NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Strategic Plan for Research

Pathways to health for all

NIH National Institute of Diabetes and Digestive and Kidney Diseases

December 2021

DIRECTOR'S MESSAGE

As the Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I am pleased to present this Strategic Plan describing scientific goals and research opportunities for the next 5 years.

NIDDK supports and conducts research on some of the most common, chronic, costly, and consequential diseases, along with research on diseases and disorders that are less widespread but nonetheless devastating in their impacts. This research includes basic, clinical, and translational studies by scientists across the country at universities, small businesses, and other institutions to discover biological processes and other contributors to health and disease, test prevention and treatment strategies, and develop approaches to scale up and broaden the reach of evidence-based interventions. NIDDK also remains committed to understanding and reducing the health disparities associated with many of the diseases in our mission. The Institute disseminates knowledge gained from its research to healthcare providers, people affected by disease and their families, and the public. NIDDK also supports research training and career development to encourage, inspire, and train the next generation of scientists.

To identify key research challenges and opportunities for the future and to maximize the value of research investments, NIDDK regularly engages in research planning focused on the diseases within our mission, including diabetes and other endocrine and metabolic diseases; liver and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases. To complement our disease-specific planning, NIDDK now has developed this overarching Strategic Plan. Extensive input from leading researchers and patient advocates across the country was integral to our planning process, as was broader public input. We are grateful for the innovative ideas and insights we received.

We have established four scientific goals for this Strategic Plan, focused on advancing basic science research, clinical studies, dissemination and implementation research, and stakeholder engagement. Several cross-cutting topics are part of each of these goals: reducing health disparities, improving women's health, and strengthening biomedical workforce diversity and training. The plan also highlights our commitment to serve as an efficient and effective steward of public resources.

This Strategic Plan presents a broad vision for accelerating research on the diseases, conditions, and scientific areas under NIDDK's mission. Many of these diseases are intertwined: some may share the same root causes; the presence of one disease may raise the risk of another; and treating one disease may improve the outcome of others. By leveraging these connections, empowering a vibrant and talented scientific workforce, and engaging our many stakeholders, we can help ensure healthier lives and improved quality of life for all and advance health equity. Thus, the overarching theme of this Strategic Plan is **Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All.**

Griffin P. Rodgers, M.D., M.A.C.P.
Director
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
U.S. Department of Health and Human Services

Table of Contents

OVERVIEW AND INTRODUCTION

NIDDK Mission and Vision

Mission and Statutory Authority

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) was established in 1950 as part of the National Institutes of Health (NIH), and acquired its current name in 1986. As authorized by Sections 426-434A of the Public Health Service Act [42 U.S.C. 285c – 285c-9], the mission of the NIDDK is to conduct and support medical research and research training and to disseminate science-based information on diabetes and other endocrine and metabolic diseases; digestive diseases, nutritional disorders, and obesity; and kidney, urologic, and hematologic diseases, to improve people's health and quality of life.

As a whole, the diseases that fall within NIDDK's mission are chronic, costly, and consequential for patients, their families, and the Nation, often with differential impact on populations that have been marginalized.

Endocrine and metabolic diseases span a range of conditions. They include diabetes, which affects an estimated 34.2 million people in the United States.[1] The most common forms of diabetes are type 1 diabetes, in which the body loses its ability to produce the hormone insulin as a result of an aberrant immune system attack; and type 2 diabetes, which is due to a combination of insulin resistance and insufficient insulin production. Women can also develop gestational diabetes, a form of the disease that is diagnosed during pregnancy and increases risk for later type 2 diabetes. There are other forms of diabetes that, although not as common, can still have devastating effects. A variety of factors increase risk for diabetes, including genetic, environmental, and other factors. Obesity is a strong risk factor for development of type 2 diabetes and gestational diabetes. Diabetes is associated with serious complications, such as heart disease and stroke, blindness, kidney failure, lower limb amputation, many forms of cancer, dementia, hearing loss, erectile dysfunction, urinary incontinence, and other adverse health conditions. Other endocrine and metabolic diseases, such as cystic fibrosis, osteoporosis, and hypothyroidism, also can be severe in their impacts.

Obesity affects more than 40 percent of U.S. adults and over 19 percent of children and adolescents.[2] Individuals with obesity may develop devastating health problems, face reduced life expectancy, and experience stigma and discrimination. Obesity results from a combination of genetic susceptibility, biological pathways related to metabolism and body weight regulation, and environmental and other factors. People who have obesity are at increased risk for type 2 diabetes, fatty liver disease, kidney disease, cardiovascular disease, cancer, and many other diseases.

Digestive diseases affect the gastrointestinal tract, liver, gallbladder, and pancreas, and also include nutrition-related disorders. Digestive diseases, which can cause serious complications such as severe pain, elevated risk of cancer, or liver failure, accounted for an estimated 66.4 million ambulatory care visits to doctor's offices, outpatient hospital clinics, and emergency departments in 2016.[3] Complex interactions among genetic, environmental, immune, microbial, and other factors contribute to the development of inflammatory bowel diseases, celiac disease, and other digestive disorders. Liver diseases can be caused by infection, such as viral hepatitis; genetic mutations; autoimmune reactions; or drug toxicity. The rise in obesity in the United States has fueled a rise in nonalcoholic fatty liver disease, which, like many liver diseases, can place individuals at higher risk for liver cancer.

Good nutrition is essential for health and survival, and dietary factors affect risk for obesity, type 2 diabetes, chronic kidney disease, fatty liver disease, and many other chronic diseases. Nutritional needs can vary depending on such factors as an individual's underlying health conditions, and can change across the lifespan, from infancy to older adulthood.

It has been estimated that 37 million U.S. adults have impaired kidney function—also called chronic kidney disease.[4] Kidney disease can lead to irreversible kidney failure and other life-threatening complications, and people with kidney failure require dialysis or a kidney transplant to live. Yet, kidney disease often has no symptoms in its early stages and can go undetected until it is very advanced. There are many different forms of kidney disease, including kidney disease related to diabetes or high blood pressure; inherited diseases such as polycystic kidney disease, congenital kidney disorders, and focal segmental glomerulosclerosis; and immune-related kidney diseases.

Urologic diseases and disorders include urinary incontinence and broad lower urinary tract dysfunction, benign prostatic hyperplasia (enlarged prostate), urinary tract infections, kidney stones, interstitial cystitis/bladder pain syndrome, chronic prostatitis/chronic pelvic pain syndrome, and congenital urological disorders, among others. These conditions can be chronic and painful, and they may lead to substantial disability and impaired quality of life. Like many other diseases in NIDDK's mission, urologic diseases and disorders are prevalent; for example, it is estimated that about 54 percent of women 20 years and older report urinary incontinence in the past year.[5]

Hematologic diseases within NIDDK's mission include serious, debilitating, and painful diseases such as thrombocytopenia, sickle cell disease, the thalassemias, aplastic anemia, iron deficiency anemia, hemolytic anemias, and the anemia of inflammation or chronic disease.

While the diseases and conditions within NIDDK's mission affect different tissues, organs, or functions of the body, many are intimately linked. For example, obesity is a risk factor for fatty liver disease and type 2 diabetes; diabetes raises the risk for kidney disease; type 1 diabetes and celiac disease share genetic predisposition; and individuals with urologic pain syndromes often have irritable bowel syndrome. Many of the diseases and conditions within NIDDK's mission have shared causes and contributors, for example, genetics, inflammation, and other biological factors, along with social and structural determinants of health such as differences in access to care, environmental exposures, availability of healthy food or places to exercise, and other external factors. As a result of the shared pathways to disease development, many individuals have more than one of these diseases and conditions. Additionally, many of these diseases and conditions are associated with health disparities, disproportionately affecting racial and ethnic minority populations,[6] American Indian/Alaska Native communities, people who live in rural areas, and other populations who are underserved.

Vision

Several principles guide NIDDK's leadership: maintain a vigorous investigator-initiated research portfolio; support pivotal clinical studies and trials; promote a steady and diverse pool of talented new investigators; foster exceptional research training and mentoring opportunities; and ensure knowledge dissemination through outreach and communications.

Additionally, to fulfill our mission today and in the future, NIDDK is committed to empowering a **multidisciplinary research community**; engaging **diverse stakeholders**; and leveraging discoveries of connections among diseases across NIDDK's mission to improve prevention, treatment, and health equity—pursuing **pathways to health for all**. This theme is addressed throughout the Strategic Plan.

Empowering a multidisciplinary research community: Through support of vigorous, multi-pronged research efforts, NIDDK strives to combat the many debilitating chronic diseases within its mission. Additionally, training and career development for researchers is critical to ensure a vibrant and experienced workforce with people from different backgrounds. Multidisciplinary research—combining the expertise and perspectives of researchers in a range of fields—is important for paving the way for groundbreaking insights and new, effective strategies to improve health.

Engaging diverse stakeholders: By engaging our stakeholder communities, we can ensure that biomedical research benefits all populations, including those who are underserved. For the Strategic Plan, the term stakeholders broadly refers to those who share an interest in improving health and quality of life for people with diseases in our mission. These stakeholders include, for example: patients, caregivers, and patient advocates; people who participate in research; those who deliver interventions studied in clinical research, including healthcare systems, healthcare providers, and community and other organizations; entities such as industry that may move the results of NIDDK-supported basic research into later stages of therapeutic development; other federal agencies; and many others. Importantly, these individuals, organizations, communities, and others can all be partners in the research process.

People living with diseases in NIDDK's mission can provide valuable perspectives to inform research. Because many of the diseases within NIDDK's mission disproportionately affect racial and ethnic minority groups and other populations who have been marginalized, the Institute will strengthen its efforts to engage stakeholders from these groups to help advance research and address health disparities. Additionally, some diseases within the Institute's mission more frequently or only affect women; thus, it is important to intensify research to improve women's health, and engage women for input in the process. NIDDK will also work to ensure substantial representation and participation of women, racial and ethnic minority populations, people living in rural communities, and other populations who are underrepresented in clinical studies and trials relevant to these diseases. It will be valuable to engage with other stakeholders as well, such as community members who could partner with researchers in recruiting study participants and delivering an intervention to be studied in their communities. Additional stakeholders who could provide important perspectives include those who may be involved in the research continuum from foundational discoveries to clinical trials to dissemination and implementation of proven interventions in clinical and community settings. As part of NIDDK's communication with stakeholders, the Institute will also continue to provide health information to improve the lives of patients, their families, and those at risk for the diseases within its mission, building on community relationships and partnerships to deliver tailored messages effectively.

Pathways to health for all can be forged by leveraging the connections shared by the diseases across NIDDK's mission, and by pursuing research avenues to benefit diverse populations. Many of these diseases have shared causes and contributors—including biological factors, social determinants of health and related structural determinants, and other environmental factors. Additionally, many people have multiple chronic diseases and conditions in NIDDK's mission. These connections also present valuable opportunities for improving prevention and treatment for multiple diseases. Finally, because the burden of many of the diseases across NIDDK's mission differs across populations, it will be critical to bolster research that eliminates disparities and achieves health equity.

Framework for the Strategic Plan for NIDDK Research

The Strategic Plan highlights four overarching Scientific Goals. These align with the Mission and Vision described above, including the theme of empowering a multidisciplinary workforce, engaging diverse stakeholders, and pursuing pathways to health for all.

Scientific Goals

- Advance understanding of biological pathways and environmental contributors to health and disease
- Advance pivotal clinical studies and trials for prevention, treatment, and cures in diverse populations
- Advance research to disseminate and implement evidence-based prevention strategies and treatments in clinics and community settings, to improve the health of all people, more rapidly and more effectively
- Advance stakeholder engagement—including patients and other participants as true partners in research

For each Scientific Goal, the Strategic Plan presents a set of broad Research Opportunities. The Goals and accompanying research opportunities will guide future research efforts to improve health and quality of life for people who have, or are at risk for, diseases and conditions across NIDDK's mission. The Institute will also pursue new research opportunities and meet new challenges as they emerge in the coming years.

Stewardship

Serving as an efficient and effective steward of public resources is critical to all of NIDDK's research, and the Strategic Plan highlights many facets of stewardship. The research opportunities described in the Strategic Plan will be pursued with the resources available to the Institute. Through careful planning and analysis, the Institute will meet the challenge of deploying its budgetary resources in the most effective and efficient ways to sustain research momentum, build on research achievements, and identify and pursue new scientific opportunities.

Cross-cutting Topics

Several cross-cutting topics crucial to NIDDK's mission are addressed throughout the Strategic Plan:

- Achieving health equity by eliminating health disparities among racial and ethnic minority populations and others who are underserved
- Improving women's health
- Strengthening biomedical research workforce diversity and training

NIDDK Organization

NIDDK is organized into several Divisions and Offices that work together to lead and support research to fulfill the Institute's mission.

Most of NIDDK's resources support extramural research, including over 4,000 research grants, career development awards, and contracts each year. The majority of this research is conducted by scientists at universities and other medical research institutions, including small businesses, throughout the United States. A limited amount of research leverages special opportunities elsewhere, for example, to address important scientific questions relevant to our research mission that could be answered more readily in another part of the world.

The NIDDK's extramural research portfolio is directed by three programmatic Divisions that support basic, clinical, and translational research, along with a fourth Division that coordinates and manages extramural activities. The Division of Diabetes, Endocrinology, and Metabolic Diseases supports research related to diabetes; obesity; cystic fibrosis and other genetic metabolic diseases; and thyroid, bone, and other endocrine diseases. The Division of Digestive Diseases and Nutrition supports research related to diseases of the esophagus, stomach, intestines, liver and biliary system, and pancreas, as well as research on obesity and nutrition. The Division of Kidney, Urologic, and Hematologic Diseases supports research related to diseases and disorders of the kidneys, urinary tract, and the blood and blood-forming organs. All three of these programmatic Divisions support research training and research career development, in addition to sponsoring scientific workshops and symposia. The Division of Extramural Activities provides leadership, oversight, tools, and guidance to help manage extramural program policies and operations, including the Institute's scientific peer-review activities, grants management, committee management, and other efforts, including analysis and evaluation activities.

The NIDDK's Division of Intramural Research is composed of government scientists who conduct research across a broad spectrum of basic and clinical topics, along with research training, at its laboratories and clinical facilities in Bethesda, Maryland, and Phoenix, Arizona.

The Office of the NIDDK Director coordinates efforts across the Institute and provides scientific and administrative leadership for the Institute, including policy guidance, strategic program development and evaluation, and overall operational and administrative harmonization. Several other Offices also support NIDDK's mission. For example, the Institute's Office of Minority Health Research Coordination develops training and mentoring programs for investigators from backgrounds underrepresented in biomedical science, and advances minority health research. These efforts complement the Divisions' support for research to eliminate health disparities and advance health equity.

