



Preventive Treatment: Chronic Diseases

Medicines in Development | 2024 Report

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A Path to Healthier Societies

Treating chronic diseases is important. But actually preventing them in the first place? That's becoming a possibility in many disease areas thanks to biopharmaceutical innovation.

Consider how new GLP-1 treatments for diabetes and obesity -- two conditions that collectively kill hundreds of thousands of people and cost the nation trillions each year -- can also prevent associated illnesses like heart and liver disease, sleep apnea and some cancers.ⁱ

Or look at PCSK9 inhibitors -- designed to lower cholesterol -- that cut the chance of heart attacks by about a third and can prevent the need for bypass surgery.ⁱⁱ

Or hepatitis C drugs that cure the fatal liver condition in nearly all cases -- thereby preventing countless cases of cirrhosis and liver cancer.ⁱⁱⁱ

Imagine the benefits of these treatments for patients and for society. Each one holds immense value and represents years of research and investment. In the past decade, PhRMA member companies alone have invested more than \$800 billion to bring new vaccines, treatments and cures to patients worldwide.

Some insurers and government officials have suggested that preventive treatments are "too expensive" when they first come to market. Their math doesn't add up. Studies have shown that GLP-1 drugs, for instance, could save society hundreds of billions of dollars by boosting productivity and reducing the need for other health care interventions.^{iv}

When insurers limit access to preventive medicines, they're not just making patients less healthy. They're also making society less wealthy in the long run.

Researchers are working tirelessly to develop the preventative treatments and cures of tomorrow -- from vaccines that ward off cancer to cell and gene therapies that fix the genetic malfunctions that cause disease.

It's up to the rest of us to ensure that patients can access those medicines -- and that society can reap the benefits.



Stephen J. Ubl

President and Chief Executive Officer
Pharmaceutical Research and Manufacturers of America

R&D Focused on Medicines that Treat and Prevent Chronic Diseases, Including Heart Disease, Cancer, Stroke, Alzheimer's Disease and More, Offer the Potential to Dramatically Reduce Burden of Illness

JUST THE FACTS

✓ **90%** of the United States' health care expenditures are spent on patients with chronic diseases each year^v

✓ **129 million** American adults have at least one chronic disease^{vi}

✓ The leading cause of death in the U.S. is heart disease and about **700,000** Americans die from it each year^{vii}

✓ **42%** of Americans have two or more chronic diseases^{viii}

Chronic diseases affect millions of patients, families and communities across the United States each day. Differing from acute diseases, which usually demand short-term care, chronic diseases often require extended and, in some cases, life-long treatment. Because of this, chronic diseases are a significant driver of health care spending and can have a detrimental impact on a patient's quality of life.

An estimated 129 million people (51.8%) in the U.S. have at least one major chronic disease.ⁱⁱ And, seven of the top 10 leading causes of death in the U.S. are strongly associated with preventable and treatable chronic diseases.ⁱⁱⁱ

Furthermore, an increasing number of American adults have multiple chronic conditions; 42% have two or more, and 12% have at least five.^{iv} As a result, chronic diseases have a substantial financial impact on the U.S. health care system, accounting for about 90% of the \$4.5 trillion spent on health care each year.ⁱ Looking ahead, the number of individuals with three or more chronic conditions is projected to reach 83.4 million by 2030, greatly increasing the economic burden imposed by these illnesses.^{ix}

These trends not only underscore that chronic illnesses are common, but they are commonly co-occurring. This is not surprising given many chronic illnesses are highly interrelated. In fact, some of the most common chronic conditions, such as heart disease, diabetes, obesity, high cholesterol and blood pressure are risk factors for each other.^x Likewise, any public health intervention to improve population health and reduce the costs of chronic illnesses must take a comprehensive approach and consider the collective role each of these illnesses play in health outcomes.

