On behalf of the National Institutes of Health (NIH), I am transmitting the Congressional Justification of the NIH request for the fiscal year (FY) 2022 budget. This request for a $52.0 billion total program level is critical to supporting NIH's mission to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to enhance health, lengthen life, and reduce illness and disability. Importantly, this budget request enables the NIH to support critical biomedical discoveries that lead to life-saving medical interventions and enables the biomedical research workforce from across the full inclusive richness of the Nation to transform inspiration into innovation.

It is hard to put into words just how remarkable the biomedical research accomplishments in response to the COVID-19 pandemic are in the history of science. A vaccine development process that used to take many years, often decades, has been condensed to about 11 months. In our efforts to combat COVID-19, we have come a long way in a short period. But there is still plenty of work to do to get this pandemic and other public health crises facing our Nation under control. The NIH FY 2022 budget ensures that NIH can prioritize innovation to develop transformational tools and technologies, discover new clinical breakthroughs, and advance the next frontier of biomedical research.

It is important to recognize that the advances made in the past year could not have happened without the efforts of many scientists working tirelessly for many years to understand fundamental aspects of life and human health prior to the pandemic. The FY 2022 budget continues to advance NIH's long-standing commitment to investing in basic research and the arc of translation into clinical practice. Fundamental research is the key to unlocking the secrets of how living systems function and remains the foundation for developing novel treatments and cures. Just as investment in basic science led to the rapid development of COVID-19 vaccines, diagnostics, and therapeutics, basic research also serves as the foundation for the NIH Helping to End Addiction Long-term (HEAL) Initiative, which aims to curb the opioid epidemic and provide non-addictive alternatives for individuals who suffer from chronic pain. As the NIH builds upon its investments in basic research to develop innovative medical treatments, we look forward to being the home to the new Advanced Research Projects Agency for Health (ARPA-H) and its exciting new capabilities to speed the application and implementation of health breakthroughs.

The FY 2022 budget allows NIH to secure the Nation's investment in this current biomedical workforce and the next generation of biomedical research scientists. As a science agency, the NIH understands that bringing diverse perspectives, backgrounds, and skillsets to address complex scientific problems enhances scientific innovation, and we are committed to ending structural racism in biomedical research. We will be instituting new ways to support diversity, equity, and inclusion which will help identify and dismantle any policies and practices that may

harm our workforce and our science. A new NIH initiative called UNITE will provide the framework for this important effort. UNITE goals are centered on ending structural racism and racial inequities across the biomedical research enterprise through short-term and long-term actions.

In conclusion, the FY 2022 budget provides resources for NIH, and the hundreds of thousands of researchers it supports, to accelerate discoveries that will enhance our ability to prevent and cure disease. I look forward to discussing the FY 2022 budget request.

Francis S. Collins, M.D., Ph.D.

TABLE OF CONTENTS

EXECUTIVE SUMMARY

OVERALL APPROPRIATIONS

SUPPLEMENTARY TABLES

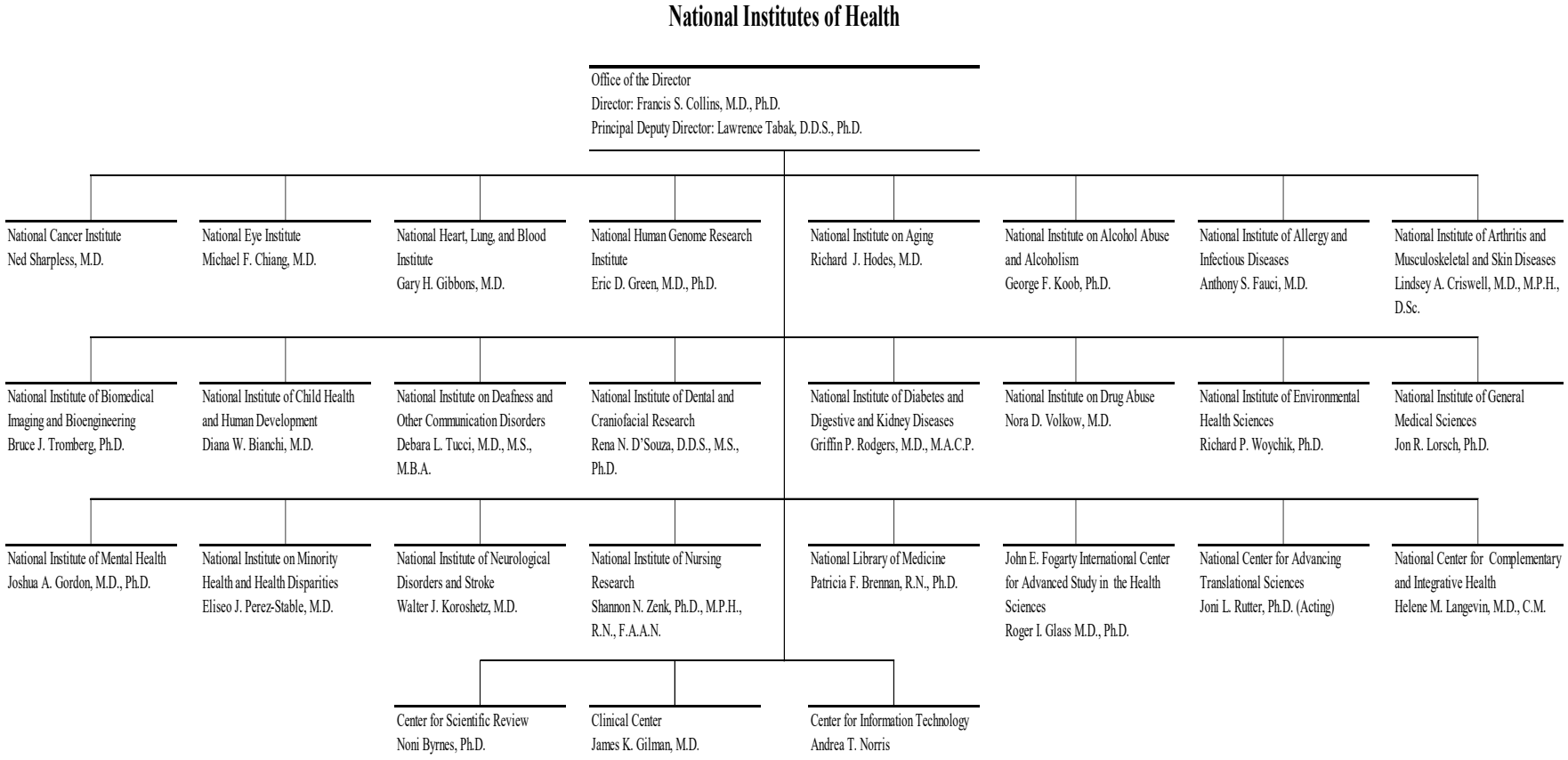
TRANS-NIH INITIATIVES

COMMON FUND

OFFICE OF AIDS RESEARCH

DRUG CONTROL PROGRAMS

ORGANIZATION CHART



INTRODUCTION AND MISSION

The mission of the National Institutes of Health (NIH) is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. In pursuit of this mission, NIH conducts and supports biomedical research focused on fostering fundamental creative discoveries, innovative research strategies, and their applications towards improving human health.

As the Nation's premier biomedical research agency, NIH plays a critical role in advancing basic and clinical biomedical research to improve human health and lay the foundation for ensuring the Nation's economic well-being, particularly as we face COVID-19, the greatest public health crisis of our generation. NIH also works to develop, maintain, and renew scientific, human, and physical resources that will ensure the Nation's capability to prevent disease and disability. The biomedical research enterprise depends upon not only NIH's support of cutting-edge science and technology, but also its wise investment of tax dollars. Through careful stewardship of public resources in pursuit of its mission, NIH strives to enhance the lives of all Americans.

OVERVIEW OF BUDGET REQUEST

Introduction

The National Institutes of Health (NIH) requests a total program level for FY 2022 of $52.0 billion, which is $9.0 billion more than the FY 2021 Enacted level. Included in the request is a bold new investment of $6.5 billion to establish the Advanced Research Projects Agency for Health (ARPA-H), which aims to drive transformational health research innovation and speed medical breakthroughs by tackling ambitious challenges requiring large-scale, sustained, and cross-sector coordination.

The request incorporates strategic investments to address several national priorities, including combatting the COVID-19 pandemic through countermeasures and researching its effects on mental health and the health of children, fighting the opioid epidemic, eradicating HIV in the United States, addressing health disparities and inequities, continuing efforts to tackle maternal mortality and morbidity, researching the human health impacts of climate change, and strengthening cybersecurity at NIH.

NIH is developing the *NIH-Wide Strategic Plan, Fiscal Years 2021–2025.* This plan will outline a vision for biomedical research to capitalize on new opportunities for scientific exploration and address new challenges for human health. Being developed with input from hundreds of stakeholders and scientific advisers, and in collaboration with leadership and staff of NIH's Institutes, Centers, and Offices (ICOs), the plan is being designed to complement the ICOs' individual strategic plans, which align with their congressionally mandated missions. The agency has also released the NIH-wide COVID-19 Strategic Plan, which provides a framework for accelerating the development of therapeutic interventions, vaccines, and diagnostics.[1]

The Buildings & Facilities (B&F) account budget request is $250.0 million, a $50.0 million increase from the FY 2021 Enacted level. NIH's backlog of maintenance and repair (BMAR) was $2.5 billion at the end of FY 2020. The budget also increases flexibility for Institutes and Centers to fund construction, repair, and improvement projects. These two proposals are part of a long-term effort to strengthen stewardship of NIH facilities. An independent review of the facility needs of NIH's main campus by the National Academies of Sciences, Engineering, and Medicine that was released in 2019 supports additional investments in NIH facilities alongside reforms to the NIH capital planning and funding process, including prioritizing projects of highest functional research value.[2] In addition to efforts to improve physical infrastructure, the request invests in NIH's information technology infrastructure through a $100.0 million increase to enhance NIH-wide cybersecurity efforts.

In striving to achieve its mission, NIH supports a world-class research workforce that aims to better understand the fundamental nature of disease. The knowledge from this research can then be harnessed to move the biomedical research enterprise forward, ultimately benefiting the human and economic health of our country.

[1] www.nih.gov/research-training/medical-research-initiatives/nih-wide-strategic-plan-covid-19-research
[2] www.nationalacademies.org/our-work/assessing-the-capital-needs-of-the-national-institutes-of-health-main-campus

More than 80 percent of the NIH's funding is awarded for extramural research, largely through almost 50,000 competitive grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in every state. A recent study showed that NIH directly supported the training of more than 9,500 pre-doctoral and almost 5,900 post-doctoral fellows through training grants.[3] To date, 163 NIH-supported researchers, including 26 intramural investigators, have been awarded the Nobel Prize.[4] The Lasker Prize, which is often called "America's Nobel," recognizes researchers and clinicians for their contributions to medicine and has been awarded to 195 NIH-supported researchers, including 33 intramural investigators to date.[5]

NIH and the biomedical research community are coming together in unprecedented ways to meet the challenges of developing safe and effective therapeutic treatments and vaccines, accurate and reliable testing technologies, and behavioral and community prevention practices in response to the COVID-19 pandemic. The community must also grapple with the unprecedented impacts and massive disruption to the research enterprise. Many NIH-supported research projects across the Nation have ground to a halt as universities and other research institutions have suspended operations. In some instances, this has resulted in the loss of critical biological resources that will have to be recreated. Similarly, the research workforce, particularly early-career scientists, faces significant challenges as the opportunity to generate and collect data has been disrupted.

Science in Service to Society

Answering the Call

NIH research has proven its value to the United States and the world over the years by rising to meet the tests of polio, AIDS, and many other formidable health challenges. Now, we face what may be the greatest public health crisis of our generation: COVID-19. To address the challenge that the COVID-19 pandemic poses to our health and economy, it is imperative that NIH and all sectors of society work together in unprecedented ways and with unprecedented speed. Enabled by the strong support of Congress and other partners in the public and private sectors, NIH has mounted a vigorous research response against COVID-19 since the beginning of the pandemic. The agency has expanded efforts to understand viral biology and pathogenesis of SARS-CoV-2 and employ this knowledge to develop the tools needed to diagnose, treat, and prevent disease. By April 2020, the agency announced the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership to develop a coordinated research strategy for prioritizing and speeding development of the most promising treatments and vaccines. Later in April 2020, NIH launched the Rapid Acceleration of Diagnostics (RADx℠) initiative to speed innovation in the development, commercialization, and implementation of technologies for COVID-19 testing. The breathtaking pace and scope of this response have been made possible by decades of NIH-funded basic research, which built a priceless foundation for the current efforts to combat COVID-19.

[3] www.ncbi.nlm.nih.gov/pubmed/26625903
[4] www.nih.gov/about-nih/what-we-do/nih-almanac/nobel-laureates
[5] www.nih.gov/about-nih/what-we-do/nih-almanac/lasker-awards

As researchers make stunning progress on treatments and vaccines to combat COVID-19, the long-term health impacts remain unclear. NIH is supporting studies in diverse populations, including pregnant women, infants, and children, supported by $1.15 billion in emergency supplemental appropriations enacted in December 2020.[6] The FY 2022 Budget request includes an additional $15.0 million for research on multisystem inflammatory syndrome in children (MIS-C) and the spectrum of SARS-CoV-2 pediatric risks. For many Americans, this pandemic has been overwhelming, affecting their mental health. Prior research on disasters and epidemics has shown that in the immediate wake of a traumatic experience, large numbers of affected people report distress, including new or worsening symptoms of depression, anxiety, and insomnia. To aid in mental health recovery from the COVID-19 pandemic, $25.0 million is requested to increase research on the impact of the pandemic on mental health and the mental health delivery system. This will be done in part by utilizing participants of the *All of Us* Research Program, who will be surveyed on the effect of the pandemic and various mitigation measures on their physical and mental health.

The public health crisis of opioid misuse and addiction in America continues, exacerbated by the coronavirus pandemic. In 2019, 70,630 people in the United States died of overdose, including 49,860 dying from opioid overdose (70.6 percent of all drug overdose deaths).[7] Moreover, more than 50 million Americans suffer from chronic pain, and of those, 25 million live with daily chronic pain and lack effective and safe non-opioid options for pain management.[8] The widespread use of opioids to treat acute and chronic pain contributed to the approximately 10.3 million people aged 12 years and older in the United States in 2018 who misused opioids, including heroin.[9] These staggering numbers are likely underestimates. They fail to capture the full extent of the damage of the opioid crisis, which reaches across every domain of family and community life — from lost productivity and economic opportunity, to intergenerational and childhood trauma, to extreme strain on community resources, including first responders, emergency rooms, hospitals, and treatment centers. NIH launched the Helping to End Addiction Long-term℠ Initiative, or NIH HEAL Initiative, to provide scientific solutions to the opioid crisis and offer new hope for individuals, families, and communities affected by this devastating crisis. The FY 2022 Budget includes total funding of $2.2 billion to address the opioid crisis across the ICOs, an increase of $626.6 million over the FY 2021 funding level. The use of opioids, together with stimulants, such as methamphetamine, is increasing; and deaths attributed to using these combinations are likewise increasing. Taking note of these trends, FY 2021 appropriation language expanded allowable used of HEAL funds to include research related to stimulant misuse and addiction. Identifying how opioids and stimulants interact in combination to produce increased toxicity will enhance our ability to develop medications to prevent and treat comorbid opioid and stimulant use disorders and overdoses associated with this combination of drugs.

[6] www.congress.gov/bill/116th-congress/house-bill/133/text
[7] www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf
[8] pubmed.ncbi.nlm.nih.gov/26028573/
[9] www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf

Another area of immense importance and concern is maternal morbidity and mortality. Maternal health spans a wide array of topics on the health of pregnant women and mothers, including pregnancy-related disorders -- preeclampsia, pregnancy-induced hypertension, gestational diabetes (GDM) preterm labor, hemorrhage, and other complications that pose acute risks and may have long-term consequences. Renewed awareness that the United States lags markedly behind other developed countries in preventing maternal mortality and morbidity lends urgency to basic and clinical research on multiple determinants of maternal health. Collaborative efforts of NIH ICOs focus on both basic mechanisms that set the course of healthy pregnancies and the disease processes that are implicated in pregnancy complications. Critical research goals are to identify new treatments, determine how to test existing therapies for safety and effectiveness in the unique physiology of pregnant women and lactating women, and develop effective strategies to prevent adverse maternal outcomes. Triggering particular urgency is the growing recognition that Black and American Indian/Alaska Native women are disproportionately affected by maternal morbidity and mortality.

In response to the rising maternal mortality (MM) in the United States, the FY 2022 Budget provides $30.0 million for the Implementing a Maternal health and Pregnancy Outcomes Vision for Everyone (IMPROVE) initiative, which will support research on how to mitigate preventable MM, decrease severe maternal morbidity (SMM), and promote health equity in the United States. The initiative will address the leading causes of SMM/MM during pregnancy, at delivery, and up to one year post-partum. It will build on ongoing efforts among federal and other partners and stakeholders to accelerate progress and maximize reach and impact by leveraging existing resources (*e.g.,* previously studied cohorts and archived biospecimens) and developing new studies. IMPROVE proposes to launch a national network of Maternal Health Research Centers of Excellence that supports integrated biological and biopsychosocial research. The research projects will incorporate local community needs and perspectives to expand and complement existing research efforts by developing, implementing, and evaluating community-tailored interventions to address health disparities in SMM/MM, as well as investigate biological, behavioral, sociocultural, and structural risk factors and mechanisms of the leading causes of SMM/MM. Through this multidimensional strategy, IMPROVE aims to build an evidence-based approach to reducing SMM/MM and its associated health disparities.

Among the still other public health crises our Nation faces are the health threats brought by climate change and gun violence. As the climate continues to change, the risks to human health will grow, exacerbating existing health threats and creating new public health challenges. While all Americans will be affected by climate change, populations of concern are disproportionately vulnerable. These populations of concern include children, the elderly, outdoor workers, and those living in disadvantaged communities. The FY 2022 Budget includes a $100.0 million increase for research on the human health impacts of climate change. Violence is a widespread public health problem that has profound impacts on lifelong health, opportunity, and well-being. When firearms are involved with violent events, the risk for injury and mortality as well as both acute and chronic physical, mental, and behavioral health conditions increases. The NIH is committed to supporting scientific research to understand and prevent injury and mortality associated with firearm violence through public health interventions. A $12.5 million increase is included in the Office of the Director (OD) for gun violence research, which doubles funding for this important research.

Closing the Gap in Health Disparities

The COVID-19 pandemic has brought into sharp focus the dramatic health disparities that exist across the American population. For example, 22 percent of U.S. counties that are disproportionately African American accounted for 52 percent of our Nation's COVID-19 cases and 58 percent of COVID-19 deaths.[10] NIH is engaging in several efforts to ensure the inclusion of minorities in COVID-19 research. One of the most notable is the RADx Underserved Populations (RADx-UP) initiative, which leverages existing community partnerships to build community-engaged implementation projects focused on understanding the factors associated with disparities in COVID-19 morbidity and mortality.[11] This initiative aims to lay the foundation to reduce disparities for those underserved and vulnerable populations who are disproportionately affected by, have the highest infection rates of, and/or are most at risk for complications or poor outcomes associated with the COVID-19 pandemic. But health disparities extend well beyond the current pandemic, and the time is right for an enhanced research agenda. The Budget proposes a $330.0 million increase for research managed by the National Institute on Minority Health and Health Disparities (NIMHD), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Nursing Research (NINR) and the Fogarty International Center to address these disparities. Also included in the request is $30.0 million for NHLBI for the Community Engagement Alliance (CEAL) Against COVID-19 Disparities,[12] an initiative connecting researchers to trusted leaders and organizations in communities hardest hit by COVID-19, helping them work together to address misinformation, increase the use of practices to prevent spread of the virus, and ensure that clinical trials include people in these communities, so that the treatments and vaccines developed will work for everyone.

Beyond COVID-19, NIMHD is leading the advancement of the science of minority health and health disparities in several ways such as by redefining minority health and health disparities research; developing a research framework that underscores the key health determinants, levels of influence, and domains of influence researchers should consider in conducting research on minority health and health disparities; and developing methods and measurements for minority health and health disparities research. As a blueprint for the new opportunities, the "NIH Minority Health and Health Disparities Strategic Plan 2021-2025: Taking the Next Steps" was released on March 31, 2021.[13] It was developed by NIMHD, in collaboration with other NIH ICOs, and outlines the agency's research, research-sustaining activities, and outreach priorities and goals for minority health and health disparities.

In addition to looking at health disparities through the lens of racial and ethnic diversity, the agency is also working to understand health inequities from other perspectives. For example, the *All of Us* Research Program is seeking a million or more participants from all backgrounds who reflect the rich diversity of the United States to ensure that all people benefit from the new biomedical advancements made with program data. *All of U*s is achieving its diversity goals through partnership with organizations that have ties to, and can guide the long-term engagement

[10] www.medrxiv.org/content/10.1101/2020.05.04.20090274v1
[11] www.nih.gov/research-training/medical-research-initiatives/radx
[12] covid19community.nih.gov/
[13] www.nimhd.nih.gov/about/strategic-plan/

of, participants from communities that have been historically underrepresented in biomedical research.

Capitalizing on Foundational Investments and Beyond

Years of basic science allowed us to respond effectively
Investments in basic research that generate fundamental knowledge about the nature and behavior of living systems provide the building blocks that allow us to respond effectively to old and new challenges. In pursuit of its mission, NIH invests more than half of its research budget in fundamental discovery, which provides the key for unlocking the secrets of how living systems function.[14] With this substantial level of support, NIH lays the groundwork for discoveries that will ultimately lead to novel interventions, treatments, and cures. In fact, a recent study found that NIH funding contributed to published research associated with every single one of the 210 new drugs approved by the Food and Drug Administration (FDA) from 2010 through 2016.[15] More than 90 percent of this NIH funding was for basic research.

From basic neuroscience to innovative technologies
The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative® is a key example of NIH's approach to fostering basic research.[16] The BRAIN Initiative aims to revolutionize our understanding of the human brain by supporting the development and application of innovative technologies that allow researchers to study how individual cells and complex neural circuits interact in both time and space. By catalyzing the development of new research technologies, the BRAIN Initiative supports advancements that will allow scientists across disciplines, not just those funded by the initiative, to push the frontiers of their research, from manipulating and monitoring neural activity at unprecedented scales to understanding the molecular "census" of the cells in the brain well enough to manipulate highly specific populations. In one study, researchers with funding from the BRAIN Initiative pioneered the pairing of a 3D live-imaging microscope with an ultra-fast camera.[17] This technique, called Swept Confocally Aligned Planar Excitation (SCAPE) 2.0 microscopy, enables scientists to image in a wide range of experiments where they can present stimuli or probe an animal's behavior—all while imaging how cells drive and depict those behaviors. Using SCAPE 2.0, researchers can rapidly image large fixed, cleared, and expanded tissues such as the retina, brain, and spinal cord—enabling tracing of the shape and connectivity of cellular circuits.

Alongside BRAIN Initiative-funded research, NIH funds other groundbreaking basic neuroscience research to build a solid foundation for new innovations or discoveries. For example, NIH-funded researchers found yet another link between sleep and brain health: sleep triggers rhythmic waves of blood and cerebrospinal fluid that appear to function much like a washing machine's rinse cycle, which may help to regularly clear the brain of toxic waste.[18] These findings and others may help explain why poor sleep or loss of sleep has previously been

[14] nexus.od.nih.gov/all/2016/03/25/nihs-commitment-to-basic-science/
[15] Galkina Cleary E. Contribution of NIH funding to new drug approvals 2010-2016. Proc Natl Acad Sci USA. 2018 115(10):2329-2334. PMID: 29440428 www.pnas.org/content/115/10/2329
[16] braininitiative.nih.gov/
[17] directorsblog.nih.gov/2019/12/05/3d-neuroscience-at-the-speed-of-life/
[18] directorsblog.nih.gov/2020/03/05/discovering-the-brains-nightly-rinse-cycle/

associated with the spread of toxic proteins and worsening memory loss in people with Alzheimer's disease.

INCLUDE high-risk, high-reward basic science
A major component of the INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) project is to fund targeted, high-risk, high-reward basic science studies on chromosome 21, which is present in an extra copy in Down syndrome.[19] INCLUDE funded projects investigate conditions that disproportionately affect individuals with Down syndrome, such as Alzheimer's disease/dementia, autism, cataracts, celiac disease, congenital heart disease and diabetes. Basic research on chromosome 21 will improve understanding of the biology of Down syndrome and support the development of new treatments for health conditions experienced by individuals with Down syndrome. With advances in technology, researchers can further explore the effects of multiple genes on chromosome 21 and identify genetic pathways that may be most responsive to new therapies for co-morbid conditions.

The Potential for Future Advances Is Extraordinary!

Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, design preventive interventions, develop better diagnostics, and discover new treatments and cures. Realizing the benefits of fundamental biomedical discoveries depends on the translation of that knowledge into the development of new diagnostics, therapeutics, and preventive measures to improve health. These strategies, which could develop a potential medication, a new vaccine, a medical device, a community-based prevention program, or a wide range of other intervention types, are then optimized and tested in clinical or real-world settings to assess their efficacy and effectiveness. NIH is deliberate in its support of translational and clinical sciences, following the guidance of the *NIH-Wide Strategic Plan, Fiscal Years 2016–2020* to fund those studies in which the scientific opportunities are ripe, and the public health needs, whether emerging or chronic, are greatest. As with basic research, NIH not only supports translational and clinical studies directly, but also supports the creation of the infrastructure, resources, and tools to provide a platform for innovation. To facilitate an integrated understanding of health and disease at all levels, from molecular underpinnings to social factors to treatment response, NIH is investing in large population studies to learn more about how we are the same and how we are different. This integration will allow for unprecedented precision in the ways in which health is addressed, making it possible for every individual to receive preventive and therapeutic care tailored specifically to their needs, ushering in an era of precision medicine.

The new Advanced Research Projects Agency for Health (ARPA-H) will be a key component to drive transformational innovation in health research. The FY 2022 Budget includes $6.5 billion for ARPA-H to build platforms and capabilities to deliver cures for cancer, Alzheimer's disease, diabetes, and other diseases. This investment in bold and emergent research opportunities is both high-risk and high-reward, and will collapse barriers and speed the development, application, and implementation of urgently needed health breakthroughs. ARPA-H will fund projects with the potential to transform entire areas of medicine and health by:

[19] www.nih.gov/include-project

- Tackling bold challenges requiring large scale, sustained, cross-sector coordination
- Creating new capabilities (*e.g.,* technologies, data resources, disease models)
- Supporting high-risk exploration that could establish entirely new paradigms
- Overcoming market failures through critical solutions, including financial incentives

Modeled after the Defense Advanced Research Projects Agency, ARPA-H will recruit visionary term-limited program managers who can identify and fund traditional and non-traditional partners to take on critical challenges that are unlikely to move forward quickly without this catalytic assistance. ARPA-H will leverage novel public-private partnerships, use directive approaches that will provide quick funding decisions to support projects that are results-driven and time-limited, and identify emergent opportunities through advanced systematic horizon scans of academic and industry efforts. Potential areas of transformative research driven by ARPA-H include an "innovation funnel" for accurate, wearable, ambulatory blood pressure technology, preparation of mRNA vaccines against common forms of cancer, or accelerating development of efficient gene/drug delivery systems to target any organ, tissue, or cell type – a zip code for the human body.

ARPA-H will be operationally unique from NIH's Institutes and Centers, with a distinctive culture and organizational structure that provides agility to advance biomedical science in bold new ways. It will make broad use of flexible hiring and procurement authorities, such as the use of Other Transactions Authority. ARPA-H will have a Federal advisory panel that will provide an avenue for interagency coordination and idea generation, and will include the heads and/or designated staff of major science agencies within and outside HHS. Importantly, this advisory panel will not set the research agenda, or oversee ARPA-H funding or programs. Decisions on funding and programs will be made by program managers in consultation with the ARPA-H Director to ensure decisions are timely, independent, and informed by project performance. Funding is requested with a three-year period of availability, which will allow for both scale-up in FY 2022 and redeployment of resources in the next two years if projects fail to meet performance milestones. Funding will support extramural research, with only a small percentage retained to support a lean workforce and administrative functions. ARPA-H will benefit from NIH's existing infrastructure and relationships with Federal and non-Federal entities. While most awards would go to industry, universities, and non-profit research institutions, ARPA-H may also enter into agreements with other Federal entities. ARPA-H will not have its own intramural program to preserve flexibility in funding bold, high-risk projects. ARPA-H is designed to complement NIH's existing research portfolio and its activities will be coordinated with other components of NIH and other HHS agencies.

Advancing testing and diagnostics for early detection of disease

The emergence of COVID-19 as a global pandemic has highlighted the importance of testing and diagnostics for early detection of infection, but the critical importance of testing and diagnostics to understanding, treating, and preventing disease is well known to health researchers. NIH-funded researchers are getting closer to a blood test to diagnose Alzheimer's disease and distinguish it from other neurodegenerative conditions. Advances like this expedite the identification and validation of biological targets of disease.

To spur the creation of new approaches that can rapidly expand access to testing for COVID-19, NIH launched the Rapid Acceleration of Diagnostics (RADx℠) program in late April 2020.[20] This effort, conducted in partnership with the Office of the Assistant Secretary of Health, the Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense, was started with $1.5 billion in emergency supplemental funding. As one component of RADx℠, the RADx-Tech initiative aims to speed the development, validation, and commercialization of innovative point-of-care and home-based tests, and improve clinical laboratory tests, that can directly detect the virus. RADx-Tech expands the Point-of-Care Technologies Research Network (POCTRN) established several years ago by NIH's National Institute of Biomedical Imaging and Bioengineering (NIBIB). The network uses a flexible, rapid process to infuse funding and enhance technology designs at key stages of development, with expertise from technology innovators, clinical testing, regulatory affairs, entrepreneurs, and business leaders. ARPA-H will be well-positioned to apply the lessons learned from RADx to a wide variety of applications.

Advances in data science: artificial intelligence, big data, and machine learning
Advances in data science, artificial intelligence, and machine learning will help to speed the analysis of data and application of the insights provided. Already, NIH-funded researchers have used artificial intelligence to classify a broad range of heart arrhythmias from individual patient ECGs, provided a low-cost mobile approach to cervical cancer screening,[21] and sped up brain tumor diagnosis.[22]

NIH supports multiple data science efforts to ensure that COVID-19 research data are findable, accessible, interoperable, and reusable (the FAIR principles).[23] By enhancing existing and creating new data science resources and analytical tools, NIH is facilitating the use of COVID-19 data to the greatest extent possible, both by those generating the data and by other researchers. These investments support the development of diagnostic tools, survey instruments, risk assessment models, public health surveillance tools, and portals to share data, among others (e.g., NIH Repository of COVID-19 Research Tools, OpenData Portal, PhenX, SHIELD [Systemic Harmonization and Interoperability Enhancement for Laboratory Data Collaborative], and SPHERES [SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance]). NIH investments to develop shared metrics and terminologies across research projects facilitate and maximize the use of a wide breadth of data, from chemical structures to clinical trial results.

To accelerate the pace of discovery of diagnostics, treatments, and vaccines for COVID-19, NIH launched the Medical Imaging and Data Resource Center (MIDRC), an ambitious effort that will harness the power of artificial intelligence and medical imaging to fight COVID-19.[24] The multi-institutional collaboration, led by NIBIB, will create new tools that physicians can use for early detection and personalized therapies for COVID-19 patients. The MIDRC goals are to lead

[20] directorsblog.nih.gov/2020/07/23/racing-to-develop-fast-affordable-accessible-tests-for-covid-19/
[21] directorsblog.nih.gov/2019/01/17/using-artificial-intelligence-to-detect-cervical-cancer/
[22] directorsblog.nih.gov/2020/01/14/artificial-intelligence-speeds-brain-tumor-diagnosis/
[23] www.nih.gov/sites/default/files/research-training/initiatives/covid-19-strategic-plan/coronavirus-strategic-plan-20200713.pdf
[24] www.nih.gov/news-events/news-releases/nih-harnesses-ai-covid-19-diagnosis-treatment-monitoring

the development and implementation of new diagnostics, including machine learning algorithms, that will allow rapid and accurate assessment of disease status and help physicians optimize patient treatment.

New tools and technologies for treatments and cures
NIH-funded researchers are achieving transformative results through technology and shedding new light on how biological systems function in health and disease. These insights are leading to faster, more accurate diagnostics, less invasive screening and treatment procedures, and hope for therapies and cures for previously intractable diseases. Gene editing, three-dimensional (3D) tissue printing, single-cell biology, and neurotechnologies are just a few of the areas in which innovative discoveries are moving towards tangible results in delivering the promise of biomedical research for human health.

Gene vector production and innovation
Gene therapy and gene editing approaches are some of the most promising treatment modalities for a growing number of disease conditions. Vectors are the "vehicle" by which a gene can be delivered to a targeted location in the body, and adeno-associated viruses (AAVs) are currently the most prevalent type of vector used in both gene therapy and gene editing studies. Wait times to produce vector therapies that meet the manufacturing standards necessary for clinical trials are long, often 1 to 2 years. Resolving this production bottleneck is critical for gene-based therapies to reach all people who need them.

One example of how gene vectors can be used as an effective therapy comes from research on sickle cell disease. Researchers at NIH have developed a new and improved viral vector—a virus-based vehicle that delivers therapeutic genes—for use in gene therapy for sickle cell disease.[25] Researchers report that the new vector was up to 10 times more efficient at incorporating corrective genes into bone marrow stem cells than the conventional vectors currently used in advanced lab tests using animal models, and its carrying capacity is up to 6 times higher. The development of the vector could make gene therapy for sickle cell disease much more effective and pave the way for wider use of it as a curative approach for the painful, life-threatening blood disorder. Sickle cell disease affects about 100,000 people in the United States and millions worldwide.

Advances in cancer treatment
Cancer remains a leading cause of death in the United States and around the world. Complicating matters is the fact that cancer is not a single disease but is a complex of more than 100 diseases in which genetic changes disrupt cell function. Given the complicated nature of cancer, it is essential to harness new technologies and approaches to treat this often-deadly condition. Leveraging new knowledge of the precise factors that influence disease, NIH is pioneering the use of precision medicine in treatment approaches to better target the right treatments to the right people.

Beau Biden Cancer Moonshot. The initiative is designed to accelerate cancer research, to make more therapies available to more patients, while also improving our ability to prevent cancer and

[25] www.nih.gov/news-events/news-releases/nih-researchers-create-new-viral-vector-improved-gene-therapy-sickle-cell-disease

detect it at an early stage.[26] Because of the broad scope of the Moonshot, this initiative has the potential to impact all cancer patients, including the 1.9 million U.S. patients who are expected to be diagnosed with cancer in 2021, and the nearly 18 million cancer survivors in the United States.[27] More effective prevention, diagnostic, and treatment methods will help to reduce the financial and psychosocial burdens placed on cancer patients and their families.

Pediatric cancers. Enormous strides have been made in the treatment of childhood acute leukemia, where the cure rate now stands at well over 90 percent. But the science of understanding other types of pediatric cancer is especially challenging, and too many children and adolescents still die from rare brain tumors, sarcomas, and other malignancies. Many others endure lifelong adverse effects from their cancers or their treatment.

The Childhood Cancer Data Initiative (CCDI) is building a data resource that will aggregate data from pediatric cancer cases and coordinate with partners that maintain data sets on pediatric patients to create a federated, comprehensive, and shared resource to support research to develop new, more effective, and safer treatments for childhood cancers, and will complement ongoing research within the National Cancer Institute (NCI) and the Cancer Moonshot. This knowledge, spanning from basic biology to clinical outcomes, can provide a path for changing the course of cancer in all children.

In June 2020, the Board of Scientific Advisors (BSA) Ad Hoc Working Group (WG) in Support of the CCDI released a report to provide general guidance to NCI regarding considerations for future CCDI priorities.[28] The report, which was unanimously accepted, provided guidance to NCI in implementing the CCDI so that this new resource will enable broad, rapid data sharing in ways that will optimally facilitate childhood, adolescent and young adult (AYA) cancer research and accelerate the development of better and less toxic therapies for the benefit of pediatric and AYA cancer patients and their families.

Disease Prevention and Health Promotion

Disease prevention has been a central component of the NIH mission from its earliest days. Today, along with investments in fundamental science and treatments and cures, the NIH continues to emphasize health promotion and disease prevention as a key strategy for advancing opportunities in biomedical research. Prevention research targets biology, individual behavior, factors in the social and physical environments, and health services, and informs and evaluates health-related guidelines, policies, and regulations. Advances in these areas are possible because of a comprehensive approach to research that includes basic, translational, clinical, population science, and epidemiology.

Vaccines

Vaccines represent the safest, most cost-effective, and efficient way to reduce the burden of infectious diseases—by preventing them altogether. Creating a safe and effective vaccine often requires understanding how a particular virus or bacteria infects the human body, as well as the

[26] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative
[27] seer.cancer.gov/statfacts/html/all.html
[28] www.cancer.gov/research/areas/childhood/childhood-cancer-data-initiative

various molecules that the immune system might use to target it, requiring a multi-pronged research approach. NIH engages in vaccine research to prevent many diseases, including both emerging threats and recurring maladies.

The COVID-19 pandemic has shone light on the importance of vaccines for a healthy and prosperous nation. Building on previous research on Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), NIH scientists and grantees were positioned to rapidly develop COVID-19 vaccine candidates for testing in clinical trials. A coordinated effort across the U.S. government is supporting the rapid conduct of these clinical trials and making sure that millions of doses of safe and effective vaccines are available to the public.[29] With major contributions from the ACTIV[30] initiative, a remarkable public-private partnership involving multiple biopharmaceutical companies, academic experts, non-profit organizations, and federal agencies, NIH experts have advised on the protocol design for each of the trials. Additionally, NIH experts are members of each trial oversight group—along with the sponsor and BARDA—that receives recommendations from the vaccine trials' Data and Safety Monitoring Board. A summary of clinical trials of COVID-19 vaccine candidates is available on the NIH ACTIV vaccines page.[31]

Eliminating HIV/AIDS

NIH-supported basic research has allowed us to gain a deep understanding of the biology of HIV. This, in turn, has led to the development of effective treatments, rapid diagnostics, and other approaches that now allow HIV-infected individuals to live a nearly normal lifespan. This is an amazing accomplishment considering that at the beginning of the HIV epidemic, there were limited treatment options, aside from palliative care, and infection meant early death.

Ending the HIV Epidemic (EHE). As part of the new effort, Centers for AIDS Research (CFAR) and HIV/AIDS Research Centers (ARCs) will build on existing relationships with local health authorities, community-based groups, and other HHS agencies involved in the EHE initiative, including the Centers for Disease Control and Prevention (CDC) and the Health Resources and Services Administration (HRSA).[32] With these partners, researchers work to identify and evaluate strategies to diagnose new cases of HIV, help connect people living with HIV or at risk of HIV acquisition with medical care and HIV prevention services, and ensure they continue to receive care to treat or prevent HIV. With much of the needed research infrastructure already in place, this effort is expected to yield critical findings with modest funding. This new initiative focuses on implementing proven HIV treatment and prevention tools. These include daily antiretroviral therapy that suppresses HIV to undetectable levels, which benefits people living with HIV and prevents sexual transmission of the virus to others (Undetectable=Untransmittable); pre-exposure prophylaxis (PrEP), a single pill that can reduce the risk of acquiring HIV by more than 95 percent when taken daily; and emergency post-exposure prophylaxis (PEP), which can prevent HIV infection if begun within three days of exposure and taken for an additional 28 days. Implementation strategies that demonstrate

[29] www.niaid.nih.gov/diseases-conditions/covid-19-vaccine-faq#OWS
[30] www.nih.gov/research-training/medical-research-initiatives/activ
[31] www.nih.gov/research-training/medical-research-initiatives/activ/sars-cov-2-vaccine-clinical-trials-using-activ-informed-harmonized-protocols
[32] www.nih.gov/news-events/news-releases/nih-bolsters-funding-hiv-implementation-research-high-burden-us-areas

success in these initial research locations will be shared as best practices to inform efforts in other jurisdictions. The FY 2022 Budget includes a $10.0 million increase for CFARs to support the EHE initiative.

Personalized Nutrition
Good nutrition is essential for healthy development and basic survival, but it is also integral to well-being and disease prevention. Health conditions linked to poor diet constitute the most frequent and preventable causes of death in the United States and are major drivers of health care costs, estimated in the hundreds of billions of dollars annually.[33] The 2020-2030 Strategic Plan for NIH Nutrition Research, released in May 2020, presents a bold, unifying vision emergent as "Precision Nutrition."[34] An important constituent of Precision Medicine, Personalized Nutrition in research and practice considers multiple, synergistic levels of influence: dietary habits, genetic background, health status, microbiome, metabolism, food environment, physical activity, socioeconomics, psychosocial characteristics, and environmental exposures. This emerging research agenda promises to deepen understanding of the interactions between what, when, why, and how we eat; how our body systems process our diet and influence the microbiome; as well as how food environments influence health and disease.

Areas of Continued Investment

This is a remarkable time in biomedical research. Truly exciting, world-class science is taking place through NIH support, and leading to breakthroughs in multiple areas as described above. However, there is still much to be done. NIH sees the opportunity for many promising areas of research in the future.

Increasing Research Capacity Through Partnerships
Translating NIH's basic research findings into treatments and cures requires efficient collaborations within NIH as well as with other government, academic, industry, and non-profit partners. NIH works closely with federal partners to streamline processes, collaborate on research projects, and share the agency's evidence base to catalyze efforts across the government to improve health for all Americans. Partnerships also enable the public and private sectors to work synergistically toward medical advances, accomplishing goals that cannot readily be achieved by acting alone. Leveraging resources and expertise, NIH is engaged in several significant partnerships addressing issues from Alzheimer's disease to HIV through bold public-private partnerships (PPPs) such as the Accelerating Medicines Partnership (AMP), the Partnership for Accelerating Cancer Therapies (PACT), and now ACTIV. In one such effort, NIH has partnered with The Bill & Melinda Gates Foundation to develop affordable, gene-based cures for sickle cell disease and HIV.[35] Continued emphasis on PPPs will ensure NIH's careful stewardship of public funds and increase the pace of research to benefit patients more quickly.

[33] www.cdc.gov/chronicdisease/about/costs/index.htm
[34] www.niddk.nih.gov/about-niddk/strategic-plans-reports/strategic-plan-nih-nutrition-research
[35] www.nih.gov/news-events/news-releases/nih-launches-new-collaboration-develop-gene-based-cures-sickle-cell-disease-hiv-global-scale

Communicating Results to Inform Future Research

NIH continues to promote policies and programs that foster and ensure a strong foundation and culture of good scientific stewardship. As critical research needs arise, NIH will respond by ensuring the scientific community has flexibility to quickly adapt and address urgent public health issues. This is exemplified by the NIH response to the COVID-19 pandemic with the rapid emergence of the OpenData COVID-19 portal,[36] expanded access to coronavirus literature through PubMed Central® (PMC),[37] as well as a preprint pilot to accelerate dissemination of research related to the SARS-CoV-2 virus and COVID-19.[38]

These new resources are built on existing NIH platforms for the communication of research results such as *PubMed* and *ClinicalTrials.gov*. *PubMed* is the most heavily used biomedical literature citation database in the world and enables the communication and discovery of scientific literature across the globe. PMC provides public access to the full text of more than 6 million scientific articles. PMC offers text mining access to over 3 million articles, facilitates linking between articles and associated data, and supports discovery of these data by aggregating data citations, data availability statements, and supplementary materials. Results from clinical studies are made available through NIH's *ClinicalTrials.gov*, the largest public clinical research registry and results database in the world. It provides patients, health care providers, and researchers with information on over 330,000 registered studies, including studies with summary results, many of which are not otherwise available through the published literature. A multi-year effort is underway to modernize *ClinicalTrials.gov* to deliver an improved user experience on an updated platform that will accommodate growth and improve efficiency.

Conclusion

The Nation's investment in NIH is born from the recognition that a healthy population is a productive and thriving population. The benefits of NIH research may be felt in the near term through development of novel health interventions and continue well into the future, as transformations in the diagnosis, prevention, and treatment of disease today become standard practice tomorrow. For example, thanks in large part to NIH research, survival rates for respiratory distress syndrome in newborns have improved from 5 percent in the 1960s to 95 percent currently. The infants who now survive what was once a deadly condition will live to become productive adults, potentially with children of their own and on into future generations.

A healthier nation is a more productive and economically sound nation. Each permanent 1 percent reduction in cancer deaths alone has been approximated to have a value of nearly $500 billion to current and future generations of Americans. A full cure could be worth more than three times today's GDP.[39]

[36] opendata.ncats.nih.gov/covid19/
[37] www.nlm.nih.gov/news/Expanding_Access_Coronavirus_Literature.html
[38] www.nlm.nih.gov/news/Preprint_Pilot.html
[39] ucema.edu.ar/u/je49/capital_humano/Murphy_Topel_JPE.pdf

NIH is at the vanguard of biomedical research, leading the world in support of groundbreaking science. Strategically investing in scientific opportunities such as those described above will help NIH ensure the United States remains at the forefront of innovation and discovery.

OVERVIEW OF PERFORMANCE

The NIH mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. Investments in basic biomedical and behavioral research make it possible to understand the causes of disease onset and progression, design preventive interventions, develop better diagnostics, and discover new treatments and cures. Realizing the benefits of fundamental biomedical discoveries depends on the translation of that knowledge into the development of new diagnostics, therapeutics, and preventive measures to improve health. Investments in translational research are leading to the identification of new targets and pathways for the development of new therapeutics.

The FY 2022 budget request reflects the Agency's longstanding commitment to invest strategically using performance-based analysis, as emphasized in the Government Performance and Results Act (GPRA) (P.L. 103-62), as amended by the GPRA Modernization Act of 2010 (P.L. 111-352). Through the continuous evaluation and strategic management of its research portfolio, NIH focuses on funding research that shows the greatest promise for improving the overall health of the American people. In addition, NIH continually seeks to identify and address high-priority scientific opportunities and emerging public health needs. By managing its research portfolio to support key research priorities, NIH ensures the most effective use of funds to achieve the greatest impact on the health and welfare of the Nation. In particular, NIH's strong peer-review process, site visits, performance monitoring, program evaluation, and performance-based contracting enable the Agency to ensure that its investments generate results for the American people.

NIH strives to achieve transparency and accountability by regularly reporting results, achievements, and the impact of its activities. To increase transparency and promote effective use of resources, NIH began reporting the amount of indirect costs paid per grant on its Research Portfolio Online Reporting Tools website (NIH RePORT[40]) in October 2013. NIH supports a wide spectrum of biomedical and behavioral research and engages in a full range of activities that enable research, its management, and the communication of research results. Because of this diversity and complexity, NIH uses a set of performance measures that is representative of its activities and is useful for tracking progress in achieving performance priorities. This representative approach has helped NIH to share progress of its performance priorities with HHS, the rest of the Executive Branch, the Congress, and the public.

Collectively, the NIH performance measures reflect the Agency's overall goals to: 1) advance the full continuum of biomedical research; 2) strengthen the scientific workforce and biomedical research infrastructure; 3) facilitate the communication of research findings and transfer of knowledge to other sectors for further development; and 4) enhance internal management processes, policies, and systems to support programmatic and organizational oversight. Furthermore, the measures support the Administration's goal of protecting and improving the health and well-being of the American people. In particular, NIH substantially contributes to HHS Strategic Goal 4 – Foster Sound, Sustained Advances in the Sciences. For example, in

[40] https://report.nih.gov/

support of Objective 4.3 (Advance basic science knowledge and conduct applied prevention and treatment research to improve health and development) under Goal 4, NIH continues to support promising research with the goals of: 1) developing, optimizing, and evaluating the effectiveness of nano-enabled immunotherapy (nano-immunotherapy) for one cancer type; 2) evaluating the safety and effectiveness of one to three long-acting strategies for the prevention of HIV; and 3) identifying risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease.

Performance Management

Performance management at NIH is an integrated and collaborative process to ensure that the Agency is achieving its mission to conduct and support research to improve public health. At the Agency level, the NIH Director sets priorities, monitors performance, and reviews results across the 27 Institutes and Centers (ICs) and the Office of the Director (OD). OD is the central office responsible for setting policy for NIH, and for planning, managing, and coordinating the programs and activities of all NIH components. The NIH Director provides leadership to the ICs and helps identify needs and opportunities, especially for efforts that involve multiple ICs. ICs and OD offices carry out priority setting, performance monitoring, and progress reviews, and also make adjustments based on progress achieved in their respective areas of science. In addition to the performance management processes that occur for the NIH research program, there are equivalent processes for administrative management functions.

The NIH performance framework includes: 1) priority setting with input from key stakeholders; 2) implementation and management of activities that support priorities; 3) monitoring and assessment of progress, and identification of successes and challenges; 4) oversight by IC leadership and OD office directors in assessing overall progress toward priorities and identification of best practices, appropriate next steps, and corrective actions (as needed); 5) incorporation of regular feedback from IC and OD office leadership to enhance activities; 6) regular reviews of priorities, progress, and outcomes by the NIH Director and IC Directors; and 7) regular review of performance and priorities by external expert review groups including grant peer-review groups, Advisory Councils, and ad hoc working groups.

Qualitative and quantitative information is used to monitor progress and help to identify successes, as well as obstacles in achieving short- and long-term goals. Supporting high-performing research is a process of adapting to new developments or newly identified barriers, or shifting resources to pursue promising unanticipated results that may provide critical new information. Moreover, the impact of research may not be immediately known and may depend on additional development or on advances in other fields. Despite these challenges, NIH leadership is able to manage performance effectively by using the best available information to assess progress toward achieving priorities and making appropriate adjustments.

The vast majority of scientific research carried out through NIH support is subjected to a rigorous and consistently applied review process. For example, the Extramural Research Program, which accounts for the majority of NIH-funded research, utilizes two levels of peer review. The first level, in which scientific excellence is assessed, consists of chartered scientific review groups composed of outside experts in particular scientific disciplines. The second level,

in which public health relevance is assessed, is conducted by National Advisory Councils of the ICs. For the Intramural Research Program, the progress of individual scientists and their laboratories is evaluated once every four years by Boards of Scientific Counselors composed of external experts. These reviews enable ongoing assessments of all intramural labs and the accomplishments of the scientists who contribute to them. It is through this well-honed system of peer review that NIH maintains its focus on supporting research of the highest possible quality with the greatest potential of furthering NIH's mission. The ARPA-H program will utilize a more nimble approach to funding decisions, following the DARPA model where expert program managers are provided with considerable flexibility in recruiting participants, and given authority to make decisions about project initiation, expansion, or termination built around rigorous milestones.

The NIH approach to performance management is undergirded by the NIH Governance Structure. That structure includes the NIH Steering Committee and standing Working Groups.[41, 42] Ad-hoc working groups are established, as needed, to address emerging issues. The premise of the structure is that shared governance, which depends on the active participation of the IC Directors with the NIH Director, will foster the collaborative identification of corporate issues and a transparent decision-making process. With active participation by the IC Directors in NIH-wide governance, NIH can maximize its perspective and expertise in the development and oversight of policies common to NIH and its ICs. Through the governance process, corporate decisions are made; these may be long-term and strategic (e.g., facilities planning, budget strategy, and research policy direction) or short-term and tactical (e.g., stipend levels, resource allocations, and compliance oversight). This process does not include issues related to the setting of scientific priorities, which is reserved for meetings of all IC Directors. The NIH Director meets with the IC Directors on a bi-weekly basis, and scientific initiatives are discussed, as well as major management issues that affect the Agency. In addition, scientists – from within and outside the Agency – are invited to present on new or emerging research opportunities. The NIH Director stays informed of priorities through regular meetings with IC and OD Office Directors. Similarly, the IC Directors monitor performance through regular meetings with the Division Directors and Scientific/Clinical Directors in their respective ICs.

Based on these reviews, leadership and their staff take appropriate actions to support research activities. For example, the reviews may lead to the development of new award programs for early-career researchers, the development of new funding announcements for promising research areas, or new collaborations across NIH and/or with other Federal and non-Federal partners. The NIH Director and senior leadership receive regular updates on the progress of the priorities, provide feedback, and incorporate the latest information into the NIH's overall planning and management efforts. This constant feedback loop enables NIH to make critical adjustments periodically to align activities and target resources in support of its research priorities.

[41] The NIH Steering Committee is composed of the NIH Director, Deputy Director (ex-officio), the Directors of the National Cancer Institute, National Heart, Lung, and Blood Institute, and National Institute of Allergy and Infectious Diseases, as well as a balance of Directors from the smaller and medium-sized institutes.
[42] The standing working groups are: Extramural Activities, Diversity, Facilities, Management and Budget, Scientific Data Council, Administrative Data Council, Data Science Policy Council, Clinical Center Governing Board, Board of Scientific Counselors, and Research Services Working Group.

ALL-PURPOSE TABLE

(Dollars in Thousands)[1,2]	FY 2020 Final[5]	FY 2020 Supplemental Funding[6]	FY 2021 Enacted[5]	FY 2021 Supplemental Funding[7]	FY 2022 President's Budget[5]	FY 2022 +/- FY 2021
Total, NIH Program Level	**$41,685,000**	**$3,587,400**	**$42,935,500**	**$1,250,000**	**$51,952,703**	**$9,017,203**
Less mandatory and funds allocated from different sources:						
PHS Program Evaluation	1,230,821		1,271,505		1,271,505	0
Mandatory Type 1 Diabetes Research	150,000		150,000		141,450	-8,550
Total, NIH Discretionary Budget Authority	**$40,304,179**	**$3,587,400**	**$41,513,995**	**$1,250,000**	**$50,539,748**	**$9,025,753**
Interior Budget Authority	81,000		81,500		83,540	2,040
Total, NIH Labor/HHS Budget Authority	**$40,223,179**	**$3,587,400**	**$41,432,495**	**$1,250,000**	**$50,456,208**	**$9,023,713**
Number of Competing RPGs	*11,395*		*11,189*		*12,664*	*1,475*
Total Number of RPGs	*41,643*		*42,083*		*44,343*	*2,260*
FTE[3]	*17,623*		*18,785*		*19,303*	*518*
NEF[4]						
Surgery, Radiology, and Laboratory Medicine Building	*212,400*		*225,000*		*NA*	*NA*
Building 10 Building Automation System Replacement	*12,600*		*0*		*NA*	*NA*

[1] Numbers may not add due to rounding.

[2] Includes 21st Century Cures Act funding.

[3] FTE levels include 4 NIH FTEs funded by PHS trust funds in FY 2020 through FY 2022.

[4] Amounts for FY 2020 reflect amounts allocated for NIH from the NEF by sec. 237 of Division A of P.L. 116-94. Amounts for FY 2021 reflect amounts allocated for NIH from the NEF by sec. 237 of Division H of P.L. 116-260.

[5] Amounts for FY 2020 through FY 2022 reflect directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

[6] Shows supplemental funds post-transfer.

[7] This column includes funding appropriated in P.L. 116-260, post-transfer.

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2021 Enacted**	**FY 2022 President's Budget**	**FY 2022 +/- FY 2021**
Research Project Grants	$24,559.013	$26,227.757	6.8%
Competing Average Cost (in thousands)	$580.276	$567.892	-2.1%
Number of Competing Awards (whole number)	11,189	12,664	13.2%
Estimated Competing RPG Success Rate	20.1%	22.1%	10.0%
Research Centers	$2,778.539	$2,872.575	3.4%
Other Research	$2,996.908	$3,096.571	3.3%
Training	$951.864	$1,019.196	7.1%
Research & Development Contracts	$3,362.683	$3,561.276	5.9%
Intramural Research	$4,548.996	$4,695.985	3.2%
Research Management and Support	$2,090.554	$2,184.166	4.5%
Common Fund (non-add)	*$648.539*	*$658.539*	*1.5%*
Advanced Research Projects Agency for Health	$0.000	$6,500.000	N/A
Buildings & Facilities Appropriation	$200.000	$250.000	25.0%
Other Mechanisms[1,2]	$1,446.943	$1,545.176	6.8%
Total, Program Level[3]	**$42,935.500**	**$51,952.703**	**21.0%**

[1] Includes Office of the Director-Other, Buildings and Facilities funding in the National Cancer Institute, and Superfund Research activities funded from the Interior appropriations bill.