In planning for the future, NIDDK will continue to seek and value external input from its Advisory Council, the broader scientific community, patient advocates, other stakeholders, and the public. Active collaboration with other components of NIH, other federal agencies, and the private sector will also remain a cornerstone of NIDDK planning efforts. Ever-increasing knowledge and the advent of new technologies bring new scientific opportunities for alleviating and conquering the many chronic diseases within NIDDK's mission. The Institute will continue to seize and maximize new opportunities to reduce the burden of disease and improve health for all.

---

[1] Centers for Disease Control and Prevention (CDC). National Diabetes Statistics Report. Atlanta, GA: HHS, 2020. www.cdc.gov/diabetes/data/statistics-report/index.html

[2] CDC. National Center for Health Statistics Data Brief No. 360. www.cdc.gov/nchs/products/databriefs/db360.htm and CDC. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2017–2018. NCHS Health E-Stats. 2020. https://www.cdc.gov/nchs/data/hestat/obesity-child-17-18/obesity-child.htm

[3] National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, CDC. https://www.cdc.gov/nchs/ahcd/index.htm

[4] CDC. Chronic Kidney Disease in the United States, 2021. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2021. https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html

[5] Urological Diseases in America, 2018 Addendum. NIDDK, NIH Publication Number 12-7865, 2018. https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/urologic-diseases-in-america

[6] The NIDDK Strategic Plan uses the terminology “racial and ethnic minority” populations (or groups), consistent with terminology used by the National Institute on Minority Health and Health Disparities in the *NIH Minority Health and Health Disparities Strategic Plan 2021-2025.* The NIDDK Strategic Plan highlights the importance of research to reduce health disparities experienced by these populations and others who are underserved.

SCIENTIFIC GOALS

Scientific Goal 1

Advance understanding of biological pathways and environmental contributors to health and disease

“Basic” or “foundational” biomedical research includes the study of the biological principles, mechanisms, and processes that underlie how life works. By investigating these fundamental biological pathways as well as the environmental factors that affect health, foundational research lays the groundwork for new approaches to prevent, treat, and cure disease. The dedication of NIDDK-supported researchers to expanding scientific understanding has led to life-changing medical breakthroughs and has opened exciting new research avenues toward further improving health. By pursuing the most compelling research opportunities, filling the gaps in knowledge in understudied areas, pursuing innovations in technology, and strengthening the scientific workforce, the NIDDK strives to build new pathways to health for all.

Challenges: NIDDK’s mission covers a broad portfolio of diseases and conditions affecting many organs and cells in the body, and NIDDK-supported researchers continue to tackle the scientific challenges in these many fields. One overarching challenge is to expand our foundational knowledge of human variation and thus to increase our understanding of the heterogeneity of disease, e.g., why people differ in their risk for diseases, why even people with the same disease may experience different disease symptoms or severity, and why treatments may work well for some people but not others. Gaps exist in our knowledge of the links between biological, environmental, and social factors affecting health, particularly factors that contribute to health disparities. Understanding these factors will be crucial if we are to capitalize on the promise of personalized or precision medicine approaches for all. Increasingly, pursuing this research requires bringing together multidisciplinary expertise, cutting-edge technologies, and the ability to collect, analyze, and integrate data from various sources. Such integrated efforts are needed to fully uncover the trends and associations within increasingly large and complex data sets that can point the way to new medical advances. Connecting researchers with existing data, biosamples, and animal models to advance their work is also an ongoing challenge, with some repositories underutilized due to lack of available tools or training for users. Finally, collaboration with varied stakeholders is also needed to ensure that all voices are heard and that foundational research studies are asking the most important questions to address the needs of all Americans.

Building on advances and discoveries: NIDDK's previous research accomplishments have demonstrated how understanding the underlying biology of health can lead to scientific breakthroughs and real-world medical advances. NIDDK-supported studies have documented the rising incidence of both type 1 and type 2 diabetes in American youth, as well as the increasing burden of type 2 diabetes on youth of racial and ethnic minority groups. NIDDK has also supported the Accelerating Medicines Partnership® program-Type 2 Diabetes, an innovative partnership among NIH, academic scientists, pharmaceutical companies, and non-profits which has developed a knowledge portal that shares vast, high-quality genetic and other data for studying diabetes and identifying potential therapeutic targets. This program recently expanded to other diseases, to become the Accelerating Medicines Partnership® program for Common Metabolic Diseases. Decades-long research into glucose management technology also laid the foundations for development of continuous glucose monitors and artificial pancreas systems for diabetes. Studying markers of disease risk, researchers found that elevated maternal blood glucose levels during pregnancy, even if not high enough to be diagnosed as gestational diabetes, increased the risk for adverse health outcomes in mother and child both at birth and years later. NIDDK-sponsored research has contributed to deciphering the important roles of the human microbiome, providing new understanding of diseases influenced by the gut microbiome, such as inflammatory bowel disease. Studies of various types of body fat tissue and how weight and appetite are regulated have shed light on the underlying mechanisms of obesity. Researchers studying kidney development and regeneration have highlighted possible targets for developing new kidney disease treatments. Other studies have advanced understanding of urinary tract infections and urinary stone disease, and have identified sub-groups within and associated risk factors for complex urologic conditions such as chronic pelvic pain syndrome and lower urinary tract dysfunction, all of which may inform future research and therapeutic strategies. Research has also yielded new information on how blood cells mature and are renewed, knowledge that may have significant implications for blood transfusion technologies and treatment of hematological diseases. Several groups of NIDDK-supported scientists have also developed miniaturized laboratory models of the liver, kidney, intestine, and pancreas, as well as modifiable, miniature "organ-on-a-chip" experimental model platforms that are already accelerating research.

These are only a handful of the many foundational discoveries that the NIDDK has supported. More NIDDK-supported research is highlighted on our website in news releases and research updates and in NIDDK's annual reports. NIDDK will continue to build on previous discoveries while taking advantage of the opportunities in this Strategic Plan to drive further progress and innovation.

Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All

Critical therapeutic advances are often made possible through foundational research discoveries of the complex connections among factors that affect health and disease, including biological processes, the physical environment, and social determinants of health. Understanding these interrelationships requires the collaboration of researchers with varied backgrounds. From the fields of organ biology and genomics, to health disparities and health equity, to data science and bioinformatics, to clinical care, multidisciplinary teams bring together the expertise from multiple perspectives and life experiences to address the most urgent research questions. Sustained and fruitful collaboration between federal agencies, academic institutions, and industry is also crucial to share ideas, expand the scope of research studies, identify understudied research areas, and accelerate the path of discovery from the bench to the bedside. Community stakeholders—including those experiencing diseases within the NIDDK mission and other individuals and organizations—are also invaluable partners. NIDDK is committed to ensuring that foundational research studies offer benefit to people of all backgrounds and from all walks of life. By expanding knowledge of a wide variety of influences on health—including those that differ among people depending upon age, sex/gender, race/ethnicity, socioeconomic status, conditions such as pregnancy, and other factors—foundational research will lead to new discoveries that will benefit all.

Research Opportunities

With the opportunities highlighted in this section of the Strategic Plan, NIDDK aims to promote health and health equity by enhancing fundamental understanding of the many biological processes and environmental factors, including social and structural factors, that contribute to human health and the diseases across our mission.

Research Opportunity 1.1: Identify and characterize factors that affect human health in diverse populations

Identifying and characterizing genetic and molecular mechanisms of health and disease: New advances in clinical care require a strong foundation of detailed biological knowledge to tackle the many diseases and conditions within the NIDDK's mission. Broadly, basic research studies provide this knowledge base by contributing to our understanding of how health is maintained in various parts of the body, how diseases develop, and how and why disorders progress. Linking genes and gene variants to the molecular processes they control, identifying the genes and proteins active or dormant during specific health or disease states, expanding our understanding of cell and organ development and function, and identifying disease-related differences between people of different sexes or ages are just a few areas that researchers should study within the NIDDK's mission areas. By increasing our knowledge of fundamental body processes, basic research studies also provide clues to what factors can be leveraged to develop better prevention strategies, treatments, and cures for all people.

Promoting interdisciplinary research into biological, environmental, and social factors that affect risk and progression of multiple diseases: The NIDDK continually seeks to maximize the value of its research efforts by emphasizing study of cross-cutting topics that are broadly applicable to many diseases and conditions within its mission. For example, researchers could pursue new insights into how the body's organs, tissues, and cells signal each other to carry out their functions and how this biological communication is disrupted in disease or during physical or psychological stress. New information on how organs self-repair could lead to “regenerative medicine” approaches to restore lost organ function. The brain-body connection is also increasingly recognized as playing a bidirectional role in many diseases and conditions. Further studies are needed to fully understand how the brain and the autonomic nervous system connecting it to the body’s organs affect the function of—and sensations of pain in—organs such as the gut and the bladder. The lymphatic and immune systems also have multiple influences on health and disease, and research in these areas is also important. For example, researchers can gain critical knowledge through studies of the aberrant immune attacks and excessive inflammation associated with autoimmune and other types of diseases within NIDDK’s mission. Another factor associated with many diseases and conditions is the microbiome, which includes the numerous bacteria and other microbes in the gut and the male and female urogenital tract. Increased study of microbiome compositions and functions could have broad impacts on health. Biological pathways throughout the body are also affected by factors such as nutrition, physical activity, and day/night cycles (circadian rhythm); research in these areas can yield deeper insight into many diseases and point to effective interventions. How gene function is regulated under varied conditions is another broad research area with exciting potential benefits. Through further study of epigenetic modifications, contributions of specialized RNA molecules, the organization of the genome in the cell nucleus, and other factors controlling the timing and levels of gene activity, researchers can illuminate how a person’s environment affects their biology. Additional research into the regulation of proteins and other molecules will advance understanding of the communication between cells and the environment. Finally, there is a great need for foundational research that takes into account data on the physical and social environment. Adding consideration of these factors, where possible, into fundamental basic research may lead to a better understanding of how behavior, psychology, and the environment interact to affect health.

Engaging stakeholders in basic research: Research volunteers help expand the reach and scope of basic research, while ensuring that biological studies are representative of the diverse backgrounds of the American people. Community partnerships can also provide a critical perspective and input for basic research planning. People living with a particular disease can give researchers unique “on the ground” insights into their experiences and priorities, which can lead to innovation and new discoveries; and they may also donate precious tissue and other biological samples to make critical discoveries possible. It is also important to engage with other stakeholders (e.g., other federal agencies, other NIH Institutes and Centers, the healthcare industry, foundations, patient advocacy groups, scientific societies, other non-governmental organizations, and others) who could collaborate in research efforts, play important roles in turning foundational discoveries into potential therapeutics and other interventions to improve health, and help pave the way toward future implementation. Stakeholder engagement is important for the other research opportunities in this Scientific Goal as well. (Additional information related to this topic is in Scientific Goal 4, which is focused on stakeholder engagement.)

Regenerative medicine: restoring tissue and organ function to improve health

Some damaged tissues—including the gut lining, kidney, liver, and other organs of NIDDK interest—have a remarkable capacity to repair themselves. The field of "regenerative medicine" seeks to harness this process to restore cell, tissue, and organ function lost due to aging, damage, or disease. Understanding how and why cells and tissues regenerate, how stem cells contribute to tissue repair, and how to induce self-repair in damaged tissues could lead to new treatments or prevention strategies for inflammatory bowel disease, diabetes, kidney disease, liver failure, hematologic diseases, and many other diseases and conditions. For example, understanding how kidneys grow and repair themselves will be key to novel approaches to repair damaged kidneys or to engineer transplantable artificial kidney replacements. Studies characterizing the factors involved in intestinal stem cell health may inform new therapies to heal the intestine during disease. Additionally, knowing how insulin-producing beta cells are damaged and how they can be protected or replaced could lead to better ways to treat, prevent, or even cure diabetes.

Research Opportunity 1.2: Analyze the links between biology, behavior, and the environment, including social determinants of health and structural factors, that contribute to disease heterogeneity and health disparities

Everyone's health is unique. Varied genetic and biochemical predispositions, environmental exposures, behavioral patterns, and social influences all contribute to overall health via a complex interplay of mechanisms that are not yet fully understood. These unique variations can result in disease heterogeneity, in which people have different risks of developing a certain disease or experience different disease symptoms, progression rates, prognoses, or responses to treatment. Unraveling the complicated reasons behind disease heterogeneity could lead to more targeted and effective disease prevention, diagnosis, and treatment, as well as contribute to data-driven strategies to address health disparities.

Pursuing interdisciplinary research into how biological, behavioral, social, and environmental factors interact to affect human health: As NIDDK-supported research refines our knowledge of the individual biological, behavioral, social, structural, and other environmental factors affecting human health, there is a growing need to understand how these different influences interact to cause disease and its heterogeneity. For example, knowing that a biological process varies with factors such as stress, lower income, or exposure to pollutants can help refine research questions and reveal previously unrecognized connections between biological responses and the environment. Researchers can investigate many aspects of these connections. Some relevant questions may include: What combinations of factors cause good or poor health, and what biological mechanisms are involved? How do environmental exposures interact with a person's genetic background to cause disease? What are the biological changes wrought by social determinants of health such as socioeconomic status or access to health-related resources? And, importantly, how can we harness this knowledge for precision medicine—personalizing treatment and prevention approaches for each individual—to improve health for all?

These critically important questions cut across a variety of disease and clinical research specialties and require the expertise of collaborative, multidisciplinary teams. Such teams could spearhead holistic investigative approaches on topics such as how specific eating habits and dietary patterns combine with a person's metabolism to affect disease risk; how diseases in

NIDDK's mission affect outcomes of other diseases (including the role of microbes in health and disease); how environmental, chemical, or other exposures can disrupt metabolic and organ function; how social determinants of health such as stress, lower income, and access to resources affect a person's microbiome, immune reactions, or brain-body interactions; and which epigenetic changes are important mediators between environmental factors and disease. Researchers can study these interrelated dynamics to gain deeper understanding that would enable precision health approaches to be developed for the "whole person"—including not just genetic and other biological predispositions but also components of the communities in which individuals live and other aspects of their lives.

Advancing health equity research by understanding factors underlying health disparities: To advance health equity, we must harness our knowledge of disease heterogeneity to understand the underlying causes of health disparities, so that research findings can be translated into health interventions for people of all backgrounds. Foundational research should be designed and conducted in ways that serve diverse communities, including populations that are understudied. Research should also take into consideration factors associated with sex/gender; for example, women's disease risks and outcomes may differ from men's. Research that addresses the health of all by developing targeted tools that work in a variety of environments and for a variety of people will promote health equity.

