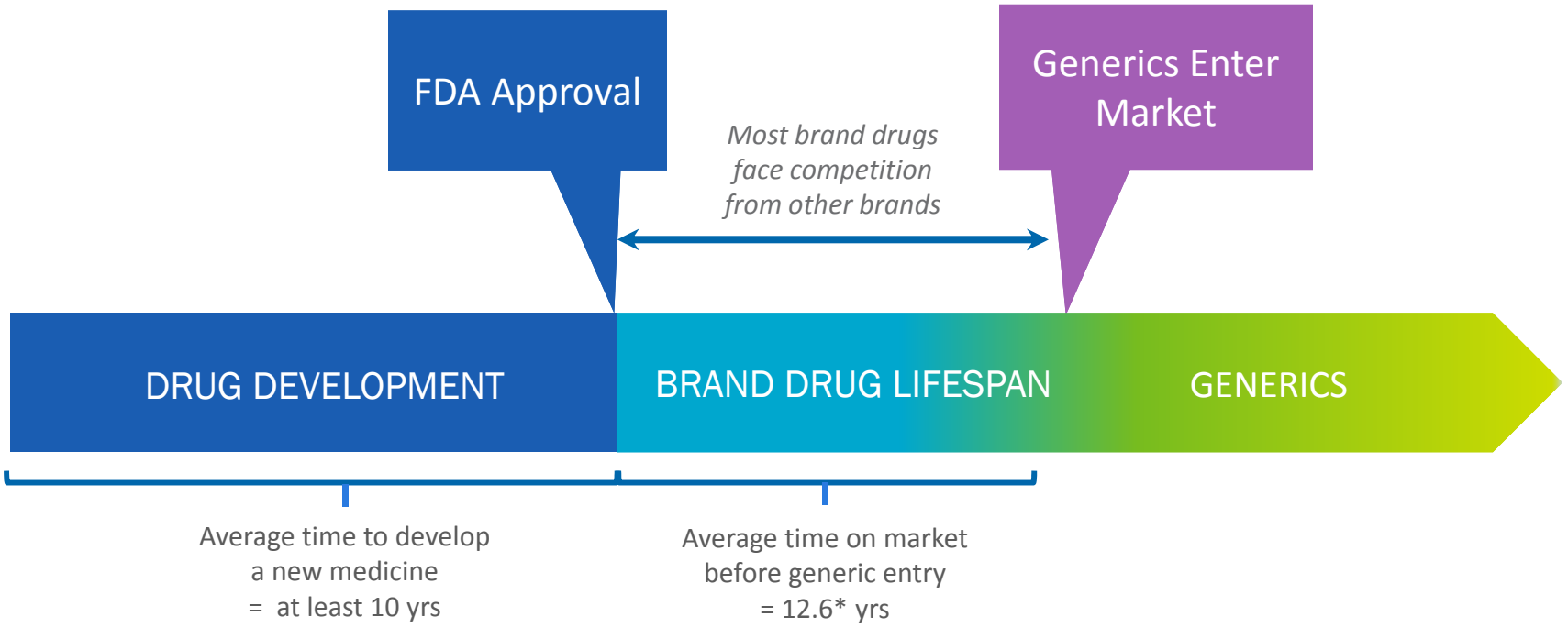
- **Improving target validation methods** to allow for greater accuracy in identifying and selecting the most promising drug candidates
- **Enhancing IT infrastructure** to improve efficiencies in translating drug discovery and preclinical data into clinical research activity
- **Using adaptive trial 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[22]

Illustrative Pharmaceutical Lifecycle

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



*For brand medicines with more than $100 million in annual sales in 2008 dollars, which account for 97% of sales of the brand medicines analyzed

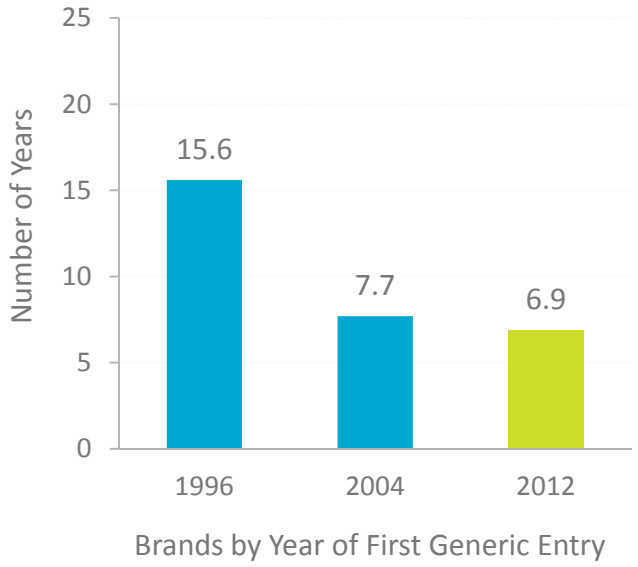
Sources: PhRMA[23]; Grabowski HG, et al.[24]; Tufts CSDD[25]

Earlier and More Frequent Patent Challenges by Generic Companies

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

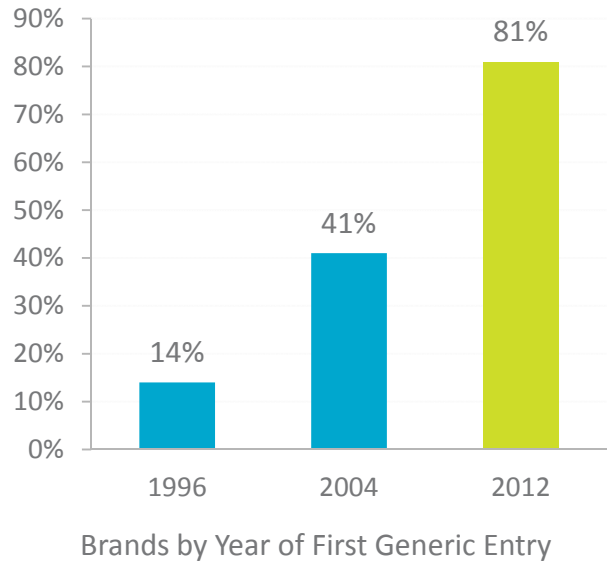
Patent challenges are occurring earlier…

Average Time from Brand Launch to Paragraph IV Patent Challenge



… and are more common

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



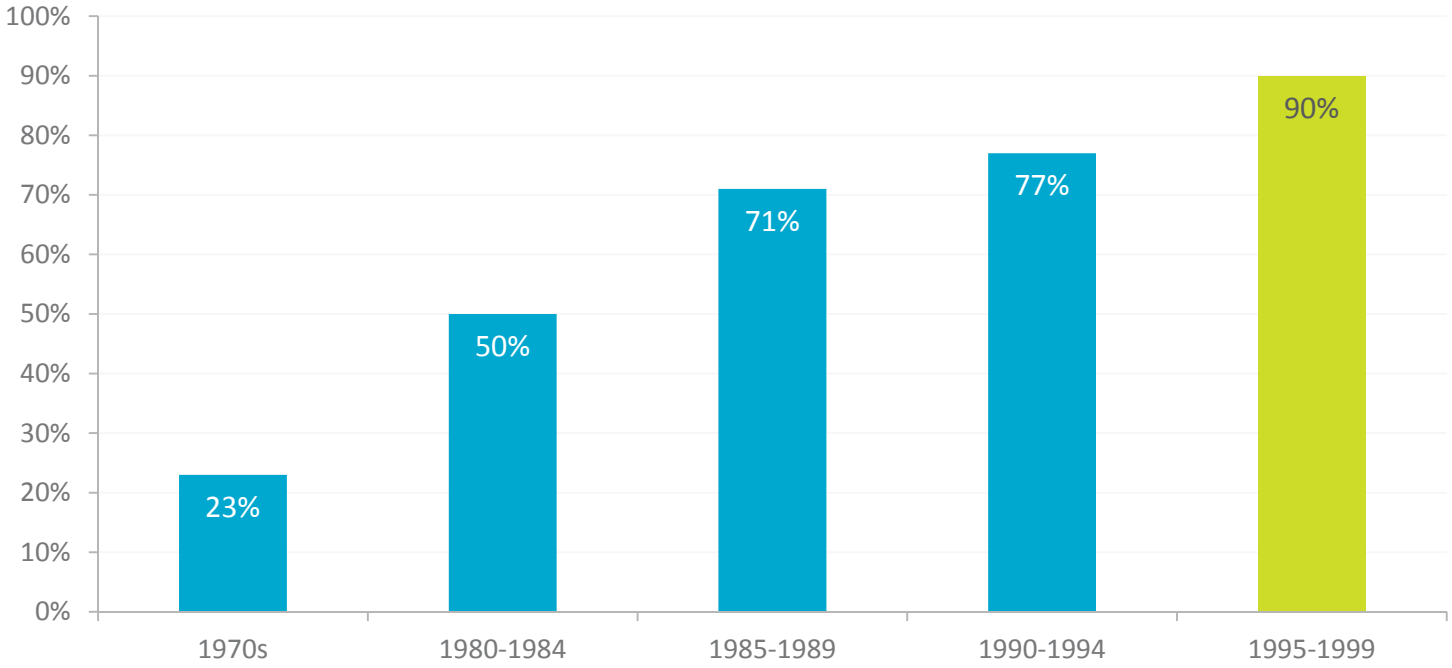
Note: All numbers are 3-year moving averages.

Source: Grabowski HG, et al.[26]

Competing Medicines Race for Approval

By 1995, nearly all first-in-class medicines being approved already had potential competitors in phase II clinical testing.

Percentage of First-in-Class Medicines with a Competitor Already in Phase II Clinical Testing at Time of Approval

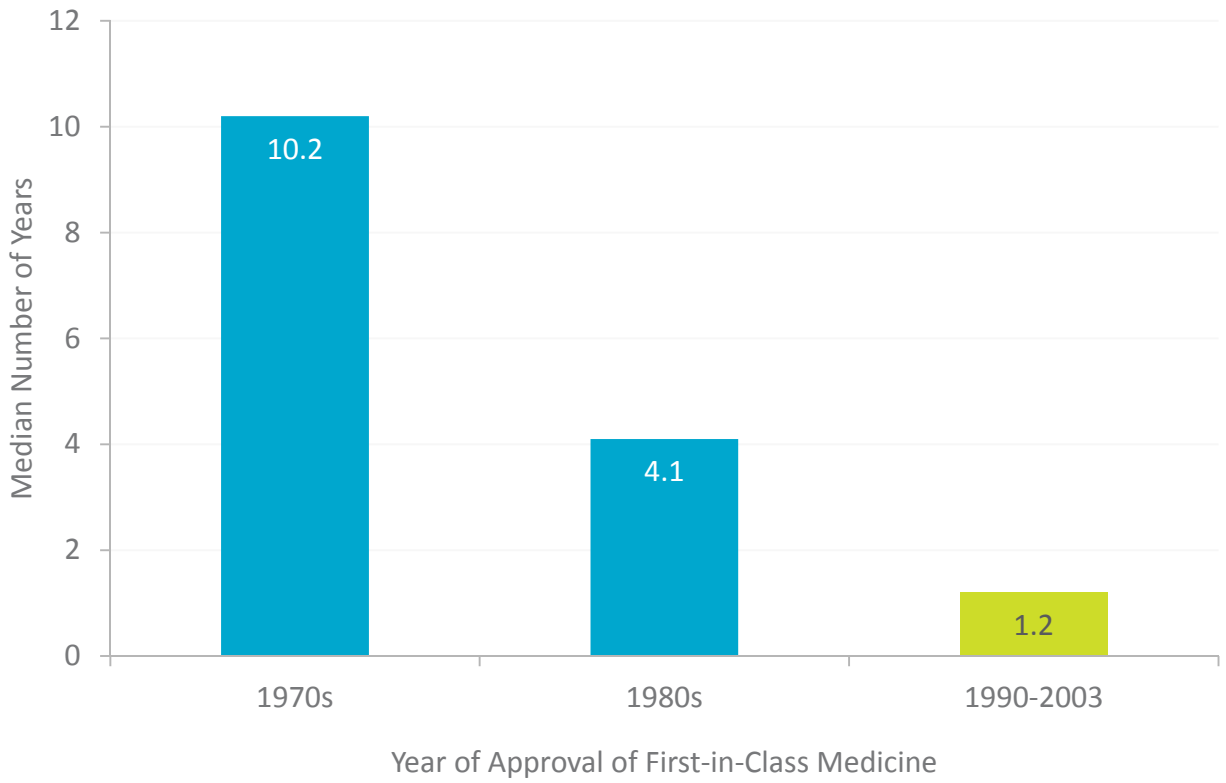


Source: DiMasi JA, Faden LB[27]

Increasing Competition Within Therapeutic Categories

The time a medicine is the only drug available in its therapeutic class has declined dramatically from a median of more than 10 years in the 1970s to less than 2 years by 1998.

Time Between Approval of First and Second Drugs in a Therapeutic Class

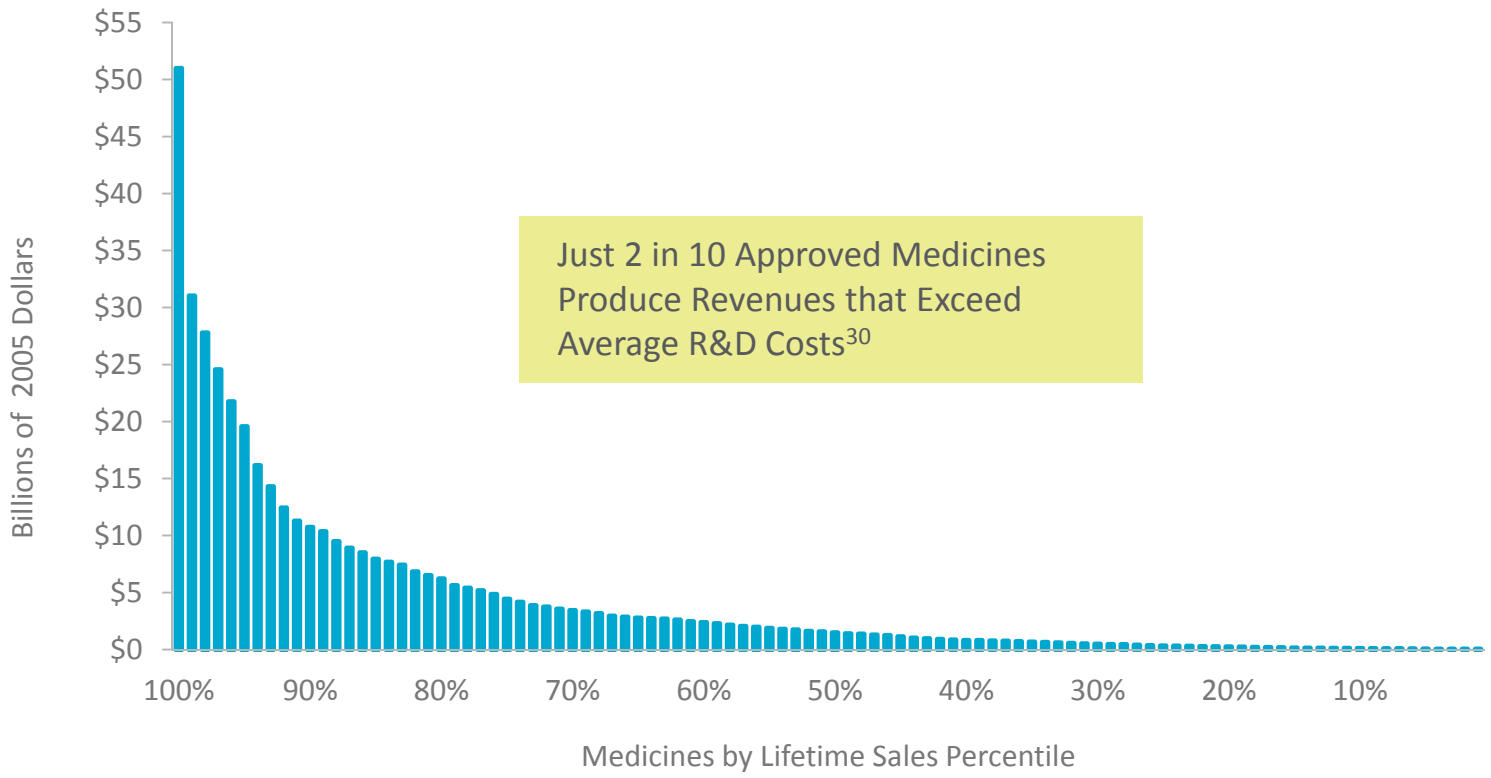


Source: Tufts CSDD[28]

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[29]



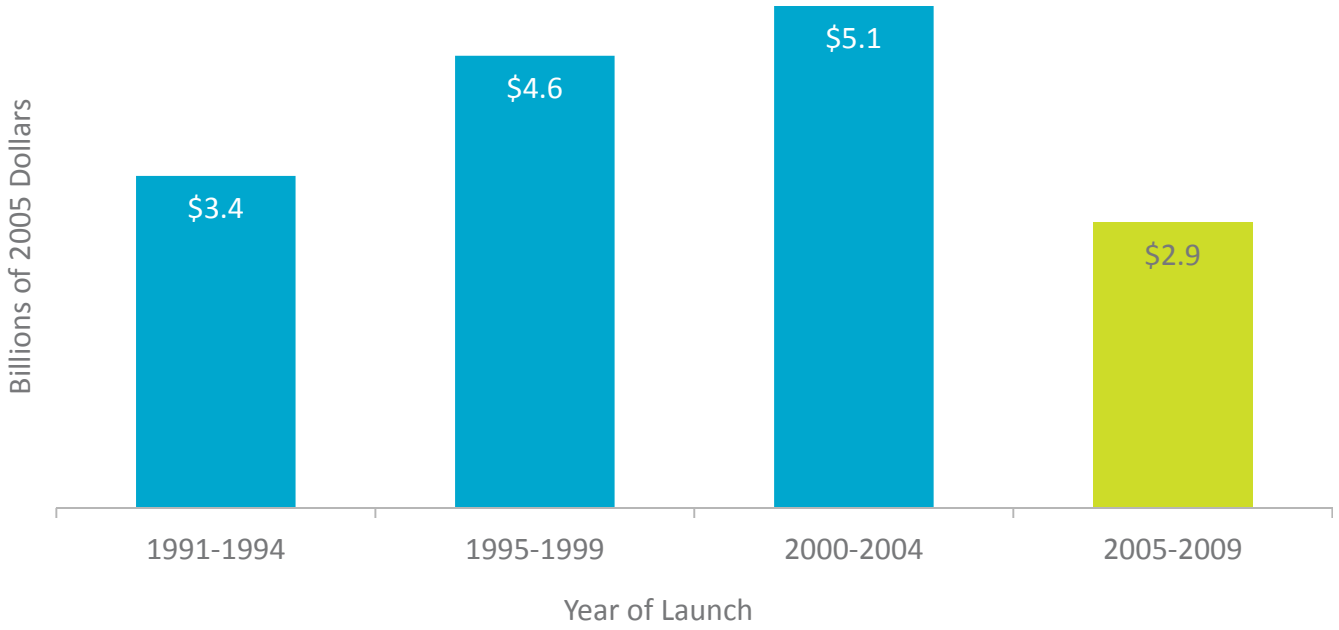
A "medicine" is defined as a novel active substance, ie, a molecular or biologic entity or combination product in which at least one element had not previously been approved by the US Food and Drug Administration. Sales are global sales net of rebates and discounts.

Sources: Berndt E, et al.[29]; Vernon JA, et al.[30]

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 companies' ability to maintain their historically high levels of innovation.