[2] Amounts reflect directive transfer of $5.0 million to the HHS Office of Inspector General.

[3] Includes discretionary budget authority received from Labor/HHS appropriations bill and the Interior appropriations bill (Superfund). Also includes program evaluation financing and mandatory budget authority derived from the Type 1 Diabetes account.

APPROPRIATIONS LANGUAGE

NATIONAL CANCER INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cancer, [$6,364,852,000]*$6,539,302,000*, of which up to $30,000,000 may be used for facilities repairs and improvements at the National Cancer Institute-Frederick Federally Funded Research and Development Center in Frederick, Maryland.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cardiovascular, lung, and blood diseases, and blood and blood products, [$3,664,811,000]*$3,845,681,000*.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to dental and craniofacial diseases, [$484,867,000]*$516,197,000*.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to diabetes and digestive and kidney disease, [$2,131,975,000]*$2,219,298,000*.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

For carrying out section 301 and title IV of the PHS Act with respect to neurological disorders and stroke, [$2,463,393,000]*$2,707,300,000*.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to allergy and infectious diseases, [$6,069,619,000]*$6,245,926,000*.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to general medical sciences, [$2,991,417,000]*$3,096,103,000*, of which $1,271,505,000 shall be from funds available under section 241 of the PHS Act: *Provided*, That not less than [$396,573,000]*$410,453,000* is provided for the Institutional Development Awards program.

EUNICE KENNEDY SHRIVER NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

For carrying out section 301 and title IV of the PHS Act with respect to child health and human development, [$1,590,337,000]*$1,942,117,000*.

NATIONAL EYE INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, [$835,714,000]*$858,535,000*.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to environmental health sciences, [$814,675,000]*$937,107,000*. (Department of Health and Human Services Appropriations Act, 2021.)

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For necessary expenses for the National Institute of Environmental Health Sciences in carrying out activities set forth in section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (42 U.S.C. 9660(a)) and section 126(g) of the Superfund Amendments and Reauthorization Act of 1986, [$81,500,000]*$83,540,000*. (Department of the Interior, Environment, and Related Agencies Appropriations Act, 2021.)

NATIONAL INSTITUTE ON AGING

For carrying out section 301 and title IV of the PHS Act with respect to aging, [$3,899,227,000]*$4,035,591,000*.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

For carrying out section 301 and title IV of the PHS Act with respect to arthritis and musculoskeletal and skin diseases, [$634,292,000]*$680,186,000*.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

For carrying out section 301 and title IV of the PHS Act with respect to deafness and other communication disorders, [$498,076,000]*$511,792,000*.

NATIONAL INSTITUTE OF NURSING RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to nursing research, [$174,957,000]*$199,755,000*.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

For carrying out section 301 and title IV of the PHS Act with respect to alcohol abuse and alcoholism, [$554,923,000]*$570,165,000*.

NATIONAL INSTITUTE ON DRUG ABUSE

For carrying out section 301 and title IV of the PHS Act with respect to drug abuse, [$1,479,660,000]*$1,852,503,000*.

NATIONAL INSTITUTE OF MENTAL HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to mental health, [$2,053,708,000]*$2,137,574,000*.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to human genome research, [$615,780,000]*$632,973,000*.

NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING

For carrying out section 301 and title IV of the PHS Act with respect to biomedical imaging and bioengineering research, [$410,728,000]*$422,039,000*.

NATIONAL CENTER FOR COMPLEMENTARY AND INTEGRATIVE HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to complementary and integrative health, [$154,162,000]*$184,323,000*.

NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES

For carrying out section 301 and title IV of the PHS Act with respect to minority health and health disparities research, [$390,865,000: *Provided*, That funds may be used to implement a reorganization that is presented to an advisory council in a public meeting and for which the Committees on Appropriations of the House of Representatives and the Senate have been notified 30 days in advance] *$652,244,000*.

JOHN E. FOGARTY INTERNATIONAL CENTER

For carrying out the activities of the John E. Fogarty International Center (described in subpart 2 of part E of title IV of the PHS Act), [$84,044,000]*$96,322,000*.

NATIONAL LIBRARY OF MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to health information communications, [$463,787,000]*$474,864,000*: *Provided*, That of the amounts available for improvement of information systems, $4,000,000 shall be available until September 30, [2022]*2023*: *Provided further*, That in fiscal year [2021]*2022*, the National Library of Medicine may enter into personal services contracts for the provision of services in facilities owned, operated, or constructed under the jurisdiction of the National Institutes of Health (referred to in this title as "NIH").

NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to translational sciences, [$855,421,000]*$878,957,000*: *Provided*, That up to [$60,000,000]*10 percent of the amounts made available under this heading* shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network[: *Provided further*, That at least $586,841,000 is provided to the Clinical and Translational Sciences Awards program].

OFFICE OF THE DIRECTOR

[(INCLUDING TRANSFER OF FUNDS)]

For carrying out the responsibilities of the Office of the Director, NIH, [$2,411,110,000]*$2,237,259,000*: *Provided*, That funding shall be available for the purchase of not to exceed 29 passenger motor vehicles for replacement only: *Provided further*, That all funds credited to the NIH Management Fund shall remain available for one fiscal year after the fiscal year in which they are deposited: *Provided further*, That [$180,000,000 shall be for the

Environmental Influences on Child Health Outcomes study: *Provided further*, That] [$635,939,000]*$645,939,000* shall be available for the Common Fund established under section 402A(c)(1) of the PHS Act: *Provided further*, That of the funds provided, $10,000 shall be for official reception and representation expenses when specifically approved by the Director of the NIH: *Provided further*, That the Office of AIDS Research within the Office of the Director of the NIH may spend up to $8,000,000 to make grants for construction or renovation of facilities as provided for in section 2354(a)(5)(B) of the PHS Act: *Provided further*, That [$50,000,000] *up to $30,000,000* shall be used to carry out section 404I of the PHS Act (42 U.S.C. [283K), relating to biomedical and behavioral research facilities]*283k) with respect to the National Primate Research Centers and Caribbean Primate Research Center*: *Provided further*, That $5,000,000 shall be transferred to and merged with the appropriation for the "Office of Inspector General" for oversight of grant programs and operations of the NIH, including agency efforts to ensure the integrity of its grant application evaluation and selection processes, and shall be in addition to funds otherwise made available for oversight of the NIH: *Provided further*, That the funds provided in the previous proviso may be transferred from one specified activity to another with 15 days prior [approval of] *notification to* the Committees on Appropriations of the House of Representatives and the Senate: *Provided further*, That the Inspector General shall consult with the Committees on Appropriations of the House of Representatives and the Senate before submitting to the Committees an audit plan for fiscal years [2021 and]2022 *and 2023* no later than 30 days after the date of enactment of this Act*: Provided further, That amounts available under this heading are also available to establish, operate, and support the Research Policy Board authorized by section 2034(f) of the 21st Century Cures Act*.

In addition to other funds appropriated for the Common Fund established under section 402A(c) of the PHS Act, $12,600,000 is appropriated to the Common Fund [from the 10-year Pediatric Research Initiative Fund described in section 9008 of title 26, United States Code,] for the purpose of carrying out section 402(b)(7)(B)(ii) of the PHS Act (relating to pediatric research), as authorized in the Gabriella Miller Kids First Research Act*, of which $3,000,000 shall be derived from the 10-year Pediatric Research Initiative Fund described in section 9008 of title 26, United States Code*. (Department of Health and Human Services Appropriations Act, 2021.)

[(INCLUDING TRANSFER OF FUNDS)]

[For an additional amount for "Office of the Director", $1,250,000,000, to remain available until September 30, 2024, to prevent, prepare for, and respond to coronavirus, domestically or internationally: *Provided*, That of the amount appropriated under this heading in this Act, $1,150,000,000 shall be provided for research and clinical trials related to long-term studies of COVID-19: *Provided further*, That of the amount appropriated under this heading in this Act, no less than $100,000,000 shall be for the Rapid Acceleration of Diagnostics: *Provided further*, That funds appropriated under this heading in this Act may be transferred to the accounts of Institutes and Centers of the National Institutes of Health (NIH): *Provided further*, That this transfer authority is in addition to any other transfer authority available to the NIH: *Provided further*, That such amount is designated by the Congress as being for an emergency requirement pursuant to section 251(b)(2)(A)(i) of the Balanced Budget and Emergency Deficit Control Act of 1985.] (Coronavirus Response and Relief Supplemental Appropriations Act, 2021.)

BUILDINGS AND FACILITIES

For the study of, construction of, demolition of, renovation of, and acquisition of equipment for, facilities of or used by NIH, including the acquisition of real property, [$200,000,000]*$250,000,000*, to remain available through September 30, [2025]*2026*. (Department of Health and Human Services Appropriations Act, 2021.)

NIH INNOVATION ACCOUNT, CURES ACT

(INCLUDING TRANSFER OF FUNDS)

For necessary expenses to carry out the purposes described in section 1001(b)(4) of the 21st Century Cures Act, in addition to amounts available for such purposes in the appropriations provided to the NIH in this Act, [$404,000,000]*$496,000,000*, to remain available until expended: *Provided*, That such amounts are appropriated pursuant to section 1001(b)(3) of such Act, are to be derived from amounts transferred under section 1001(b)(2)(A) of such Act, and may be transferred by the Director of the National Institutes of Health to other accounts of the National Institutes of Health solely for the purposes provided in such Act: *Provided further*, That upon a determination by the Director that funds transferred pursuant to the previous proviso are not necessary for the purposes provided, such amounts may be transferred back to the Account: *Provided further*, That the transfer authority provided under this heading is in addition to any other transfer authority provided by law. (Department of Health and Human Services Appropriations Act, 2021.)

ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to advanced research projects for health, $6,500,000,000, to remain available through September 30, 2024.

GENERAL PROVISIONS

SEC. 216. Not to exceed [$45,000,000] *1 percent* of funds appropriated by this Act to the *offices,* institutes and centers of the National Institutes of Health may be [used for alteration, repair, or improvement of facilities, as necessary for the proper and efficient conduct of the activities authorized herein, at not to exceed $3,500,000 per project] *transferred to and merged with funds appropriated under the heading "National Institutes of Health-Buildings and Facilities": Provided, That the use of such transferred funds shall be subject to a centralized prioritization and governance process: Provided further, That the Director of the National Institutes of Health shall notify the Committees on Appropriations of the House of Representatives and the Senate at least 15 days in advance of any such transfer: Provided further, That this transfer authority is in addition to any other transfer authority provided by law*. (Department of Health and Human Services Appropriations Act, 2021.)

LANGUAGE ANALYSIS

Language Provision to be Changed	Explanation/Justification
NATIONAL INSTITUTE ON MINORITY HEALTH AND HEALTH DISPARITIES [: *Provided*, That funds may be used to implement a reorganization that is presented to an advisory council in a public meeting and for which the Committees on Appropriations of the House of Representatives and the Senate have been notified 30 days in advance].	This provision may be removed, since the reorganization of NIMHD is expected to be completed by the end of FY 2021.
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES *Provided*, That up to [$60,000,000]*10 percent of the amounts made available under this heading* shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network	The unique authorities associated with the Cures Acceleration Network (CAN) – use of Other Transactions Authority (OTA) and matching funding – give NCATS flexibility to quickly create or terminate parts of an initiative based on programmatic need and scientific priority. Specifying the CAN ceiling as a percentage of the overall NCATS budget ensures that CAN funding adjusts relative to overall funding levels and enables NCATS to plan CAN activities more strategically.
NATIONAL CENTER FOR ADVANCING TRANSLATIONAL SCIENCES [: *Provided further*, That at least $586,841,000 is provided to the Clinical and Translational Sciences Awards program].	The removal of this provision would give NCATS flexibility in the amounts allocated to the Clinical and Translational Sciences Awards (CTSA) program in order to preserve flexibility in managing its budget within the President's Budget request level.
OFFICE OF THE DIRECTOR [$180,000,000 shall be for the Environmental Influences on Child Health Outcomes study: *Provided further*, That]	The removal of this provision permits a planned transfer of the ECHO program from OD to NICHD.
OFFICE OF THE DIRECTOR That [$50,000,000] *up to $30,000,000* shall be used to carry out section 404I of the PHS Act (42 U.S.C. [283K), relating to biomedical and behavioral research facilities]*283k) with respect to the National Primate Research*	The FY 2022 President's Budget does not request continued funding for the construction and renovation of extramural research facilities. It proposes refocusing funding on non-human primate infrastructure.

Language Provision to be Changed	Explanation/Justification
Centers and Caribbean Primate Research Center	
OFFICE OF THE DIRECTOR *Provided further*, That the funds provided in the previous proviso may be transferred from one specified activity to another with 15 days prior [approval of] *notification to* the Committees on Appropriations of the House of Representatives and the Senate	Revised text clarifies that the requirement in this provision is for Congressional notification of transfers between activities.
OFFICE OF THE DIRECTOR *Provided further, That amounts available under this heading are also available to establish, operate, and support the Research Policy Board authorized by section 2034(f) of the 21st Century Cures Act.*	This provision authorizes the use of funds for the establishment, operation, and support of the Research Policy Board.
OFFICE OF THE DIRECTOR [from the 10-year Pediatric Research Initiative Fund described in section 9008 of title 26, United States Code,] for the purpose of carrying out section 402(b)(7)(B)(ii) of the PHS Act (relating to pediatric research), as authorized in the Gabriella Miller Kids First Research Act*, of which $3,000,000 shall be derived from the 10-year Pediatric Research Initiative Fund described in section 9008 of title 26, United States Code.*	The 10-Year Pediatric Research Initiative Fund is expected to have insufficient balances in FY 2022 to make the $12.6 million appropriation. The provision specifies that the Pediatric Fund will provide the first $3.0 million of the appropriation and the general fund of the Treasury will support the remaining amount.
ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH *For carrying out section 301 and title IV of the PHS Act with respect to advanced research projects for health, $6,500,000,000, to remain available through September 30, 2024.*	This provision provides appropriations for the Advanced Research Projects Agency for Health (ARPA-H).

BUDGET MECHANISM TABLE

Budget Mechanism - Total[1,2,3]

(Dollars in Thousands)[1,2,3]	FY 2020 Final[7,8]		FY 2021 Enacted[7,8]		FY 2022 President's Budget[7,9]		FY 2022 +/- FY 2021	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	28,415	$15,903,452	29,040	$16,402,139	29,718	$17,350,182	678	$948,043
Administrative Supplements[3]	*(2,723)*	555,090	*(2,573)*	509,636	*(2,388)*	456,192	*(-185)*	-53,443
Competing	11,395	$6,395,871	11,189	$6,492,703	12,664	$7,191,779	1,475	$699,075
Subtotal, RPGs	39,810	$22,854,413	40,229	$23,404,478	42,382	$24,998,153	2,153	$1,593,675
SBIR/STTR	1,833	1,127,734	1,854	1,154,534	1,961	1,229,604	107	75,069
Research Project Grants	41,643	$23,982,147	42,083	$24,559,013	44,343	$26,227,757	2,260	$1,668,744
Research Centers:								
Specialized/Comprehensive	999	$1,937,294	1,063	$2,036,557	1,104	$2,132,854	41	$96,297
Clinical Research	70	432,804	67	419,359	66	418,554	-1	-805
Biotechnology	73	125,526	64	102,802	59	93,653	-5	-9,149
Comparative Medicine	48	138,385	51	141,435	52	141,514	1	79
Research Centers in Minority Institutions	21	74,111	22	78,386	25	86,000	3	7,614
Research Centers	1,211	$2,708,120	1,267	$2,778,539	1,306	$2,872,575	39	$94,036
Other Research:								
Research Careers	4,461	$835,776	4,558	$862,683	4,761	$896,618	203	$33,935
Cancer Education	59	14,878	83	20,939	85	21,439	2	500
Cooperative Clinical Research	272	498,295	265	501,540	268	508,255	3	6,715
Biomedical Research Support	125	89,486	131	91,397	130	90,994	-1	-403
Minority Biomedical Research Support	286	98,392	257	88,594	190	66,696	-67	-21,898
Other	2,127	1,273,872	2,265	1,431,756	2,454	1,512,570	189	80,814
Other Research	7,330	$2,810,700	7,559	$2,996,908	7,888	$3,096,571	329	$99,663
Total Research Grants	50,184	$29,500,967	50,909	$30,334,460	53,537	$32,196,903	2,628	$1,862,443
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,919	$186,323	4,005	$196,857	4,106	$209,440	101	$12,584
Institutional Awards	13,089	720,929	13,550	755,007	13,843	809,755	293	54,748
Total Research Training	17,008	$907,252	17,555	$951,864	17,949	$1,019,196	394	$67,332
Research & Develop. Contracts	2,304	$3,295,504	2,355	$3,362,683	2,521	$3,561,276	166	$198,593
(SBIR/STTR) (non-add)[3]	*(109)*	*(71,684)*	*(116)*	*(76,634)*	*(121)*	*(82,267)*	*(5)*	*(5,632)*
Intramural Research		$4,460,682		$4,548,996		$4,695,985		$146,989
Res. Management & Support		1,979,165		2,090,554		2,184,166		93,612
Res. Management & Support (SBIR Admin) (non-add)[3]		*(7,762)*		*(10,128)*		*(10,116)*		*(-11)*
Office of the Director - Appropriation[3,4]		*(2,163,516)*		*(2,283,867)*		*(2,394,859)*		*(110,992)*
Office of the Director - Other		1,230,430		1,335,443		1,431,636		96,194
ORIP (non-add)[3,4]		*(293,976)*		*(299,885)*		*(304,684)*		*(4,798)*
Common Fund (non-add)[3,4]		*(639,111)*		*(648,539)*		*(658,539)*		*(10,000)*
ARPA-H		0		0		6,500,000		6,500,000
Buildings and Facilities[5]		230,000		230,000		280,000		50,000
Appropriation[3]		*(200,000)*		*(200,000)*		*(250,000)*		*(50,000)*
Type 1 Diabetes[6]		-150,000		-150,000		-141,450		8,550
Program Evaluation Financing[6]		-1,230,821		-1,271,505		-1,271,505		0
Subtotal, Labor/HHS Budget Authority		**$40,223,179**		**$41,432,495**		**$50,456,208**		**$9,023,713**
Interior Appropriation for Superfund Research		81,000		81,500		83,540		2,040
Total, NIH Discretionary Budget Authority		**$40,304,179**		**$41,513,995**		**$50,539,748**		**$9,025,753**
Type 1 Diabetes		150,000		150,000		141,450		-8,550
Total, NIH Budget Authority		**$40,454,179**		**$41,663,995**		**$50,681,198**		**$9,017,203**
Program Evaluation Financing		1,230,821		1,271,505		1,271,505		0
Total, Program Level		**$41,685,000**		**$42,935,500**		**$51,952,703**		**$9,017,203**

1 All Subtotal and Total numbers may not add due to rounding.
2 Includes 21st Century Cures Act funding and excludes supplemental financing.
3 All numbers in italics and brackets are non-add.
4 Number of grants and dollars for the Common Fund and ORIP components of OD are distributed by mechanism and are noted here as non-adds. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.
5 Includes B&F appropriation and monies allocated pursuant to appropriations acts provisions such that funding may be used for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
6 Number of grants and dollars for mandatory Type 1 Diabetes (T1D) and NIGMS Program Evaluation financing are distributed by mechanism above; therefore, T1D and Program Evaluation financing amounts are deducted to provide subtotals for Labor/HHS Budget Authority.
7 Reflects transfer of $5.0 million to the HHS OIG.
8 Amounts are adjusted for comparability with the proposed transfer of ECHO and INCLUDE from OD to NICHD in FY 2022.
9 Reflects Type 1 Diabetes Research sequestration of $8.55 million.

AUTHORIZING LEGISLATION

(Dollars in Thousands)	FY 2021 Amount Authorized	FY 2021 Amount Appropriated	FY 2022 Amount Authorized	FY 2022 President's Budget
National Institutes of Health Activity:				
1. Biomedical Research under Section 301 and title IV of the PHS Act:				
General Authorization: Section 402A(a)(1) of the PHS Act[1]	TBD	42,292,400	TBD	51,224,113
Pediatric Research Initiative: Section 402A(a)(2) of the PHS Act	12,600	12,600	12,600	12,600
2. Superfund Research Program: Section 311(a) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, and Section 126(g) of the Superfund Amendments and Reauthorization Act of 1986	Indefinite	81,500	Indefinite	83,540
3. 21st Century Cures Act:				
Precision Medicine: Section 1001(b)(4)(A)	109,000	109,000	150,000	150,000
BRAIN Initiative: Section 1001(b)(4)(B)	100,000	100,000	152,000	152,000
Cancer Moonshot: Section 1001(b)(4)(C)	195,000	195,000	194,000	194,000
4. Special Diabetes Programs: Section 330B(b) of the PHS Act[2]	150,000	150,000	150,000	141,450

[1]The authorization of appropriations expired as of September 30, 2020.

[2]The amount for the Special Diabetes Programs in the FY 2022 President's Budget reflects the reduction due to sequestration.

APPROPRIATIONS HISTORY

Fiscal Year	Budget Request to Congress	House Allowance	Senate Allowance	Appropriation [1]
FY 2013				
Base	$30,852,187,000		$30,810,387,000	$30,929,977,000 [2]
Sequestration				-1,552,593,211
Subtotal	$30,852,187,000		$30,810,387,000	$29,377,383,789
FY 2014	$31,323,187,000		$31,176,187,000	$30,142,653,000
FY 2015	$30,353,453,000		$30,084,304,000	$30,311,349,000 [3]
FY 2016	$31,311,349,000 [4]	$31,411,349,000	$32,311,349,000	$32,311,349,000 [5]
FY 2017	$33,136,349,000 [6]	$33,463,438,000	$34,311,349,000	$34,229,139,000 [7]
FY 2018	$26,919,710,000 [8]	$35,184,000,000	$36,084,000,000	$37,311,349,000 [9]
FY 2019	$34,766,707,000 [10]	$38,564,000,000	$39,312,349,000	$39,313,000,000 [11]
FY 2020	$34,367,629,000 [10]	$41,154,000,000	$42,084,000,000	$41,690,000,000 [12]
FY 2021	$39,133,215,000 [10]	$42,071,000,000	$43,536,500,000	$42,940,500,000 [13]
FY 2022 PB	$51,957,703,000 [14]			

[1] Does not reflect comparability adjustments. Interior appropriation's Superfund Research allocation included for all years. Special Type 1 Diabetes Research mandatory funding included. Includes CURES amounts of $352,000,000 in FY 2017, $496,000,000 in FY 2018, $711,000,000 in FY 2019, $492,000,000 in FY 2020, $404,000,000 in FY 2021, and $496,000,000 in the FY 2022 Request.

[2] Reflects: Full-year continuing resolution base. Does not include Section 3004 OMB 0.2 percent across-the-board rescission.

[3] Includes Program Evaluation Financing of $715,000,000. Excludes Ebola-related funding.

[4] Includes Program Evaluation Financing of $847,489,000.

[5] Includes Program Evaluation Financing of $780,000,000. Excludes Ebola-related and Zika-related funding.

[6] Includes Program Evaluation Financing of $847,489,000.

[7] Includes Program Evaluation Financing of $824,443,000.

[8] Includes Program Evaluation Financing of $780,000,000.

[9] Includes Program Evaluation Financing of $922,871,000. Excludes supplemental hurricane funding of $50,000,000 to the Office of the Director for extramural construction.

[10] Includes Program Evaluation Financing of $741,000,000.

[11] Includes Program Evaluation Financing of $1,146,821,000. Does not reflect $5,000,000 transfer from NIH to the HHS Office of the Inspector General or hurricane disaster supplemental of $1,000,000 for National Institute of Environment Health Sciences.

[12] Includes Program Evaluation Financing of $1,230,821,000. Does not reflect $5,000,000 transfer from NIH to HHS Office of the Inspector General. Also does not reflect three COVID-19 supplementals totaling $3,587,400,000: the amounts are $836,000,000 in P.L. 116-123, $945,400,000 in P.L. 116-136, and $1,806,000,000 in P.L. 116-139 that was provided to NIH through directive transfer from the PHSSEF.

[13] Includes Program Evaluation Financing of $1,271,505,000. Does not reflect $5,000,000 transfer from NIH to HHS Office of the Inspector General. Also does not reflect COVID-19 supplemental of $1,250,000,000 in P.L. 116-260 for the Office of the Director.

[14] Includes Program Evaluation Financing of $1,271,505,000 and reflects the sequestration of the mandatory funding for the Special Type 1 Diabetes Research account. Does not reflect $5,000,000 transfer from NIH to HHS Office of the Inspector General.

APPROPRIATIONS NOT AUTHORIZED BY LAW

	Last Year of Authorization	Authorization Level	Appropriations in Last Year of Authorization	Appropriations in FY 2021
NIH Labor/HHS Budget Authority[1]	FY 2020	$36,472,442,775	$40,954,400,000	$42,292,400,000

[1]Appropriations under general authorization of appropriations in Section 402A(a)(1) of the PHS Act. Excludes appropriations related to the Cures Act and the Gabriella Miller Pediatric Research Initiative.

NARRATIVE BY ACTIVITY TABLE/HEADER TABLE

(Dollars in Thousands)	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Program Level[1,2,3,4]	$41,685,000	$42,935,500	$51,952,703	$9,017,203
FTE[5]	17,623	18,785	19,303	518

[1] All years reflect directive transfer of $5.0 million to the HHS Office of Inspector General.

[2] Includes 21st Century Cures Act funding, Mandatory Type 1 Diabetes, and Superfund in all years; includes Program Evaluation financing of $1,230.8 million in FY 2020 and $1,271.5 million in FY 2021 and FY 2022.

[3] Excludes supplemental appropriations.

[4] Reflects sequestration of $8.55 million for Mandatory Type 1 Diabetes in FY 2022.

[5] Represents NIH target FTE level, including direct funded and reimbursable funded FTE.

Authorizing Legislation: Section 301 and Title IV of the Public Health Act, as amended.

Allocation Methods: Competitive Grants; Contract; Intramural; Other

PROGRAM DESCRIPTIONS AND ACCOMPLISHMENTS

NIH Contributions and Scientific Advances Towards Improving Human Health

NIH is the largest public funder of biomedical research in the world, investing over $40 billion in taxpayer dollars each year to achieve its mission to enhance health, lengthen life, and reduce illness and disability. In pursuing this mission, NIH improves health by promoting treatment and prevention, contributes to society by stimulating economic growth and productivity, and expands the biomedical knowledge base by supporting cutting-edge research and investing in the biomedical workforce of the future.

NIH-funded scientists are making ground-breaking contributions across the full arc of biomedical science — from basic and translational research to clinical research studies. Since the beginning of 2020, NIH has focused intensively on research related to SARS-CoV-2 and COVID-19, including standing up an unprecedented set of efforts to understand this new disease and develop diagnostics, therapeutics, and vaccines to combat the pandemic. The pandemic has posed challenges to conducting research in other areas, but that research continues with necessary precautions. NIH efforts related to SARS-CoV-2 and COVID-19 are described below, followed by examples of selected other recent NIH-funded research accomplishments.

Speeding Towards Treatments, Vaccines and Diagnostics for COVID-19

NIH is part of the trans-governmental effort being led by the Department of Health and Human Services and part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics. In April 2020, NIH received up to $483 million in support for Moderna's then-candidate vaccine for COVID-19 (co-developed with NIH and described further below), which received a fast-track designation from the Food and Drug Administration (FDA) and was authorized for use in December 2020. Additionally, the Department continues to support NIH clinical trials under the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership (ACTIV-2 and ACTIV-3), described further below, to develop monoclonal antibody treatments for COVID-19. The Department will also ensure harmonization among efforts at NIH and those at other agencies including the Biomedical Advanced Research and Development Authority (BARDA), the FDA, the Centers for Disease Control and Prevention (CDC) and the Department of Defense.

NIH-Wide Strategic Plan for COVID-19 Research

To address the unprecedented challenge that the COVID-19 pandemic poses to public health and economy, NIH has mounted a vigorous research response against COVID-19 in coordination with Congress, HHS, the Department of Defense, and partners in the private and public sector. The NIH-Wide Strategic Plan for COVID-19 Research[43] provides a framework for improving, advancing, and optimizing COVID-19-related research in five key areas: fundamental knowledge, detection and diagnosis, treatment, prevention, and health disparities in an effort to improve basic understanding of SARS-CoV-2 and COVID-19 and develop the necessary tools and approaches to better diagnose, prevent, and treat this disease. The Plan includes efforts to expand the capacity for and accuracy of testing and an unprecedented public-private partnership to accelerate development of therapeutics and vaccines. NIH research also will tackle the disturbing disparities seen in the COVID-19 response, with the aim of developing effective,

[43] www.nih.gov/research-training/medical-research-initiatives/nih-wide-strategic-plan-covid-19-research

evidence-based methods to ensure that diagnostics, treatments, and vaccines reach all populations, particularly those disproportionately affected by this devastating disease. Implementation of components of the strategic plan has already begun as NIH develops and tests diagnostics through the Rapid Acceleration of Diagnostics (RADx) effort,[44] develops therapeutics via the ACTIV public-private partnership (PPP)[45] and the COVID-19 Prevention Network,[46] and ramps up testing of a number of candidate vaccines through clinical trials.[47,48] In December 2020, NIH released a Request for Information (NOT-OD-21-018)[49] inviting public comment on the Strategic Plan and anticipates the release of an updated NIH-Wide Strategic Plan for COVID-19 Research, incorporating both public input and evolutions in the COVID-19 pandemic response and research, in mid-2021.

Breakthroughs and Partnerships to Development Therapies and Vaccines for COVID-19
Announced in April 2020, NIH has assembled a distinguished team of senior scientists from government, industry, and academia to lead the ACTIV partnership. This exciting new PPP has four fast-track focus areas, each led by a working group of experts that is developing a collaborative, streamlined forum to identify preclinical treatments, accelerate clinical testing of the most promising vaccines and treatments, improve clinical trial capacity and effectiveness, and speed the evaluation of vaccine candidates to enable rapid authorization or approval. Together, this group has already put into place a framework for advancing COVID-19 therapeutics, vaccines and clinical trials in a matter of months that would normally take years to develop.

Six clinical trial initiatives (ACTIV-1 through ACTIV-6) are currently being developed and launched through this effort. These trials test a wide range of medical countermeasures in both inpatient and outpatient settings, including immune modulators, monoclonal antibodies for prevention and therapy, antithrombotics, and a host of repurposed drugs that have been tested for other indications. As part of this overarching effort, in early August 2020, NIH announced the launch of two ACTIV clinical trials. ACTIV-2 is a phase 2 clinical trial to evaluate monoclonal antibodies (mAbs), including LY-CoV555, in patients who have mild to moderate disease not requiring hospitalization.[50] In November 2020, the FDA issued an Emergency Use Authorization (EUA) for LY-CoV555 for this indication as a result of clinical data from this study. More recent clinical studies have shown that addition of another monoclonal antibody, called etesevimab, to LY-CoV555 provides enhanced clinical benefit and this combination will be pursued together as a new therapy. In April 2021, FDA revoked the EUA for the use of LY-CoV555 alone for treating mild-to-moderate COVID-19 in adults and certain pediatric patients due to issues caused by SARS-CoV-2 variants. Another clinical trial, ACTIV-3, a global Phase 3 randomized, controlled trial testing multiple mAb treatments for COVID-19 (including LY-

[44] www.nih.gov/research-training/medical-research-initiatives/radx
[45] www.nih.gov/research-training/medical-research-initiatives/activ
[46] www.niaid.nih.gov/news-events/niaid-clinical-trials-monoclonal-antibodies-prevent-covid-19-now-enrolling
[47] www.nih.gov/news-events/news-releases/phase-3-clinical-trial-investigational-vaccine-covid-19-begins
[48] www.niaid.nih.gov/news-events/nih-launches-clinical-trials-network-test-covid-19-vaccines-and-other-prevention-tools
[49] grants.nih.gov/grants/guide/notice-files/NOT-OD-21-018.html
[50] www.nih.gov/news-events/news-releases/nih-clinical-trial-test-antibodies-other-experimental-therapeutics-mild-moderate-covid-19

CoV555)[51] using an adaptive two-phase study design that can be modified to test additional experimental therapeutics as they emerge. ACTIV-3 also supports concurrent testing in COVID-19 patients hospitalized with differing levels of disease severity and leverages the clinical trial resources and infrastructure of the National Institute of Allergy and Infectious Diseases (NIAID) and the National Heart, Lung, and Blood Institute (NHLBI). Initial results from ACTIV-3 indicated that LY-CoV555 did not provide any benefit to hospitalized patients with COVID-19.

In addition to these activities supported through ACTIV, NIH has also launched other clinical trials to test additional therapies for COVID-19, including existing antiviral agents known to be effective against related coronaviruses which cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome. In February 2020, the Adaptive COVID-19 Treatment Trial (ACTT) was launched and demonstrated the safety and efficacy of remdesivir in shortening time to recovery. ACTT has since improved on those results, showing additive benefit of baricitinib in hospitalized patients. ACTT provided high quality, interpretable data that contributed to the FDA's licensure of remdesivir and the EUA of baricitinib.

Building upon existing research on related coronaviruses at the NIAID Vaccine Research Center and a research collaboration with Moderna, NIAID scientists were able to initiate development of an mRNA vaccine candidate for COVID-19 as soon as viral sequences were posted on international databases. Sixty-five days later, a Phase 1 clinical trial was launched to evaluate this promising vaccine candidate, and within one year, the vaccine received an EUA by the FDA. By capitalizing on established clinical research infrastructure, NIH facilitated the rapid testing of additional vaccine candidates. These efforts provided the critical data for the FDA issuance of EUAs for two additional vaccine candidates to alleviate the public health crisis caused by COVID-19. Additionally, as variants of SARS-CoV-2 emerge, the need to update these vaccines is imperative. As such, NIH initiated a Phase 1 clinical trial of the Moderna vaccine candidate against the B.1.351 variant to evaluate its safety and immunogenicity.

Lastly, a cancer drug called acalabrutinib, a Bruton tyrosine kinase inhibitor, is known to suppress an overactive immune response found in certain cancers such as lymphoma. In a joint study supported by the National Cancer Institute (NCI) and NIAID published in June 2020, this drug was shown to reduce the need for supplemental oxygen in patients with COVID-19,[52] and is also thought to be part of the disease process in response to SARS-CoV-2 infection. This finding is now being used to design a randomized, controlled clinical trial to further assess the efficacy of this drug in treating severe COVID-19.

Since May 2020, using emergency supplemental appropriations, NCI evaluated more than 100 commercial assays at the COVID-19 Serology Lab in Frederick, Maryland, to assist FDA regulatory decisions. In December 2020, the NCI lab produced the U.S. Serology Standard, a tool that scientists conducting serology studies can use to calibrate their research, to harmonize assays that measure SARS-CoV-2 antibodies, and to make comparisons across studies including different candidate vaccines.

[51] www.nih.gov/news-events/news-releases/nih-launches-clinical-trial-test-antibody-treatment-hospitalized-covid-19-patients

[52] www.nih.gov/news-events/nih-research-matters/cancer-drug-may-reduce-symptoms-severe-covid-19

The NCI Serology Lab is part of an array of programs NCI launched with the emergency appropriation from Congress. Other examples include –

- SeroNet, a large, highly coordinated effort to understand immune response to SARS-CoV-2, the virus responsible for the pandemic. SeroNet involves 25 academic institutions along with the NIAID, other NIH Institutes, and others working to answer fundamental questions about the virus and support vaccine development.
- SeroHub, an NCI effort launched in collaboration with NIAID and the CDC. SeroHub is a central repository for studies of SARS-CoV-2 seroprevalence. Seroprevalence shows how the virus is spreading within the population and allows scientists to better understand populations most at risk for the disease. SeroHub's interactive dashboard allows scientists, clinicians, and policymakers to compare seroprevalence by geography, testing date, and other factors.
- Digital Health Solutions funds businesses and universities to develop user-friendly tools, smartphone apps, and wearable devices to support pandemic response, such as efficiently identifying and tracing contacts with infected individuals. In partnership with the National Institute of Biomedical Imaging and Bioengineering, this NCI initiative is supporting new technologies to meet pandemic-related needs.

Rapid Acceleration of Diagnostics (RADx) for COVID-19

In complement to the efforts focused on therapies and vaccines for COVID-19, the NIH RADx program is a $1.5 billion effort designed to address the COVID-19 pandemic by speeding innovation, commercialization, and implementation of SARS-CoV-2 diagnostic testing.[53] This four-part effort will fund innovative technologies and novel approaches to enhance the speed and accessibility of SARS-CoV-2 tests while seeking opportunities to evaluate effective and equitable strategies for testing and implementation. Across all four RADx initiatives, NIH is working closely with other agencies, including the FDA, CDC and BARDA, to advance these goals and increase the availability of accurate, innovative diagnostic testing.

The four parts of RADx are outlined below, and each component has published calls for applications and ideas, with awards and contracts being awarded starting in late July through 2021.

RADx Tech, which aims to advance innovative technologies, is supporting scientists and inventors through a nationwide competition to expand access to new technologies for SARS-CoV-2 diagnostics and laboratory-based testing. RADx-Advanced Technology Platforms (ATP) reduces barriers for scaling up advanced technologies to increase the capacity for rapid, high-throughput testing infrastructure. These initiatives use a phased review process to identify and advance the most promising candidates. Thirty successful candidates have begun the Phase 2 of the competition.[54] The Phase 2 point-of-care awards include a hand-held device to test for SARS-CoV-2 genetic material with results in 30 minutes, a test kit for nursing homes to detect viral proteins and provide results in 15 minutes, and a compact device which uses isothermal amplification of genetic material and optical detection to provide results in 30 minutes. The promising lab-based approaches include a scale-up of next generation sequencing, a combination of automated testing and bulk shipping of test kits, a microfluidics platform utilizing saliva

[53] www.nih.gov/research-training/medical-research-initiatives/radx
[54] www.nibib.nih.gov/covid-19/radx-tech-program/radx-tech-dashboard

samples, and finally a CRISPR gene-editing system to detect pieces of SARS-CoV-2 genetic material. Together, RADx Tech and RADx-ATP have increased national testing capacity by 6.1 million diagnostic tests per day and supported 17 FDA authorized tests including one over-the-counter test for at-home use as of February 2021.

RADx-Radical (RADx-rad) advances nontraditional approaches and repurposing of existing approaches for SARS-CoV-2 testing such as community-level wastewater surveillance, chemosensory technologies for SARS-CoV-2 detection, and methods to detect COVID-19 severity in children.[55] Other RADx-rad components will support the development of electronic nose technology aiming to detect compounds in breath, saliva, or skin associated with both symptomatic and asymptomatic COVID-19. If successful, this program will lead to a safe, effective, and noninvasive method for detecting SARS-CoV-2 infected individuals in everyday settings. With longer development timelines, RADx-rad projects will address gaps in SARS-CoV-2 testing that may be used in future outbreaks of COVID-19 and other as yet unknown infectious diseases.

RADx-Underserved Populations (RADx-UP) leverages existing partnerships to develop and implement strategies to enable and enhance SARS-CoV-2 testing of underserved, under-resourced, rural, and/or vulnerable populations across the United States. Sites within RADx-UP use large consortiums, multi-site trials, centers and other current networks that have adequate capacity, infrastructure, and established community relationships to support and expand testing efforts. A key feature of RADx-UP is the development of testing strategies to utilize the advances made by the other RADx initiatives in real-world settings. This initiative is also specifically examining the range of social, ethical, and behavioral issues associated with testing/diagnostic technologies and information/data (including stigma associated with a positive test result) in research, clinical, or other settings. Comprised of two phases, the first phase of RADx-UP focused on communities with well-established research infrastructure and partnerships to better understand SARS-CoV-2 testing patterns and approaches. The second phase will advance the scientific mission described above while being responsive to the changing diagnostic landscape, continued need for behavioral mitigation strategies, and the effects of the implementation and scale-up of COVID-19 vaccine distribution efforts. Research will be focused on understanding COVID-19-related disparities and implementing testing interventions to mitigate these disparities in the context of vaccine implementation and uptake among underserved and vulnerable populations.

This includes developing and implementing testing interventions for school settings to enable evidenced-based approaches for safely returning students and staff to in-person school. Further, establishing partnerships with other COVID-19 programs will continue to ensure the needs of vulnerable and disproportionately affected communities are addressed.

The entire RADx program is supported by the Data Management for Testing for Safe Release Project, which is working to build an infrastructure and coordination of the various data management needs for the many COVID-19 efforts. This Project is developing a platform to integrate individual and population level data from a variety of sources, including serology and

[55] www.nih.gov/research-training/medical-research-initiatives/radx/funding#radx-rad

genetic test results, self-reported symptoms, and demographic data, to provide a source of indexed, searchable data and analytical tools for additional research including longitudinal studies.

Addressing Health Disparities through Research

Multiple lines of evidence have highlighted disparities in health outcomes among racial and ethnic minorities, social disadvantaged groups, rural residents, and other populations. In response to this need, NIH is supporting multidisciplinary research on health disparities across a range of populations, diseases, and disorders. Recent developments in this area include a study supported by both NHLBI and the National Institute on Minority Health and Health Disparities (NIMHD), which announced its findings in April 2020. The study found that African American men and women who had severe sleep apnea or other disrupted sleep patterns had higher blood sugar levels than those who slept normally. African American men and women are up to two times more likely to develop diabetes over their lifetimes than white Americans. These findings suggest that screening and treatment of sleep apnea and supporting better sleep habits may be another strategy to reduce the risk of diabetes in African Americans.[56]

Recent studies have also found that racial and ethnic minorities are disproportionately affected by COVID-19. Specifically, African Americans, Latinos, American Indians, and Pacific Islanders are more likely to acquire SARS-CoV-2 infection and African Americans especially are more likely to become seriously ill with COVID-19 and have greater mortality from the disease. In addition to the RADx-UP effort described above, NIH has launched trans-agency COVID-19 science initiatives, with a special focus on racial/ethnic minorities, such as the Social, Behavioral, and Economic Health Impacts of COVID-19 (SBE). Co-led by NIMHD, the National Institute of Mental Health (NIMH), the National Institute on Aging (NIA), the Office of Behavioral and Social Sciences Research (OBSSR) and the Office of Extramural Research (OER), and engaging with 24 Institutes and Centers (ICs) and offices, this effort is both leveraging existing opportunities at NIH and also actively soliciting applications to address secondary impacts of the pandemic in health disparity and other vulnerable populations. In FY 2020, 52 projects spanning research on alcohol, substance abuse, and mental health outcomes, public health mitigation impacts and adherence, and chronic health conditions were supported.[57] An important aspect of FY 2020 support was to supplement longitudinal studies to capture initial and longer-term effects of the pandemic on population health and health disparities. For example, the Understanding America Study tracks a nationally representative sample of adults across the pandemic, providing rapid access to data to support SBE research that has yielded early results on topics including adherence to pandemic mitigation interventions, childcare and parental mental health and use of protective behaviors.[58] In order to better understand how

[56] www.nih.gov/news-events/nih-research-matters/poor-sleep-linked-higher-blood-sugar-levels-african-americans
[57] grants.nih.gov/grants/guide/notice-files/NOT-OD-20-118.html
[58] Understanding America Study data and publications can be found on their website (uasdata.usc.edu/index.php). Example papers: Gema Zamarro and María J. Prados , "Gender differences in couples' division of childcare, work and mental health during COVID-19. " Review of Economics of the Household Vol. 19, pp 11-40 (2021); Robert F. Schoeni, Emily E. Wiemers, Judith A. Seltzer and Kenneth M. Langa, "Association Between Risk Factors for Complications From COVID-19, Perceived Chances of Infection and Complications, and Protective Behavior in the US" JAMA Netw. Open 4(3) (2021); Matthew Crane, Kenneth Shermock and Saad Omer, "Change in Reported Adherence to Nonpharmaceutical Interventions During the COVID-19 Pandemic, April-November 2020" JAMA January 22 (2021).

pandemic associated economic change (e.g., income insecurity caused by unemployment) influenced health, SBE supplemented research by the National Bureau of Economic Research which has already produced findings referenced in academic journals and the popular press.[59] Additionally in FY 2021, the workgroup is funding new research on community and digital healthcare interventions to leverage and extend the limited healthcare workforce to address social, behavioral, and economic impacts of the pandemic as well as initiatives to access, extract, integrate, share, and analyze existing data from various sources with broad population coverage including underserved and vulnerable populations to understand short and long-term impacts of the pandemic on healthcare use and health.

Maternal Mortality

U.S. rates of maternal deaths (approximately 700 each year) and complications are higher than in any other developed country and continue to rise, with black women and other women of color facing higher risks than white women. NIH increased efforts in FY 2020 to address maternal morbidity and mortality (MMM) in disproportionately affected populations (i.e., African American, American Indian/Alaska Native, women with advanced maternal age, people with disabilities, low socioeconomic status, or rural locales) by supporting initiatives targeted at geographical, racial, and ethnic disparities, including an initiative focused on determining mechanisms underlying racial and ethnic disparities in MMM. Led by the NIH Maternal Mortality Task Force, the new Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative, which provided supplemental research awards in FY 2020, focuses on biological, behavioral, sociocultural, and structural factors that affect pregnancy-related or -associated morbidity and mortality (PRAMM) and addresses leading causes of death and disability, including cardiovascular disease, infection and immunity, and significant morbidity associated with mental health for disproportionately affected populations. Awards include topics ranging from expanding telehealth obstetrics programs in rural Midwestern hospitals to studying the contribution of lifetime trauma in Black women to increased maternal morbidity risks.

Additional research in FY 2020 lent insight into PRAMM related to infection and immunity, cardiovascular disease, and severe maternal morbidity. One NIH-funded study found that among women readmitted to hospitals for sepsis, 61 percent of readmissions occurred after six weeks—the time point at which women generally have their postpartum visit.[60] For cardiovascular disease, the NuMoM2b Heart Health Study[61] showed an association of adverse pregnancy outcomes in a first pregnancy with maternal hypertension two to seven years postpartum, suggesting that preventive care for women should include a detailed history of pregnancy when determining hypertension risk. Researchers also sought insight into severe maternal morbidity by analyzing maternal birth outcomes from nearly 6.5 million health records of women. They found that women who have stillbirths are at substantially higher risk of severe maternal

[59] Examples include Cutler, David and Lawrence Summers. 2020. "The COVID-19 Pandemic and the $16 Trillion Virus." JAMA, doi:10.1001/jama.2020.19759; https://www.washingtonpost.com/business/2021/01/25/lockdowns-job-losses/;

[60] pubmed.ncbi.nlm.nih.gov/31529451/

[61] pubmed.ncbi.nlm.nih.gov/31564189/

morbidity than women with live births.[62] All of these studies revealed factors that play into the risk of complications and long-term health impacts associated with or related to pregnancy.

To align and support these and other collaborative maternal health initiatives, NIH remains actively engaged in coordinated efforts across HHS, including the HHS Task Force on Research Specific to Pregnant Women and Lactating Women,[63] the Surgeon General's Call to Action to Address Maternal Mortality and Morbidity, and the Healthy Women, Healthy Pregnancies, Healthy Futures: The U.S. Department of Health and Human Services' Action Plan to Improve Maternal Health in America.

Scientific Breakthroughs Across NIH

As the largest funder of public health research in the U.S., the mission of NIH includes a broad range of biomedical and public health research and services. To accomplish that mission, the ICs of the NIH each support research in specific areas of health, the human body, and disease, and each take varied approaches to funding biomedical research and the scientific workforce. While each IC is unique, all have supported critical scientific breakthroughs over the last year, and a few examples are provided below to illustrate their breadth and scope:

The National Institute of Dental and Craniofacial Research (NIDCR) recently announced a new bone-regenerating system in mice which uses nanoparticles released from a biodegradable scaffold near damaged areas to deliver a bone growing drug to nearby stem cells.[64] These stem cells, once triggered by the drug, regenerate new bone leading to an observed decrease in the size of damage averaging 50 percent after 6 weeks. This work has the potential to regenerate bone on-site, eliminating the need for bone grafts, the current standard of care, which increase risk of infection and nerve damage.

In response to research on the increase in mortality and morbidity for older adults transitioning to a care facility, scientists supported by the National Institute of Nursing Research (NINR) developed a novel sensor technology to monitor daily movement patterns, such as restlessness in bed, of new facility residents.[65] These sensors generate a report for nurses and physicians to monitor for clinically relevant changes in behavior and to predict approaching or worsening illnesses 10-14 days before symptoms begin, leading to earlier detection and treatment and potentially saving lives.

A team of scientists supported jointly by the National Center for Complementary and Integrative Health (NCCIH) and the National Institute of Neurological Disorders and Stroke (NINDS) announced the discovery of a new technique to manipulate two genes (NGN2 and BRN3A) in developing stem cells, triggering them to grow into sensory neurons which can detect cold temperatures and touch.[66] Individuals with a rare genetic disorder called PIEZO2 deficiency lack both a sense of touch and body position. The team found that cells from these

[62] pubmed.ncbi.nlm.nih.gov/31306335/
[63] www.nichd.nih.gov/about/advisory/PRGLAC
[64] www.nidcr.nih.gov/news-events/news/2020/scientists-take-crack-bone-regeneration
[65] www.ninr.nih.gov/all-stories-of-discovery
[66] www.nccih.nih.gov/research/research-results/stem-cell-technology-helps-scientists-generate-a-previously-unknown-type-of-sensory-neuron

individuals could be genetically corrected with this new technique and CRISPR Cas-9 to restore the senses in individuals with PIEZO2 deficiency. This discovery shows how stem cells can be a vital tool in advancing the field of sensory biology.

Researchers supported by NCCIH recently released findings that acupuncture can relieve inflammation through several independent mechanisms. Using mice as a model, the team investigated how distinct types of stimulation from acupuncture relieved systemic inflammation with what is known as a somatotropic organization, meaning stimulating a specific area produced an effect in a specific, corresponding tissue.[67] Varying intensities of stimulation also altered the effect. Comparing manual to electroacupuncture, the investigation showed electroacupuncture to be more effective as it is easier to control. These findings should lead to improved acupuncture practices and the potential for more optimized treatment.

Finally, researchers supported by the National Institute on Deafness and Communication Disorders (NIDCD) discovered a potential new drug for slowing hearing loss caused by nerve damage.[68,69] Previously considered irreversible with no approved medications, this type of hearing loss, known as sensorineural hearing loss, is the most common cause of age-related hearing loss. A new study found that a drug for preventing bone density loss given to mice dramatically reduced nerve damage and restored cochlear function 24 hours after exposure to loud, damaging noises. This discovery has the potential to lead to clinical trials to determine if this same drug type could prevent hearing loss in people.

NIH will continue to serve in its critical role of advancing basic and clinical biomedical research to advance knowledge of human disease and enhance public health. Through careful stewardship of taxpayer dollars and broad investment in cutting-edge ideas and the scientific workforce, NIH will build on these and other breakthroughs to further champion human health.

Harnessing Computational Biology/Data Science and Artificial Intelligence to Advance Biomedical Research

NIH is leveraging advanced computational and data science techniques, including artificial intelligence (AI) and machine learning (ML), to accelerate and expand biomedical and clinical research and improve clinical care. Researchers are using computational biology and data science to unravel the inner workings of intricate biological processes, including those that impact mental health, aging, and infectious diseases. For example, NIH is supporting research analyzing neural networks to help with early diagnosis of Alzheimer's disease and to discover and optimize treatments for mental illnesses, emotional disturbance, and abnormal behavior.[70,71] In clinical care, NIH-supported research is incorporating AI and ML techniques to facilitate interpretation of imaging results for radiological diagnosis of diseases (e.g., cancer[72] and COVID-19[73]), remote telehealth monitoring using wearable devices, and clinical decision

[67] www.nccih.nih.gov/research/research-results/new-findings-suggest-acupuncture-stimulation-reduces-systemic-inflammation
[68] hms.harvard.edu/news/dramatic-effect
[69] www.nidcd.nih.gov/research
[70] www.nibib.nih.gov/science-education/science-topics/artificial-intelligence-ai
[71] grants.nih.gov/grants/guide/pa-files/PAR-19-344.html
[72] directorsblog.nih.gov/2020/01/14/artificial-intelligence-speeds-brain-tumor-diagnosis/
[73] www.nih.gov/news-events/news-releases/nih-harnesses-ai-covid-19-diagnosis-treatment-monitoring

support systems that use health observations and case knowledge to assist with treatment decisions.[74] Telehealth and clinical decision support systems could be particularly useful in rural and other under-resourced areas where patients have limited access to health care and specialized health care providers. For example, an ongoing study is testing a ML approach on maternal delivery hospitalization data from Maryland state databases to develop a predictive risk assessment tool for severe maternal morbidity (SMM). Such a tool could help clinicians without specialized training identify women at high-risk of SMM to help avoid or minimize adverse outcomes.[75]

Data science can also be used to address emerging public health needs. A major challenge for clinicians is the rapid and accurate assessment of SARS-CoV-2-infected hearts and lungs on medical images to predict COVID-19 disease severity and treatment response. Across NIH, several institutes are supporting the Medical Imaging and Data Resource Center (MIDRC)[76] for Rapid Response to COVID-19 Pandemic. MIDRC aims to develop and implement new diagnostics, including ML algorithms, that will allow rapid and accurate assessment of disease status and help physicians optimize patient treatment. NIH also has joined with the AI community, the White House, and key industry and university leaders to develop text mining tools to help analyze the thousands of scholarly articles for insights on coronavirus through the COVID-19 Research Data Set (CORD-19).[77] A complementary effort by NIH's Office of Portfolio Analysis created a sortable, machine readable comprehensive listing of COVID-19 publications and preprints to assist researchers.[78] The tool can drill down through a variety of data facets and includes visualizations to group articles into clusters based on key terms.

To unleash the full potential that data science has to offer in aiding scientific discovery and clinical care, NIH must take steps to ensure that appropriate infrastructure, resources, and expertise are available to drive advances. To this end, the NIH Office of Data Science Strategy (ODSS) continues to implement the NIH Strategic Plan for Data Science.[79] These trans-NIH collaborative approaches are building resources, unifying efforts, training staff, recruiting new talent, and enabling broad use of data science and computational approaches in biomedical research. NIH is also engaging stakeholders to identify priorities and opportunities specifically for AI and ML. Plans are in progress to implement many of the recommendations derived through workshops and working groups, including the NIH Advisory Committee to the Director AI Working Group.[80]

All of Us Genomic Program and Expansion of the Workbench

The *All of Us* Research Program is preparing to launch one of the largest genomic sequencing activities in the world and continues its progress to build one of the largest and most diverse datasets to advance health research, in partnership with its more than 381,000 and counting participants as of April 2021. *All of Us* began genotyping and sequencing participant biosamples

[74] www.nibib.nih.gov/science-education/science-topics/artificial-intelligence-ai
[75] projectreporter.nih.gov/project_info_details.cfm?aid=9767258&icde=0
[76] www.nih.gov/news-events/news-releases/nih-harnesses-ai-covid-19-diagnosis-treatment-monitoring
[77] www.kaggle.com/allen-institute-for-ai/CORD-19-research-challenge
[78] nexus.od.nih.gov/all/2020/04/15/new-nih-resource-to-analyze-covid-19-literature-the-covid-19-portfolio-tool/
[79] datascience.nih.gov/strategicplan
[80] acd.od.nih.gov/working-groups/ai.html

in August 2020, and initial genomic data, including robust sets of whole genome sequences and arrays, are anticipated to be available to approved researchers in late 2021 or early 2022 The scale of this program – both participants and data collected – will set it apart from other studies. In the future, the program will expand the data available within, functionality of, and access to its Researcher Workbench, the platform researchers use to access *All of Us* data. *All of Us* began beta testing the Researcher Workbench in May 2020, allowing researchers to start using the program's initial dataset and tools in studies and comment on what is working and what the program can improve. This early version of its Researcher Workbench includes data generously shared with the program from more than 315,000 of its first participants, 80 percent of whom are from communities that are historically underrepresented in research, and more than 50 percent of diverse races and ethnicities. The platform will grow more robust over time with additional data and tools, including genomics, wearable device data, and linkages to other datasets. The program plans regular releases of new data and will continue to explore expanding access to the platform beyond the current beta audience, including citizen and community scientists and researchers in the private sector. The Researcher Workbench's expansion aims to enable research that will increase wellness and resilience, and promote healthy living; reduce health disparities and improve health equity; develop improved risk assessment and prevention strategies to preempt disease; provide earlier and more accurate diagnosis to decrease illness burden; and improve health outcomes and reduce disease burden through improved treatment and development of precision interventions.