Precision phenotyping: new windows into understanding health and disease

Diabetes, kidney disease, digestive diseases, obesity, and other diseases and conditions within the NIDDK's mission can progress differently depending on a person's genes and metabolism, social determinants of health, and other biological, behavioral, and environmental factors that vary among individuals. Precision phenotyping—analyzing comprehensive, integrated information on these factors—could reveal new ways to detect, prevent, and treat disease. Information from precision phenotyping could answer questions such as who is at high risk for developing diabetes or its complications, how best to help a person lose excess weight, how various forms of chronic kidney disease differ, how rapidly kidney disease will progress in different people, and who will benefit from certain inflammatory bowel disease treatments. Wearable devices that track organ function or measure markers of disease could help monitor disease progression and treatment success. Additionally, enhanced phenotyping that includes social determinants of health, which are often not measured, could help pinpoint how these factors contribute to disease.

Research Opportunity 1.3: Develop innovative technologies and resources and expand data science to advance scientific progress and enhance health

Basic research advances can lead not just to new ideas, treatments, and cures but also to improved techniques and tools that accelerate the pace of scientific discovery. Thus, the impact of foundational discoveries can ripple far into the future, opening novel fields of inquiry and shedding new light on existing research questions. Feeding this technological pipeline today with research to develop next-generation tools will expand scientific horizons tomorrow.

Promoting technological development to advance the search for new drugs, diagnostics, and devices: Advancing biomedical research and development technologies could lead to new treatments and interventions to help people across the lifespan. New advances in biochemistry, immunology, biophysics, and materials science are needed to accelerate the development of promising and potentially life-saving technologies such as artificial organs. Researchers can also design improved methods for screening promising therapeutic targets in the laboratory to enhance our ability to identify potential new drugs and thus shorten drug development times. Identifying and standardizing more biomarkers could provide safe, noninvasive ways to diagnose or measure progression of disease, and could make it easier to test the efficacy of new therapies in people. Improved biomarkers could also warn of possible health issues in the clinic by helping healthcare providers monitor currently difficult-to-track health factors such as nutritional health, physical frailty, physical or psychological stress, or general metabolic health. Such tools could also provide physicians with valuable information on how to identify which personalized treatment approaches are right for which person. Finally, to deliver some of those personalized treatments to organs that are currently difficult to access, researchers can develop new gene therapy and drug delivery technologies.

Developing and improving research technologies: Technical breakthroughs in laboratory procedures and tools can increase the scope, efficiency, and accuracy of research. For example, through advances in imaging technology, researchers could visualize and record data from under the microscope or within living people in unprecedented detail. Another area of opportunity is in the development of new research model systems. By generating new cell lines, animal models, organoids, and tissue- or organ-on-a-chip systems that more accurately reflect human health and disease, researchers can enhance the relevance of basic research results and accelerate study in many NIDDK mission areas. New preclinical animal or tissue models of rare disease states could also aid in foundational research by providing novel insight into the function and disruption of biological pathways. For diseases that currently lack useful laboratory models, such advanced research tools could be game-changing, opening new areas of inquiry and promoting new advances. Researchers can also test their hypotheses in multiple model systems that accurately reflect human physiology, as described earlier, to reduce potential error and to ensure that results are reproducible and as relevant as possible to human health.

Advancing data repository/biorepository science and management to enhance utility and user adoption: Resources such as data and biospecimen repositories are invaluable assets for maximizing the scientific value of donated biological samples and research data, and they provide excellent opportunities to enhance the study of diseases across NIDDK's mission. Repositories allow centralized access to consolidated data and clinical samples from multiple research institutions, which can be critical to studies of diseases that are rare or are caused by a complex web of multiple factors. Repositories linking patient-reported data such as behavioral, psychosocial, and environmental factors with biological samples and data could greatly accelerate investigations into how all these factors affect health. Where repository resources are underutilized, there is a great need to identify and address the barriers hindering repository use, to implement best practices in repository organization and administration, and to improve repository navigation and analysis tools to facilitate research. It is also important to ensure that repository data and samples reflect diverse populations. (Additional discussion of biorepositories, along with data and biosample sharing and management, is in the Stewardship section.)

Expanding the use of data science to improve foundational research: Through multidimensional studies linking large-scale proteomic, molecular, genomic, and psychosocial data with clinical, geographical, and environmental data, researchers can identify health-modifying factors and generate new knowledge of disease causes and contributors. However, unlocking the power of such "big data" often requires decoding the complex patterns and associations hidden within various streams of evidence. Thus, there is a need to recruit and integrate computational biologists and bioinformaticians into basic research to bring their expertise to bear on existing foundational research. Additionally, researchers can use new mathematical modeling, machine learning, and artificial intelligence approaches to facilitate analysis of complex data sets such as those available on cellular protein networks, disease mechanism pathways, and therapeutic target candidates. Finally, basic and clinical researchers can use data science advances to develop innovative, data-driven algorithms to implement precision medicine approaches, matching a person's unique background with appropriate medical recommendations.

Finding connections: the autonomic nervous system in health and disease

The autonomic nervous system connects the brain to organs throughout the body. It also controls important involuntary functions. Digestion, for example, is regulated by the largest component of the autonomic nervous system—the enteric nervous system—that encases the gut. Damage to the autonomic nerves, such as from long-term diabetes, can affect the functions of the kidneys, digestive tract, and genitourinary system. One way NIDDK-supported researchers can better understand autonomic nerve damage and resulting organ dysfunction is by leveraging advances from NIH's Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, which is generating maps of the autonomic nervous system along with other tools and technologies. Such tools would also aid research on diagnosis and treatment of disorders such as incontinence and diabetic kidney disease. Studies to develop and utilize cellular models of the autonomic nervous system, such as enteric nerves derived from intestinal stem cells, can also help advance our understanding of the molecular origins of disease.

Research Opportunity 1.4: Strengthen the research investigator pipeline by enhancing and diversifying workforce development and training of basic and translational investigators

Advancing discovery and innovation requires a world-class research workforce with the varied training and experience needed to solve tomorrow's complex and increasingly multidisciplinary research questions.

Promoting and retaining a steady and diverse pool of new investigators: The NIDDK is committed to recruiting and training a steady stream of talented, innovative thinkers of all backgrounds, including by increasing the representation of populations who are currently underrepresented. Expanded training and mentorship opportunities in basic/foundational and translational research are needed to achieve these goals. Recruiting the scientists of tomorrow can also start early—for example, with programs for high school and undergraduate students. (Additional information related to the research workforce is in the Stewardship section.)

Facilitating interdisciplinary, multi-institution research collaboration and data sharing programs: Many of the research opportunities identified in this Strategic Plan require the attention and expertise of multidisciplinary teams. Through collaborations such as these, researchers can reduce the "siloing" of information and studies within their specific fields or institutions. Bringing together basic, clinical, translational, and population science researchers can also spark new ideas and allow the sharing of data, perspectives, skills, and resources. Input from physician-scientists (including surgeon scientists) can be particularly valuable in basic research, helping to bridge the gap between knowledge discovery and real-world clinical needs. Collaborations between the NIDDK and varied private, academic, and federal institutions can also broaden the Institute's scientific reach to expand studies, develop new research partnerships, pursue new programs, and tackle multidisciplinary questions.

Encouraging training in emerging research areas and cutting-edge technologies: Research training and career development opportunities are key to creating and maintaining a robust and flexible scientific workforce. As new research techniques and tools are developed, the research community should in parallel develop training opportunities for both early-stage and established investigators. One example is the current need for bioinformatics and "big data" analysis training to help integrate these techniques into ongoing research projects. Additionally, training in cutting-edge techniques and technologies in areas such as bioengineering, imaging, genomics, proteomics, and social science can provide new tools applicable to the pursuit of a broad array of research studies. Overall, enhanced opportunities for hands-on career development training will help the scientific workforce remain nimble and ready to face emerging research challenges.

We envision a future

in which expanded knowledge and novel discoveries of biological, environmental, and social contributors to health and disease lead to new prevention strategies, treatments, and cures for all people throughout our Nation who have, or are at risk for, diabetes and other endocrine and metabolic diseases; liver, intestinal, and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases.

Scientific Goal 2

Advance pivotal clinical studies and trials for prevention, treatment, and cures in diverse populations

Clinical studies can deepen our understanding of human health and identify new ways to detect, diagnose, and reduce the chance of developing a disease. They can also determine whether a treatment is safe and effective, constituting a critical step in the journey from discovery to therapy. Indeed, clinical studies provide opportunities to improve the health of all populations affected by some of the most common, chronic, costly, and consequential diseases.

Challenges: There are many challenges that must be overcome to make clinical studies successful. Clinical trials that are testing or developing novel diagnostics, therapeutics, and prevention strategies can be immense undertakings. Furthermore, many diseases in NIDDK's mission take years to develop, which makes prevention studies particularly difficult because the assessment of outcomes must be done over many years. As many of these diseases are also common across the country's diverse population, clinical studies need to recruit similarly diverse cohorts of participants so that the results are applicable to a vast array of people with different biological and social determinants of health. There are hurdles to recruitment, however, including costs, some people's reluctance to volunteer for studies, challenges to reaching out effectively to communities that are underserved, and logistical burdens to both participants and researchers. Long-term follow-up studies present challenges as well, due to factors such as high costs and declining participant retention. Additionally, clinical studies require a well-trained, innovative, diverse, and sustainable workforce not only to design and conduct the study, but also to carry out other critical tasks such as participant recruitment, study coordination, and data analysis. Integrating constantly evolving technologies into clinical studies is also challenging. This is particularly pertinent to data science, where new tools and methods could enable more extensive analysis of vast amounts of data generated in large clinical studies, but training in this emerging field is needed. A further challenge is the costly and time-consuming process required to set up clinical studies. Mitigating costs, improving efficiency, and streamlining the clinical study set-up process require innovative approaches to enhance the infrastructure for clinical research.

Building on advances and discoveries: The NIDDK has a rich history of supporting clinical studies and trials to understand and combat the diseases within its mission. These studies have provided critical evidence about which therapies yield the best results, and this research can also inform future studies to improve prevention and treatment strategies. For example, NIDDK-supported clinical trials have paved the way to U.S. Food and Drug Administration approval of a new artificial pancreas device for children and adults with type 1 diabetes. The NIDDK also established an international clinical trials network, TrialNet, that has been testing agents that have shown positive effects to slow progression toward clinically overt type 1 diabetes, such as a drug that slowed the progression to clinical type 1 diabetes in high-risk individuals. In other research, the Restoring Insulin Secretion (RISE) Consortium has been testing ways to prevent the loss of insulin secretion among individuals at high risk for type 2 diabetes or in early stages of the disease, and, along with other research, has shown that this disease is more difficult to treat in youth. Clinical trials have shown that in people with severe obesity, bariatric surgery resulted in substantial improvements in type 2 diabetes and blood pressure along with substantial weight loss. Other research showed that people ate more and gained more weight when eating ultra-processed foods. Studies of weight gain in pregnant women with obesity yielded findings that could inform calorie intake recommendations. Underscoring the many factors that can contribute to disease, scientists showed that a combination of clinical, genetic, and immunologic tests can be used to predict response to standard medical therapy for children with a form of inflammatory bowel disease (IBD). In recent NIDDK-supported clinical studies on liver disease, researchers in the Childhood Liver Disease Research Network (ChiLDReN) developed a screening strategy for earlier diagnosis of the liver disease biliary atresia in infants, with implications for earlier treatment, and identified a gene signature to help predict how quickly the disease will progress. Similarly, NIDDK-supported clinical research studies have identified genetic factors, circulating molecules, and physiological indicators in study participants that can help predict how quickly kidney function may decline, paving the way for more tailored healthcare strategies for kidney diseases. In other research, findings from studies of lower urinary tract symptoms have led to a more comprehensive subgrouping of people with these conditions based on symptom flares, knowledge that could lead to new strategies for managing this condition.

These are only a few examples of NIDDK-supported clinical research; these studies and others are highlighted on our website in news releases and research updates and in NIDDK's annual reports. In charting future directions, NIDDK will build on the advances and discoveries that emerge from the opportunities in the Strategic Plan, to drive further progress and innovation.

Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All

Technological advances have led to a time in which data-intensive science plays a central role in clinical studies, and researchers must increasingly traverse disciplinary boundaries to work on large collaborative projects such as population studies that aggregate data from many sources. Clinical studies require a diverse workforce to serve as a wellspring of innovation, along with broad recruitment of participants, including those from groups currently underrepresented in research, so that the study results will be applicable to the entire population. Many of the diseases across NIDDK's mission have common pathways with shared biological and social underpinnings; therefore, gaining a better grasp on how to best treat or prevent a disease may lead to new therapeutic approaches for others.

Research Opportunities

With the opportunities highlighted in the clinical studies section of the Strategic Plan, NIDDK aims to enhance and expedite the development of approaches to prevent, diagnose, manage, and treat diseases across our mission that impact diverse populations.

Research Opportunity 2.1: Enhance the development and testing of diagnostics, therapeutics, and prevention strategies

Understanding and eliminating health disparities to achieve health equity: Many diseases in NIDDK's mission disproportionately affect racial and ethnic minority populations, rural communities, as well as people with lower incomes. They may also affect males and females differently; many of the diseases and conditions within NIDDK's mission affect women solely, disproportionately, or in unique ways. Health disparities may stem partly from biological differences, such as genetic risk factors that are more prevalent in one population than in another. They may also stem from social and structural determinants of health—systemic differences in access to quality healthcare, environmental exposures, other external factors, and other root causes that shape these inequities. For this reason, clinical researchers studying health disparities should focus not only on biological factors, but also on conditions in the environments in which people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks. This includes research on how these social determinants of health intersect with biological factors to affect disease risk, and research on interventions to reduce or prevent disadvantageous social determinants of health or mitigate their ill effects.

Evaluating the removal of race-based tools in the diagnosis, prognosis, and treatment of disease: As predictive algorithms are increasingly being used to support decision-making in medicine, it is important to address bias in these tools. Several diagnostic algorithms and practice guidelines adjust their outputs on the basis of a person's race or ethnicity to make risk assessment and guide clinical decisions. However, race is not a reliable proxy for disease-related genetic differences, and including adjustment for race in these equations ignores the substantial diversity within self-identified racial or ethnic minority study participants, as well as other factors that contribute to disease. By evaluating these race-based tools and eliminating those that are detrimental, researchers can improve the accuracy of disease diagnosis, prognosis, and treatment.