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



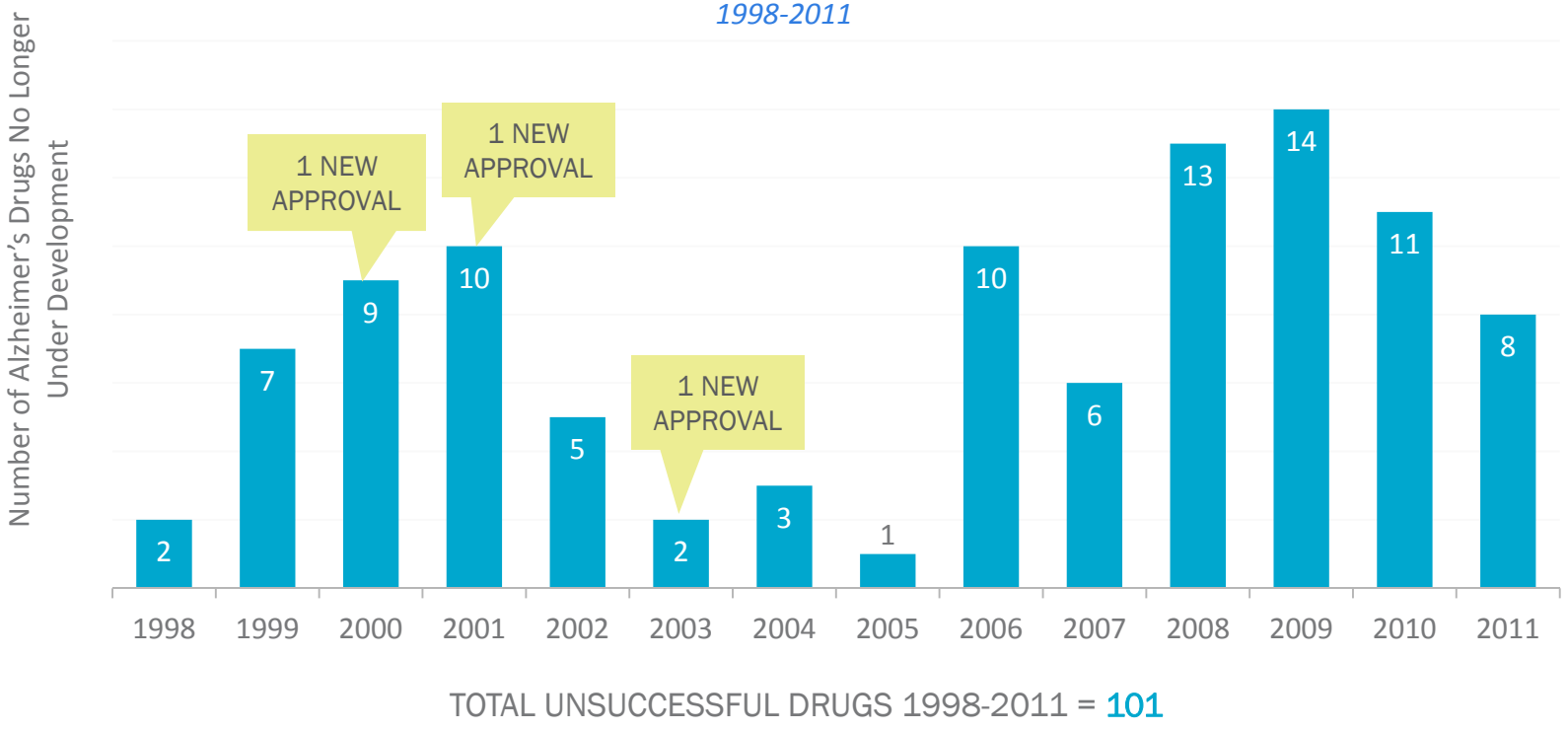
A "medicine" is defined as a novel active substance, ie, a molecular or biologic entity or combination product in which at least one element had not previously been approved by the Food and Drug Administration. Sales are global sales net of rebates and discounts.

Source: Berndt E, et al.[31]

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

Since 1998, 101 medicines in development for the treatment of Alzheimer's disease have not made it through clinical trials, with only 3 gaining FDA approval. These setbacks highlight the complexity of the R&D process. Though disappointing, they provide important knowledge to fuel future research.

Unsuccessful Alzheimer's Drugs in Development
1998-2011



Source: PhRMA[32]

Cancer Researchers Build on Knowledge Gained from Setbacks in Order 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

*Setbacks and advances from 1998 to 2014

Source: PhRMA[33]

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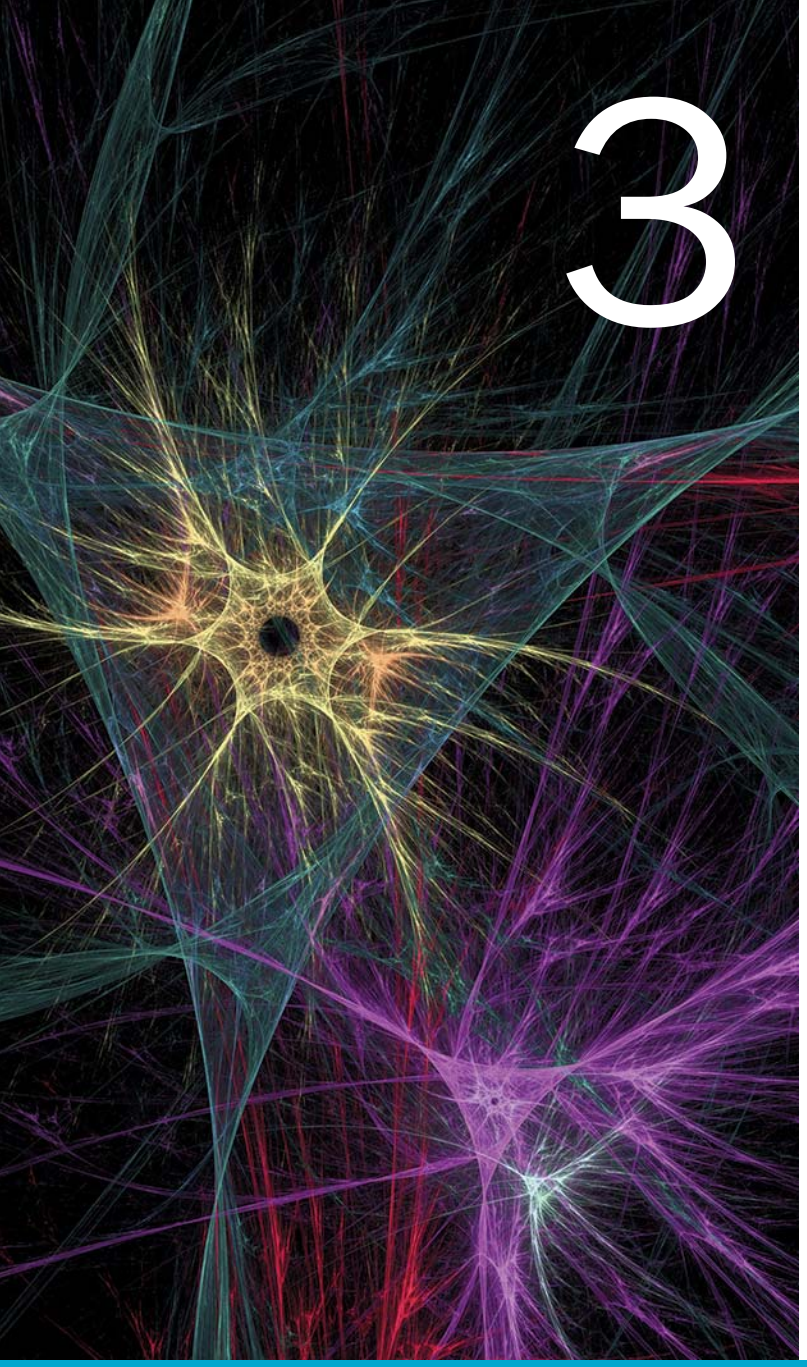


3 SPENDING AND COSTS

Understanding Spending on Medicines

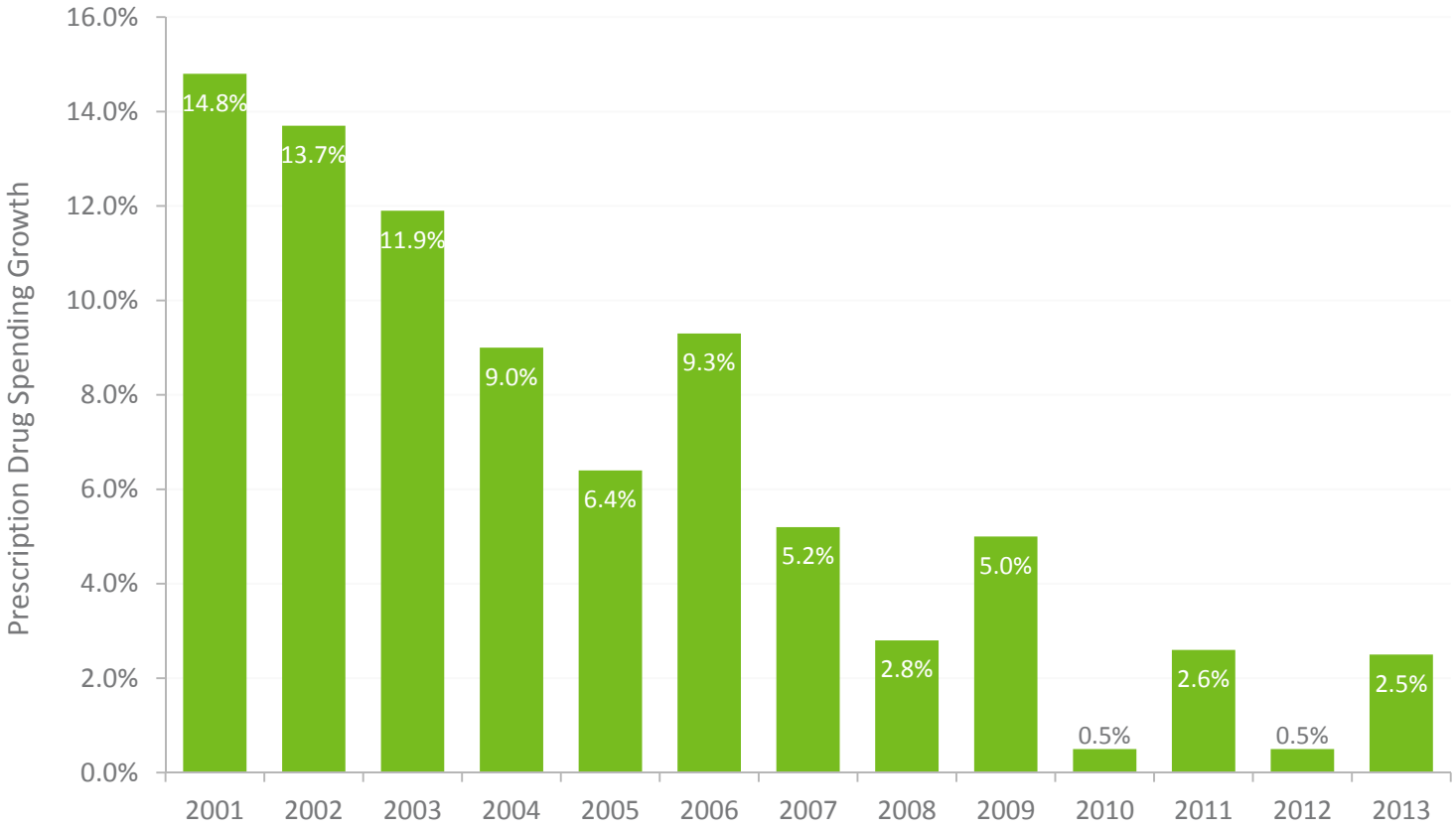
Prescription medicines represent a small share of national health spending. Growth in prescription drug spending has slowed markedly over the past decade, and grew more slowly than overall health spending. Government estimates project this trend will continue over the coming decade.

Innovator pharmaceutical companies produce medical advances through pioneering scientific work and large-scale investments. Innovators' work and investment lead to new medicines and may, over time, lead to generic drugs and biosimilars that consumers can use at lower cost for many years.

Health plans have many tools such as tiered formularies and cost sharing to steer use toward generics and biosimilars. Payers also typically require patients to pay a higher share of the costs of medicines out of pocket compared with other health services. Changes in the design of drug benefits have led to high out-of-pocket costs for some medicines, creating access barriers for some patients with serious and chronic health conditions.

Sharply Declining Prescription Medicine Spending Growth: 2001-2013*

Spending growth for prescription medicines has slowed dramatically over the past decade, with historically low rates of growth observed in recent years.

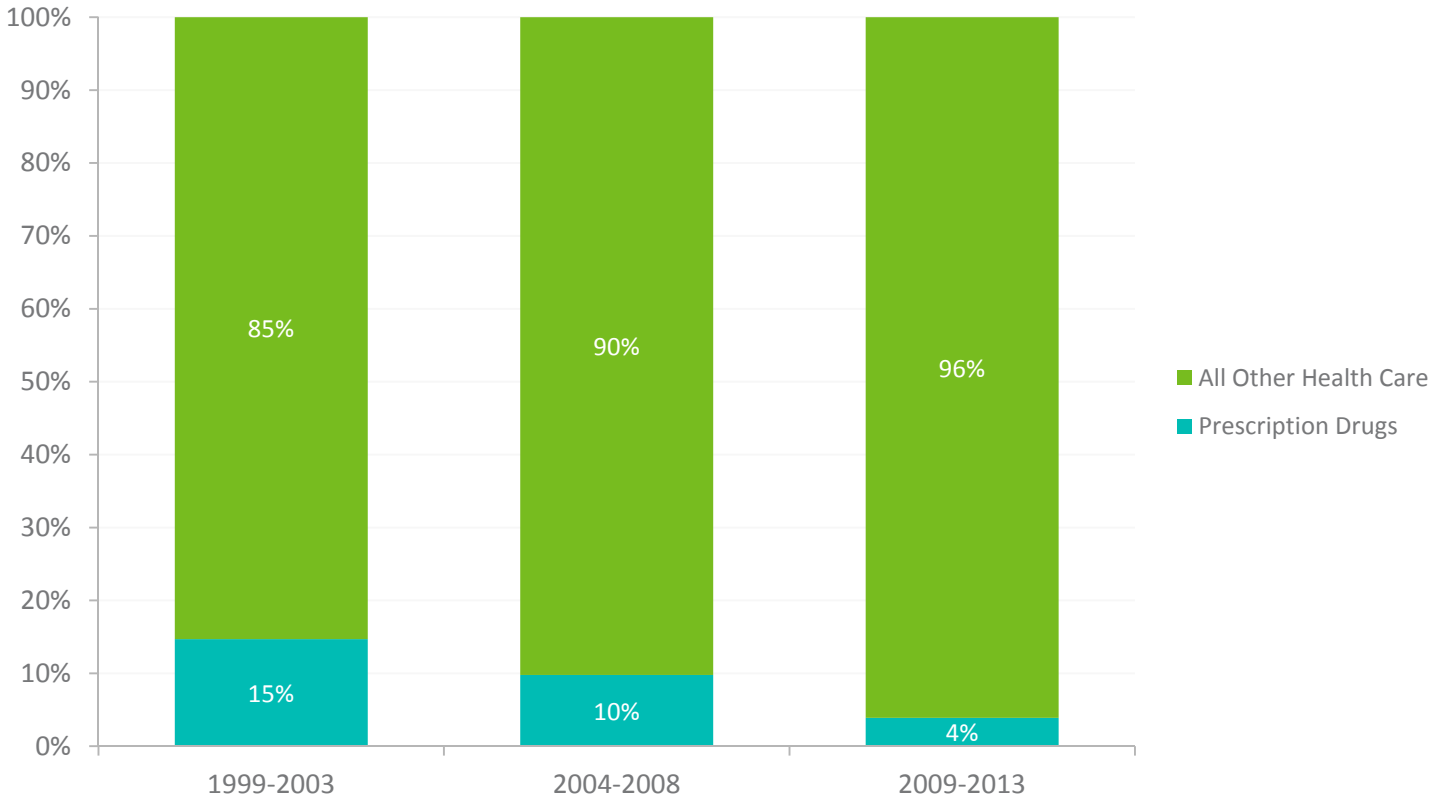


*Total retail sales including brand medicines and generics

Source: Centers for Medicare & Medicaid Services (CMS)[1]

Medicines Account for a Small and Declining Share of Health Care Spending Growth

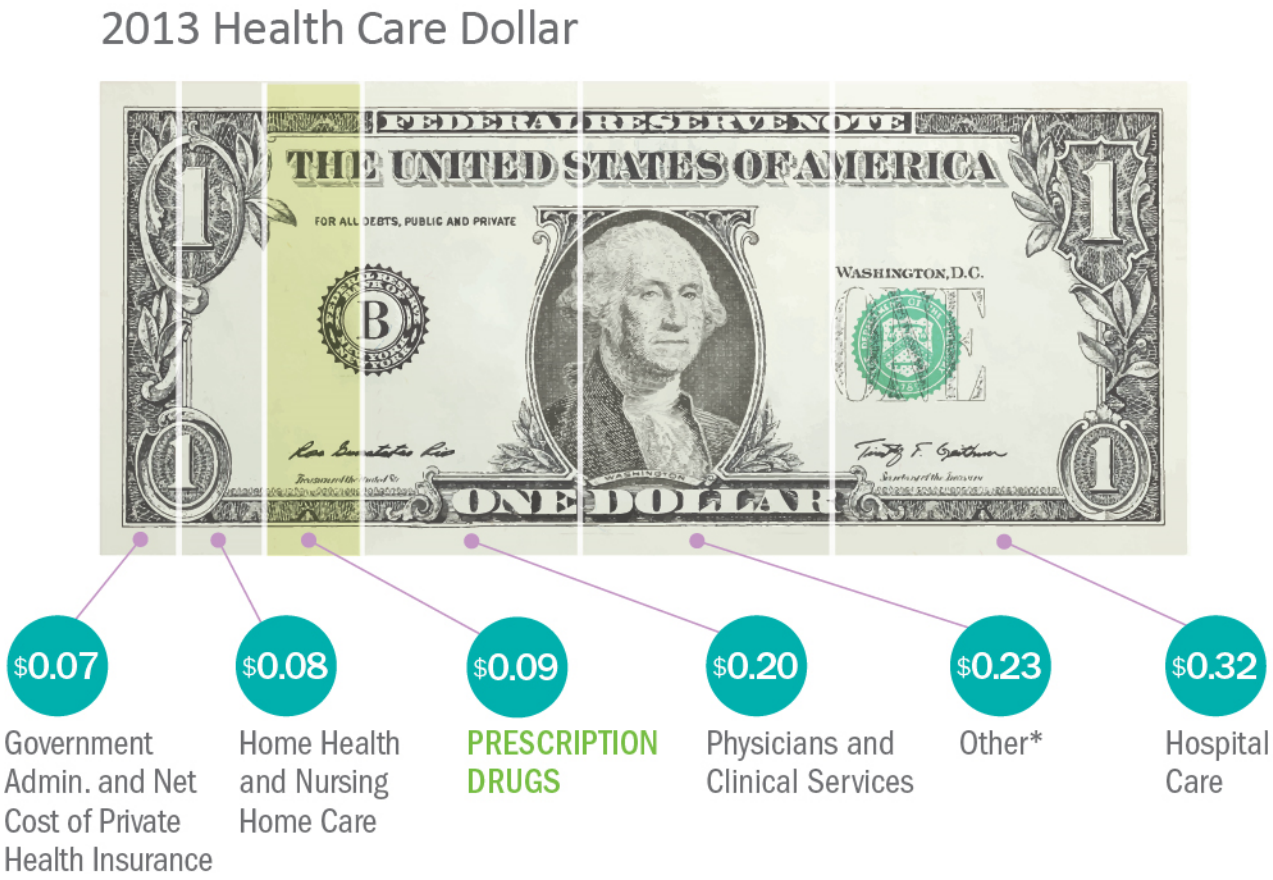
Growth in Health Care Expenditures Attributable to Prescription Drugs, 1999-2013