The *All of Us* Research Program also has risen to the challenge of addressing the COVID-19 pandemic.[81] *All of Us* tested blood samples from over 24,000 participants for the presence of SARS-CoV-2 antibodies, indicating prior infection. Researchers tested samples collected in March 2020 and worked backwards until positive samples were no longer found to help determine the prevalence, rates of infection, and timing of SARS-CoV-2 infection in regions across the country. Additionally, *All of Us* is collecting relevant information from the electronic health records of more than 240,000 participants, some of whom have been diagnosed with COVID-19 or sought healthcare for related symptoms to help researchers look for patterns and learn more about COVID-19 symptoms and the effects of different medicines and treatment. Another effort focuses on understanding the mental and physical impacts of the COVID-19 pandemic on participants and includes questions on symptoms, stress, social distancing, and economic impacts. As data become available from all of these efforts, researchers will look for new leads that may bring greater precision to the diagnosis, treatment, and prevention of COVID-19, including those communities that have been hit the hardest.

Accelerating Precision Nutrition Research

The National Institutes of Health Nutrition Research Task Force (NRTF) was established in 2016 to coordinate and accelerate progress in nutrition research across the NIH, and to guide the development and implementation of the first NIH-wide strategic plan for nutrition research for the next 10 years.[82] In May 2020, the task force released the 2020-2030 Strategic Plan for NIH Nutrition Research, reflecting the wide range of nutrition research supported across NIH and

[81] directorsblog.nih.gov/2020/06/16/nihs-all-of-us-program-joins-fight-against-pandemic/

[82] National Institute of Diabetes and Digestive Kidney Disease. *NIH Nutrition Research Task Force*. www.niddk.nih.gov/about-niddk/advisory-coordinating-committees/nih-nutrition-research-task-force

accounting for over $1.9 billion in FY 2019.[83] The strategic plan emphasizes cross-cutting, innovative opportunities to advance nutrition research across a wide range of areas, from basic science to experimental design to research training.[84] These opportunities complement and enhance ongoing research efforts across NIH to improve health and to prevent or combat diseases and conditions affected by nutrition.

Several areas in nutrition research that are ripe for further development include rapidly advancing technologies, such as high throughput "omics" (genomics, epigenomics, proteomics, metabolomics, etc.) and artificial intelligence, combined with the growing emphasis on personalized medicine approaches. To support the goals of NRTF and the strategic plan on nutrition research, the *All of Us* Research Program is developing the Nutrition for Precision Health program. This initiative will aim to understand individual responses to diet, enabling tailored dietary recommendations to be provided by physicians, as well as development of tools to allow individuals to make more informed decisions about healthy food choices.

Eliminating HIV/AIDS

Decades of research sponsored by the NIH, led by NIAID, has provided the critical treatment and prevention toolkits to theoretically end the HIV epidemic in the United States. With effective antiretroviral therapy (ART), a person with HIV now can expect a near-normal lifespan. The *Ending the HIV Epidemic (EHE) in the U.S.*[85] initiative aims to implement major scientific strategies and interventions to reduce new HIV transmissions by 75 percent over the next 5 years and by 90 percent by 2030. The strategy focuses on implementing evidence-based HIV treatment and prevention tools in geographic and demographic "hot spots" in this country where more than 50 percent of new HIV infections are concentrated.

NIH-sponsored clinical trials have demonstrated that individuals who receive ART and have achieved and maintained an undetectable viral load cannot sexually transmit the virus to others – the evidence-base for the concept, Undetectable=Untransmittable, or U=U. NIH-sponsored studies have demonstrated that ART used daily as pre-exposure prophylaxis (PrEP) can also protect those who are at risk of HIV acquisition. NIAID is supporting research on the optimal implementation of these strategies and on novel approaches to improve diagnosis, linkage to care, and treatment of people with HIV and to protect those at risk of acquiring HIV.

NIAID, the NIH Office of AIDS Research, and NIMH provided supplemental funding to institutions participating in the NIH-funded Centers for AIDS Research (CFAR)[86] and AIDS Research Center (ARC)[87] programs to conduct pilot and exploratory studies that will enhance the knowledge base needed for future implementation of science-based interventions to support the

[83] National Institutes of Health. (2020, May 27). NIH releases strategic plan to accelerate nutrition research over next 10 years [Press release]. www.nih.gov/news-events/news-releases/nih-releases-strategic-plan-accelerate-nutrition-research-over-next-10-years

[84] National Institute of Diabetes and Digestive Kidney Disease. *2020-2030 Strategic Plan for NIH Nutrition Research*. www.niddk.nih.gov/about-niddk/strategic-plans-reports/strategic-plan-nih-nutrition-research

[85] www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview

[86] www.niaid.nih.gov/research/centers-aids-research

[87] www.nimh.nih.gov/about/organization/dar/aids-research-centers-program/aids-research-centers-program.shtml

EHE Initiative. In FY 2020, this partnership has extended and expanded these programs and added important new topics for reducing HIV incidence in at-risk populations. Notably, clinical trials funded by NIAID, the National Child Health and Human Development (NICHD), and NIMH showed that use of the dapivirine vaginal ring decreased women's risk of acquiring HIV.[88] This ring has recently been given a positive opinion by the European Medicines Agency for use in low- and middle-income countries. Further studies are examining the safety of the dapivirine ring during adolescence and pregnancy, when the risk of HIV acquisition is heightened. NIAID is continuing to develop new and improved HIV treatment and prevention tools, as well as the translation of basic and clinical biomedical research findings into strategies and modalities that are user- friendly and can be effectively and efficiently taken up in real-world settings by diverse communities. Several approaches aimed at achieving these treatment goals include: eradication of HIV from the body (i.e., achieving a "cure"), long-acting anti-retroviral therapry (ART) that could be taken intermittently, and broadly neutralizing antibodies (bNAbs). Novel prevention strategies being pursued include: long-acting pre-exposure prophylaxis (PrEP), bNAbs, and vaccine candidates.

Developing A Universal Flu Vaccine

FY 2021 appropriations included $220 million to bolster the ongoing efforts of NIAID to develop a "universal" influenza vaccine that will provide robust, long-lasting protection against multiple strains of influenza virus, including emerging strains that could spread globally. This includes developing state-of-the-art vaccine platforms, such as DNA, mRNA, virus-like particles, viral vectors, and nanoparticles, that are easier to produce and adapt. Scientists at the NIAID Vaccine Research Center (VRC) built on previous studies suggesting that vaccines targeting the "stem" region of the influenza hemagglutinin (HA) protein on the surface of the virus offer broader protection than existing strain-specific influenza vaccines that typically target the HA "head" region, which varies from year to year. NIAID VRC is testing experimental vaccine candidates using nanoparticle platform technology to target the HA stem, and in FY 2020, one nanoparticle vaccine candidate was proven to be safe and immunogenic in a Phase 1 clinical trial. A second vaccine candidate will be tested in a similar trial in FY 2021. In addition, a "mosaic nanoparticle"–based vaccine candidate that displays multiple influenza HAs is currently being manufactured by the VRC for testing in a Phase 1 clinical trial. In collaboration with industry partners, NIAID scientists in the Division of Intramural Research recently completed a Phase 2 clinical trial assessing a novel peptide-based candidate vaccine in a human influenza challenge model. The experimental vaccine, called FLU-v, targets several proteins conserved across influenza strains and yielded promising efficacy results. Advances in the areas of influenza virology, structural biology, protein engineering, immunology, and vaccinology result from many NIAID-supported research programs, including the Collaborative Influenza Vaccine Innovation Centers (CIVICS), the Infectious Diseases Clinical Research Consortium (IDCRC) network, and the Adjuvant Discovery and Development Programs. NIAID will continue targeted investments to generate critical information for the development of safe and effective universal vaccine candidates against both seasonal and pandemic influenza.

[88] www.nih.gov/news-events/news-releases/vaginal-ring-hiv-prevention-receives-positive-opinion-european-regulator

Gene Therapy Cures for Sickle Cell Disease and HIV

In an effort to develop affordable, gene-based cures for sickle cell disease (SCD) and HIV, the NIH launched a new collaboration with the Bill & Melinda Gates Foundation (Gates Foundation) to fund research that develops curative strategies using gene-based treatments. Together, the NIH and the Gates Foundation will invest at least $200 million to advance safe, effective, and durable gene-based cures to clinical trials in the United States and relevant countries in sub-Saharan Africa within the next 7 to 10 years.[89] To accomplish these goals, the partnership will focus on two areas of coordination – identifying potential candidates for curing SCD and HIV for pre-clinical and clinical evaluation and defining long-term opportunities to work together on advancing promising candidates to late-phase clinical trials.[90]

To meet the goal of a scalable HIV cure, a number of approaches are being considered[91] and will improve coordination with ongoing research efforts, thereby accelerating studies into early phase clinical trials to safely test promising tools and interventions. An approach of interest is to identify the location of the reservoir of infected cells that still harbor integrated HIV genomes after treatment and target those DNA sequences with gene editing technology.

Recently, NIH studies targeting SCD demonstrated the effectiveness of correcting defective genes outside the body and infusing them into the body of SCD patients to reverse the disease.[92] Although a substantial breakthrough, the process is time intensive and involves many complex manufacturing and clinical steps. Under the collaboration with the Gates Foundation, the goal for SCD is to develop an easy-to-administer, gene-based intervention to correct the SCD gene mutations or promote fetal hemoglobin gene expression to achieve normal hemoglobin function. The path to a cure will rely in part on the development of gene-based delivery systems capable of selectively targeting hematopoietic stem cells, which will result in the precise correction of gene mutations or the addition of a gene to promote sufficient levels of normal hemoglobin expression and function.[93]

Another NIH initiative targeting SCD is the Cure Sickle Cell Initiative (CureSCi) launched in 2018 by NHLBI to move the most promising gene-based therapies safely into clinical trials within five to ten years.[94] Accomplishments include development of a data consortium to collect and harmonize existing SCD datasets, support for research and platforms toward the launch of clinical trials (e.g., an SCD stem cell biobank, manufacture of Good Manufacturing Practice

[89] NIH Director's Blog. (2019, October 28). Joining Forces Against Sickle Cell Disease and HIV Infection. directorsblog.nih.gov/2019/10/28/joining-forces-against-sickle-cell-disease-and-hiv-infection/

[90] National Institutes of Health. Backgrounder: NIH Collaboration on Gene-Based Cures for SCD and HIV. www.nih.gov/news-events/news-releases/backgrounder-nih-collaboration-gene-based-cures-scd-hiv

[91] National Institutes of Health. (2019, October 23). NIH launches new collaboration to develop gene-based cures for sickle cell disease and HIV on global scale. www.nih.gov/news-events/news-releases/nih-launches-new-collaboration-develop-gene-based-cures-sickle-cell-disease-hiv-global-scale

[92] National Institutes of Health. Backgrounder: NIH Collaboration on Gene-Based Cures for SCD and HIV. www.nih.gov/news-events/news-releases/backgrounder-nih-collaboration-gene-based-cures-scd-hiv

[93] National Institutes of Health. (2019, October 23). NIH launches new collaboration to develop gene-based cures for sickle cell disease and HIV on global scale. www.nih.gov/news-events/news-releases/nih-launches-new-collaboration-develop-gene-based-cures-sickle-cell-disease-hiv-global-scale

[94] National Heart, Lung, and Blood Institute. Data Consortium. curesci.azurewebsites.net

(GMP) vectors, new clinical outcome measures and biomarkers), in addition to patient, caregiver, and provider engagement.

These initiatives are some examples of many gene therapy efforts, including the NIH Common Fund's Somatic Cell Genome Editing (SCGE) program, that will help to reduce the burden of common and rare diseases caused by genetic changes, and potentially develop curative treatments.[95]

Identifying and Addressing Structural Racism

NIH is committed to bringing diverse perspectives, backgrounds, and skillsets to enhance scientific productivity and solve complex biomedical and health research problems. To identify new ways of supporting diversity, equity, and inclusion and dismantle policies and practices that may harm our workforce and our ability to advance critical scientific discoveries and improve lives, NIH launched the UNITE initiative in February 2021.

The goal of the UNITE initiative is to identify and address structural racism within the NIH community and the greater biomedical research community. UNITE is comprised of five core activities with coordinated objectives to address racism and discrimination in science and develop methods to promote diversity and inclusion in biomedical research:

- **U**nderstanding stakeholder experiences through listening and learning
- **N**ew research on health disparities, minority health, and health equity
- **I**mproving the NIH culture and structure for equity, inclusion and excellence
- **T**ransparency, communication, and accountability with internal and external stakeholders
- **E**xtramural research ecosystem: changing policy, culture and structure to promote workforce diversity

The UNITE initiative will work to address challenging issues stemming from structural racism such as attracting and retaining scientists from underrepresented groups; addressing disparities in success rates for grants supporting Black/African American scientists; improving transparency of race-based demographic data; increasing funding of research for minority health, health disparities, and health equity; and addressing racism in the NIH workplace. Led by the NIH Office of the Director, the 5 core areas of the UNITE initiative bring together nearly 80 appointed members representing all of the 27 ICs of the NIH. As these critical efforts begin, the UNITE initiative will engage these members as well as the scientific community and the public to bolster the NIH's effort to increase diversity within the scientific workforce, achieve racial equity on the NIH campus, and enhance opportunity and achievement within the scientific community.

Protecting U.S. Biomedical Intellectual Innovation

NIH recognizes the importance of scientific collaborations to advance its mission, and NIH and the biomedical research enterprise have a long history of international collaborations with rules of engagement that allow science to advance while protecting intellectual capital and proprietary

[95] National Institutes of Health. (2019, October 23). Somatic Cell Genome Editing (SCGE). commonfund.nih.gov/editing

information. However, in August 2018, the NIH Director issued a statement about incidents that violate core principles and threaten the integrity and academic competitiveness of U.S. biomedical research and innovation.[96] Such incidents include failure by some researchers at NIH-funded institutions to disclose contributions of resources from other organizations, diversion of intellectual property produced by NIH-supported biomedical research, and sharing of confidential information by peer reviewers or otherwise attempting to influence funding decisions.

NIH has taken a number of steps to address these risks, including convening a working group of the Advisory Committee to the Director (ACD) to advise on how best to address it.[97] NIH has also communicated these concerns to over 10,000 recipient institutions within the research community and has contacted over 90 institutions regarding specific concerns about scientists who may have failed to disclose foreign affiliations, financial conflicts of interest, and/or research support from foreign governments. The agency has also extensively communicated the responsibilities of all participants in the NIH peer review process and the consequences of a breach of review integrity. NIH continues to address this issue by implementing ACD working group recommendations, outreach and communication within NIH and with the broader research community, as well as active partnerships with other Federal departments and agencies, scientific professional societies, and recipient institutions to establish best practices to protect the integrity of NIH-supported science. NIH appreciates the proactive efforts many institutions are taking to address these serious issues, such as updating institutional disclosure policies and providing outreach to faculty and staff regarding reporting requirements to ensure that U.S. institutions and the American public benefit from their investment in biomedical research.

[96] www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-protecting-integrity-us-biomedical-research

[97] acd.od.nih.gov/working-groups/foreign-influences.html

FUNDING HISTORY (FIVE-YEAR FUNDING TABLE)

Fiscal Year	Amount[1, 2]
2018	$37,311,349,000
2019	$39,313,000,000
2020	$41,690,000,000
2021	$42,940,500,000
2022 Budget Request[3]	$51,957,703,000

[1] Appropriated amounts include discretionary budget authority received from both Labor/HHS appropriations that fund ICs as well as the Interior, Environment & Related Agencies appropriation that supports NIH Superfund Research activities. Also includes mandatory budget authority derived from the Special Type 1 Diabetes account. Includes NIGMS Program Evaluation financing of $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, $1,230,821,000 in FY 2020, $1,271,505,000 in FY 2021 and $1,271,505,000 in the FY 2022 request. Includes CURES amounts of $496,000,000 in FY 2018, $711,000,000 in FY 2019, $492,000,000 in FY 2020, $404,000,000 in FY 2021 and $496,000,000 in the FY 2022 request.

[2] Excludes supplemental appropriations and permissive and directive transfers.

[3] Reflects sequestration of the mandatory funding for the Special Type 1 Diabetes Research account.

SUMMARY OF REQUEST NARRATIVE

The FY 2022 President's Budget request provides a program level of $52.0 billion for NIH, which is $9.0 billion more than the FY 2021 Enacted level of $42.9 billion. This request includes $6.5 billion to establish a new Advanced Research Projects Agency for Health (ARPA-H) within NIH.

The following summary references program level funding, which is the sum of discretionary budget authority in the Department of Labor, Health and Human Services, and Education, and Related Agencies appropriations ($50.5 billion in FY 2022); discretionary budget authority in the Department of the Interior, Environment, and Related Agencies appropriations dedicated to the Superfund Research Program ($83.5 million in FY 2022); mandatory budget authority provided for Type 1 Diabetes research ($141.4 million in FY 2022[98]); and Program Evaluation Financing for the National Institute of General Medical Sciences under Section 241 of the Public Health Service Act ($1,271.5 million in FY 2022).

The primary budget mechanisms discussed below include allocations by mechanism of Program Evaluation Financing and Type 1 Diabetes funds. The Superfund Research program is a lump-sum amount within the NIH mechanism tables.

In FY 2022, NIH will continue providing upfront funding for certain research projects, as appropriate, to facilitate efficient management of resources across multiple years. In general, NIH discretionary research project grants are awarded for more than one year and funded incrementally; each year's commitment is obligated from that year's appropriation. Grants are classified as Competing in the first year of award or renewal, and Non-competing in the remaining years of each award. Certain categories of NIH grants are awarded for multiple years with the full funding provided up front. This includes the NIH Director's New Innovator Award (DP2) and the NIH Research Enhancement Award (R15). The latter consists of two programs, the Academic Research Enhancement Award (AREA) for Undergraduate-Focused Institutions, and the Research Enhancement Award Program (REAP) for Health Professional Schools and Graduate Schools. In addition, full funding can be provided up front for other NIH grants and cooperative agreements as appropriate in special circumstances. Situations that may benefit from such an approach can include, but are not limited to, appropriations for new programs, rapid increases in funding, or variable outyear funding streams (e.g., under the 21st Century Cures Act). The use of upfront funding for new programs makes some base funding available for competing awards in the following year. Up-front funding has increased over the last few years, due in part to the large Congressional increases for Alzheimer's disease research.

Research Project Grants (RPGs)

The FY 2022 President's Budget provides $26.2 billion for RPGs, which is $1.7 billion more than the FY 2021 level. This amount would fund 12,664 Competing RPGs, or 1,475 more than for the FY 2021 level. It would also support 29,718 Noncompeting RPGs, 678 more than the FY 2021 level. In addition, the projected average cost for Competing RPGs of approximately $568,000 would be 2.1% below the FY 2021 projected average cost of $580,000.

[98] Reflects a mandatory appropriation of $150.0 million, reduced by $8.6 million for sequestration pursuant to the Budget Control Act.

- **Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) RPGs.** The FY 2022 President's Budget provides $1,229.6 million for SBIR/STTR program grants, which is $75.1 million above the FY 2021 level. The statutory minimum set-aside requirement of 3.65% for NIH-wide SBIR/STTR support is achieved in FY 2022.

Research Centers
The FY 2022 President's Budget provides $2,872.6 million for Research Centers, which is $94.0 million more than the FY 2021 level. This amount would fund 1,306 grants, 39 more than the FY 2021 level.

Other Research
The FY 2022 President's Budget provides $3,096.6 million for this mechanism, which is $99.7 million more than the FY 2021 level. This amount would fund 7,888 grants, which is 329 more than the number of awards projected for FY 2021.

Training
The FY 2022 President's Budget provides $1,019.2 million for research training, which is $67.3 million above the FY 2021 level. This amount would fund 17,949 Full-Time Trainee Positions (FTTPs), which is 394 more than planned for FY 2021, and would fund a new child care subsidy allowance for individual and institutional trainees that was phased in starting in FY 2021.

Research & Development (R&D) Contracts
The FY 2022 President's Budget provides $3,561.3 million for R&D contracts, which is $198.6 million more than the FY 2021 level. The requested amount would fund an estimated 2,521 contracts, or 166 more than the FY 2021 level.

- **SBIR/STTR R&D Contracts.** The FY 2022 President's Budget includes a $82.3 million set-aside within the R&D Contracts mechanism for support of qualified SBIR/STTR contracts.

Intramural Research (IR)
The FY 2022 President's Budget provides $4,696.0 million for IR, which is $147.0 million more than the FY 2021 level.

Research Management and Support (RMS)
The FY 2022 President's Budget provides $2,184.2 million for RMS, which is $93.6 million more the FY 2021 level.

Office of the Director (OD)
The FY 2022 President's Budget provides $2,394.9 million for OD, which is $111.0 million more than the FY 2021 level.

- **Common Fund (CF)**
  Funding of $658.5 million is allocated for CF-supported programs. This amount is $10.0 million more than the FY 2021 level.

- **Office of Research Infrastructure Programs (ORIP)**
  Funding of $304.7 million is allocated for ORIP. This amount is $4.8 million above the FY 2021 level.

- **Other**
  The $1,431.6 million allocated for OD components other than the Common Fund or ORIP is a net increase of $96.2 million from the FY 2021 level. This is due, in part, to an increase in the portion of funding authorized by the 21st Century Cures Act that is managed by OD, from $109.0 million to $150.0 million for the *All of Us* Research Program.

Advanced Research Projects Agency for Health (ARPA-H)
The FY 2022 President's Budget provides $6.5 billion to establish ARPA-H as a new research entity within NIH. ARPA-H will complement the research portfolio of NIH's existing Institutes and Centers, investing in breakthrough health technologies and strategies to accelerate the development of evidence-based, real-world-driven cures for and transformative advances in a range of biomedical and health research areas and diseases.

Buildings & Facilities (B&F)
The FY 2022 President's Budget provides $280.0 million for infrastructure sustainment projects associated with the B&F program, which is $50.0 million more than the FY 2021 level. This amount includes $250.0 million for NIH's Buildings and Facilities appropriation, an increase of $50.0 million from the FY 2021 level, and $30.0 million within the appropriation for the National Cancer Institute (NCI) for facility repair and improvement activities at NCI's Frederick, Maryland, facility.

Superfund Research Program
The FY 2022 President's Budget provides $83.5 million for the Superfund Research Program, which is $2.0 million more than the FY 2021 level.

Program Evaluation Financing
The FY 2022 President's Budget provides $1,271.5 million for Program Evaluation Financing purposes in NIGMS, which is the same as the FY 2021 level.

OUTPUTS AND OUTCOMES

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
SRO-1.5 By 2020, increase our understanding of cancer trends and outcomes in the context of disparities and population subgroups through expansion of coverage and representation of the US population in the Surveillance, Epidemiology and End Results (SEER) Program registries. (Outcome)	FY 2020: With the recent expansion, SEER is able to provide trends and rates specific to the clinically relevant cancer subtypes represented by molecular characterization of each tumor. This expansion was implemented by adding U.S. cancer registries that include more underserved and ethnic and racial minority populations. Target: Provide trends and rates specific to the clinically relevant cancer subtypes represented by molecular characterization of each tumor. (Target Met)	N/A	N/A	N/A
SRO-1.6 By 2020, determine the effectiveness of an evidence-based, patient-centered multicomponent fall injury prevention strategy in adults 75 years of age and older. (Outcome)	FY 2020: Analyses of secondary outcome data were completed. Target: Complete analyses of secondary outcome data. These outcomes include patient concerns about falling, all falls, all fall-related injuries, physical function, disability, anxiety and depression. (Target Met)	N/A	N/A	N/A
SRO-2.1 By 2021, develop, optimize, and evaluate the effectiveness of nano-enabled immunotherapy (nano-immunotherapy) for one cancer type. (Output)	FY 2020: Two nanodelivery systems, which were identified as top candidates, were further optimized and are currently being tested in cancer patients who have advanced stages of cancer. Target: Further optimize	Further optimize the top candidate nanoformulation for co-delivery of antigens, adjuvants and immuno-modulators and evaluate its efficacy towards near and distance metastatic	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	the top candidate nanoformulation for co-delivery of antigens, adjuvants and immuno-modulators and evaluate its efficacy and long-lasting immunity (over 3 months) in preclinical models with established tumors. (Target Met)	lesions in preclinical models with established tumors.		
SRO-2.4 By 2025, increase the number of potential treatment options for communication disorders that are being tested in clinical trials by adding one new treatment option per year. (Outcome)	FY 2020: This study is not currently enrolling participants due to COVID-19 restrictions. Target: Initiate testing one new potential treatment option for a taste disorder. (Target Not Met)	Initiate testing one new potential treatment option for a disorder affecting voice, speech, or language.	To be determined[99]	N/A
SRO-2.5 By 2021, develop three non-invasive imaging technologies that can image retinal cell function and circuitry. (Output)	FY 2020: Four novel imaging technologies have been translated from animal studies into human participants. Some of the teams have completed their work ahead of schedule. Target: Translate two novel imaging technologies from animal studies into human participants. (Target Exceeded)	Complete development of three non-invasive imaging technologies which image retinal cell function and circuitry.	N/A	N/A
SRO-2.6 By 2020, investigate the pathways and mechanisms of how seven environmental agents can alter epigenetic processes such as DNA methylation, recruitment of specific histone	FY 2020: Researchers identified sex differences in six additional environmentally induced epigenomic signatures in five different mouse tissues. Target: Determine and	N/A	N/A	N/A

[99] The longer-term impact of COVID-19 on patient recruitment is unknown at this time.

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
modifications, and chromatin remodeling to better determine if these changes can be inherited. (Output)	identify, if present, sex differences in four additional environmentally induced epigenomic signatures in three different mouse tissues. (Target Exceeded)			
SRO-2.7 By 2022, file Phase II Investigational New Drug (IND) application with the FDA for a therapy to treat geographic atrophy in age-related macular degeneration (AMD) using patient-derived stem cells. (Outcome)	FY 2020: FDA approved the IND application in December 2019. Three initial patients were enrolled and were preparing to receive the transplant, but the COVID-19 pandemic prevented implementation of treatment. Target: Recruit three AMD patients into Phase I clinical trial. (Target Not Met)	Complete Phase I trial enrollment to treat a total of 12 AMD patients.	To be determined[100]	N/A
SRO-2.8 By 2023, advance the development of three novel drug or biologic therapeutic candidates for Alzheimer's disease (AD) or related dementias toward the point of entry into Phase I human studies. (Output)	FY 2020: Proof-of-concept animal model studies were completed for eight new candidate therapeutics. Target: Complete preclinical proof of concept in animal models of AD for 3-5 new candidate therapeutics. (Target Exceeded)	Initiate Investigational New Drug (IND)-enabling studies for 2-3 new candidate therapeutics.	Complete IND-enabling studies for 2-3 new candidate therapeutics.	N/A
SRO-2.9 By 2022, evaluate the safety and effectiveness of 1-3 long-acting strategies for the prevention of HIV. (Outcome)	FY 2020: NIH-funded investigators completed follow-up of participants in two studies testing the safety, tolerability, and effectiveness of VRC01.	Strategy 1: Analyze data of two studies testing the safety, tolerability, and effectiveness of VRC01 broadly	Initiate an open label extension of two studies, HPTN 083 and HPTN 084, investigating the safety and efficacy of the long-acting	N/A

[100] The longer-term impact of COVID-19 on patient recruitment and treatment implementation is unknown at this time.

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	Target: Strategy 1: Complete follow-up of participants in at least one of the studies testing the safety, tolerability, and effectiveness of VRC01. (Target Met)	neutralizing antibody (bnAb).	injectable antiretroviral drug cabotegravir (CAB).	
SRO-2.10 By 2024, develop methods for the regeneration of functional tissues of the human dental, oral, and craniofacial complex to enable initiation of human Phase I clinical trials. (Outcome)	FY 2020: Pre-clinical testing has been completed for a bone adhesive biomaterial. Target: Initiate pre-clinical animal studies that will lead to the development of regenerative medicine therapies of human dental, oral, and craniofacial diseases and conditions. (Target Met)	The Resource Centers will facilitate the development of five Investigational New Drug (IND)/ Investigational Device Exemption (IDE) applications from the current pool of Interdisciplinary Translational Projects.	One FDA application for a tissue regeneration combination product will be approved and one Phase 1 clinical trial protocol will be developed.	N/A
SRO-2.12 By 2021, develop, validate, and/or disseminate 3-5 new research tools or technologies that enable better understanding of brain function at the cellular and/or circuit level. (Output)	FY 2020: The Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative supported the development of novel technologies for brain stimulation and recording and efforts to disseminate resources and integrate them into neuroscience research practice. Target: Provide broad access to new research approaches and techniques for acquiring fundamental insight about how the nervous system functions in health and disease. (Target Met)	Expand our understanding of brain function at the cellular or circuit level using 3-5 new tools and technologies.	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
SRO-2.13 By 2023, advance the development of 1-2 new drugs and/or other therapeutic candidates for neurological diseases from lead optimization or device development toward the point of preparedness for first-in-human studies. (Output)	FY 2020: Animal toxicology studies have been initiated and/or completed for a total of seven neurotherapeutic/ device candidates. Target: Initiate animal toxicology studies for 1-2 therapeutic or device candidates. (Target Exceeded)	Determine the margin of safety for 1-2 therapeutic or device candidates.	Demonstrate efficacy of trial-ready formulation of 1-2 therapeutic or device candidates in preclinical disease models.	N/A
SRO-3.1 By 2025, identify neurobehavioral precursors or consequences of adolescent substance use or other childhood experiences. (Outcome)	FY 2020: Researchers investigated the relationships among childhood trauma, functional brain connectivity, executive dysfunction, and the development of binge drinking during adolescence. Target: Examine how individual differences in neurobiology contribute to adolescent substance taking behavior and related health outcomes. (Target Met)	Conduct preclinical studies to identify persistent neurobiological adaptations that occur as a result of exposure to alcohol during adolescence.	Continue preclinical research to identify brain-based predictors of alcohol use initiation and misuse among adolescents.	N/A
SRO-3.2 By 2023, establish the feasibility of using one emerging technology to safely and non-invasively obtain real time data on human placenta development and function during pregnancy. (Outcome)	FY 2020: NIH-funded research that identified two biomarkers associated with placental function and pregnancy complications. Target: Identify two biomarkers that are associated with placental development and/or function.	Utilize one innovative technology to characterize longitudinal changes in normal vs. abnormal placenta during pregnancy.	To be determined[101]	N/A

[101] Research activities were temporarily halted due to COVID-19. The longer-term impact of COVID-19 on these research activities is unknown at this time.

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	(Target Met)			
SRO-3.9 By 2020, identify two molecular-targeted therapies for disorders of the immune system that affect children. (Outcome)	FY 2020: Researchers completed an interventional clinical study and published results from four patients with treatment-resistant juvenile dermatomyositis (JDM) who responded to treatment with a Janus Kinase (JAK) inhibitor. Patients improved clinically by standard research laboratory measures and have exhibited a sustained response. Target: Complete an interventional clinical study of a molecularly targeted therapy for a disorder of the immune system that affects children. (Target Met)	N/A	N/A	N/A
SRO-4.1 By 2020, enable 1-3 Bridging Interventional Development Gaps (BrIDGs) projects to have sufficient pre-clinical data for therapeutic agents in order to apply for Investigational New Drug (IND) approval from the FDA. (Output)	FY 2020: BrIDGs researchers and their collaborators filed an Investigational New Drug (IND) application with the FDA and initiated clinical evaluation in late FY 2019. Target: Enable 1-3 BrIDGs projects to have sufficient pre-clinical data for therapeutic agents in order to apply for IND approval from the FDA. (Target Met)	N/A	N/A	N/A
SRO-4.3 By 2020, advance our characterization and understanding of the cellular and genetic	FY 2020: Studies of tumor composition by the Cancer Systems Biology Consortium and the Physical Sciences	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
components that make up the diverse composition of most tumors. (Outcome)	Oncology Network led to the development of six computational models that enhance understanding of dynamic tumor biology and enable predictions of cancer patient outcomes. Target: Based on new understanding of tumor composition, develop three computational models to explore new knowledge and treatments. (Target Exceeded)			
SRO-4.9 By 2023, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD). (Output)	FY 2020: NIH conducted a pre-clinical development study of a novel long-acting formulation of nalmefene for treating OUD, and a clinical study of a novel long-acting implant that delivers naltrexone, an effective treatment for OUD. Target: Conduct one pre-clinical and one clinical study of a longer acting formulation of a medication for the treatment of opioid use disorders or opioid overdose. (Target Met)	Conduct a Phase I clinical trial of an anti-opioid vaccine and a new medication to treat OUD.	Conduct a clinical trial of a medication for relapse prevention of OUD or overdose.	N/A
SRO-4.10 By 2020, design and develop novel dental composite resins that demonstrate superiority over the currently used restorative materials. (Output)	FY 2020: A filling has been developed that is stronger and longer lasting than current fillings, resulting in two patents. Target: One patent application of a novel resin will be completed, reflecting the priorities identified by the FDA.	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	(Target Met)			
SRO-4.11 By 2020, create a model system that recreates key features of human type 1 diabetes (T1D) autoimmunity for use in therapeutics development and testing. (Outcome)	FY 2020: Mouse models carrying induced pluripotent stem cell (iPSC)-derived human beta cells were used to test the efficacy of two approaches aimed at enhancing beta cell viability. Target: Use in vivo model(s) carrying iPSC-derived human beta cells to test the efficacy of two approaches aimed at enhancing beta cell viability and/or expansion. (Target Met)	N/A	N/A	N/A
SRO-4.14 By 2020, identify a total of three effective strategies to reduce modifiable health risk factors associated with premature mortality in people with serious mental illness (SMI). (Outcome)	FY 2020: Researchers tested three additional health risk reduction models that have the potential to reduce premature mortality in people with SMI. Target: Conduct testing of an additional three health risk reduction models that have potential to reduce premature mortality in adults with SMI. (Target Met)	N/A	N/A	N/A
SRO-4.15 By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations. (Output)	FY 2020: Researchers tested the effectiveness of multiple behavioral interventions for reducing alcohol use and other harmful behaviors in underaged incarcerated and homeless youth. Target: Test a behavioral	Test another behavioral therapy for intervening with alcohol misuse in an underage population.	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	therapy for intervening with alcohol misuse in an underage population. (Target Met)			
SRO-5.1 By 2020, develop and test the effectiveness of two strategies for translating cancer knowledge, clinical interventions, or behavioral interventions to underserved communities in community-based clinical settings. (Outcome)	FY 2020: Building on earlier efforts, two U54 Partnerships to Advance Cancer Health Equity (PACHE) validated strategies to help translate basic cancer knowledge and clinical or behavioral interventions to underserved communities across the United States and U.S. territories. These partnerships continue to work with various community-based organizations to disseminate these interventions and to assess their effectiveness in promoting health equity. Target: Finalize testing and validating the strategies to translate basic cancer knowledge, clinical or behavioral interventions to underserved communities and into clinical practice. (Target Met)	N/A	N/A	N/A
SRO-5.2 By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders (SUD). (Outcome)	FY 2020: Nine prevention pilot studies were conducted as part of the Helping to End Addiction Long-term (HEAL℠) Initiative. Target: Conduct 3-5 pilot studies to test the efficacy of promising prevention interventions for SUD.	Launch 1-2 clinical trials, based on pilot study results, to test the effects of a prevention intervention for opioid use disorder.	Conduct 1-2 studies to test the effectiveness of prevention interventions focused on electronic nicotine delivery systems (including vaping).	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	(Target Exceeded)			
SRO-5.3 By 2023, identify risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease. (Output)	FY 2020: Data analysis for the Alzheimer's Disease Sequencing Project (ADSP) Discovery follow-up Phase continued. Ongoing data analysis includes analysis from genomic regions of interest in ethnically diverse cohorts with increased sample size and data comparison on genomic regions of interest by ethnicity. Target: Continue analysis of ADSP Discovery Follow-Up Phase in ethnically diverse cohorts. Continue confirmation of genomic regions of interest from Discovery Phase and Discovery Follow-Up Phase in ethnically diverse datasets. Compare data on genomic regions of interest by ethnicity. (Target Met)	Continue analysis of ADSP Discovery Follow-Up Study in ethnically diverse cohorts. Continue confirmation of genomic regions of interest from Discovery Phase and Discovery Follow-Up Phase in ethnically diverse datasets. Begin harmonization of phenotypic data with ADSP genetic data across multiple types of study approaches from large epidemiology and clinical cohorts that are outside of the ADSP.	Continue analysis of ADSP Discovery Follow-Up Study in ethnically diverse cohorts. Continue confirmation of genomic regions of interest from Discovery Phase and Discovery Follow-Up Phase in ethnically diverse datasets. Continue harmonization of phenotypic data with ADSP genetic data across multiple types of study approaches from large epidemiology and clinical cohorts that are outside of the ADSP. Begin analysis of ADSP genetic data using artificial intelligence approaches.	N/A
SRO-5.8 By 2022, obtain pre-clinical and clinical data from newly initiated and current studies to evaluate 1-2 HIV vaccine candidate(s). (Outcome)	FY 2020: Findings from three NIH-funded studies have helped advance understanding of correlates of protection in non-human primates. Target: Further explore identification of correlates of protection in non-human primate animal models. (Target Met)	Enroll 25 percent - 50 percent of the 3,800 participants needed for a Phase III vaccine study.	Collect clinical data from a Phase IIb vaccine efficacy study.	N/A
SRO-5.10 By 2020, assess the effectiveness of five to seven	FY 2020: Five projects finalized their interventions and initiated dissemination	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
interventions that focus on eliminating health disparities by utilizing community partnerships to conduct intervention research that will foster sustainable efforts at the community level that will impact disparate conditions. (Output)	of results through scientific publications. Target: Complete analyses of five to seven community-based participatory research interventions to determine effectiveness in impacting health disparity conditions. (Target Met)			
SRO-5.12 By 2020, develop and/or characterize three mouse models for investigation of properties and functions of skin stem cells that can be used to advance research on wound healing, tissue engineering, or skin cancer. (Outcome)	FY 2020: Researchers made a mouse melanoma model that mimics the initial radial growth phase of human melanoma. Another mouse model uncovered a mechanism in which skin stem cells with a cancer-driving mutation multiply more but balance this by reducing their renewal rate. Target: Describe the role of stem cells in skin cancer development by creating traceable stem cells that allow researchers to study cancer development from its earliest events. (Target Met)	N/A	N/A	N/A
SRO-5.13 By 2022, complete research to the pre-clinical stage of development of a new or significantly improved targeted, minimally invasive biomodulation technology for therapy. (Outcome)	FY 2020: Researchers created a technology using acoustic waves to direct small objects like kidney stones out of the body without the need for surgery. Target: Initiate research of a prototype technology that	Conduct research on continued development and preliminary testing of one prototype technology that uses acoustic, optical, or electromagnetic waves to manipulate cells for treatment of a specific	To be determined[102]	N/A

[102] Research activities were temporarily halted due to COVID-19. The longer-term impact of COVID-19 on these research activities is unknown at this time.

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	uses acoustic, optical, or electromagnetic waves as a test case in a specific disease. (Target Met)	disease and begin to develop a plan for initiating the regulatory process.		
SRO-5.14 By 2020, evaluate the effectiveness of one intervention to reduce death and/or neurodisability in pre-term or in full term infants with life-threatening conditions. (Outcome)	FY 2020: Completed follow-up on 310 subjects enrolled in a study of Laparotomy vs. Drainage for Infants with Necrotizing Enterocolitis (NEST). Target: Complete follow-up on subjects enrolled in a comparative-effectiveness study on two surgical procedures to treat intestinal perforation due to necrotizing enterocolitis in infants. (Target Met)	N/A	N/A	N/A
SRO-5.15 By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations. (Outcome)	FY 2020: Researchers developed and tested three technology-based interventions to prevent and reduce underage drinking. Target: Develop a digital technology-based intervention to prevent or reduce alcohol misuse in underage individuals. (Target Met)	Disseminate information to the public about evidence-based interventions for underage populations.	Develop and/or evaluate preventive interventions to address underage alcohol use among specific underserved populations.	N/A
SRO-5.16 By 2021, conduct research to support pharmaceutical labeling changes for five drugs, to reflect safe and appropriate dosing and use specifically in children. (Outcome)	FY 2020: The Pediatric Trials Network has completed study enrollment for nine off-patent drugs and is enrolling patients to gather data on an additional 23 drugs. Due to the COVID-19 pandemic, there have been delays in patient enrollment.	Assess pharmacokinetics, pharmacodynamics, and safety of five drugs in pediatric populations.	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	Target: Obtain preliminary pharmacokinetic results to help assess the safety for mothers and infants of at least three common, off-patent drugs when used by breastfeeding women. (Target Not Met)			
SRO-5.17 By 2022, develop and test the effectiveness of three strategies to enhance end-of-life and palliative care. (Outcome)	FY 2020: Research developed culturally tailored interventions to improve advanced care planning for diverse populations. Target: Develop and test one novel strategy for improving end-of-life/palliative care through better support of family members and informal caregivers. (Target Met)	Develop and test at least one effective intervention for improving quality of life for patients at the end of life through enhanced shared decision-making and support of informal caregivers.	Develop and test at least three effective interventions to enhance end-of-life and palliative care by: improving quality of life for patients; providing support for family members and informal caregivers; and/or facilitating shared decision-making.	N/A
SRO-5.18 By 2026, enhance understanding of how five health information technologies can be applied effectively to improve minority health or to reduce health disparities. (Output)	Note: SRO-5.18 will begin reporting in December 2021.	Develop an adaptive smoking cessation intervention targeting adolescents of health disparity populations using the quitStart mobile application.	Determine if a mobile phone app is effective in promoting physical activity or reducing weight among racial and ethnic minority populations.	N/A
SRO-6.1 By 2023, perform comparative effectiveness studies to test five therapies for prevention or treatment of type 2 diabetes. (Outcome)	FY 2020: The final visits were completed and the data analyzed from the Restoring Insulin Secretion (RISE) adult medication study. Target: Complete final visits and analyze the data from the Restoring Insulin Secretion adult medication study.	Complete all final participant visits in the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study, according to the study protocol.	Analyze the primary outcome results from Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	(Target Met)			
SRO-6.2 By 2025, advance 1-2 new or repurposed compounds that act on neurobiological targets that may have the potential for treating alcohol or other substance use disorders. (Outcome)	FY 2020: Researchers examined the effects of ghrelin and ghrelin receptor blockade, a potential pharmacotherapy for alcohol use disorder, on inflammation in individuals with chronic heavy alcohol use. Target: Evaluate one compound with potential for treating alcohol and other substance use disorders in a clinical trial. (Target Met)	Conduct a preclinical evaluation of a novel or repurposed compound that acts on neurobiological targets implicated in alcohol use disorder.	Evaluate the efficacy of a candidate compound used in combination with a behavioral therapy for the treatment of alcohol use disorder.	N/A
SRO-7.3 By 2020, develop and/or evaluate two treatment interventions using health information technology (HIT) to improve patient identification, treatment delivery or adherence for substance use disorders and related health consequences. (Output)	FY 2020: NIH completed testing for two FDA approved digital therapeutic interventions for substance use disorder treatment. These projects focused on developing or testing health IT-based interventions to prevent or treat substance use disorders or to improve medication adherence. Target: Develop and test 1-2 FDA-approved digital therapeutic interventions for substance use disorder treatment and/or medication adherence. (Target Met)	N/A	N/A	N/A
CBRR-1.1 Provide research training for predoctoral trainees and fellows that promotes greater retention and long-term success in	FY 2020: Award rate to comparison group reached 11 percent. Target: N ≥ 10%	N ≥ 10%	N ≥ 10%	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
research careers. (Output)	(Target Met)			
CBRR-1.2 Provide research training for postdoctoral fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2020: Award rate to comparison group reached 16 percent and exceeded target by 6 percent. Target: N ≥ 10% (Target Exceeded)	N ≥ 10%	N ≥ 10%	N/A
CBRR-2 Promote data sharing and provide information in real time through the NIH Business System (NBS) by developing, integrating, deploying and maintaining business modules. (Output)	FY 2020: NBS implemented priority deployment activities for the Fund Configuration Initiative as planned. Target: (Deployment [Dep]) Conduct priority deployment activities for the Funds Configuration Initiative to comply with one of the NIH Corrective Action Plan remediation efforts. (Target Met)	(Development [Dev]) Continue to conduct priority deployment activities for the NIH Corrective Action Plan remediation efforts.	(Development [Dev]) Initiate development of planned business modules to build capacity and functionality of the NIH Business System.	N/A
CBRR-4 By 2021, produce and phenotype 2,500 knockout mouse strains to enhance the capacity of researchers to investigate the in vivo function of mammalian genes and identify new models of human disease. (Outcome)	FY 2020: Over 600 knockout juvenile lines were characterized (phenotyped). Target: Deliver phenotyping on 600 knockout juvenile lines (Target Exceeded)	Provide a cumulative total of 2,500 knockout mouse juvenile lines and associated resources to support research into gene function and human diseases.	N/A	N/A
CBRR-9 By 2020, enroll a total of 3,010 participants in GenomeConnect, ClinGen's Patient Registry. (Output)	FY 2020: A cumulative 3,106 participants were enrolled in GenomeConnect. Target: Enroll a total of 3,010 participants in GenomeConnect, ClinGen's Patient Registry.	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	(Target Exceeded)			
CBRR-10 By 2020, enroll 180 children into the Pediatric Heart Network (PHN) to support a research resource for investigators conducting research in congenital heart disease across the age spectrum. (Output)	FY 2020: More than 50 children were enrolled in the PHN in 2020. Target: Enroll 50 children with complex congenital heart disease in a clinical research study (Target Met)	N/A	N/A	N/A
CBRR-18 By 2021, develop and validate a new protocol for dementia assessment for use in large nationally representative samples. (Outcome)	FY 2020: Baseline Harmonized Cognitive Assessment Protocol (HCAP) data collection is complete in the US, Mexico, England, China and India. Data and documentation have been publicly released. Follow-up studies were planned but not initiated due to the COVID-19 pandemic. Target: Make data from the HCAP publicly available to the research community and initiate a follow-up study to the HCAP. (Target Not Met but Improved)	Complete follow-up assessment in the Health and Retirement Study using the refined HCAP.	N/A	N/A
CBRR-20 By 2020, advance the preclinical development of ten candidate products (e.g., vaccines, therapeutics) to combat infectious diseases. (Outcome)	FY 2020: Four vaccine and therapeutic products were advanced in FY 2020. Target: Advance the preclinical development of four vaccine and/or therapeutic candidate products. (Target Met)	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
CBRR-21 By 2020, establish and implement a national collaborative Pilot and Feasibility (P&F) program that utilizes specialized equipment, and expertise in nonmalignant hematology that are available through the Cooperative Centers of Excellence in Hematology (CCEH). (Output)	FY 2020: Eight pilot and feasibility projects involving collaborations outside the hematology Centers were supported in FY 2020. Target: Support four P&F projects involving collaboration outside the hematology Centers. (Target Met)	N/A	N/A	N/A
CBRR-22 By 2020, establish a reference map that will serve as the framework to understand the development of the human urinary tract. (Outcome)	FY 2020: Comparative atlases of the human and mouse prostate and kidney were generated and released to the general public. Target: Generate and release the human/mouse comparative atlases to the general public. (Target Met)	N/A	N/A	N/A
CBRR-25 Increase the total number of mentored research career development experiences for trainees from diverse backgrounds, including groups underrepresented in biomedical research, to promote individual development and to prepare them for a range of research-related careers. (Output)	FY 2020: Trainees from diverse backgrounds received a total of 3,779 career development experiences across all career stages. Target: 3,539 career experiences across all career stages (Target Exceeded)	3,540 career experiences across all career stages	3,545 career experiences across all career stages	N/A
CBRR-26 Maintain the yearly number of undergraduate students with mentored research experiences through the IDeA (Institutional	FY 2020: Due to the COVID-19 pandemic, the INBRE program was not able to provide summer research programs during FY 2020.	Sustain the number of undergraduate mentored research experiences from 2020 level.	Sustain the number of undergraduate mentored research experiences from FY 2021 level.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
Development Award) Networks of Biomedical Research Excellence (INBRE) program in order to sustain a pipeline of undergraduate students who will pursue health research careers. (Output)	Target: Sustain the number of undergraduate mentored research experiences from 2019 level. (Target Not Met)			
CBRR-27 By 2020, develop a suicide risk validated assessment tool that can easily be implemented in emergency care settings. (Output)	FY 2020: Researchers validated the Computerized Adaptive Screen for Suicidal Youth (CASSY). Target: Validate risk stratification approaches in emergency care settings for youth, and test clinical decision-making approaches based on risk stratification. (Target Not Met but Improved)	N/A	N/A	N/A
CBRR-28 Collect and distribute human tissue samples and molecular and genetic data from human tissues to the scientific community with the purpose of supporting research on brain and behavior. (Output)	FY 2020: Brain tissue from 30 new donors was obtained and tissue or data were distributed to 35 researchers. Target: Collect brain tissue from an additional 50 new donors and distribute tissue samples or data derived from tissue to 20 researchers studying mental or neurological disorders. (Target Not Met but Improved)	Collect brain tissue from an additional 30 new donors and distribute tissue samples or data derived from tissue to 20 researchers studying mental or neurological disorders.	Collect brain tissue from an additional 50 new donors and distribute tissue samples or data derived from tissue to 25 researchers studying mental or neurological disorders.	N/A
CBRR-29 By 2020, establish an interactive consortium to facilitate efficient data collection and sharing for biomarker studies of	FY 2020: Multi-site validation studies have been initiated for 10 additional biomarker candidates, bringing the total to 11 biomarker	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
vascular contribution to cognitive impairment and dementia (VCID). (Output)	candidates undergoing instrumental and clinical multi-site validation within the Consortium. Target: Initiate multi-site validation studies for two additional biomarker candidates. (Target Exceeded)			
CBRR-30 By 2024, expand the use of program-focused versus target-focused award mechanisms by National Institute of General Medical Sciences (NIGMS) investigators. (Output)	Note: CBRR-30 will begin reporting in December 2021.	Expand NIGMS investigator participation in the Maximizing Investigators' Research Award (MIRA) program by 2 percentage points.	Expand NIGMS investigator participation in the Maximizing Investigators' Research Award (MIRA) program by 2 percentage points.	N/A
CTR-7 By 2022, engage a national community in the development, dissemination, and implementation of a comprehensive national strategy to address the burden of Chronic Obstructive Pulmonary Disease (COPD) in the US. (Output)	FY 2020: NIH analyzed information from completed webinars and meetings and briefed stakeholders on National Action Plan progress. Target: Analyze completed webinars and meetings, and brief stakeholders on Action Plan progress. (Target Met)	Launch COPD National Action Plan Community Action Tool for stakeholders to capture Action Plan progress and conduct webinar and other promotional activities to encourage its use.	Analyze Action Plan implementation activities reported by stakeholders.	N/A
CTR-8 By 2020, improve the breadth of available metrics used to assess the number of scientists seeking research awards from NIH, and report on these expanded measures to both inform agency funding decisions, and promote transparency regarding the agency's funding strategies. (Output)	FY 2020: NIH developed summary reports to characterize grantee organizations that receive funding using multiple classification schemes, including the Department of Education Carnegie Classification. The framework provides a landscape of higher education granting postsecondary organizations.	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	Target: By 2020, develop a central standard report to describe NIH research investments to organizations receiving R01-equivalent and Research Project Grant support according to Carnegie Classification and Funding Institute/Center. (Target Met)			
MPO-3 Address diverse workforce recruitment needs to ascertain highly qualified staff to conduct or support biomedical research. (Ongoing) (Output)	FY 2020: NIH examined the use of the shared recruitment approach to determine if hiring goals were being met. The success of shared recruitments identified in the evaluation process led NIH to implement an even more proactive solution involving an entire schedule of shared recruitments that launched in the fall of 2020. Target: Examine (EX) key area to enhance recruitment. Examine use of the shared recruitment approach, using data gathered in first year of full-time practice, to determine if hiring goals are being met. [IM 2021/AS 2022] (Target Met)	Assess [AS] results of implementation. Assess process in place to identify the most opportune times throughout the year for NIH to recruit for varying occupations. [EX 2019/IM 2020]	Assess [AS] results of implementation. Assess the shared recruitment approach, using data gathered in first year of full-time practice, to determine if hiring goals are being met. [EX 2020/IM 2021]	N/A
MPO-4 Reallocate laboratory resources based on external reviews by Boards of Scientific Counselors. (Output)	FY 2020: 25 percent of Principal Investigators were reviewed resulting in approximately 25 percent of resources recommended to be reallocated.	Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources.	Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	Target: Conduct Board of Scientific Counselors (BSC) reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources. (Target Met)			
MPO-5 Improve facility conditions in order to reach and maintain a Condition Index (CI) weighted average of 85 or above (CIwa=85). (Ongoing) (Output and Efficiency)	FY 2020: The condition of the facilities portfolio reached a CIwa of 80.16. Target: CIwa = 77.78 (Target Exceeded)	CIwa = 77.63	CIwa = 76.95	N/A
MPO-7 Manage all Buildings and Facilities (B&F) line item projects so it is completed within 100 percent of the final approved project cost. (Ongoing) (Output)	FY 2020: 37 of the 45 active projects at the Facility Project Approval Agreement (FPAA) level threshold were effectively managed to ensure completion within 100 percent of the final approved cost. Target: 25 Active Projects (Target Exceeded)	21 Active Projects	28 Active Projects	N/A
MPO-8 Manage design and construction of capital facility projects funded by B&F so that no more than 10 percent of the projects may incorporate plus or minus 10 percent adjustments of the approved scope. (Ongoing) (Output)	FY 2020: NIH managed the design and construction of 37 of the 45 funded projects without a plus or minus 10 percent adjustment to the scope. Target: 25 Active Projects (Target Exceeded)	21 Active Projects	28 Active Projects	N/A
MPO-9 Utilize performance-based contracting (PBC). (ongoing) (Output)	FY 2020: Obligated 47 percent of eligible service contracting dollars to PBC. Target: Obligate the FY 2020 goal of eligible	Obligate the FY 2021 goal of eligible service contracting dollars to PBC.	Obligate the FY 2022 goal of eligible service contracting dollars to PBC.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2021 Target	FY 2022 Target	FY 2022 Target +/-FY 2021 Target
	service contracting dollars to PBC. (Target Met)			
MPO-11 Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation. (Output)	FY 2020: Of the 120 grant awards, 90 instruments (75 percent) were installed within 18 months of the Notice of Award date. Target: Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 18 months after award. (Target Met)	Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 18 months after award.	Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 18 months after award.	N/A
MPO-12 By 2020, enhance the management, oversight, and transparency of NIH-funded clinical trials through reforms to clinical trials grant applications, peer review, and tracking of awards. (Outcome)	FY 2020: NIH has deployed an enterprise-wide system for improved stewardship of NIH-funded clinical trials. The system has the ability to identify NIH-funded clinical trials and to receive and manage Clinical Trial data for grants, contracts and intramural projects and integrate with ClinicalTrials.gov to enhance availability of data and compliance. Target: Deploy an enterprise-wide system for improved stewardship of NIH-funded clinical trials that will enhance the management and oversight of NIH-funded clinical trials. (Target Met)	N/A	N/A	N/A

Grant Awards Table

	FY 2020 Final Allocation*,3	FY 2021 Enacted*,3	FY 2022 President's Budget a,3
Number of Awards	50,184	50,909	53,537
Average Award (in Whole $s)	$587,856	$595,857	$601,395
Range of Awards (in Whole $s)[1,2]	$1,000 to $32,595,654	$1,000 to $38,339,743	$1,000 to $37,780,409

[1] Award range excludes minimum values of zero to under $1,000 related primarily to no-cost extensions and co-funded actions.

[2] Award maximum estimates are based on an extrapolation from the most recent historical actual while accounting for expected budget policies applicable to each future fiscal year. The actual year-to-year fluctuations are roughly eight million dollars, plus or minus.

[3] Includes 21st Century Cures Act funding.

[*] To make the figures for FY 2020 and FY 2021 comparable to FY 2022, grant awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years, adding 103 and 89 awards to the NIH total figures, respectively.