Strengthening the integration between basic and clinical research: It is important to build upon basic scientific discoveries by translating them into new therapies, diagnostics, devices, or medical procedures; thus, clinical studies can be the culmination of decades of basic research. For example, researchers can conduct translational research that moves basic research on markers of disease onset or progression into clinical studies to develop prevention or treatment strategies. Likewise, the results of clinical studies can spur further basic research by broadening our understanding of how some treatments work—and why they might not work for everyone. Researchers can also conduct bedside-to-bench research on successful interventions to explore their mechanistic bases and expand their therapeutic potential. One important way to bridge basic and clinical research is to promote team science, with physician-scientists collaborating with basic researchers, data scientists, and others with complementary expertise. (See Research Opportunity 2.3 for further discussion.) Additionally, population studies will be important, for example, to gather data for prevention approaches. Furthermore, the development and optimization of clinical trials could be streamlined by conducting preclinical and clinical studies in parallel where appropriate, and integrating data from these studies in real time.

Developing precision health approaches: Many of the diseases under NIDDK's umbrella are heterogeneous—that is, they can affect people in different ways. Treatment responses can vary from person to person, between women and men, or among different age groups, for example. It is important to undertake clinical studies on the underpinnings of disease heterogeneity and translate that knowledge into clinical trials to aid the development of prevention or treatment approaches that are tailored to the individual.

Preventing and treating diseases in children: It is important to increase focus on how to reduce risk and slow progression of chronic diseases that can develop at an early age, including studies to develop and test cost-effective disease prevention and treatment strategies for children and teens. In addition to improving health during childhood, these research avenues have the potential for health benefits throughout life.

Making research participation and healthcare more feasible by using and improving technology: As home-based tools such as wearable devices for taking health, activity, and behavioral measurements have become more popular, researchers can undertake studies to improve how participants share health data. For example, these devices could provide a new way to monitor how nutrients, metabolites, and hormones fluctuate in the body over time. The integration of accurate, user-friendly, and convenient technological tools can significantly ease burdens on study participants, present a clearer picture of the participants' health in real-world settings, and allow for the development of more personalized treatment approaches. Research must also address ways to optimize the use of these technologies in different populations and address the challenges to implementing them, such as lack of access, understanding, and acceptability.

Improving study efficiency by examining several outcomes at once: Many of the chronic diseases and conditions under NIDDK's mission are interrelated, such that many individuals have more than one of these diseases. For example, people with obesity are also at high risk for type 2 diabetes and the liver disease nonalcoholic steatohepatitis, and people with diabetes are at high risk for kidney disease. By looking at more than one outcome at once (e.g., progression of diabetes and kidney disease), researchers can gain important information on effects of therapies in people with multiple chronic diseases and conditions, broaden the scope of use for treatments, and deepen the understanding of how these diseases interact.

Incorporating innovative clinical trial designs: The structure of a clinical study can strongly influence its efficiency and the applicability of the results. In many cases, researchers can improve clinical studies by incorporating innovative trial designs. Examples of these would be adaptive design clinical trials (which allow researchers to modify aspects of the trial, such as treatment selection, based on accumulating study data), pragmatic trials (which would reveal outcomes more applicable to real-world settings), master protocol trials (which could bolster study efficiency by testing several therapies for one disease, or one therapy for several diseases), and stepped-wedge trials (in which an intervention is administered to all participants, but at different times).

Improving the degree to which people adhere to therapeutic recommendations: Adherence to therapy is important for controlling chronic conditions, treating acute or temporary conditions, and overall long-term health and well-being. Studies should be undertaken to understand heterogeneity among different individuals' responses to adherence strategies and to test new ways to improve adherence, such as the development of new tools to enhance or maintain communication between patients and their clinicians or other healthcare providers.

Health at every age: improving chronic disease management across the lifespan

Many chronic diseases in NIDDK's mission manifest early in life and thus necessitate management throughout the lifespan. Even with advances in treatments, such as new technologies for glucose management, the benefits of those advances are not always shared equally across all racial, ethnic, and age groups, contributing to disparities in health outcomes. Thus, it is critical to improve chronic disease management to address individuals' unique needs at different life stages. For example, adolescence remains a vulnerable time for people with chronic diseases such as diabetes, kidney disease, and inflammatory bowel disease. Clinical trials and population data will be important. Research in diverse populations could identify ways to optimize the transition from pediatric to adult care for people with these and other chronic diseases, including finding strategies to improve adherence to therapies. Research could also lead to more precise ways to predict which individuals are at high risk for developing chronic diseases at different life stages, such as type 2 diabetes in youth, so that targeted prevention approaches could be developed and tested.

Research Opportunity 2.2: Increase the diversity of participants in clinical trials

A vital component of clinical trials is making sure that the participants reflect the populations who could benefit from the treatments, diagnostics, or preventative measures being tested.

Developing more participant-centered research: Selection of an appropriate outcome measure is a key factor that affects the ultimate value of results from clinical studies, but what patients prioritize may sometimes differ from outcome measures selected by researchers and physicians. It is important that researchers include participant-centered outcomes, such as quality of life and other outcomes that are respectful to the participants' values, needs, and concerns. This could help to build trust between research scientists and the broader community.

Increasing adequate representation of women, racial and ethnic minority populations, and other populations underrepresented in clinical trials to help understand the underpinnings of health disparities and promote health equity: When studying diseases that exhibit health disparities, researchers should ensure that women and racial and ethnic minority groups are well-represented in the participant cohort, so that researchers can learn whether an intervention being tested works for these populations, and whether, for example, there may be different outcomes for men and women. To help broaden clinical trial participation, it will be important to build and maintain a diverse workforce and engage key stakeholders. For example, community members can help with developing strategies to ensure representation of racial and ethnic minority populations, women, and other groups who have been marginalized or underrepresented in prior studies. In addition, investigators should clearly and thoroughly identify who is affected by the disease or condition under study, and whether the planned participant composition is appropriate.

Promoting participant engagement: There are several hurdles to enrolling a diverse cohort, including a reluctance of some to volunteer for studies due to factors that have led to a lack of trust, and various burdens on research participants. Overcoming these challenges requires innovative and inclusive outreach strategies, along with the development of infrastructure to assist investigators with strategies to cover unanticipated costs. For example, researchers can improve the process of enrolling in clinical trials by considering language and literacy when developing and distributing consent forms. Clinical researchers can also reduce participants' burden by utilizing community health centers in clinical studies, so that participants would not have to travel a great distance, could potentially attend study visits at times that would better fit their schedules, and could discuss the studies with their physician. Researchers should also partner with trusted organizations to document the life experiences of study participants. These types of approaches to increase enrollment and trust across populations will become even more important as studies move toward remote recruitment. (Further discussion of participant and other stakeholder engagement is in Scientific Goal 4, which is focused on this topic.)

Promoting pragmatic data collection: By incorporating ways to record health data in real-world settings (i.e., not in the controlled environment of a clinical trial), researchers could facilitate equitable research across populations and ease some of the burden on the participants (e.g., of traveling to a clinic). This approach could also result in a more accurate picture of study participants' health. These measurements could be performed by the study participants themselves, and could include wearable devices (see Research Opportunity 2.1) or other tools to record health data, such as digital recorders for audio journal entries. Retrospective and prospective cohort studies utilizing electronic health records (EHRs, see section 2.4) could be carried out to gain insights into interventions tested in "real world" settings. It would also be important to train people in the use of these data collection technologies and to overcome the challenges of providing them to communities that are underserved.

Research Opportunity 2.3: Bolster workforce development and training to increase and diversify the pipeline of clinical investigators

To ensure that NIDDK remains a leader in stimulating biomedical discovery, it is critical to promote and nurture an innovative and well-trained workforce to drive the clinical research necessary to tackle the diseases within NIDDK's mission. It is also important that the workforce—in clinical research as in other biomedical research fields—includes representation from all populations, including women, people from diverse racial and ethnic populations, sexual and gender minority groups (which include, but are not limited to, individuals who identify as lesbian, gay, bisexual, asexual, transgender, Two-Spirit, queer, and/or intersex), and others currently underrepresented.

Increasing and retaining the number of women and people of racial, ethnic, and sexual and gender minority groups who are conducting clinical research: Diverse teams outperform homogeneous teams, as scientists and trainees from varied backgrounds and life experiences bring different perspectives, innovative ideas, and individual enterprise to address complex scientific problems. A diverse workforce is also important if significant progress is to be made to reduce health inequities. Thus, as with other areas of research, it is important to bolster the number of scientists from populations that are underrepresented, including women and people of racial, ethnic, and sexual and gender minority groups, and to retain these individuals in the workforce. It is also important to address structural supports to promote and sustain this workforce at research institutions.

Addressing the workforce pipeline at earlier career stages: As with other fields of science, the path to becoming a clinical researcher often begins with opportunities and choices early in one's education. Thus, it is important to reach out early, such as through programs for high school and undergraduate students.

Involving trainees in the design and implementation of clinical trials: Getting trainees more involved in designing and carrying out clinical trials would provide hands-on experience to help propel their careers in clinical research. In particular, the biomedical research enterprise would greatly benefit if trainees from different backgrounds were more involved in clinical trials, as this would bring more perspectives and ideas to the research, bolster the trainees' competitiveness in their careers, and help achieve a more diverse and equitable workforce.

Fostering interactions between clinical researchers and basic, behavioral, population, and public health researchers: It is important to encourage efforts that help graduate students and trainees in basic, behavioral, population, public health, or discovery science engage with the medical community, and medical students and trainees engage with the research community. These interactions would broaden the research experience of those in the biomedical research workforce pipeline and help to build bridges across disciplines.

Training diverse staff with critical roles in clinical research: As part of efforts to enhance the research workforce, it will be important to recruit and train people who would have a variety of roles in clinical research, including not only those who would lead a research effort, but also clinical study coordinators and others to advance clinical trials. Additionally, it will be valuable for researchers to engage with and train community partners. These partners could help enroll study participants, help deliver interventions being studied in communities, and assist with general outreach.

(Additional information related to the research workforce is in the Stewardship section.)

Research Opportunity 2.4: Utilize data science to improve clinical studies

Leveraging existing data for clinical research: Researchers could use existing data such as electronic health records (EHRs), healthcare claims data (e.g., data on appointments and billing), and data from existing population cohorts in clinical studies on disease detection and diagnosis, which could, in some cases, be more efficient and cost-effective than recruiting and observing research participants over time to gather similar data. EHRs offer the promise of supporting both discovery science and improved healthcare processes and outcomes, such as through comparative effectiveness studies that, for example, compare the benefits of different treatments that are already being used in practice. EHRs may also provide information on treatment patterns, which would be useful when evaluating adherence to guidelines. There is a tremendous amount of data in EHRs, and it is increasing with the inclusion of data from wearable devices, clinical laboratory tests, and patient comments. A further advantage to using EHRs is that they may portray long-term or even lifelong observations of individuals, and they have been widely adopted in clinical settings. Claims data, like EHRs, contain a vast amount of information on large numbers of people, so researchers can use these data for epidemiological studies and also analyze groups of patients with rare diseases. Research should also address bias in EHR and other health data to improve the validity of study findings for different populations.

Incorporating "big data" technologies into analyses of new or existing data: With the tremendous growth in data collection, coupled with advances in computing power and data accessibility, researchers can apply artificial intelligence (AI) technologies, such as machine learning, in many scientific disciplines to enhance analysis of complex medical images and data. Key ethical concerns include protecting individual privacy and ensuring that the results of research with big data benefit all populations equitably. There is also a need to mitigate potential bias that could result, for example, from using unrepresentative data to train AI technologies—as risk and other assessments generated on the basis of incorrect analyses and interpretations could potentially stigmatize communities and perpetuate or exacerbate health inequities. AI technologies are rapidly becoming important data science-based analytic tools across biomedical discovery, clinical research, medical diagnostics and devices, and precision health. Such tools and systems can uncover new possibilities for researchers, physicians, and patients, to enhance efficiency and enable more informed care decisions for treating or preventing disease.

Providing health research training to data scientists: A strong pool of investigators trained in data analysis and big data technologies would be critical if these skills are to be applied to clinical studies. Therefore, it is important to provide health science training to individuals with strong backgrounds in data science. Likewise, it is important to provide data science training to health science researchers. These training opportunities would pave the way for interdisciplinary research, and applying data analysis tools and technologies could help to reach across different research areas.

Developing and incorporating common data elements into clinical studies: Data elements, or information that describes a piece of data to be collected in a study (such as age or blood glucose level), are important components of clinical studies. Researchers can use common data elements (CDEs), or data elements that can be used in multiple clinical studies, for systematically collecting and analyzing information, and for ensuring that the collected data are high quality and are comparable across multiple studies. This would allow researchers to streamline data collection, investigate relationships between data from different studies, and increase the potential for reuse of their shared data to build upon research findings. NIH maintains a searchable repository that researchers can use to find, create, and share CDEs for clinical studies.

Filling the gap: funding studies not supported by the private sector or other entities

NIDDK is in a unique position to sponsor impactful clinical studies that are not likely to be supported by the pharmaceutical industry or other funders. There are opportunities to support research such as behavioral studies for treatment and prevention of obesity, kidney disease, or urological disorders; comparative effectiveness studies to determine the best available treatments for diabetes; and clinical trials that test the efficacy of existing generic drugs and devices as therapies for pancreatitis, liver disease, and other diseases and conditions under NIDDK's mission. Other areas of research include studies that might not have a sufficiently large market size to attract attention of pharmaceutical companies, like studies that test precision medicine/precision health-based approaches for subpopulations of people with kidney disease or inflammatory bowel disease. These types of studies have the potential to identify new therapies or improve current treatment approaches to make them more effective and economical.

Research Opportunity 2.5: Optimize clinical infrastructure and resources for clinical studies

Promoting prospective cohort studies: A prospective cohort study follows over time groups of individuals who are alike in many ways but differ by a certain characteristic (for example, sleep duration) and compares them for a particular outcome (such as diabetes). Although they could be lengthy, prospective cohort studies are valuable because they allow observation of a large population over time and data collection at regular intervals, which investigators can use to answer many questions about the associations between risk factors and disease outcomes. These types of observational studies could be particularly valuable when studying the diseases in NIDDK's mission, many of which develop slowly over a long period of time. Indeed, these kinds of studies have provided important and meaningful insights into the origins of disease, which, in turn, could lead to new ways to prevent and treat disease. Moreover, using different care settings in cohort studies, such as non-academic centers and private practices, would allow for the generation of meaningful and useful real-world data.

Transitioning from initial observational studies to clinical trials for disease prevention and treatment: As noted above, observational studies provide valuable insight into the potential contributors to disease. Researchers should continue using the foundational knowledge gained from observational studies to design and test therapies—including behavioral, medical, surgical, and alternative therapies to prevent and treat disease—through clinical trials. Furthermore, observational studies are useful platforms to collect scientific data from participants in real-world settings (as opposed to the tightly controlled environments of typical clinical trials), which can then be used to design pragmatic clinical trials.