"Preventing and changing the course of disease is at the heart of what we mean by getting ahead of disease together. By harnessing our science and technology, we have an opportunity to prevent disease in the first place, as well as change the course of a disease, helping to prevent progression of an illness and limit long-term complications. Our expertise in vaccines and medicines means we are uniquely placed to focus on connections between prevention and treatment." - GSK

Preventive treatments for chronic illness are defined as those that prevent or avoid illness or mitigate the progression of a disease. Preventive treatments can help lower health care costs by reducing chronic diseases and comorbidities.

Innovative biopharmaceutical research companies are working to develop new medicines to prevent and treat many chronic diseases. Today, there are **1,181** preventive treatments in development^{xi} addressing chronic conditions providing hope that people of all ages can live longer, healthier lives. This report seeks to shine a light on the growing burden of chronic disease in the United States and its impact on patients, our health care system and society.

Innovation for Disease Prevention and Public Health

The biopharmaceutical industry is at the forefront of developing groundbreaking preventive treatments and vaccines that have the potential to save lives and reduce health care costs in the long term. Biopharmaceutical researchers are deeply committed to advancing public health through the development of vaccines, therapies and other preventive measures that address a wide range of diseases and health challenges.

Medical Benefits Stemming from Chronic Disease Prevention Innovations

Preventive treatments not only improve health outcomes, but also well-being by reducing the burden of disease and allowing individuals to lead longer, healthier, more productive lives.

This is especially relevant for older adults, who are at higher risk for chronic conditions like diabetes, osteoporosis, and Alzheimer's disease.^{xii} More than two-thirds of Medicare beneficiaries 65 years or older have two or more chronic conditions and more than 15% have six or more.^{xiii} Preventive treatments for chronic conditions affecting older Americans can contribute to healthy aging by reducing the need for long-term care and improving the quality of life for older adults.

Some examples have shown how preventive treatments can offer good value to patients and the U.S. health care system:

- SGLT2 inhibitors are approved for the treatment of diabetes and to reduce the risk of cardiovascular death and hospitalizations, as well as kidney disease in patients with a range of co-occurring chronic conditions. In a study compared with placebo, SGLT2 inhibitors reduced the risk of major adverse cardiovascular events (myocardial infarction, stroke, or cardiovascular death) by 11% and hospitalization for heart failure or cardiovascular death by 23%.^{xiv}
- Cholesterol-lowering medicines called PCSK9 inhibitors are approved to prevent a wide range of cardiovascular outcomes, including heart attacks and strokes. Compared against a placebo, PCSK9 inhibitors have been shown to lower LDL cholesterol (LDL-C) by 60% as well as reductions in cardiovascular events.^{xv}
- Another group of cholesterol-lowering medicines called HMG-CoA reductase inhibitors, commonly referred to as statins, are also approved for lowering LDL cholesterol levels. The first statin was introduced in the 1980s^{xvi} and can lower LDL-C levels by as much as 60%. Statins also are effective in reducing triglyceride levels associated with hypertriglyceridemia.^{xvii}
- A medicine approved to prevent migraine has been shown in studies to reduce migraine days by 75% or more in some people who experience a migraine 4-14 days a month. And some people saw a 100% reduction.^{xviii} Migraines are a neurological disorder that causes severe, and sometimes prolonged headaches, disrupting daily life with many people living with pain for half of every month. About 68% of people say that migraines have made them less productive at work.^{xix}
- A GLP-1 agonist approved for the treatment of obesity was additionally approved to lower the risk of major adverse cardiovascular events (MACE) or overweight. Compared to placebo, the medicine reduced the risk of MACE by 20% when added to standard of care. Additionally, the medicine reduced the risk of cardiovascular death by 15% and a risk reduction of death from any cause by 19%.^{xx}

"We are uniquely positioned at Bristol Myers Squibb to harness the power of science and discover next generation treatments that will transform patients' lives. The cornerstone of our research strategy is based on three key principles: selecting targets with strong causal human biology, matching the right therapeutic modality to a molecular mechanism of action, and identifying a clear path to clinical proof-of-concept. We have capabilities and platforms at BMS that are truly differentiating, particularly in the areas of targeted protein degradation, cell therapy and radiopharmaceutical therapeutics (RPTs). We also have amazing team members from around the world who are passionate about helping patients prevail over serious diseases. We believe that together, these factors will help us deliver high-quality medicines with greater speed and an increased probability of success."