[a] Figures do not include any awards related to the proposed ARPA-H program.

NEF NARRATIVE

Budget Summary
(Dollars in Thousands)

	FY 2020	FY 2021	FY 2022[103]
Notification[104]	--	--	TBD
Congressional Direction	$225,000	$225,000	TBD

Authorizing Legislation:

Authorization……..…. Section 223 of Division G of the Consolidated Appropriations Act, 2008
Allocation Method……..……..…….Direct Federal, Competitive Contract

Program Description and Accomplishments

The Nonrecurring Expenses Fund (NEF) permits HHS to transfer unobligated balances of expired discretionary funds from FY 2008 and subsequent years into the NEF account. Congress authorized use of the funds for capital acquisitions necessary for the operation of the Department, specifically information technology (IT) and facilities infrastructure acquisitions.

In recent years, the NEF has provided funds for critical infrastructure needs for NIH buildings, structures, and facilities, as a supplement to the regular NIH Building and Facilities (B&F) appropriations. The projects described below received NEF funds in FY 2016, FY 2017, FY 2019, FY 2020, and FY 2021.

FY 2016

In FY 2016, NIH received $162.1 million from the NEF for the renovation of the E-Wing in the NIH Clinical Center Complex (CCC) - Building 10 (B10). The CCC on the Bethesda Campus is a group of facilities that collectively support the NIH biomedical research mission by serving research hospital and laboratory functions. B10 is a 66-year-old facility built over two years beginning in 1950 that provides clinical services, laboratories, and supporting office space. With failing infrastructure, the condition of B10 has impaired its ability to fully support its role in this mission-critical complex. Without major renovation of its infrastructure, NIH is at risk of:

- Impacting accreditation by The Joint Commission and College of Anatomical Pathologists relating to the proximity of the Anatomical Pathology area located in the adjoining F-wing,
- Failing to provide the necessary functional adjacency to the existing Institutes and the Center's outpatient clinics, and

[103] HHS has not notified Congress in FY 2022.
[104] Pursuant to Section 223 of Division G of the Consolidated Appropriation Act, 2008, notification is required of planned use.

- Failing to fulfill its mission.

The renovation of the E-Wing in B10 provides major new research laboratory space replacing laboratories from aged distal wings in the complex and provides replacement of critical clinical programs, including the Department of Transfusion Medicine. It also provides critical new state-of-the-art current Good Manufacturing Practice (cGMP) facilities to further develop Cellular Engineering initiatives for all Institutes requiring Cell Processing.

FY 2017

In FY 2017, NIH received $35.3 million from the NEF for R22 Refrigerant Chiller replacement. This project involves replacing one of the six existing R22 chillers, a York 5,000-ton dual steam turbine/electric driven chiller (CH-16) in Building 11, with two new 3,000-ton variable speed electric chillers and associated cooling towers. Three additional chillers (CH-17,18 and 19) will be replaced between FY 2021 and FY 2024 using B&F funds. Due to the efficiency achieved in the chilled water upgrades accomplished between 2013 and 2015, and the additional efficiency and capacity of the two new chillers, the remaining R22 chillers (CH-20 and 21) will not have to be replaced. The refrigerant removed from the demolished chillers will be used as backup for the four remaining chillers if needed.

Also, in FY 2017, NIH received $16.5 million from the NEF for Emergency Generators to support the Central Utility Plant (CUP). The original scope of this project was to install three 2,500-kilowatt (KW) emergency generators and associated electrical gear adjacent and within the Building 11 CUP to feed enough power to run three steam-driven Chillers (21, 22 and 23). The Cogeneration (COGEN) Plant at NIH, which runs on natural gas, is unique in that it is believed to be the most efficient source of electrical power and steam from a stand-alone system in the world. The plant has the capability of delivering 22 megawatts (MW) of power to various substations on the Bethesda Campus, which in turn feeds the CUP. The new scope of work for this project is to direct the new emergency power generator or generators (2000 KW total) toward the startup of the COGEN plant should a loss of power occur from the local electrical utility service. In order to protect the critical mission of the NIH from disruption if the electric utility service for any reason suffers a severe voltage reduction or loss of the electrical system, the COGEN system and campus electric distribution system would automatically shut down and restart by energizing the COGEN plant through the new emergency generation system. This system will guarantee uninterrupted cooling and steam service to the most critical facilities on campus.

FY 2019

In FY 2019, NIH received $63.5 million from the NEF for a new CCC Utility Vault and Parking Garage. This project is for the completion of a new, 330,000 gross square foot (GSF) Utility Vault and Multi-Level Parking Garage to serve the CCC. The project will also include several enabling tasks for the proposed Surgery, Radiology, and Laboratory Medicine (SRLM) building, to be built as an addition to the Clinical Research Center (CRC). The enabling tasks include a new 2MW generator and switchgear for the SRLM building and the Clinical Data Center, as well as replacement of the electrical duct bank currently serving the CRC, which is in the footprint of

the new SRLM building. Also, repairs include a new CO2 storage tank, a new electrical feeder from Building 63 to the utility vault and parking garage, and utility vault housing for the future Building 59 & 59A (emergency generators and switchgear) replacement.

In FY 2019, NIH also received $19.5 million from the NEF for Electrical Power Reliability at the CCC. The CCC is composed of three major structures, including the original B10, the Ambulatory Care Research Facility (ACRF), and the CRC, built in 1952, 1980, and 2005, respectively. This project consists of two major initiatives in order to achieve electrical power reliability in the CCC, including electrical vault decommissioning and upgrades to existing electrical vaults. NIH will decommission the existing vaults and fully remove existing equipment in vaults 6 and 10, including environmental requirements for removal of transformers contaminated with Polychlorinated biphenyls. NIH will replace and upgrade electrical vaults 7, 8 and 9, one vault at a time, while maintaining full functional service to the CCC in subsequent years using B&F funds.

FY 2020

In FY 2020, NIH received $225 million from the NEF through Congressional direction, and allocated $12.6 million to upgrade and replace the obsolete Building Automation System of the CCC (inclusive of the original B10, ACRF, and CRC) with a new state-of-the-art, cost-effective, contiguous, simple, and secure system. The upgrade includes replacement of primary network controllers, controllers serving air-moving equipment and associated sensors, controllers serving hydronic systems and associated sensors, and replacement of pneumatic actuators with electronic actuators (except for speed-critical and high-torque devices). In order to minimize disruption to operations, terminal unit (VAV box) controllers and interfaces to Phoenix airflow control systems will remain and integrate into the new system. To a large extent, existing network and end device wiring will remain and be reused. This project was originally included in the FY 2019 NEF notification to Congress, and it continues to be one of the most pressing facility needs for NIH.

In FY 2020, NIH also allocated $212.4 million for its highest priority construction project, the SRLM building. This project will construct a new addition and repurpose two floors of the West Laboratory Wing of the CRC. The project will include the CCC Departments of Perioperative Medicine and Interventional Radiology, Radiology and Imaging Sciences, and Laboratory Medicine, now located in the ACRF's Wings S&T, and the National Cancer Institute's (NCI) research labs located on floors 1W and 3W of the CRC West Laboratory Wing. The total project will consist of 629,440 GSF, including new construction of 547,290 GSF and 82,150 GSF of renovation. The new wing will be an 8-story above-grade structure (with interstitial floors), plus one floor below grade and a mechanical penthouse. A below-grade Cardiovascular Intervention Program suite is also planned. The addition will be located on the west end of the CRC-West Laboratory Wing. Once the new addition is completed, four floors of the West Lab wing will be renovated after the existing NCI Research Labs are moved to the new addition.

The most recent Building Condition Index conducted by NIH has the ACRF, built in 1982, in the POOR category. Some of the major deficiencies include the following: 1) functional space

inadequacies/ inefficiencies; 2) inefficient routes of circulation; 3) numerous limitations restricting the facility's reliability of operations/flexibility/adaptability to address growth and change; 4) deficient and unreliable infrastructure systems (major areas of concern include normal and emergency power, communication systems, heating, cooling, and ventilation); and 5) structural problems (light steel structure), resulting in unacceptable vibration levels in some areas of the building.

Of the $212.4 million of FY 2020 NEF funds devoted to the SRLM, NIH plans to use $12.0 million to further the development of the SRLM bridging documents and conduct an independent cost estimate. This work will also include developing plans to get final approval from the National Capital Planning Commission and the Maryland Department of the Environment concept plans approved, construction logistics plan, air entrainment studies, traffic studies, analysis of potential crane usage/safety, materials staging, worker access, utilities shutdowns, and more.

FY 2021

While the SRLM project was shovel-ready in FY 2020, NIH did not have sufficient funds from its B&F appropriation and the NEF to award the $492.0 million construction contract. NIH carried over $200.4 million of the FY 2020 NEF funds, which are available until expended, to make the construction award in late FY 2021 or early FY 2022 using both FY 2020 and FY 2021 resources. In FY 2021, NIH intends to devote an additional $225.0 million in NEF funds, in addition to $62.6 million of FY 2020 and $4.0 million of FY 2021 B&F appropriations, to SRLM to award the construction contract using the remaining FY 2020 and new FY 2021 funds. The current target for issuing the solicitation for a Design-Build Contract is May 2021, with the target date for awarding the contract in the first quarter of FY 2022.

BUDGET REQUEST BY IC (SUMMARY TABLE)

(Dollars in Thousands)[1]	FY 2020 Final[6]	FY 2021 Enacted[6]	FY 2022 President's Budget[7]
NCI	$6,440,438	$6,558,805	$6,733,302
NHLBI	$3,625,258	$3,664,703	$3,845,681
NIDCR	$477,679	$484,843	$516,197
NIDDK[2]	$2,265,146	$2,281,931	$2,360,748
NINDS	$2,446,577	$2,510,913	$2,783,300
NIAID	$5,876,195	$6,067,071	$6,245,926
NIGMS[3]	$2,937,218	$2,991,417	$3,096,103
NICHD[4]	$1,797,780	$1,837,972	$1,942,117
NEI	$823,325	$835,521	$858,535
NIEHS[5]	$883,598	$896,168	$1,020,647
NIA	$3,545,869	$3,899,926	$4,035,591
NIAMS	$624,889	$634,286	$680,186
NIDCD	$490,692	$498,073	$511,792
NIMH	$2,042,966	$2,105,902	$2,213,574
NIDA	$1,457,724	$1,480,309	$1,852,503
NIAAA	$546,696	$554,882	$570,165
NINR	$172,363	$174,936	$199,755
NHGRI	$604,118	$616,012	$632,973
NIBIB	$404,638	$410,726	$422,039
NIMHD	$335,812	$391,586	$652,244
NCCIH	$151,877	$154,079	$184,323
NCATS	$832,888	$855,421	$878,957
FIC	$80,827	$84,013	$96,322
NLM	$456,911	$462,138	$474,864
OD[4]	$2,163,516	$2,283,867	$2,394,859
ARPA-H	---	---	$6,500,000
B&F	$200,000	$200,000	$250,000
Total, NIH Program Level	**$41,685,000**	**$42,935,500**	**$51,952,703**
Special Type 1 Diabetes Research	-$150,000	-$150,000	-$141,450
PHS Program Evaluation	-$1,230,821	-$1,271,505	-$1,271,505
Interior Approp. (Superfund Research)	-$81,000	-$81,500	-$83,540
Total, NIH Labor/HHS Budget Authority	**$40,223,179**	**$41,432,495**	**$50,456,208**

[1] Includes funding derived by transfer from the NIH Innovation Account under the 21st Century Cures Act.

[2] Includes Type 1 Diabetes mandatory funding as shown later in the table.

[3] Includes Program Evaluation financing as shown later in the table.

[4] FY 2020 and FY 2021 levels for OD and NICHD are adjusted for comparability with the proposed transfer of ECHO and INCLUDE to NICHD in FY 2022.

[5] Includes Interior Appropriations for Superfund Research activities as shown later in the table.

[6] Amounts for FY 2020 and FY 2021 reflect directive transfer of $5.0 million from OD to the HHS Office of Inspector General, and HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research.

[7] Reflects directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

APPROPRIATIONS ADJUSTMENT TABLE FOR FY 2020

(Dollars in Thousands)	FY 2020 Enacted	Permissive Transfer (NIH Innovation Account)[3]	OIG Transfer[4]	HIV/AIDS Transfer[5]	Subtotal	Comparable Adjustments	Comparable Budget Authority
NCI	$6,245,442	$195,000		-$4	$6,440,438		$6,440,438
NHLBI	$3,624,258			$1,000	$3,625,258		$3,625,258
NIDCR	$477,429			$250	$477,679		$477,679
NIDDK[1]	$2,264,314			$832	$2,265,146		$2,265,146
NINDS	$2,374,687	$70,000		$1,890	$2,446,577		$2,446,577
NIAID	$5,885,470			-$9,275	$5,876,195		$5,876,195
NIGMS	$2,937,218				$2,937,218		$2,937,218
NICHD	$1,556,879			$30	$1,556,909	$240,871	$1,797,780
NEI	$824,090			-$765	$823,325		$823,325
NIEHS[2]	$883,598				$883,598		$883,598
NIA	$3,543,673			$2,196	$3,545,869		$3,545,869
NIAMS	$624,889				$624,889		$624,889
NIDCD	$490,692				$490,692		$490,692
NIMH	$1,968,374	$70,000		$4,592	$2,042,966		$2,042,966
NIDA	$1,462,016			-$4,292	$1,457,724		$1,457,724
NIAAA	$545,373			$1,323	$546,696		$546,696
NINR	$169,113			$3,250	$172,363		$172,363
NHGRI	$606,349			-$2,231	$604,118		$604,118
NIBIB	$403,638			$1,000	$404,638		$404,638
NIMHD	$335,812				$335,812		$335,812
NCCIH	$151,740			$137	$151,877		$151,877
NCATS	$832,888				$832,888		$832,888
FIC	$80,760			$67	$80,827		$80,827
NLM	$456,911				$456,911		$456,911
OD	$2,744,387	-$335,000	-$5,000		$2,404,387	-$240,871	$2,163,516
B&F	$200,000				$200,000		$200,000
Total, NIH Program Level	**$41,690,000**	**$0**	**-$5,000**	**$0**	**$41,685,000**	**$0**	**$41,685,000**
Less funds allocated from different sources:							
Mandatory Type 1 Diabetes Research	-$150,000				-$150,000		-$150,000
PHS Program Evaluation	-$1,230,821				-$1,230,821		-$1,230,821
Total, NIH Discretionary Budget Authority	**$40,309,179**	**$0**	**-$5,000**	**$0**	**$40,304,179**	**$0**	**$40,304,179**
Interior Budget Authority	-$81,000				-$81,000		-$81,000
Total, NIH Labor/HHS Budget Authority	**$40,228,179**	**$0**	**-$5,000**	**$0**	**$40,223,179**	**$0**	**$40,223,179**

[1]Includes Type 1 Diabetes.

[2]Includes Superfund Research activity.

[3]Reflects redistribution of NIH Innovation account for the 21st Century Cures Act.

[4]Reflects directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

[5]Reflects HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research.

APPROPRIATIONS ADJUSTMENT TABLE FOR FY 2021

(Dollars in Thousands)	FY 2021 Enacted	Permissive Transfer (NIH Innovation Account)[3]	OIG Transfer[4]	HIV/AIDS Transfer[5]	Subtotal	Comparable Adjustments	Comparable Budget Authority
NCI	$6,364,852	$195,000		-$1,047	$6,558,805		$6,558,805
NHLBI	$3,664,811			-$108	$3,664,703		$3,664,703
NIDCR	$484,867			-$24	$484,843		$484,843
NIDDK[1]	$2,281,975			-$44	$2,281,931		$2,281,931
NINDS	$2,463,393	$50,000		-$2,480	$2,510,913		$2,510,913
NIAID	$6,069,619			-$2,548	$6,067,071		$6,067,071
NIGMS	$2,991,417				$2,991,417		$2,991,417
NICHD	$1,590,337			$2,635	$1,592,972	$245,000	$1,837,972
NEI	$835,714			-$193	$835,521		$835,521
NIEHS[2]	$896,175			-$7	$896,168		$896,168
NIA	$3,899,227			$699	$3,899,926		$3,899,926
NIAMS	$634,292			-$6	$634,286		$634,286
NIDCD	$498,076			-$3	$498,073		$498,073
NIMH	$2,053,708	$50,000		$2,194	$2,105,902		$2,105,902
NIDA	$1,479,660			$649	$1,480,309		$1,480,309
NIAAA	$554,923			-$41	$554,882		$554,882
NINR	$174,957			-$21	$174,936		$174,936
NHGRI	$615,780			$232	$616,012		$616,012
NIBIB	$410,728			-$2	$410,726		$410,726
NIMHD	$390,865			$721	$391,586		$391,586
NCCIH	$154,162			-$83	$154,079		$154,079
NCATS	$855,421				$855,421		$855,421
FIC	$84,044			-$31	$84,013		$84,013
NLM	$463,787			-$1,649	$462,138		$462,138
OD	$2,827,710	-$295,000	-$5,000	$1,157	$2,528,867	-$245,000	$2,283,867
B&F	$200,000				$200,000		$200,000
Total, NIH Program Level	**$42,940,500**	**$0**	**-$5,000**	**$0**	**$42,935,500**	**$0**	**$42,935,500**
Less funds allocated from different sources:							
Mandatory Type 1 Diabetes Research	-$150,000				-$150,000		-$150,000
PHS Program Evaluation	-$1,230,821				-$1,230,821		-$1,230,821
Total, NIH Discretionary Budget Authority	**$41,559,679**	**$0**	**-$5,000**	**$0**	**$41,554,679**	**$0**	**$41,554,679**
Interior Budget Authority	-$81,000				-$81,000		-$81,000
Total, NIH Labor/HHS Budget Authority	**$41,478,679**	**$0**	**-$5,000**	**$0**	**$41,473,679**	**$0**	**$41,473,679**

[1]Includes Type 1 Diabetes.

[2]Includes Superfund Research activity.

[3]Reflects redistribution of NIH Innovation account for the 21st Century Cures Act.

[4]Reflects directive transfer of $5.0 million from OD to the HHS Office of Inspector General.

[5]Reflects HIV/AIDS transfers across ICs under the authority of the Office of AIDS Research.

BUDGET MECHANISM TABLE

Budget Mechanism - Total[1,2,3]

(Dollars in Thousands)[1,2,3]	FY 2020 Final[7,8]		FY 2021 Enacted[7,8]		FY 2022 President's Budget[7,9]		FY 2022 +/- FY 2021	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	28,415	$15,903,452	29,040	$16,402,139	29,718	$17,350,182	678	$948,043
Administrative Supplements[3]	*(2,723)*	555,090	*(2,573)*	509,636	*(2,388)*	456,192	*(-185)*	-53,443
Competing	11,395	$6,395,871	11,189	$6,492,703	12,664	$7,191,779	1,475	$699,075
Subtotal, RPGs	39,810	$22,854,413	40,229	$23,404,478	42,382	$24,998,153	2,153	$1,593,675
SBIR/STTR	1,833	1,127,734	1,854	1,154,534	1,961	1,229,604	107	75,069
Research Project Grants	41,643	$23,982,147	42,083	$24,559,013	44,343	$26,227,757	2,260	$1,668,744
Research Centers:								
Specialized/Comprehensive	999	$1,937,294	1,063	$2,036,557	1,104	$2,132,854	41	$96,297
Clinical Research	70	432,804	67	419,359	66	418,554	-1	-805
Biotechnology	73	125,526	64	102,802	59	93,653	-5	-9,149
Comparative Medicine	48	138,385	51	141,435	52	141,514	1	79
Research Centers in Minority Institutions	21	74,111	22	78,386	25	86,000	3	7,614
Research Centers	1,211	$2,708,120	1,267	$2,778,539	1,306	$2,872,575	39	$94,036
Other Research:								
Research Careers	4,461	$835,776	4,558	$862,683	4,761	$896,618	203	$33,935
Cancer Education	59	14,878	83	20,939	85	21,439	2	500
Cooperative Clinical Research	272	498,295	265	501,540	268	508,255	3	6,715
Biomedical Research Support	125	89,486	131	91,397	130	90,994	-1	-403
Minority Biomedical Research Support	286	98,392	257	88,594	190	66,696	-67	-21,898
Other	2,127	1,273,872	2,265	1,431,756	2,454	1,512,570	189	80,814
Other Research	7,330	$2,810,700	7,559	$2,996,908	7,888	$3,096,571	329	$99,663
Total Research Grants	50,184	$29,500,967	50,909	$30,334,460	53,537	$32,196,903	2,628	$1,862,443
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,919	$186,323	4,005	$196,857	4,106	$209,440	101	$12,584
Institutional Awards	13,089	720,929	13,550	755,007	13,843	809,755	293	54,748
Total Research Training	17,008	$907,252	17,555	$951,864	17,949	$1,019,196	394	$67,332
Research & Develop. Contracts	2,304	$3,295,504	2,355	$3,362,683	2,521	$3,561,276	166	$198,593
(SBIR/STTR) (non-add)[3]	*(109)*	*(71,684)*	*(116)*	*(76,634)*	*(121)*	*(82,267)*	*(5)*	*(5,632)*
Intramural Research		$4,460,682		$4,548,996		$4,695,985		$146,989
Res. Management & Support		1,979,165		2,090,554		2,184,166		93,612
Res. Management & Support (SBIR Admin) (non-add)[3]		*(7,762)*		*(10,128)*		*(10,116)*		*(-11)*
Office of the Director - Appropriation[3,4]		*(2,163,516)*		*(2,283,867)*		*(2,394,859)*		*(110,992)*
Office of the Director - Other		1,230,430		1,335,443		1,431,636		96,194
ORIP (non-add)[3,4]		*(293,976)*		*(299,885)*		*(304,684)*		*(4,798)*
Common Fund (non-add)[3,4]		*(639,111)*		*(648,539)*		*(658,539)*		*(10,000)*
ARPA-H		0		0		6,500,000		6,500,000
Buildings and Facilities[5]		230,000		230,000		280,000		50,000
Appropriation[3]		*(200,000)*		*(200,000)*		*(250,000)*		*(50,000)*
Type 1 Diabetes[6]		-150,000		-150,000		-141,450		8,550
Program Evaluation Financing[6]		-1,230,821		-1,271,505		-1,271,505		0
Subtotal, Labor/HHS Budget Authority		**$40,223,179**		**$41,432,495**		**$50,456,208**		**$9,023,713**
Interior Appropriation for Superfund Research		81,000		81,500		83,540		2,040
Total, NIH Discretionary Budget Authority		**$40,304,179**		**$41,513,995**		**$50,539,748**		**$9,025,753**
Type 1 Diabetes		150,000		150,000		141,450		-8,550
Total, NIH Budget Authority		**$40,454,179**		**$41,663,995**		**$50,681,198**		**$9,017,203**
Program Evaluation Financing		1,230,821		1,271,505		1,271,505		0
Total, Program Level		**$41,685,000**		**$42,935,500**		**$51,952,703**		**$9,017,203**

1 All Subtotal and Total numbers may not add due to rounding.
2 Includes 21st Century Cures Act funding and excludes supplemental financing.
3 All numbers in italics and brackets are non-add.
4 Number of grants and dollars for the Common Fund and ORIP components of OD are distributed by mechanism and are noted here as non-adds. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.
5 Includes B&F appropriation and monies allocated pursuant to appropriations acts provisions such that funding may be used for facilities repairs and improvements at the NCI Federally Funded Research and Development Center in Frederick, Maryland.
6 Number of grants and dollars for mandatory Type 1 Diabetes (T1D) and NIGMS Program Evaluation financing are distributed by mechanism above; therefore, T1D and Program Evaluation financing amounts are deducted to provide subtotals for Labor/HHS Budget Authority.
7 Reflects transfer of $5.0 million to the HHS OIG.
8 Amounts are adjusted for comparability with the proposed transfer of ECHO and INCLUDE from OD to NICHD in FY 2022.
9 Reflects Type 1 Diabetes Research sequestration of $8.55 million.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING TYPE 1 DIABETES

(Dollars in Thousands)[1]

Object Classes	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Personnel Compensation			
Full-Time Permanent (11.1)	$1,116,657	$1,181,512	$64,855
Other Than Full-Time Permanent (11.3)	561,071	584,236	23,165
Other Personnel Compensation (11.5)	58,144	60,051	1,907
Military Personnel (11.7)	17,474	18,153	679
Special Personnel Services Payments (11.8)	207,271	213,584	6,313
Subtotal Personnel Compensation (11.9)	**$1,960,617**	**$2,057,536**	**$96,919**
Civilian Personnel Benefits (12.1)	639,521	689,172	49,651
Military Personnel Benefits (12.2)	13,667	14,120	454
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,613,805**	**$2,760,829**	**$147,024**
Travel & Transportation of Persons (21.0)	19,957	21,660	1,702
Transportation of Things (22.0)	6,452	6,546	94
Rental Payments to GSA (23.1)	25,682	25,482	-200
Rental Payments to Others (23.2)	1,454	1,404	-50
Communications, Utilities & Misc. Charges (23.3)	25,805	25,940	135
Printing & Reproduction (24.0)	241	240	0
Consultant Services (25.1)	1,382,675	1,452,680	70,004
Other Services (25.2)	1,470,793	1,488,960	18,166
Purchase of goods and services from government accounts (25.3)	3,049,930	3,200,055	150,125
Operation & Maintenance of Facilities (25.4)	68,179	68,685	506
R&D Contracts (25.5)	1,506,025	1,610,862	104,836
Medical Care (25.6)	36,371	37,515	1,144
Operation & Maintenance of Equipment (25.7)	162,482	165,034	2,551
Subsistence & Support of Persons (25.8)	7	7	0
Subtotal Other Contractual Services (25.0)	**$7,676,464**	**$8,023,797**	**$347,333**
Supplies & Materials (26.0)	223,730	226,523	2,793
Equipment (31.0)	240,702	282,806	42,103
Land and Structures (32.0)	215,816	216,554	738
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	30,532,328	39,005,820	8,473,491
Insurance Claims & Indemnities (42.0)	0	0	0
Interest & Dividends (43.0)	58	56	-2
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$38,968,690**	**$47,836,829**	**$8,868,139**
Total Budget Authority	**$41,582,495**	**$50,597,658**	**$9,015,163**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING SSF AND MF

(Dollars in Thousands)[1]

Object Classes	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Personnel Compensation			
Full-Time Permanent (11.1)	$1,556,025	$1,648,850	$92,825
Other Than Full-Time Permanent (11.3)	613,349	637,703	24,354
Other Personnel Compensation (11.5)	96,949	101,128	4,179
Military Personnel (11.7)	26,972	27,915	943
Special Personnel Services Payments (11.8)	214,043	220,510	6,467
Subtotal Personnel Compensation (11.9)	**$2,507,339**	**$2,636,107**	**$128,768**
Civilian Personnel Benefits (12.1)	825,072	889,461	64,389
Military Personnel Benefits (12.2)	19,530	20,147	617
Benefits to Former Personnel (13.0)	1,218	1,218	0
Total Pay Costs	**$3,353,159**	**$3,546,932**	**$193,773**
Travel & Transportation of Persons (21.0)	21,826	23,624	1,798
Transportation of Things (22.0)	11,963	12,088	125
Rental Payments to GSA (23.1)	84,830	84,642	-188
Rental Payments to Others (23.2)	63,462	63,413	-49
Communications, Utilities & Misc. Charges (23.3)	127,695	130,935	3,240
Printing & Reproduction (24.0)	252	252	0
Consultant Services (25.1)	630,822	661,296	30,474
Other Services (25.2)	2,775,618	2,850,800	75,181
Purchase of goods and services from government accounts (25.3)	870,644	917,550	46,906
Operation & Maintenance of Facilities (25.4)	229,415	245,944	16,529
R&D Contracts (25.5)	1,506,378	1,611,216	104,839
Medical Care (25.6)	51,162	53,258	2,096
Operation & Maintenance of Equipment (25.7)	361,980	370,460	8,480
Subsistence & Support of Persons (25.8)	41	43	2
Subtotal Other Contractual Services (25.0)	**$6,426,060**	**$6,710,567**	**$284,506**
Supplies & Materials (26.0)	400,613	413,398	12,785
Equipment (31.0)	299,232	343,961	44,729
Land and Structures (32.0)	260,800	261,754	953
Investments & Loans (33.0)	0	0	0
Grants, Subsidies & Contributions (41.0)	30,532,328	39,005,820	8,473,491
Insurance Claims & Indemnities (42.0)	0	0	0
Interest & Dividends (43.0)	274	272	-2
Refunds (44.0)	0	0	0
Subtotal Non-Pay Costs	**$38,229,336**	**$47,050,726**	**$8,821,390**
Total Budget Authority	**$41,582,495**	**$50,597,658**	**$9,015,163**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

SALARIES AND EXPENSES

(Dollars in Thousands)[1]

Object Classes	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Personnel Compensation			
Full-Time Permanent (11.1)	$1,116,657	$1,181,512	$64,855
Other Than Full-Time Permanent (11.3)	561,071	584,236	23,165
Other Personnel Compensation (11.5)	58,144	60,051	1,907
Military Personnel (11.7)	17,474	18,153	679
Special Personnel Services Payments (11.8)	207,271	213,584	6,313
Subtotal Personnel Compensation (11.9)	**$1,960,617**	**$2,057,536**	**$96,919**
Civilian Personnel Benefits (12.1)	639,521	689,172	49,651
Military Personnel Benefits (12.2)	13,667	14,120	454
Benefits to Former Personnel (13.0)	0	0	0
Total Pay Costs	**$2,613,805**	**$2,760,829**	**$147,024**
Travel & Transportation of Persons (21.0)	19,957	21,660	1,702
Transportation of Things (22.0)	6,452	6,546	94
Rental Payments to Others (23.2)	1,454	1,404	-50
Communications, Utilities & Misc. Charges (23.3)	25,805	25,940	135
Printing & Reproduction (24.0)	241	240	0
Other Contractual Services:			
Consultant Services (25.1)[2]	1,267,494	1,316,389	48,895
Other Services (25.2)	1,470,793	1,488,960	18,166
Purchase of goods and services from government accounts (25.3)[2]	2,004,747	2,108,390	103,643
Operation & Maintenance of Facilities (25.4)[2]	68,179	68,685	506
Operation & Maintenance of Equipment (25.7)	162,482	165,034	2,551
Subsistence & Support of Persons (25.8)	7	30,007	30,000
Subtotal Other Contractual Services	**$4,973,702**	**$5,177,465**	**$203,763**
Supplies & Materials (26.0)	223,730	226,523	2,793
Subtotal Non-Pay Costs	**$5,251,341**	**$5,459,779**	**$208,437**
Total Salaries and Expense / Administrative Costs	**$7,865,147**	**$8,220,608**	**$355,461**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, supplemental financing, and Program Evaluation Financing.

[2] Excludes obligations from accounts (OC 25.1, 25.3 and 25.4) supporting Program Evaluations and Inter-agency Agreements related to the Research and Development Contracts mechanism.

DETAIL OF FULL-TIME EQUIVALENT EMPLOYMENT (FTE)

Institutes and Centers	FY 2020 Actual	FY 2021 Estimate	FY 2022 Estimate
NCI	2,993	3,090	3,193
NHLBI	817	962	962
NIDCR	230	247	252
NIDDK	632	666	666
NINDS	525	549	607
NIAID	1,969	2,051	2,051
NIGMS	171	184	184
NICHD[1]	520	561	602
NEI	269	282	282
NIEHS	625	662	672
NIA	438	478	520
NIAMS	219	238	238
NIDCD	130	140	140
NIMH	548	577	589
NIDA	363	388	388
NIAAA	219	238	238
NINR	85	96	111
NHGRI	334	351	370
NIBIB	92	102	102
FIC	59	61	61
NIMHD	66	71	107
NCCIH	71	79	90
NCATS	187	239	277
NLM	647	741	741
OD[1]	875	952	975
ARPA-H	---	---	50
Central Services:			
OD - CS	792	841	851
CC	1,883	1,995	2,035
CSR	409	422	427
CIT	227	257	257
ORS	512	539	539
ORF	716	726	726
Subtotal Central Services[2]	**4,539**	**4,780**	**4,835**
PHS Trust Fund (non-add)[3]	*4*	*4*	*4*
CRADA (non-add)[4]	*6*	*6*	*6*
Total	**17,623**	**18,785**	**19,303**

[1] Includes transfer of 11 ECHO FTEs from OD to NICHD in FY 2022.

[2] Reflects FTE associated with Central Services positions whose payroll costs are financed from the NIH Management Fund and the NIH Service and Supply Fund.

[3] PHS Trust Fund positions are incorporated within the IC's Direct-funded civilian FTE category and are treated as non-add values.

[4] CRADA positions are distributed across multiple ICs and are treated as non-add values.

PROGRAMS PROPOSED FOR ELIMINATION

The FY 2022 request for the National Institutes of Health does not propose any programs for elimination.

PHYSICIAN'S COMPARABILITY ALLOWANCE WORKSHEET

		FY 2019 Actual	FY 2020 Actual	FY 2021 Estimate[1]	FY 2022 Estimate
1) Number of Physicians Receiving PCAs		130	123	126	126
2) Number of Physicians with One-Year PCA		23	22	21	21
3) Number of Physicians with Multi-Year PCA		107	101	105	105
4) Average Annual Physician Pay (without PCA payment)		$168,551	$174,272	$174,452	$178,420
5) Average Annual PCA Payment		$17,445	$18,770	$20,744	$21,216
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position				
	Category II Research Position	130	123	124	124
	Category III Occupational Health				
	Category IV-A Disability Evaluation			1	1
	Category IV-B Health and Medical Admin.	0	0	1	1

7) If applicable, list and explain the necessity of any additional physician categories designated by your agency (for categories other than I through IV-B). Provide the number of PCA agreements per additional category for the PY, CY and BY.

N/A

8) Provide the maximum annual PCA amount paid to each category of physician in your agency and explain the reasoning for these amounts by category.

Maximum annual PCA amounts for category II and IV-B vary based on grade level, amount of federal service and length of the PCA agreement. The monetary range is between $4,000 and $30,000. These flexible amounts are necessary to recruit and retain the caliber of physician needed to carry out the NIH mission which directly impacts the health of the nation.

9) Explain the recruitment and retention problem(s) for each category of physician in your agency (this should demonstrate that a current need continues to persist).(Please include any staffing data to support your explanation, such as number and duration of unfilled positions and number of accessions and separations per fiscal year.)

NIH strives to make progress recruiting and retaining qualified physicians to the Federal service. However, due to competition and more lucrative compensation in the private sector it continues to be challenging. NIH consistently has had a high turnover rate for physicians. NIH physicians require unique and specialized qualifications that make it difficult to fill vacancies.

10) Explain the degree to which recruitment and retention problems were alleviated in your agency through the use of PCAs in the prior fiscal year. (Please include any staffing data to support your explanation, such as number and duration of unfilled positions and number of accessions and separations per fiscal year.)

In FY 2020, there were a total of 123 PCA recipients across NIH. In FY 2021 and beyond, as indicated by the minimal increase in recipients to-date relative to the prior year, the critical need continues to exist for highly qualified, specialized physicians to support the NIH mission. NIH still requires compensation flexibilities such as PCA to attract and retain qualified physicians.

11) Provide any additional information that may be useful in planning PCA staffing levels and amounts in your agency.

N/A

[1] FY 2021 data will be approved during the FY 2022 Budget cycle.

HISTORY OF OBLIGATIONS BY IC

(Dollars in Thousands)	FY 2012	FY 2013	FY 2014	FY 2015[1]	FY 2016[1]	FY 2017[1,6]	FY 2018[1,6,7]	FY 2019[1,6,8]	FY 2020[1,6,9]	FY 2021[1,6,10] Enacted	FY 2022[1,6,10,11] President's Budget
NCI	$5,062,763	$4,789,014	$4,932,368	$4,944,593	$5,206,169	$5,636,393	$5,948,569	$5,993,599	$6,418,988	$6,755,147	$6,733,302
NHLBI	$3,073,302	$2,903,768	$2,988,415	$2,995,546	$3,109,062	$3,209,843	$3,374,154	$3,482,237	$3,624,863	$3,664,703	$3,845,681
NIDCR	$409,947	$387,309	$397,833	$397,672	$412,788	$424,782	$446,656	$460,613	$477,644	$484,843	$516,197
NIDDK[2]	$1,943,706	$1,837,027	$1,884,377	$1,899,088	$1,963,738	$2,009,448	$1,989,700	$2,099,265	$2,220,977	$2,526,624	$2,360,748
NINDS	$1,623,344	$1,533,793	$1,588,899	$1,604,581	$1,692,830	$1,778,684	$1,949,067	$2,413,897	$2,443,099	$2,517,496	$2,783,300
NIAID	$4,482,369	$4,235,094	$4,401,185	$4,417,529	$4,749,884	$4,905,708	$5,262,398	$5,567,138	$5,880,084	$6,085,200	$6,245,926
NIGMS[3]	$2,425,522	$2,293,044	$2,366,429	$2,372,199	$2,508,868	$2,646,059	$2,780,954	$2,821,806	$2,937,142	$2,991,417	$3,096,103
NICHD	$1,318,943	$1,246,140	$1,283,314	$1,286,797	$1,338,280	$1,376,541	$1,449,613	$1,508,603	$1,556,841	$1,837,972	$1,942,117
NEI	$701,407	$657,055	$675,551	$676,726	$707,002	$731,203	$770,483	$793,767	$823,310	$835,521	$858,535
NIEHS[4]	$763,225	$721,331	$743,002	$745,533	$769,730	$789,860	$826,646	$850,793	$883,808	$896,168	$1,020,647
NIA	$1,120,391	$1,040,565	$1,171,656	$1,197,459	$1,596,005	$2,048,792	$2,571,438	$3,080,043	$3,545,814	$3,899,926	$4,035,591
NIAMS	$534,791	$505,206	$520,314	$521,480	$540,874	$556,568	$585,240	$602,907	$624,832	$634,286	$680,186
NIDCD	$415,500	$392,540	$404,237	$405,168	$422,311	$435,877	$458,876	$472,988	$490,687	$498,073	$511,792
NIMH	$1,477,516	$1,396,006	$1,419,632	$1,433,603	$1,516,325	$1,604,624	$1,754,423	$1,869,653	$2,044,852	$2,107,924	$2,213,574
NIDA	$1,051,410	$993,404	$1,017,957	$1,015,695	$1,048,971	$1,070,813	$1,161,149	$1,621,334	$1,457,683	$1,480,309	$1,852,503
NIAAA	$458,665	$433,247	$446,282	$447,152	$466,713	$482,449	$508,398	$525,282	$546,691	$554,882	$570,165
NINR	$144,500	$136,516	$140,553	$140,837	$145,701	$149,930	$157,633	$163,165	$172,342	$174,936	$199,755
NHGRI	$512,258	$483,650	$498,076	$498,648	$512,486	$528,316	$556,741	$575,361	$604,083	$616,012	$632,973
NIBIB	$337,728	$319,062	$326,989	$327,223	$342,997	$356,971	$376,700	$388,079	$404,616	$410,726	$422,039
NIMHD	$275,927	$260,671	$268,439	$270,480	$280,264	$287,640	$304,372	$313,195	$335,799	$391,586	$652,244
NCCIH	$127,820	$120,767	$124,368	$124,046	$129,760	$134,373	$141,667	$145,933	$151,871	$154,079	$184,323
NCATS	$574,297	$542,598	$633,571	$632,629	$684,366	$704,248	$754,080	$847,430	$832,856	$855,421	$878,957
FIC	$69,493	$65,627	$67,575	$67,576	$69,996	$71,813	$75,534	$77,894	$80,811	$84,013	$96,322
NLM[5]	$373,087	$325,088	$334,383	$336,653	$393,074	$406,250	$424,789	$441,645	$456,584	$462,138	$474,864
ORIP	$303,525	$290,042	$294,486	$294,662	$295,783	$279,130	$289,205	$288,096	$293,970	$299,885	$304,684
Common Fund	$544,930	$513,461	$531,146	$545,607	$675,628	$695,430	$600,707	$619,166	$639,111	$648,539	$658,539
OD - Other	$608,713	$608,584	$477,293	$573,328	$599,263	$714,058	$1,016,632	$1,185,155	$1,467,130	$1,398,785	$1,431,636
B&F	$125,308	$106,676	$88,880	$123,464	$79,883	$113,415	$106,434	$211,107	$108,709	$200,000	$250,000
ARPA-H	---	---	---	---	---	---	---	---	---	---	$6,500,000
Total, NIH Program Level	**$30,860,387**	**$29,137,284**	**$30,027,205**	**$30,295,974**	**$32,258,751**	**$34,149,217**	**$36,642,258**	**$39,420,151**	**$41,525,195**	**$43,466,612**	**$51,952,703**
Less funds allocated from different sources:											
Mandatory - Special type 1 Diabetes Research	-$150,000	-$142,350	-$139,200	-$150,000	-$150,000	-$139,650	-$26,292	-$73,923	-$105,893	-$150,000	-$141,450
PHS Program Evaluation	-$8,200	-$8,200	-$8,200	-$715,000	-$780,000	-$824,443	-$922,871	-$1,146,821	-$1,230,821	-$1,271,505	-$1,271,505
Total, NIH Discretionary Budget Authority	**$30,702,187**	**$28,986,734**	**$29,879,805**	**$29,430,974**	**$31,328,751**	**$33,185,124**	**$35,693,095**	**$38,199,407**	**$40,188,481**	**$42,045,107**	**$50,539,748**
Interior Budget Authority	-$78,928	-$74,864	-$77,345	-$77,349	-$77,252	-$77,337	-$77,342	-$78,988	-$80,993	-$81,500	-$83,540
Total, NIH Labor/HHS Budget Authority	**$30,623,259**	**$28,911,870**	**$29,802,460**	**$29,353,625**	**$31,251,499**	**$33,107,787**	**$33,021,788**	**$38,120,419**	**$40,107,488**	**$41,963,607**	**$50,456,208**

[1] Excludes Ebola, Zika and other supplemental funding or transfers.

[2] Includes Special type 1 Diabetes Research mandatory account funding (through FY 2021). FY 2020 includes carryover of $123,707,707 from FY 2018 and $76,493,143 from FY 2019.

[3] Includes PHS Program Evaluation financing of $715,000,000 in FY 2015, $780,000,000 in FY 2016, $824,443,000 in FY 2017, $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, $1,230,821,000 in FY 2020 and $1,271,505,000 in FY 2021 and FY 2022.

[4] Includes Interior Appropriation allocation for Superfund Research activities.

[5] Includes PHS Program Evaluation financing of $8,200,000 for years before FY 2015.

[6] Includes funds under the 21st Century Cures Act.

[7] Includes obligations of $60,647,563 of 21st Century Cures carryover from FY 2017.

[8] Includes obligations of $429,883,740 of FY 2018 Opioids carryover in various ICs and $42,852,637 of 21st Century Cures carryover from FY 2017 and FY 2018 in various ICs and $415,197 of T1D carryover.

[9] Includes CURES carryover obligations of $230,278,992

[10] Amounts represent estimated or requested budget authority as opposed to obligations displayed in historical years.

[11] The FY 2022 Budget proposes a new Advanced Research Projects Agency for Health (ARPA-H).

HISTORY OF OBLIGATIONS BY TOTAL MECHANISM

(Dollars in Thousands)[1]	FY 2012 Actual	FY 2013 Actual	FY 2014 Actual	FY 2015 Actual [4]	FY 2016 Actual [4]	FY 2017 Actual [4]	FY 2018 Actual [4, 5]	FY 2019 Actual [4, 6]	FY 2020 Actual [4, 7]	FY 2021 Enacted [4, 8]	FY 2022 President's Budget [4, 9, 10]
Research Project Grants	$16,550,486	$15,445,463	$16,168,246	$16,441,843	$17,839,691	$19,105,304	$20,756,893	$22,493,313	$23,744,187	$24,876,534	$26,227,757
Research Centers	$3,040,375	$2,708,744	$2,723,203	$2,663,064	$2,573,774	$2,536,308	$2,581,750	$2,680,161	$2,713,731	$2,791,905	$2,872,575
Other Research	$1,808,138	$1,783,481	$1,846,841	$1,802,719	$2,019,736	$2,181,261	$2,371,164	$2,698,036	$2,753,289	$3,010,048	$3,096,571
Subtotal, Research Grants	**$21,398,999**	**$19,937,688**	**$20,738,290**	**$20,907,625**	**$22,433,201**	**$23,822,873**	**$25,709,807**	**$27,871,510**	**$29,211,207**	**$30,678,487**	**$32,196,903**
Research Training	$761,934	$733,524	$738,429	$758,017	$803,869	$827,397	$855,844	$865,305	$907,010	$951,864	$1,019,196
R & D Contracts	$2,937,188	$2,927,077	$2,990,037	$2,826,971	$2,913,224	$3,046,759	$3,072,406	$3,124,750	$3,283,765	$3,440,135	$3,561,276
Intramural Research	$3,401,506	$3,247,193	$3,373,601	$3,409,362	$3,682,831	$3,780,181	$3,972,054	$4,179,250	$4,462,022	$4,595,200	$4,695,985
Res. Mgt. & Support	$1,530,874	$1,485,575	$1,527,131	$1,619,784	$1,653,230	$1,747,406	$1,813,738	$1,886,087	$1,974,360	$2,090,641	$2,184,166
Office of the Director[2]	$609,530	$608,584	$477,293	$573,328	$599,263	$701,864	$1,016,633	$1,185,155	$1,467,130	$1,398,785	$1,431,636
Subtotal	**$30,640,031**	**$28,939,641**	**$29,844,781**	**$30,095,088**	**$32,085,618**	**$33,928,465**	**$36,440,482**	**$39,112,057**	**$41,305,493**	**$43,155,112**	**$45,089,163**
Buildings & Facilities[3]	$133,228	$114,580	$96,880	$123,464	$95,883	$143,415	$124,434	$229,107	$138,709	$230,000	$280,000
Interior- Superfund	$78,928	$74,864	$77,345	$77,332	$77,252	$77,337	$77,342	$78,988	$80,993	$81,500	$83,540
ARPA-H	---	---	---	---	---	---	---	---	---	---	$6,500,000
Total	**$30,852,187**	**$29,129,085**	**$30,019,005**	**$30,295,884**	**$32,258,753**	**$34,149,217**	**$36,642,258**	**$39,420,151**	**$41,525,195**	**$43,466,612**	**$51,952,703**

[1] Obligations for actual years exclude lapse. Amounts for all years include Special Type 1 Diabetes. All Subtotal and Total numbers may not add due to rounding. FY 2017 through FY 2021 includes 21st Century Cures Act funding. All years exclude Ebola-related and supplemental funding.

[2] Excludes obligations for the Common Fund and the Office of Research Infrastructure Programs, which are distributed by mechanism.

[3] Includes B&F appropriation and monies allocated ($18,000,000 in FY 2018, $18,000,000 in FY 2019, $30,000,000 in FY 2020, $30,000,000 in FY 2021, and $30,000,000 in FY 2022) pursuant to appropriations acts provisions that funding may be used for facilities repairs and improvements at the NCI Federally funded Research and Development Center in Frederick, Maryland.

[4] Includes Program Evaluation Financing resources of $715,000,000 in FY 2015, $780,000,000 in FY 2016, $824,443,000 in FY 2017, $922,871,000 in FY 2018, $1,146,821,000 in FY 2019, $1,230,821,000 in FY 2020, $1,271,505,000 in FY 2021 and $1,271,505,000 in FY 2022.

[5] Includes obligations of $60,647,563 of 21st Century Cures Act funding which was appropriated in FY 2017, but carried over into FY 2018.

[6] Includes obligations of $42,852,637 of 21st Century Cures Act funding which was appropriated in FY 2017 and FY 2018, but carried over into FY 2019. Similarly, includes $429,883,740 of Opioids funding and $415,917 of Type 1 Diabetes funding carried over from FY 2018. Obligations of carryover funding are distributed by mechanism.

[7] Includes obligations of $230,278,992 of 21st Century Cures Act funding which was appropriated in FY 2017 through FY 2019, but carried over into FY 2020. Similarly, includes $200,200,850 of Type 1 Diabetes funding carried over from FY 2018 and FY 2019. Obligations of carryover funding are distributed by mechanism.

[8] Includes estimated obligations of $268,290,203 of 21st Century Cures Act funding which was appropriated in FY 2017 through FY 2020, but carried over into FY 2021. Similarly, includes $244,692,931 of Type 1 Diabetes funding carried over from FY 2018 through FY 2020. Obligations of carryover funding are distributed by mechanism.

[9] Fhe FY 2022 Budget proposes a new Advanced Research Projects Agency for Health (ARPA-H).

[10] FY 2022 figures based on requested budget authority.

STATISTICAL DATA: DIRECT AND INDIRECT COSTS AWARDED

(Dollars in Thousands)	Direct Cost Awarded	Indirect Cost Awarded	Percent of Total		Percent Change	
			Direct Cost Awarded	Indirect Cost Awarded	Direct Cost Awarded	Indirect Cost Awarded
FY 2010	$16,040,991	$6,193,567	72.1%	27.9%	2.3%	2.8%
FY 2011	$15,849,082	$6,173,769	72.0%	28.0%	-1.2%	-0.3%
FY 2012	$15,978,032	$6,182,900	72.1%	27.9%	0.8%	0.2%
FY 2013	$14,915,599	$5,755,617	72.2%	27.8%	-6.7%	-6.9%
FY 2014	$15,568,553	$5,908,275	72.5%	27.5%	4.4%	2.7%
FY 2015	$15,645,282	$6,020,843	72.2%	27.8%	0.5%	1.9%
FY 2016	$16,791,158	$6,445,133	72.3%	27.7%	7.3%	7.1%
FY 2017[1]	$17,799,515	$6,838,801	72.2%	27.8%	6.0%	6.1%
FY 2018[1,3]	$19,599,758	$7,481,452	72.4%	27.6%	10.1%	9.4%
FY 2019[1,2]	$20,544,931	$7,953,747	72.1%	27.9%	4.8%	6.3%
FY 2020 Final[*,1]	$21,971,965	$8,436,254	72.3%	27.7%	7.0%	6.1%
FY 2021 Enacted[*,1]	$22,627,128	$8,659,196	72.3%	27.7%	3.0%	2.6%
FY 2022 President's Budget[a,1]	$24,008,509	$9,207,590	72.3%	27.7%	6.9%	7.1%

Note: Data for fiscal years 2021 and later represent estimates and will change as actual data are received.

[1] Includes 21st Century Cures Act funding.

[2] Figures include estimates of BA carried over into later years.

[3] Figures reflect BA carried over into later years.

[*] To make the figures for FY 2020 and FY 2021 comparable to FY 2022, the costs of awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years, adding $236.5 and $239.6 million to the total NIH award amounts, respectively. As a result, the "Percent of Total" figures in the comparable case differ by less than about 0.015% from the not-comparable case.

[a] Figures do not include any awards related to the proposed ARPA-H program.

RPGS – TOTAL NUMBER OF AWARDS AND FUNDING

(Dollars in Thousands)	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017 Final[3]	FY 2018 Final[3,5]	FY 2019 Final[3,4]	FY 2020 Final Allocation[*,3]	FY 2021 Enacted[*,3]	FY 2022 President's Budget[a,3]
No. of Awards:										
Competing	8,234	9,168	9,540	10,364	10,123	11,116	11,020	11,395	11,189	12,664
Noncompeting	25,140	23,504	23,261	23,528	24,638	25,780	27,624	28,415	29,040	29,718
Subtotal	33,374	32,672	32,801	33,892	34,761	36,896	38,644	39,810	40,229	42,382
SBIR/STTR	1,466	1,660	1,578	1,689	1,807	2,034	2,023	1,833	1,854	1,961
Total	**34,840**	**34,332**	**34,379**	**35,581**	**36,568**	**38,930**	**40,667**	**41,643**	**42,083**	**44,343**
Average Annual Cost:										
Competing RPGs	$418	$489	$452	$484	$522	$527	$573	$561	$580	$568
Total RPGs[1]	444	474	479	502	523	546	552	574	582	590
Percent Change in Average Cost from Prior Year[2]										
Competing RPGs	-0.8%	17.0%	-7.5%	7.2%	7.8%	1.0%	8.7%	-2.0%	3.4%	-2.1%
Total RPGs[1]	-3.3%	6.7%	1.2%	4.8%	4.0%	4.4%	1.1%	4.1%	1.3%	1.4%
Average Length of Award in Years	**3.5**	**3.5**	**3.5**	**3.6**	**3.6**	**3.6**	**3.6**	**3.6**	**3.6**	**3.6**

NOTE: Includes awards supported by the Common Fund program (for all years) and the Type 1 Diabetes mandatory account.

[1] Includes Noncompeting RPGs and Administrative Supplements. Excludes SBIR/STTR awards.

[2] Based on average costs in whole dollars.

[3] Includes 21st Century Cures Act funding.

[4] Figures include estimates of BA carried over into later years.

[5] Figures reflect BA carried over into later years.

[*] To make the figures for FY 2020 and FY 2021 comparable to FY 2022, RPG awards and dollars for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years, adding 58 and 72 RPGs and $175.8 and $175.6 million to the NIH-total figures, respectively.

[a] Figures do not include any awards related to the proposed ARPA-H program.

RPGS – SUCCESS RATES

INSTITUTES & CENTERS[+,1,2]	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017 Final[6]	FY 2018 Final[6,8]	FY 2019 Final[6,7]	FY 2020 Final Allocation[*,6]	FY 2021 Enacted[*,6]	FY 2022 President's Budget[6,a]
NCI	13.7%	14.1%	13.0%	12.0%	11.7%	11.3%	11.9%	12.9%	13.4%	13.3%
NHLBI	16.9%	18.2%	21.9%	24.2%	23.5%	25.1%	22.3%	22.2%	21.1%	21.8%
NIDCR	19.9%	21.5%	22.0%	19.9%	17.8%	22.2%	23.8%	21.7%	24.5%	27.3%
NIDDK	21.0%	22.9%	20.3%	20.1%	17.8%	21.6%	20.3%	24.4%	24.2%	26.5%
NINDS	19.8%	18.7%	20.5%	19.8%	17.7%	22.4%	20.4%	23.7%	20.5%	22.1%
NIAID	18.8%	22.0%	21.5%	23.8%	19.1%	22.9%	22.1%	23.9%	22.2%	23.9%
NIGMS	19.9%	24.8%	29.6%	29.6%	30.6%	29.2%	32.6%	32.3%	33.2%	24.7%
NICHD[*]	10.8%	12.5%	11.5%	13.2%	16.1%	18.4%	19.5%	18.8%	20.8%	21.8%
NEI	23.7%	26.7%	21.4%	25.7%	24.9%	26.7%	28.4%	29.6%	26.2%	27.2%
NIEHS	15.3%	15.0%	14.7%	14.2%	15.0%	17.1%	14.8%	14.2%	15.9%	35.7%
NIA	13.6%	15.9%	17.7%	22.8%	26.6%	28.9%	29.2%	25.8%	27.5%	26.1%
NIAMS	15.9%	18.1%	16.7%	16.0%	17.0%	16.7%	17.1%	18.0%	17.5%	22.2%
NIDCD	22.5%	25.8%	24.9%	26.7%	24.4%	27.1%	25.2%	24.2%	21.7%	22.3%
NIMH	18.7%	19.4%	20.4%	22.9%	20.9%	22.2%	24.8%	22.5%	21.1%	21.9%
NIDA	19.5%	18.0%	19.6%	15.4%	19.7%	19.4%	17.5%	16.9%	12.0%	33.7%
NIAAA	19.5%	19.2%	16.4%	18.8%	22.0%	26.7%	20.9%	21.4%	17.8%	24.5%
NINR	9.1%	11.6%	8.0%	9.0%	8.9%	10.3%	9.3%	10.8%	10.2%	16.6%
NHGRI	20.5%	17.7%	18.8%	25.6%	23.9%	28.0%	19.2%	21.8%	18.6%	13.1%
NIBIB	13.7%	13.1%	12.0%	14.6%	13.0%	16.8%	18.3%	19.8%	15.7%	17.0%
NIMHD	4.3%	11.9%	13.7%	19.3%	21.5%	10.7%	7.5%	7.9%	12.1%	41.6%
NCCIH[3]	11.6%	8.7%	10.8%	13.9%	16.7%	20.3%	12.5%	11.6%	12.3%	22.5%
NCATS[4]	N/A	16.7%	66.7%	27.7%	21.8%	36.4%	20.7%	25.2%	21.5%	28.0%
FIC	14.6%	9.1%	9.7%	29.5%	10.8%	19.5%	20.6%	19.7%	15.7%	25.4%
NLM	12.3%	19.4%	19.8%	13.0%	14.9%	17.7%	18.4%	13.4%	14.2%	12.1%
ORIP & SEPA[5]	20.0%	19.6%	21.5%	18.8%	16.5%	17.8%	34.2%	29.6%	29.2%	29.2%
Common Fund	9.2%	10.0%	12.1%	12.6%	11.8%	10.9%	11.0%	9.5%	8.8%	6.5%
NIH	**16.7%**	**18.0%**	**18.3%**	**19.1%**	**18.7%**	**20.3%**	**20.1%**	**20.7%**	**20.1%**	**22.1%**

[+] Success Rates identified in FY 2021 and beyond are estimates, and will change as applications are received and selected for funding.