Leveraging the research value of repositories: Repositories are an important component of scientific collaboration because they make data and biological samples from clinical studies available to other researchers. By establishing and using repositories, and by making it easier to find and access repository collections, researchers can ensure that datasets and biological samples are maintained and accessible even after a study ends. Repositories or databases can also link genomic, metabolomic, and other "omics" data to phenotypic data (i.e., data on presence or absence of a disease, hormone levels, other physical traits, and behaviors). Researchers can repurpose these collections, thus facilitating the testing of hypotheses without the need for new data generation or sample collection. It is important to ensure that repositories include data and samples from diverse populations.

It would also be important to establish repositories for study fields that do not yet have any. (Additional discussion of data and repository management is in the Stewardship section.)

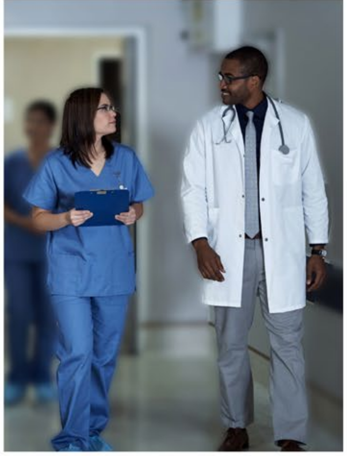
Facilitating the start-up process for clinical studies: Clinical studies require potentially expensive and time-consuming efforts such as gaining regulatory approval to conduct the study, developing a participant recruitment plan, setting up quality control systems and data analysis tools, and bringing in people necessary to carry out these tasks. This clinical research infrastructure is usually developed on a study-by-study basis, resulting in the establishment of substantial resources that are subsequently disbanded after the study is completed. It would be beneficial to researchers if this set-up process were streamlined. For example, researchers could develop approaches for re-using existing infrastructures, with minimal changes as necessary, for additional clinical studies. Furthermore, researchers could establish an overarching infrastructure that incorporates features of both research networks and investigator-initiated studies, to facilitate resource sharing and rapid participant recruitment and follow-up.

Dealing with unanticipated challenges in real time: The COVID-19 pandemic has challenged all aspects of the biomedical enterprise—from studies with populations who experience health disparities and other disadvantages, to the viability of investigators' careers, to overall research progress. NIDDK has engaged in a rapid, multifaceted response, including supporting COVID-19-related research and taking actions to reinvigorate research across the Institute's mission. This response can serve as an example for future unanticipated challenges. Furthermore, researchers can leverage lessons learned to enhance research both during emergencies and more normal times, such as using remote labs, telemedicine for follow-up visits, and at-home data collection, to potentially reduce costs and lessen study burdens on participants, including those from communities that are underserved.

Prioritizing use of NIDDK resources in clinical research to complement, not duplicate, what is being done by other funders: To promote efficiency and responsible stewardship, it is important that research priorities avoid redundancies and overlaps with other entities, such as industry, foundations, and other federal agencies, that are funding high-quality clinical research. Collaborations with external partners and other NIH Institutes should be nurtured to promote innovation. Other NIH-funded studies or participant cohorts should be leveraged where possible, such as through efforts to add measures or endpoints applicable to NIDDK, leveraging NIH Common Fund investments, and integrating EHR systems with clinical trials to facilitate long-term assessments after the trials are completed. Furthermore, clinical investigators have the opportunity to complement industry research by undertaking the types of studies that the private sector does not typically prioritize, such as comparative effectiveness trials, preventative medicine, the testing of non-pharmacologic therapies, or exploration of further uses for generic medications. NIDDK-supported researchers can also continue to partner with industry to streamline the development of therapies.

We envision a future

in which clinical studies strengthen and accelerate the development of successful prevention strategies and treatments to improve health of all people in our Nation who have, or are at risk for, diabetes and other endocrine and metabolic diseases; liver, intestinal, and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases.




Scientific Goal 3

Advance research to disseminate and implement evidence-based prevention strategies and treatments in clinics and community settings, to improve the health of all people, more rapidly and more effectively

As researchers find successful approaches to prevent or treat diseases within NIDDK's mission, we can amplify the health benefits by developing strategies for disseminating the findings broadly and implementing evidence-based interventions in a range of real-world settings, to expand their reach. It is also imperative that we study how best to disseminate and implement evidence-based interventions for diverse populations, so that our research benefits all, equitably.

Challenges: There are substantial challenges, however, to dissemination and implementation, whether an intervention is clinic-, home-, or community-based. Because diseases in NIDDK's mission are chronic, managing them requires continuous attention to medications, devices, and what may be a "new normal" of other changes to daily life. Treatment regimens can be difficult, time-consuming, and costly; and many people have the added burden of multiple chronic conditions. Some lifestyle approaches to prevention or treatment may be difficult to maintain outside the context of a clinical study. Some medications that worked in clinical trials are not used by as many people as would benefit, for reasons that may not be well understood and might vary for different individuals; and some have not been tested in diverse populations. Surgical interventions, including organ transplants and other procedures, may require long-term follow-up monitoring and treatment. Healthcare and community organizations may view even a highly effective intervention as too costly to implement, or as simply not compatible with their standard processes. Dissemination and implementation strategies need to be acceptable, accessible, and tailored to people who face different life circumstances. For example, many people experience adverse effects of social determinants of health (e.g., socioeconomic disadvantage, underlying structural factors such as policies and systems that reinforce inequities), and it will be crucial for research efforts to address these inequities. An additional challenge in this area is to ensure a talented, diverse, and trained research workforce, along with skilled and trusted people who could deliver an intervention effectively, long after the research study ends.

Building on advances and discoveries: NIDDK's previous accomplishments in this area demonstrate the importance and impact of dissemination and implementation research and can also inform future studies. For example, research has highlighted the value of approaches in different community settings for screening for and preventing type 2 diabetes in different populations. One such study adapted a lifestyle intervention to prevent type 2 diabetes based on the landmark Diabetes Prevention Program clinical trial; the findings led to a nation-wide program. Research on children who had liver transplants highlighted the need for additional implementation efforts to improve adherence to required medications. A collaborative study with the Agency for Healthcare Research and Quality reported a successful effort to prevent catheter-associated urinary tract infection in people residing in nursing homes. Other research demonstrated the benefits of artificial pancreas technology for people with type 1 diabetes as they lived their normal day-to-day lives. NIDDK also pursues administrative approaches to facilitate science, such as an accelerated grant review and award process, developed with others at NIH, that has enabled time-sensitive evaluation of a variety of obesity-related policies and programs. NIDDK-supported research is highlighted on our website in news releases and research updates and in NIDDK's annual reports. In charting future directions, NIDDK will build on the advances and discoveries that emerge from the opportunities in the Strategic Plan, to drive further progress and innovation.

Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All

Dissemination and implementation research will require multidisciplinary approaches and collaboration among scientists with expertise in these areas, as well as expertise in intervention delivery, health equity research, and the diseases in NIDDK's mission. Engaging a broad range of stakeholders will be critical—including those who could implement and disseminate evidence-based interventions in different settings, and those who would benefit from these interventions. Successful research efforts for one disease may yield insights that would be applicable to other diseases with related biological, social, and other environmental causes and contributors.

Research Opportunities

With the opportunities highlighted in the dissemination and implementation research section of the Strategic Plan, NIDDK aims to accelerate and expand the impact of evidence-based interventions for diseases across our mission, to improve health for all.

Research Opportunity 3.1: Improve dissemination and implementation research, to accelerate the reach of prevention and treatment strategies proven successful in clinical trials

A variety of factors can inform research on strategies to adapt, scale up, and spread an intervention shown to work in clinical trials. These include the nature of the intervention, characteristics of the study participants and broader populations who could benefit, and potential barriers and facilitators.

Improving implementation research for different types of interventions: Some interventions for NIDDK diseases are developed for and evaluated in a particular population and setting, while others are designed as "one-size-fits-all." Thus, research should focus both on broader, scalable, real-world implementation of tailored interventions, and on exploring strategies to adapt one-size-fits-all interventions for different settings and populations of adults and children. To boost the chances of effective implementation, researchers can test innovative strategies, such as multi-level approaches that link medical settings with other organizations (e.g., social services, housing) to treat the whole person; leverage telehealth and novel technologies (e.g., for implementing behavior change and other types of interventions); study stepped-care approaches (increasing treatment intensity if needed); glean insights from and partner with community groups; and pursue approaches that leverage peer support in community settings, among other strategies.

Improving dissemination research strategies: For more effective dissemination of accurate information about NIDDK diseases and evidence-based interventions, researchers can tailor and personalize messages to be meaningful to people and consistent with their values. Researchers can also harness a range of cutting-edge technologies and social and other media, to reach diverse populations. Strategies could include partnering with stakeholders in communities and healthcare, and engaging experts in fields beyond the health and medical disciplines for new ideas to inform messaging and dissemination approaches.

Understanding the populations we want to reach and the challenges they face: To advance health equity, researchers should identify and characterize populations who are not being reached with current intervention delivery strategies, including people who have not been sufficiently included in research. Such populations include racial and ethnic minority groups who are disproportionately affected by diseases in NIDDK's mission; women—whose disease risks, symptoms, and treatment outcomes can differ from men's; people who live in rural areas; those with limited internet access; sexual and gender minority groups; people of different ages, including older adults, youth who are underserved, and other children of diverse backgrounds who may face life-long disease and unique challenges in treatment both during childhood and in the transition to adulthood; people who have multiple chronic conditions within NIDDK's mission; and other populations. Researchers can then use this knowledge to improve dissemination and implementation strategies, for example, by addressing the perspectives and life experiences of different populations.

Evaluating dissemination and implementation strategies with representative study participants: To ensure relevance of research results, it is critical for researchers to engage diverse and relevant stakeholders and recruit study participants who are representative of the populations the intervention is designed to benefit. By generating evidence as to what works and doesn't for different people, this research can also increase trust in the applicability of scientific findings. Such efforts are important across the research continuum, not only in dissemination and implementation, but also at earlier stages of research, when developing and testing interventions in clinical trials.

Advancing understanding of social and structural determinants of health, both as causes of disease and as targets for intervention: To optimize research toward achieving health equity, it is crucial to develop and evaluate strategies to mitigate the adverse effects of social determinants of health. These determinants include, for example, aspects of communities where people live and work that contribute to health or disease, such as socioeconomic status, healthcare access and quality (as relevant to disease prevention, diagnosis, and treatment), and the "built environment" (e.g., types of food establishments and availability of healthy and affordable foods in a community, places to exercise); structural racism; and other factors. As an example of one research avenue, researchers can design strategies to lessen the impact of societal inequities by helping people compensate or adapt. In another approach, researchers can develop novel strategies that target social determinants of health directly, to inform how to reduce or eliminate these causes of disparities.

Addressing other barriers and challenges to widespread dissemination and implementation: In addition to mitigating social determinants of health, approaches are needed to address related challenges and other potential barriers. For example, researchers should identify and include appropriate and trusted people who could deliver the intervention to be implemented—both during the study and beyond. To inform study design, researchers should also identify individual preferences among those who would receive the intervention. Also needed is research to address the challenges of implementing a new intervention into existing healthcare systems, standard medical care practices, and reimbursement models. Widespread dissemination and implementation could also be promoted through connecting research efforts and findings with major public health initiatives, in partnership with other federal agencies or other stakeholders. Future study design would benefit from taking into account costs (to patients, healthcare systems, and others); time needed and scheduling flexibility; challenges experienced by those who are managing multiple chronic conditions; health literacy; the availability of health information and resources in different languages; medical mistrust; biases among healthcare providers; and stigma faced by populations that have been marginalized and by people with diseases in NIDDK's mission. Implementation strategies for behavioral interventions need to address neighborhood and community characteristics that may facilitate or impede healthy behavior change. To advance dissemination efforts, researchers can develop ways to counteract inaccurate health information that is circulating and ensure that evidence-based information captures people's attention.

Sustainability of dissemination and implementation: It is critical to incorporate sustainability as a feature of research design to enable the continuation of intervention delivery in healthcare or community settings over time, after the research project period has concluded. For example, strategies can use existing healthcare delivery systems and programs, public health mechanisms, or community partnerships (e.g., through community-based participatory research)—infrastructure and people already in place to sustain the efforts. Engaging stakeholders in the research will help identify what would be needed for sustainable implementation. Finally, for iterative learning and continuous improvement, dissemination and implementation efforts should build in mechanisms for stakeholders to obtain feedback on the effectiveness of their efforts.

Overcoming barriers: research toward health equity

Chronic diseases across NIDDK's mission disproportionately affect racial/ethnic minority populations and others who are underserved. Contributors to these disparities include structural racism, socioeconomic disadvantages, inequitable healthcare access and quality, and related factors. To advance health equity, it is crucial to develop dissemination and implementation strategies that mitigate these social determinants of health. For example, the availability of nutritious, affordable food in a community would affect the implementation of dietary interventions for obesity, type 2 diabetes, or fatty liver disease. Racial disparities in kidney disease treatment and transplants need to be addressed. Individuals from racial/ethnic minority groups are less likely to use technologies for managing type 1 diabetes; new research on potential barriers (e.g., healthcare access) could reduce this disparity. Researchers can explore partnerships between healthcare and community organizations to address both medical and health-related social needs (food, housing, transportation) for those with chronic disease. Researchers can also evaluate obesity and other health-related policies and programs designed by communities, and identify opportunities for broader implementation of those with beneficial effects.

Research Opportunity 3.2: Evaluate large health programs and policies initiated by communities and others ("natural experiments") – research toward broader implementation

Because the diseases in NIDDK's mission place substantial burden on public health, many organizations, communities, and policymakers have pursued efforts toward disease prevention or management. For example, some policies and programs relate to expanding the availability of healthy foods (such as fruits and vegetables) or making neighborhoods more conducive to physical activity. These "natural experiments" provide valuable opportunities for researchers to learn what works in real-world settings. Studies can evaluate the effects on health, determine why a program or policy may work in some communities but not others, identify unintended consequences, and explore whether there are disparities in who is benefitting (e.g., based on socioeconomic status). By including implementation science and stakeholder engagement in these studies, researchers can also bring to light the challenges and opportunities for disseminating and implementing promising efforts in other settings and for different populations.

When a program or policy is put in place with limited advance notice, it is important for researchers to initiate studies expeditiously. For example, there may be a time-sensitive opportunity to collect baseline data before the program or policy starts, for comparison when analyzing subsequent health outcomes and stakeholder perspectives. To facilitate such studies, NIDDK developed a flexible and rapid grant application review process for obesity-related research, and this review process could be expanded to more diseases across our mission.