Source: CMS[2]

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

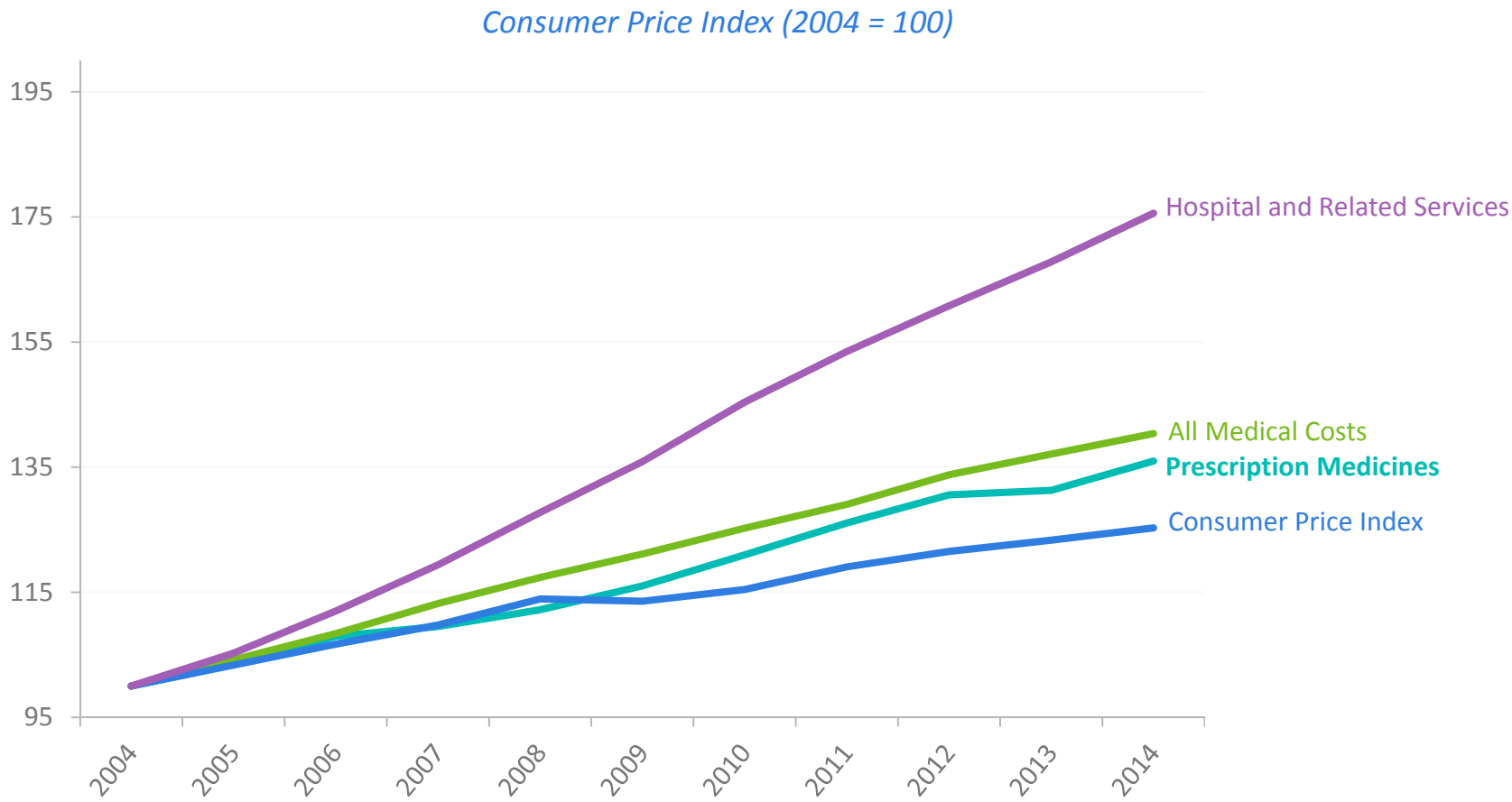
Prescription medicines today account for about 10% of health care spending in America, the same percentage as in 1960.



*Other includes dental, home health, and other professional services as well as durable medical equipment costs.

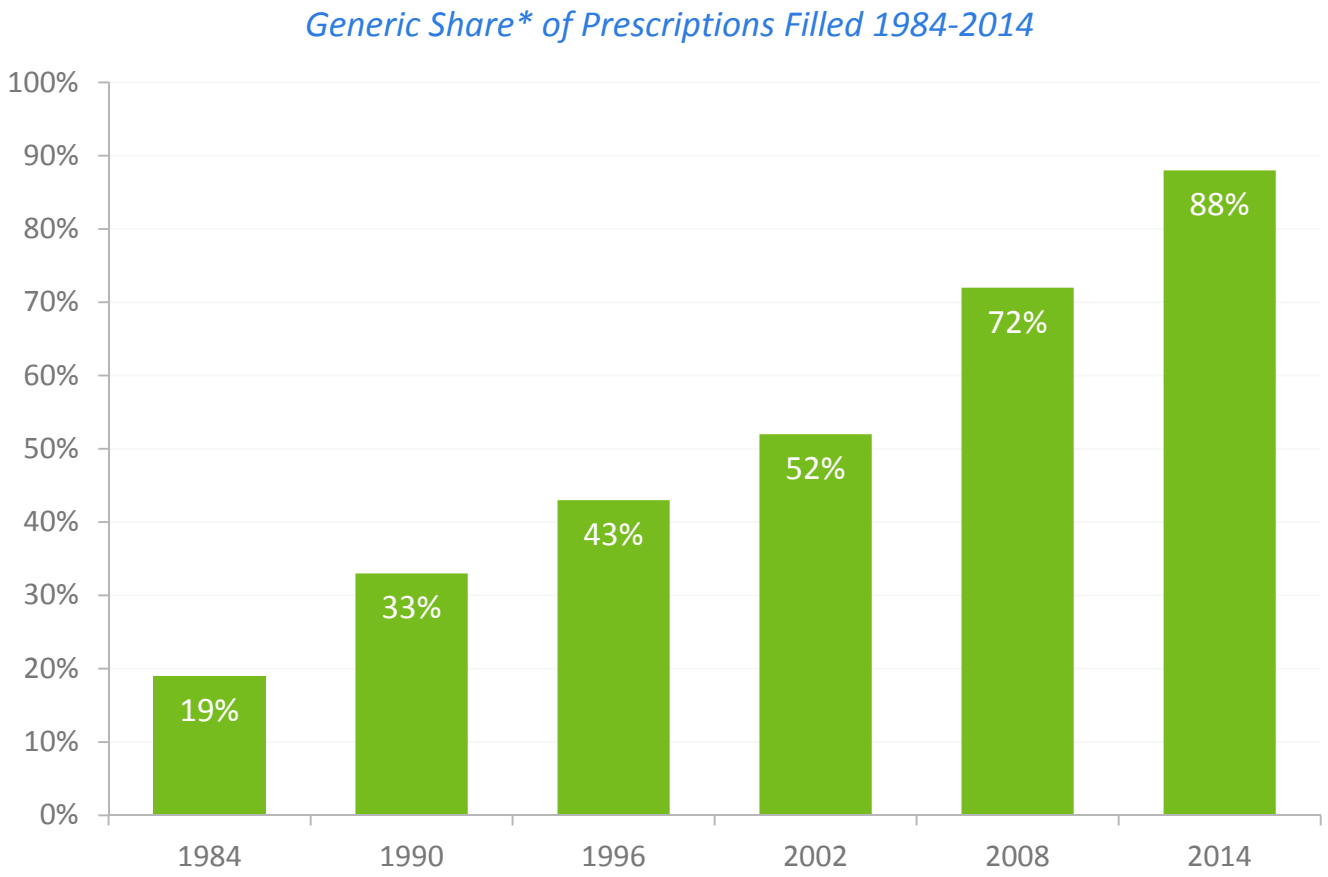
Source: PhRMA analysis based on CMS[3]

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



Source: PhRMA analysis based on US Bureau of Labor Statistics[4]

Nearly 9 Out of Every 10 US Prescriptions Are Filled With Generics



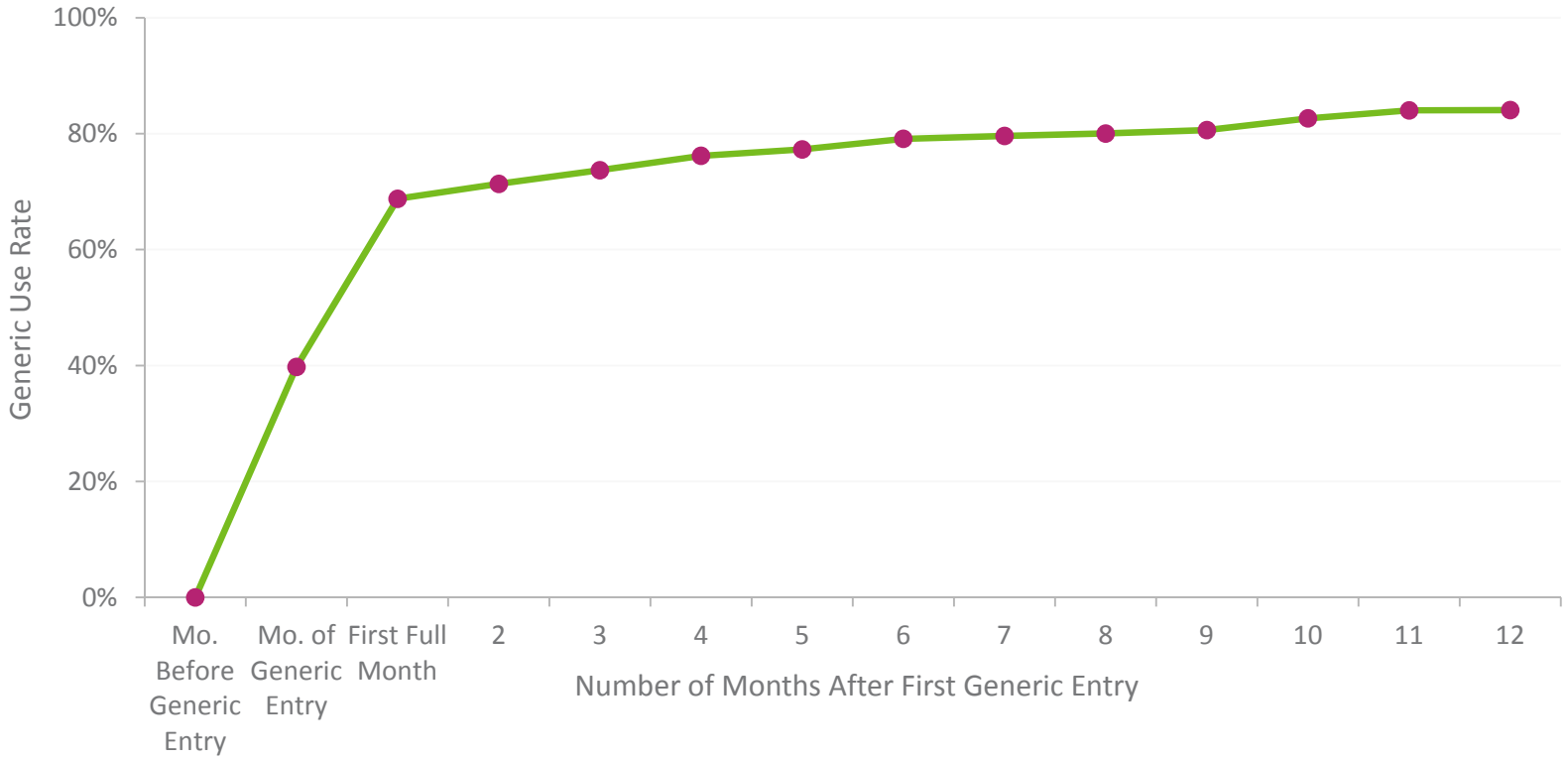
*Generic share includes generics and branded generics. "Other" category from IMS National Prescription Audit™ not included in calculation.

Source: IMS Health[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,[6] and some capture as much as 90% by that time.[7]

*Average Generic Share of Total Use Following Launch of a Brand Medicine's First Generic, 2011-2012**



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

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

The US Prescription Drug Lifecycle Promotes Innovation and Affordability

Incredible advances by innovator 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 M[8]

Powerful Purchasers Negotiate on Behalf of Patients

A small number of large purchasers dominate the US prescription drug market.

Prescription Volume by **PHARMACY BENEFIT MANAGEMENT (PBM)** Companies, 2012

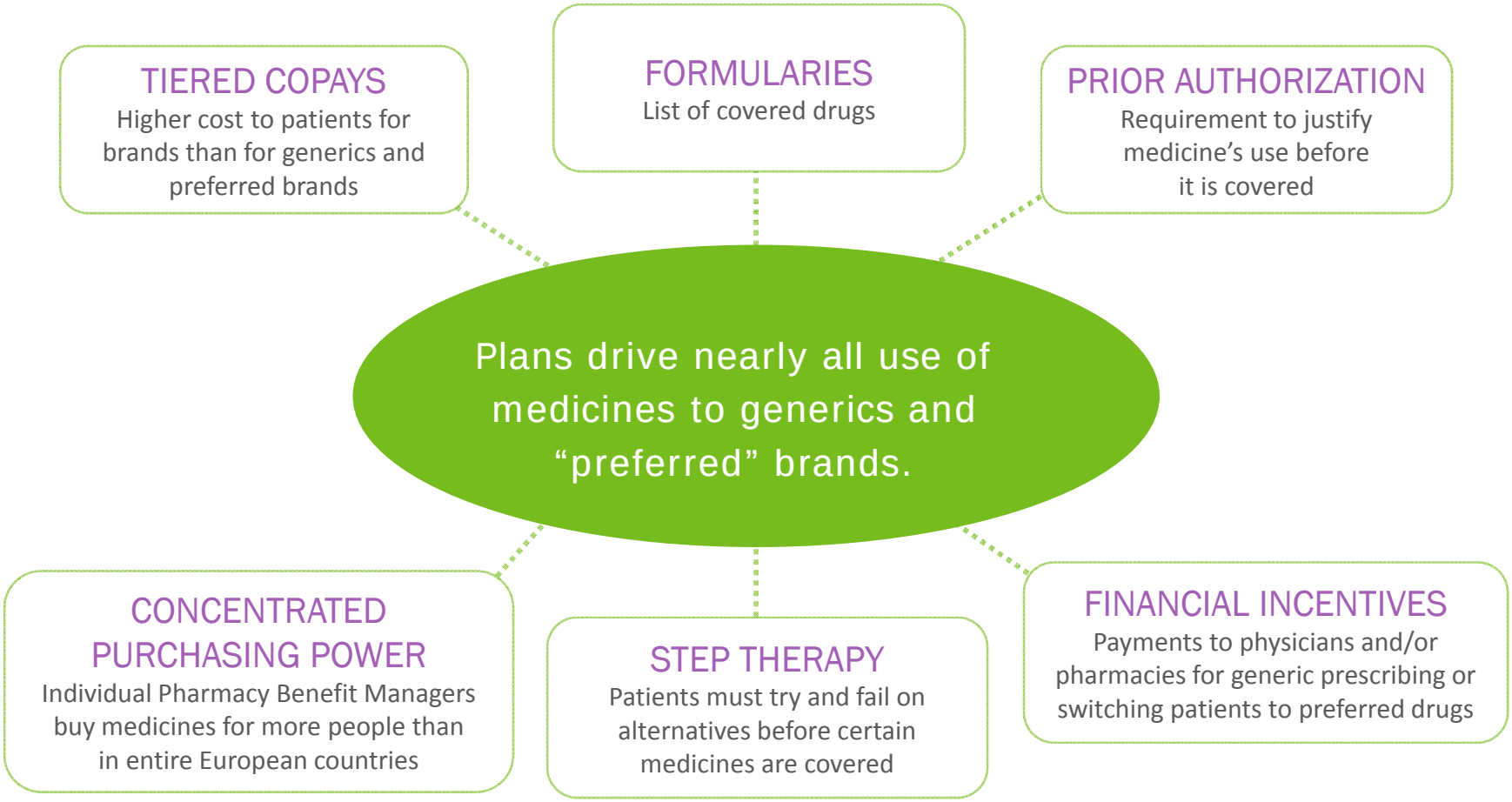
PBMs		PRESCRIPTIONS (millions)	MARKET SHARE*
top 5	1 Express Scripts/Medco Health Solutions**	1,411	29.5%
	2 CVS/Caremark	775	16.2%
	3 Argus Health Systems	504	10.5%
	4 OptumRx, Inc.	319	6.7%
	5 ACS, Inc.	250	5.2%
	TOTAL	3,259	68.2%
top 10		4,107	85.9%
top 15		4,584	95.9%
all PBMs in US		4,780	100%

*Figures may not sum to totals due to rounding.

**Medco was acquired by Express Scripts in April 2012. Figure for Express Scripts/Medco is the sum of the individual script totals for each entity for the most recently reported 12-month period in 2012.

Source: Atlantic Information Services, Inc[9]

In the US System, Health Plans Have Powerful Tools to Reduce Spending on Medicines

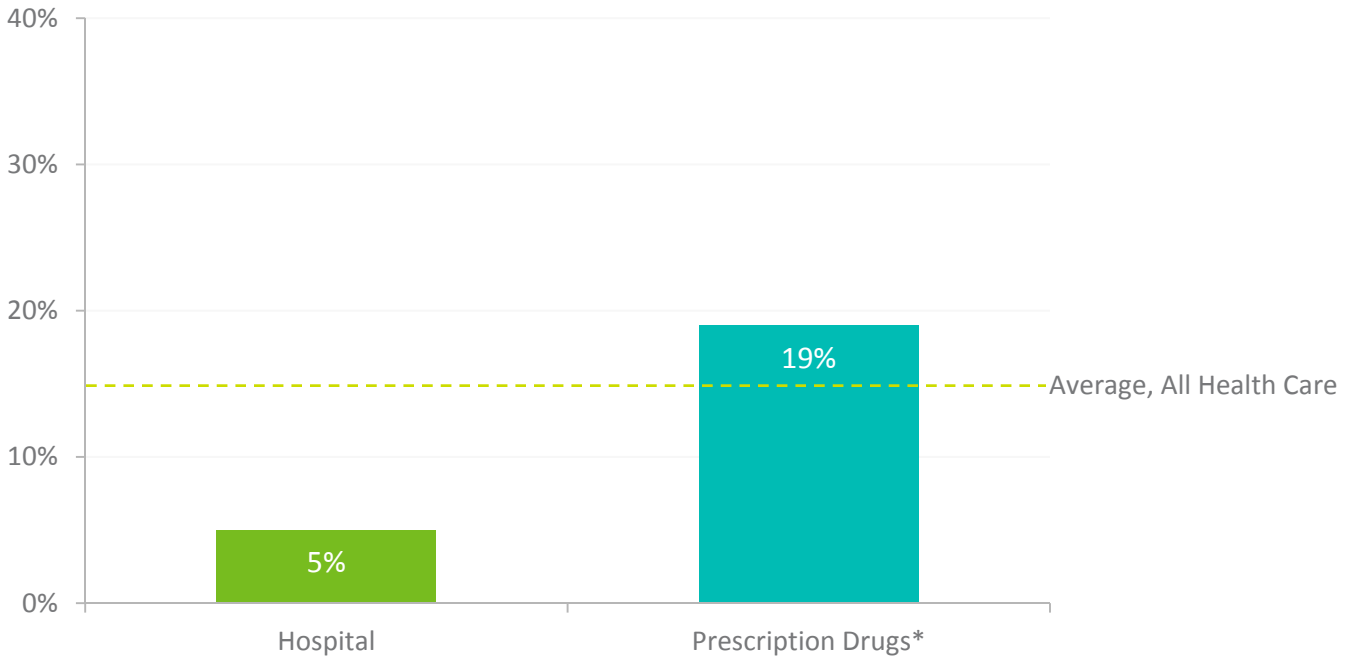


Source: IMS Health[10]

Insurance Covers a Lower Share of Prescription Drug Costs Than of Other Medical Services

On average, patients pay out of pocket nearly 20% of their total prescription drug spending, compared to 5% of spending for hospital care.[11]

Average Share of Health Costs Patients Pay Out of Pocket, All Ages[12]



*Includes brand and generic

Sources: PhRMA analysis based on Medical Expenditure Panel Survey (MEPS)[11]; Cunningham PJ[12]

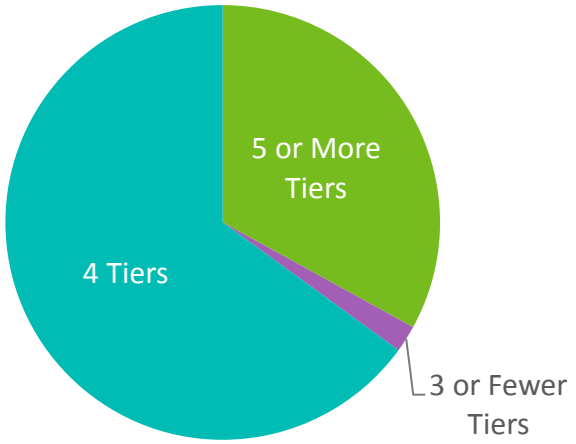
Plans Increasingly Subject Certain Medicines to Higher Cost Sharing

Patients taking medicines placed on higher cost-sharing “tiers" can face higher out-of-pocket costs relative to lower tiers. Patients needing these medicines commonly face serious and chronic health conditions.