- Robert Plenge, MD, PhD, EVP, Chief Research Officer, Bristol Myers Squibb

Prevention Can Reduce Health Care System Costs

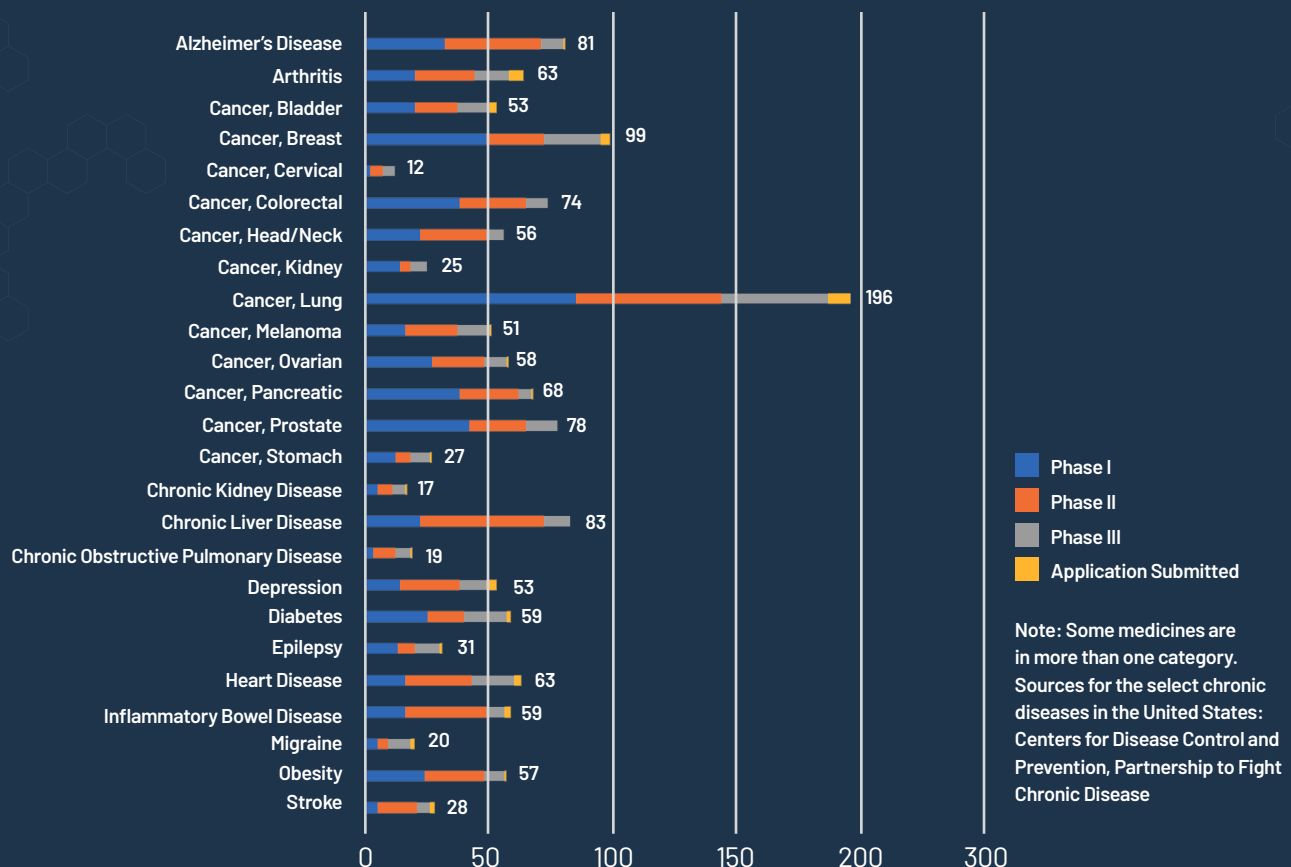
The combined costs of managing chronic diseases account for two-thirds of all health care costs and 93% of Medicare spending.^{xxi} While untreated and poorly controlled chronic illness imposes a heavy burden in the United States, the opportunity to improve health and drive savings through the use of medicines offer tremendous potential to control health care costs in the years ahead.