Research Opportunity 3.3: Study major unanticipated events – toward future implementation of preparedness and response efforts

Along with studies of planned efforts, researchers can gain critical insights from the study of unanticipated events—pandemics, natural disasters, and other crises. Such research could aid not only the recovery from the emergency at hand, but also the implementation of preparedness efforts and responses to future events. Researchers should examine the impacts on health as related to diseases within NIDDK's mission, including in populations who are underserved and experience disproportionate impact. These health impacts may arise from the crisis itself (such as a circulating virus or social injustice) or from new barriers to standard care for NIDDK diseases. Implementing interventions for chronic disease is difficult in normal times, but in extraordinary times, the hurdles are even higher; thus, research could address these new challenges. Researchers can also evaluate the effects of community and healthcare responses to crises. As an innovative way to enhance such efforts, researchers could participate in initial response teams to study the event itself, help with developing response strategies (such as modifications that may be needed to existing interventions due to crisis conditions, incorporation of telehealth and other technologies, etc.), and evaluate the effects of the response. Flexible and nimble grant mechanisms, noted above, can facilitate this avenue of research as well.

Research Opportunity 3.4: Engage and partner with stakeholders in dissemination and implementation research

As with other areas of research, dissemination and implementation research will benefit from enhancing engagement with multiple stakeholders:

A range of stakeholders: Stakeholders include those involved in disseminating and implementing interventions, and those who would benefit. By engaging with stakeholders who would disseminate and implement evidence-based prevention strategies and treatments, researchers can learn what their priorities are and what is feasible for them (e.g., costs), and they can incorporate this information into research design and methods, and form partnerships. Depending on the intervention, these stakeholders may include healthcare systems, providers/clinicians, payors, state health departments, school districts, others involved in policy and payment decisions, digital health technology vendors, community leaders and organizations, federal partners, foundations, patient and professional organizations, and others. Similarly, by engaging with stakeholders whom an intervention is intended to benefit, researchers can assess the perspectives, values, preferences, priorities, and lived experiences of people with diseases in NIDDK's mission, along with their views of treatment acceptability and feasibility—knowledge that would inform dissemination and implementation strategies. These stakeholders include not only people with or at risk for diseases, but also families and other caregivers, patient advocacy groups, nonprofits, and others. For effective and impactful stakeholder engagement, it will be important to develop engagement approaches tailored to diverse groups and individuals, and actively involve them to help shape the research approaches and decisions that impact them.

Stakeholder-researcher collaboration: Stakeholders should be viewed both as potential partners in investigator-initiated research ideas and also as initiators of dissemination and implementation efforts that investigators could join, bringing relevant expertise. To advance research collaboration, a repository could be developed to share information about evidence-based interventions that have potential for great benefit through efforts to expand their reach, and such a repository could also share information about dissemination and implementation efforts being developed by NIDDK stakeholders. Collaboration between researchers and stakeholders on dissemination and implementation research strategies could also increase the likelihood of uptake, i.e., that people would be willing to use the interventions.

Educating stakeholders and researchers: To advance future studies, researchers can pursue educational efforts to enhance the participation of stakeholders in research and to help them understand how scientific research benefits health. Such efforts can also help stakeholders understand and use research findings, including new knowledge that may overturn previous views about disease causes or treatments. Educational efforts can be bidirectional; for example, those who have a disease can educate researchers about what is important to them and can help scientists better communicate the value of their research in grant applications and other venues. Patient advocacy and community-based organizations can offer perspectives on meaningful communication with people who have diseases in NIDDK's mission, including populations who are disproportionately affected. Organizations of healthcare professionals can provide information on challenges encountered by practitioners in caring for their patients. Researchers can also gain ideas from experts in different fields (e.g., science education) to inform these efforts.

(Further discussion of stakeholder engagement is in Scientific Goal 4, which is focused on this topic.)

A holistic approach to health: tackling chronic disease through multidisciplinary care

Chronic diseases are prevalent across the country, particularly in under-resourced areas, and many people face the burden of multiple chronic conditions, such as diabetes, obesity, and kidney disease, as well as urologic and digestive diseases. It is critical to improve strategies for disseminating and implementing interventions so that people are empowered with information they trust and understand and with integrated treatment options that are feasible and sustainable within their life circumstances. For example, enhancing the interoperability and sharing of electronic health data across multiple settings could help providers coordinate and improve treatment for people with kidney and other diseases. Multidisciplinary approaches to care could improve health of young people with liver or other organ transplants as they navigate the challenges of taking medications over the long-term to ensure transplant success. Innovative research to improve diabetes self-management could combine individual behavior change, family engagement, and strategies to address barriers within the healthcare system and other social determinants of health.

Research Opportunity 3.5: Enhance the dissemination and implementation research workforce and multidisciplinary studies

Dissemination and implementation research moving forward will require an innovative, trained, and diverse workforce; multidisciplinary collaboration; and enhancements to study design.

Invigorating the research workforce—research training and diversity: To promote a pipeline of scientists in dissemination and implementation research, training should include knowledge and methods for this field. In parallel, it will be valuable to train the next generation of scientists working in other stages of the research continuum—including basic and clinical research—to consider potential future dissemination and implementation of their research. Such training could inform the development of interventions that would be more amenable to future widespread adoption.

As with all areas of biomedical research, increasing workforce diversity will be key to successful dissemination and implementation. To promote innovation, it will be important to recruit and retain people from minority groups underrepresented in the research workforce, women, those with a range of life experiences and understanding of social determinants of health, and people with different skills and expertise. These efforts will help bring talented, innovative people into research careers, and their perspectives will enhance dissemination and implementation efforts in diverse communities. (Additional information related to the research workforce is in the Stewardship section.)

Multidisciplinary, collaborative research: In addition to collaborating with scientists from different disciplines and partnering with a variety of stakeholders, as noted above, researchers can also develop novel dissemination and implementation approaches by learning from different sectors. For example, insights from industries skilled at promoting behaviors (e.g., advertising, video gaming) could inform implementation of lifestyle interventions and guide behavior change among providers, to improve care.

We envision a future

in which evidence-based prevention and treatment strategies are scaled up and adapted to improve the health of all people throughout our Nation who have, or are at risk for, diabetes and other endocrine and metabolic diseases; liver, intestinal, and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases.

Scientific Goal 4

Advance stakeholder engagement—including patients and other participants as true partners in research

Sustained, meaningful input from people who have diseases within NIDDK's mission and other stakeholders can have enormous value and benefit to biomedical research. Stakeholders should therefore be viewed as partners with researchers, including clinical and basic researchers (who may, for example, be studying tissue donated by a research participant). Through engagement along the research continuum, stakeholders can provide a critical voice to help identify issues of greatest importance to them and give context to scientists to understand the life experiences of those whom the research aims to benefit. Stakeholder engagement can also help ensure that clinical study cohorts reflect the demographics of people with the particular disease being studied, leading to research that effectively generates consequential results that can improve peoples' lives.

This section of the Strategic Plan focuses primarily on patients and other research participants, caregivers, and patient advocacy and community-based organizations. It is also important to engage other stakeholders as well, such as healthcare organizations who may deliver interventions tested in research, others involved in policy and payment decisions, industry, nonprofits, and other federal agencies. A range of stakeholders are addressed in the other Scientific Goals, along with discussion of the importance of stakeholder engagement in basic (foundational), clinical, and dissemination and implementation research.

Challenges: There are numerous challenges to engaging a diverse range of stakeholders. For example, outreach to racial and ethnic minority populations, who are at higher risk for many diseases, is essential, but hesitancy to participate and the need to build trust must be acknowledged and addressed. Scientists need to be educated about the value that patients bring to research to avoid missed opportunities for making findings more relevant to those with diseases within NIDDK's mission. Importantly, practical issues, such as time and potential costs associated with research participation, and challenges to reaching out to remote communities, need to be addressed for effective engagement efforts. In addition, it is important to recognize that effective stakeholder engagement will require strategies tailored to different communities, rather than a "one size fits all" approach.

Building on advances and discoveries: While stakeholder voices are becoming more widely recognized as critical for patient-centered research, few major studies to date have included stakeholder engagement. Notably, however, three NIDDK-supported studies—the Kidney Precision Medicine Project (KPMP), the APOL1 Long-term Kidney Transplantation Outcomes Research Network (APOLLO), and the Hemodialysis Opioid Prescription Effort (HOPE) consortium—have included patient voices at many stages of research design. For example, patients have served on leadership committees, provided valuable contributions to consent document development, and helped identify and address critical challenges such as insurance coverage for potential complications. Therefore, KPMP, APOLLO, and HOPE can serve as useful models of successful stakeholder engagement to build a foundation of best practices to benefit research across the broad range of diseases within NIDDK's mission.

Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All

Stakeholder engagement is critical for advancing research that ultimately will lead to improved prevention, treatment, and health equity for people with, or at risk for, diseases in NIDDK's mission. By building trust and sustained relationships between the research and diverse stakeholder communities, NIDDK-supported research will better reflect, and subsequent findings will more likely improve, the health of populations most affected by these diseases.

Research Opportunities

With the opportunities highlighted in the stakeholder engagement section of the Strategic Plan, NIDDK aims to comprehensively engage stakeholders across the research continuum as true partners in research.

Research Opportunity 4.1: Comprehensively involve diverse stakeholders in each step of the research process, including patients, caregivers and family members, patient advocacy groups, and community-based organizations

To maximize the benefit of research for those affected by diseases within NIDDK's mission, stakeholder engagement must be promoted along the broad continuum of the research process. Potential opportunities for stakeholder engagement include, for example: providing input into priorities and goals for research, the design of research studies (such as studies that involve volunteers or analysis of human tissue samples or data), participant recruitment, and development of consent forms that are understandable and relevant to potential research volunteers; participating in conferences and workshops; participating in grant application review (where appropriate); helping to draft manuscripts and other reports describing study results; and providing input into dissemination of research findings. Such stakeholders would include patients and their families/caregivers and could also include organizations such as patient advocacy groups, community organizations, nonprofits, and others, where appropriate and applicable. Fostering training opportunities for researchers and stakeholders will enhance interactions and communication, leading to improved relationships between the two communities to help guide research efforts toward consequential results that can improve peoples' lives.

Stakeholders as leaders in clinical studies: Clinical research studies are often guided by committees that provide leadership, expertise, and oversight to ensure integrity of research design and safety for human participants. Stakeholders, such as patients and community members, would provide great value in leadership roles on steering committees; oversight committees, such as Data and Safety Monitoring Boards and Observational Study Monitoring Boards; External Expert Panels; and other committees. Furthermore, individual stakeholders would bring their own unique sets of skills, experiences, and expertise, which could ultimately improve the research process.

Stakeholder engagement in research proposals: In grant proposals, including an explanation of how results from a proposed study will be meaningful and beneficial to patients, caregivers, and communities (similar to the Public Health Relevance Statements currently in grant applications) may help researchers consider multiple stakeholder perspectives as they develop research proposals. Funding Opportunity Announcements could similarly request that research proposals include detailed plans for stakeholder engagement that would be relevant and meaningful.

Partnering with stakeholder organizations: Patient advocacy organizations help elevate the voices of those living with different diseases, highlighting the needs and challenges that are the highest priorities of the people they represent. Partnering with these and other stakeholder organizations will improve research on diseases within NIDDK's mission in myriad ways, such as helping to strengthen relationships with patient communities. For example, stakeholder organizations could assist researchers with participant recruitment and could aid in dissemination of research results broadly to those with the diseases being studied. Fostering strategic partnerships with organizations with an interest in health outcomes of racial and ethnic minority populations may be valuable in outreach efforts.

Research Opportunity 4.2: Ensure stakeholders who engage in research are representative of the populations affected by diseases in NIDDK's mission

Stakeholder engagement efforts must reflect the populations that are most affected by the diseases being studied. Therefore, we must recognize the inherent inequities experienced by populations that have been marginalized and identify ways to make involvement in research feasible for and appealing to these stakeholders. Potential research participants, including people who might not be readily reached in healthcare settings, should be engaged in the variety of different settings in which they live. Engagement cannot be limited to inclusion of study participants; clinical research panels and committees, as described earlier, should also include community stakeholders who represent the populations most affected by the particular disease.

Promoting diversity in clinical research: Research findings are most durable and implementable when research participation closely reflects the populations most affected by the diseases being studied. It is therefore essential to promote diversity in all relevant demographic categories. These include women; people of different ages, from children to older adults; racial and ethnic minority populations and other minority groups; people who live in rural areas and other geographically diverse communities; people with lower incomes and other socioeconomic disadvantages; and other groups historically underrepresented in research. For example, reaching out to sexual and gender minority communities can help identify research opportunities within NIDDK's mission.

Building trust between scientists and communities affected by diseases in NIDDK's mission: It is essential to build trust between scientists and the patient communities whose lives they endeavor to improve, particularly populations who have been underrepresented and underserved. For stakeholder engagement to be most effective, it will be important to develop strategies for reciprocal relationship-building, co-learning between communities, transparent and honest dialogue, and cultural humility. Conducting stakeholder needs assessments, such as through partnerships with local sites, media, and community leaders, could be of great benefit to study design and to relationship-building efforts. Furthermore, the relationships between researchers and patient communities can be strengthened by promoting sustained engagement, even after a particular study has completed, through consultation with study participants to determine their preferences of ways to keep in contact. Continued engagement would also facilitate broader implementation of research findings. Additionally, promoting diversity in the biomedical research workforce, including those leading clinical studies, research coordinators, research assistants, and other participant-facing positions, could help build trust and enhance recruiting efforts in underrepresented communities.

Educating scientists on the history of unethical research: The history and cultural legacy of unethical research on racial and ethnic minority communities must be acknowledged and addressed in order to make necessary strides in diverse stakeholder engagement. For example, educational opportunities should be made available to inform the research community about the history of unethical clinical research in African American and other communities, how those practices have changed, the current ethical standards in clinical research, and identification of areas for continued improvement in clinical research and practice.

Research Opportunity 4.3: Develop new ways to address barriers to stakeholder engagement

For a variety of reasons, participating in clinical research can be challenging for some people. It is therefore critical to identify and reduce existing barriers to stakeholder engagement, particularly for underrepresented communities. For example, improved awareness of available research studies may broaden opportunities for participation. Flexibility in engagement would enable studies to accommodate the needs of research participants. It may also be helpful to identify new ways to improve the consent process and to review clinical study policies to identify any that may present unnecessary obstacles to participation. Addressing medical literacy may help tailor stakeholder engagement efforts and training. Additionally, for some diseases and conditions, potential research participants and the public may benefit from education about symptoms for which embarrassment is an issue (e.g., urinary incontinence). Strategies, tools, and resources could be developed to help investigators engage with stakeholders, such as instruments (e.g., surveys) to receive real-time feedback from study participants about their experiences. Additionally, opportunities to help investigators learn from other stakeholder engagement efforts could be pursued.