[1] Application success rates represent the percentage of applications that are awarded during the fiscal year.

[2] Includes Special type 1 Diabetes Research program administered by NIDDK. Excludes NIEHS Superfund Research and OD Other awards.

[3] The National Center for Complementary and Alternative Medicine (NCCAM) was renamed in December 2014 to the National Center for Complementary and Integrative Health (NCCIH).

[4] The National Center for Advancing Translational Sciences (NCATS) was established concurrent with the dissolution of National Center for Research Resources (NCRR) effective FY 2012.

[5] The SEPA program transitioned to NIGMS in FY 2017 from the NIH Office of Research Infrastructure Program (ORIP).

[6] Includes 21st Century Cures Act funding.

[7] Figures include estimates of BA carried over into later years.

[8] Figures reflect BA carried over into later years.

[*] To make the success rates for FY 2020 and FY 2021 comparable to FY 2022, competing RPG awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years. Those tables include 22 and 20 competing awards, respectively. Application counts are not adjusted. Those competing awards increase the success rates for NICHD in those years by about 0.8%, whereas the NIH total success rate remains unchanged, to within the displayed digits.

[a] Figures do not include any awards or applications related to the proposed ARPA-H program.

TOTAL R01 EQUIVALENT DATA FOR FIRST TIME AND ESTABLISHED INVESTIGATORS

R01 Equivalent Grants[X,1,2,3,4,5]	FY 2020 Final Allocation[*]	FY 2021 Enacted[*]	FY 2022 President's Budget[a]
Applications			
Received	37,413	39,248	41,961
Funded	**8,169**	**8,321**	**9,773**
Total Investigators			
Received	32,888	34,598	36,992
Funded	**9,962**	**10,234**	**12,127**
Established Investigators			
Received	20,442	21,203	22,535
Funded	**7,231**	**7,300**	**8,628**
First-time Investigators			
Received	12,446	13,395	14,457
Funded	**2,731**	**2,934**	**3,499**

[X] R01 Equivalent Grants form a subset of all RPG awards. In FY 2020 they comprised roughly 72% of Funded Applications, 75% of Funded Total Investigators, 84% of Funded Established Investigators and 59% of Funded First-time Applicants.

[1] Grant data is based on linear extrapolation of five years of latest actual data.

[2] Excludes applications and awards associated with reimbursable agreements and Superfund Research.

[3] Estimates for received applications reflect consolidations of Institute/Center validated refinements to linear extrapolation of five years of latest actual data.

[4] Includes 21st Century Cures Act funding.

[5] Figures include estimates of BA carried over into later years.

[*] To make the figures for FY 2020 and FY 2021 comparable to FY 2022, RPG awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years. As a result the comparable figures for FY 2020 and FY 2021 are slightly larger than the non-comparable figures: 1) there are about 15 more Funded Applications, and 2) there are about 19 more Funded Investigators (5 of which are First-time Investigators).

[a] Figures do not include any applications or awards related to the proposed ARPA-H program.

COMPETING RPGS BY LENGTH OF AWARD

(Dollars in Thousands)	FY 2020 Final Allocation*		FY 2021 Enacted*		FY 2022 President's Budget[a]	
	No.	Amount	No.	Amount	No.	Amount
Competing RPGs:[1,2]						
One-Year Awards	1,671	$1,424,460	1,293	$1,346,182	1,463	$1,491,126
Two-Year Awards	2,210	$500,099	2,535	$601,442	2,869	$666,200
Three-Year Awards	445	$252,864	505	$307,578	571	$340,696
Four-Year Awards	2,033	$1,123,379	2,069	$1,191,495	2,341	$1,319,784
Five or More Year Awards	5,036	$3,095,069	4,787	$3,046,006	5,420	$3,373,973
Total Competing RPGs	11,395	$6,395,871	11,189	$6,492,703	12,664	$7,191,779

[1] The distribution of awards with durations of 1, 2, 3, 4 and 5+ years is based on historical data.

[2] Includes 21st Century Cures Act funding.

[*] To make the figures for FY 2020 and FY 2021 comparable to FY 2022, RPG awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism table for those years, adding 22 and 20 competing RPGs and $38.6 and $35.7 million to the NIH-total figures, respectively.

[a] Figures do not include any awards related to the proposed ARPA-H program.

NON-COMPETING COMMITMENTS

(Dollars in Thousands)	FY 2020 Final Allocation*[4]	FY 2021 Enacted*[4]	FY 2022 President's Budget[a,4]
Research Project Grants (RPGs)			
Noncompeting:			
Number	28,415	29,040	29,718
Amount	$15,903,452	$16,402,139	$17,350,182
Administrative Supp	$555,090	$509,636	$456,192
Competing:			
Number	11,395	11,189	12,664
Amount	$6,395,871	$6,492,703	$7,191,779
SBIR/STTR:			
Number	1,833	1,854	1,961
Noncompeting	944	810	780
Amount[1]	$1,127,734	$1,154,534	$1,229,604
Noncompeting	$581,069	$504,224	$488,957
Subtotal, RPGs:			
Number	41,643	42,083	44,343
Amount	$23,982,147	$24,559,013	$26,227,757
Research Centers:			
Number	1,211	1,267	1,306
Noncompeting	985	889	1,033
Amount	$2,708,120	$2,778,539	$2,872,575
Noncompeting	$2,203,389	$1,949,775	$2,272,126
Other Research:			
Number	7,330	7,559	7,888
Noncompeting	5,798	5,015	6,203
Amount	$2,810,700	$2,996,908	$3,096,571
Noncompeting	$2,223,230	$1,988,488	$2,435,118
Training:			
FTTPs	17,008	17,555	17,949
Noncompeting	12,588	13,555	13,288
Amount	$907,252	$951,864	$1,019,196
Noncompeting	$671,492	$734,993	$754,546
Total Extramural Research[2]	**$30,408,219**	**$31,286,324**	**$33,216,099**
Noncompeting Number/FTTPs	48,730	49,309	51,022
Competing Number/FTTPs	18,462	19,155	20,464
Noncompeting Amount	$22,137,722	$22,089,255	$23,757,121
Competing Amount	$8,270,497	$9,197,069	$9,458,978
Total Percent Change	**6.7%**	**2.9%**	**6.2%**
Total Discretionary Budget Authority[3]	**$41,535,000**	**$42,785,500**	**$45,311,253**
Percent Change	**6.4%**	**3.0%**	**5.9%**

[1] The 3.65% combined SBIR/STTR program threshold is achieved in FY 2020 and sustained in subsequent years.

[2] Includes both grants and FTTPs for Noncompeting and Competing numbers.

[3] Includes Labor/HHS appropriations, the Interior Superfund Research account, 21st Century Cures Act funding, as well as Program Evaluation financing resources. Excludes mandatory accounts such as Type 1 Diabetes.

[4] Includes 21st Century Cures Act funding.

* To make the figures for FY 2020 and FY 2021 comparable to FY 2022, competing and noncompeting awards for the ECHO & INCLUDE programs have been added to the NICHD mechanism tables for those years. The only significant differences are for the RPGs and Other Research mechanisms, for which the award totals in the comparable case are about 0.8% and 2.2% larger than in the non-comparable case, respectively.

[a] Figures exclude awards and total discretionary budget aurthority related to the proposed ARPA-H program.

MF GENERAL STATEMENT

The NIH Management Fund (MF) was established on June 29, 1957, by Public Law 85-67. The MF was created to finance a variety of centralized support services and administrative activities that are required for the efficient and effective operation of all NIH programs and facilities. The services provided by the MF include a research hospital and outpatient clinic; receipt, review and referral of research and training grant applications; and police, fire, security, and general administrative support services. The MF is financed through offsetting collections from the NIH Institutes and Centers representing charges for services provided. Funds credited to the NIH Management Fund remain available for one fiscal year after the fiscal year in which they are deposited.

MF BUDGET AUTHORITY BY ACTIVITY

Budget Authority by Activity
(Dollars in thousands)

	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Detail:								
Clinical Center	1,883	$604,145	1,995	$651,872	2,035	$684,466	40	$32,594
Center for Scientific Review	409	128,341	422	128,597	427	135,027	5	6,430
Office of Research Services, Development & Operations and Administrative services	258	80,851	272	81,094	272	85,149	0	4,055
TOTAL	**2,550**	**$813,337**	**2,689**	**$861,563**	**2,734**	**$904,642**	45	$43,079

MF BUDGET AUTHORITY BY OBJECT CLASS

(Dollars in thousands)

		2021 Enacted	FY 2022 President's Budget	Increase or Decrease
Total compensable workyears:				
	Full-time employment	2,689	2,734	45
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$194	$194	1
	Average GM/GS grade	11.3	11.3	0
	Average GM/GS salary	$109	$112	3
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$110	$113	3
	Average salary of ungraded positions	104	107	3
	OBJECT CLASSES	**FY 2021 Enacted**	**FY 2022 President's Budget**	**Increase or Decrease**
	Personnel Compensation:			
11.1	Full-time permanent	$224,186	$238,457	$14,271
11.3	Other than full-time permanent	43,897	44,896	999
11.5	Other personnel compensation	27,007	28,588	1,581
11.7	Military personnel	6,291	6,466	175
11.8	Special personnel services payments	6,743	6,897	154
	Total, Personnel Compensation	**308,124**	**325,304**	**17,180**
12.0	Personnel benefits	99,920	107,856	7,936
12.2	Military personnel benefits	4,235	4,352	117
13.0	Benefits for former personnel	0	0	0
	Subtotal, Pay Costs	**412,279**	**437,512**	**25,233**
21.0	Travel and transportation of persons	1,650	1,724	74
22.0	Transportation of things	750	781	31
23.1	Rental payments to GSA	236	247	11
23.2	Rental payments to others	10	10	0
23.3	Communications, utilities and miscellaneous charges	4,850	5,044	194
24.0	Printing and reproduction	12	12	0
25.1	Consulting services	37,235	37,607	372
25.2	Other services	129,483	129,533	50
25.3	Purchase of goods and services from government accounts	77,093	81,129	4,036
25.4	Operation and maintenance of facilities	8,417	9,157	740
25.5	Research and development contracts	37	39	2
25.6	Medical care	11,934	12,829	895
25.7	Operation and maintenance of equipment	25,849	28,305	2,456
25.8	Subsistence and support of persons	35	36	1
25.0	**Subtotal, Other Contractual Services**	**290,083**	**298,635**	**8,552**
26.0	Supplies and materials	124,161	130,990	6,829
31.0	Equipment	24,250	26,190	1,940
32.0	Land and structures	3,260	3,475	215
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	0	0	0
42.0	Insurance claims and indemnities	0	0	0
43.0	Interest and dividends	22	22	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**449,284**	**467,130**	**17,846**
	Total Budget Authority by Object	**861,563**	**904,642**	**43,079**

MF DETAIL OF POSITIONS

GRADE	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
Total, ES Positions	4	4	4
Total, ES Salary	$763,595	$774,658	$776,599
GM/GS-15	110	115	116
GM/GS-14	330	336	339
GM/GS-13	367	383	391
GS-12	530	482	491
GS-11	478	480	488
GS-10	35	34	35
GS-9	113	119	121
GS-8	100	99	100
GS-7	217	224	227
GS-6	47	49	53
GS-5	26	21	22
GS-4	8	9	9
GS-3	10	7	8
GS-2	3	3	2
GS-1	1	1	1
Subtotal	2,375	2,362	2,403
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	14	13	13
Senior Grade	16	14	14
Full Grade	13	13	13
Senior Assistant Grade	15	15	15
Assistant Grade	1	1	1
Subtotal	59	56	56
Ungraded	285	245	249
Total permanent positions	2,413	2,455	2,461
Total positions, end of year	2,723	2,667	2,712
Total full-time equivalent (FTE) employment, end of year	2,550	2,689	2,734
Average ES salary	190,899	193,664	194,150
Average GM/GS grade	11.3	11.3	11.3
Average GM/GS salary	103,149	108,728	111,664

SSF GENERAL STATEMENT

The NIH Service and Supply Fund (SSF) was established on July 3, 1945, under 42 U.S.C. 231. The SSF was created to finance a variety of centralized research support services and administrative activities that are required for the efficient and effective operation of all NIH programs and facilities. The SSF provides a single means for consolidating the financing and accounting of business-type operations, including the sales of services and commodities to customers. The services provided through the SSF include mainframe computing, enterprise IT software planning and development, facilities engineering, planning and design, facility use and maintenance including leased buildings, printing, telecommunications, procurement, shipping and receiving, motor pool, research animals, fabrication and maintenance of scientific equipment, utilities and plant maintenance, finance and accounting operations, government-wide contracting for IT, biomedical engineering, security, consolidated human resources, collaborative computer science research, and other administrative support services. The SSF is financed through offsetting collections from the NIH Institutes and Centers representing charges for goods and services provided.

SSF Budget Authority by Activity

Budget Authority by Activity
(Dollars in thousands)

	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Detail:								
Research Support and Administrative (OD & includes CIF, ORS)	1,046	$1,493,350	1,108	$1,581,458	1,118	$1,660,519	10	$79,061
Office of Research Facilities Development & Operations (ORF)	716	552,212	726	584,793	726	614,032	0	29,240
Information Technology (CIT)	227	403,821	257	427,647	257	449,029	0	21,382
TOTAL	**1,989**	**$2,449,384**	**2,091**	**$2,593,898**	**2,101**	**$2,723,581**	10	$129,683

SSF BUDGET AUTHORITY BY OBJECT

(Dollars in Thousands)

		FY 2021 Enacted	FY 2022 President's Budget	Increase or Decrease
Total compensable workyears:				
	Full-time employment	2,091	2,101	10
	Full-time equivalent of overtime and holiday hours	0	0	0
	Average ES salary	$196	$199	3
	Average GM/GS grade	12.2	12.3	0
	Average GM/GS salary	$117	$120	3
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$105	$107	2
	Average salary of ungraded positions	147	150	3
	OBJECT CLASSES	**FY 2021 Enacted**	**FY 2022 President's Budget**	**Increase or Decrease**
	Personnel Compensation:			
11.1	Full-time permanent	$215,183	$228,881	$13,699
11.3	Other than full-time permanent	8,381	8,572	191
11.5	Other personnel compensation	11,798	12,489	691
11.7	Military personnel	3,207	3,296	89
11.8	Special personnel services payments	29	29	1
	Total, Personnel Compensation	**238,597**	**253,267**	**14,670**
12.0	Personnel benefits	85,631	92,433	6,801
12.2	Military personnel benefits	1,629	1,674	45
13.0	Benefits for former personnel	1,218	1,218	0
	Subtotal, Pay Costs	**327,075**	**348,591**	**21,516**
21.0	Travel and transportation of persons	218	240	22
22.0	Transportation of things	4,761	4,761	0
23.1	Rental payments to GSA	58,912	58,912	0
23.2	Rental payments to others	61,999	61,999	0
23.3	Communications, utilities and miscellaneous charges	97,040	99,951	2,911
24.0	Printing and reproduction	2	2	0
25.1	Consulting services	29,912	30,959	1,047
25.2	Other services	1,175,342	1,232,307	56,965
25.3	Purchase of goods and services from government accounts	380,078	404,638	24,561
25.4	Operation and maintenance of facilities	152,820	168,102	15,282
25.5	Research and development contracts	316	316	0
25.6	Medical care	2,857	2,914	57
25.7	Operation and maintenance of equipment	173,649	177,122	3,473
25.8	Subsistence and support of persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**1,914,972**	**2,016,357**	**101,385**
26.0	Supplies and materials	52,722	55,885	3,163
31.0	Equipment	34,279	34,965	686
32.0	Land and structures	41,725	41,725	0
33.0	Investments and loans	0	0	0
41.0	Grants, subsidies and contributions	0	0	0
42.0	Insurance claims and indemnities	0	0	0
43.0	Interest and dividends	194	194	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**2,266,824**	**2,374,991**	**108,167**
	Total Budget Authority by Object	**2,593,897**	**2,723,581**	**129,684**

SSF DETAIL OF POSITIONS

GRADE	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
Total, ES Positions	6	7	7
Total, ES Salary	$1,169,410	$1,374,485	$1,395,715
GM/GS-15	96	107	112
GM/GS-14	314	336	346
GM/GS-13	637	665	674
GS-12	291	304	306
GS-11	120	128	129
GS-10	7	7	7
GS-9	100	105	106
GS-8	20	21	21
GS-7	51	54	54
GS-6	6	6	6
GS-5	9	10	10
GS-4	16	15	15
GS-3	14	9	9
GS-2	10	6	6
GS-1	9	6	6
Subtotal	1,700	1,779	1,807
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	7	7	7
Senior Grade	7	7	7
Full Grade	11	11	11
Senior Assistant Grade	3	3	3
Assistant Grade	1	1	1
Subtotal	29	29	29
Ungraded	328	337	339
Total permanent positions	1,982	2,037	2,062
Total positions, end of year	2,063	2,152	2,182
Total full-time equivalent (FTE) employment, end of year	1,989	2,091	2,101
Average ES salary	194,902	196,355	199,388
Average GM/GS grade	12.1	12.2	12.3
Average GM/GS salary	113,726	116,882	120,052

DIGITAL MODERNIZATION

Modernization of the Public-Facing Digital Services – 21st Century Integrated Digital Experience Act

The 21st Century Integrated Digital Experience Act (IDEA) was signed into law on Dec. 20, 2018. It requires data-driven, user-centric website and digital services modernization, website consolidation, and website design consistency in all Executive Agencies. Departments across the federal landscape are working to implement innovative digital communications approaches to increase efficiency and create more effective relationships with their intended audiences. The American public expects instant and impactful communications – desired, trusted content available when they want it, where they want it, and in the format they want it. If the consumer is not satisfied they move on and the opportunity for impact is lost.

Modernization Efforts

In FY 2019, HHS engaged Department leadership and developed a Digital Communications Strategy that aligns with the requirements of IDEA. In FY 2020, HHS Digital Communications Leaders began implementation of the Strategy in alignment with IDEA, beginning to align budgets to modernization requirements.

As the result of a comprehensive review of costs associated with website development, maintenance, and their measures of effectiveness, HHS will prioritize:

- modernization needs of websites, including providing unique digital communications services, and
- continuing to developing estimated costs and impact measures for achieving IDEA.

Over the next four years, HHS will continue to implement IDEA by focusing extensively on a user-centric, Digital First approach to both external and internal communications and developing performance standards. HHS will focus on training, hiring, and tools that drive the communication culture change necessary to successfully implement IDEA.

Over the next year, HHS Agencies and Offices will work together to continue to implement IDEA and the HHS Digital Communications Strategy across all communications products and platforms.

Trans-NIH Initiatives

CONGRESSIONAL JUSTIFICATION

FY 2022

Department of Health and Human Services

National Institutes of Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Trans-NIH Initiatives

FY 2022 Budget Table of Contents Page No.

Introduction

The National Institutes of Health (NIH) seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. To achieve these goals, the NIH supports research on the causes, prevention, and treatment of human diseases and disorders; processes in healthy development and aging; and methods for collecting and disseminating data and health information. In addition, the NIH Institutes, Centers, and Offices (ICOs) leverage existing strengths and resources by collaborating in innovative and creative ways, to develop multidisciplinary approaches to answering complex and crucial questions about human health and preventing disease.

Trans-NIH collaborative efforts have led to the development of special initiatives and innovative research programs across the agency. For example, the Accelerating Medicines Partnerships (AMP), a federal and private collaboration, aims to increase the number of available diagnostic tools and therapeutics for major diseases including Type 2 diabetes and Parkinson's disease. The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative, a public-private partnership, focuses on innovative technologies which allow researchers to gain a new understanding of the brain to ultimately lead to discoveries in treatments, cures, and preventions for brain disorders. Other examples of trans-NIH collaborative efforts include the NIH Maternal Mortality and Morbidity Task Force, which is focused on increasing support for research on maternal health to reduce disparities and advancing foundational knowledge of the risk factors associated with maternal mortality and morbidity in the United States. The National Institute on Aging (NIA), in collaboration with 23 ICOs across NIH, has made substantial efforts in Alzheimer's disease and related dementia (ADRD) research. Research on ADRD has led to new tools and biomedical knowledge such as expansive data sharing platforms, new disease biomarkers and targets for treatment, and training programs designed to enhance diversity in the research workforce. NIH ICOs have partnered to develop data science, including artificial intelligence, to help NIH meet the challenges ahead by introducing new analytical methodologies and expanded capabilities. This includes the ability to flexibly and automatically analyze images and large datasets for many areas of biomedical research, including diagnostics and precision medicine.

A broad range of expertise focused on basic, translational, and clinical research is needed to guide and support research and related policies across the biomedical enterprise. The Advisory Committee to the Director (ACD) Working Groups, for instance, bring together experts from within NIH and the scientific community to address complex issues, such as ending the culture of sexual harassment and enhancing scientific rigor in animal research. NIH supports early-stage investigators through the Next Generation Researchers Initiative (NGRI). In alignment with the recommendations of the ACD Working Group on the NGRI, NGRI encourages ICOs to prioritize funding opportunities for early-stage investigators, track the impact of that funding on investigator careers and develop policies responsive to the needs of these investigators.

The ultimate example of trans-NIH collaborative efforts came with the emergence of the COVID-19 pandemic. NIH quickly responded to this public health challenge by establishing new multi-ICO programs, including the Accelerating COVID-19 Therapeutics Interventions and Vaccines (ACTIV) partnership and the Rapid Acceleration of Diagnostics (RADx[SM]) initiative.

Together, these initiatives support the development of promising therapeutic, vaccine, and diagnostic approaches to usher in an end to the pandemic. ACTIV brings together key partners from federal, private, academic, and nonprofit organizations to align efforts and resources across four areas of opportunity: preclinical treatments, clinical therapeutics, clinical trial capacity, and vaccine development. RADx is working to expand the development and distribution of COVID-19 diagnostics with trans-NIH support for promising testing technologies, advancement of existing testing platforms, development of novel approaches to testing, and identification of effective strategies to make testing available to all, especially underserved and/or vulnerable populations. In addition to developing new initiatives, existing trans-NIH efforts quickly shifted to meet the growing emergency and public health need associated with COVID-19. The Helping to End Addiction Long-term (HEAL^{SM}) Initiative, a trans-agency effort developed to address the national opioid crisis, leveraged its existing partnerships and research infrastructure to respond to COVID-19 and its intersection with the opioid epidemic by funding research on the best approaches to treat those with opioid use disorder who are at a higher risk of respiratory illnesses and providing additional support to ongoing studies to direct resources to the COVID-19 pandemic. The *All of Us* Research Program leveraged its large and diverse cohort by testing participant samples collected prior to March 2020 for antibodies against SARS-CoV-2, which may indicate if a participant has been exposed. This testing will enhance understanding of when the virus first arrived in the United States and how it has spread since. Participants also are being surveyed on the effect of COVID-19 on their physical and mental health. To help researchers study common symptoms and treatments, the *All of Us* Research Program is also collecting and standardizing electronic health record information of those affected by COVID-19 for secondary analysis.

During FY 2022, NIH will continue to facilitate partnerships across ICOs to leverage infrastructure and scientific strengths and effectively advance biomedical research and public health. Building partnerships and leveraging existing relationships are important for NIH to support and facilitate research discoveries to prevent illness and disease and promote health. By answering the call of urgent public health needs, closing gaps in health disparities, and capitalizing on foundational research investments, NIH will continue turning discovery into health.

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

Program Overview

The COVID-19 pandemic is an unprecedented global crisis that has been met with a swift and extraordinary response. One of the ways the NIH has addressed this public health need with great urgency is by establishing and leading the new public-private partnership, the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership,[105] to develop a coordinated research strategy for prioritizing and speeding development of the most promising treatments and vaccines. Announced April 17, 2020, and managed by the Foundation for the National Institutes of Health (FNIH), ACTIV brings NIH together with the Biomedical Advanced Research and Development Authority (BARDA); Centers for Disease Control and Prevention (CDC); Food and Drug Administration (FDA); Department of Defense (DOD); Department of Veterans Affairs (VA); the trans-governmental collaborative effort formerly known as Operation Warp Speed; European Medicines Agency (EMA); and representatives from numerous biopharmaceutical companies, academia, and philanthropic organizations.

The ACTIV governance consists of a Leadership Group, an Executive Committee, and four working groups. The Leadership Group, which includes representatives from all ACTIV partners, meets regularly to review the progress of ACTIV. The Executive Committee, comprised of scientific executives from government and industry, oversees the activities and operations of the working groups, including reviewing recommendations for preclinical testing and therapeutic agents selected to enter ACTIV clinical trials using master protocols. NIH Institute Directors and Deputy Directors, including those from the National Center for Advancing Translational Sciences (NCATS), the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Allergy and Infectious Diseases (NIAID), and the Office of the Director (OD), actively participate on the ACTIV Leadership Group, and some also serve on the ACTIV Executive Committee. Four working groups have focused on fast-track areas most ripe for opportunity: preclinical, therapeutics clinical, clinical trial capacity, and vaccines. The working groups include senior scientists from government, industry, academia, and philanthropic organizations.

In an unprecedented timeframe, ACTIV has made numerous accomplishments by developing a collaborative framework for prioritizing candidate therapeutics that fall into four categories (antivirals, immunomodulators, supportive therapies, and neutralizing antibodies), streamlining clinical trials, coordinating regulatory processes, and leveraging assets among all partners to rapidly respond to the COVID-19 and future pandemics.

The preclinical working group was charged with standardizing and sharing preclinical evaluation resources and methods and accelerating testing of candidate therapies and vaccines to support entry into clinical trials.[106] The working group has developed a master inventory of preclinical testing resources, including for nonhuman primates (NHPs), small animal models, and biosafety level 3/4 laboratories. A national strategy for NHP research was developed, which aims to maximize the research value of scarce NHP resources that are needed for preclinical testing of

[105] www.nih.gov/research-training/medical-research-initiatives/activ
[106] www.nih.gov/research-training/medical-research-initiatives/activ/preclinical-working-group

some vaccines and certain therapeutics during the pandemic. The working group has established standard operating procedures for accelerated preclinical agent development in response to a pandemic. They have also completed a prioritization framework for evaluating and prioritizing preclinical compounds for further preclinical testing. Together with the therapeutics clinical working group, the preclinical working group helped to establish an ACTIV COVID-19 Clinical and Preclinical Candidate Compound Survey to collect information for an inventory of potential candidates for preventing or mitigating COVID-19 infection.[107] The preclinical working group has created a virtual preclinical testing network to streamline access to testing resources. They have also created a public database for sharing preclinical data, which will help to facilitate interpretation and comparison of results from multiple experiments on multiple agents that could provide insight on SARS-CoV-2 and treatment approaches not apparent from a single study.[108] As new viral variants have emerged, they are generating a process to assess viral variant effects on vaccines and therapeutics. The working group has published scientific papers related to the group's efforts, including preclinical paths to support rapid development of therapeutics and preclinical models for vaccines and therapeutics.[109,110]

The therapeutics clinical working group was charged with designing an adaptive master protocol strategy and prioritizing therapeutic agents for testing within clinical trial networks identified by the clinical trial capacity working group.[111] The working group has developed a process to prioritize clinical agents for rapid testing, evaluated hundreds of publicly available agents, and prioritized promising compounds for clinical testing. Based on the results of several waves of agent prioritization, ACTIV clinical trials have been launched in numerous NIH-supported networks using selected candidates, including monoclonal antibodies, antivirals, immunomodulators, and anticoagulants/anti-platelet agents. These rapid launches were made possible by the development of master protocols by the working group, which allow for the efficient evaluation of multiple investigational agents as they become available and for the standardization of primary endpoints to enable the comparison of trial data. The ACTIV-1 master protocol, led by NCATS and launched in October 2020, tests promising immune modulator compounds, a class of drugs that help minimize the deleterious effects of an overactive immune response to SARS-CoV-2 infection, in a Phase 3 trial of hospitalized patients.[112] ACTIV-2, led by NIAID and launched in August 2020, is designed as a Phase 2 trial that can expand seamlessly to Phase 3 testing of monoclonal antibodies and other types of therapeutics in outpatients.[113] ACTIV-3, also led by NIAID and launched in August 2020, is a Phase 3 trial testing monoclonal antibodies and other types of therapeutics in hospitalized patients.[114] ACTIV-4, led by NHLBI, consists of three adaptive platform Phase 3 clinical trials to test antithrombotics in three patient populations. The outpatient and inpatient trials were

[107] redcap.ncats.nih.gov/redcap/surveys/index.php?s=DAE87WPTE7
[108] opendata.ncats.nih.gov/covid19/databrowser
[109] www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30522-9
[110] www.cell.com/cell-host-microbe/fulltext/S1931-3128(20)30521-7
[111] www.nih.gov/research-training/medical-research-initiatives/activ/therapeutics-clinical-working-group
[112] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ1
[113] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ2
[114] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ3

launched in September 2020, and the third trial involving post-hospitalized patients launched in March 2021.[115] The ACTIV-5 master protocol, led by NIAID and launched in October 2020, is designed to test other promising therapies in a series of Phase 2 trials of hospitalized patients.[116] The ACTIV-6 master protocol, starting in May 2021, will test the efficacy of repurposed medications in an outpatient setting.[117] In addition to the ACTIV clinical trials, some of which have yielded results, several ACTIV-associated trials, which are other NIH-funded flagship COVID-19 therapeutic trials of ACTIV-prioritized agents using protocols informed or endorsed by the ACTIV partnership, are underway or complete.[118]

The clinical trial capacity working group was charged with developing an inventory of clinical trial capacity, including networks from the NIH Institutes and Centers (ICs) and contract research organizations (CROs), to serve as potential settings in which to efficiently implement COVID-19 clinical trials.[119] The working group developed and launched a series of clinical trial capacity surveys that included questions designed to identify the capabilities of more than 60 networks, over 700 clinical trial sites, and over 30 CROs and site management organizations. The results of these surveys were combined with geographic mapping, COVID-19 disease incidence data, and visualization capabilities into a unique "geotracking tool" that has enabled the therapeutics clinical working group and trial sponsors to choose the most effective networks and sites to support ACTIV master protocols and associated trials. This effort included multiple NIH ICs involved in the ACTIV partnership, including NCATS, NHLBI, NIAID, and OD. The working group created a reference guide for novel clinical trial innovations along with a resource map of available solutions to help enable the safe and efficient conduct of ACTIV clinical trials under the unique conditions imposed by the COVID-19 pandemic.

The vaccines working group was charged with accelerating the evaluation of vaccine candidates by supporting harmonized clinical efficacy trials and a parallel effort to generate biomarkers and other evidence for more rapid approval/authorization.[120] The working group coordinated and contributed to the development of harmonized protocols for vaccine evaluation in clinical trials, which allows for the simultaneous assessment of multiple vaccine candidates through analyses of correlates of protection across trials. SARS-CoV-2 vaccine clinical trials using these ACTIV-informed harmonized protocols include Phase 3 trials of the Moderna mRNA-1273 vaccine using a messenger RNA delivery platform, the AstraZeneca AZD1222 vaccine using a non-replicating adenovirus delivery system, the Johnson & Johnson JNJ-78436725 vaccine using a non-replicating adenovirus delivery system, and the Novavax NVX-CoV2373 protein subunit vaccine.[121] The Phase1/2 trial of the Sanofi/GlaxoSmithKline COVID-19 adjuvanted recombinant protein-based vaccine is also using a harmonized protocol. These trials activated at

[115] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ4
[116] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ5
[117] clinicaltrials.gov/ct2/show/NCT04885530?term=ACTIV-6&draw=2&rank=1
[118] www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials#activ6
[119] www.nih.gov/research-training/medical-research-initiatives/activ/clinical-trial-capacity-working-group
[120] www.nih.gov/research-training/medical-research-initiatives/activ/vaccines-working-group
[121] www.nih.gov/research-training/medical-research-initiatives/activ/sars-cov-2-vaccine-clinical-trials-using-activ-informed-harmonized-protocols

sites that are part of the NIAID COVID-19 Prevention Network (CoVPN).[122] The vaccine sponsors, ACTIV, and NIH leadership work closely with the networks on recruitment strategies and communication to promote enrollment of a diverse population in the vaccine trials. This working group has developed scientific publications, assessing practical considerations and prerequisites for using controlled human challenge studies to support SARS-CoV-2 vaccine development and potential vaccine-associated enhanced disease in SARS-CoV-2 vaccine development.[123,124]

Next Steps/Goals

Both the vaccines and clinical capacity working groups officially completed their charges as of July 31, 2020. The vaccines working group continues to meet on an ad-hoc basis to provide recommendations for ongoing vaccine trials. The majority of ACTIV trials are at capacity for agents to be assessed. Therapeutic agents received through the ACTIV COVID-19 Clinical and Preclinical Candidate Compound Survey continue to be considered by the ACTIV preclinical and clinical therapeutics working groups in case additional capacity becomes available in any of the trials.

[122] coronaviruspreventionnetwork.org/
[123] stm.sciencemag.org/content/early/2020/10/16/scitranslmed.abe0948
[124] science.sciencemag.org/content/368/6494/948

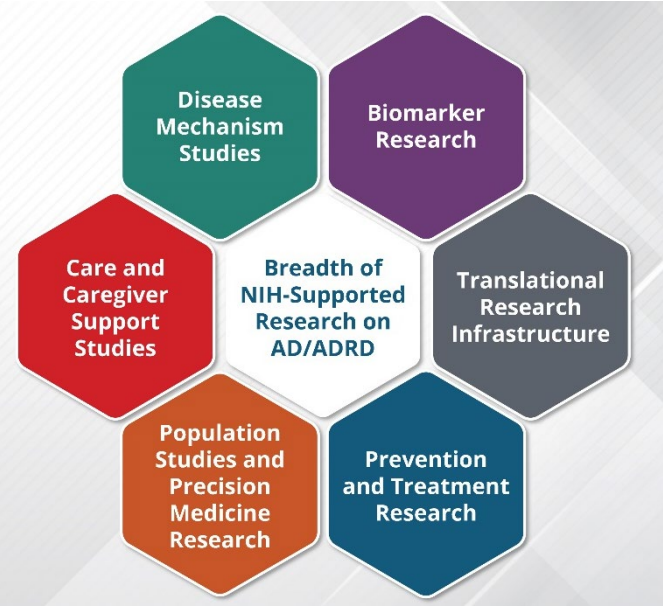
Alzheimer's Disease and Related Dementias

Program Overview

In 2020, as many as 5.8 million Americans 65 years and older had Alzheimer's disease, and the prevalence in the United States is projected to increase to 13.8 million by 2050. Alzheimer's is the most common dementia diagnosis and the sixth leading cause of death for Americans. In addition, many people have other forms of Alzheimer's disease related dementias, such as Lewy body disease, frontotemporal dementia, and vascular cognitive impairment/dementia, either alone or more commonly mixed with Alzheimer's pathology.

Since the passage of the National Alzheimer's Project Act (NAPA) in 2010, Congress has expressed continuing interest and support of Alzheimer's research through additional Alzheimer's-focused legislation including the mandate for an annual professional judgment budget and appropriations report language targeting increased funds for Alzheimer's research.

NIH leads an ambitious research agenda designed to better understand, diagnose, prevent, and treat these devastating diseases. NIH now progresses more quickly, connects scientific discoveries more precisely, increases the diversity of its research workforce as well as clinical trial participants, and builds new research resources such as extensive data sharing platforms. Indeed, today NIH is pursuing the answers to fundamental questions that could not be addressed just a few years ago. Even with everything learned so far, the path toward effective prevention and treatment remains challenging; however, NIH is unwavering in its commitment to combat these complicated diseases. NIH is poised to build on the current momentum and capitalize on the recent funding increases in this area, which have enabled significant progress in:



Disease Mechanism Studies: NIH investments in research to identify underlying biological mechanisms that cause Alzheimer's and related dementias are fundamental for the discovery of potential drugs targeting those processes. Today, scientists have identified variants in more than 50 genetic areas that may increase risk for the disease. Ten years ago, we knew of just 10 genes associated with Alzheimer's disease, and 20 years ago, we knew of only four. These genetic regions appear in clusters that point toward what may be highly relevant molecular pathways and specific biological processes, such as cell trafficking, lipid transport, inflammation, and immune responses. These discoveries are providing researchers with multiple new clues that suggest potential preventions, treatments and cures for Alzheimer's and related dementias.

Studies of toxic proteins are also providing important clues to possible disease mechanisms underlying Alzheimer's and related dementias. As one example, recent NIH-supported research has demonstrated that the features of abnormal protein folding may contribute to their toxicity and accumulation in brain diseases that cause dementia.[125,126,127] Specifically, researchers have demonstrated differences in the structure of abnormal tau protein filaments that collect in the brains of people with Alzheimer's versus two other neurodegenerative conditions.

With nearly 100 billion neurons and 100 trillion connections, the human brain remains one of the greatest mysteries in science and one of the greatest challenges in medicine. Advances in basic science research, such as those described above, will produce greater knowledge about disease mechanisms that will have clinical implications and ultimately improve human health. To accelerate progress toward that goal, 10 institutes are collaborating on the Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative. Launched in 2013, the initial focus has been on understanding the basic mechanisms underlying the function of the healthy brain, often in cellular and animal models. BRAIN Initiative advances are now setting the stage for groundbreaking human neuroscience research aimed at understanding the human brain, including diagnosing and treating its disorders. Over time this project will provide new tools and knowledge to combat human brain diseases, such as Alzheimer's and related dementias.

Biomarker Research: Biomarkers — characteristics that can be objectively measured and evaluated as an indicator of normal biological processes, disease processes, or responses to therapeutic intervention — can facilitate a more accurate diagnosis by helping researchers and clinicians discern between the different diseases that cause dementia. NIH funding has enabled significant recent progress in developing, testing, and validating biomarkers for diagnosing Alzheimer's and related dementias. These technological advances have helped scientists discover that changes in the brain that occur during Alzheimer's are evident long before a person shows outward signs of cognitive impairment or dementia. Emerging research also shows that beta amyloid plaques, tau proteins, and other biomarkers not only are present in the brain and spinal fluid but also circulate in the bloodstream.

In 2019 and early 2020, NIH-supported scientists reported advances in the development of blood-based tests that could enable rapid screening of volunteers who wish to enroll in studies. These blood tests could help detect pathological Alzheimer's in people who are showing signs of dementia or even detect abnormal levels of protein prior to cognitive symptoms. Blood tests that are at the most advanced stage of development detect the accumulation of amyloid or tau proteins. Using blood tests for screening and tracking response to treatment could help reduce the number of research volunteers needing to undergo invasive procedures such as a spinal tap or expensive positron emission tomography (PET) imaging. In the future, improved blood-based biomarkers may help not just researchers but also physicians to detect and diagnose Alzheimer's and related neurodegenerative disorders earlier, when interventions are more likely to be effective. In addition to blood tests, other NIH-supported research projects are designed to look beyond current measures to detect signs of dementia even earlier. These include changes in

[125] doi: 10.1186/s40478-019-0787-2
[126] doi: 10.1038/s41586-019-1026-5
[127] doi: 10.1038/s41586-020-2043-0

vision and pupil responses that may signal Alzheimer's, or a combined decline in memory and walking speed as a sign of dementia. New NIH programs are also working to develop biomarkers for small vessel diseases of the brain and vascular contributions to cognitive impairment and dementia (VCID). The MarkVCID consortium — led by the National Institute of Neurological Disorders and Stroke (NINDS) — has developed and is currently testing 11 different biomarker kits, which include several types of vascular imaging and fluid-based biomarkers, across several clinical research sites.

Translational Research Infrastructure: NIH has been able to augment investments in key research areas necessary for laying the groundwork for a precision medicine approach to treatment and prevention of Alzheimer's and related dementias. To accelerate the discovery of effective treatments that will become broadly available to the public, NIH has developed programs to make data, knowledge, and research tools widely available to all researchers. NIH has launched a number of programs over the past six years to provide researchers with an infrastructure for developing their ideas for medicines and other products, including: the Alzheimer's Disease Sequencing Project, Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD), the Model Organism Development and Evaluation for Late-Onset Alzheimer's Disease (MODEL-AD) consortium, and TaRget Enablement to Accelerate Therapy Development for Alzheimer's Disease (TREAT-AD) consortium. A hallmark of these programs is that every one of them brings together scientists from academia and industry who are working in many different disciplines, from epidemiology and genetics to data science and computational biology, molecular and cell biology, and medicinal chemistry and pharmacology. Working collaboratively, the researchers utilize an open-science/open-source approach to the key steps of the translational process. They are discovering new and better targets for treatment; producing and analyzing comprehensive and shareable sets of molecular data; and developing high quality translational research tools.

Complementing the new translational infrastructure is support for new cross-disciplinary training programs funded through NIH's Institutional Training Programs to Advance Translational Research on Alzheimer's Disease and AD-Related Dementias, which is designed to support a new and more diverse generation of translational scientists with expertise in biology, data science, engineering, and drug development, who are able to participate and lead team-science programs from target discovery to clinical trials. In addition, the National Institute on Aging (NIA)-funded Alzheimer's Clinical Trials Consortium (ACTC), a clinical trials infrastructure to accelerate and expand studies for therapies in Alzheimer's and related dementias, continues to provide centralized resources and shared expertise to researchers nationwide to hasten the development of effective interventions. In 2020, the ACTC launched the Institute on Methods and Protocols for Advancement of Clinical Trials in Alzheimer's and related dementias (IMPACT-AD) course that aims to educate and promote diversity among research professionals and future researchers in the Alzheimer's field.

Prevention and Treatment Research: Scientists have been able to pursue many avenues simultaneously as they study promising treatments that act upon many different targets. Some approaches do not rely on drugs; rather, they focus on behavior changes and lifestyle choices such as the careful control of high blood pressure, which is an established risk factor for dementia. For example, a previously supported NIH study called SPRINT Memory and

Cognition in Decreased Hypertension (SPRINT MIND) demonstrated that people who intensively control their blood pressure with one or more drugs can significantly reduce their risk of developing mild cognitive impairment (MCI).[128] This study provided what is perhaps the most promising randomized clinical trial evidence to date supporting a role for active primary prevention in the cognitive trajectory of dementia.

NIH will build on the current momentum by continuing to support a broad range of treatment targets. NIH currently supports approximately 270 clinical trials on Alzheimer's and related dementias, from pilot studies to large-scale trials, on a wide range of interventions for diagnosis, treatment, prevention, care, and caregiving. While amyloid continues to be a target of clinical investigation, 40 of the 57 pharmacological trials supported by NIH are investigating other targets. More than 120 current trials test nonpharmacological interventions, while more than 80 others are aimed at care and caregiving for people living with dementia. NIH has taken significant steps to modernize and speed up trials to test potential interventions earlier in the disease continuum, examine how therapies can be delivered pragmatically in real-world settings, and foster new partnerships with organizations and individuals in the design and operation of trials.

Ensuring greater racial, ethnic, gender, and socioeconomic diversity among participants and researchers is central to these efforts. Inclusion is critical to understanding and addressing disparities in the incidence and prevalence of disease and identifying unique care needs for diverse populations. As part of a broader effort to improve inclusivity, NIA has recently awarded a contract to develop an institute-wide informatics system to track, report, and manage NIA's clinical research data, activities, and portfolio in real time. This system will also enable NIA to better manage clinical research, identify and support sites not able to meet diverse recruitment goals, learn from top-performing sites, and provide transparency regarding its recruitment efforts and successes.

Population Studies and Precision Medicine Research: Because of the accelerated pace of research in recent years, we now know that Alzheimer's and related dementias are complex conditions that stem from the interplay of genetic, lifestyle, and environmental factors. NIH-supported researchers continue to study large, diverse groups of people, to better understand the reasons why some people develop these conditions and others do not, and which genes, lifestyle choices, and other factors seem to be associated with the disease.

Developing a better understanding of how and why many diseases affect diverse communities in different ways is paramount in our search for treatments and prevention for Alzheimer's and related dementias. NIH-supported studies in health disparities have already found that: 1) those who do not graduate from high school are at higher risk; 2) the risk of dementia is highest among African Americans and American Indians or Alaska Natives; intermediate for Latinos, Pacific Islanders, and non-Latino whites; and lowest for Asian Americans; and 3) women are at potentially higher risk of dementia than men, at least in part due to greater overall longevity. These discoveries, paired with knowledge of genetic and other factors, can be used to design clinical trials to test whether these factors truly confer risk or offer protection.

[128] doi: 10.1001/jama.2019.10551

Care and Caregiver Support Studies: NIH is also committed to enabling better outcomes for people with Alzheimer's and related dementias, as well as for their caregivers. NIH-supported efforts have led to improved quality of care and quality of life for those living with these conditions and the development of resources designed to help ease burdens on care providers. Our efforts to encourage broad sharing of data and resources include raising awareness about evidence-based social and behavioral interventions. In 2019, NIA expanded its network of Edward R. Roybal Centers for Translational Research on Aging to focus on the development of behavioral interventions for dementia care providers. The Roybal network, which was established in 1993, is designed to translate findings from basic behavioral and social research into evidence-based interventions and programs that can be shared and implemented in the community. The four new centers, called collectively the Roybal Centers for Translational Research on Dementia Care Provider Support, will develop and pilot test dementia-related interventions and their related materials for feasibility, acceptability, and efficacy.

Also in 2019, NIH funded a new effort called the IMbedded Pragmatic Alzheimer's disease and related dementias Clinical Trials (IMPACT) Collaboratory to meet the urgent public health need to deliver high quality, evidence-based care to people living with dementias and their caregivers. Through this effort, researchers will develop and test care interventions in real world settings such as hospitals, assisted living facilities, nursing homes, and adult day care centers. In general, a "pragmatic clinical trial" means participants are enrolled as part of a real-world setting, rather than selected from a broader community based on narrowly defined criteria.

Additionally, the costs of dementia care and the challenges families face as caregivers continue to be a priority area of research. A recent analysis of Medicare and Medicaid data shows that the costs of health care for people with dementia are much higher than for those without dementia, and the burden of those higher costs falls disproportionately on people with dementia and their families.[129]

Trans-NIH Collaboration

NIA spearheads the NIH effort in Alzheimer's and related dementias, in close collaboration with NINDS. Many other NIH ICOs also contribute, and major international research summits hosted by NIH contribute significantly to the development of detailed operational plans. These summits focus on 1) treatment and prevention of Alzheimer's disease (hosted by NIA); 2) treatment and prevention of Alzheimer's related dementias, including vascular cognitive impairment/dementia, Lewy body dementia (LBD), and frontotemporal dementias (hosted by NINDS); and 3) better approaches to care, services, and support (hosted by NIA). The research summits are held annually with a three-year rotation by topic. The summit focused on treatment and prevention of Alzheimer's disease took place in April 2021. Extensive summit-related discussion and feedback from a wide range of key stakeholders informs NIH's future Alzheimer's and related dementias research efforts. Additionally, representatives from NIA, NINDS, and other NIH ICOs meet annually to discuss opportunities for research collaborations and joint funding initiatives in Alzheimer's and related dementias. To foster greater collaboration and spur new research ideas, NIA offers Alzheimer's and related dementias supplement awards to researchers with grants from any of the ICOs, including those focused on non-Alzheimer's topics. NIA also supports Alzheimer's and related dementias projects at other ICOs that are within the NIA pay

[129] doi: 10.1111/jgs.16414

line. In 2019 NIA launched the collaborative intramural Center for Alzheimer's and Related Dementias (CARD) in partnership with NINDS, and also including the National Center for Advancing Translational Sciences, and the NIH Clinical Center. CARD will be housed in newly constructed headquarters on the NIH main campus. The Center will combine the power of NIH intramural science with the work of researchers around the globe to push boldly ahead in basic, translational and clinical AD/ADRD research. CARD will also emphasize teamwork, innovation, transparency, data sharing and advanced technology to speed up the translation of scientific findings into real-world applications.

Next Steps/Goals

NIH has embarked on an ambitious research agenda, making much progress toward better understanding these complex diseases. NIH continues to make significant advances in discovering approaches that may prevent, diagnose, and treat them, while at the same time continuing to advance research on dementia care and caregiving. Future work in this area will focus on a deeper understanding of different forms of dementia, as well as the development of effective prevention approaches and care interventions that can improve quality of life for patients and caregivers. NIH will work toward precision medicine for Alzheimer's and related dementias research, making it possible in the future to treat the right patients with the right drugs at the right time of disease progression.

Faculty Institutional Recruitment for Sustainable Transformation (FIRST)

Program Overview

As our nation's population grows increasingly diverse, there is an urgent need to ensure that scientific talent is nurtured, recognized, and supported in researchers from diverse backgrounds. Fostering inclusive environments in the biomedical research workforce will allow creative minds the opportunity to contribute to realizing our national research and health goals. Efforts to increase the diversity of the biomedical research workforce are anticipated to lead to the recruitment of talented researchers from all backgrounds, enrich the training environment, balance and broaden the perspective in setting research priorities, improve the ability to recruit subjects from all backgrounds into clinical research protocols, and expand the nation's capacity to address and eliminate health disparities.

Despite recognizing the pressing need to enhance diversity in National Institutes of Health (NIH)-funded institutions across the United States, success in accomplishing this goal has largely been limited to trainee populations, leaving biomedical research faculty diversity as an ongoing challenge. Institutional cultures lacking necessary elements of inclusion and equity are an important contributing factor to faculty-level disparities. However, many previous efforts to enhance diversity have focused on the individual and have not addressed the critical issue of institutional culture.

Early indications from the intramural NIH Distinguished Scholars Program,[130] as well as other cohort-based recruitment programs, suggest that recruitment of a critical mass of investigators committed to diversity and inclusion may foster the institutional changes needed to create meaningful improvement in diversity at the faculty level. Building upon this hypothesis, NIH is launching the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program.[131] FIRST aims to create cultures of inclusive excellence at NIH-funded institutions, to establish and maintain scientific environments that cultivate and benefit from a full range of talent. This goal will be achieved by implementing a set of well-integrated, evidence-based strategies and evaluating their impact on prespecified metrics of institutional culture, inclusion, and diversity. FIRST will establish a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. Ultimately, successful strategies can be adopted by additional institutions, leading to meaningful improvements in the diversity of biomedical research faculty.

FIRST consists of two independent, but linked, components. The first component is support for institutions in their efforts to develop and implement faculty cohort models for simultaneous hiring of a cohort of research faculty committed to promoting diversity and scientific excellence. Highly-Resourced Institutions and Limited-Resourced Institutions[132] may apply independently or in a partnership arrangement to develop and implement faculty cohort models for the

[130] diversity.nih.gov/programs-partnerships/dsp
[131] commonfund.nih.gov/first
[132] Limited-Resourced Institutions must award doctoral degrees in the health professions or health-related sciences and have received less than $50 million average in annual NIH funds within the three years prior to the time of application. These criteria are also used for the Research Centers in Minority Institutions (RCMI) program.

simultaneous hiring of a diverse cohort of research faculty. Any individual who is competitive for a new tenure track faculty position and who has demonstrated a strong commitment to promoting diversity and scientific excellence is eligible for FIRST faculty support.

Faculty in the cohort will receive multilevel mentoring, sponsorship, and professional and research development embedded within institutions that are actively implementing integrated, systems-level approaches for sustainable culture change. Each institutional cohort is expected to include at least 6 to 10 faculty, and may be comprised of small clusters of scientists (no fewer than 3) within several scientific areas, such as neuroscience, cardiovascular disease, cancer, minority health and health disparities, behavioral, social, or other research area within the NIH mission. FIRST will support three cycles of faculty cohorts; awardee institutions will begin with a planning year in the first year of the award, and then bring new cohort faculty on board in the second year. The first planning year of awards is anticipated in FY 2021, and the first year of faculty cohort support will start in FY 2022.

The second component of the FIRST program is support for a Coordination and Evaluation Center (CEC), which will facilitate evaluation of institutional culture change. The FIRST CEC will establish consortium-wide evaluation plans and develop common metrics of inclusive excellence. Working collaboratively with the individual institutions supporting faculty cohorts, the CEC will coordinate submission of data across institutions and objectively assess progress towards achieving consortium-wide metrics. Evaluation activities will include three levels of analysis: cohort-level, department-level, and institution-wide. The CEC will also coordinate consortium-wide activities and disseminate knowledge generated through FIRST to inform national institutional policies, programs, and practices. The CEC award is expected to start in FY 2021.

The FIRST program is funded through the NIH Common Fund and managed in collaboration with the National Cancer Institute, the National Institute on Minority Health and Health Disparities, the Office of Scientific Workforce Diversity, the National Institute of Neurological Disorders and Stroke, and the National Heart, Lung, and Blood Institute. Additional program management is provided by trans-NIH Working Group members from 17 ICOs. The robust trans-NIH participation in the FIRST program demonstrates that supporting a diverse biomedical research workforce is a high priority across NIH. Fostering a workforce that better reflects the diversity of our nation will advance the missions of all NIH ICOs by ensuring talented individuals from all backgrounds can use their skills and creativity to address current challenges and opportunities in biomedical research.

Harnessing Artificial Intelligence (AI) for Health

Program Overview

Biomedical science has made, and continues to make, enormous progress in studying fundamental components of human biology. The challenge ahead will increasingly be to systematically learn how the components work together—an endeavor in which technological advances will undoubtedly foster progress and expedite discoveries. The extraordinary capability of artificial intelligence (AI) to learn, infer, and make predictions can be harnessed as a powerful tool to advance biomedical science and develop treatments. However, this requires new approaches to data collection, integration, and labeling to create large datasets that are "AI-ready." It requires dynamic application of algorithms that include detailed model descriptions to enable their transparent interpretation and reuse. As technologies advance, the public will need to be assured that data and algorithms are developed with the highest ethical standards to address bias and transparency and ensure safe and trustworthy adoption in the biomedical research community. To achieve these goals, a well-rounded and multidisciplinary workforce fluent in biomedical and computational challenges and well-versed in ethics, social, and behavioral sciences will be critical. The National Institutes of Health (NIH) is developing new programs that focus on data development and ethics, building training programs that will engage a diverse workforce, and employing AI for a broad array of applications—like addressing public health needs, closing the gaps in disparities, and expanding on fundamental discoveries.

Through the Common Fund's leadership, NIH assembled an internal group of leaders to start implementing a large subset of the recommendations put forth by the 2018 AI Working Group of the Advisory Committee to the Director.[133] The National Human Genome Research Institute (NHGRI), National Institute of Biomedical Imaging and Bioengineering (NIBIB), and National Library of Medicine (NLM) in partnership with the Common Fund are leading the new program, which was approved as a concept at the May 2020 Council of Councils. The new program, Bridge to Artificial Intelligence (Bridge2AI), will be run by a trans-NIH team, which is developing funding announcements and planning for program launch. Bridge2AI is now possible because of extraordinary technological advances in AI and drastic increases in the ability to collect and store massive amounts of biologically relevant data.

FY 2021 appropriations included $50 million to expand the number of machine learning (ML)-focused grants focused on the use of AI to address chronic diseases. This initiative will leverage NIH Office of Data Science Strategy (ODSS) programs and allow NIH to develop unbiased, ethical, and transparent datasets; link massive datasets together across programs; develop AI algorithms that take advantage of the capabilities of cloud and Industries of the Future-based infrastructures and transparent, explainable models to improve understanding of the causes and early treatments of chronic disease; and to account for important social and behavioral factors that affect health outcomes across heterogenous populations.

Across NIH, individual institutes and centers continue to support mission-specific AI efforts, several of which are detailed below.