Better disease management achieved through use of prescription medicines has long been credited with avoiding health complications and spending on other costly health care services such as emergency room visits, hospital stays, surgeries and long-term care. These features make medicines a central component of any strategy to improve health while controlling costs, including in the communities of color disproportionately impacted by them.

Illustrating this point:

- Medicare savings due to better use of medicines may be three to six times greater than estimated by the Congressional Budget Office (CBO) for seniors with common chronic conditions, including heart failure, diabetes and hypertension.^{xxii}
- Improved medicine adherence can lead to avoided hospital stays savings Medicare billions of dollars – \$4.5 billion for diabetes, \$5.1 billion for hyperlipidemia, \$5.6 billion for heart failure and \$13.7 billion for hypertension.^{xxiii}
- One study found that roughly half of the marked slowdown in Medicare spending growth between 1999 and 2012 was the result of slower growth in spending for cardiovascular diseases. Importantly, greater use of cardiovascular medicines accounted for one-quarter of the overall slowdown in medical care spending during this period.^{xxiv}

Medicines in Development Preventive Treatment and Chronic Diseases



"Cancer is one of the most challenging health crises of our lifetime and we urgently need more innovative treatment options. At Pfizer, we are making significant investments to deliver transformative therapies for some of the world's most common cancers. Through our robust and diverse oncology pipeline, we will continue to advance our vision of accelerating breakthroughs to help people with cancer live better, longer lives."

- Jeff Settleman, Ph.D., Chief Scientific Officer
Pfizer Oncology

"Research and innovation have reached an era where we have the opportunity to redefine how we treat chronic immunologic diseases. Our deepening understanding of the science and patient needs has yielded the development of medicines like bimekizumab that have the power to, in many cases for the first time, selectively target the root causes of disease."

- Christopher Cioffi, Ph.D.
Global Development Head for Bimekizumab, UCB

Promise of the Preventive Medicine Pipeline

The **1,181** medicines in development for prevention by biopharmaceutical research companies are being investigated to prevent certain cancers, heart disease, Alzheimer's disease and other chronic diseases. Preventive treatments in development include:

- A monoclonal antibody (mAb) is in development for the reduction of **asthma attacks** in severe asthma with type 2 inflammation (a condition that elevates white blood cell levels, which increase asthma symptoms). Type 2 inflammation is responsible for more than 80% of severe asthma cases and can lead to exacerbations of the disease (increased coughing, shortness of breath or wheezing). The mAb in development targets the action of interleukin-5 (IL-5), a protein known to play a key role in the growth, activity and survival of eosinophils associated with type 2 inflammation in severe asthma. In clinical trials, the medicine has shown significant reductions in exacerbations over 52 weeks versus placebo.^{xxv}
- Post-approval research of an amyloid-beta protein inhibitor for the treatment of mild **Alzheimer's disease** is being studied as a treatment for preclinical Alzheimer's disease (the disease stage when changes in the brain are occurring but before any symptoms are seen). The medicine works by targeting the build up of amyloid beta plaques in the brain, a key element in the development of Alzheimer's disease. Amyloid plaques appear between nerve cells in the brain and disrupt cell function. It is being studied to determine its ability to reduce brain amyloid accumulation and possibly prevent the disease from progressing.
- An oral PCSK9 inhibitor is in development for the reduction of low-density lipoprotein (LDL) **cholesterol**, or "bad cholesterol." Currently, approved PCSK9 inhibitors are all injectable medicines. PCSK9 plays a key role in cholesterol by lowering levels of LDL receptors, which are responsible for removing LDL cholesterol from the blood. Inhibiting the interaction of PCSK9 and LDL receptors results in a greater number of LDL receptors to remove LDL cholesterol. Elevated LDL cholesterol is a major risk factor for atherosclerotic cardiovascular disease, which can lead to heart attacks and strokes.
- A medicine approved to improve blood sugar along with diet and exercise in adults with type 2 diabetes and to reduce the risk of cardiovascular events in adults with type 2 diabetes and heart disease is also being studied in **chronic kidney disease (CKD)**. The medicine, a GLP-1 agonist, is in development for the reduction in risk of kidney disease-related events in patients with type 2 diabetes and CKD. CKD is a common complication of type 2 diabetes with about 40% of people with type 2 diabetes also having CKD. In clinical trials, the medicine demonstrated a 24% reduction in the risk of kidney disease progression and death from cardiovascular and kidney-related causes compared to placebo.^{xxvi}