Logistical and practical challenges are often obstacles to research participation, so reducing existing burdens may help broaden stakeholder engagement. We must strive to identify practical ways that researchers can make involvement in the research process feasible for and appealing to stakeholders, such as minimization of up-front costs and addressing other financial issues, time, childcare logistics, addressing the needs of people with disabilities, and transportation needs. Additionally, the use of technologies may promote greater engagement with remote communities (e.g., web-based meetings, telemedicine); technological improvements and adaptations made during the COVID-19 pandemic may help with this challenge for other research areas as well.

(Additional discussion of stakeholder engagement is in the other Scientific Goals of the Strategic Plan.)

We envision a future

in which stakeholders are true partners with researchers in the scientific research enterprise through meaningful, sustainable engagement, together striving to achieve health equity for people who have, or are at risk for, diabetes and other endocrine and metabolic diseases; liver, intestinal, and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases.

Measuring progress toward achieving the Scientific Goals

- *Scientific Goal 1: Advance understanding of biological pathways and environmental contributors to health and disease.*
- *Scientific Goal 2: Advance pivotal clinical studies and trials for prevention, treatment, and cures in diverse populations.*
- *Scientific Goal 3: Advance research to disseminate and implement evidence-based prevention strategies and treatments in clinics and community settings, to improve the health of all people, more rapidly and more effectively.*
- *Scientific Goal 4: Advance stakeholder engagement—including patients and other participants as true partners in research.*

For each of the Scientific Goals of the Strategic Plan—described in the preceding pages and listed above—NIDDK will assess and monitor progress toward achieving the Goals to respond to new challenges, identify areas for strengthening efforts, build on discoveries, and pursue emerging research opportunities.

For example, we will continue to analyze our research portfolio for existing gaps and potential opportunities. We will also identify advances in knowledge, prevention, and treatments resulting from research across our mission; evaluate the progress of large research efforts; monitor research training efforts; and assess stakeholder engagement. We will also explore methods to track research progress from initial discoveries to clinical studies of potential prevention or treatment strategies to implementation of findings in clinical practice or community settings, as such analyses could identify challenges and opportunities for further research. Additionally, we will continue to develop and enhance our analysis and assessment metrics and methods to address an evolving research landscape. As we pursue research efforts, we will also consider the unique challenges and opportunities associated with different diseases and related scientific areas. To inform research directions, NIDDK will continue to seek external input from our research and patient advocacy communities. Finally, NIDDK will share the findings from these analyses and progress toward our goals with our stakeholders, through the Institute's annual report and other venues.

STEWARDSHIP

Serving as an Efficient and Effective Steward of Public Resources

The NIDDK recognizes that careful stewardship of public resources is critical to all its efforts. Through thoughtful planning and analysis with input from a variety of stakeholders, NIDDK will deploy its resources in the most effective and efficient ways to support research along the spectrum of discovery to dissemination, communicate advances and health information to the public, promote a diverse and talented biomedical research workforce, and prepare to tackle new challenges as they emerge.

This section describes opportunities for a wide range of topics including workforce diversity, training, and career development; rigor and reproducibility in research; partnerships; innovation; management and accountability; and other critical areas.

Planning and Priority Setting

Planning and priority setting approaches: NIDDK takes multiple approaches to research planning and priority setting to maximize the public investment in research and remain dynamic as science advances and new challenges and opportunities emerge. These strategic planning approaches include developing formal plans and reports, as well as internal planning processes led by staff across NIDDK's scientific research programs. Planning and priority setting are also informed by burden of disease data; identification of research gaps, which may reflect understudied areas; scientific trends and new opportunities; research challenges; findings from evaluations of existing programs; and, importantly, input from the broader research community, people with diseases in the Institute's mission, and others.

Stakeholder input: NIDDK seeks stakeholder input through multiple venues, including advisory and coordinating committees, scientific meetings and workshops, meetings with professional societies and patient advocacy organizations, and public requests for information. NIDDK also reaches out to those with diseases/conditions in the Institute's mission to hear about the priorities and perspectives of these communities and use this input to inform research efforts. The Institute works closely with other NIH Institutes, Centers, and Offices, as well as its sister agencies at the Department of Health and Human Services (HHS). (Additional discussion of stakeholder engagement is in the Scientific Goals section.)

NIDDK workforce for effective stewardship: NIDDK will strive to ensure Institute staff and those in leadership roles (both scientific and administrative) have expertise that reflects the research opportunities in the Strategic Plan; recognize that a diverse, inclusive, and respectful workforce is crucial to our mission; and are committed to research to improve health, including critical research to advance health equity among populations disproportionately affected by diseases within NIDDK's mission.

Multidisciplinary Researchers, Diverse Stakeholders, Pathways to Health for All

Good scientific stewardship requires the attention and efforts of everyone involved in the biomedical research enterprise. The challenges are significant and varied; thus, a range of expertise, experiences, and input is needed from NIDDK staff and leadership, researchers, stakeholders, and research participants. Working together, and ensuring that all voices are heard, we can ensure that public resources are administered wisely, public trust is protected, and health equity is achieved.

Scientific Stewardship – Opportunities

With the opportunities highlighted in the Stewardship section of the Strategic Plan, NIDDK aims to promote efficient and effective ways to serve as a trusted steward of public resources and support research for diseases across our mission.

For many of the topics below, additional information is presented in the Scientific Goals section of the Strategic Plan.

Increase Diversity of the Biomedical Research Workforce

The NIDDK recognizes that the scientific challenges and opportunities within its mission require a workforce of individuals with different backgrounds and experiences and a range of skills, perspectives, and creative approaches both within the Institute itself and in the broader extramural research community. While scientific talent is well represented across all populations, opportunity is not. Efforts to provide biomedical research training to people from backgrounds underrepresented in research are not new, but they have generated limited success in increasing the diversity of the workforce overall. Thus, intensified efforts and novel strategies are required.

One approach would be to bring opportunities directly to communities to help individuals maintain their community support networks, improve their chances for success, and build resources. For example, opportunities in data science could be implemented even in communities with few existing resources, as extensive laboratory and medical research infrastructure would not be required. Another strategy to expand NIDDK's outreach would be to increase partnerships with colleges, universities, and other institutions that serve racial and ethnic minority groups and other populations who have been underrepresented in research. Individuals could be recruited and supported by promoting the NIH Loan Repayment Program—a set of programs established by Congress to repay advanced educational debt in in return for a commitment to engage in NIH mission-relevant research.

Effective mentoring is critical for career advancement in biomedical research, particularly at early career stages; thus, another approach to improving diversity is to enhance mentoring programs to help overcome challenges faced by trainees and faculty from groups who are underrepresented in biomedical research. For example, one opportunity would be to strengthen engagement of NIDDK-supported researchers in providing quality mentoring specifically to individuals in early career stages. The development of mentorship programs across institutions could increase the number of mentors and promote diversity among mentors. In addition to mentorship from more senior scientists, peer mentoring—both within and across institutions—can provide a valuable support network. Additional approaches to enhance mentoring are described in the section on research training and career development.

NIDDK will also leverage and build on the success of programs it has developed to provide research experiences and career development support for talented individuals from communities underrepresented in biomedical research. For example, the STEP-UP program provides high school and undergraduate students with biomedical research opportunities for the summer. At the graduate school level, NIDDK provides scholarship support to students from communities who are underrepresented and underserved to complete their Ph.D. or M.D./Ph.D. degrees. For individuals at various stages of their research careers post-doctoral and higher, NIDDK established the Network of Minority Health Research Investigators to provide mentoring and other information and support. NIDDK's Diversity Supplement Program provides support for promising researchers as they gather preliminary data to apply for their own independent research awards. NIDDK also partners with professional organizations in efforts to enhance diversity in the scientific workforce and workforce leadership. Many of these programs are coordinated by NIDDK's Office of Minority Health Research Coordination.

Women and others who are marginalized in the scientific workforce, including sexual and gender minority groups, people with disabilities, and others, also face significant challenges to careers in biomedical research. Strategies to reduce barriers need to be tailored to the unique challenges faced by different groups and individuals. NIDDK will continue to collaborate with its NIH partners to identify barriers and develop strategies to support women and other communities that have been marginalized in biomedical research—from entry, recruitment, and retention, to career development and leadership opportunities.

NIDDK is also actively engaged in NIH- and HHS-wide efforts, including NIH's UNITE initiative, to develop and implement strategies to increase diversity in science and break down barriers of structural racism. NIDDK will promote diversity in groups that provide input to the Institute, such as study section panels, NIDDK's Advisory Council, and others. NIDDK will continue to explore ways to promote a diverse, inclusive, and respectful workforce in Institute staff and leadership, both scientific and administrative, as well as in the extramural research community.

As further analyses continue to highlight other factors and biases affecting workforce diversity, these should be addressed, so that the biomedical research enterprise benefits from the ideas, perspectives, creativity, and leadership of people from all communities. (Other opportunities are discussed in the Scientific Goals sections of this Plan.)

Enhance Research Training and Career Development

As discussed throughout this Plan, it is imperative to foster exceptional research training and mentoring opportunities to cultivate the next generation of scientists. The Institute supports the training and career development of medical and graduate students, postdoctoral fellows, and physician/surgeon scientists through institutional and individual grants to extramural researchers and through its Intramural Research Program. NIDDK is committed to enhancing efforts to recruit and support talented individuals and to optimize their experiences and likelihood of success.

The importance of mentorship to training and career development is paramount. Important avenues include increasing mentoring opportunities, including peer mentoring; training and incentivizing mentors at all stages of their careers; and evaluating mentoring programs to develop best practice resources. Additionally, by seeking input from next-generation researchers about their experiences and scientific career goals, NIDDK will be able to build training and career development programs that better meet their needs.

There are several transition points in research training and career development where talented trainees and early career scientists face significant challenges. By focusing efforts on these transition points, the Institute can mitigate these barriers. For example, NIDDK will continue to hold workshops for its career development awardees and new principal investigators to help these individuals advance their scientific careers. The Institute also emphasizes support of emerging scientific careers through special funding consideration for talented new and early-stage investigators.

To promote broader research experience and build bridges across disciplines, NIDDK will encourage efforts to engage doctoral students in basic or discovery science with the medical community, and to engage medical students with the research community. NIDDK will also encourage recruitment of talent from varied scientific disciplines to the Institute's research areas. As an additional approach, at earlier stages of education, programs linking undergraduate and high school students with research training opportunities in both foundational science and clinical research can help fuel interest in scientific research and spark new careers to strengthen the scientific workforce for years to come. (Other aspects of research training are described in the Scientific Goals sections of the Strategic Plan.)

Attract and Retain Physician/Surgeon Scientists

Physician/surgeon scientists are an essential part of the biomedical workforce; however, recent efforts have not yielded a steady, sustainable pool of early-stage researchers with medical degrees. As residency and medical fellowship training often provide limited time for research, many trainees interested in a career as a physician/surgeon scientist struggle to compete successfully for individual career development awards due to a lack of scientific publications and prior research experience.

To counter this, NIDDK will foster the development of innovative approaches to strengthen efforts to attract and retain these individuals. Mentorship opportunities, as discussed in previous sections, are important for this group and need to be increased. Another consideration would be timing of research training and career development with respect to the structure of clinical/surgical training. Promoting team science, pairing physician/surgeon scientists with researchers with complementary expertise, could enhance comprehensive research design and foster a multidisciplinary research environment. Connecting physician/surgeon scientists with the growing field of data science could also help to attract and retain these individuals in research. Data science research can be flexible to be woven into clinical training, and collaboration between clinical researchers and data scientists could enhance translation of big data into clinical application. Another potential avenue is promoting the NIH Loan Repayment Program to physician/surgeon scientists, along with other potential strategies to enhance recruitment and retention of clinician scientists in research.

Promote Innovation

Creativity and innovation are hallmarks of biomedical research and drive improvements in health and healthcare. The ingenuity and problem-solving capabilities of individual investigators are crucial for research progress. NIDDK supports meritorious, investigator-initiated research that capitalizes on the ideas and expertise of scientists working in the NIDDK research mission. The Institute will continue to harness the creativity of individual scientists by maintaining a vigorous investigator-initiated research portfolio across its mission. High-risk, high-reward programs also promote innovation by supporting novel scientific directions for major scientific challenges, with the potential for broad impact. Pioneering solutions to complex biomedical research problems and engineering novel medical technologies also require the ingenuity of specialists from different backgrounds working across disciplines and along the spectrum of basic, clinical, translational, and implementation science. NIDDK will seek ways to promote, support, and sustain trans-disciplinary team science within its research mission. Additionally, NIDDK will continue to utilize the Small Business Innovation Research Program to stimulate technological innovation and increase small business participation in Federal research and development in NIDDK mission areas. NIDDK will also seek other ways to promote innovative and transformative research.

Improve Rigor and Reproducibility in Research

Scientific rigor is instrumental to the generation of data that is robust, and full transparency in reporting experimental details is essential so that others may reproduce and extend the findings. NIDDK will continue to support NIH policies and reporting guidelines to improve rigor and reproducibility in research, including implementation of a data sharing policy that requires researchers to plan for data management, preservation, and sharing.

NIDDK will promote good experimental practices in the design, conduct, and analysis of research to ensure that conclusions are valid and reproducible. For example, standardization and harmonization of data and samples as they are collected, analyzed, and stored enhances their utility by allowing results to be compared across multiple studies.

NIDDK will also promote approaches such as use of unique identifiers for datasets and reagents to allow unambiguous tracking of these across the scientific literature, standardization of metadata (additional information about scientific data, e.g., origin of the data, date the data were collected or generated, and methodology), and application of clinical research design principles to pre-clinical research.

NIDDK will also continue to support resources to promote rigor and reproducibility and maximize investments in research. For example, the NIDDK Information Network, dkNET, promotes sharing of information among researchers; ensures that data and resources can easily be found, used, and re-used; and provides services to promote transparency and reproducibility.

Promote Data Science

The complexity and volume of data generated by biomedical researchers offers numerous opportunities and challenges. To take advantage of these data, NIDDK, working with its NIH partners, must promote proper collection including use of data standardization methods and common data elements, storage, and sharing, as well as training efforts so that researchers are able to analyze and use the data to the fullest potential.

It will be valuable to increase training in bioinformatics and biostatistics for the scientific community overall, as well as foster a talented and diverse data science-focused workforce. Additionally, increasing awareness of and access to bioinformatics and biostatistics tools, resources, and expertise could help NIDDK-funded researchers analyze their data successfully. Connecting data scientists with NIDDK researchers focused on diseases within the Institute's mission could encourage interdisciplinary relationships and promote innovation.