[133] acd.od.nih.gov/documents/presentations/12132019AI_Report.pdf

Addressing Urgent Public Heath Challenges

Efforts in AI are addressing public health needs with great urgency. Through support from the CARES Act, NIBIB, in collaboration with multiple NIH institutes, launched the Medical Imaging and Data Resource Center[134] to support rapid analysis and dissemination of coronavirus disease 2019 (COVID-19) related imaging and associated data. This large database will fill several unmet needs, including (1) use of machine intelligence for quality assurance/quality control to ensure optimal image quality, (2) biomedical discovery (radiogenomics, deep learning, and predictive modeling to affect public health), and (3) virtual clinical trials. In other efforts to respond to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, the NCI researchers and NVIDIA,[135] an AI computing company, partnered to develop high-throughput AI classification algorithms for detecting COVID-19 in computerized tomography (CT) scans from patients.

NLM and NIAID are funding research to devise algorithms for chest x-ray screening and visualization.[136] The algorithms are being applied to detect tuberculosis infections in chest radiography images from children with and without HIV.

The NIAID Tuberculosis Portals[137] program supports NIAID's efforts to rapidly respond to a potential drug-resistant tuberculosis outbreak in the United States. Through an international partnership, the portal collects tuberculosis case data—including chest x-rays and CT scans—and uses AI and image processing techniques to process, analyze, and organize the images bases on similarity metrics. Other examples include applying natural language processing to medical records and image analysis for TB diagnostics and selection of potential compounds targeting SARS-CoV-2.

Combating Health Disparities

Other AI applications are helping to close the gap in health disparities. For example, the National Eye Institute supported work that led to an FDA-approved AI diagnostic system, IDx-DR. The system analyzes retinal images to screen and detect diabetic retinopathy, an important step in managing a disease that causes vision loss in more than 30 million Americans. As IDx-DR is implemented in clinics and more data are produced, this tool can transform the field by improving access to rural and underserved populations.

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) is supporting an ML framework to predict severe maternal morbidity.[138] Severe maternal morbidity, or life-threatening pregnancy complications at delivery, has been increasing steadily, affecting more than 50,000 women in the United States in 2014. Researchers aim to analyze population-based data from Maryland state databases and hospital surveys to develop techniques that can predict maternal risks early. Identifying key predictors of severe maternal

[134] www.nibib.nih.gov/news-events/newsroom/nih-harnesses-ai-covid-19-diagnosis-treatment-and-monitoring
[135] www.nature.com/articles/s41467-020-17971-2#Abs1
[136] reporter.nih.gov/project-details/10016025
[137] tbportals.niaid.nih.gov/
[138] projectreporter.nih.gov/project_info_description.cfm?aid=9767258

morbidity can help ascertain health disparities, strengths and weaknesses in obstetric care, and prevent adverse maternal and neonatal outcomes.

Capitalizing on Foundational Investments and Beyond

NCI has hosted multiple innovation labs, or short, intensive opportunities for cross-disciplinary teams to form de novo, rapidly generate novel ideas, and receive pilot funds to jump-start projects. These opportunities bring together diverse expertise to develop new algorithms for application to understanding cancer disease mechanisms, cancer epidemiology, and approaches to cancer care. Recent innovation labs include "Towards Development of a Cancer Digital Twin",[139] and "Advancing Cancer Biology at the Frontiers of Machine Learning and Mechanistic Models".[140]

The National Institute of Dental and Craniofacial Research (NIDCR)-supported FaceBase Consortium[141] generates, integrates, and distributes diverse data on craniofacial development and associated disorders that researchers can analyze to make new discoveries. For example, FaceBase Consortium researchers combined 3D facial imaging and AI to create a tool to more quickly diagnose children with rare genetic diseases that affect facial features.

National Institute of Mental Health (NIMH) investigators are developing an objective, passive, ML algorithm that uses biosensor data to measure depression symptom severity.[142] The algorithm analyzes biological, physiological, and behavioral data to monitor symptoms in natural settings, allowing clinicians to evaluate patients outside the clinic, and optimize and expedite treatment options.

Progress in AI is in many ways inspired by neuroscience research on how animal and human brains "compute." Researchers from the National Institute of Neurological Disorders and Stroke (NINDS) and the Brain Research through Advancing Innovative Neurotechnologies® Initiative are increasingly applying AI to help understand the brain and to treat brain diseases. In one recent example, researchers used brain signals recorded from epilepsy patients (whose brain electrical activity was monitored as part of their treatment) to program a computer to mimic natural speech.[143] This strategy could one day restore the ability of certain patients to communicate.

Unique Challenges

Addressing ethical considerations and training—two key issues in AI—will help enable broad, trustworthy, and ethical application of AI technologies to biomedical and clinical research. Incorporating ethics and training into AI activities will help achieve the broader goal of conducting science in service to society. Several recent activities highlight NIH's dedication in these areas.

[139] events.cancer.gov/cbiit/dtwin2020/
[140] www.hub.ki/groups/mechanisticapproachesinnovationlab
[141] www.facebase.org/
[142] projectreporter.nih.gov/project_info_description.cfm?aid=9839684&icde=50836319
[143] www.nature.com/articles/s41586-019-1119-1

In July 2020, ODSS led an International Society for Computational Biology workshop[144] focused on "Ethics, Bias, and the Application of AI in Biomedicine." Leaders in the field presented and discussed challenges related to trustworthy AI and training a workforce ready to address these challenges with creative solutions. To incorporate lessons from these discussions into practice, ODSS is part of the trans-NIH team developing Bridge2AI initiatives on training and ethics, bias, and transparency in AI data and algorithms.

In the training space, the National Institute of Nursing Research hosted an AI boot camp in August 2020[145] to provide the next generation of nurse scientists with the basic knowledge of AI for use in clinical applications and research to improve health care and health outcomes across diverse patient populations.

In October 2020, the Office of Behavioral and Social Sciences Research (OBSSR) and its partner institutes (NICHD, NIMH, the National Institute on Drug Abuse, the National Institute on Minority Health and Health Disparities, and the National Heart, Lung, and Blood Institute) launched the Training in Advanced Data Analytics for Behavioral and Social Sciences Research program designed to infuse data science training into existing BSSR predoctoral programs and produce a cohort of specialized health-related researchers with competencies intersecting the social sciences and data science.[146]

Future directions include continued integration of AI methodologies into biomedical research activities. NIH will also plan events—such as ethics workshops and trainings—to reach more users, diversify the workforce, and increase skill bases. For example, ODSS will collaborate across NIH to place computer science students and professionals in projects focused on using ML for biomedicine or streamlining administrative tasks and will build programs to engage underrepresented communities for future AI-focused codeathons, trainings, and data science bootcamps.

[144] www.iscb.org/cms_addon/conferences/ismb2020/tracks/odss
[145] www.ninr.nih.gov/newsandinformation/events/bootcamp2020
[146] obssr.od.nih.gov/obssr-t32-training-in-advanced-data-analytics-for-behavioral-and-social-sciences-research-grants-awarded/

NIH Helping to End Addiction Long-term (HEAL) Initiative

Program Overview

The crisis of opioid misuse, addiction, and overdose in the United States is a rapidly evolving and urgent public health emergency. In 2019, 70,630 people in the United States died of overdose, including 49,860 dying from opioid overdose (70.6 percent of all drug overdose deaths).[147] More than 2 million Americans have Opioid Use Disorder (OUD) while 10 million Americans misuse opioids, taking them differently than prescribed.[148] An additional 50 million Americans experience chronic pain, putting them at increased risks for opioid use and misuse.[149,150] The magnitude of the crisis has made clear the need for collaborative and innovative scientific solutions, including the need for safe and effective pain management interventions; additional user-friendly and effective options for the treatment of OUD; and strategies to implement evidence-based interventions for pain and addiction.

In response to this historic crisis, in 2018 NIH launched the Helping to End Addition Long-term (HEAL) Initiative, a trans-NIH effort spanning basic, translational, clinical and implementation science on opioid misuse, addiction, and pain. By the end of FY 2020, HEAL funded over $1.5 billion in research, representing more than 500 research projects across the United States. These projects aim to identify new therapeutic targets for both pain and opioid use disorder, reduce the risk of opioids through nonpharmacological strategies for pain management, and improve opioid addiction treatment in a variety of settings.

Progress in efforts to reduce opioid overdose and death has been affected by the COVID-19 pandemic, which has fueled increases in opioid use, addiction, and overdose. Since the declaration of a public health emergency for COVID, overdoses increased 42 percent in May 2020 compared to May 2019.[151] For patients receiving treatment for addiction and chronic pain, access to support systems, medications to treat opioid use disorder, and mental health care have been significantly interrupted or shifted to virtual platforms. In addition, social support is closely tied to better treatment adherence and recovery outcomes, therefore social distancing measures and the stress of social isolation intensifies challenges for people with pain and addition, and makes it difficult for individuals to maintain their mental health.

Addressing the Opioid Crisis During the COVID-19 Pandemic

The colliding opioid and COVID crisis is affecting individuals, families and communities in deadly ways. Since the declaration of a public health emergency for COVID, fentanyl and heroin use increased by 32 percent and 13 percent respectively. The use of stimulants and other illicit drugs, together with opioids, is also increasing leading to an overall dramatic rise in

[147] www.cdc.gov/drugoverdose/data/statedeaths.html
[148] Center for Behavioral Health Statistics and Quality (CBHSQ). 2017 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2018.
[149] Collins, Koroshetz, Vo www.cdc.gov/drugoverdose/data/statedeaths.html
[149] Center fo lkow. (2018). Research plan for the HEAL Initiative. *JAMA,* 320(2), 129-130.
[150] Dahlhamer, Lucas, Zelaya, Nahin, Mackey, DeBar, Kerns, Von Korff, Porter, Helmick. (2018). Prevalence of chronic pain and high-impact chronic pain among adults — United States, 2016. *CDC Morbidity and Mortality Weekly Report,* 67(36);1001–1006. www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm#References
[151] ODMAP. (2020). Overdose Detection Mapping Application Program. http://www.odmap.org/

overdose and overdose death. Disruptions of treatment and recovery services, limited access to mental health and peer recovery support, and increased stress provide drive this increase and create new barriers to recovery. Economic impacts from job losses may also contribute to despair, and fatalities from misuse relapse, overdose, and suicide. Additional risks face people with OUD such as housing instability and incarceration where social distancing is difficult. Vulnerable and underserved populations, particularly economically disadvantaged, geographically remote, and ethnic minority communities affected by poverty, lack access to adequate prevention, treatment, and recovery resources, putting them at especially high risk.

The COVID pandemic has also complicated efforts to address the need for safe and non-addictive pain management. For the 50 million Americans in chronic pain, significant disruptions to healthcare access occurred as providers moved resources to intensive care units and other critical COVID care sites. Nonurgent needs, such as routine management of chronic pain, or outpatient, elective procedures needed to treat chronic pain, have been delayed to avoid the risk of transmitting the SARS-CoV-2 virus.[152] It is not yet known how this unmanaged and untreated pain has contributed to the rise of opioid misuse, addiction and overdose.

To match the urgency of these combined epidemics, the NIH HEAL initiative is leveraging expertise across NIH Institutes and Centers to approach the crisis from all angles and disciplines. NIH leadership, intramural and extramural investigators, and key stakeholders have collaborated to monitor impact of COVID on communities, provision of treatment services, and available outcome data. Research progress is closely monitored on the impact of COVID. Additionally, NIH has responded by supplementing ongoing research to collect additional measures to understand the impact of COVID on HEAL communities. The initiative is harnessing its collaborative structure to adapt to the COVID crisis while continuing to make progress toward key goals: identifying new therapeutic targets for both pain and opioid use disorder, reducing the risk of opioids through nonpharmacological strategies for pain management, and improving opioid addiction treatment in a variety of real-world settings. Examples of high impact programs are listed below:

Advancing Clinical Trials in Neonatal Opioid Withdrawal Syndrome (ACT NOW). Infants exposed to maternal opioid use while in the womb can experience neonatal opioid withdrawal syndrome (NOWS), which has an estimated frequency of 7 per 1,000 hospital births. Every 15 minutes an infant is born with NOWS.[153, 154] The NIH HEAL Initiative has funded $41.7 million of research through *ACT NOW* to identify best practices for the management of NOWS and to improve our understanding of health outcomes of these infants. Specifically, the *ACT NOW Eat Sleep and Console* (ESC) clinical research trial is testing the effects of function-based assessments for NOWS among 864 families over two years. The *ACT NOW Weaning Trial* will test the effectiveness of two different pharmacological treatments for NOWS among over 500 infants. Despite COVID-19's impact, both *ACT NOW* trials began recruitment in 2020. In

[152] Volkow, N. (2020). Collision of the COVID-19 and opioid epidemics. *Annals of Internal Medicine.* doi:10.7326/M20-

[153] NIH HEAL Initiative. (2020). Advancing clinical trials in neonatal opioid withdrawal. (ACT NOW). heal.nih.gov/research/infants-and-children/act-now

[154] Bremer, A. September 1, 2020 NIH HEAL Multidisciplinary Working Group Meeting (MDWG). Addressing the medical and social needs of children affected by opioids: The ACT NOW Program. heal.nih.gov/files/2020-09/MDWG%20for%20website%20day%202%20v2_0.pdf

addition to the clinical trials, the ACT NOW Longitudinal Study will use neuroimaging to measure the effects of prenatal opioid exposure on neurodevelopment, as well as how maternal and environmental factors interact to influence development and behavior. These efforts complement the HEALthy Brain and Child Development (HBCD) Study, which is a comprehensive study of early brain development to study the impact of opioid exposure together with other environmental factors influencing child development. Additional research is planned to compare the effectiveness of specific pharmacological approaches for treating NOWS. Together, these studies will rapidly provide key evidence to help inform clinical guidance of infants born with NOWS.

New Strategies to Prevent and Treat Opioid Addiction. Through HEAL, NIH has invested $157 million to date on studies aimed at new prevention and treatments strategies for OUD. This research includes prevention studies for at-risk adolescents and young adults, as well as other groups at the highest risk for opioid initiation and misuse. Prevention research is also underway to test ways to reduce the likelihood that individuals who misuse opioids or those with low-severity OUD progress to more severe OUD. Research on new strategies to treat OUD include studies defining the role of sleep dysfunction in OUD and recovery, an issue highlighted as of special importance to people in treatment for OUD and those with lived experience. Additional research is testing how integrated approaches to mental health and substance use disorder treatment affects outcomes for the 40 percent of patients with OUD who also have a diagnosed mental health condition. This research has been delayed by COVID-related effects on patient recruitment and care, but has benefited from creative approaches in virtual enrollment and engagement of research participants. Together, this research will provide insight into the full experience of addiction during the COVID pandemic, and will open new avenues for novel therapeutic strategies, OUD prevention and treatment approaches, and ways to sustain long-term recovery.

HEALing Communities Study. NIH has devoted $209.2 million to support the HEALing Communities Study, an unprecedented effort to test the integration of prevention, overdose reversal, and medication-based treatment for OUD, with an ambitious goal of a 40 percent reduction in opioid overdose deaths in select rural and urban communities hit hard by the opioid crisis.[155] During the COVID pandemic, community engagement and coalition building activities in the study were transitioned to a virtual format. Despite these challenges, baseline data were collected, and the first wave communities have selected and begun implementing locally appropriate interventions, such as novel approaches to distribute naloxone for overdose reversal. This research is strengthened by complementary efforts through the Justice Community Opioid Innovation Network (JCOIN) to test approaches to provide evidence-based treatment for OUD within justice settings, and by the Behavioral Research to Improve Medication-Based Treatment (BRIM) program, which tests the use of non-pharmacologic strategies to help individuals stay on lifesaving medications for the treatment of OUD. Together, these programs seek to inform strategies to integrate evidence-based treatments for OUD in specific settings where they will be of the greatest benefit.

[155] NIH HEAL Initiative. (2020). Translation of research to practice for the treatment of opioid addiction. *HEALing Communities Study*. heal.nih.gov/research/research-to-practice/healing-communities

Precision Medicine in Pain Management. NIH has invested $207 million to date for research in clinical research in pain management. To reduce the risk of opioids and enhance management of pain, HEAL supports Phase III trials on pharmacological and nonpharmacological therapies for pain conditions including post-surgical pain, musculoskeletal pain, osteoarthritis, and cancer pain through the Pain Management Effectiveness Research Network. With the goal of increasing uptake of effective pain treatments, HEAL tests how best to embed effective non-pharmacological treatments for pain into large health care settings, including a virtual intervention to treat chronic low back pain in the Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM) program. Chronic low back pain is one of the most common forms of chronic pain among adults worldwide, and there are multiple contributions and treatment interventions. Through the Back Pain Consortium (BACPAC) Research Program, researchers test an iterative model to inform precision medicine using interdisciplinary methods and exploring innovative technologies.[156] Pain is also a common problem in end-stage renal disease and patients receiving hemodialysis. The Hemodialysis Opioid Prescription Effort (HOPE) received an FDA Investigational New Drug (IND) Application for the use of buprenorphine for pain management as part of multidisciplinary approach.[157] Although the COVID pandemic has resulted in some delays in enrollment across study sites, studies that have been able to continue are modifying protocols to increase the use of telehealth where appropriate, as well as alternative means to collaborate through research projects.

Preclinical and Translational Research in Pain. Through a suite of targeted trans-NIH efforts, HEAL research is accelerating the development of safe and effective therapeutics to treat pain with little or no addiction liability. To date, HEAL has invested $223 million in preclinical research, including programs to validate novel therapeutic targets for non-addictive medications for pain that would reduce reliance on opioids. HEAL research on the translation of promising technologies, such as implanted devices and noninvasive technologies that target areas of the brain associated with pain, will yield next-generation medical devices to diagnose and treat pain. To improve the efficacy of clinical trials for pain treatments, and to increase the chance that new therapeutics will advance along the regulatory path to approval, HEAL tests the development of biomarkers to objectively measure pain, including pain associated with sickle cell disease, musculoskeletal disease, nerve pain and headache. Promising biomarkers identified through this program may advance to clinical validation through the Early Phase Pain Investigation Clinical Network (EPPIC-Net). Findings from these studies could improve quality of life for millions of people in the United States who experience pain daily; however, the COVID pandemic poses a new unprecedented challenge. In many cases, disruptions to research caused by lab closures and long startup times impacted scientific collaboration and data collection. NIH staff closely monitors efforts needed to reestablish these studies and works with investigators to avoid further disruptions.

Medication Development to Treat Opioid Use Disorders and Prevent Overdose. Through the HEAL Initiative, NIH supports over 70 targeted studies to accelerate medication development of treatments for OUD, including novel medications and biologic agents, as well as novel formulations of approved medications to treat OUD and prevent opioid overdose. To date, 16

[156] heal.nih.gov/research/clinical-research/back-pain
[157] heal.nih.gov/research/clinical-research/hemodialysis

Investigational New Drug applications were filed with the FDA and authorized to for human studies. These studies focus on a variety of drug targets, as well as vaccines that could prevent opioids from entering the brain. Despite this success, COVID-19 greatly impacted progress across studies. For example, many of these projects were delayed by closures of labs and clinical facilities, and the pipeline of analgesic candidate development pipeline may be slowed across the portfolio. NIH staff are working closely with investigators to help manage budgets and FDA review processes to accomplish research goals despite COVID-19 delays.

Trans-NIH Collaboration

Through its trans-NIH design, the NIH HEAL Initiative builds on scientific expertise across NIH Institutes and Centers and cross-cutting collaborations across disciplines and sectors. For example, recent HEAL awards will evaluate the best approaches to treat people with both OUD as well as common mental health conditions and/or suicidality. In addition, interdisciplinary HEAL research is addressing stigma as a barrier to treatment of both painful conditions and OUD, as people with chronic pain and people with OUD face stigma from their healthcare providers, family, friends, coworkers, the health care system. HEAL is building collaborations across NIH to enhance ongoing studies to reduce the burden of chronic pain and OUD in vulnerable populations, diversify recruitment in clinical trials to better represent patient populations, and accelerate diversity inclusion policies, processes, and programs.

HEAL Data Ecosystem: As currently funded projects are completed, the HEAL initiative will rapidly disseminate research findings and results to patients, providers, institutions, and organizations so that they can rapidly put them into practice across the United States. A platform for accessing HEAL research data will make studies across HEAL and other NIH datasets accessible for investigators and the public, while protecting the privacy and confidentiality of research participants. HEAL will continue to maximize the availability of publications and the sharing of underlying data to promote dissemination of new knowledge, enhance reproducibility and accelerate the ability of researchers to build upon HEAL research to make new discoveries. This platform will form the foundation for an ecosystem for data management, analysis, and interaction through the HEAL initiative, and accelerate scientific solutions to the opioid crisis.

Next Steps and Goals

Although HEAL research has initiated a remarkably diverse set of scientific programs, there is more work to be done. HEAL has encouraged innovative approaches and bold new research into prevention and treatment interventions for substance misuse and addiction. Examples of planned research areas are summarized below:

Opioid Use in the Context of Polysubstance Use: Seventy percent of drug overdose deaths involved opioids, and the use of illicitly manufactured fentanyl in combination with stimulants is driving a new wave of overdose deaths. There is an urgent need for research to address polysubstance use. Leveraging HEAL infrastructure to accelerate development of safe and effective prevention and treatment interventions, including novel medications and collaborative treatment approaches, will provide much-needed options for individuals who misuse opioids together with psychostimulants such as methamphetamine and cocaine.

Advancing Health Equity: There are wide disparities in provision of care and treatment for pain and addiction, which result in both inappropriate treatment with opioids, increased risk of addiction and overdose, and lack of evidence-based non-pharmacological options for managing pain and lifesaving medications for OUD. Planned expansion to HEAL includes the development and implementation of culturally appropriate interventions for the prevention and management of pain and addiction in diverse populations, with a focus on interventions that target health disparities at multiple levels and those which can be rapidly implemented by healthcare systems.

Coordinated Approach to Pain Management: Research that is guided by individuals and joins together scientists, caregivers, people with lived experience, and other key community partners to build and test approaches for treating pain is essential for long term pain management. HEAL researchers will work in collaboration with clinicians and federal partners to test multi-disciplinary multimodal approach to pain management and uncover successful strategies for managing pain and preventing progression to opioid misuse and addiction.

Harnessing the Power of Innovation to Treat Pain: Recent discoveries in human genetics and molecular biology will be incorporated into the development of a novel team-based platform to rapidly test targets and candidate therapeutics for diverse human pain conditions and share finding with the wider pain research community. This research will address pain systems and allow for a variety of research questions including conditions of chronic analgesic use, other drug use, SUDs and other co-morbid conditions, and will enable and accelerate human gene and cell-based validation of pain therapeutic targets through the HEAL initiative and other pipelines. This will build on existing HEAL research, which has invested $223 million to date on preclinical and translational research in pain, and ongoing efforts to accelerate the development of novel treatments for pain.

High-Risk, High-Reward Research

Program Overview

Scientific progress often advances in modest steps, building upon a strong foundation of previous research and preliminary data. In contrast, more rapid advances in science can be stimulated by approaches that foster innovation and risk taking, and/or allow investigators flexibility to "follow their noses" to surprising and fortuitous discoveries. Such research is often referred to as "high-risk, high-reward" research. NIH is committed to supporting high-risk research with the potential for exceptionally large impact, balanced with support for incremental, yet extremely important, research that also advances our understanding of human health and disease.

Awards designed to support high-risk research may emphasize different criteria during peer review compared to more traditional grant mechanisms, weighting innovation and potential impact more heavily than feasibility and preliminary data. Thus, these awards provide an opportunity for investigators and projects that might not fare well in typical peer review due to a lack of preliminary data and/or ideas that appear inherently risky. "High risk" in this context refers to the type of science supported, which is often more innovative and paradigm-shifting than traditional research studies. "High risk" does not refer to risks posed to research participants. As with all NIH-funded studies involving people, any risks posed to participants are carefully evaluated by institutional or tribal review boards and explained to participants so that their consent is fully informed.

A major source of support for high-risk, high-reward research is the Common Fund's High-Risk, High-Reward (HRHR) program.[158] The HRHR program supports research projects that span the entire NIH mission, and is managed by a trans-NIH Working Group that includes members from 28 ICOs. The HRHR program consists of the following initiatives:

- NIH Director's Pioneer Award: supports individual scientists of exceptional creativity who propose pioneering or transformative approaches to major challenges in biomedical and behavioral research.
- NIH Director's New Innovator Award: supports promising new investigators proposing highly innovative research that may lack the preliminary data necessary to fare well in traditional peer review.
- NIH Director's Transformative Research Award: supports individual investigators or teams proposing exceptionally innovative and/or unconventional research projects with the potential to overturn fundamental paradigms.
- NIH Director's Early Independence Award: provides a mechanism for exceptional early career scientists to move rapidly into independent research positions and launch innovative research programs as early in their careers as possible by omitting the traditional post-doctoral training period.
- Transformative Research to Address Health Disparities and Advance Health Equity – launched in FY 2021, this initiative supports research in developing, disseminating, or

[158] commonfund.nih.gov/highrisk

> implementing innovative and effective interventions that prevent, reduce, or eliminate health disparities and health inequities; it also aims to expand the capacity for health disparities research at minority serving institutions.[159]

The HRHR awards often forge new ground, providing foundations upon which future research can build. These awards have supported significant technological breakthroughs that enable a wide range of research questions to be explored. For example, HRHR support contributed to the development of revolutionary techniques that allow researchers to precisely control the activity of neurons (optogenetics)[160] and expand the contents of tissue samples to allow detailed viewing of fine subcellular structures (expansion microscopy).[161] HRHR awardees are also advancing public health, including identification of celebrity endorsements and advertisements of unhealthy food and beverages during television programming popular with children and adolescents,[162,163] and development of a low-cost device based on a children's toy that could be used to diagnose diseases such as malaria.[164] Independent evaluations of the Pioneer[165] and New Innovator[166] Awards concluded that these awards support research that is more innovative and impactful compared to more traditional NIH research awards.

The Common Fund's HRHR program is a trans-NIH endeavor, with Working Group members from across NIH helping to coordinate and oversee the program. In addition to the HRHR awards supported by the Common Fund, ICs may also support HRHR awards that address exciting scientific projects relevant to their missions. Awards can be co-funded by multiple ICs, representing innovative research projects with the potential for high impact across multiple disciplines and subject areas. For example, a Transformative Research Awardee supported by the National Institute on Aging and the National Institute for Neurological Disorders and Stroke found that the ages of cells within multiple organ tissues can vary widely, even within tissues that have high or low overall rates of turnover, providing a fundamentally new characterization of the aging process.[167] In FY 2020, 18 New Innovator, 1 Pioneer, and 3 Early Independence Awards were funded by ICs, and 3 New Innovator awards were co-funded by Common Fund and other ICs or OD offices.

In addition to participating in the Common Fund's HRHR program, many ICs support awards that target exceptionally creative and innovative researchers and high-risk projects within the IC's mission. Some of these awards were launched based on the success of the HRHR program,

[159] commonfund.nih.gov/healthdisparitiestransformation
[160] www.eurekalert.org/pub_releases/2007-04/su-al040207.php
[161] directorsblog.nih.gov/2015/03/26/diaper-compound-brings-change-to-cell-microscopy/
[162] commonfund.nih.gov/earlyindependence/programhighlights#Celebrity
[163] commonfund.nih.gov/earlyindependence/programhighlights#Unhealthy%20Promotions
[164] commonfund.nih.gov/newinnovator/programhighlights#Paperfuge
[165] commonfund.nih.gov/sites/default/files/HRHR%20PA%20FY%202004-2006%20Outcome%20Evaluation.pdf
[166] commonfund.nih.gov/sites/default/files/HRHR%20New%20Innovator%20Award%20Outcomes%20Evaluation%202007-2009_508%20compliant.pdf
[167] www.salk.edu/news-release/how-old-are-your-organs-to-scientists-surprise-organs-are-a-mix-of-young-and-old-cells/

demonstrating the trans-NIH value of this approach. Examples of IC-supported awards for high-risk, high-reward research include:

- Avant-Garde Award Program for HIV/AIDS and Drug Use Research (National Institute on Drug Abuse):[168] supports individual scientists of exceptional creativity who propose high-impact research that will open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS among drug abusers.
- Avenir Award Program (National Institute on Drug Abuse):[169] supports early stage investigators who propose pioneering research approaches to HIV/AIDS/substance abuse research as well as epigenetics research.
- Biobehavioral Research Awards for Innovative New Scientists (BRAINS; National Institute of Mental Health):[170] helps exceptional early-career scientists launch innovative research programs that have the potential to transform mental health research.
- Outstanding New Environmental Scientist (ONES) Program (National Institute of Environmental Health Sciences):[171] fosters the careers of outstanding scientists while supporting innovative environmental health research.
- Research Innovations for Scientific Knowledge (RISK; National Institute of Arthritis and Musculoskeletal and Skin Diseases):[172] fosters innovative research by encouraging researchers to pursue unusual observations, test imaginative hypotheses, investigate creative concepts, and build ground-breaking paradigms, all of which deviate significantly from the current prevailing theories or practice.
- Multiple ICs support R35 awards, which aim to provide long term support to an investigator with an outstanding record of research productivity. This support is intended to encourage investigators to embark on long-term projects of unusual potential.

Moving forward, the NIH will continue to support a robust portfolio of high-risk, high-reward research. Within the Common Fund's HRHR program, several new activities aim to increase the diversity of the applicant pool to reflect the investigator and institutional diversity of the nation's research workforce, while maintaining a focus on supporting the best science. Based on recommendations from the Advisory Committee to the Director Working Group on High-Risk, High-Reward Programs[173] and input from the scientific community, the HRHR program is increasing outreach to underrepresented groups, strengthening language in funding opportunities to encourage applicant diversity, making institutional diversity a program priority, taking steps to mitigate potential bias against some scientific topics, and piloting anonymized review within the Transformative Research Award.[174] Additionally, to address specific pressing public health needs, the HRHR program is supporting two new scientific focus areas in FY 2021: 1) COVID-19-related funding opportunities within the Transformative Research and Early Independence

[168] www.drugabuse.gov/about-nida/organization/offices/aids-research-program-arp/avant-garde-award-hivaids-research
[169] www.drugabuse.gov/news-events/subject-area-experts/avenir-award-winners
[170] grants.nih.gov/grants/guide/rfa-files/RFA-MH-20-525.html
[171] www.niehs.nih.gov/research/supported/training/ones/index.cfm
[172] www.niams.nih.gov/grants-funding/funding-opportunities/research-innovations-scientific-knowledge-risk
[173] acd.od.nih.gov/documents/presentations/06132019HRHR.pdf
[174] dpcpsi.nih.gov/sites/default/files/CoC_Jan_2020_845_concept_clearance_HRHR_slides.pdf

Awards,[175, 176] and 2) Accelerating Leading-edge Science in ALS (ALS^2) within the Transformative Research Awards.[177]

[175] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-020.html
[176] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-021.html
[177] grants.nih.gov/grants/guide/notice-files/NOT-RM-20-019.html

Maternal Mortality and Morbidity—Closing the Gap in Health Disparities

Program Overview

An estimated 700 women die each year in the United States from conditions related to or associated with pregnancy or childbirth, and over 50,000 women experience severe maternal morbidity (SMM).[178] Over a 25-year period, the global maternal mortality ratio (MMR) of deaths per 100,000 live births declined from 385 in 1990 to 216 in 2015, a relative decline of 44 percent.[179] In contrast, the MMR increased in the United States during the same period and, at 17.4 per 100,000 in 2018,[180] is currently the highest among developed nations. High rates of maternal mortality (MM) and SMM disproportionately affect specific racial and ethnic minority populations. In particular, African American and American Indian/Alaska Native women are two to four times more likely to die from pregnancy-related or -associated causes compared to White women. Furthermore, African American, Hispanic/Latina, Asian, Pacific Islander, and American Indian/Alaska Native women all have higher incidence of SMM compared to White women.[181] Age, disabilities, and geographical disparities also affect MM and SMM, as do social determinants of health, including education, racism, and socioeconomic standing.

One-third of pregnancy-related deaths occur during pregnancy, one-third occur during or in the week after delivery, and one-third occur between one week to one year postpartum.[182] Causes of MM and SMM are multifaceted. In the United States, the leading causes are cardiovascular disease, hemorrhage, and infection. Drug overdose and suicide are major factors, particularly during the postpartum period. Other significant contributing factors include comorbid conditions such as obesity, mental health, and substance use disorders, and structural and health care system characteristics. It is estimated that 60-70 percent of maternal deaths in the United States are preventable.[183] Therefore, implementing multifaceted strategies to address preventable contributors to pregnancy-related and pregnancy-associated morbidity, particularly MM and SMM in disproportionately affected populations, has the potential to drastically reduce disparities in pregnancy-related maternal deaths and morbidity.

NIH supports a broad portfolio of research on MM and SMM, including research focused on disproportionately affected populations. NIH has taken steps to emphasize the inclusion of disadvantaged and high-risk pregnant and lactating women in clinical studies. In concurrence with recommendations from the Congressionally mandated Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), NIH plans to implement additional

[178] www.cdc.gov/vitalsigns/maternal-deaths/index.html#:~:text=about%201%2F3%20of%20deaths,week%20to%201%20year%20postpartum.
[179] www.unfpa.org/publications/trends-maternal-mortality-1990-2015#:~:text=Estimates%20by%20WHO%2C%20UNICEF%2C%20UNFPA,the%20United%20Nations%20Population%20Division&text=The%20global%20maternal%20death%20ratio,an%20estimated%20303%2C000%20in%202015.
[180] www.cdc.gov/nchs/maternal-mortality/index.htm
[181] www.cdc.gov/vitalsigns/maternal-deaths/index.html#:~:text=about%201%2F3%20of%20deaths,week%20to%201%20year%20postpartum.
[182] www.cdc.gov/vitalsigns/maternal-deaths/index.html#:~:text=about%201%2F3%20of%20deaths,week%20to%201%20year%20postpartum.
[183] www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/mmr-data-brief.html

recommendations from this group to strengthen its efforts.[184,185] These recommendations highlight the potential for leveraging existing federal resources, implementing systematic data collection, and developing new research tools and strategies, among other key approaches to addressing MM and SMM research. Developing scientifically validated, safe and effective interventions for pregnant and lactating women is difficult, as many researchers routinely exclude these women from clinical research. Researchers often do not consider potential risks of untreated maternal disorders to both the mother or the fetus and worry about safety and exposure of the fetus to experimental treatments. In conducting research on promising therapeutics to be used by pregnant and lactating women, researchers will need to over-sample racial and ethnic minority women to better understand the differential impact of maternal health disorders. NIH clinical research networks have supported extensive research on interventions to reduce maternal morbidity and mortality, with a special emphasis on reducing health disparities. Scientists found that a quality improvement initiative undertaken at 99 California hospitals benefitted African American women more than White women by reducing disparities in the risk of obstetric hemorrhage.[186] Current efforts include clinical research studies and trials on reducing the risk of preeclampsia and prophylactic interventions to prevent postpartum hemorrhage after cesarean delivery.

Other research efforts across NIH have made advances in reducing pregnancy-related and -associated morbidity and mortality (PRAMM). Population health researchers supported by NIH were quick to alert the nation to alarming rates of maternal mortality and have continued using large-scale data approaches to shed light on disparities. Researchers found that Black women were particularly at risk for cardiopulmonary complications shortly after delivery, with a risk of postpartum pulmonary edema (fluid in the lungs) and/or acute heart failure more than twice as high as that of Non-Hispanic White women.[187] Results from the NuMoM2b Heart Health Study showed that women who experienced adverse outcomes in a first pregnancy were more likely to have hypertension two to seven years postpartum, compared to women without such pregnancy history.[188] Another study with support from multiple NIH ICOs determined that among women readmitted postpartum for sepsis, 61 percent occurred after six weeks, the normal time for postpartum visits. These results support the need for a flexible continuum of postpartum care for mothers that could extend well beyond the traditional check-in at six weeks after delivery.[189]

Although NIH and NIH-supported researchers have made strides in addressing PRAMM and its associated health disparities, the agency recognized the need for a trans-NIH initiative targeted at this issue. In 2020, NIH convened a trans-NIH Maternal Mortality Task Force led by the NIH Immediate Office of the Director, NICHD, and the Office of Research on Women's Health (ORWH) to coordinate collaborative research efforts across NIH to address maternal mortality and drive a new initiative under development at NIH called Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE).[190] IMPROVE aims to use an integrated approach to understanding biological, behavioral, sociocultural, and structural factors

[184] www.nichd.nih.gov/about/advisory/PRGLAC
[185] www.nichd.nih.gov/about/advisory/PRGLAC/recommendations
[186] pubmed.ncbi.nlm.nih.gov/31978432/
[187] pubmed.ncbi.nlm.nih.gov/30786255/
[188] pubmed.ncbi.nlm.nih.gov/31564189/
[189] pubmed.ncbi.nlm.nih.gov/31529451/
[190] www.nih.gov/research-training/medical-research-initiatives/improve-initiative

that affect PRAMM by building an evidence base for improved care and outcomes. IMPROVE is a multipronged innovative research initiative designed to target health disparities associated with PRAMM by 1) implementing and evaluating community-engaged interventions for disproportionately affected women (e.g., African American, American Indian/Alaska Native, advanced maternal age, low socioeconomic status, or rural populations), and 2) identifying risk factors and the underlying biological mechanisms associated with leading causes of PRAMM, including cardiovascular disease, infection and immunity, and mental health.

To address the leading causes of PRAMM during pregnancy, at delivery, and up to one year postpartum, IMPROVE will build on ongoing efforts among federal and other key partners to accelerate progress and maximize reach and impact by leveraging existing resources including previously studied cohorts and archived biospecimens, and developing new studies. IMPROVE will expand and complement existing research efforts that incorporate local community needs and perspectives to address health disparities in PRAMM. Supported projects will develop, implement, and evaluate community-tailored interventions, as well as investigate biological, behavioral, sociocultural, and structural risk factors and mechanisms of the leading causes of PRAMM. Through this multidimensional strategy, IMPROVE aims to create an evidence-based approach to reducing PRAMM and its associated health disparities. In FY 2020, IMPROVE kicked off by supporting 36 supplements to existing research projects that incorporate community partnerships in high-risk areas and populations, expand research on the leading causes of, or build the knowledge base for PRAMM.

Other activities across NIH align with the priorities of IMPROVE and primarily address PRAMM in disproportionately affected populations. The ORWH developed and maintains the Maternal Morbidity and Mortality Web Portal that offers maternal health and pregnancy-related resources to the public.[191] NIH also engaged the research community in workshops to consider priorities and gaps in research to address underlying factors that contribute to PRAMM and methods or care models that reduce inequities in maternal health. In FY 2020, multiple NIH institutes supported two projects to target different facets of PRAMM. One included multidisciplinary research to advance the understanding, prevention, and reduction of PRAMM in racial and ethnic minorities and socially disadvantaged populations.[192] The second project will encourage women's health research in Institutional Development Award (IDeA) states that have historically received low levels of NIH funding.[193] These states often have a large proportion of rural or minority populations that are disproportionately affected by PRAMM.

NIH synergizes its own activities through internal collaborations as well as external collaborations with other agencies within U.S. Department of Health and Human Services (HHS) and other governmental agencies on maternal health topics. Multiple NIH ICOs participate in the HHS Maternal Mortality and Morbidity (MMM) Working Group to address MMM in diverse populations across operating divisions. NIH led the congressionally mandated PRGLAC, which brings together clinical, research, advocacy, public health, regulatory, and pharmaceutical industry leaders to address the significant gaps in research on safety, efficacy, and dosing of medications currently used to manage pregnancy-related and other conditions of pregnant and

[191] orwh.od.nih.gov/research/maternal-morbidity-and-mortality
[192] grants.nih.gov/grants/guide/rfa-files/RFA-MD-20-008.html
[193] grants.nih.gov/grants/guide/notice-files/NOT-GM-20-017.html

lactating women. Plans for implementing the PRGLAC recommendations, published in September 2018, are already underway.[194] NIH also contributed to the Health Resources and Services Administration's Maternal and Child Health Bureau Grand Challenge on Remote Pregnancy Monitoring focused on technology-based solutions for remote health monitoring of pregnant women, and maternal mortality action plans from HHS and the Surgeon General.

Next Steps

In FY 2021, IMPROVE will include a multipronged initiative to accelerate understanding of the impact of structural racism and discrimination in the context of the COVID-19 pandemic on maternal health outcomes and up to one year postpartum[195] and technology-focused initiatives to improve maternal health outcomes.[196] IMPROVE plans will be complemented by other efforts across NIH, including the planned continuation of the NuMoM2b Heart Health Study that will continue follow-up for 6 to 15 years with a cohort of geographically and ethnically diverse group of women enrolled during their first pregnancies to explore the occurrence and mechanisms of cardiovascular disease development in women with and without adverse pregnancy outcomes.[197]

[194] www.nichd.nih.gov/sites/default/files/inline-files/PRGLAC_Implement_Plan_083120.pdf
[195] grants.nih.gov/grants/guide/notice-files/NOT-OD-21-071.html
[196] grants.nih.gov/grants/guide/notice-files/NOT-EB-21-001.html
[197] reporter.nih.gov/project-details/9085357

Next Generation Researchers Initiative: Investing in the Future of the Biomedical Workforce

Program Overview

The National Institutes of Health (NIH) has long recognized that the most critical assets in the biomedical research enterprise are the scientists who comprise its workforce. The biomedical research enterprise relies upon a pipeline of highly trained investigators to convey new insights, develop innovative ideas, and advance the translation of scientific research into improved health for all. Intense competition for funding, however, can pose a challenge for researchers trying to embark upon and sustain independent research careers. NIH understands this challenge and, as such, is continuing to invest in the future through initiatives that strengthen and diversify the biomedical research workforce.

In September 2017, with support from the 21st Century Cures Act (P.L. 114-255), NIH launched the Next Generation Researchers Initiative (NGRI) to cultivate and support talent entering the biomedical and behavioral research workforce.[198] This initiative aims to bolster opportunities for early-stage investigators (ESIs).[199] ESIs are defined as those within 10 years of completing their highest advanced research degree or postgraduate clinical training and who have not previously competed successfully for a substantial NIH independent research award. In addition, applications from ESIs are given special consideration during peer review as well as at the time of funding consideration.

NIH Institutes and Centers prioritize funding for ESIs as part of NGRI. The initiative also tracks the impact of funding decisions on ESIs, such as subsequent grant submission and success. As a result of this initiative, NIH has substantially increased support for ESIs – from less than 600 ESIs in 2013 to 1,412 in FY 2020.

Moving forward, NGRI will continue to support novel approaches to expand pathways for funding ESIs. One such pathway is available through the new ESI award named in honor of Stephen I. Katz, M.D., Ph.D., who was profoundly dedicated to mentoring the next

Caption: Dr. Stephen Katz with early career scientists in 2018.

[198] grants.nih.gov/ngri.htm
[199] grants.nih.gov/grants/guide/notice-files/NOT-OD-17-101.html

generation of scientists.[200] Dr. Katz led the National Institute of Arthritis and Musculoskeletal and Skin Diseases from 1995 to his passing in 2018. ESIs may apply for this new opportunity, issued in November 2020, to support their innovative ideas if they are proposing research that is a change in direction from their past work and experience, and for which they have no preliminary data.

In addition to the Katz Award, NIH has several other established programs targeted to those early in their research career, such as:

- NIH Director's New Innovator Award Program[201]
- Maximizing Investigators' Research Award[202]
- NIH Pathway to Independence Award[203]
- NIH Director's Early Independence Award[204]
- High Priority, Short-Term Project/Bridge Award[205]
- Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program[206]

Also as part of NGRI, NIH is implementing methods to identify and support meritorious investigators (new or established) who are at-risk for losing all NIH funding and who do not have significant research support from other sources. The Advisory Committee to the NIH Director NGRI Working Group also called for special funding consideration for "at-risk" investigators in their December 2018 NGRI report.[207,208] Early data suggest that, since NGRI began, the outlook for at-risk investigators has improved somewhat in 2018 and 2019, but still their funding rates are lower than those for established investigators who are assured of continuing funding for at least one more fiscal year.[209]

NGRI also aims to strengthen diversity in the future biomedical workforce. Scientists and trainees from diverse backgrounds and life experiences bring different perspectives and creative approaches to solving the scientific problems we face as a nation. NIH recognizes that its ability to help ensure that the nation remains a global leader in biomedical scientific discovery and innovation is dependent upon a pool of highly talented scientists from diverse backgrounds who will help to further NIH's mission. Today and going forward, NIH will analyze NGRI policies to ensure its efforts continue supporting career development for women and individuals from nationally underrepresented backgrounds in biomedicine.

NIH has several programs aimed at promoting diversity and enhancing progress to an independent career. As an example, the BRAIN Initiative Advanced Postdoctoral Career

[200] grants.nih.gov/funding/katz-esi-r01.htm
[201] commonfund.nih.gov/newinnovator
[202] www.nigms.nih.gov/research/mechanisms/mira/pages/default.aspx
[203] grants.nih.gov/grants/guide/pa-files/PA-20-188.html
[204] commonfund.nih.gov/earlyindependence
[205] grants.nih.gov/grants/funding/r56.htm
[206] www.nigms.nih.gov/training/careerdev/Pages/MOSAIC.aspx
[207] acd.od.nih.gov/working-groups/nextgen.html
[208] acd.od.nih.gov/documents/presentations/12132018NextGen_report.pdf
[209] nexus.od.nih.gov/all/2020/02/07/whats-happening-with-at-risk-investigators/

Transition Award to Promote Diversity (K99/R00) program enhances biomedical research workforce diversity and fosters a strong cohort of new, highly skilled and well trained, NIH-supported, independent investigators from diverse backgrounds.[210] The MOSAIC program, referenced earlier, facilitates the transition of cohorts of talented postdoctoral researchers from diverse backgrounds into independent faculty careers in research-intensive institutions.

In addition, NIH has developed and implemented a range of approaches to improve the representation of women in the biomedical research pipeline. NIH implemented automatic extensions of ESI status for childbirth within the ESI period.[211] In FY 2020, an automatic extension of one year was also implemented for childbirth within the four-year K99 eligibility window.[212] Additionally, NIH offers support for early-career investigators with high potential to re-enter an active research career after an interruption for family responsibilities or other qualifying circumstances.[213,214]

NIH remains strongly committed to the goals of NGRI to fund more early-career investigators, protect and retain meritorious at-risk scientists, and enhance the diversity of the biomedical research workforce. NIH will continue to incorporate guidance from the Advisory Committee to the NIH Director NGRI working Group and the National Academies of Sciences, Engineering, and Medicine (NASEM) report "The Next Generation of Biomedical and Behavioral Sciences Researchers: Breaking Through" in the future design, testing, implementation, and evaluation of policies and programs to enhance the success of the next generation of talented biomedical researchers.[215] To address concerns raised in the NASEM report, NIH will continue to collect and analyze workforce-related data to assess workforce trends.

[210] grants.nih.gov/grants/guide/rfa-files/rfa-ns-19-043.html
[211] grants.nih.gov/grants/guide/notice-files/NOT-OD-18-235.html
[212] grants.nih.gov/grants/guide/pa-files/pa-18-592.html
[213] grants.nih.gov/grants/guide/notice-files/NOT-OD-20-054.html
[214] grants.nih.gov/grants/guide/notice-files/NOT-OD-20-055.html
[215] www.nap.edu/catalog/25008/the-next-generation-of-biomedical-and-behavioral-sciences-researchers-breaking

Nutrition Research

Program Overview

The National Institutes of Health (NIH) funds a broad array of basic, clinical, and applied research to further understand nutrition as it relates to health and disease. The goal of the recently released *2020-2030 Strategic Plan for NIH Nutrition Research,*[216] the first NIH-wide plan for nutrition research, is to advance nutrition research and address diet-related diseases through interventions focused on nutrition across the lifespan, including the use of food as medicine. To elevate attention to and ensure a coordinated approach to nutrition research across NIH, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Office of Nutrition Research (ONR) was moved to the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) in the NIH OD in FY 2021.

The Strategic Plan for NIH Nutrition Research

The *Strategic Plan for NIH Nutrition Research* was developed by the NIH Nutrition Research Task Force (NRTF),[217] which coordinated with NIH ICOs. The NRTF completed their work developing the plan in 2020 and its implementation will be overseen by the newly created ONR with the assistance of an NIH-wide Senior Liaison Group and topic-specific Implementation Work Groups.[218] The strategic plan calls for expanded collaboration across NIH ICOs to accelerate nutrition science and uncover the role of human nutrition in maintaining and improving public health and reducing diseases that contribute to the top causes of death, disability, and high health care costs in the United States. The strategic plan reflects the wide range of nutrition research supported across NIH—over an estimated $1.9 billion in FY 2020 **(Figure 1)**.

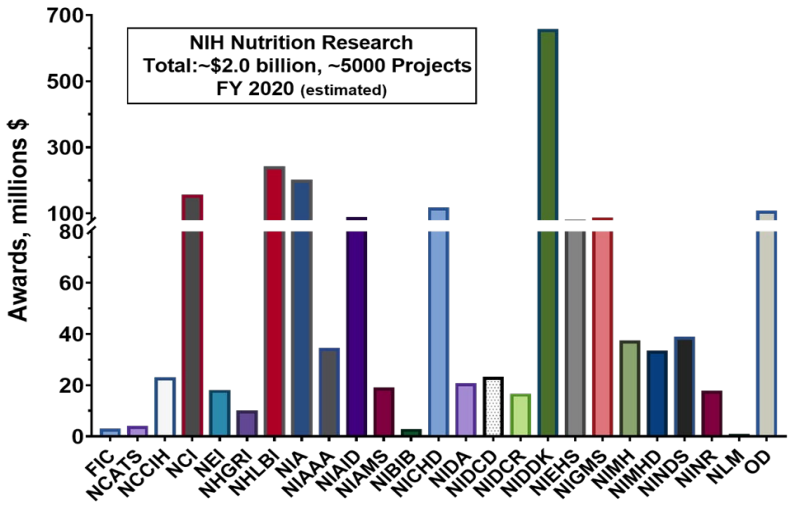


Figure 1. Estimated Nutrition Research Funding, Fiscal Year (FY) 2020.

With a focus on precision nutrition, the plan is a multifaceted approach—spanning basic to clinical discovery—toward developing comprehensive and dynamic nutrition recommendations relevant to both individual and population health.

[216] dpcpsi.nih.gov/onr/nih-nutrition-report
[217] dpcpsi.nih.gov/onr/nutrition-research-committees-and-working-groups
[218] dpcpsi.nih.gov/onr/iwg

NIH is implementing the strategic plan and will monitor and encourage progress. ONR, along with ICO partners, is pursuing opportunities to advance the priorities identified in each of the strategic plan goals and cross-cutting research areas and catalyze nutrition research at NIH-funded universities and institutions and in NIH labs. The ONR will continue to develop new concepts to implement the strategic plan, such as a Human Milk Informatics and Longitudinal Composition Initiative, to characterize components of human milk in a diverse population, and the Developmental Origins of Health and Disease Initiative, to evaluate parents and offspring for contributions of early nutrition to future health and disease.

As the plan is put into action, NIH will continue to seek input from the nutrition community and others. For example, in January 2021, NIDDK, the National Heart, Lung, and Blood Institute (NHLBI), and the DPCPSI Office of Disease Prevention (ODP) held a related workshop[219] to identify research gaps and opportunities in precision nutrition.

In addition to activities related to the strategic plan, NIH supports ongoing nutrition research studies, which will be coordinated and leveraged to advance nutrition science. Examples of new nutrition advances are in the NIH Nutrition Research Report, 2017-2019.[220]

Nutrition for Precision Health, powered by the *All of Us* Research Program

Designed to implement aspects of the strategic plan, the new Common Fund program, Nutrition for Precision Health,[221] is powered by the *All of Us* Research Program.[222] Research is needed to provide more precise and dynamic nutritional recommendations than currently possible through population-wide guidance. This in turn will facilitate a deeper understanding of how individual human biological systems and molecular pathways interact with or mediate the relationships among dietary patterns, environmental, social, and behavioral factors to influence health status.

The Nutrition for Precision Health program aims to catalyze precision nutrition research by establishing predictive algorithms to inform targeted dietary approaches. Plans for phase 1 of the program will leverage the *All of Us* Research Program by recruiting a subset of 10,000 participants—the largest precision nutrition study to date **(Figure 2)**. Subsets of these individuals will be asked to undergo more detailed dietary regimens and analyses. Each module will involve assessment of social, community, and other behavioral and contextual factors that could be sources of individual variability in dietary responses, along with microbiome, physiological, proteomic, and metabolomic assays. The diverse study population in the *All of Us* Research Program will illuminate important insights into diet-related health disparities. Artificial intelligence and other data science tools will be used to generate predictive dietary intervention algorithms that may be useful for patients and doctors for improving health and quality of life. If successful, a second stage of the program would support studies to validate

[219] www.niddk.nih.gov/news/meetings-workshops/2021/Precision-Nutrition-Workshop
[220] www.niddk.nih.gov/about-niddk/strategic-plans-reports/nih-nutrition-report
[221] commonfund.nih.gov/nutritionforprecisionhealth
[222] allofus.nih.gov/

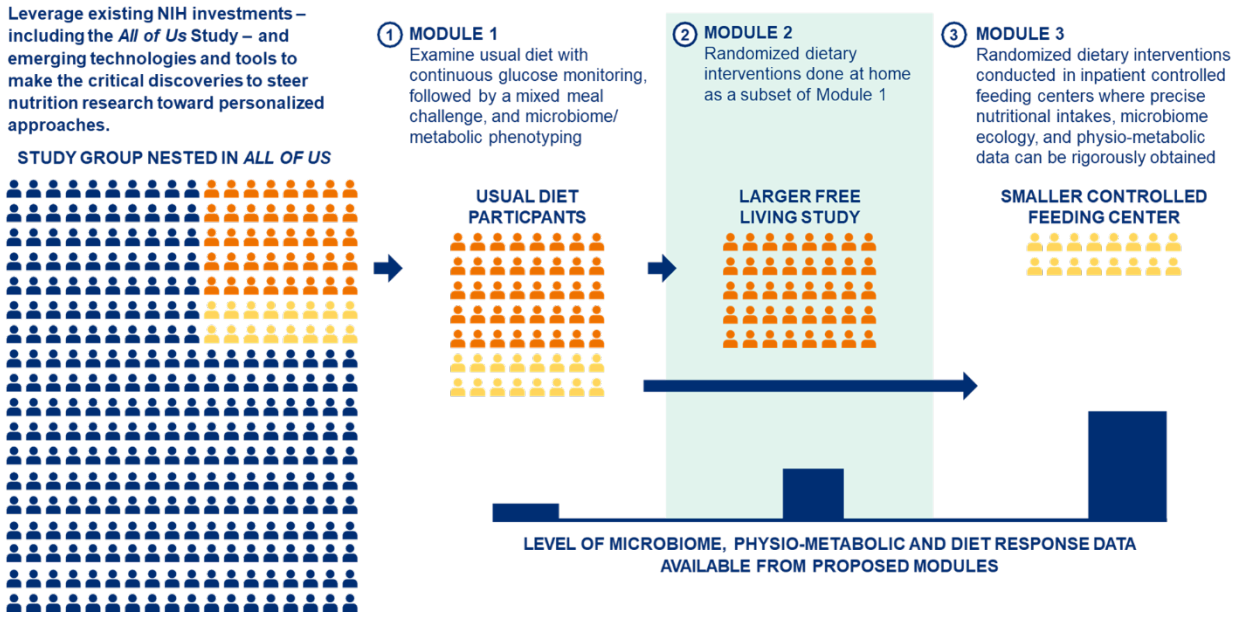


Figure 2. The Nutrition for Precision Health, powered by the *All of Us* Research Program. The Nutrition for Precision Health program aims to use data collected from the large, diverse *All of US* Research Program cohort to determine what individuals should eat to stay healthy. In phase 1, participants will be divided into modules involving usual diet, controlled feeding, and/or domiciled studies.

those algorithms that predict responses to diet. Although funded by the Common Fund, the Nutrition for Precision Health program will be managed by 17 ICOs collaborating across NIH.

Next Steps and Goals for Nutrition Research at NIH

To fully realize the vision of the strategic plan, the new DPCPSI ONR will undertake a number of research initiatives, workshops, and other activities designed to implement the goals of the strategic plan.