- A medicine approved to improve glycemic control in people with type 2 diabetes and obesity is continuing to be studied in adults with **heart failure** with preserved ejection fraction (HFpEF) and who are obese. HFpEF accounts for nearly half of all people with heart failure cases and 60% of those are also clinically obese. The medicine is a dual acting GIP (glucose-dependent insulintropic polypeptide) and GLP-1 (glucagon-like peptide-1), which are receptors found in areas of the brain that regulate appetite. In clinical trials, the medicine reduced the risk of heart failure events – urgent care visits, hospitalization, the need for additional oral diuretics or cardiovascular death – by 38% compared to placebo. It also led to a 15.7% weight loss in clinical trial participants and a significant improvement in heart failure symptoms and physical limitations.^{xxvii} It is also being studied for the reduction of morbidity and mortality associated with obesity and for the reduction of adverse cardiovascular outcomes in patients with type 2 diabetes.
- A factor XIa (FXIa) inhibitor is being developed for the prevention of **secondary ischemic** stroke in patients who have had a stroke or who are at high-risk for transient ischemic attack (TIA). Many patients are untreated or undertreated for the risk of blood clots (thrombosis) due to the risk of bleeding. Factor XIa is a key factor in the process promoting clot formation but with reduced risk of bleeding compared to other factors. FXIa inhibitors may reduce clot formations while maintaining the body’s ability to respond to bleeding events.

Impact of Prevalent Chronic Diseases on Society

Different chronic diseases impact patients, caregivers and communities in different and varied ways. Unlike acute diseases, which usually require short-term care, chronic diseases often require longer management, and, in some cases, life-long treatment. Having a chronic disease can influence a person’s ability to work, in addition to causing physical limitations that restrict activities and can lead to emotional challenges.

Below are examples of different chronic diseases and their impact:

Alzheimer’s Disease

An estimated 6.9 million Americans are living with Alzheimer’s disease. Of those, 26% are age 65 to 74 and 73% are age 75 or older. The long duration of Alzheimer’s disease contributes significantly to the public health impact because much of that time is spent in a state of severe disability and dependence. Alzheimer’s also impacts more than the person with the disease with more than 11 million Americans providing unpaid care for a family member or friend with the disease. This unpaid care is valued at nearly \$350 billion. In 2024, health and long-term care costs for people living with Alzheimer’s and other dementias are projected to reach \$360 billion.^{xxviii}

Cardiovascular Disease

In the U.S, heart disease is the leading cause of death for most Americans. Someone in the U.S. dies every 33 seconds from cardiovascular disease. In 2023, 680,980 people died from heart disease – about 1 in every 5 deaths. And another 162,640 people died from stroke (cerebrovascular disease).ⁱⁱⁱ Heart disease costs from health care services, medicines and lost productivity due to death, cost the nation about \$252.2 billion from 2019 to 2020.^{xxix}