THE USE OF 4 OR MORE COST-SHARING TIERS

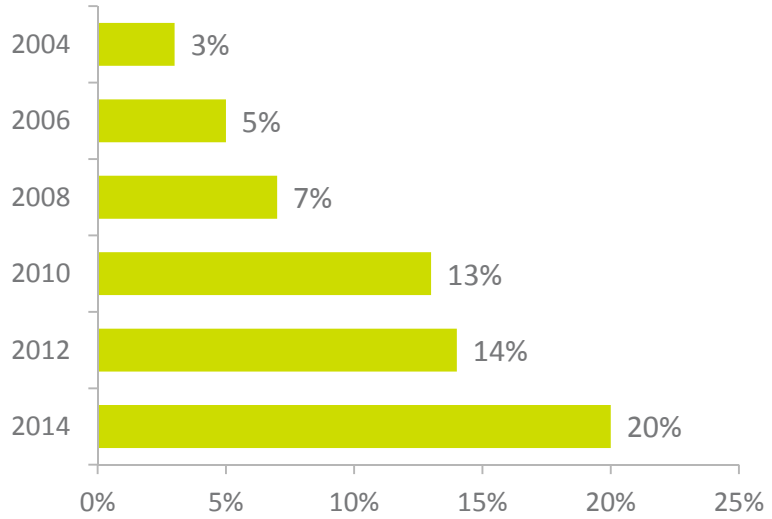
…is the norm for plans in Health Insurance Exchanges

*Share of Silver Plans by Number of Tiers[13]**



…and is becoming more common in employer plans

Share of Workers in Plans With 4 or More Tiers[14]



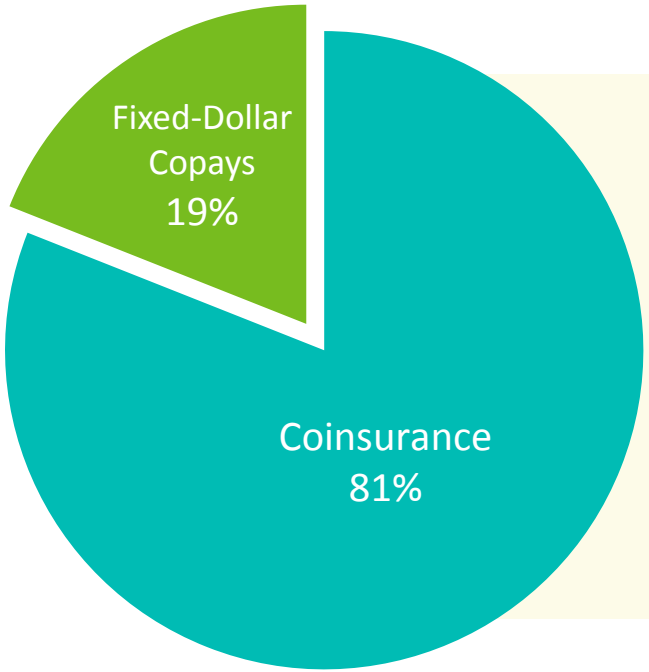
*Silver Plans account for a majority of Health Insurance Exchange enrollment. ”Tiers” refer to the different levels of cost sharing that plans require patients to pay for different groupings of medicines.

Sources: Avalere *PlanScape*© Database[13]; KFF/HRET[14]

Plans Increasingly Charge Patients a Percentage of a Medicine's Total Cost Rather Than Fixed Copays

For example, in the most frequently purchased type of Health Insurance Exchange plan, coinsurance for certain medicines is common: 81% of these plans require enrollees to pay a percentage of a specialty tier medicine's total cost, with 41% of plans requiring coinsurance of more than 30% of the cost.

*Cost Sharing in Specialty Tiers of 2015 Silver Plans**



COINSURANCE

is a percentage of costs a patient is responsible for paying with his or her own money (out of pocket). Coinsurance can make a patient's out-of-pockets costs difficult to predict—and potentially much higher—than fixed-dollar copays.

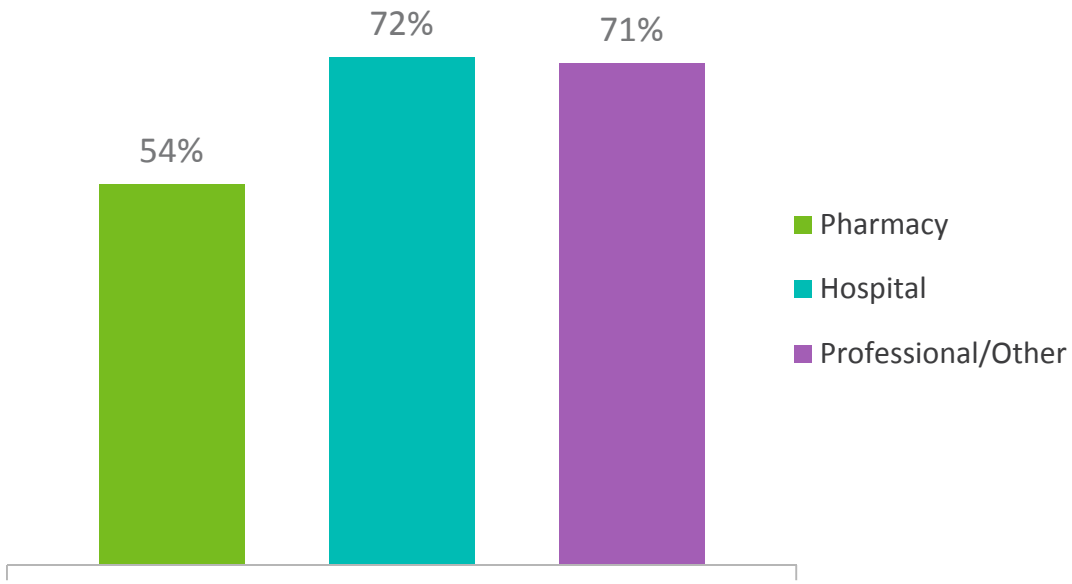
*Silver Plans are shown here because they account for a majority of Health Insurance Exchange enrollment. Figure excludes the 2% of Silver Plans that do not use a specialty tier. Plans subject different medicines to different levels of cost sharing, or "tiers." Medicines assigned to a "specialty tier" typically require the highest level of cost sharing.

Source: Avalere *PlanScape*© Database[15]

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 for other covered 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**

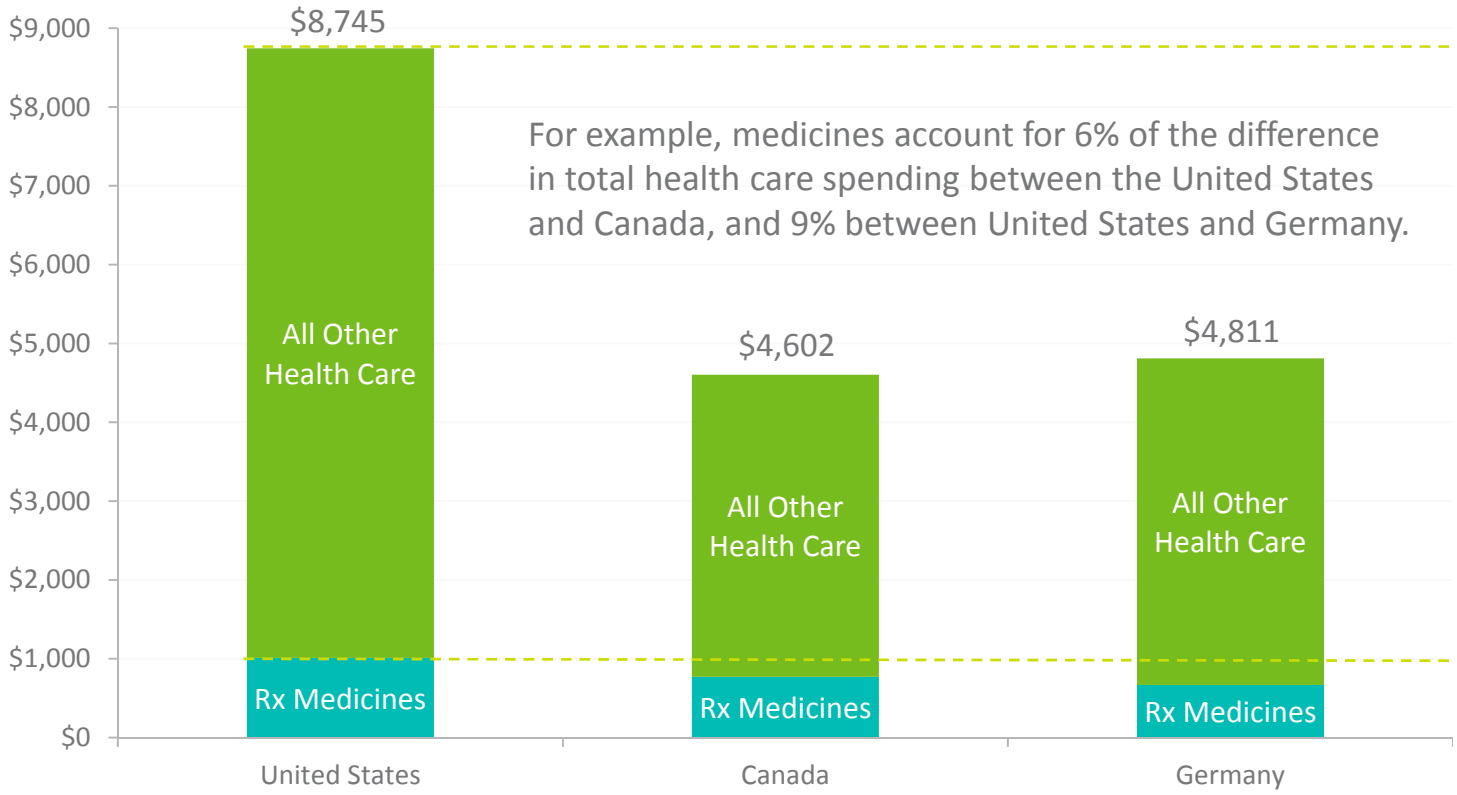


*Silver Plans accounted for a majority of Health Insurance Exchange enrollment, and combined deductibles were the most common type of deductible arrangement among these plans. A deductible is the amount patients must pay annually with their own money (out of pocket) before a health plan will pay for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

Source: Milliman, Inc[16]

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

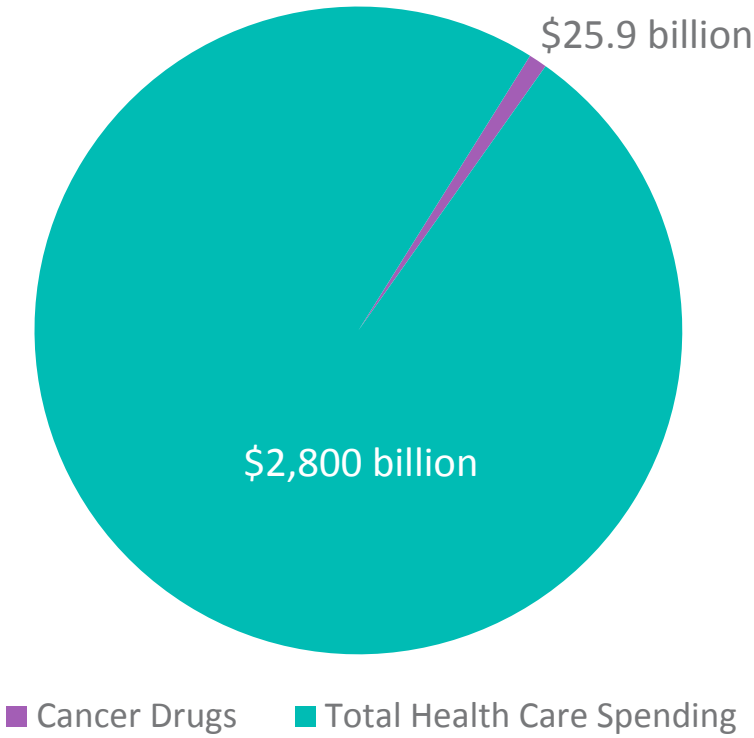
Per Capita Health Care Spending in the United States, Canada, and Germany, 2012



Source: PhRMA analysis based on Organisation for Economic Co-operation and Development[17]

Spending on Cancer Medicines Represents Less than 1% of Overall Health Care Spending

Cancer Medicines as a Portion of Total US Health Care Spending, 2012

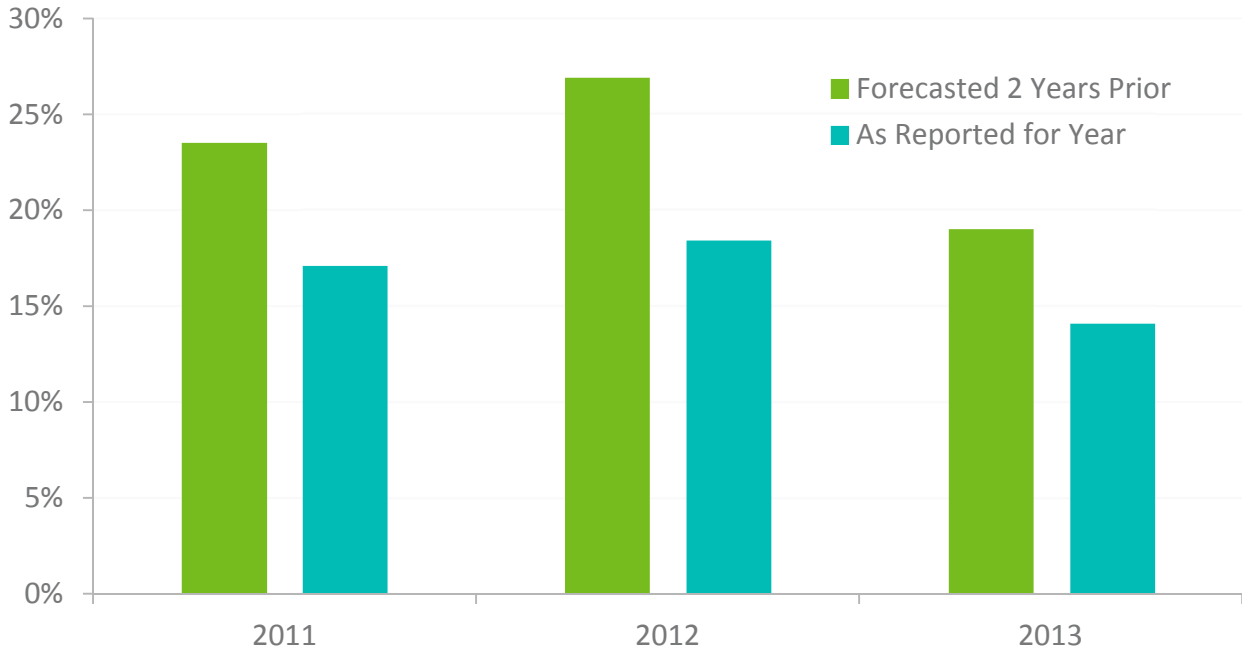


Source: IMC[18]; Martin AB[19]

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 the Annual Drug Trend Reports from Express Scripts, Inc.

Source: Milliman, Inc[20]

Notes and Sources

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4 OUTCOMES AND SAVINGS

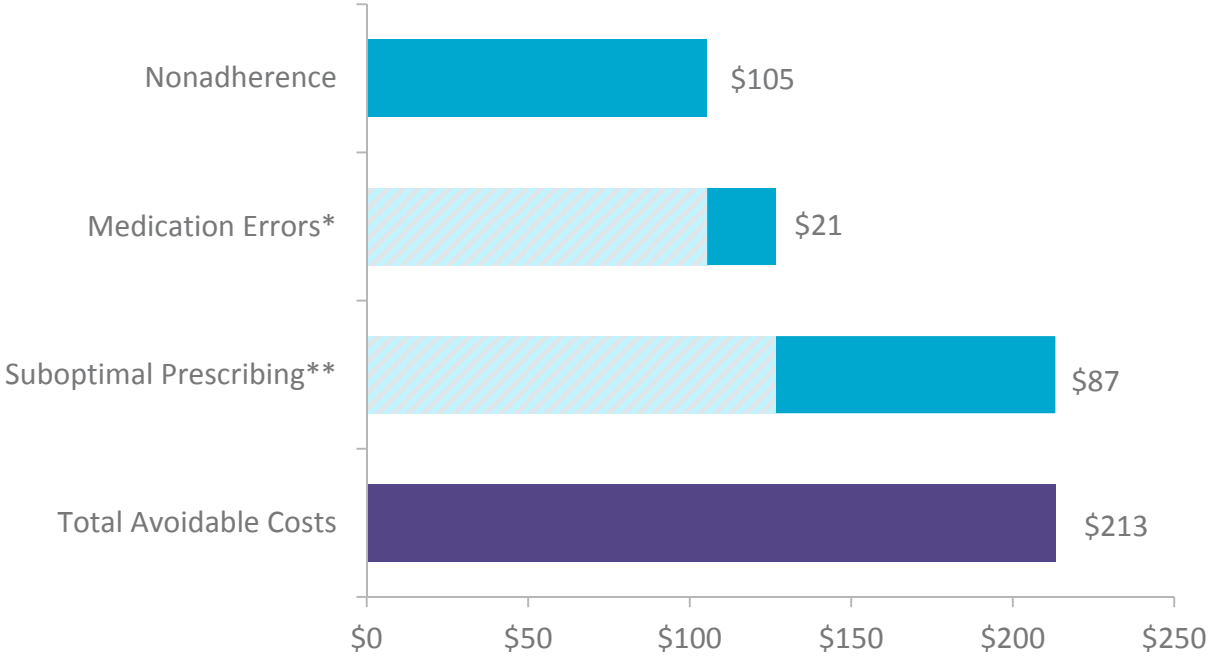
Overcoming Gaps in Treatment, Improving Outcomes, and Reducing Costs Through Better Use of Medicines

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.