One way to maximize the impact of ONR is to launch time-limited goal-driven programs focused on nutrition. Common Fund programs represent strategic investments in biomedical and behavioral research designed to achieve high impact goals and catalyze discovery within a defined timeframe not to exceed 10 years. These programs address challenges and opportunities that are of high priority for NIH as a whole and include an emphasis on project management to track attainment of milestones and to ensure that goals are met. The 10-year limit to funding ensures a constant churn of funds that enables new programs to be established.

Past examples of transformative programs that informed nutrition research include the Human Microbiome Project (HMP), supported by the Common Fund from 2007-2016, which developed numerous research resources to enable the study of the microbial communities that live in and on the human body and the roles these communities play in health and disease. The gut microbiome, which is highly variable between individuals, has been linked to disease susceptibility, as well as to individual variability in behavioral and physiological responses to diet. The human gastrointestinal microbiota not only influence what nutrients an individual can extract from one's diet, but may also affect that individual's physiology, behavior, and

susceptibility to diet-related chronic diseases. The Nutrition for Precision Health program will build upon this knowledge to advance our understanding of the microbiome and its influences on diet and overall health at the individual and population level. In addition, the Common Fund Metabolomics Program has developed nationwide capabilities to measure metabolic responses and to identify metabolites. This will be essential for the Nutrition for Precision Health program.

The Common Fund itself supports a continuously changing set of topics and would not be able to support repeated projects devoted to the same topic, such as nutrition. However, coordinating Common Fund-like programs through ONR will provide a tested research strategy for repeatedly delivering transformation in the nutrition field.

Rapid Acceleration of Diagnostics (RADx) — Answering the Call of COVID-19

Program Overview

The coronavirus pandemic has presented a significant challenge to public health and safety across the United States. To stem the spread of the novel coronavirus (SARS-CoV-2), communities must have access to efficient and reliable diagnostic testing. In response to this urgent public health need, the Rapid Acceleration of Diagnostics (RADx℠) initiative, a major effort coordinated through the NIH OD, was launched in April 2020. This initiative is a national call for scientists and engineers to present innovative ideas to speed the development, validation, commercialization, and implementation of COVID-19 testing and ensure fast and accurate testing to support nation-wide efforts to reduce the spread of COVID-19 and return to normal activities. With the goal of making millions of tests available each week, the RADx℠ initiative is also pursuing opportunities to study and refine testing methods and approaches for distribution through engagement with underserved and vulnerable communities, with a special focus on those at higher risk of COVID-19.

NIH launched the RADx℠ initiative in partnership with several other federal agencies, including the Office of the Assistant Secretary of Health (OASH), Department of Defense (DOD), the Biomedical Advanced Research and Development Authority (BARDA), U.S. Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC).

The RADx℠ initiative consists of five programs uniquely designed to meet the need of COVID-19 testing:

- RADx Tech: NIH established the RADx Tech program to quickly identify, validate, and scale up production of promising new technologies for point-of-care and laboratory COVID-19 testing. The RADx Tech program invited bioengineers and entrepreneurs to submit ideas for testing technologies that could be rapidly developed and deployed. This program is an accelerated milestone-driven approach that, through vigorous vetting, identifies the most promising solutions in which to invest. Experts help awardees simultaneously address technical, regulatory, clinical, and commercialization requirements throughout the phased approach.

  The program expanded on the Point-of-Care Technologies Research Network (POCTRN), established by NIH's NIBIB in 2007, which uses a flexible, rapid process to support promising technologies at key stages of development to advance technologies with clinical applications.

- RADx-ATP: The RADx Advanced Technology Platforms (RADx-ATP) program seeks to enhance testing capacity and throughput by identifying existing and late-stage testing technologies ready to be scaled up or expanded to increase their geographic reach. This two-year effort began in 2020 by leveraging the established RADx Tech proposal review process and market research infrastructure to identify high-potential applicants. RADx-ATP has placed special emphasis on different testing technologies with the capability to distinguish between SARS-CoV-2 and influenza infections and has built collaborations with key industry partners.

To date, RADx Tech and RADx-ATP have provided support and funding to 150 organizations with promising testing technologies. Projects chosen for advancement through the phased selection process represent a broad range of test types, including both point-of-care and laboratory-based tests. The tests utilize a range or sample types, methods, and technologies all of which have or are near to receiving FDA authorization. Diversifying the available diagnostic tests enhances the ability to develop effective tests for many environments.

- RADx-rad: The RADx Radical (RADx-rad) program supports research and development for new, innovative techniques and new applications of existing approaches to address current gaps in COVID-19 testing. The goal of RADx-rad is to enhance the usability, accessibility, and accuracy of novel COVID-19 testing. Non-traditional approaches supported by RADx-rad include community wastewater analysis and surveillance, sensory detection for early disease, and integration of artificial intelligence systems with digital health technologies for screening and prognostics. RADx-rad has supported 49 projects to address gaps in SARS-CoV-2 testing through technology platforms that can be used in future outbreaks of COVID-19 and that could be applicable to other, yet unknown, infectious organisms.

  RADx-rad is coordinated by a trans-NIH committee with partnerships across 25 NIH ICOs. A RADx-rad data coordination effort (RADx Data Hub) will assure harmonized data collection, storage, management and access, and linkages to data from other RADx initiatives, which will provide opportunities for secondary analysis to further explore early findings and identify promising approaches to understand the novel SARS CoV-2 virus. Beyond the current crisis, the technologies advanced through RADx-rad will likely be applicable to the early identification and prevention of other, as yet unknown, infectious disease agents.

- RADx-UP: As part of the NIH-wide effort to address the COVID-19 pandemic, the RADx Underserved Populations (RADx-UP) program was developed to enable and expand COVID-19 testing for underserved and vulnerable populations. RADx-UP addresses the increased burden of COVID-19 on populations with health disparities, particularly African Americans, Hispanics or Latinos, and American Indians/Alaska Natives, older adults, pregnant women, those in underserved rural or urban communities, the homeless, and those who are incarcerated. To partner with these communities, RADx-UP created a consortium of community-engaged research projects designed to evaluate and implement effective COVID-19 interventions. RADx-UP established a collaborative network of clinical research projects to examine COVID-19 infection patterns and efforts to increase access and effectiveness of diagnostic methods. These two-year research projects seek to examine COVID-19 transmission patterns, assess the use and effectiveness of COVID-19 diagnostic tools, and ultimately enable rapid, accurate COVID-19 testing within underserved and vulnerable populations that have been disproportionately affected by the COVID-19 pandemic. In FY 2021, RADx-UP plans to expand this testing network to include studies that focus on testing in the context of vaccination, a new emphasis on testing strategies to safely return children and staff to the in-person school setting, and ways to leverage and build partnerships between RADx-UP and other aligned NIH programs focused on underserved and vulnerable populations.

The RADx-UP Social, Ethical, and Behavioral Implications (SEBI) research program will identify, analyze, and address the social, ethical, and behavioral factors likely to influence access to and uptake of COVID-19 testing in underserved and vulnerable populations. RADx-UP will strengthen the available data on infection rates, disease progression and outcomes, and identify strategies to reduce disparities seen in COVID-19 diagnostics.

The RADx-UP Coordination and Data Collection Center will serve as a national resource to coordinate research activities, guide administrative operations and logistics, and provide analytical infrastructure and expertise for COVID-19-related research activities. RADx-UP also supports the application of technological advances emerging from other RADx efforts to underserved and vulnerable populations in real-world settings, such as distributing home diagnostic kits.

- Data Management: In support of these and other COVID-19 related efforts, NIH is constructing an infrastructure to support coordination of the data management needs of COVID-19 efforts. The goal of this effort is to develop a platform to integrate data on individuals and populations from a variety of sources, including testing results, self-reported symptoms, and electronic medical record data. All RADx℠ initiatives will be undergirded by a data coordinating effort, which will intake and collect data from the various RADx projects through project-focused coordination centers. This effort will also work with the project coordination centers, todevelop and implement common data elements and models, and facilitate harmonized data sharing on a secure cloud-based data platform.

Trans-NIH Collaboration

The RADx℠ initiative has overarching trans-NIH governance, including the RADx Executive Committee, specific governance mechanisms for each initiative, and trans-NIH working groups to utilize diverse subject matter expertise from across the agency. RADx also includes collaborations across HHS, including BARDA, FDA, and CDC. These collaborations are a priority for tracking and routing NIH-supported projects, coordinating efforts, implementing review processes, and coordinating communications strategies.

Next Steps

The RADx programs are developing opportunities to expand and support ongoing and new COVID-19 diagnostic research activities. Through the RADx℠ initiative, the NIH will continue to evolve and adapt efforts to meet the changing circumstances of the COVID-19 pandemic.

UNITE Initiative

Program Overview

The NIH has spent over a year addressing the COVID-19 pandemic, which has made painfully clear that health disparities and inequities continue to contribute to morbidity and mortality in our nation. In addition, the events of 2020 highlighted our nation's continued struggle with systemic and structural racism. As a science agency, the NIH understands that bringing diverse perspectives, backgrounds, and skillsets to complex scientific problems enhances scientific productivity. NIH is committed to instituting new ways to support diversity, equity, and inclusion, and identifying and dismantling any policies and practices that may harm the NIH workforce and its ability to make important discoveries that improve health and save lives.

NIH launched the UNITE Initiative at a special meeting of the Advisory Committee to the Director (ACD) on February 26, 2021[223] with the goal of identifying and addressing structural racism within the NIH community and the greater biomedical research community. UNITE[224] is comprised of five workstreams with separate but coordinated objectives to tackle the problem of racism and discrimination in science, while developing methods to promote diversity and inclusion across the biomedical enterprise. These workstreams include:

- U - Understanding stakeholder experiences through listening and learning
- N - New research on health disparities, minority health, and health equity
- I - Improving the NIH culture and structure for equity, inclusion and excellence
- T - Transparency, communication, and accountability with our internal and external stakeholders
- E - Extramural research ecosystem: changing policy, culture and structure to promote workforce diversity

Through this NIH-wide, collaborative effort, UNITE will work to address challenging issues stemming from structural racism with which the NIH is currently grappling.

Attracting and Retaining Scientists from Underrepresented Groups: The NIH will be instituting several efforts to attract and retain scientists from underrepresented groups including expanding the Distinguished Scholars Program[225] to Senior Investigators hired with tenure, and enhancing recruitment of researchers from underrepresented groups as candidates for open tenure-track investigator positions. This program is led through a collaboration between the Office of Scientifc Workforce Diversity (SWD) and the Intramural Research Program.

Addressing Disparities in the Success Rates for Grants Supporting Black Scientists: In 2011, Ginther et al. reported a significant racial gap apparent in NIH R01 funding.[226] The funding rate for R01 applications from Black/African American scientists was 10 percentage points lower than for all other groups. This urged NIH and the biomedical community to look closely at

[223] acd.od.nih.gov/meetings.html
[224] www.nih.gov/ending-structural-racism/unite
[225] diversity.nih.gov/programs-partnerships/dsp
[226] www.ncbi.nlm.nih.gov/pmc/articles/PMC3412416/

individual and systemwide potential contributors and solutions, codified in 13 recommendations by the NIH ACD.[227] Today, there are still far too few Black applicants and applicants from other groups underrepresented in the biomedical workforce (Figure 1). While success rates for receipt of R01 equivalent grants from Black applicants have increased slightly,[228] further work remains to eliminate the well-documented funding gap.

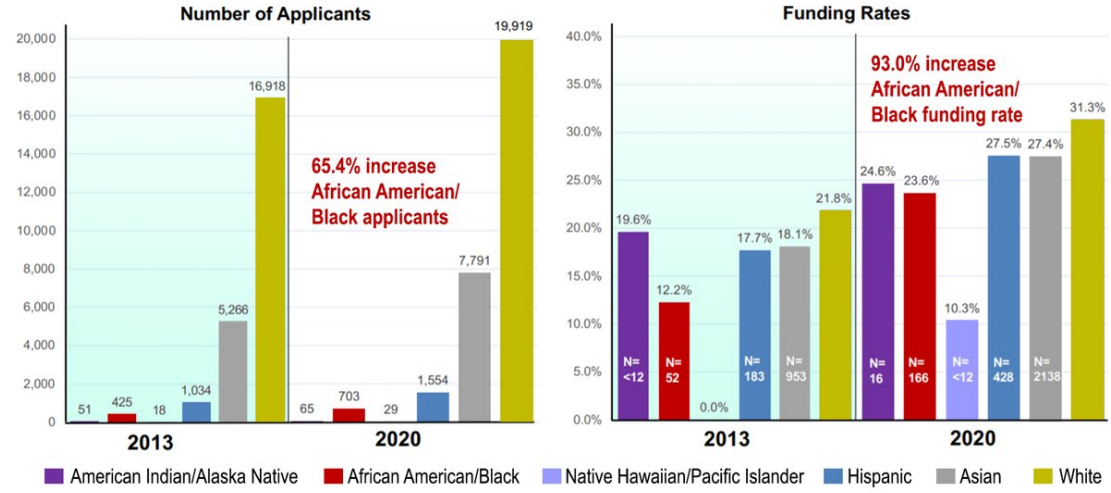


Fig. 1. Disparities in NIH R01 Grant Application and Funding Rates. Disparities in number of applicants and funding rates between NIH R01 grants that support non-White investigators and NIH R01 grants that support White investigators. From 2013 to 2020, both application and funding rates for grants that support African American/Black investigators increased, but differences with White investigators still remained.

Improving Transparency of Race-Based Demographic Data: The NIH workforce is composed of both an extramural scientific workforce of division directors, program officers, policy analysts, etc. and an intramural scientific workforce of lab heads, biologists, trainees, as well as a clinical center running clinical trials. In the scientific workforce, disparities have been identified based on race and ethnicity (Figure 2).

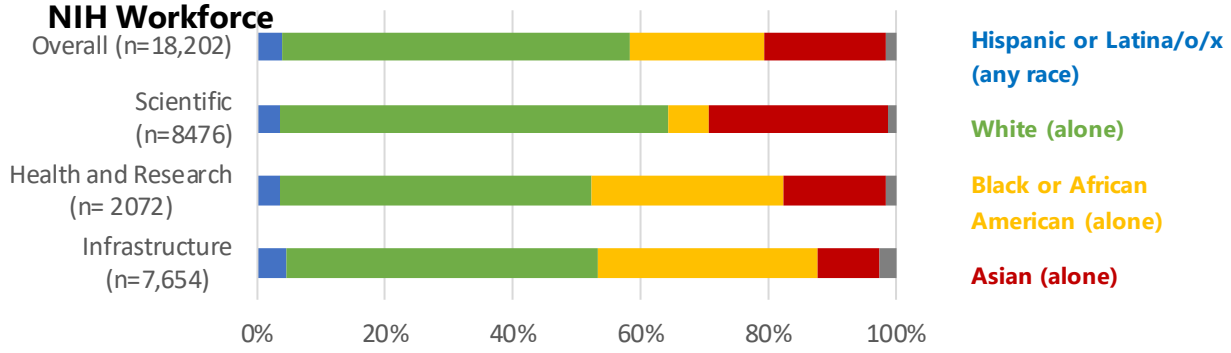


Fig. 2. Demographics of NIH FTE Workforce. This figure demonstrates the NIH's current FTE workforce data. Scientific Workforce leads or has oversight over research (e.g., investigator, staff scientist, health science administrator); Heath and Research Workforce supports research (e.g., nurse, lab technician); and Infrastructure Workforce undergirds the scientific enterprise but not "scientific" or "health and research" (e.g., program analyst, grants management, IT). Disparities in the Scientific Workforce are seen in the underrepresentation of Black/African Americans and American Indian, Alaska Native,

[227] acd.od.nih.gov/documents/reports/DiversityBiomedicalResearchWorkforceReport.pdf
[228] diversity.nih.gov/sites/coswd/files/images/docs/SWD_Progress_2021_Infographic.pdf

Native Hawaiian, Pacific Islander, and Two or More Races compared to the overall workforce demographics where Whites are overrepresented.

In addition, when examining NIH Leadership positions (IC Directors, Deputy Directors, Scientific Directors, Clinical Directors, and Executive Officers), data indicate a disparity with the overall NIH workforce in that Whites are overrepresented compared to others (Figure 3). NIH's goal is to develop a sustainable, systematic process to gather and make public demographic data for both the intramural and extramural biomedical research workforces, extending across all job categories to better empower the work of NIH.

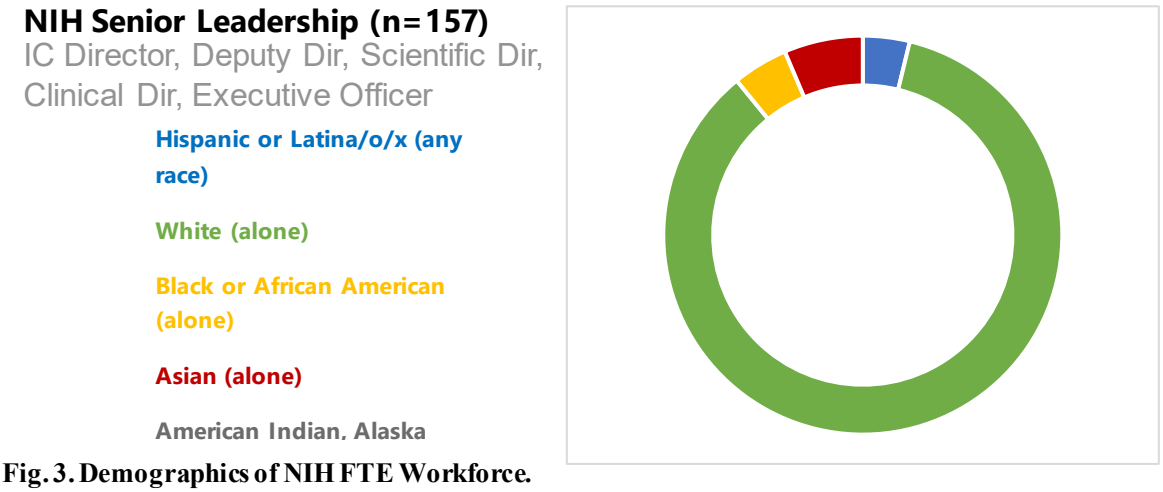


Fig. 3. Demographics of NIH FTE Workforce.
This figure demonstrates the NIH's current Senior Leadership demographic data. This indicates an underrepresentation of Black/African Americans and American Indian, Alaska Native, Native Hawaiian, Pacific Islander, and two or More Races compared to the overall workforce demographics where Whites are overrepresented.

Increasing Funding of Research for Minority Health, Health Disparities, and Health Equity:
All NIH institutes and centers, led by the National Institute of Minority Health and Health Disparities (NIMHD), will seek to expand and enhance research on health disparities and health equity. As part of this, the NIH Common Fund, led by DPCPSI, has announced a new 5-year, $60 million program to support innovative investigator-initiated projects aimed at reducing health disparities and inequalities.[229] Emphasis will be placed on projects aimed at developing effective interventions, and institutions that serve minority populations will be prioritized for select awards. NIH is also providing robust support to the NIMHD funding opportunity announcement,[230] *Understanding and Addressing the Impact of Structural Racism and Discrimination on Minority Health and Health Disparities*, announced on March 23, 2021, with 22 ICOs signed on with their support.

Addressing Racism in the NIH Workplace:
The NIH has identified accounts of racism in the workplace reported by people of color throughout the biomedical research enterprise both through personal accounts and through

[229] grants.nih.gov/grants/guide/rfa-files/RFA-RM-21-021.html and, grants.nih.gov/grants/guide/rfa-files/RFA-RM-21-022.html.
[230] grants.nih.gov/grants/guide/rfa-files/RFA-MD-21-004.html

Notification and Federal Employee Antidiscrimination and Retaliation (NoFEAR) Act data collected and shared by the Office of Equity, Diversity, and Inclusion (EDI).[231] To address racism in the NIH workplace, NIH will publicly identify and correct any NIH policies or practices that may have helped to perpetuate structural racism. This includes revisiting and revising NIH manual chapters. Additionally, input was sought from the public and stakeholder organizations though a Request for Information that was issued on March 1, 2021 and remained open through April 23, 2021.[232] Other opportunities to gather feedback from both the extramural community and the internal NIH workforce through listening sessions, focus groups, and town halls are in development. NIH will also ensure that each of its 27 ICs appoint a diversity, equity, and inclusion officer who will have direct access to the institute or center director, and who, among other things, will track the institute or center's diversity and inclusion efforts.

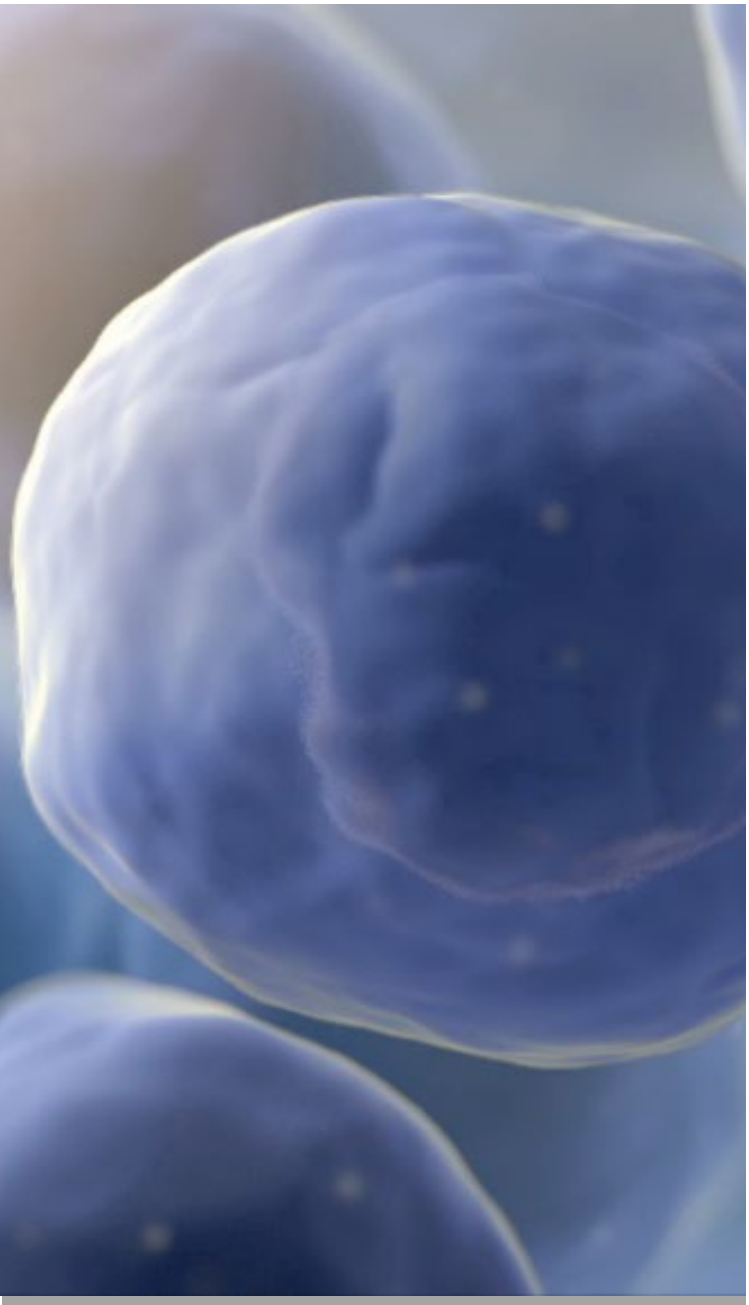
NIH-wide Collaboration

UNITE is spearheaded by the Immediate Office of the Director and co-chaired by the Acting Chief Officer for Scientific Workforce Diversity, the Deputy Director for Management, and the Principal Deputy Director. The five interrelated, but distinct, workstreams of UNITE have nearly 80 members from across the NIH workforce with representation from each of NIH's 27 ICs as well as the OD. Members of UNITE were nominated by NIH ICO Leadership. UNITE works in collaboration with a number of NIH key stakeholders including EDI, SWD, the Office of Human Resources (OHR), OHR/Civil Program, the Office of Communications and Public Liaison, DPCPSI, and others. The UNITE Initiative reports to the NIH Steering Committee and reports its findings and activities to the NIH ACD.

Next Steps/Goals

This is just the beginning of a multifaceted effort to achieve racial equity across the biomedical enterprise. These efforts to improve recruitment and retention of scientists from underrepresented groups; address funding disparities; ensure transparency of race-based demographic data; increase research for minority health, health disparities, and health equity; and address racism in the NIH workplace will take time but will propel NIH's work in biomedical research and discovery. The NIH mission is "to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability." Ensuring that this fundamental knowledge includes diverse perspectives, backgrounds, and skillsets to address complex research questions not only enhances innovation and scientific productivity but is also key to enhancing the health of our nation.

[231] edi.nih.gov/no-fear-act
[232] grants.nih.gov/grants/guide/notice-files/NOT-OD-21-066.html



NIH Common Fund

CONGRESSIONAL JUSTIFICATION

FY 2022

Department of Health and Human Services

National Institutes of Health

NIH National Institutes of Health
Office of Strategic Coordination - The Common Fund

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NIH Common Fund

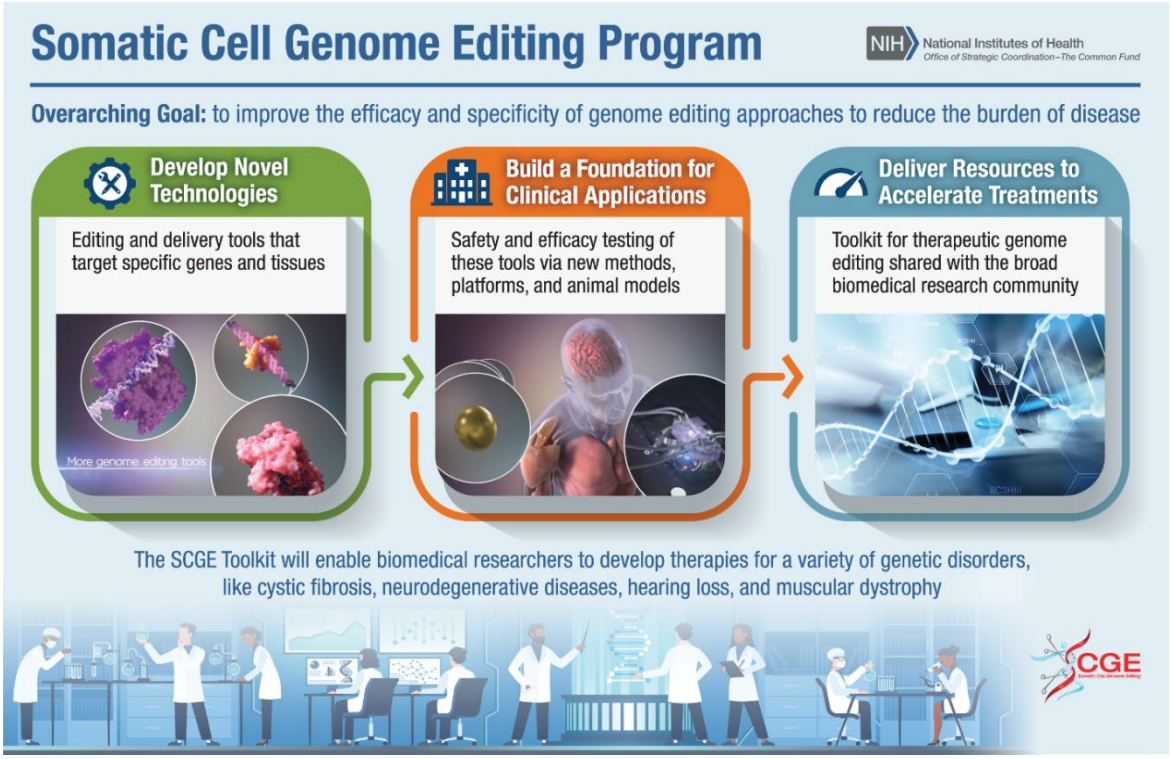
FY 2022 Budget Table of Contents Page No.

Director's Overview

Elizabeth Wilder, Ph.D., Director, Office of Strategic Coordination

The National Institutes of Health (NIH) Common Fund (CF) is a unique and exciting component of the NIH, specifically designed to address challenges and opportunities that are of high priority for the NIH as a whole. We support research in areas of emerging scientific opportunities, public health challenges, and knowledge gaps that deserve special emphasis; would benefit from strategic coordination and planning across NIH Institutes and Centers (IC); and are designed to achieve specific, high-impact goals and milestones within a 5-10 year timeframe.[233] These bold scientific programs often accelerate emerging science, enhance the biomedical research workforce, remove research roadblocks, or support high-risk, high-reward science in ways that no other entity is likely or able to do. Many CF programs are designed to produce specific deliverables, such as data sets, tools, technologies, or fundamental scientific paradigms. We intend for these deliverables to spur subsequent scientific advances that would not be possible without our strategic investment.

Often, CF programs assemble consortia of multidisciplinary, innovative researchers who collaborate to tackle a shared, ambitious goal. For example, researchers from the Somatic Cell



[233] commonfund.nih.gov/

Genome Editing[234] (SCGE) program (pictured above) are working together to improve the efficacy and specificity of gene editing approaches to help reduce the burden of diseases caused by genetic mutation. One initiative is developing improved human gene editing tools and targeted delivery systems to precisely transport editors to the correct cells and tissues. A complimentary initiative is developing new methods for assessing safety and efficacy, and applying these methods to test the novel tools and delivery systems developed in the first initiative. The tools, technologies, data, methods, and best practices developed through the program will make up the SCGE Toolkit, which will be broadly disseminated to the biomedical research community by another initiative focused on dissemination and coordination.

CF programs provide a venue for NIH to respond to critical needs and scientific opportunities using a trans-agency approach, complementing IC-specific programs and activities. CF programs play an important role in addressing NIH priority areas, including answering the call of urgent public health needs, diversifying the workforce, and capitalizing on foundational investments.

Answering the call of urgent public health needs

One of the purposes of the CF is to respond to public health challenges through interdisciplinary approaches that complement research supported by ICs. Since the inception of the CF, we have supported programs that address complex public health challenges, such as the need to engage health care systems in research that determines the best way to treat patients in real world settings, or the need to determine which patients are likely to suffer from chronic pain following surgery and may therefore be at higher risk for opioid use disorder.

The recent emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus and the disease it causes, coronavirus disease 2019 (COVID-19), have required an unprecedented scientific response to address this global pandemic. With $30 million provided by the Coronavirus Aid, Relief, and Economic Security (CARES) Act, 2020,[235] we are supporting research to prevent, prepare for, and respond to coronavirus, domestically or internationally. In FY 2020, we supported emergency competitive revisions to existing CF grants and cooperative agreements to conduct innovative research on COVID-19 and coronavirus. Projects funded through these supplements include research on host and viral genes influencing infection severity, generation of genetically diverse mouse models susceptible to SARS-CoV-2, rapid screening for neutralizing antibodies, and understanding causes of disparities in COVID-19 severity across socioeconomic groups.

We also issued new FY 2021 Funding Opportunity Announcements for the Transformative Research[236] and Early Independence Awards[237] to bring new, innovative perspectives to COVID-19 and coronavirus research. These awards, part of the High-Risk, High-Reward program, support highly innovative research that is expected to have exceptional impact. Any

[234] commonfund.nih.gov/editing
[235] www.congress.gov/116/plaws/publ136/PLAW-116publ136.pdf
[236] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-020.html
[237] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-021.html

relevant area of SARS-CoV-2 research is welcome, including behavioral/social science research, research on health disparities, novel therapeutics, and other related topics.

Diversifying the workforce and closing the gap in health disparities

The NIH has a long-standing interest in supporting a diverse scientific workforce that fosters contributions from creative and talented individuals from all backgrounds. Within the CF, we support several efforts designed to test new approaches for attracting and retaining biomedical researchers from groups underrepresented in the workforce, rigorously evaluate these approaches to determine their effectiveness in different contexts, and disseminate information about proven approaches so that institutions everywhere can implement strategies that are known to be effective.

The Enhancing the Diversity of the NIH-Funded Workforce program, also known as the Diversity Program Consortium (DPC),[238] is developing, implementing, assessing, and disseminating innovative and effective approaches to engaging, training, and mentoring students; enhancing faculty development; and strengthening institutional research training infrastructure to enhance the participation and persistence of individuals from underrepresented backgrounds in biomedical research careers. The DPC is comprised of several integrated initiatives: awards to undergraduate institutions to develop and implement approaches to engage, retain, and prepare students from diverse backgrounds in biomedical research; a national mentoring network; a coordination and evaluation center; support for Offices of Sponsored Programs at educational institutions; and awards to use DPC experimental methods to study the effectiveness of a training, mentoring, or capacity building intervention.

The Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program[239] aims to address the persistent challenge of achieving meaningful levels of diversity at the faculty level by targeting institutional culture change. The FIRST program aims to create cultures of inclusive excellence at NIH-funded institutions, establishing and maintaining scientific environments that can cultivate and benefit from a full range of talent. This program is examining whether recruitment of a critical mass of investigators committed to diversity and inclusion will foster the institutional changes needed to create sustainable improvements in faculty diversity. FIRST supports a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts.

While NIH has long supported programs to improve the diversity of the scientific workforce, those efforts have not been sufficient to achieve racial equity across the biomedical research enterprise. Through a new initiative called UNITE[240], NIH has begun to identify short-term and long-term actions to end structural racism and racial inequities throughout the biomedical research enterprise. Part of ending racial inequities in biomedical research will be to ensure NIH-supported research benefits the health of all populations, especially those whose health is

[238] commonfund.nih.gov/diversity
[239] commonfund.nih.gov/first
[240] www.nih.gov/ending-structural-racism

negatively impacted by racism. For this reason, conducting new research into health disparities, minority health, and health inequities is an important goal of UNITE.

As part of UNITE, the Common Fund and UNITE team members are developing new initiatives to bolster innovation, solve challenges, and address emergent opportunities in health disparities research. In FY 2021, the Common Fund launched the Transformative Research to Address Health Disparities and Advance Health Equity initiative. This initiative supports innovative projects in developing, disseminating, or implementing effective interventions that prevent, reduce, or eliminate health disparities and health inequities, and also expands the research base dedicated to health disparities research at minority serving institutions.

Capitalizing on foundational investments

Science often advances by building upon previous discoveries, leveraging prior investments to propel research forward. CF programs are designed to be catalytic, either capitalizing on emerging scientific opportunities or removing research roadblocks to accelerate progress across a wide range of biomedical research fields. Many CF programs produce resources, such as data sets, tools, technologies, or methods, that are designed to spur subsequent biomedical advances. Additionally, CF programs often aim to establish new paradigms in biology, generating foundational knowledge to support new and emerging fields. Therefore, CF programs often represent foundational investments in biomedical research that are expected to have extraordinarily high impact.

Examples of foundational CF programs include:

- Human BioMolecular Atlas Program (HuBMAP) – HuBMAP is developing a framework for mapping the human body at cellular resolution as a basis for understanding human health and diagnosing, monitoring, and treating disease. This will be achieved through a globally coordinated effort to develop new technologies; generate foundational tissue maps; and make data findable, accessible, interoperable, and reusable.
- Molecular Transducers of Physical Activity in Humans – This program aims to uncover the molecules that underlie the health benefits of physical activity across many tissues/organs, and where possible, to associate these molecules with individual differences in response to exercise. This "molecular map" is anticipated to catalyze the development of therapeutic strategies that mimic components of the physical activity response and inform development of more specific exercise recommendations. Additional funding in FYs 2018 and 2019 enabled a more detailed analysis of human tissues after exercise, pilot analyses of how exercise may affect the microbiome, and analyses of how the microbiome may influence the health benefits of exercise.
- Extracellular RNA Communication (ERC) – The ERC program aims to generate new paradigms for cell-to-cell communication through the analysis of extracellular RNAs. Once thought to exist only inside cells, the evolving understanding that RNA is exported from cells hints at previously unknown processes through which cells in one tissue influence cells in another tissue to maintain or disrupt health. These extracellular RNAs may also provide new diagnostic or therapeutic strategies. Resources developed through the ERC program are catalyzing this emerging field of research.

We make significant efforts to evaluate programs during their lifetime and assess outcomes as programs end. Continuous evaluation during program implementation allows flexibility to modify program management and/or budgets in response to rapidly evolving scientific landscapes, technical challenges, or other unforeseen challenges or opportunities. New challenges and opportunities will be supported in FY 2022 from funds made available as other programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Overall Budget Policy. The FY 2022 President's Budget request for the CF is $658.5 million, an increase of $10.0 million from the FY 2021 Enacted level. This level of funding will support high-priority activities within existing programs and support the launch of the Nutrition for Precision Health, powered by the *All of Us* Research Program. This new program will develop algorithms to predict individual responses to diet through partnership with the *All of Us* program. Additionally, a program to explore somatic mosaicism in various human tissues is being considered for launch in FY 2022, as explained later in this narrative.

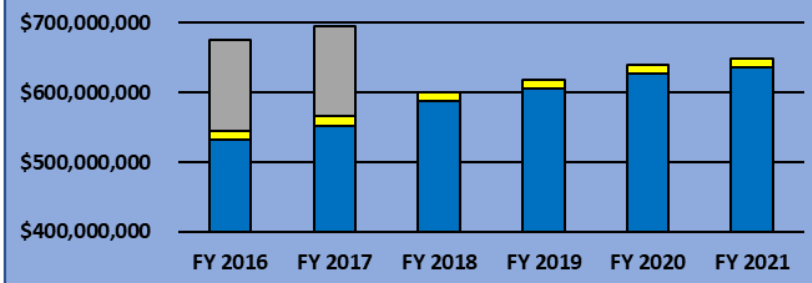
National Institutes of Health
Office of Strategic Coordination - The Common Fund

About the NIH Common Fund

The NIH Common Fund provides a dedicated source of support for trans-NIH scientific programs with the potential for extraordinary impact. Common Fund programs are time-limited, goal-driven investments that accelerate emerging science, remove research roadblocks, enhance the biomedical workforce, and/or support high-risk, high-reward science. These programs often involve multi-disciplinary, innovative researchers who work together to tackle a shared, ambitious goal. Common Fund programs span the NIH mission, addressing scientific opportunities and research challenges in some of the most cutting-edge areas of biomedical research, including genome editing, pain biomarkers, undiagnosed and rare diseases, data science, and bioelectronic medicine.

Elizabeth Wilder, Ph.D., has been the Director of the Office of Strategic Coordination since 2010. She received a Ph.D. in Molecular/Cellular Biology from Northwestern University and was a faculty member at the University of Pennsylvania School of Medicine before joining the NIH in 2002.

Common Fund Appropriations History



The FY 2022 President's Budget request is $658.5 million

Blue indicates Common Fund base appropriation; yellow indicates the Pediatric Research Initiative Fund; gray indicates the Precision Medicine Initiative (moved out of the Common Fund to the Office of the Director in FY 2018).

Common Fund Research Accomplishments

- The Genotype-Tissue Expression (GTEx) program is revolutionizing our understanding of how genes are expressed in different tissues in the body, how they are regulated, and how variations in gene expression result in a wide range of human diseases.
- The Undiagnosed Diseases Program (UDP) is establishing a new model for meeting the pressing need for diagnosis of rare diseases. In the first 20 months of operation, UDP accepted over 600 patients, provided a diagnosis in 35 percent of patients evaluated, and discovered 31 new syndromes.
- The Regenerative Medicine Program supported research leading to the first United States phase I/IIa clinical trial to test the safety of a novel stem cell therapy to treat age-related macular degeneration.
- The Knockout Mouse Phenotyping Program (KOMP2) systematically described genes with previously unknown function, providing information on hearing, embryonic development, metabolism, aging, and more.

Facts and Figures

- 21 Scientific Programs in FY 2020
- 561 Principal Investigators (PI)*
  - 175 High-Risk, High Reward awardees*
  - 104 early career High-Risk, High-Reward awardees*
- 139 competing Research Project Grants*
- In the past 10 years, Common Fund-supported researchers have published over 28,000 papers
- In FY 2020, Common Fund supported research in 38 states and 7 countries.

*Data represent yearly averages from FY 2016 – FY 2020

National Institutes of Health
Office of Strategic Coordination - The Common Fund

Current Activities

The Common Fund supports scientific programs that span the mission of the entire NIH. Examples of exciting ongoing activities include:

- **Somatic Cell Genome Editing** – working to improve the efficacy and specificity of gene editing approaches to help reduce the burden of common and rare diseases caused by genetic mutations.
- **Transformative Research to Address Health Disparities and Advance Health Equity** – developing, disseminating, and implementing innovative and effective interventions to prevent, reduce, or eliminate health disparities and health inequities.
- **Stimulating Peripheral Activity to Relieve Conditions** – accelerating the development of novel therapeutic devices that modulate nerve function by providing foundational data and tools

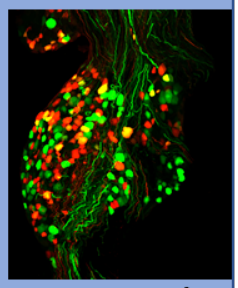


Image from the SPARC program shows sensory (vagal) neurons in a mouse

Future Initiatives

As Common Fund programs end, funds are freed to invest in new challenges and opportunities. One potential program is undergoing planning activities and may be implemented in FY 2022:

- **Somatic Mosaicism Across Human Tissues** - to investigate the causes and effects of genetically distinct cells within a single individual (mosaicism)

Image Credit: Darryl Leja, NHGRI

High-Risk, High-Reward Research Program

Science often advances step-by-step, with each new discovery adding a modest, yet important, piece in a complex biological puzzle. However, rapid scientific advancement also requires research that is innovative and flexible, allowing researchers to follow their ideas into novel territory. NIH provides dedicated support for this type of "high-risk, high-reward" research. The Common Fund's High-Risk, High-Reward (HRHR) Research program supports exceptionally creative scientists pursuing highly innovative and impactful research on any topic within the NIH mission. HRHR awardees are developing breakthrough technologies and making paradigm-shifting discoveries. For example, HRHR awardees are exploring how blood platelets could be engineered to fight cancer, whether a gut-brain connection may play a role in autism spectrum disorder, and what maps of all the neural networks involved in memory look like. In FY 2021, the Common Fund launched a new Transformative Research to Address Health Disparities and Advance Health Equity initiative to support research in developing, disseminating, or implementing innovative and effective interventions that prevent, reduce, or eliminate health disparities and inequities.

NIH DIRECTOR'S PIONEER AWARD

NIH DIRECTOR'S TRANSFORMATIVE RESEARCH AWARD

NIH DIRECTOR'S NEW INNOVATOR AWARD

NIH DIRECTOR'S EARLY INDEPENDENCE AWARD

MAJOR CHANGES IN THE PRESIDENT'S BUDGET REQUEST

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note there may be overlap between budget mechanisms and activity detail, and these highlights will not sum to the total change for the FY 2022 President's Budget Request for the Common Fund, which is $10.0 million more than the FY 2021 Enacted level, for a total of $658.5 million.

Research Project Grants (-$19.4 million; total $350.1 million): The Common Fund expects to support a total of 379 Research Project Grant (RPG) awards in FY 2022, down from 393 in FY 2021. Estimated awards for FY 2022 include 277 Noncompeting RPGs and 102 Competing RPGs. The decrease in RPGs reflect the planned ramping down of several programs. Additionally, a change in the funding approach for the NIH Director's New Innovator awards results in a temporary decline in funding levels while maintaining a similar number of New Innovator awards. Prior to FY 2021, New Innovator awards provided all five years of funding in the first fiscal year of the research project. However, to enhance financial stewardship, starting in FY 2021, New Innovator awards now provide support for years one to three of the project in the first fiscal year, and then provide support for years four and five in the fourth fiscal year.

Research Centers (+$31.9 million; total $88.2 million): The estimated increase in support for Research Centers is due to planned ramping up or launch of programs that include specialized/comprehensive centers, including Bridges to Artificial Intelligence (Bridge2AI), Cellular Senescence Network (SenNet), Faculty Institutional Recruitment for Sustainable Transformation (FIRST), Human BioMolecular Atlas Program (HuBMAP), and Nutrition for Precision Health (NPH) programs.

BUDGET MECHANISM

(Dollars in Thousands)	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021 Enacted	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	258	$197,806	262	$222,728	277	$233,054	15	$10,326
Administrative Supplements	*(34)*	5,265	*(40)*	6,164	*(53)*	8,273	*(13)*	2,109
Competing:								
Renewal	0	0	0	0	0	0	0	0
New	137	146,739	131	140,582	102	108,763	-29	-31,819
Supplements	0	0	0	0	0	0	0	0
Subtotal, Competing	137	$146,739	131	$140,582	102	$108,763	-29	-$31,819
Subtotal, RPGs	395	$349,810	393	$369,474	379	$350,090	-14	-$19,384
SBIR/STTR	0	0	0	0	0	0	0	0
Research Project Grants	395	$349,810	393	$369,474	379	$350,090	-14	-$19,384
Research Centers:								
Specialized/Comprehensive	26	$28,435	35	$38,286	65	$71,449	30	$33,163
Clinical Research	10	18,343	7	12,046	6	10,762	-1	-1,284
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	4	4,320	6	5,996	6	5,997	0	1
Research Centers in Minority Institutions	0	0	0	0	0	0	0	0
Research Centers	40	$51,097	48	$56,328	77	$88,208	29	$31,880
Other Research:								
Research Careers	0	$0	0	$0	0	$0	0	$0
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	0	0	0	0	0	0	0	0
Biomedical Research Support	0	0	0	0	0	0	0	0
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	114	195,084	105	179,354	105	178,853	0	-501
Other Research	114	$195,084	105	$179,354	105	$178,853	0	-$501
Total Research Grants	549	$595,991	546	$605,156	561	$617,151	15	$11,995
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	0	$0	0	$0
Institutional Awards	430	10,268	526	12,758	439	10,631	-87	-2,127
Total Research Training	430	$10,268	526	$12,758	439	$10,631	-87	-$2,127
Research & Develop. Contracts		$577	0	$0	0	$0	0	$0
(SBIR/STTR) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Intramural Research	0	13,703	0	7,439	0	7,460	0	21
Res. Management & Support	0	18,572	0	23,186	0	23,297	0	111
Res. Management & Support (SBIR Admin) (non-add)	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*	*(0)*
Construction		0		0		0		0
Buildings and Facilities		0		0		0		0
Total, Common Fund	549	$639,111	546	$648,539	561	$658,539	15	$10,000

[1] All items in italics and brackets are non-add entries.

BUDGET BY PROGRAM

Common Fund Program	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget
4D Nucleome	28,614	28,394	28,378
Acute to Chronic Pain Signatures	16,636	15,132	6,432
Bridge to Artificial Intelligence (Bridge2AI)	0	0	32,000
Cellular Senescence Network (SenNET)	0	25,000	40,350
Enhancing the Diversity of the NIH-Funded Workforce	53,682	48,968	44,222
Extracellular RNA Communication	6,753	11,845	10,841
Faculty Institutional Recruitment for Sustainable Transformation (FIRST)	0	4,000	27,217
Gabriella Miller Kids First Pediatric Research	12,984	13,000	13,063
Global Health	11,376	9,567	0
Glycoscience	13,349	5,358	0
Harnessing Data Science for Health Discovery and Innovation in Africa (DSI-Africa)	525	12,493	12,455
Health Care Systems Research Collaboratory	1,750	1,750	225
High-Risk Research	196,948	197,140	173,830
NIH Director's Pioneer Award	*51,701*	*50,520*	*51,333*
NIH Director's New Innovator Award Program	*83,719*	*62,437*	*51,450*
Transformative Research Award	*38,249*	*38,664*	*40,248*
NIH Director's Early Independence Award Program	*23,280*	*21,519*	*20,799*
Transformative Health Disparities Research	*0*	*24,000*	*10,000*
Human BioMolecular Atlas Project (HuBMAP)	27,021	28,661	44,676
Illuminating the Druggable Genome	13,369	14,763	13,390
Knockout Mouse Phenotyping Program	10,981	429	0
Library of Integrated Network-Based Cellular Signatures (LINCS)	82	0	0
Metabolomics	12,397	12,397	106
Molecular Transducers of Physical Activity	46,089	44,007	40,493
Nutrition for Precision Health	0	0	22,549
NIH Center for Regenerative Medicine (NCRM)	5,736	0	0
Science of Behavior Change	168	0	0
Somatic Cell Genome Editing	34,449	45,695	50,433
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	45,000	42,623	25,000
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	51,769	37,490	19,890
Undiagnosed Diseases Network	24,389	22,400	16,400
Strategic Planning, Evaluation, and Infrastructure	25,043	27,428	25,386
Subtotal Common Fund	639,111	648,539	647,336
New Initiatives in Common Fund	0	0	11,203
Total Common Fund	639,111	648,539	658,539

JUSTIFICATION OF BUDGET REQUEST

NIH Common Fund

Authorizing Legislation: Section 301 and title IV of the Public Health Service Act, as amended.

Budget Authority (BA):

	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
BA	$639,111,000	648,539,000	658,539,000	$10,000,000
FTE	0	0	0	0

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

PROGRAM DESCRIPTIONS

The CF supports over 20 programs, most of which consist of a series of integrated initiatives that collectively address a set of goals aiming to transform the way research is conducted, the way that health and disease are understood, and/or the way that diseases are diagnosed or treated – within five to ten years. Planned activities and budgets for Common Fund programs are strategically developed, with clear milestones defined throughout the lifetime of the program to enable measurement of progress towards pre-defined goals. Therefore, Common Fund programs often undergo planned budget shifts driven by the needs and activities for each program.

Two CF programs will receive their last year of support in FY 2021; funds are therefore not requested in FY 2022. These are Glycoscience[241] and Global Health.[242] Information on these programs and their accomplishments can be found on the program websites.

Highlighted below are programs that exemplify the science to be supported in FY 2022.

Acute to Chronic Pain Signatures (A2CPS)

As part of the NIH response to the growing opioid crisis, the A2CPS[243] program aims to further understanding of the transition from acute to chronic pain. Acute pain following injury resolves

[241] commonfund.nih.gov/Glycoscience
[242] commonfund.nih.gov/globalhealth
[243] commonfund.nih.gov/pain

in many patients, but the pain can become chronic for a large number of people, even after the injury itself has healed. This transition is poorly understood and therefore prevention or treatment is difficult. A2CPS is addressing this challenge by developing an objective set of biomarkers (a "signature") to predict susceptibility of transitioning from acute to chronic pain. The A2CPS program enhances the objectives of the NIH Helping to End Addiction Long-term℠ (HEAL) Initiative, a trans-agency effort to speed scientific solutions to end the opioid public health crisis. A2CPS will benefit the HEAL research priority to enhance pain management. The decrease in funds requested for FY 2022 is driven by planned ramping down of clinical studies collecting data from patients following an acute pain event.

Budget Policy. The FY 2022 President's Budget request is $6.4 million, a decrease of $8.7 million or 57.5 percent compared to the FY 2021 Enacted level. This decrease reflects the planned ramping down of clinical studies and will support data generation, analysis, and integration.

Bridge to Artificial Intelligence (Bridge2AI)

Rapid advancements in artificial intelligence and machine learning hold great promise for biomedical research. Many NIH ICs are investing in these promising technologies, and the NIH is dedicating significant effort to developing strategic and cross-agency activities to accelerate the use of artificial intelligence in biomedical research, clinical research, and medicine. Based on recommendations from the NIH's Advisory Committee to the Director on how to capitalize on recent advances in artificial intelligence technologies, the Bridge2AI program is fostering the use of artificial intelligence strategies for biomedical and behavioral research through the generation of new biomedically relevant data sets amenable to machine learning analysis at scale. FY 2022 funds will be used to launch activities aiming to generate rubrics to measure amenability of data sets to machine learning approaches, develop tools to accelerate AI-readiness, enhance existing data generation efforts to improve AI-readiness, generate gold-standard data sets that adhere to these rubrics, and use the rubrics to evaluate and update select existing public biomedical research data.

Cellular Senescence Network (SenNET)

As we age, tissues throughout the body accumulate small numbers of specialized cells that no longer divide, called senescent cells. Under some conditions, senescent cells may accumulate and release molecules that can cause damage to nearby tissue, while in other conditions, senescent cells can protect health by preventing tumor growth or promoting the growth of new tissues. There are many unanswered questions about how, when, why, and where senescent cells form, but their rarity and diversity make them difficult to study. The SenNet program aims to comprehensively identify and characterize the differences in senescent cells across the body, across various states of human health, and across the lifespan. SenNet will provide publicly accessible atlases of senescent cells, the differences among them, and the molecules they secrete, using data collected from multiple human and model organism tissues. To identify and characterize these rare cells, SenNet will develop innovative tools and technologies that build upon previous advances in single cell analysis, such as those from the Common Fund's Human Biomolecular Atlas Program[244] and Single Cell Analysis Program.[245] Lastly, SenNet aims to unite cellular senescence researchers by developing common terms and classifications for senescent cells.

[244] commonfund.nih.gov/HuBMAP
[245] commonfund.nih.gov/Singlecell

Budget Policy. The FY 2022 President's Budget request is $40.4 million, an increase of $15.4 million or 61.4 percent from the FY 2021 Enacted level. The increase in funding will support ramping up of the tissue mapping centers, as well as technology development and application projects, and a consortium organization and data coordination center.

Harnessing Data Science for Health Discovery and Innovation in Africa (DS-I Africa)

The DS-I Africa program will leverage data science technologies and prior NIH investments to develop solutions to Africa's most pressing public health problems through a robust ecosystem of new partners from academic, government, and private sectors. Despite recent progress, Africa carries a disproportionate share of the global burden of disease. However, extensive mobile phone coverage in Africa has led to major innovations that could bring the clinic to the patient through data science technologies. This could have applications to rural and underserved populations in the United States and worldwide. Additionally, substantial investment in African research and research training by NIH ICs, the Common Fund, and other organizations has provided resources and expertise that can be leveraged to impact health in Africa and around the world. This program aims to promote sustainability of the African health research enterprise by encouraging these innovative partnerships, and will also consider ethical, legal, and social issues (ELSI) for data science research and its applications to public health in Africa. Funds requested in FY 2022 will support industry partnerships for innovation, training programs, an open data science platform and coordinating center, oversight and coordination activities, and ELSI research.

Faculty Institutional Recruitment for Sustained Transformation (FIRST)

As the nation's population grows increasingly diverse, there is an urgent need to ensure that scientific talent is nurtured, recognized, and supported in researchers from diverse backgrounds. The FIRST program aims to establish a more inclusive and diverse biomedical research workforce through support of faculty cluster hiring and institutional culture change efforts. Based on early results from other cohort-based hiring programs, FIRST will explore whether hiring a critical mass of faculty committed to diversity and scientific excellence will promote institutional culture changes necessary to foster inclusive environments that create meaningful improvements in researcher diversity. FIRST will support a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts. Funds requested in FY 2022 will be used to support hiring of the first round of faculty cohorts and ramping up of the coordination and evaluation center.

Budget Policy. The FY 2022 President's Budget request is $27.2 million, an increase of $23.2 million or 580.4 percent over the FY 2021 Enacted level. This increase in support will be used to hire the first round of faculty cohorts and ramp up coordination and evaluation activities.

Gabriella Miller Kids First Pediatric Research Program (Kids First)

The Kids First[246] program aims to generate new insights into childhood cancer and birth defects through development of a widely accessible data resource containing high-quality genetic and clinical data from pediatric patient cohorts, along with associated computational tools to facilitate data analysis. There is considerable evidence for undiscovered connections between childhood cancer and structural birth defects, and therefore examining these data sets together will facilitate new discoveries and novel ways of thinking about these conditions. Funds requested in FY 2022 will be used to support pediatric research, consistent with the Gabriella Miller Kids First Research Act, and remain constant at the statutory level set by this legislation. A small amount to support program management activities is requested from the general Common Fund appropriation. In FY 2022, the Kids First program will launch a second stage, building on the successes within the program thus far to strengthen the value of the Kids First Data Resource and sustain the resource after Common Fund support. During stage 2, Kids First will continue to generate data, develop new initiatives to identify underlying mechanisms of these pediatric conditions, and strengthen Kids First's ability to work with other data resources.

Budget Policy. The FY 2022 President's Budget request is $13.1 million, an increase of $0.1 million, or 0.5 percent from the FY 2021 Enacted level. Programmatic funding remains constant at the $12.6 million statutory level and will be used to conduct pediatric research in the second stage of this program. The remainder of the funds are requested in the regular CF appropriation to support research management activities.