“A potential first-in-class disease-modifying therapy that targets the underlying pathophysiology of IgA nephropathy, also known as Berger’s disease, is currently in development. IgA nephropathy is a progressive, autoimmune, chronic kidney disease characterized by the accumulation of immune complexes containing galactose-deficient IgA1 (Gd-IgA1) and associated autoantibodies in the kidneys. Proper identification and diagnosis of IgA nephropathy are crucial as most patients progress to end-stage kidney disease within their lifetime. This new potential therapy aims to offer a promising approach of inhibiting APRIL (A Proliferation-Inducing Ligand), a cytokine in the tumor necrosis factor (TNF) family, that is integral to the development and progression of IgA nephropathy. By targeting APRIL, it is possible to reduce the production of the pathogenic galactose-deficient IgA1 (Gd-IgA1) and the formation of harmful immune complexes.”

– John Kraus, M.D., Ph.D., Executive Vice President and Chief Medical Officer, Otsuka

Diabetes

An estimated 38.4 million Americans – 11.6% of the U.S. population – have type 1 or type 2 diabetes. Of those, 29.7 million people are diagnosed with diabetes and another 8.7 million people have the disease but are undiagnosed. People with diabetes have a long list of risk factors for disease-related complications, such as being a smoker, excess weight or having obesity, physical inactivity, high A1C levels, high blood pressure and high cholesterol.^{xxx} In 2022, the financial burden of diabetes in the U.S. was estimated to be \$412.9 billion, including \$306.6 billion in direct medical costs and \$106.3 billion in indirect costs. People with diagnosed diabetes now account for one of every four health care dollars spent in the U.S.^{xxxii}

“We’re committed to helping those living with serious and chronic diseases with high unmet needs by delivering innovative medicines. Cardiometabolic conditions, like cardiovascular disease and obesity, are public health threats with trends curving in the wrong direction. With nearly 20 years of leadership in lipid and cardiometabolic research, Amgen is focused on addressing urgent diseases caused by unmanaged LDL cholesterol, Lp(a), obesity and obesity-related conditions. We look forward to the potential these pipeline therapies may have for patients, but also realize they are just one piece of the puzzle. We are committed to advancing a bold ambition alongside leading experts in the cardiovascular community: to cut the number of heart attacks and strokes in the U.S. in half by 2030. Through our cardiometabolic pipeline and working with the community on a real-world call-to-action, we aim to make meaningful progress for people with serious and chronic conditions.”

- Saptarsi Haldar, Vice President of Research, Head of Cardiometabolic Disorders, Amgen

Obesity

Obesity is a common and burdensome chronic disease, affecting more than 100 million Americans and this number is projected to grow to about 50% by 2030.^{xxxii, xxxiii} Nearly 20% of children have obesity. Additionally, among today’s children the majority are expected to have obesity by age 35.^{xxxiv} Obesity is associated with at least 236 other medical problems, including heart disease, stroke, type 2 diabetes, arthritis, respiratory problems, fatty liver disease, depression, sleep apnea, musculoskeletal problems and many forms of cancer. The impact of the obesity and overweight epidemic has been widely documented in the U.S. with an estimated cost of \$1.72 trillion (9.3% of U.S. GDP) in medical costs and loss of productivity.^{xxxv} Over the next 10 years the combined Medicare and Medicaid spending on obesity and related chronic illness will total \$4.1 trillion.^{xxxvi}

Effective treatment of obesity can help drive savings through the health care system by limiting comorbidities.