Potential Savings From Better Use of Medicines

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

Avoidable Annual US Health Care Costs (Billions, 2012)



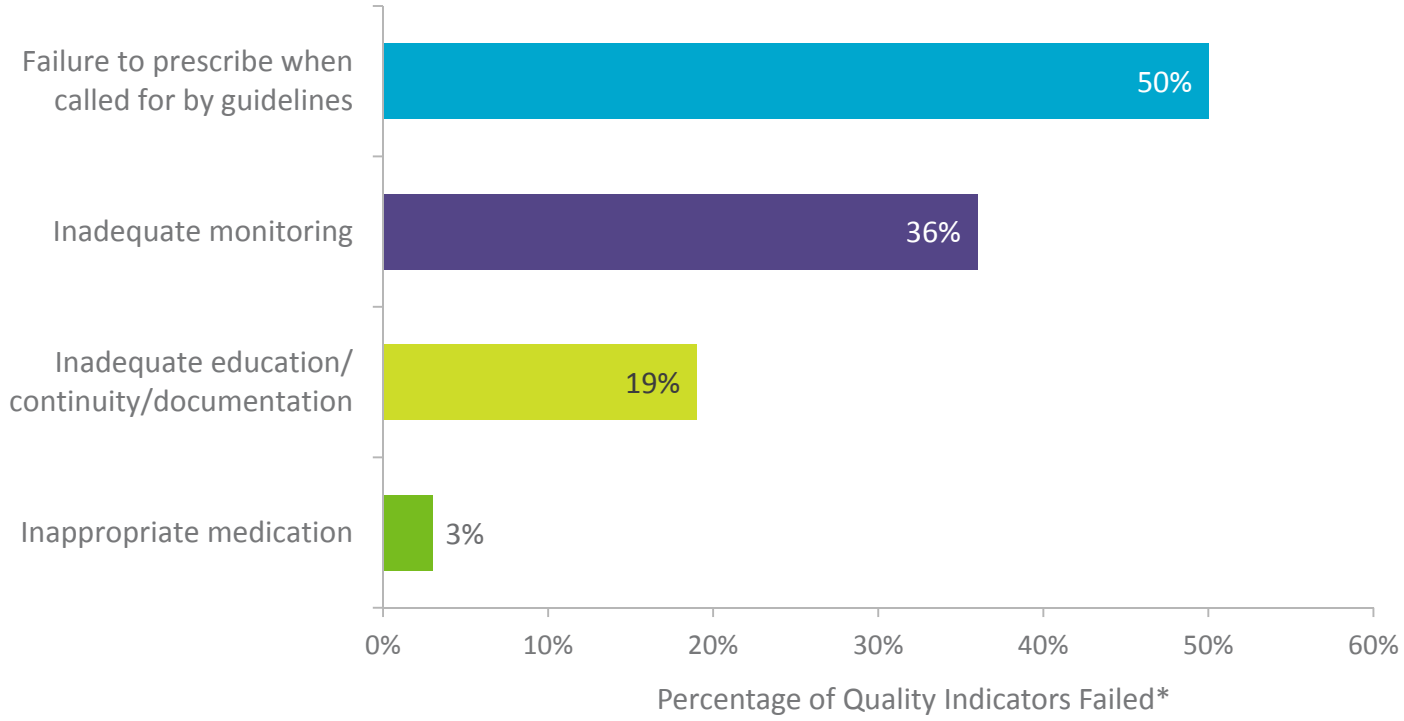
*Category includes: medication errors ($20 billion) and mismanaged polypharmacy ($1 billion)
**Category includes: untimely medicine use ($40 billion), inappropriate antibiotic use ($35 billion), and suboptimal generic use ($12 billion)

Source: IMS[1]

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 is inappropriate medicine use.

Quality Problems Among Vulnerable Older Patients

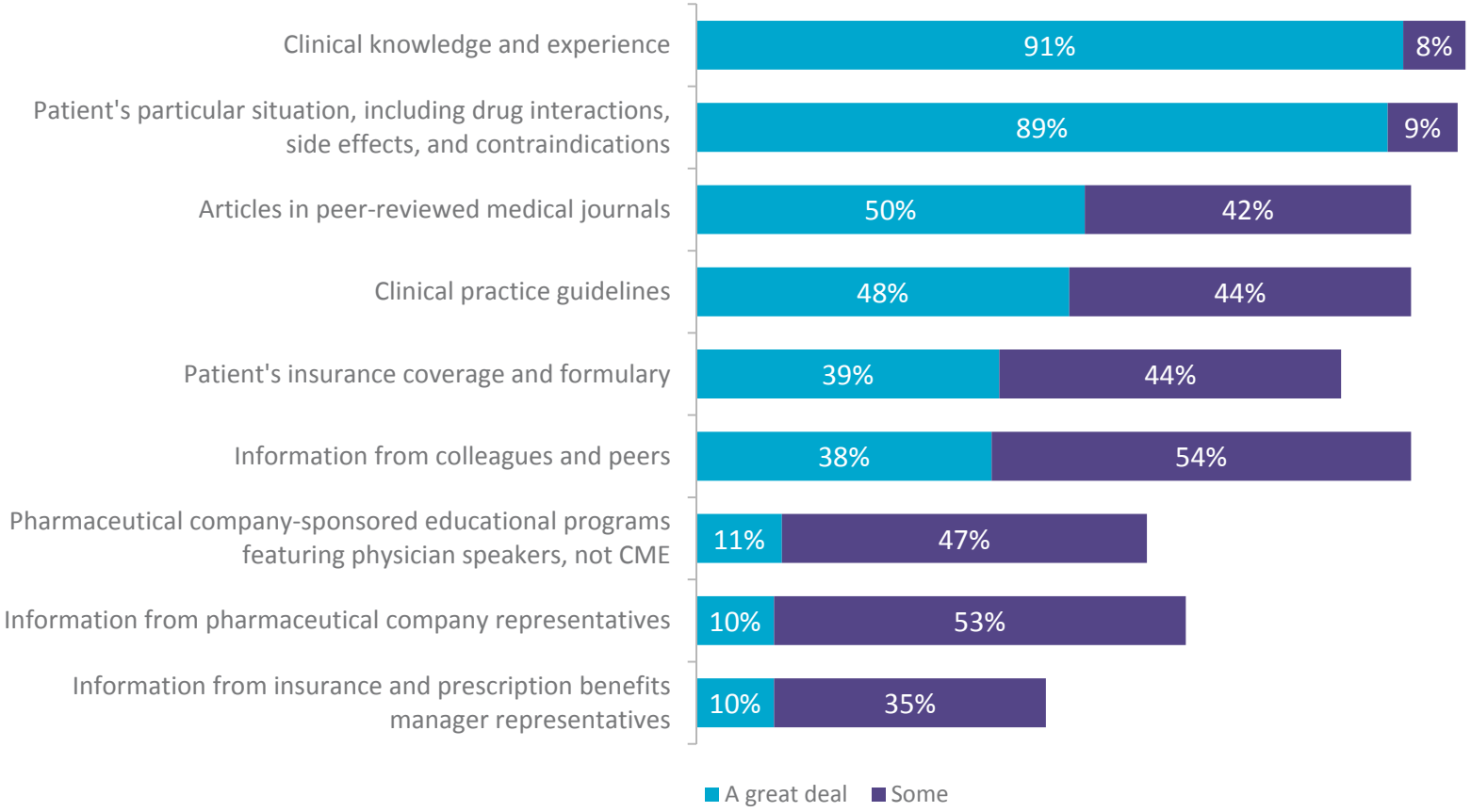


*Quality indicators were developed and implemented based on systematic literature reviews and multiple layers of expert judgment.

Source: RAND Health[2]

Many Factors Affect Physicians' Prescribing Decisions

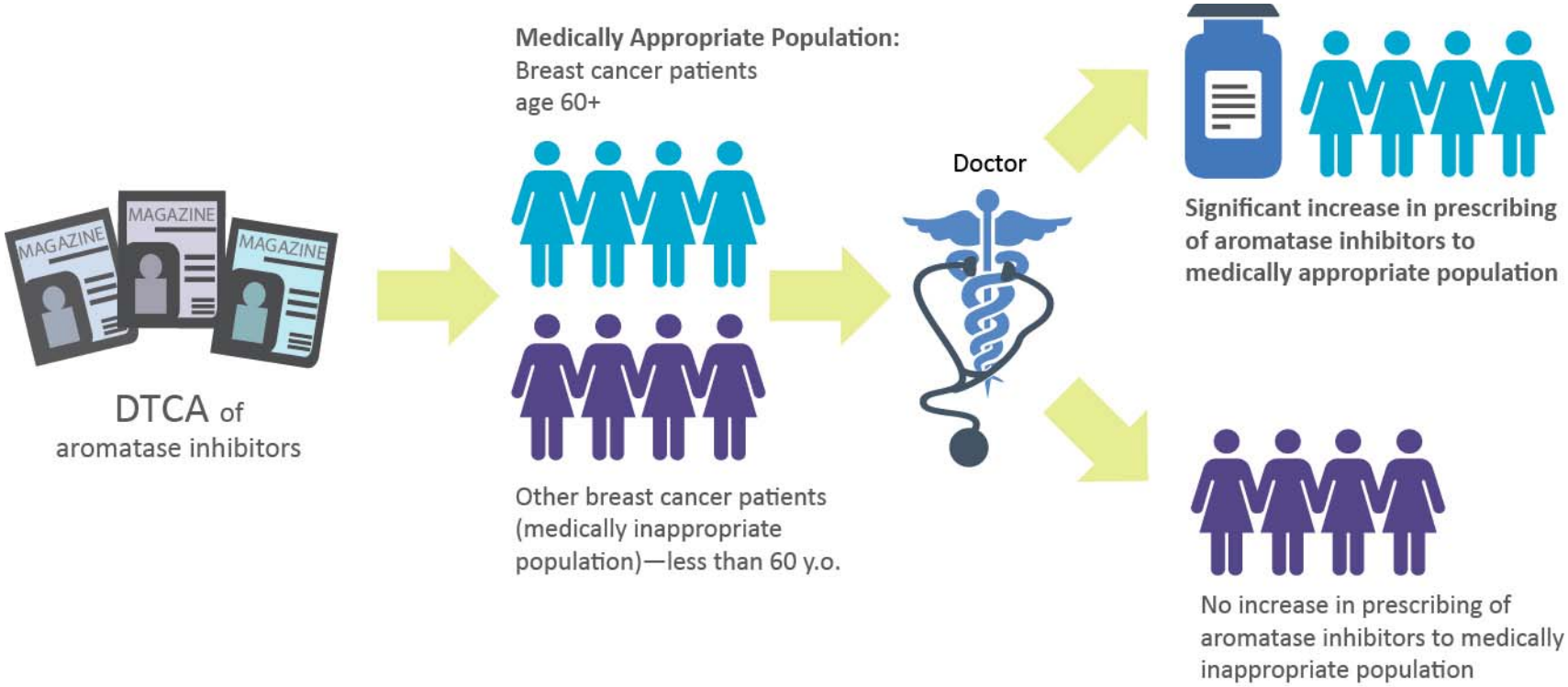
Factors Influencing Prescribing Decisions in the United States in 2013



Source: KRC Research[3]

Direct-to-Consumer Advertising Encourages Appropriate Use of Medicines

Study finds direct-to-consumer advertising (DTCA) promoted appropriate use of oral breast cancer therapies and did not promote inappropriate use.*

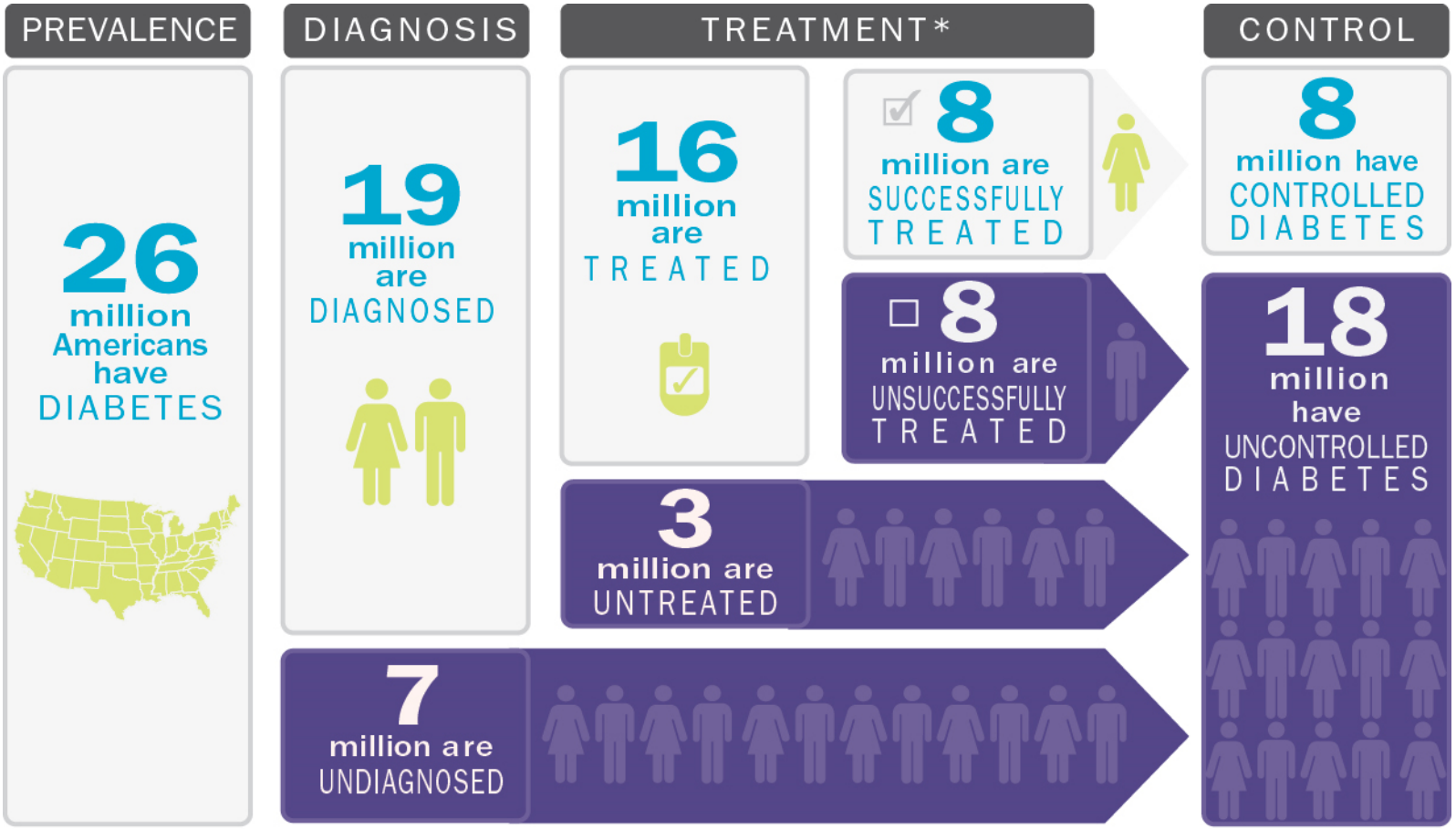


*Study measured the effect of DTCA on patients and doctors regarding the use of aromatase inhibitors (AIs) consistent with medical practice guidelines. The study found that DTCA spending on AIs was associated with an overall new AI prescription increase of 0.18% after 3 months (approximately 118 new 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.[4]

Diabetes: An Example of Underdiagnosis and Undertreatment

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

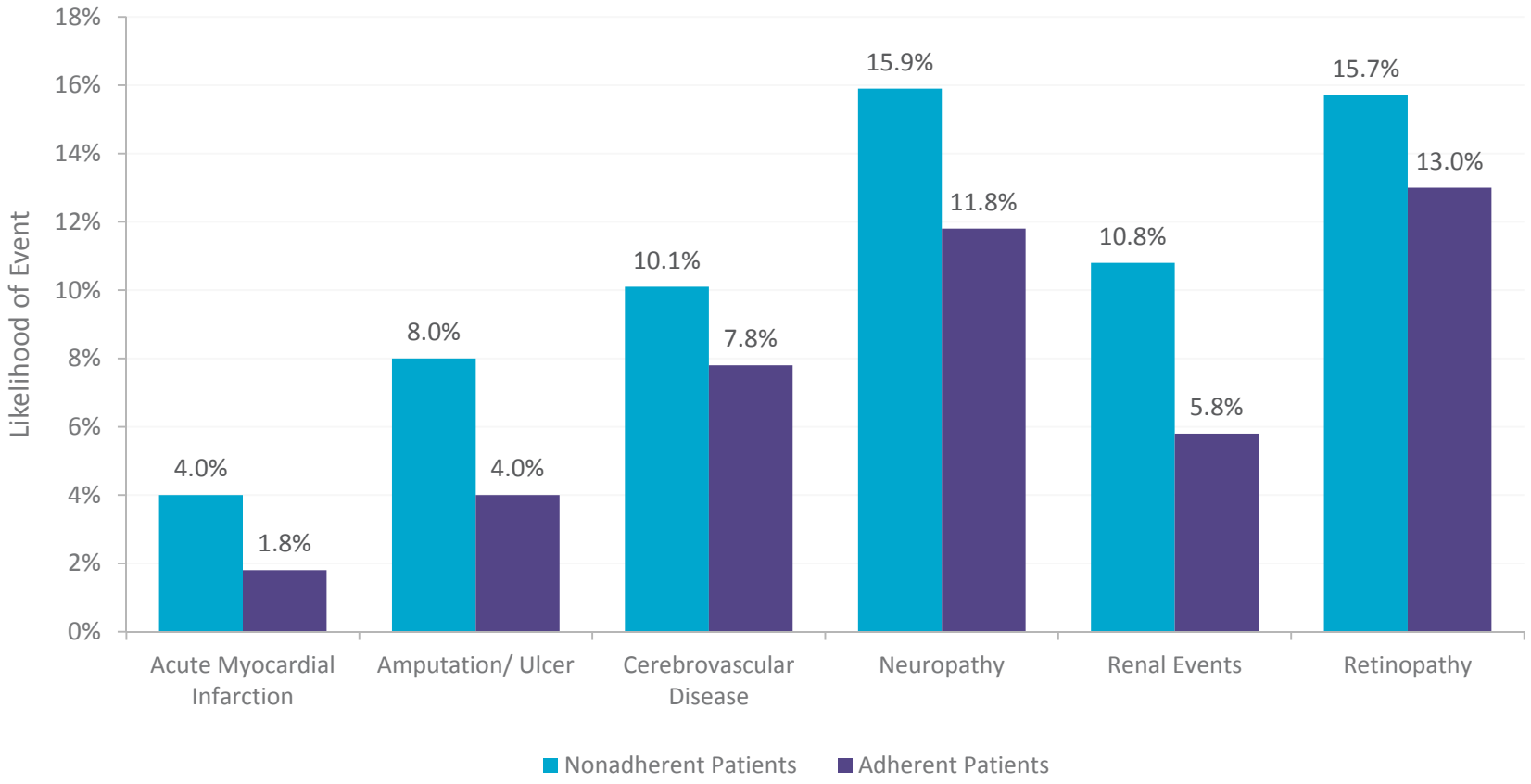


*Treatment includes blood sugar control (medicines, diet, and exercise) and testing to prevent complications.

Sources: Centers for Disease Control and Prevention (CDC)[5]; Analysis based on National Health and Nutrition Examination Survey[6]

Better Use of Medicines Improves Patient Health

Diabetes patients who take their medicines as prescribed experience fewer diabetes-related complications.