Planning for data and biosample sharing and reuse should be part of a study's design from the outset, to ensure standardized collection of data, metadata, and participant consent documentation alongside biospecimen collection. After a study's goals are completed, making data and biosamples available for reuse should be an essential component of the lifecycle of a research project. (See also the Biorepositories section below.)

Other data science opportunities are discussed in other sections of this Plan.

Strengthen Biorepositories

As discussed in the Scientific Goals section, biorepositories can increase the value of research investments by enabling reuse and novel analyses of previously collected data and biosamples. Repository management policies should maximize the reach of repository resources among the broad research community, such as by connecting repository data and samples with scientists who have innovative new ideas for their use, all done in a way that preserves participant privacy and that is respectful of the concerns of populations experiencing disproportionate impact. To accomplish this, it would be important not only to promote the establishment and use of repositories, but also to make it easier to find and access their collections. Additionally, improved data repository navigation and analysis tools could make it easier for researchers to generate and test hypotheses. Where useful, data and biosampling standards for repositories should also be adopted so that archived resources can be compared across studies and can fit easily within a prospective repository user's research. It will also be important to establish training for best practices, expectations, and opportunities for biorepository utilization for researchers, as well as enhance training in repository organization and administration.

For example, the NIDDK Central Repository fosters sharing of web-enabled data, biosample, and genetic repositories from many NIDDK-funded clinical studies with the broader scientific community. NIDDK will explore strategies to enhance and to increase use of these resources.

Enhance Partnerships

NIDDK partners with industry, academia, patient advocacy organizations, professional societies, community-based organizations, non-governmental organizations, and others to support and conduct biomedical research under the NIDDK mission. Each partner brings unique resources and strengths and the resulting synergy speeds progress toward common goals and reduces duplication of efforts. NIDDK will seek opportunities to collaborate and break down “silos” with its external partners; NIH Institutes, Centers, and Offices; and sister agencies within HHS as well as other relevant agencies.

NIDDK additionally engages in collaborations that leverage international research opportunities in mission-relevant areas. Such collaborations benefit from scientific expertise and resources in other countries along with unique opportunities to study disease risk factors and prevention and treatment strategies. Insights gained from these efforts advance scientific progress to improve the health of people in the U.S. and beyond.

Enhance Ability to Respond to Unanticipated Events

NIDDK and the research community must be able to respond to unanticipated events such as pandemics, natural disasters, and other public health emergencies, not only in sustaining current research programs, but also in pivoting to new research questions and challenges. To enhance the Institute’s ability to act in these situations, NIDDK must be flexible and dynamic. Many of the strategies developed during the COVID-19 pandemic can be utilized in other situations, and the Institute will continue to develop flexible approaches to respond to these events.

Management and Accountability – Opportunities

Enhance Use of Evidence/Data in Decision-Making

The use of evidence and data to inform programmatic, operational, and policy decisions is critical to good stewardship. For example, NIDDK regularly reviews and evaluates its research and training programs and uses the resulting data to measure progress and inform decisions about future support and new directions. By enhancing efforts to generate data on research studies, research administration, and the scientific workforce, NIDDK will ensure judicious and transparent decision-making.

Enhance Risk Management Practices

NIDDK is committed to proactively identifying and managing risks that could jeopardize or impede the Institute’s mission and will continue to spearhead and collaborate with its NIH partners to improve processes and strategies for risk management. For example, the Institute will build tools for NIDDK staff to enhance identification and management of external and internal conflicts of interest.

Reduce Administrative Burden

Working with its NIH partners, NIDDK will continue efforts to optimize and streamline administrative processes and enhance efficiency while retaining quality and accountability. Reducing administrative burden for the scientific research community will enable scientists to spend more time on their research activities. NIDDK will also work to reduce administrative burden for its staff to harmonize efforts across the Institute, facilitate transparency, improve data quality to strengthen decision-making, foster nimbleness in response to emerging opportunities, and enable increased efficiency and effectiveness toward the NIDDK mission.

Enhance Communications to Stakeholders and the Public

Knowledge dissemination is paramount to ensuring that people benefit from NIDDK-supported research and to increasing scientific knowledge of the public. The Institute translates science-based knowledge gained from NIDDK-funded research into plain language and shares it efficiently and broadly. NIDDK also builds on community relationships and partnerships to deliver targeted messages effectively. The Institute also posts annual reports on its public website, highlighting research advances, personal perspectives of research participants and others living with diseases in NIDDK's mission, and analyses of research workforce and funding trends, among other topics. In addition, NIDDK will take advantage of new and emerging technologies for communicating valuable health and research information.

DESCRIPTION OF THE STRATEGIC PLANNING PROCESS

In 2019, the NIDDK embarked on a process to develop the Institute-wide Strategic Plan, with a broad vision for accelerating research into the causes, treatment, and prevention of diseases and conditions under the NIDDK's mission. This overarching, 5-year trans-NIDDK Strategic Plan will complement our disease-specific planning efforts.

Establishment of the Strategic Plan Working Group of Council

The process began with a series of discussions within NIDDK to develop an initial draft framework for the Plan, which was presented to the Institute's Advisory Council for input. NIDDK then established a Working Group of Council, comprising 44 external scientists and patient advocates, including a subset of the members of NIDDK's Advisory Council and others with expertise across the range of NIDDK's mission areas. The Working Group also included NIDDK staff to work in concert with the external members on development of the Plan. Through a series of virtual meetings and other communication, the Working Group contributed ideas for research opportunities, the biomedical research workforce, stakeholder engagement, and effective stewardship of public resources. (The Working Group members are listed on the following pages.)

Gathering Broad Stakeholder and Public Input

As part of the strategic planning process, the Institute invited broad external input with a public Request for Information (RFI), which was open from March through July 2020. NIDDK received approximately 80 responses to the RFI, with thoughtful comments from organizations representing the views of their membership (scientists, healthcare professionals, and patient advocates), whose areas of focus span across NIDDK's mission, along with responses from individual researchers, people living with diseases in NIDDK's mission, and others. The Institute also continued to receive input from the Working Group and from its Advisory Council. Regular progress updates were presented at NIDDK's Advisory Council meetings throughout the Plan's development. The NIDDK also provided updates on the planning process on its public website and in other communications.

Based on input from the Working Group, the 2020 RFI, and Council, the Institute prepared a first draft of the Strategic Plan and circulated it to the external Working Group members for comment. NIDDK then posted the draft on the web for public comment via another RFI in the summer of 2021. Approximately 70 responses were received; and as with the earlier RFI, these included thoughtful comments from organizations, individual researchers, and people living with diseases in the Institute's mission. NIDDK then incorporated the input and provided the revised draft to the Working Group for another opportunity to review. The revised draft was then provided to NIDDK's Advisory Council for review and then to the NIH Office of the Director for review, before being finalized and released to the public.

National Institute of Diabetes and Digestive and Kidney Diseases

Strategic Plan Working Group and Other Participants

The NIDDK Strategic Plan Working Group was assembled to include experts in the range of diseases within NIDDK's mission, such as diabetes and other endocrine and metabolic diseases; liver, intestinal, and other digestive diseases; nutritional disorders; obesity; and kidney, urologic, and hematologic diseases. In addition, the expertise of the Working Group members included basic science, clinical research, dissemination and implementation research, patient advocacy, and science administration.

External Members of the Working Group

E. Dale Abel, M.D., Ph.D.
University of Iowa

Clara Abraham, M.D.
Yale University

Cindy L. Amundsen, M.D.
Duke University

Gary Bennett, Ph.D.
Duke University

Linda Brubaker, M.D.
University of California, San Diego

Kirk Campbell, M.D.
Icahn School of Medicine, Mount Sinai

Sheila Crowe, M.D.
University of California, San Diego

Mark Donowitz, M.D.
Johns Hopkins University

Barry I. Freedman, M.D.
Wake Forest University

Crystal Gadegbeku, M.D.
Cleveland Clinic

Allan Goldstein, M.D.
Massachusetts General Hospital
Harvard University

Penny Gordon-Larsen, Ph.D.
University of North Carolina
Co-chair: Dissemination and Implementation Research Subgroup

Jennifer Green, M.D.
Duke University

Debra Haire-Joshu, Ph.D.
Washington University, St. Louis

William Herman, M.D., M.P.H.
University of Michigan

Felicia Hill-Briggs, Ph.D.
Johns Hopkins University

Jane Holt, B.A.
National Pancreas Foundation

Tamara Isakova, M.D., M.M.Sc.
Northwestern University

Barbara Kahn, M.D., M.S.
Beth Israel Deaconess Medical Center
Harvard Medical School
Co-chair: Stewardship Subgroup

Lee Kaplan, M.D., Ph.D.
Massachusetts General Hospital
Harvard University

Richard Knight, M.B.A.
American Association of Kidney Patients
Co-chair: Stakeholder Engagement Subgroup

Zachary Knight, Ph.D.
University of California, San Francisco

Davida Kruger, M.S.N.
Henry Ford Health System

Mitchell Lazar, M.D., Ph.D.
University of Pennsylvania

Ruth Loos, Ph.D.
Icahn School of Medicine, Mount Sinai

Jacquelyn Maher, M.D.
University of California, San Francisco

Sandeep K. Mallipattu, M.D.
Stony Brook University

Denise Marciano, M.D., Ph.D.
University of Texas Southwestern Medical Center

Maryann Martone, Ph.D.
University of California, San Diego

Rajnish Mehrotra, M.D.
University of Washington

Monica Peek, M.D., M.P.H.
University of Chicago

Terry Powley, Ph.D.
Purdue University

Don Rockey, M.D.
Medical University of South Carolina

Ceciel Rooker, B.S.
International Foundation for Gastrointestinal Disorders

Clifford Rosen, M.D.
Maine Medical Center Research Institute

Kathleen M. Sakamoto, M.D., Ph.D.
Stanford University

Maike Sander, M.D.
University of California, San Diego

Robert Sandler, M.D., M.P.H.
University of North Carolina

Elizabeth Seaquist, M.D.
University of Minnesota
Co-chair: Clinical Studies and Trials Subgroup

Sanja Sever, Ph.D.
Massachusetts General Hospital
Harvard University

Katherine Tuttle, M.D.
Providence Medical Research Center

Hunter Wessells, M.D.
University of Washington

Deborah Wexler, M.D.
Massachusetts General Hospital
Harvard University

Gary Wu, M.D.
University of Pennsylvania
Co-chair: Biological Pathways and Environmental Contributors Subgroup

NIDDK Working Group Members and Other Participants

Griffin P. Rodgers, M.D., M.A.C.P.
Director, NIDDK

Gregory G. Germino, M.D.
Deputy Director, NIDDK

Kevin Abbott, M.D., M.P.H.

Kristin Abraham, Ph.D.

Beena Akolkar, Ph.D.

Tamara Bavendam, M.D.

Henry Burch, M.D.

William T. Cefalu, M.D.

Rebecca J. Cerio, Ph.D.
Strategic Plan Lead Development Team

Sandeep Dayal, Ph.D.
Strategic Plan Lead Development Team

Mary Evans, Ph.D.

Lisa J. Gansheroff, Ph.D.
Lead: Strategic Plan Lead Development Team

Erica R. Hennes, B.A.

Jay Hoofnagle, M.D.

Stephen P. James, M.D.

Teresa Jones, M.D.

Paul Kimmel, M.D.

Ziya Kirkali, M.D.

Michael W. Krause, Ph.D.

Ellen Werber Leschek, M.D.
Co-chair: Stakeholder Engagement Subgroup

Barbara Linder, M.D., Ph.D.

Christopher Lynch, Ph.D.

Karl F. Malik, Ph.D.

Christine Maric-Bilkan, Ph.D.

Chris Mullins, Ph.D.
Co-chair: Biological Pathways and Environmental Contributors Subgroup

Jenna Norton, Ph.D., M.P.H.

Voula Osganian, M.D., Sc.D., M.P.H.

Afshin Parsa, M.D., M.P.H.

Peter Perrin, Ph.D.

Matthew E. Portnoy, Ph.D.
Co-chair: Stewardship Subgroup

Heather Rieff, Ph.D.

David Saslowsky, Ph.D.

Sheryl Sato, Ph.D.

Anna Sadusky, Ph.D.

Terez Shea-Donohue, Ph.D.

Averell H. Sherker, M.D.
Co-chair: Clinical Studies and Trials Subgroup

Philip Smith, Ph.D.

Lisa Spain, Ph.D.

Victoria Spruance, Ph.D.

Robert A. Star, M.D.

Pamela L. Thornton, Ph.D.
Co-chair: Dissemination and Implementation Research Subgroup

Robert W. Tilghman, Ph.D.
Strategic Plan Lead Development Team

Aynur Unalp-Arida, M.D., M.Sc., Ph.D.

Julie A. Wallace, Ph.D.
Strategic Plan Lead Development Team

Susan Yanovski, M.D.

ACCELERATING MEDICINES PARTNERSHIP and AMP are registered service marks of the U.S. Department of Health and Human Services.

Image credits:

The photo of Dr. Rodgers in the Director's Message was taken by Chai-Chi Chang in NIH Events Management Public Affairs.

The microscopy images in the Scientific Goal 1 chapter image collage are reprinted with permission from the copyright holders.

- Top image: Reprinted by permission from Springer Nature: *Nature*, Subepithelial telocytes are an important source of Wnts that supports intestinal crypts, Shoshkes-Carmel M, Wang YJ, Wangensteen KJ, Toth B, Kondo A, Massasa EE, Itzkovitz S, Kaestner KH. 557: 242-246, Copyright 2018.
- Middle image: From Kimberly A. Homan (Harvard University), Navin Gupta (Brigham and Women's Hospital), Jennifer A. Lewis (Harvard University), and Ryuji Morizane (Brigham and Women's Hospital).
- Bottom image: Reprinted from *Cell Metabolism*, 27:3, Almaça J, Weitz J, Rodriguez-Diaz R, Pereira E, and Caicedo A, The pericyte of the pancreatic islet regulates capillary diameter and local blood flow, 630-644, Copyright 2018, with permission from Elsevier.

All other photos are stock photography licensed from the copyright holder. The photo of a scientist on the cover is licensed via 123rf.com. The photo of the woman in the top left of the cover photo collage, as well as the photos for the Scientific Goal 4 and Stewardship sections, are licensed via shutterstock.com. The image of the city in the Scientific Goal 3 image collage is licensed via gettyimages.com. All other photos are licensed via iStockphotos.com.

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NIH National Institute of Diabetes and Digestive and Kidney Diseases

NIH Publication Number:
21-DK-8159