Chronic Disease and Impact on Different Populations

Chronic diseases affect different populations at different rates and also in varying degrees. For instance, in 2018, prevalence of multiple chronic conditions was higher among women, non-Hispanic white adults, older adults, adults aged 18 to 64 on Medicaid, dual-eligible adults (Medicare and Medicaid) and adults in rural areas.ⁱⁱ Additionally, residents of impoverished communities are at increased risk for mental illness, chronic disease, higher mortality and lower life expectancy.^{xxxvii}



Focus: Older Adults

In 2022, 57.8 million Americans were age 65 and older and this population is projected to reach 78.3 million by 2040 and 88.8 million by 2060.^{xxxviii} Older adults are disproportionately affected by chronic diseases, such as diabetes, arthritis and heart disease. Nearly 95% have at least one chronic disease, and nearly 80% have two or more.^{xxxix}



Focus: Children

In the U.S., more than 40% of school-aged children and adolescents have at least one chronic health condition, such as asthma, obesity, other physical conditions, and behavior/learning problems. The healthcare needs of children with chronic illness can be complex and continuous and includes both daily management and addressing potential emergencies.^{xi}



Focus: Women

In 2021, 4 of the 5 leading causes of death of American women were chronic diseases.^{xii} Women also have a higher prevalence of many chronic diseases compared to men, such as Alzheimer's disease and depression. Prevalence of multiple chronic diseases is higher among women (28.4%) than men (25.9%) and increased with advancing age.ⁱⁱ

The Patient Perspective



Anna B., Epilepsy Patient
North Carolina

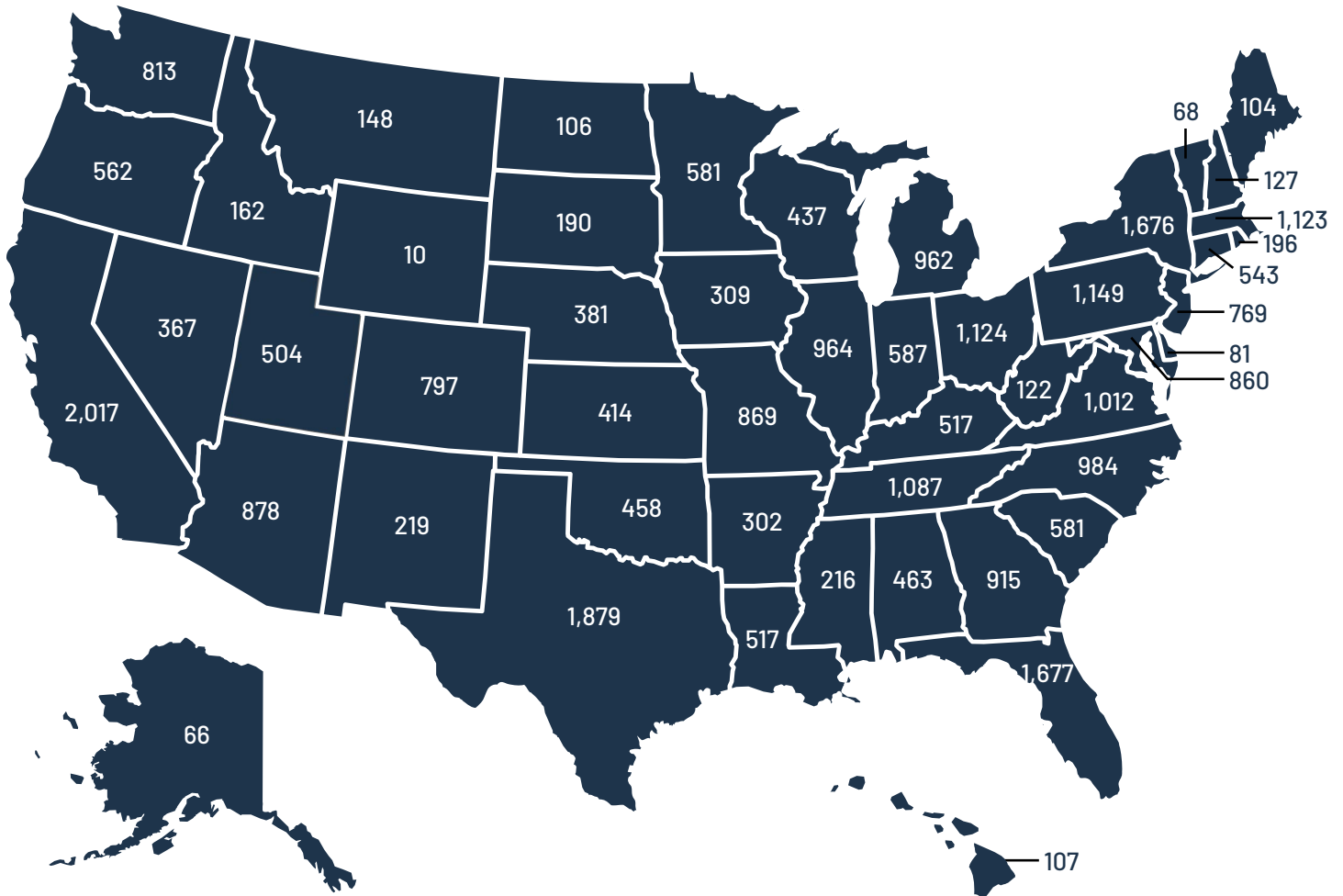
Living with chronic brain condition like epilepsy can be challenging, but I've found that the right medications can be truly lifesaving. Before I began treatment, the unpredictability of seizures made everyday life feel uncertain and frightening. However, once my neurologist identified the right combination of medications, the frequency and intensity of my seizures dramatically decreased. This newfound stability allowed me to regain control over my life, fully participate in work and social activities, and not live each day in fear.