Source: Gibson TB, et al.[7]

Recommended Medicines Can Save Lives and Dramatically Improve Health

> *"...achieving effective blood pressure control would be approximately equivalent to eliminating all deaths from accidents, or from influenza and pneumonia combined."*
>
> — David Cutler, PhD, Harvard University

Annual Hospitalizations and Deaths Avoided Through Use of Recommended Antihypertensive Medications

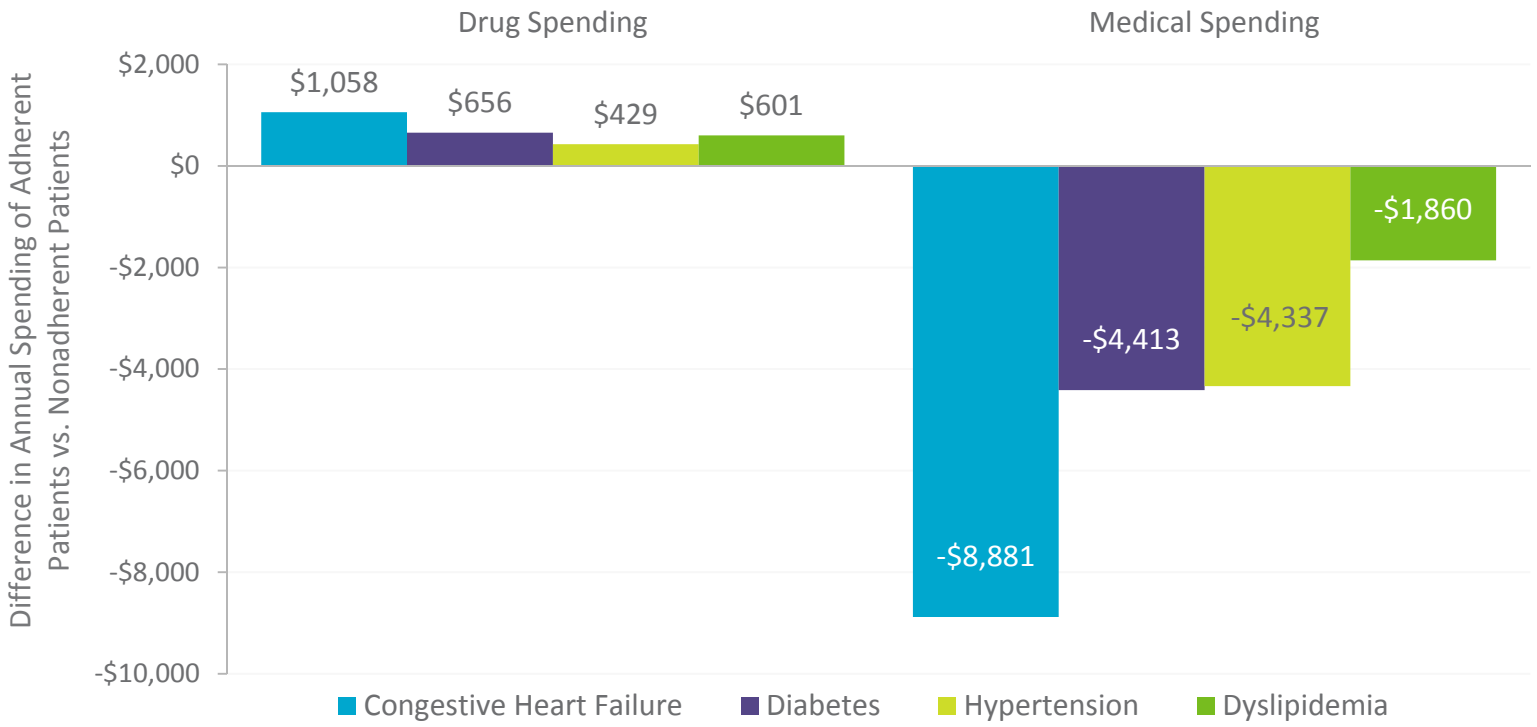
	Annual Hospitalizations Avoided	Annual Premature Deaths Avoided
Prevention Achieved: Based on Current Treatment Rates	833,000	86,000
Potential Additional Prevention: If Untreated Patients Received Recommended Medicines	420,000	89,000

Source: Cutler DM, et al.[8]

Prescription Medicines Are Part of the Solution to Reducing Medical Spending

Better use of medicines reduces use of avoidable medical care, resulting in reductions in medical spending.

Adherence to Medicines Lowers Total Health Spending for Chronically Ill Patients

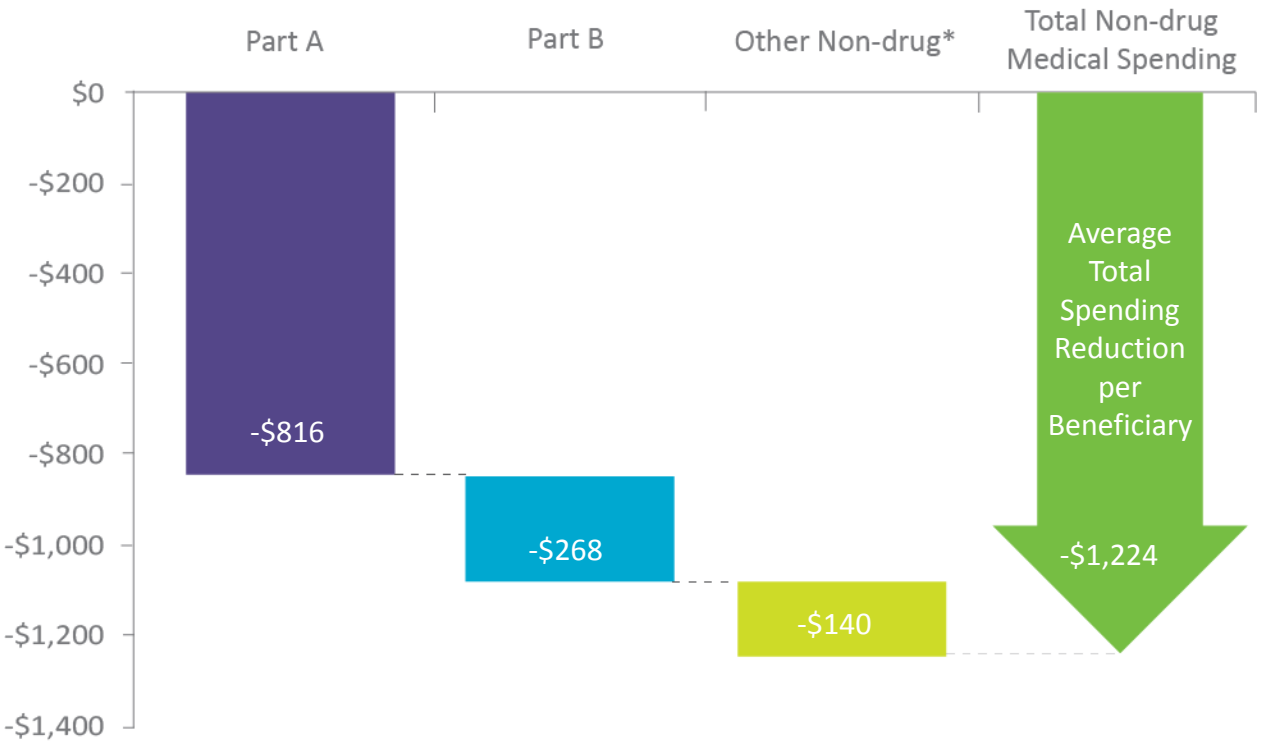


Source: Roebuck MC, et al.[9]

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[10] and an overall savings of $13.4 billion in 2007, the first full year of the program.[11]

Average Reduction in Medical Spending in 2006 and 2007, for Beneficiaries Gaining Drug Coverage Through Part D



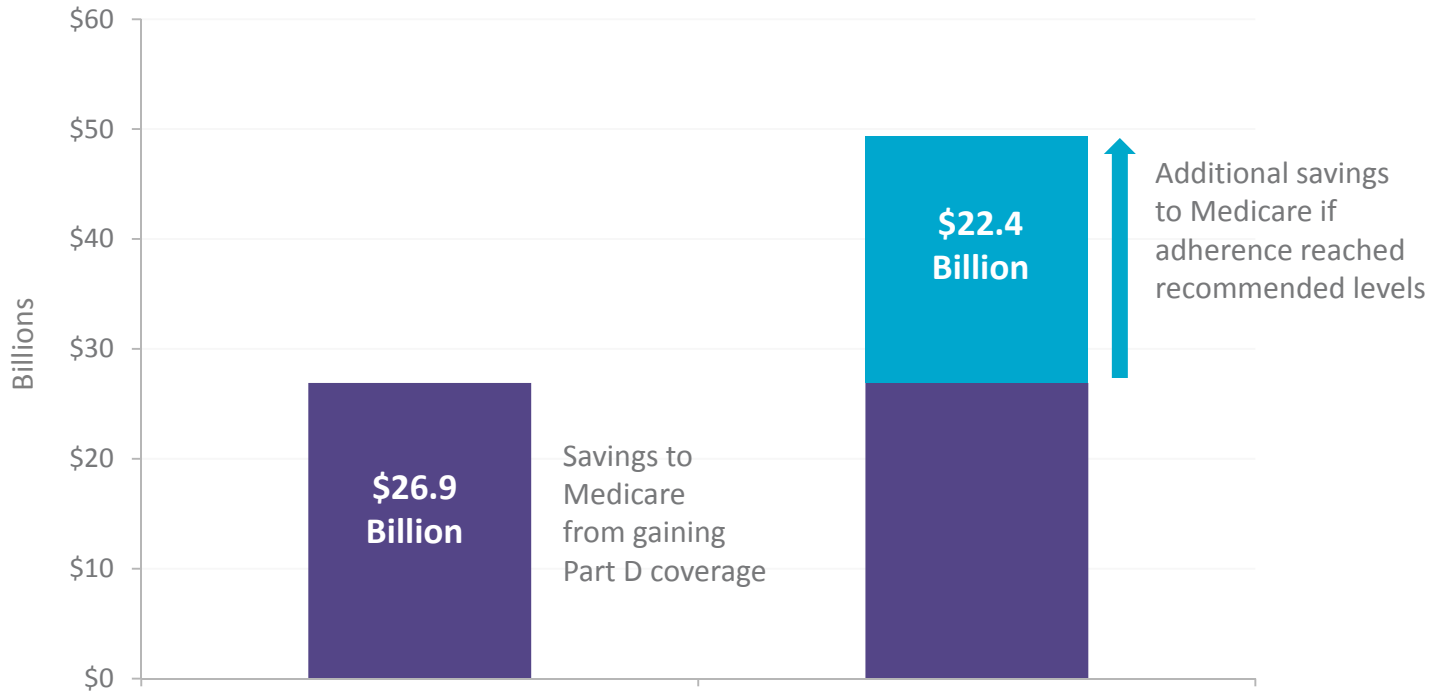
*Home health, durable medical equipment, hospice, and outpatient institutional services

Sources: McWilliams JM, et al.[10]; Afendulis CC, et al.[11]

Improving Adherence Could Yield Additional Savings

Improving adherence to congestive heart failure (CHF) medicines could result in federal savings of $22.4 billion over 10 years.

Estimated 10-Year Savings to Medicare From Improved Adherence to CHF Medications, 2013-2022



Source: Dall TM, et al.[12]

Better Use of Medicines Yields Significant Health Gains and Savings on Other Services

Due to a growing body of evidence, in 2012 the Congressional Budget Office (CBO) began recognizing reductions in other medical expenditures associated with 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[13]

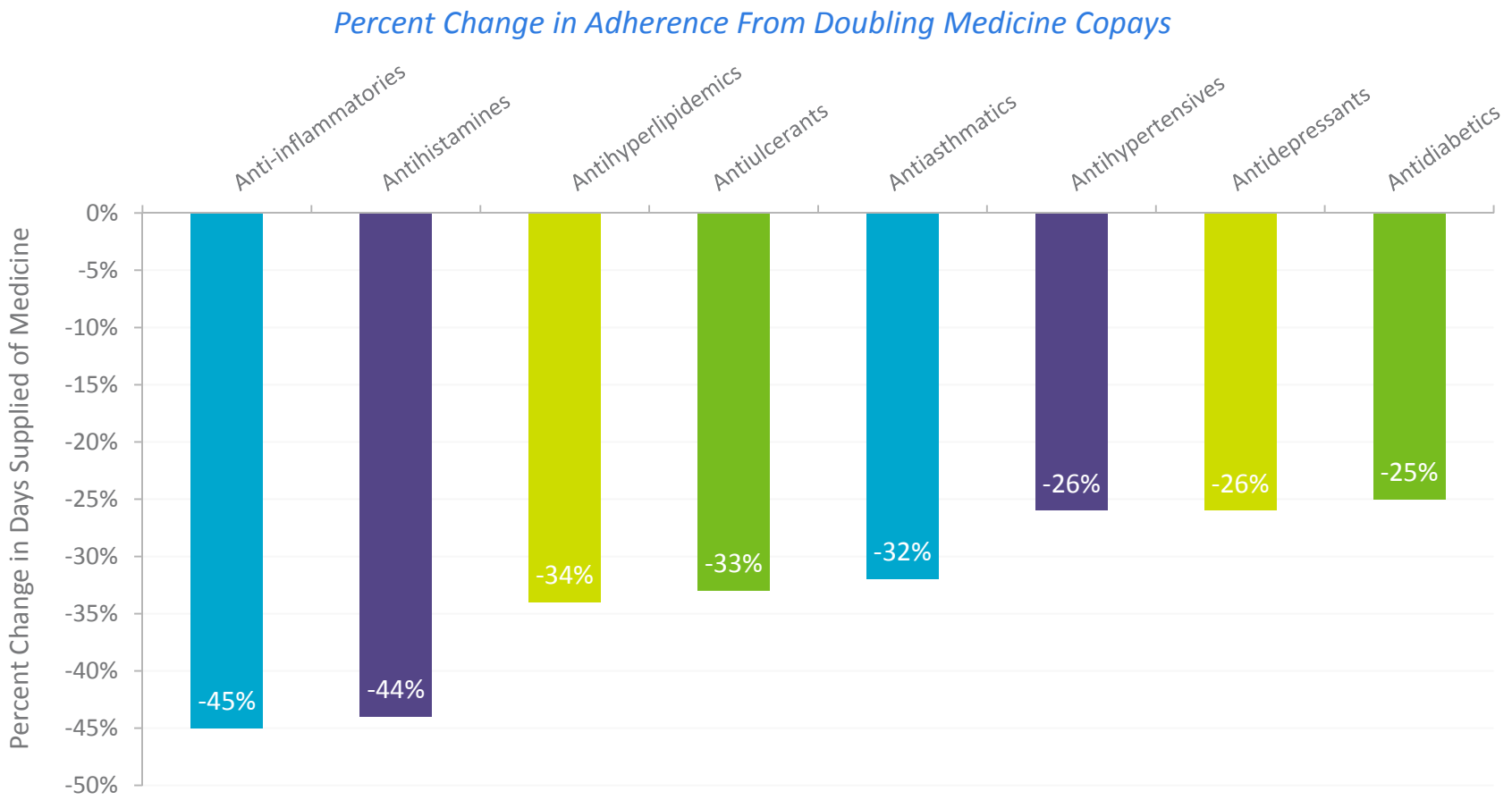
Recent evidence suggests Medicare savings due to better use of medicines may be 3 to 6 times greater than estimated by the CBO for seniors with common chronic conditions[14]:

- High cholesterol: more than 3 times greater
- Congestive heart failure: nearly 4 times greater
- Diabetes: more than 4 times greater
- Hypertension: nearly 6 times greater

Sources: CBO[13]; Roebuck MC[14]

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.

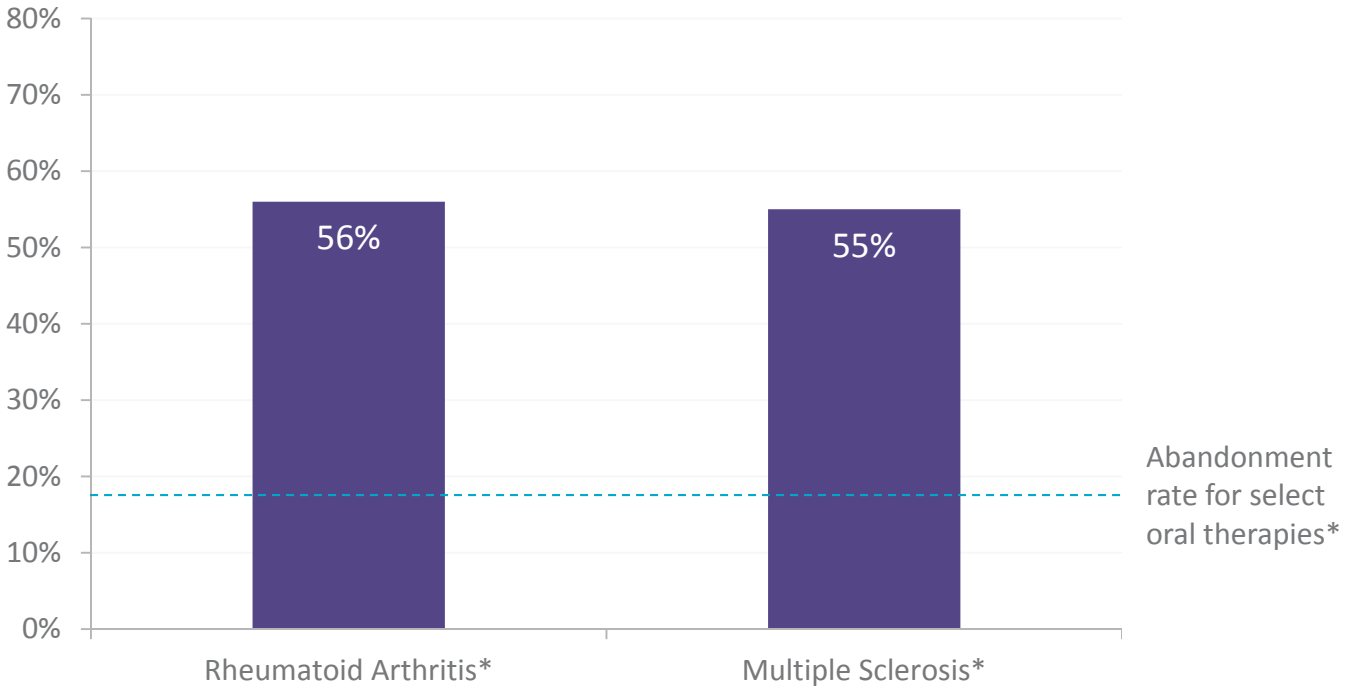


Source: Goldman DP, et al.[15]

Patients Facing High Cost Sharing Commonly Abandon Their Medicines

Patients taking medicines on a specialty tier, such as medicines to treat rheumatoid arthritis and multiple sclerosis, face high out-of-pocket expenses and often do not return to the pharmacy to pick up prescriptions after they have been filled.

Average Abandonment Rates, 2009-2011



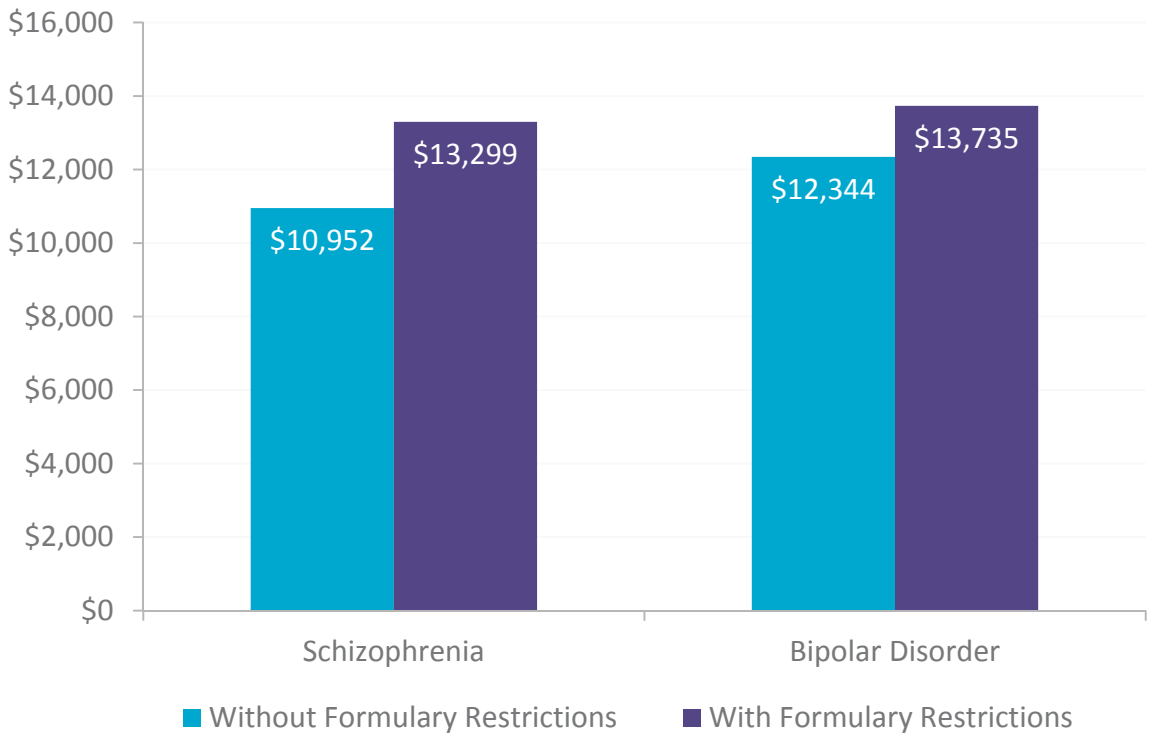
*Select therapies include those treating patients with Parkinson's disease and dyslipidemia.

Source: King A, et al.[16]

Patients Facing Access Restrictions Incur 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.

Medicaid Total Annual Medical Expenditures, Per Patient (2008)



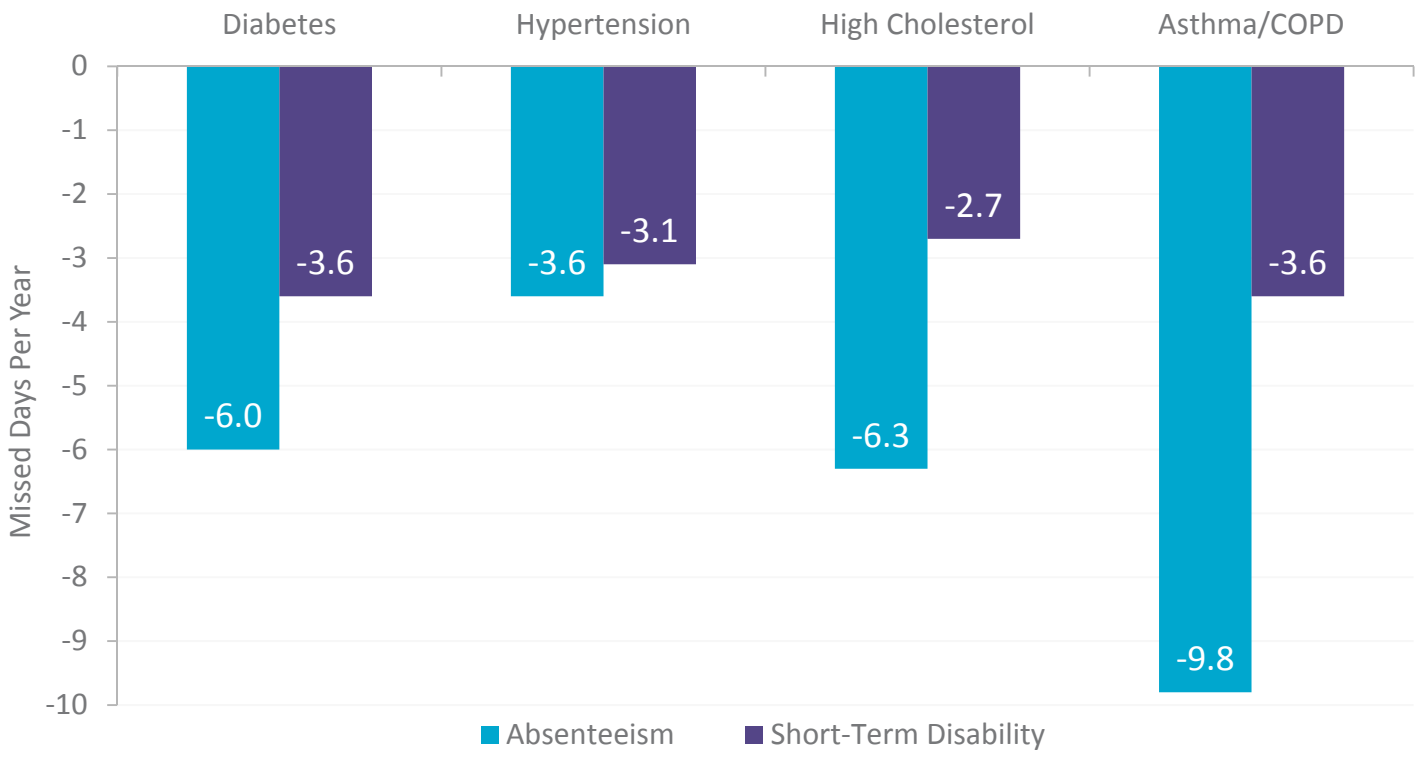
*Restrictions examined: prior authorization, step therapy, and quantity limits

Source: Seabury SA, et al.[17]

Improving Adherence Increases Productivity

Adherent patients miss fewer days of work and experience less short-term disability. For workers with asthma/chronic obstructive pulmonary disease (COPD), better adherence results in more than $3,100 in savings on average per worker annually.

Fewer Days of Absence and Short-Term Disability for Adherent Patients as Opposed to Nonadherent Patients



Source: Carls GS, et al.[18]

Notes and Sources

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5 ECONOMIC IMPACT

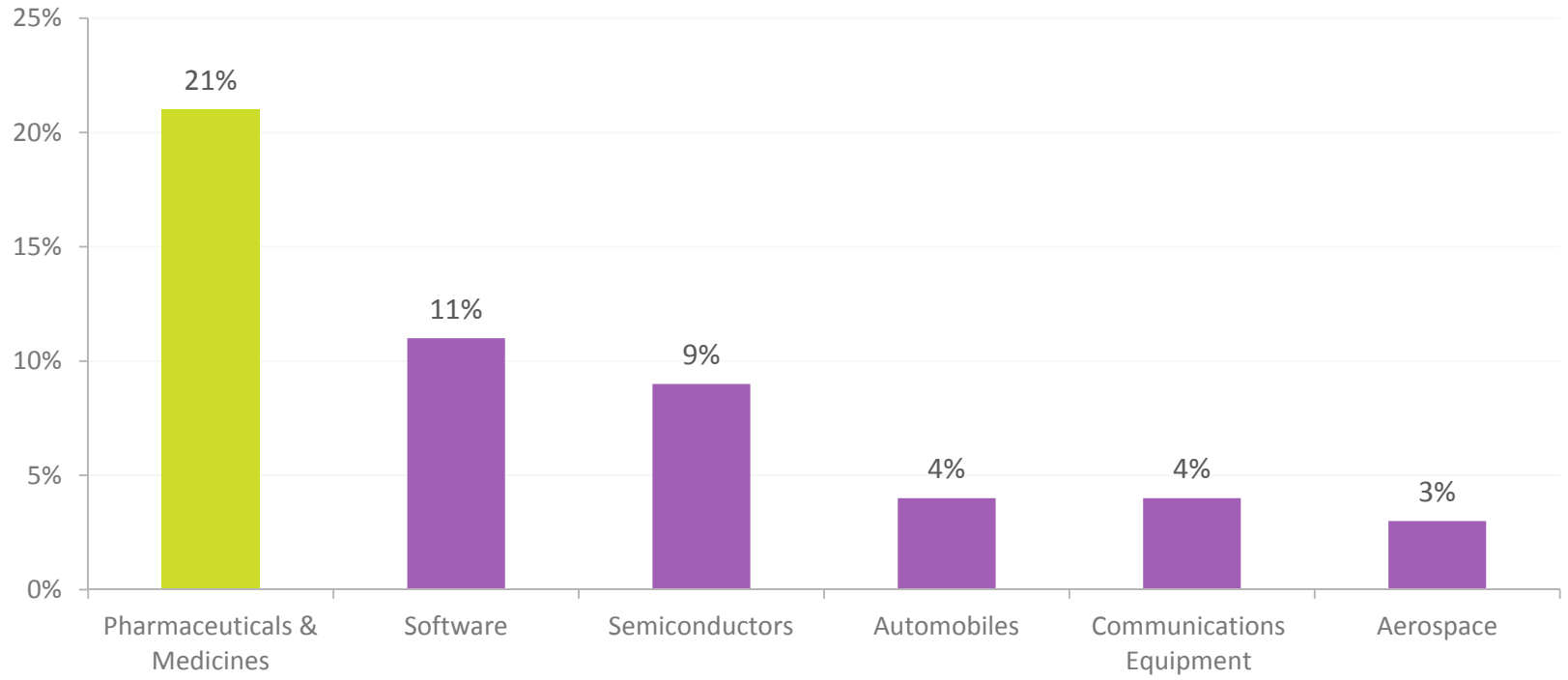
The Biopharmaceutical Sector's Role in the Economy

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 5 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. In addition, American biopharmaceutical research companies are also leaders in charitable contributions.

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

The biopharmaceutical sector accounts for the single largest share of all US business R&D, representing 21% of all domestic R&D funded by US businesses.

*Share of Total US Business R&D by Industry, 2011**



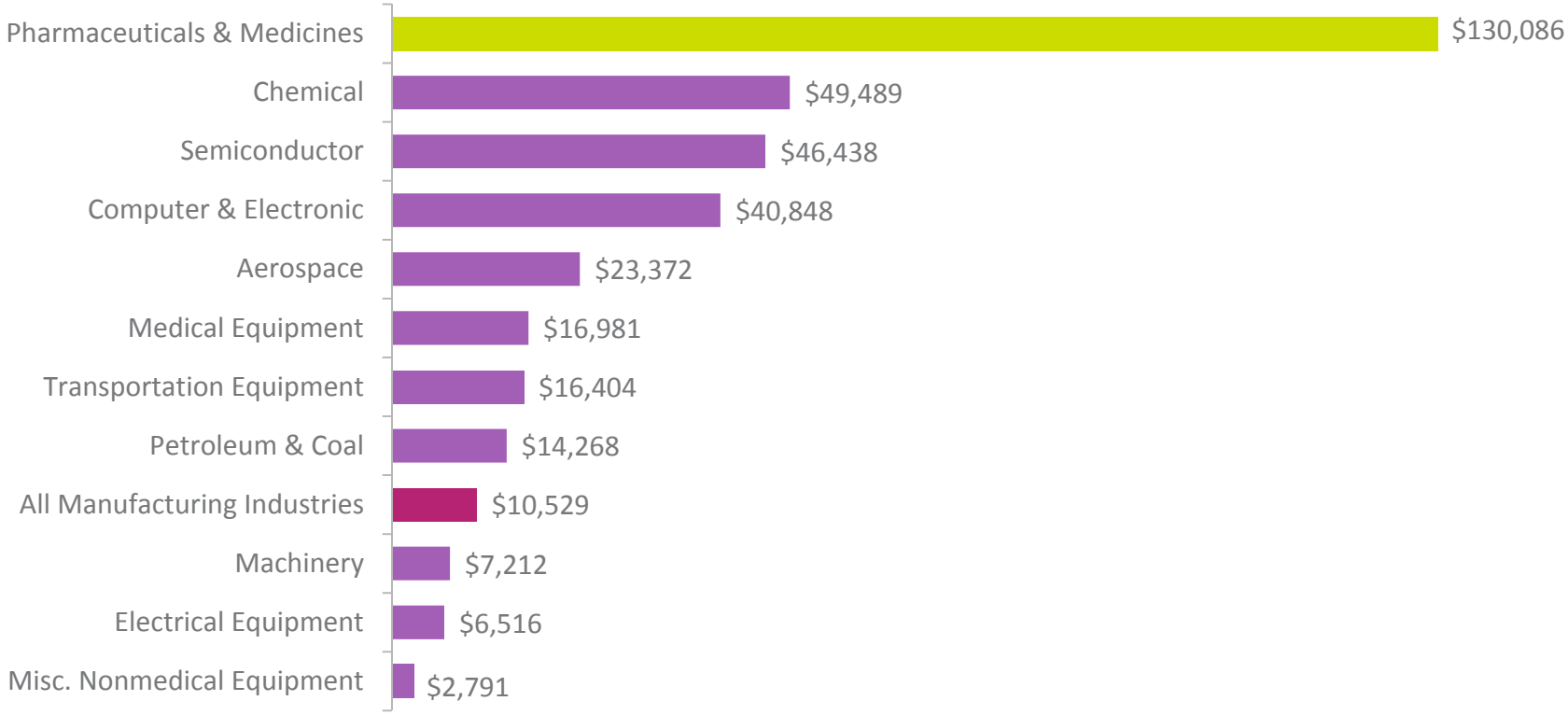
*The remaining 48% share of business R&D spending is conducted by other industries including subsectors of the machinery sector, the electrical equipment sector, and the professional, scientific, and technical services sector among others.

Source: National Science Foundation[1]

The Biopharmaceutical Sector Is the Most R&D Intensive in the United States

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

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

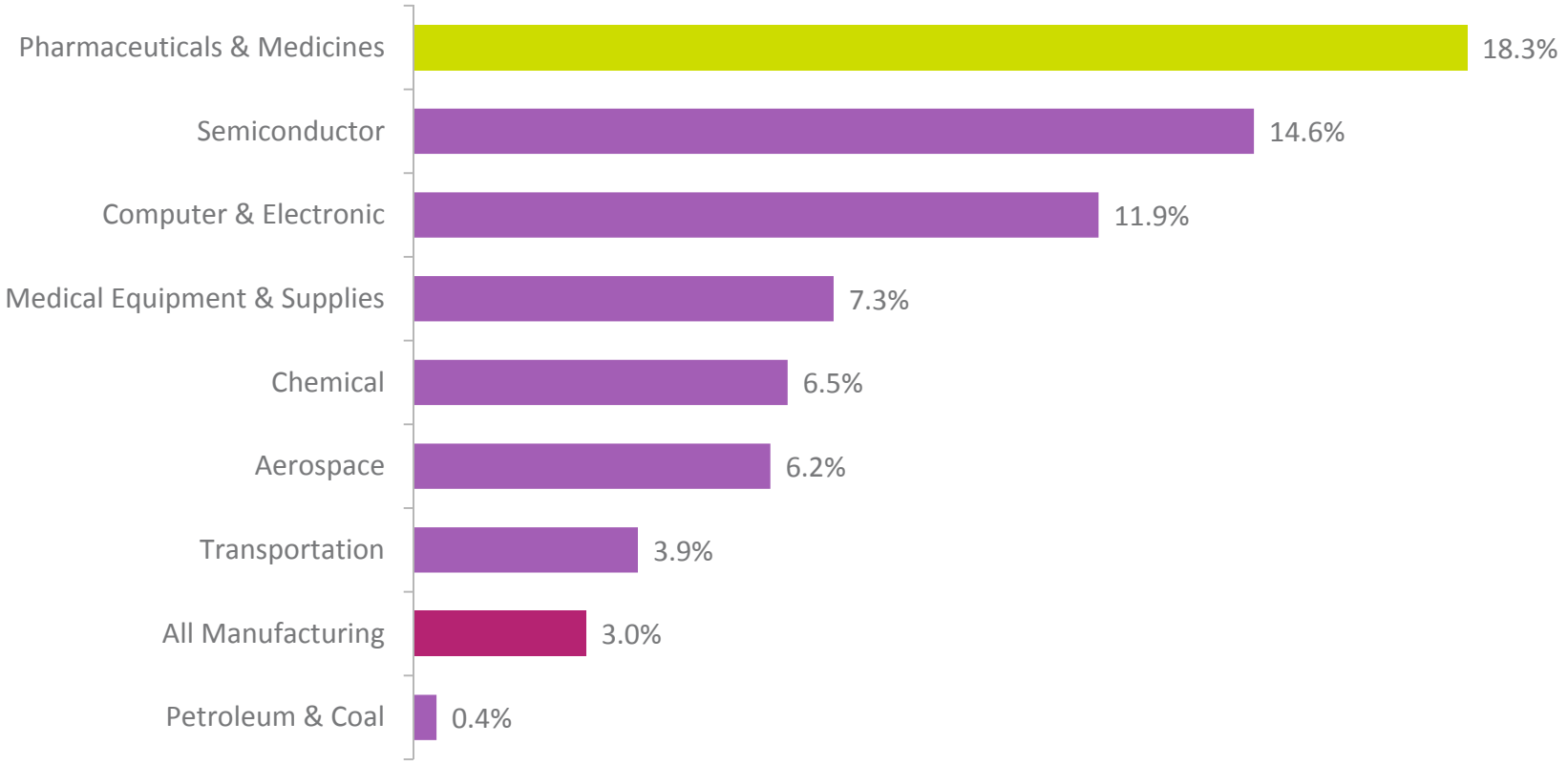


Source: NDP Analytics[2]

The Biopharmaceutical Sector Invests More in R&D Relative to Sales Than Other Manufacturing Industries

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



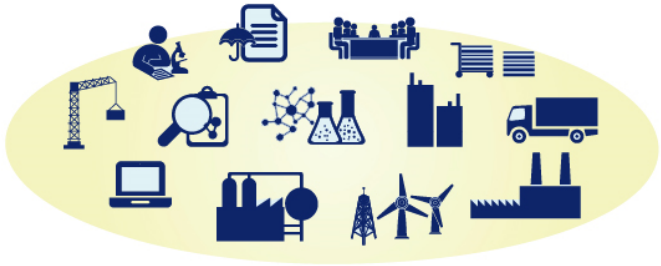
Source: NDP Analytics[3]

The Economic Reach of the US Biopharmaceutical Industry

814,000
direct jobs

Innovative Biopharmaceutical Industry

1,022,000
indirect jobs



Vendors and Suppliers

1,528,000
induced jobs

Additional Private Economic Activity

3,364,000
TOTAL JOBS

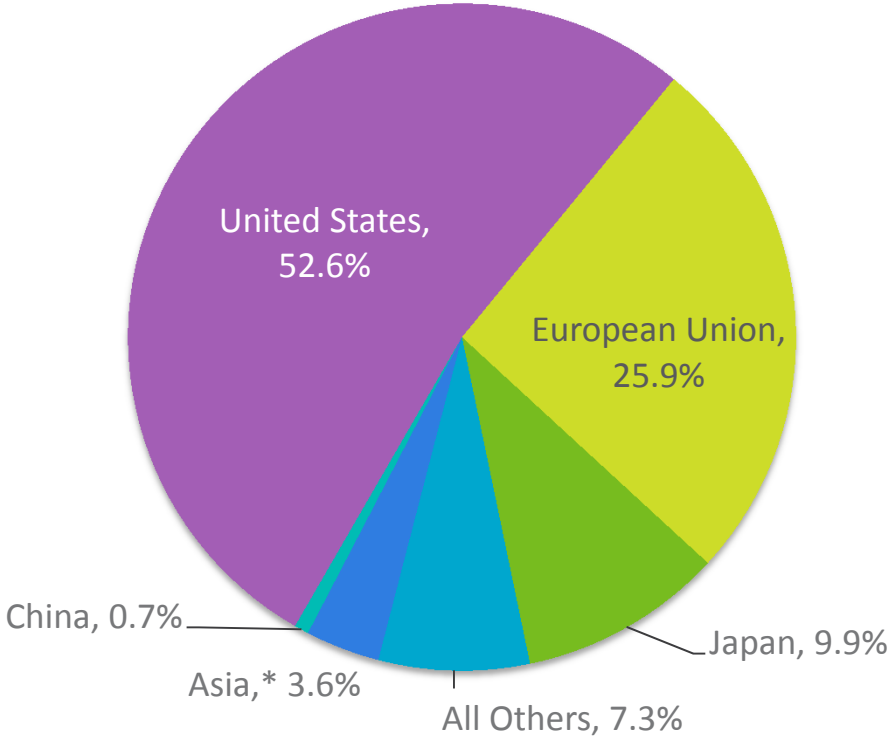
The biopharmaceutical industry supported 3.4 million jobs across the US economy in 2011.