The impact of these medications goes beyond just managing my seizures. By effectively controlling my condition, I've significantly reduced my risk of developing complications or comorbidities associated with epilepsy. For instance, my risk of injury from falls or accidents during a seizure has been minimized, which is a huge relief for both me and my family. Additionally, having my medications on hand has lowered my stress levels, which is crucial since stress is often a trigger for epilepsy patients.

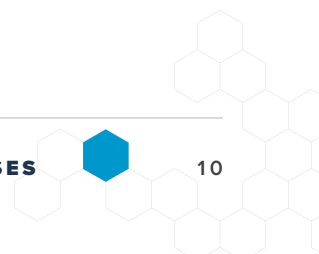
The right medicines have transformed my life. I feel healthier, more confident, and less at risk for future health issues related to epilepsy. I am able embrace everyday moments that I once feared, and for that I am grateful.



Number of Clinical Trials



Source: www.clinicaltrials.gov. Search criteria: State, United States; Phase: Early Phase I, Phase I, Phase II, Phase III; Industry only. Search performed 9/19/2024. Included clinical trials are Active, not recruiting; Recruiting, Not yet recruiting and Expanded access available. Note: many medicines are tested in more than one clinical trial at a time and at several sites across the country.



Intellectual Property Protections

Robust and reliable Intellectual property protections in the United States have provided biopharmaceutical manufacturers with the certainty needed to make the long-term investments necessary to research and develop chronic disease medicines and drive progress for patients. These incentives have fostered a favorable environment for innovation, driving unprecedented advancements in medicine and improving global health outcomes.

Price Setting

While history has demonstrated that increased access to prescription medicines not only improves health but also curbs overall health care spending, price-setting policies like those enacted under the Inflation Reduction Act (IRA) move our health care system in the opposite direction by discouraging investment in R&D to bring forward new chronic disease medicines. CMS' initial list of drugs eligible for price setting illustrates this disincentive in action as the entire list is comprised of medicines to treat common chronic illnesses such as heart disease, diabetes, cancer and autoimmune diseases.^{xliii}

Concerningly, CMS is expected to continue to select medicines that treat chronic disease for price setting in the years ahead due in large part to the high burden chronic illness imposes on the Medicare population. Public policies should focus on incentivizing and expanding access to innovative medicines that prevent and treat chronic illnesses as they provide our best opportunity to reduce the burden of these diseases while controlling health care costs in the years ahead.

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