Source: Battelle Technology Partnership Practice[4]

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, Selected Years 1997-2012, Location of Inventor by Region/Country



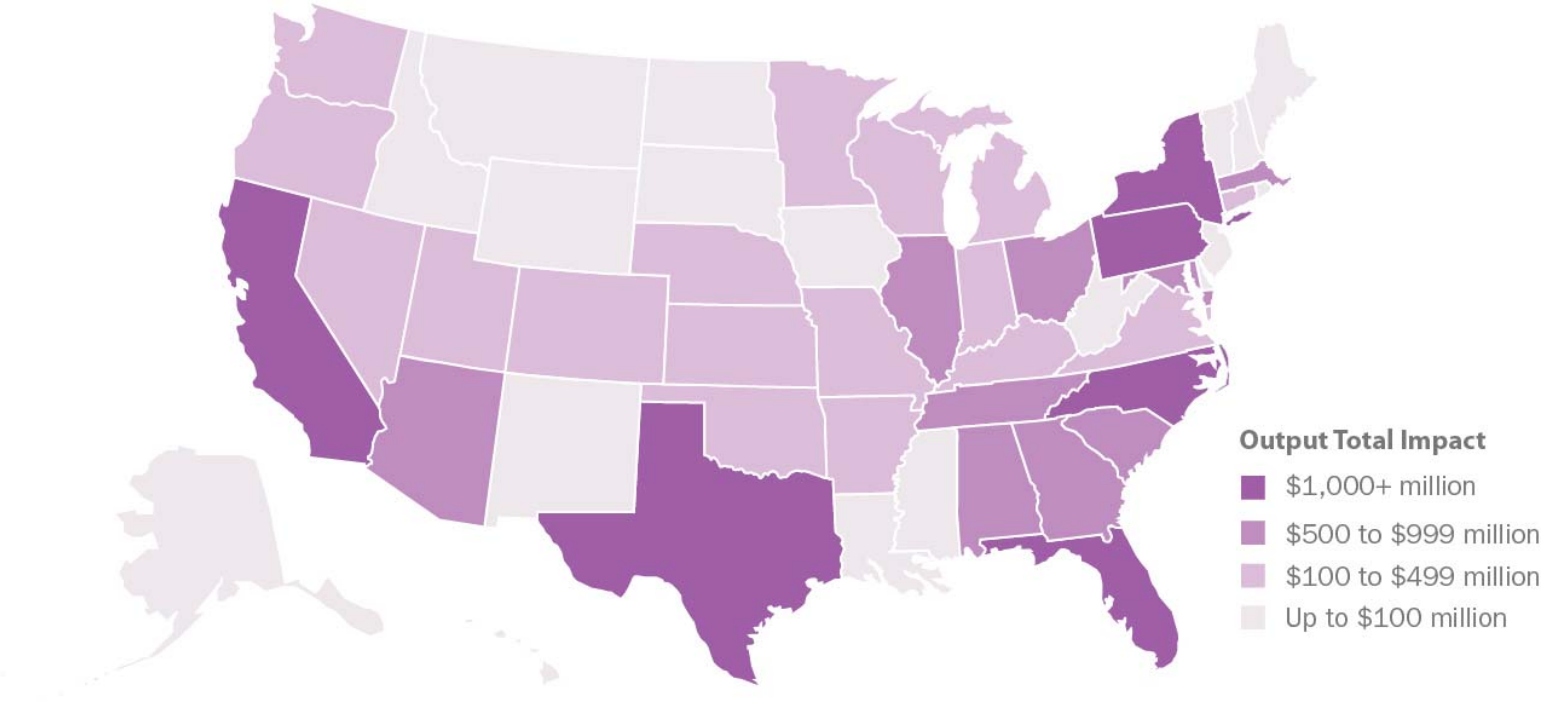
*Asia includes India, Malaysia, Singapore, South Korea, Taiwan, and others (but excludes China and Japan).

Source: National Science Foundation[5]

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 spread across all 50 states and the District of Columbia.*

Estimated Economic Impact from Industry-Sponsored Clinical Trial Sites Across the United States, 2013

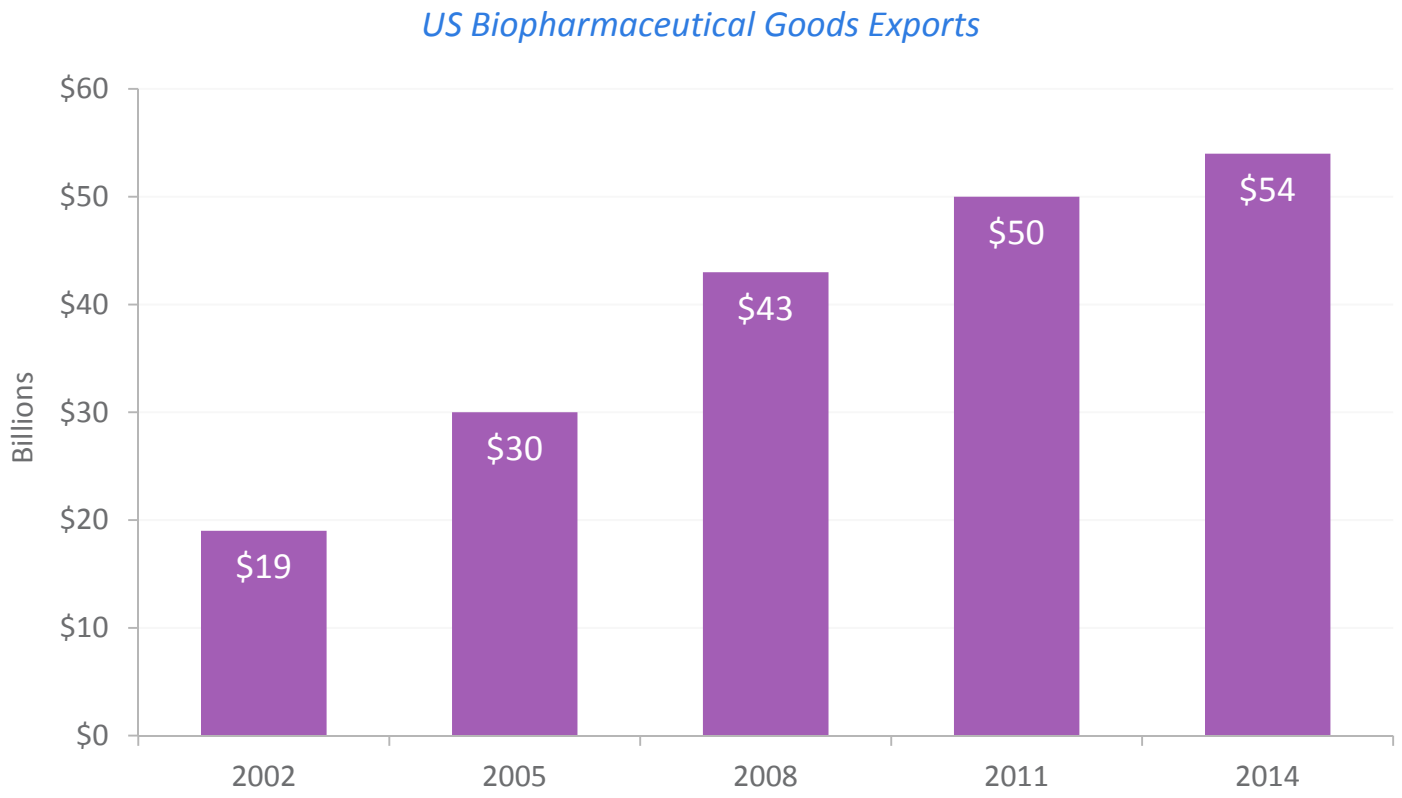


*Estimates reflect only those activities occurring at clinical trial sites and exclude more centralized, cross-site functions such as coordination and data analysis. Also excludes non-clinical R&D such as basic and preclinical research and the significant economic contribution from non-R&D activities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

Source: Battelle Technology Partnership Practice[6]

US Biopharmaceutical Exports Have Grown

Biopharmaceutical exports have nearly tripled over the 13-year period between 2002 and 2014, accounting for 3.3% of all US exports by 2014.



Source: US Department of Commerce, International Trade Administration. TradeStats Express™: national trade data[7]

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."* [8]
>
> — Frederic Scherer, AEI-Brookings Joint Center for Regulatory Studies

> *". . . the 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."* [9]
>
> — Congressional Budget Office

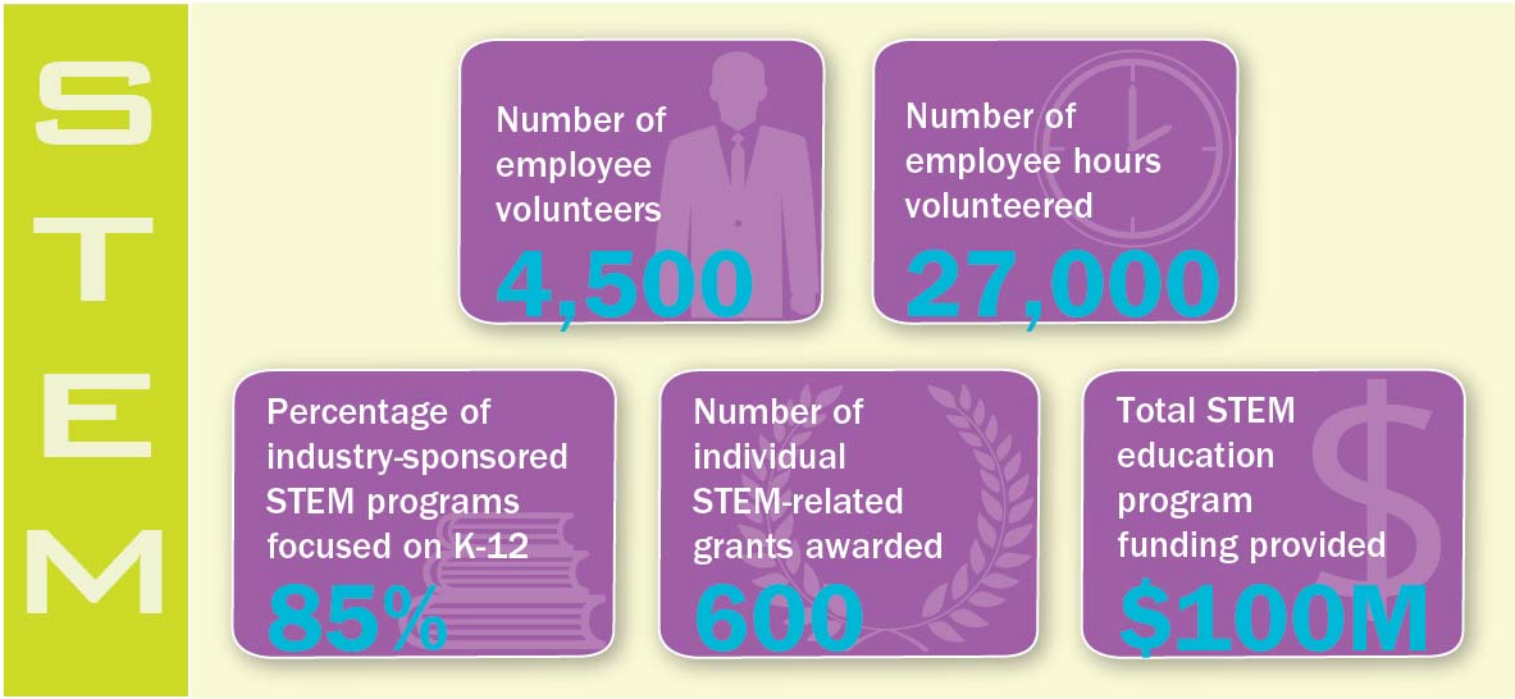
> *"Usual profit figures greatly overstate the industry's economic profit rate."* [10]
>
> — Joseph Newhouse, Harvard University

Sources: Scherer FM[8]; Congressional Budget Office[9]; Newhouse JP[10]

Biopharmaceutical Industry Advancing STEM Education in the United States

The science, technology, engineering, and mathematics (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[11]

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.

Average Corporate Giving by Sector	Total Giving as % of Pre-Tax Profit	Total Giving per Employee
All Companies	1.0%	$644
Biopharmaceuticals	19.4%	$24,453
Energy	0.8%	$2,912
Utilities	1.2%	$1,092
Information Technology	1.1%	$666
Consumer Staples	1.1%	$608
Industrials	0.8%	$244

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

Source: Committee Encouraging Corporate Philanthropy[12]

Policies Are Essential in Fostering Future Growth of the US Biopharmaceutical Industry and Its Ability to Innovate

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

COVERAGE AND PAYMENT

policies that support and encourage medical innovation

A well-functioning, science-based

REGULATORY SYSTEM

Strong

INTELLECTUAL PROPERTY

protections, including patents and data protection

Sources: Battelle Technology Partnership Practice[13]; Deloitte Consulting[14]

Notes and Sources

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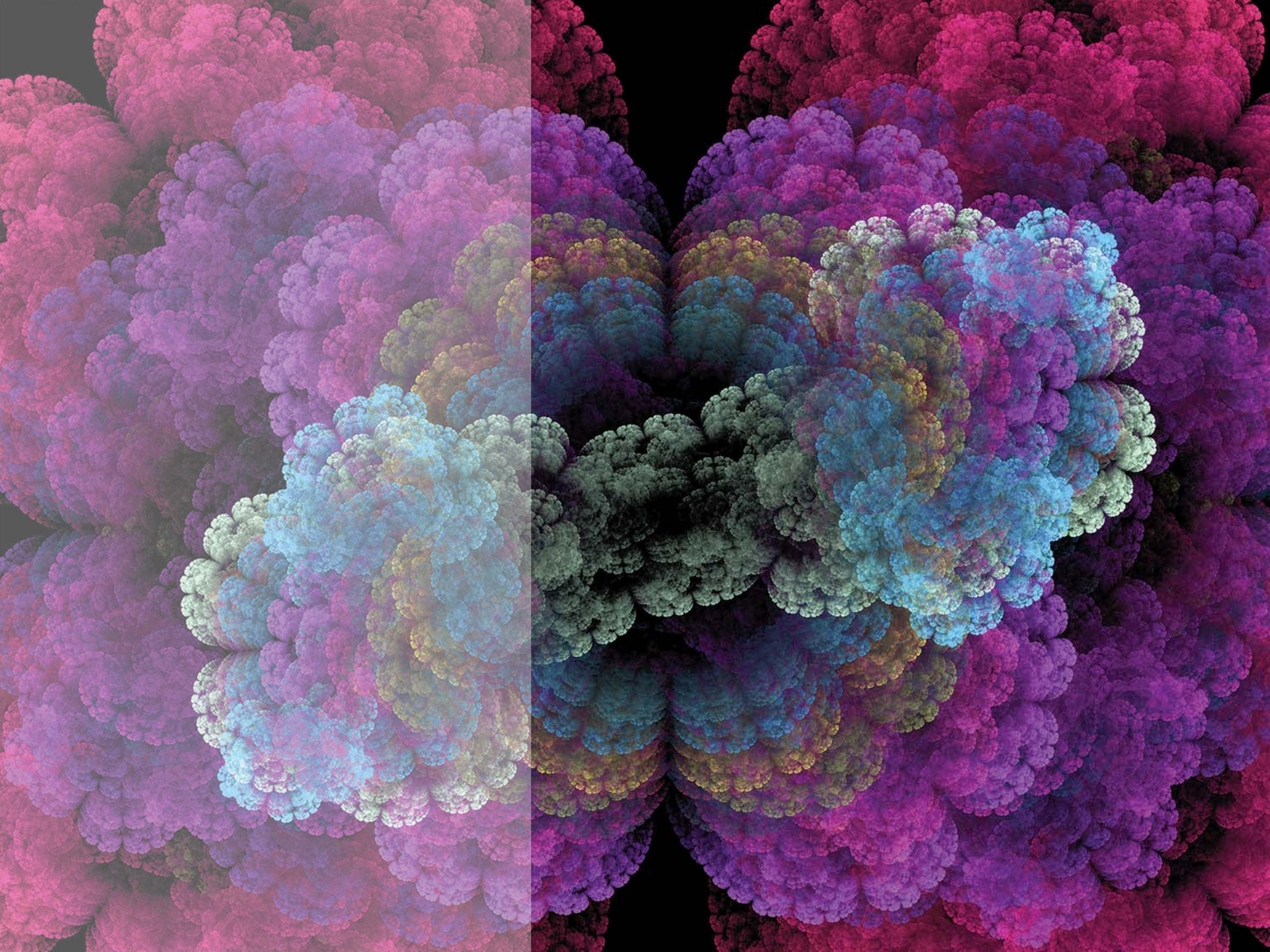

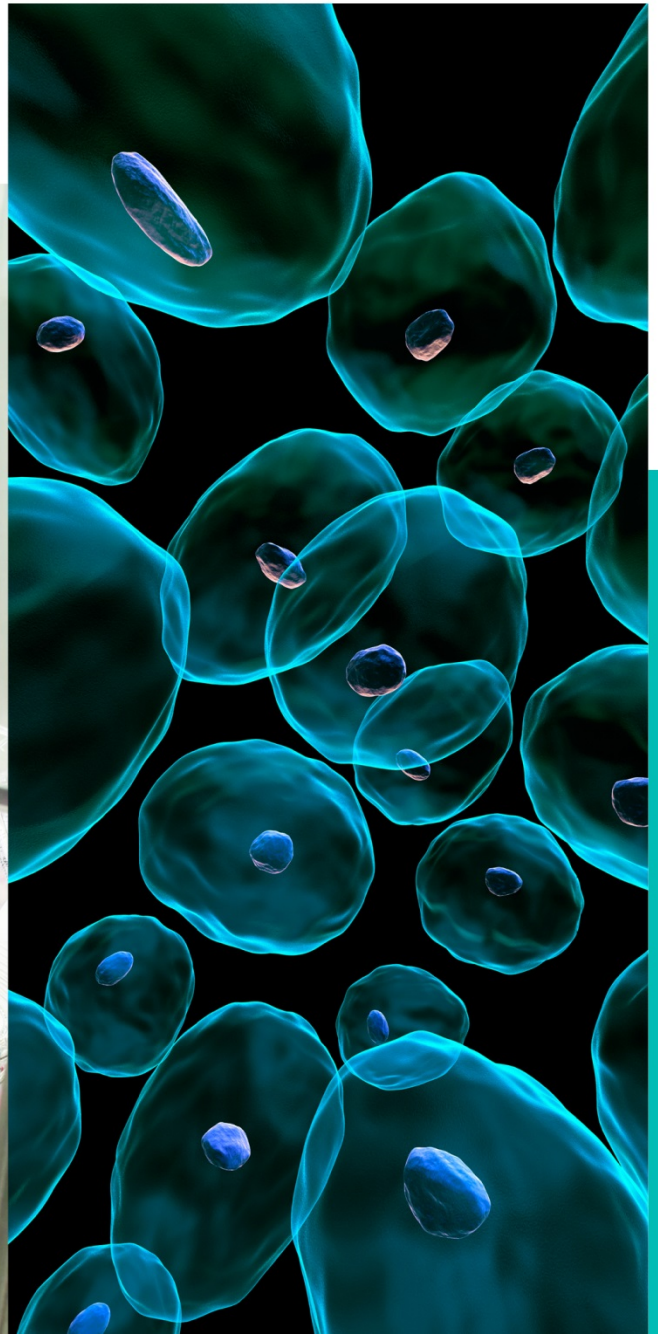

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