High-Risk, High-Reward (HRHR) Research Program

The HRHR[247] program supports exceptionally creative scientists proposing innovative and transformative research in any scientific area within the NIH mission through complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award. These awards are intended to support transformative science that is inherently difficult and may appear risky because preliminary data are not required, but is necessary to accelerate the pace of scientific discovery and advance human health. For all HRHR awards, "high risk" does not imply that additional risk is posed to research participants, as these awards use the same rigorous procedures to protect research participant safety as all other NIH-funded studies involving human subjects. Although the majority of HRHR funds are dedicated to innovative ideas on biomedical research topics proposed by the investigator, funds in FY 2021 were used to address to specific areas of pressing public health need: 1) COVID-19-related funding opportunities within the Transformative Research and Early Independence Awards,[248, 249] supported via the Coronavirus Aid, Relief, and Economic Security (CARES) Act, 2020, and 2) Accelerating Leading-edge Science in ALS (ALS^2) within the Transformative Research Awards.[250] Funds requested in FY 2022 will be used to support additional innovative, high priority projects with the potential for extraordinary impact.

[246] commonfund.nih.gov/KidsFirst
[247] commonfund.nih.gov/highrisk
[248] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-020.html
[249] grants.nih.gov/grants/guide/rfa-files/RFA-RM-20-021.html
[250] grants.nih.gov/grants/guide/notice-files/NOT-RM-20-019.html

Additionally, in FY 2021, the Common Fund launched a new Transformative Research to Address Health Disparities and Advance Health Equity initiative[251] to support research in developing, disseminating, or implementing innovative and effective interventions that prevent, reduce, or eliminate health disparities and health inequities. This initiative also aims to expand the capacity for health disparities research at minority serving institutions. This effort is part of NIH's UNITE[252] initiative, which is identifying short- and long-term actions to end structural racism and racial inequities throughout the biomedical research enterprise. Conducting new research into health disparities, minority health, and health inequities is an important goal of UNITE, and this Common Fund initiative is one component of the NIH-wide strategy to achieve this goal. Awards for this initiative were issued in FY 2021, using multiyear funding to provide support for the first two years of the awards and annual funding to support years three through five. An additional round of awards to support health disparities research at minority serving institutions will be funded in FY 2022.

Budget Policy. The FY 2022 President's Budget request is $173.8 million, a decrease of $23.3 million or 11.8 percent from the FY2021 Enacted level. The reduction in support reflects a change in funding approach for the NIH Director's New Innovator awards and does not reflect a decrease in the anticipated number of awards provided. To improve financial stewardship, starting in FY 2021, the New Innovator awards provide support for years one through three of the project in the first fiscal year, and then provide support for years four and five in the fourth fiscal year. Prior to FY 2021, New Innovator awards provided all five years of funding in the first fiscal year; thus, this change in funding approach results in a temporary decline in funding levels while maintaining similar numbers of expected awards.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP[253] is developing a framework for mapping the human body at single cell resolution to provide a new foundation for understanding human health and diagnosing, monitoring, and treating disease. Since the cell is the fundamental unit of the human body, an understanding of normal and disease processes at this level is anticipated to lead to more specific and effective therapies, and lead to new insights into human health, growth, development, and aging. In recent years, technologies that enable the analysis of single cells within the context of tissues have made mapping the human body at the level of single cells feasible. However, this is an enormous challenge, given that there are approximately 37 trillion cells in the body. HuBMAP will address this challenge through a globally coordinated effort to develop an open and global platform to map healthy cells in the human body, generate foundational tissue maps, and develop tools, technologies, and resources for broad dissemination to the entire biomedical research community. Increased funds requested in FY 2022 will support additional efforts in tissue mapping, technology development, and data coordination, integration, and analysis.

[251] commonfund.nih.gov/healthdisparitiestransformation
[252] www.nih.gov/ending-structural-racism
[253] commonfund.nih.gov/HuBMAP

Budget Policy. The FY 2022 President's Budget request is $44.7 million, an increase of $16.0 million or 55.9 percent from the FY 2021 Enacted level. This increased level of funding will support the additional efforts described above.

Illuminating the Druggable Genome (IDG)

Most drugs target proteins within four families – G-protein coupled receptors, nuclear receptors, ion channels, and protein kinases. However, only a small number of proteins within each of these families are well-studied, and these are typically proteins that are present in many cells throughout the body. Therefore, drugs that target these proteins may cause widespread adverse effects in cells and tissues that are not affected by disease. In contrast, the lesser known members of these protein families may be present in fewer tissues, and thus have potential as specific drug targets leading to fewer side effects. IDG, originally launched as a pilot in FY 2014, initially aimed to compile data about the uncharacterized proteins within the four protein classes that are most frequently targeted by drugs. An integral part of this effort was the development of publicly available resources integrating information about understudied proteins so that researchers everywhere can leverage this information to catalyze their own research. In the second, or implementation, stage, IDG is capitalizing on the information gathered and technologies developed in the pilot to further elucidate the function of uncharacterized proteins within three of the families that are least characterized – G-protein-coupled receptors, ion channels, and protein kinases. IDG is also expanding the informatics tools developed in the pilot stage and disseminating the IDG-generated resources to the biomedical research community. Funds requested in FY 2022 will continue these efforts.

Budget Policy. The FY 2022 President's Budget request is $13.4 million, a decrease of $1.4 million or 9.3 percent from the FY 2021 Enacted level. IDG will continue efforts initiated in the implementation stage, providing information, tools, and resources to the broad biomedical research community on uncharacterized proteins within three protein families of interest for drug development.

Molecular Transducers of Physical Activity

Physical activity has been demonstrated to contribute to health via a wide variety of measures, and lack of physical activity is at the root of many common chronic health problems. Despite this, researchers have a poor understanding of the molecular mechanisms by which the benefits of physical activity are realized. A better understanding of the molecules that underlie the benefits of physical activity could lead to the development of improved, personalized exercise recommendations as well as therapies for individuals who are unable to exercise due to illness or disability. The Molecular Transducers of Physical Activity Consortium (MoTrPAC) will improve understanding of the molecular mechanisms by which physical activity improves health by extensively cataloguing the biological molecules affected by physical activity in people and in animals, identifying some of the key molecules that underlie the systemic effects of physical activity, and characterizing the function of these key molecules. Support requested in FY 2022 will continue to support clinical and animal studies, analysis of biological samples, and coordination and data management.

Budget Policy. The FY 2022 President's Budget request is $40.5 million, a decrease of $3.5 million or 8.0 percent from the FY 2021 Enacted level. This funding level will continue to support data collection, analysis, and coordination.

Nutrition for Precision Health, powered by the *All of Us* Research Program (NPH)

Nutrition plays an integral role in human development and in the prevention and treatment of disease. However, there is no such thing as a perfect, one-size-fits-all diet. The goal of the **NPH program**[254] is to develop algorithms that predict individual responses to food and dietary patterns. The NPH program will build on recent advances in biomedical science, including artificial intelligence (AI) and microbiome research, as well as the infrastructure and large, diverse participant group of the *All of Us* Research Program. These advances provide unprecedented opportunities to generate new data to provide insight into personalized, or precision, nutrition. Designed to implement aspects of the Strategic Plan for NIH Nutrition Research,[255] the NPH program will conduct a study nested in the *All of Us* Research Program to explore how individuals respond to different diets. Ultimately, the predictive algorithms developed through NPH are anticipated to enable tailored dietary recommendations to be provided by physicians, as well as development of tools to allow individuals to make more informed decisions about healthy food choices.

Budget Policy. The FY 2022 President's Budget request is $22.5 million, an increase of $22.5 million from the FY 2021 Enacted level. The first year of funding for this program will support clinical centers; data generation centers; an AI, data modeling, and bioinformatics center; a biobank; data and study coordination; and oversight and coordination.

Stimulating Peripheral Activity to Relieve Conditions (SPARC)

The SPARC[256] program is accelerating the development of novel therapeutic devices that modulate electrical activity in nerves to improve organ function. Foundational data and tools from SPARC are allowing researchers to design more effective and specific devices. Modulation of nerve activity has the potential to treat a variety of diseases and conditions, but there is an urgent need to better understand the precise pattern of connections between nerves and their end organs, so that the nerves can be precisely and specifically stimulated. SPARC is addressing this need by generating maps and tools to identify and influence therapeutic targets within the neural circuitry of a wide range of organs and tissues. Ultimately, this therapeutic strategy could offer new treatment options for diverse diseases and conditions such as hypertension, heart failure, gastrointestinal disorders, type II diabetes, inflammatory disorders, and more. The first stage of the SPARC program ends in FY 2021, and a second stage beginning in FY 2022 plans to engage industry to help catalyze development of next-generation bioelectronic medicines by providing access to therapeutic targets and devices, high-value datasets, and computational science resources.

[254] commonfund.nih.gov/nutritionforprecisionhealth
[255] niddk.nih.gov/about-niddk/strategic-plans-reports/strategic-plan-nih-nutrition-research
[256] commonfund.nih.gov/sparc

Budget Policy. The FY 2022 President's Budget request is $25.0 million, a decrease of $17.6 million or 41.4 percent from the FY 2021 Enacted level. This level of funding will support the second stage of the SPARC program, which will build on the capabilities and resources of the first stage to accelerate bioelectronic medicines.

Transformative High Resolution Cryo-Electron Microscopy (CryoEM)

The CryoEM[257] program is enabling novel discoveries in structural biology by broadening access to cutting-edge cryo-electron microscopy techniques and training. Cryo-electron microscopy enables researchers to determine the structures of a wide range of biological molecules with greater accuracy, which helps identify new therapeutic targets for vaccines and drugs. However, the high cost of cryo-electron microscopes means that access to this technology is out of reach for many scientists. By providing greater access, the CryoEM program is anticipated to catalyze fundamental biological discoveries, as well as accelerate development of vaccines and therapeutics. In FY 2022, there is a planned decrease in support as the centers for cryo-electron microscopy and cryo-electron tomography, a related technology, have completed their purchase of high-end equipment and are focused on processing samples to enable the biomedical research community and accelerate development of drugs and vaccines to combat many diseases and conditions.

Budget Policy. The FY 2022 President's Budget request is $19.9 million, a decrease of $17.6 million or 47.0 percent from the FY 2021 Enacted level. This decrease in funding reflects the completion of high-end equipment purchases and will support processing samples for the biomedical research community.

Undiagnosed Diseases Network (UDN)

The UDN[258] is fostering a nationwide network of clinicians and laboratory scientists to improve diagnosis of rare and undiagnosed diseases. Based on the success of the NIH Clinical Center's Undiagnosed Diseases Program, the UDN expanded this approach to academic health centers across the county, working through challenges associated with implementation in different clinical settings and economic models. UDN promotes the use of state-of-the-art genomic sequencing technologies in disease diagnosis and engages basic researchers to uncover underlying disease mechanisms so that treatments may be identified. In the first 20 months of operation, UDN accepted 601 participants undiagnosed by traditional medical practices. Of those who completed their UDN evaluation during this time, 35 percent were given a diagnosis. Many of these diagnoses were rare genetic diseases, including 31 previously unknown syndromes. Now in its second stage, UDN is focusing on forming a sustainable national resource to diagnose both rare and new diseases, advancing laboratory and clinical research, enhancing global coordination and collaboration among laboratory and clinical researchers, and sharing resulting data and approaches throughout the scientific and clinical communities. As part of the planned effort to build a sustainable, long-term national model for the use of genomic

[257] commonfund.nih.gov/CryoEM
[258] commonfund.nih.gov/Diseases

data in disease diagnosis, the program will begin to transition to other sources of support in FY 2022.

Budget Policy. The FY 2022 President's Budget request is $16.4 million, a decrease of $6.0 million or 26.8 percent from the FY 2021 Enacted level. This decrease in support reflects the planned transition of UDN centers to sustainable sources of support as the program ramps down, thereby enabling a national, long-term approach for diagnosing patients with rare and undiagnosed diseases.

Strategic Planning, Evaluation, and Infrastructure

Management of the Common Fund requires that certain activities be undertaken for the benefit of the Common Fund as a whole. In addition to long-standing investments in strategic planning and evaluation, described below, the Common Fund has more recently expanded investments in infrastructure to address challenges facing programs that are increasingly employing data-intensive strategies to achieve their goals. This infrastructure, referred to as the Common Fund Data Ecosystem (CFDE),[259] is helping to ensure that all Common Fund data sets are Findable, Accessible, Interoperable, and Reusable (FAIR), providing training for users to operate on the data in a cloud environment, and ensuring that Common Fund data continue to be available after individual programs are completed. The CFDE will amplify the impact of many CF programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before. The CFDE is also being designed in parallel with NIH IC data platforms to enable crosstalk between Common Fund and IC data sets and to address NIH-wide data management objectives described in the NIH Strategic Plan for Data Science.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities. CF strategic planning encompasses both the identification of broadly relevant scientific challenges and opportunities for strategic investments (Phase 1 planning), and the articulation of specific goals, milestones, and implementation plans for each broadly defined potential program topic (Phase 2 planning). Phase 1 strategic planning often involves gathering broad input from stakeholders with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. Phase 2 strategic planning involves specific consultations with external experts, analysis of NIH and worldwide research portfolios, and literature reviews to articulate specific gaps and areas of research where opportunities for transformative progress are possible.

Since Common Fund programs are goal-driven, evaluation is critical to monitoring progress and developing strategies to adapt program management. Evaluation includes both formal and informal evaluative activities. Informal evaluation involves convening grantees and NIH-wide teams to review progress, discuss new challenges, and develop strategies to adapt as part of routine program management. It also involves gathering input from external consultants and using their input, together with internal analysis, to help guide the implementation of the program. Formal evaluations involve the development of baseline data for new programs and

[259] commonfund.nih.gov/dataecosystem

the development of multiple metrics of outcomes. The utility of data, resources, technologies, and other program outputs is assessed through surveys, expert opinion, and the analysis of bibliometric data such as citation analyses.

Funds Available for New Initiatives

Planning for potential new FY 2022 programs involved gathering ideas from across the NIH community, leveraging the wide-ranging expertise of the NIH's scientific staff and senior leaders. From this process, two promising ideas emerged. One, the Cellular Senescence Network, was able to be launched on an accelerated timeframe in FY 2021. Another idea, Somatic Mosaicism across Human Tissues (SMaHT) is currently undergoing planning for a potential launch in FY 2022. SMaHT will investigate the causes and effects of genetically distinct cells within a single individual (mosaicism).

Office of AIDS Research

CONGRESSIONAL JUSTIFICATION

FY 2022

Department of Health and Human Services

National Institutes of Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research (OAR)

FY 2022 Budget Table of Contents Page No.

NIH, Office of the Director, Office of AIDS Research (OAR)

Located within the NIH Office of the Director, OAR is authorized to:

- Oversee, coordinate, and manage all NIH HIV-related research;
- Establish research priorities and develop the strategic plan for HIV research;
- Ensure that funds are invested in the areas of highest scientific priority; and
- Address emerging opportunities.

Mission

To ensure that NIH HIV/AIDS research funding is directed at the highest priority research areas and to facilitate maximal return on the investment.

Director's Overview

Maureen M. Goodenow, Ph.D.

Associate Director for AIDS Research and
Director, Office of AIDS Research
National Institutes of Health

NIH investments in HIV and AIDS research over more than three decades have produced groundbreaking advances in understanding the basic virology, immunology, and pathogenesis of HIV. Research discoveries led to the development and implementation of safe, effective antiretroviral treatments to extend the lifespan of people with HIV and innovative interventions to prevent HIV transmission and acquisition. Nonetheless, globally and in the United States, new infections continue at rates that are increasing or remain unchanged, reflecting inequalities by race, ethnicity, sex, gender, age, socioeconomic status, and geography. While the HIV pandemic will continue to affect virtually every nation in the world well into the next century, the NIH will continue to lead the investment in basic, clinical, and translational research to discover cutting-edge solutions for the ongoing challenges of the HIV pandemic.

To provide leadership in setting the national and global HIV research agenda, the NIH Office of AIDS Research (OAR) was established in 1988 through Section 2353 of the Public Health Service Act.

OAR operationalizes its authorities through activities related to the four Strategic Goals outlined in the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*[260]:

[260] www.oar.nih.gov/hiv-policy-and-research/strategic-plan

Advance rigorous and innovative research to end the HIV pandemic and improve the health of people with, at risk for, or affected by HIV across the lifespan: OAR works to catalyze multidisciplinary and novel approaches in HIV prevention, treatment, cure, co-morbidities research; and to support research to address and mitigate underlying HIV-associated medical and social inequalities.

Ensure that the NIH HIV research program remains flexible and responsive to emerging scientific opportunities and discoveries: Examples from the past six years (2016 to 2021) include: the rapid focus on potential effects of the drug dolutegravir on fetal neural tube development; reconstruction of the Puerto Rico non-human primate facilities destroyed by Hurricane Maria; and the continued response to the emergent SARS-CoV-2/COVID-19 pandemic by elucidation and application of lessons learned from HIV science; development of clinical guidelines; and mitigating the effects of the COVID-19 experience on the conduct and recovery of HIV research.

Promote dissemination and implementation of research discoveries for public health impact across agencies, departments, and stakeholders within the U.S. Government and globally: OAR continued its collaboration with the HIV Antiretroviral and Opportunistic Infections Guidelines Working Groups of OARAC which recently issued *Interim Guidance for COVID-19 and Persons with HIV*. The AIDS*info*.nih.gov and *info*SIDA.nih.gov websites moved from the National Library of Medicine to OAR and their content was shifted to HIVinfo.nih.gov and Clinicalinfo.hiv.gov. OAR expanded its program of Listening Sessions and Community Conversations held in multiple sites across the country; and continued support for international HIV-related conferences to ensure broad access to the latest scientific knowledge.

Strengthen human resource and infrastructure capacity to enhance sustainability of HIV research discovery and the implementation of findings by a diverse and multi-disciplinary workforce: OAR is committed to work with the NIH Institutes, Centers, and Offices (ICOs) to ensure that the HIV research program and mechanisms of funding focus on under-represented communities and populations, and to consider novel ways to conduct research that are cost-saving, culturally and ethically appropriate, and attentive to the needs of early career investigators.

The Strategic Goals provide the framework for how OAR promotes the NIH Director's theme of *Science in Service to Society*.

Answering the Call: OAR works to address HIV and related public health needs with urgency and flexibility to ensure that science is in service to all of society. We continue to advance the basic biomedical, behavioral, and social science that is foundational to HIV prevention, treatment, and cure; ensure that discoveries are translated and disseminated widely; and place focus on addressing and strengthening capacity among populations most affected by HIV and related health issues to conduct and apply research. Key initiatives in this regard are:

- ***Implement NIH discoveries in the Ending the HIV Epidemic in the U.S. (EHE) initiative:*** OAR catalyzes research to expand discovery of new modes of prevention and treatment. These include effective vaccines and antibody mediated strategies; diversity of formulations and methods of delivery (oral, injectable, ring) of pre-exposure prophylaxis (PrEP); new antiretroviral therapies that are less toxic and easier to use; and long-acting injectable products for prevention or treatment. We also support efforts to build and leverage across NIH frameworks, such as the Centers for AIDS Research (CFAR), AIDS Research Centers (ARC), Research Centers in Minority Institutions (RCMI), to enhance academic-community-public health collaborations to accelerate the translation and implementation of basic research discoveries.

- ***Contribute knowledge from HIV science to address other, emergent infectious disease epidemics:*** Many of the lessons already learned and the clinical trials infrastructure built through the NIH HIV research program can and are being employed to respond to other epidemics that threaten our nation and the world. For example, when SARS CoV-2/ COVID-19 emerged, OAR: worked with partners inside and outside NIH on the rapid development and dissemination of clinical guidelines for COVID-19 and HIV; appointed an OAR COVID-19 and HIV Task Force to monitor the implications of the COVID-19 pandemic on the HIV pandemic and the HIV research program and to provide guidance on HIV research recovery efforts; and leveraged the HIV/AIDS Trials Networks to support clinical trials of promising COVID-19 prevention and treatment strategies.

- ***Apply the latest technological advances to HIV research:*** OAR stimulates research to advance the development and deployment of promising tools, such as: rapid, point-of-care diagnostics and self-administered viral load testing; 3-D printing; artificial intelligence (including machine learning); big data mining; geospatial modeling; advanced bioinformatics; and genetics. We also support research on the use of digital and social media in designing effective HIV prevention and treatment interventions that focus on end users as well as health care providers.

Closing the gap in health disparities: OAR works with its partners and stakeholders to effect progress in redressing HIV and associated health inequalities experienced by populations characterized by race, ethnicity, age, gender, sexual orientation, or other demographic or social features. We support research, infrastructure, and capacity strengthening focused on under-represented and disenfranchised populations. Priorities include:

- ***Reduce disparities in HIV prevention and treatment:*** OAR supports efforts to engage and retain key populations in HIV prevention and treatment research, and to diversify and expand the research workforce to ensure creative and diverse thinking about discovery, translation, and implementation of HIV prevention, treatment, and care strategies.

- ***Examine and address intersectional stigma related to HIV:*** OAR supports HIV-related research that investigates how overlapping experiences of stigma related to race, gender, sexual orientation, and other psycho-social characteristics affect HIV prevention, treatment, and care among individuals and groups.

- ***Continue Listening Sessions and Community Conversations:*** OAR continues to convene diverse stakeholders from academic, community, and public health organizations to better understand the complexities of HIV-associated health disparities and inequalities at the community and regional level, and to identify priority research questions and mechanisms to address them.

Capitalizing on foundational investments and beyond: The dedicated investment in NIH's basic HIV research program over more than three decades resulted in the transition of HIV from a fatal disease to a chronic and manageable condition, allowing millions of people world to live long and productive lives. With ever-more sophisticated technologies, diversity of thinking, and continued investment, the potential for further advances—including an HIV cure—is extraordinary. OAR works with the ICOs to build on this foundation in a number of ways to:

- ***Expand basic science discoveries in virology, cell biology, and human immunology:*** OAR supports and augments research funded through the ICOs to understand how the virus replicates within cells and perturbs complex cellular interactions, and the complexities of immune responses needed for novel vaccine, treatment, and cure strategies.

- ***Transform NIH practices to facilitate interdisciplinary collaboration and discovery:*** OAR continues to promote interdisciplinary research in high priority areas, particularly in support of the HIV clinical trials networks and cores, shared facilities, infrastructure and capacity building for multipurpose research at academic institutions, including minority-serving institutions through the RCMI Program and to institutions in states historically receiving low levels of support from NIH through the Institutional Development Award Program.

- ***Augment the NIH commitment to the development of the next generation of HIV researchers:*** To enhance the pipeline of HIV researchers in multiple disciplines, OAR has launched an initiative to expand support for early-stage investigators (ESI), with particular attention to women and underrepresented populations from institutions within the United States and globally. To reverse a trend in declining ESI HIV R01-equivalent awards, OAR is working with the ICs to increase opportunities to promote and support ESI applications.

- ***Leverage the NIH HIV research framework, outcomes, and products:*** OAR works with partners inside and outside the NIH to: provide the evidence base for EHE; contribute to SARS-CoV-2/COVID-19 treatment and vaccine research, including cost-sharing with ICs; and apply research findings on factors influencing health behaviors, disparities, and stigma to COVID-19 and other emerging epidemics.

- ***Address the prevalence of co-morbidities, co-infections, and complications with the greatest effects on people living with HIV:*** OAR encourages research that combines epidemiological, clinical, behavioral and social, and implementation science to better address conditions coexisting with HIV, such as tuberculosis, cancer, substance use disorders, cognitive decline, among others.

National Institutes of Health
Office of AIDS Research

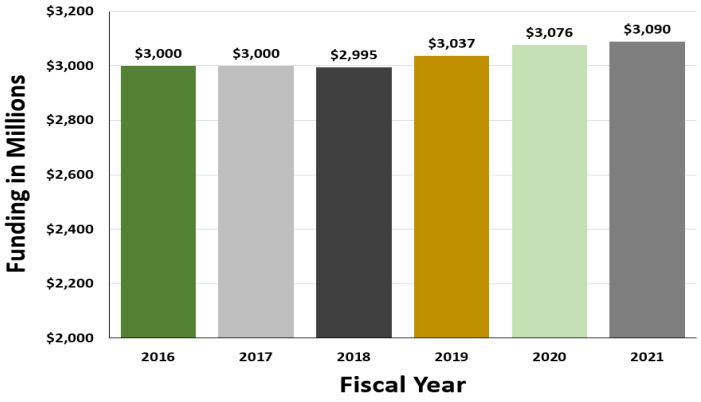
In 1988, the U.S. Congress authorized the establishment of the Office of AIDS Research (OAR) to oversee, coordinate, and manage NIH HIV/AIDS-related research. Located within the Office of the NIH Director, specifically within the Division of Program Coordination, Planning, and Strategic Initiatives, OAR:

- Establishes NIH HIV/AIDS research priorities,
- Allocates research funds in line with scientific priorities,
- Manages HIV/AIDS research across the NIH, and
- Collaborates across the U.S. government and with groups and organizations globally.

OAR Vision: ***Advance research to end the HIV pandemic and improve health outcomes for people with HIV.***

OAR Mission: ***Ensure that NIH HIV/AIDS research funding is directed at the highest priority research areas and facilitate maximal return on the investment.***

NIH HIV/AIDS Funding History FY 2016–2021



The FY 2022 President's Budget Level for the NIH-wide HIV/AIDS research agenda is $3,100.0 million, an increase of $10.0 million or 0.3 percent compared to the FY 2021 Enacted Level.

Research Highlights

- Long-acting injectables show exciting promise—the recent HPTN 083 study demonstrated the superiority of the long-acting form of cabotegravir for the prevention of HIV.
- Studies on an intravaginal ring with the microbicide dapivirine suggest a reduced risk of acquiring HIV infection.
- NIH-supported studies are using an interdisciplinary approach combining epidemiology, statistics, operations research, and decision science by studying three interlocking epidemics—opioid use disorder, HIV, and hepatitis C virus—among people who use drugs.

Maureen M. Goodenow, Ph.D.

Associate Director for AIDS Research and Director, Office of AIDS Research

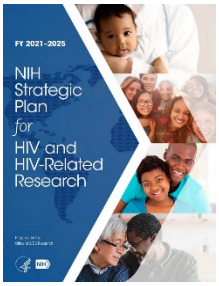
OAR Facts

- With 27 FTEs, OAR coordinates the largest public investment (~$3 B annually) in HIV/AIDS research globally.
- OAR supports HIV/AIDS-related research in more than 24 of the NIH ICOs.
- The NIH Revitalization Act of 1993 authorized OAR to plan, coordinate, and evaluate HIV/AIDS research; set scientific priorities for the NIH research agenda; and determine budgets for all NIH HIV/AIDS research.
- The NIH AIDS Executive Committee (NAEC) facilitates communication between OAR and all ICOs that use HIV/AIDS funding.
- The OAR Advisory Council (OARAC) provides advice to the OAR Director on the planning, coordination, and evaluation of research and other HIV/AIDS activities conducted or supported by NIH.
- Previous OAR Directors include Drs. Anthony Fauci, William Paul, Neal Nathanson, Jack Whitescarver, and Robert Eisinger (Acting).

National Institutes of Health
Office of AIDS Research

Recent Accomplishments

- Development and release of the *FY 2021–2025 NIH Strategic Plan for HIV and HIV-Related Research*, which includes four strategic goals:
  (1) advance rigorous and innovative research,
  (2) ensure flexibility and responsiveness,
  (3) promote dissemination and implementation of research discoveries, and
  (4) build human resource and infrastructure capacity.



- Collaboration with the HIV Antiretroviral and Opportunistic Infections Guidelines Working Groups of OARAC, which are responsible for updating the HHS HIV/AIDS Treatment Guidelines, and recently issued Interim Guidance for COVID-19 and Persons with HIV.
- Transition of the AIDS*info*.nih.gov and *info*SIDA.nih.gov websites from the National Library of Medicine to OAR. As part of this transition, the content has been rebranded and shifted to HIVinfo.nih.gov and Clinicalinfo.hiv.gov.

Current Activities

- Exploring opportunities to leverage NIH-supported HIV research platforms and the clinical trial networks to tackle unanticipated research questions related to other emerging HIV epidemics, such as COVID-19.
- Working with ICs on an initiative to enhance support for early stage investigators—with particular attention to women and those from underrepresented populations and institutions within the U.S. and globally—to enhance the pipeline of HIV researchers through mentoring by NIH program staff and external senior and mid-career investigators.
- Leading NIH's support of the Administration's Ending the HIV Epidemic in the U.S. initiative (EHE).

Ending the HIV Epidemic

- Continuing OAR's series of listening sessions and community engagement meetings in geographically defined locations to bring local and regional focus to discussions of NIH HIV research priorities, translation and dissemination efforts, and capacity-building activities.

Future Initiatives

- Effective HIV vaccines and antibody mediated protection strategies.
- Innovative technology approaches including 3-D printing, artificial intelligence (including machine learning), advanced bioinformatics, genetics, big data mining, and geospatial modeling for advanced discovery.
- New methods and delivery of pre-exposure and post-exposure prophylaxis, multi-purpose prevention technologies, and community-level behavioral and social-structural interventions.
- Novel diagnostics and treatment strategies for viral suppression and sustained ART-free viral remission for a cure for HIV.
- Prevalent HIV-associated coinfections, chronic conditions, and syndemics.
- Complications from virus exposure, long-term HIV disease, immune dysfunction, and/or ART for treatment or prevention across the lifespan: from development in infants, children and youth to aging.
- Strategies for mitigating HIV-associated stigma and discrimination.
- Efforts to increase the number and diversity of early stage investigators in the HIV research pipeline.
- Implementation strategies to improve systematic uptake of evidence-based prevention, care, and treatment interventions in diverse settings and populations.

Budget Policy Statement

The FY 2022 President's Budget request for the NIH-wide HIV/AIDS research program is $3,100.0 million, an increase of $10.0 million or 0.3 percent compared to the FY 2021 Enacted level. Funding at this level will expedite NIH efforts to pursue emerging discoveries in focused areas of HIV pandemic research, enhance the pipelines of novel HIV prevention and treatment products, ensure a diverse pool of HIV investigators, and expand partnerships with stakeholders inside and outside of government to make greater inroads into mitigating inequalities and ending the HIV epidemic in the United States and globally.

The NIH will continue a multipronged strategy to develop and advance the most promising HIV vaccine candidates. In particular, the NIH will continue to support the development of promising mRNA-based HIV vaccine approaches, building on the success of the COVID-19 mRNA-based vaccines that establish the utility of the mRNA platform in vaccine development and showcase the advantages of the approach. The NIH continues to support a broad HIV/AIDS vaccine research portfolio encompassing basic, pre-clinical, and clinical research, including studies to identify and better understand potentially protective immune responses in HIV-infected individuals and studies of improved animal models for the pre-clinical evaluation of vaccine candidates.

The NIH will also continue to support research related to HIV across the lifespan. Although there has been progress in the reduction of the number of HIV-infected infants through expansion of programs for perinatal prevention of mother-to-child transmission (PMTCT), pediatric infection by breast-feeding continues as a challenge. Because the number of HIV-exposed but uninfected (HEU) infants is increasing worldwide, studies to compare rates of pre-term delivery, mortality, growth, and other outcomes are critical to better understand how HIV exposure impacts the health and well-being of a child, long after exposure to both HIV and antiretroviral therapy (ART) has ended. At the other end of the spectrum, as the number of older people living with HIV increases, chronic HIV infection, extended exposure to ART, and aging may all interact to increase risk of neurological impairment, other comorbid conditions, and mortality. Therefore, basic science, epidemiological, clinical, and translational research studies, focused on HIV in aging populations and utilizing multi-disciplinary research teams, are critically necessary.

HIV-related stigma is an underlying feature of health inequalities and is a pervasive challenge to efforts to achieve successful HIV prevention, treatment, and care. The impact of stigma on HIV-related health outcomes is well documented; more research is needed on the intersectional nature of stigma based on multiple aspects of people's identities, social positions, and health status to develop and successfully implement strategies to best mitigate the effects of stigma on people affected by HIV.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority by Institute, Center, and Office
(Dollars in Thousands)

Institute, Center, and Office	FY 2020 Final	FY 2021 Enacted [1]	FY 2022 President's Budget	FY 2022 +/- FY 2021
NCI	$241,975	$241,238	$241,238	$0
NHLBI	84,715	84,715	84,715	0
NIDCR	18,984	18,984	18,984	0
NIDDK	34,135	34,135	34,135	0
NINDS	41,082	38,655	38,655	0
NIAID	1,779,113	1,788,843	1,798,843	10,000
NICHD	144,895	147,716	147,716	0
NEI	388	195	195	0
NIEHS	5,342	5,342	5,342	0
NIA	22,622	23,350	23,350	0
NIAMS	4,587	4,587	4,587	0
NIDCD	2,128	2,128	2,128	0
NIMH	183,991	186,421	186,421	0
NIDA	261,140	262,123	262,123	0
NIAAA	31,879	31,879	31,879	0
NINR	16,350	16,350	16,350	0
NHGRI	3,302	3,538	3,538	0
NIBIB	1,839	1,839	1,839	0
NIMHD	22,780	23,530	23,530	0
NCCIH	748	666	666	0
FIC	24,389	24,389	24,389	0
NLM	9,322	7,685	7,685	0
OD	140,355	141,692	141,692	0
OAR	62,256	63,593	63,593	0
ORIP	78,099	78,099	78,099	0
Subtotal, OD	140,355	141,692	141,692	0
TOTAL, NIH	**$3,076,061**	**$3,090,000**	**$3,100,000**	**$10,000**

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Mechanism – AIDS [1]
(Dollars in Thousands)

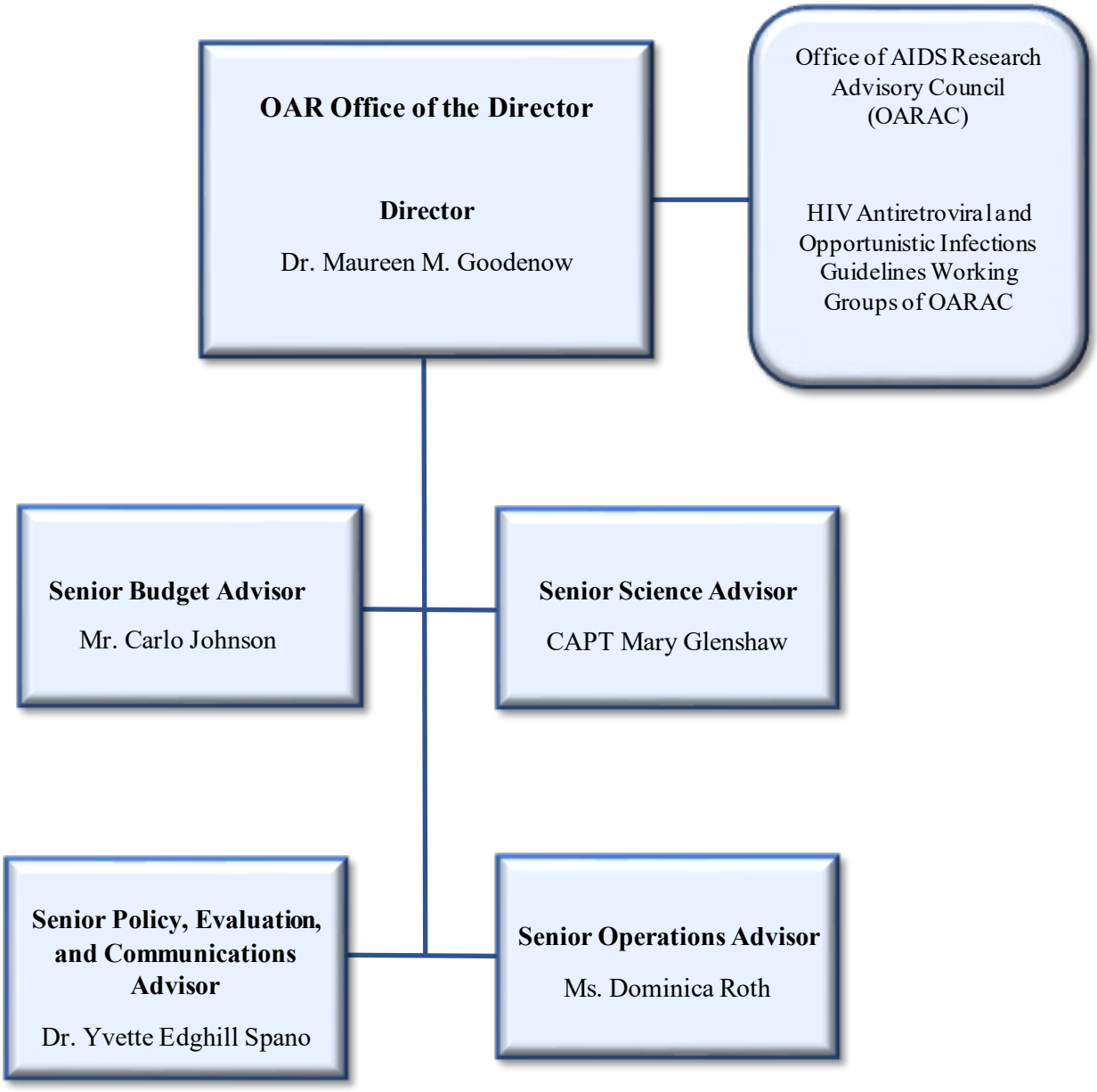
Mechanism	FY 2020 Final		FY 2021 Enacted		FY 2022 President's Budget		FY 2022 +/- FY 2021	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,388	$1,399,826	1,541	$1,080,998	1,456	$1,405,045	-85	$324,047
Administrative Supplements	*(102)*	21,304	*(58)*	17,234	*(50)*	6,699	*(8)*	-10,535
Competing	515	352,038	523	646,265	600	363,836	77	-282,429
Subtotal, RPGs	1,903	$1,773,168	2,064	$1,744,497	2,056	$1,775,580	-8	$31,083
SBIR/STTR	30	15,798	31	17,850	29	17,145	-2	-705
Research Project Grants	1,933	$1,788,966	2,095	$1,762,347	2,085	$1,792,725	-10	$30,378
Research Centers:								
Specialized/Comprehensive	51	$132,976	59	$139,969	56	$151,562	-3	$11,593
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0	0	0
Comparative Medicine	17	72,680	19	72,298	19	71,427	0	-871
Research Centers in Minority Institutions	0	0	0	1,143	0	1,143	0	0
Research Centers	68	$205,656	78	$213,410	75	$224,132	-3	$10,722
Other Research:								
Research Careers	257	$45,798	260	$45,554	254	$44,182	-6	-$1,372
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	2	1,999	0	3,114	11	4,495	11	1,381
Biomedical Research Support	1	1,628	29	1,600	31	2,000	2	400
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	116	64,796	100	61,131	110	59,930	10	-1,201
Other Research	376	$114,221	389	$111,399	406	$110,607	17	-$792
Total Research Grants	2,377	$2,108,843	2,562	$2,087,156	2,566	$2,127,464	4	$40,308
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	68	$3,114	78	$3,609	80	$3,748	2	$139
Institutional Awards	241	14,619	236	15,075	225	15,276	-11	201
Total Research Training	309	$17,733	314	$18,684	305	$19,024	-9	$340
Research & Develop. Contracts	108	$370,739	75	$402,086	89	$361,945	14	-$40,141
(SBIR/STTR) (non-add)	*(8)*	*(6,551)*	*(9)*	*(6,744)*	*(9)*	*(5,744)*	*(0)*	*(1,000)*
Intramural Research		$354,815		$352,328		$354,902		$2,574
Res. Management and Support		161,675		166,153		173,072		6,919
Res. Management & Support (SBIR Admin) (non-add)		*0*		*0*		*0*		*0*
Office of the Director - Appropriation [2]		*140,355*		*141,692*		*141,692*		*0*
Office of the Director - Other		62,256		63,593		63,593		0
ORIP (non-add) [2]		*78,099*		*78,099*		*78,099*		*0*
Total, NIH Discretionary B.A.		**$3,076,061**		**$3,090,000**		**$3,100,000**		**$10,000**

[1] All items in italics and brackets are non-add entries.

[2] Number of grants and dollars for the ORIP component of OD are distributed by mechanism and are noted here as a non-add. Office of the Director - Appropriation is the non-add total of these amounts and the funds accounted for under OD - Other.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

ORGANIZATION CHART



NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority by Activity
(Dollars in Thousands)

Overarching Priorities	FY 2018 Actual [1]	FY 2019 Actual [1]	FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
Reduce the Incidence of HIV	$714,553	$741,401	$719,217	$706,497	$691,639	-$14,858
Develop Next-Generation HIV Therapies	364,484	368,912	345,378	350,198	351,466	$1,268
Research Toward a Cure for HIV	175,757	187,777	209,133	210,025	211,730	$1,705
Address HIV-Associated Comorbidities, Coinfections, and Complications	517,884	531,440	554,452	559,382	552,747	-$6,635
Cross-Cutting Areas	1,222,703	1,207,770	1,247,881	1,263,898	1,292,418	$28,520
Total	**$2,995,381**	**$3,037,300**	**$3,076,061**	**$3,090,000**	**$3,100,000**	**$10,000**

[1] Reflects effects of Secretary's transfer.

JUSTIFICATION OF BUDGET REQUEST

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

Budget Authority (BA)

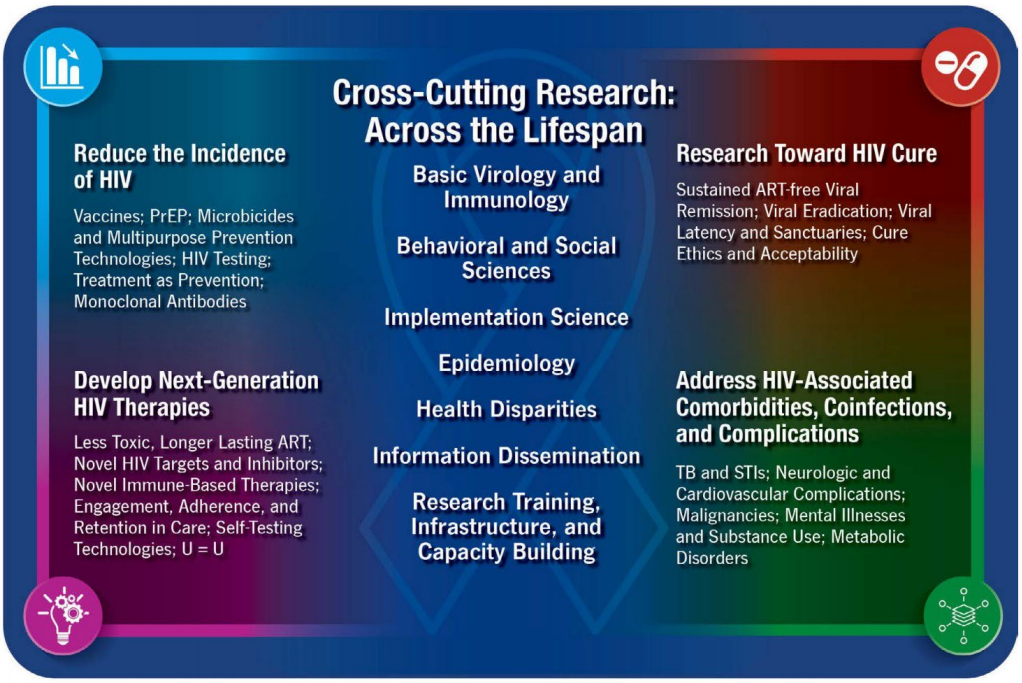
FY 2020 Final	FY 2021 Enacted	FY 2022 President's Budget	FY 2022 +/- FY 2021
$3,076,061,000	$3,090,000,000	$3,100,000,000	$10,000,000

Program funds are allocated as follows: Competitive Grants/Cooperative Agreements; Contracts; Direct Federal/Intramural and Other.

PROGRAM DESCRIPTIONS, ACCOMPLISHMENTS, AND FUTURE DIRECTIONS

The following selected programs and activities focus on the highest HIV research priorities as they further the NIH Director's theme of *Science in Service to Society*.

NIH Priorities for HIV and HIV-related Research



Reduce the Incidence of HIV

Given persistent high rates of new HIV infections globally, developing an effective preventive vaccine against HIV remains a critical research goal, although it has proven to be a formidable challenge. In 2009 a key milestone was reached with results from the RV144 vaccine trial, supported by the U.S. Department of Defense, NIH, and the government of Thailand, which showed partial efficacy (31 percent) in a large-scale field trial of an experimental vaccine regimen. However, the follow-on study, HVTN 702, carried out in South African populations, was halted because the vaccine strategy failed to prevent HIV infection.

One of the lessons learned from these and other HIV vaccine studies is the value of forming multidisciplinary teams of researchers across different fields of basic and translational science and incorporating behavioral and social science early in the development process. The scientific complexity and cost of these endeavors has led to the establishment of public/private partnerships to advance the evaluation of vaccine candidates. NIH currently is partnering with pharmaceutical companies in two large-scale, multi-national trials—Imbokodo (HVTN 705) and Mosaico (HPTN 706) that are testing a novel mosaic vaccine regimen.

Basic, clinical, and translational research to evaluate the human immune response to vaccine remains a critical priority. Advances in imaging technologies have led to the development of vaccine candidates that more closely mimic HIV envelope structural components and could provide the foundation for improved vaccines to induce protective immunity. In preparation for an increased number of vaccine efficacy clinical trials, NIH has strategically invested in expanding vaccine product manufacturing capabilities to meet future research demands.
In parallel with vaccine-based prevention strategies, antibody-mediated protection studies are testing biologicals as alternatives for prevention in uninfected individuals. Studies in multiple countries are in progress to determine whether or not periodic infusions or injections of certain broadly neutralizing antibodies (bNAbs) can prevent HIV acquisition in different populations.

Along with vaccine strategies, NIH will continue to pursue the development of other HIV prevention approaches, such PrEP. NIH has supported studies demonstrating that daily, oral antiretroviral therapy (ART)-based PrEP can reduce the risk of HIV acquisition by nearly 100 percent if taken as prescribed. For many people, however, "a pill a day" is not optimal and adherence can be a challenge. Consequently, NIH is expanding research into long-acting formulations for PrEP (as well as for HIV treatment) including research into bNAbs and long-acting small molecules as antiretroviral agents. This research will expand from the NIH-funded study, HPTN 083, which demonstrated that a PrEP regimen containing long-acting cabotegravir injected once every eight weeks was superior to daily oral tenofovir/ emtricitabine for HIV prevention in cisgender men and transgender women who have sex with men. Other long-acting alternatives under development include intra-vaginal rings, implants, transdermal patches and additional injectables.

NIH will continue to support the efforts for the development of multipurpose technologies that use HIV prevention interventions with other sexually transmitted infection (STI) preventives and/or contraceptives. Such methods will offer the advantages of discreet, self-initiated, and

long-acting HIV prevention options for women providing simultaneous protection against multiple health risks.

In concert with product development, NIH will continue to support behavioral, social, and implementation sciences research to better understand how reach, uptake, and adherence to prevention interventions may be optimized for different populations. Primary prevention options, such as PrEP are only administered to people without HIV. To determine HIV status in ways that are acceptable to those at risk of HIV infection, NIH is continuing to partner with organizations to develop new HIV testing technologies, in particular self-testing methods.

Budget Policy: The FY 2022 President's Budget request to reduce the incidence of HIV is $691.6 million, a decrease of $14.9 million or 2.1 percent compared to the FY 2021 Enacted level.

Develop Next-Generation HIV Therapies

NIH-sponsored research has led to the development of combination ART that has significantly improved the health outcomes, including the quality and length of life, of people with HIV. With effective treatment, HIV infection has changed from a rapidly fatal disease to a chronic condition. Consistent use of ART reduces damage to the immune system by suppressing viral replication, delaying the development of viral resistance, and leading to undetectable viral loads, thereby preventing sexual transmission of HIV to an uninfected partner. This has led to the highly effective "Uninfected = Untransmittable" (U=U) campaign. However, even with simplified, effective daily one-pill treatment regimens capable of suppressing HIV, only 23 million (60 percent) of the approximately 38 million people with HIV worldwide currently receive ART.

Barriers to uptake and adherence to ART include treatment unavailability, high cost, the need for daily doses, interactions with other drugs, psychosocial factors, and the potential for drug resistance and/or adverse events. Stigma and disparities in access to ART also adversely affect health outcomes in people with HIV across race, ethnicity, sex, gender, age, socioeconomic status and geographic location.

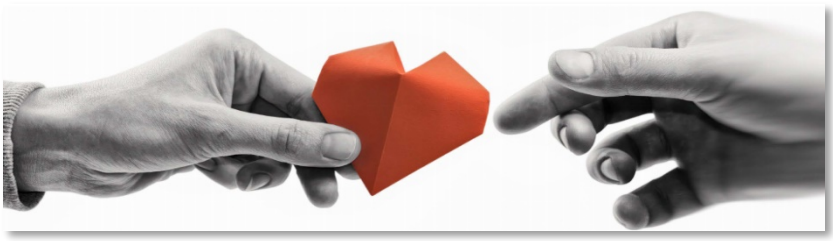
Budget Policy: The FY 2022 President's Budget request to develop next-generation HIV therapies is $351.5 million, an increase of $1.3 million or 0.4 percent compared to the FY 2021 Enacted level.

Research Toward a Cure for HIV

Significant challenges to cure HIV continue because of the persistence of HIV as integrated DNA in latently infected cells and other reservoirs. To date, only three people in the world have been cured of HIV: two individuals achieved long term ART-free suppression of HIV through a complex and costly bone marrow transplant procedure, and one individual cleared HIV through a genetic variation in her immune system that controlled the virus. While these cases provide optimism that cure of HIV is achievable, intensive focus on understanding the dynamics of viral reactivation and the nature of viral reservoirs in achieving long-term HIV suppression is a vital and essential step towards cure. Further fundamental research using novel technologies, such as clustered regularly short palindromic repeats—discovered by NIH-funded and recent Nobel Prize-winning investigators—will be supported to better understand genomic and epigenetic features of integration sites as well as to characterize, quantify, eliminate or control the viral

reservoir in different anatomical sites, cell types and to test the efficacy of novel cure strategies in appropriate animal models and human clinical trials.

NIH will invest in cure strategies with a "back to basics" approach that focuses on fundamental virology and cell biology. The aim is to better understand mechanisms of virus/host cell interactions that will lead to rational design of innovative strategies for extended viral suppression and ultimately viral elimination.



A range of techniques, including single-cell and imaging technologies, are being used to identify and describe the HIV reservoir and discover mechanisms of viral reactivation from latently infected cells. Experimental treatments in development include therapeutic vaccines, genetically engineered immune cells that are resistant to HIV infection, drugs that reactivate latent HIV to make the virus visible to the immune system so that the virus can be cleared, cure-inducing immunotherapies, and interventions to prolong the time between antiretroviral treatments from one day to a few months or longer for an ART-free viral remission.

In parallel to basic and clinical research, NIH is supporting behavioral and social science research to ascertain what kind of cure strategies will be perceived as feasible and desirable among different groups of people with HIV. A core question under exploration is how the risks and benefits of potential HIV cure strategies (including participation in the associated research) are weighed, particularly in the context of living a healthy life and maintaining viral suppression under currently available, highly effective ART. In the end, the goal of integrated HIV cure research is to develop safe, scalable, and sustainable strategies for cure for the 38 million people with HIV.

Budget Policy: The FY 2022 President's Budget request to promote research toward a HIV cure is $211.7 million, an increase of $1.7 million or 0.8 percent compared to the FY 2021 Enacted level.

Address HIV-Associated Comorbidities, Coinfections and Complications

Effective ART has ushered in a new era for the HIV epidemic. People with HIV can now achieve nearly normal lifespans, but are more likely to suffer from multiple, chronic comorbidities, coinfections, and complications (CCCs) resulting from virus exposure, long-term HIV disease, immune dysfunction, and/or ART for treatment or prevention, which can severely impact their quality of life. These include neurocognitive and cardiovascular complications, malignancies, metabolic and bone disorders, mental health impairments, substance use, and others. HIV interacts with other infectious and non-communicable diseases in significant ways. Among people with HIV globally, tuberculosis is the greatest cause of mortality. Viral hepatitis, and some viral-associated cancers also are challenges for people with HIV. HIV often occurs concomitantly with other STI and/or in association with alcohol, tobacco, and drug misuse, violence and trauma, mental illness, and other behavioral and psychosocial issues. The

overlapping etiologies and consequences of HIV-associated diseases need to be better understood in order to improve the health and well-being of people with HIV across the lifespan.

Budget Policy: The FY 2022 President's Budget request to address HIV-associated comorbidities, coinfections, and complications (CCCs) is $552.7 million, a decrease of $6.6 million or 1.2 percent compared to the FY 2021 Enacted level.

Cross-Cutting Areas

Basic Science: Basic biomedical research has generated fundamental knowledge to improve understanding of HIV virology, immunology and pathogenesis that can inform the development of effective prevention, treatment, and cure strategies. Nonetheless, significant gaps remain in areas that could lead to innovations in vaccine development, better therapies, and cure approaches. NIH will continue to invest in research to enhance understanding of fundamental aspects of innate immunity, B and T cell immunology, virology, and interplay between the virus and host, and basic mechanisms involved in host cellular interactions with HIV. Systems biology approaches to examine HIV risk, immunity, treatment response, and disease progression in diverse populations will provide additional scientific value.

Behavioral and Social Science: Insights about human behavior, social networks, community institutions, and social forces that influence the emergence and spread of HIV epidemics have contributed to the development of important HIV prevention, care, and social-structural interventions. Further research will be supported to better understand and address key individual, relational, community, and social-structural dynamics that fuel or mitigate HIV epidemics in diverse populations and settings. This includes attention to addressing intersectional stigma as a continuing challenge to information about, access to, and uptake of HIV prevention and treatment methods in at-risk communities.

Epidemiology: Epidemiologic methods provide accurate, real-time information to better understand the global HIV/AIDS pandemic and its associated CCCs, inform prevention and treatment approaches, and determine where research should be conducted. The use of surveillance, big data science, machine learning, modeling, registries, phylodynamics, and other epidemiologic approaches will contribute to improved outcomes across the HIV prevention and care continua.

Health Disparities: Research to better understand and address disparities and inequalities based on such things as sex, gender, race, ethnicity, socioeconomic status, age, sexual orientation and behavior, substance use behavior, and geographic location—including through community-based participatory research methods—will be supported to improve HIV testing and engagement and retention in prevention and care services, and to enhance the health and wellbeing of persons living with and at risk for HIV in underserved and marginalized communities.

Implementation Science: To have the greatest impact on domestic and global HIV programs and policies and help move from efficacy to effectiveness, the NIH will support implementation science to promote and improve the systematic uptake of evidence-based HIV prevention, care, and treatment interventions in diverse settings. Further understanding of the processes and factors that influence scale-up and sustainability of effective strategies will help achieve the

goals of the *National HIV/AIDS Strategy for the United States* and *Ending the HIV Epidemic in the U.S.*, and the UNAIDS global *95-95-95* targets.

Information Dissemination: A critical component of the NIH HIV research program is ensuring that research findings are shared with diverse communities and stakeholders, including patients, clinicians, researchers, public health practitioners, policy-makers, and the general public. NIH will utilize emerging technologies and venues to develop accurate, timely, and culturally responsive communication approaches, including social media, that target underserved populations.

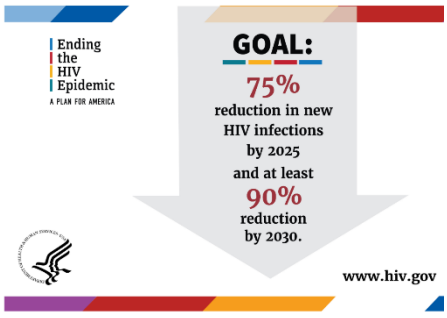
Training, Infrastructure, and Capacity-building: To ensure that the priority areas of HIV science are addressed with novel, innovative, and culturally responsive approaches, the NIH will augment its commitment to the development of the next generation of HIV researchers, particularly those from underrepresented populations and institutions. This includes providing both human resources (e.g., mentoring) and support for infrastructure (e.g., laboratories).

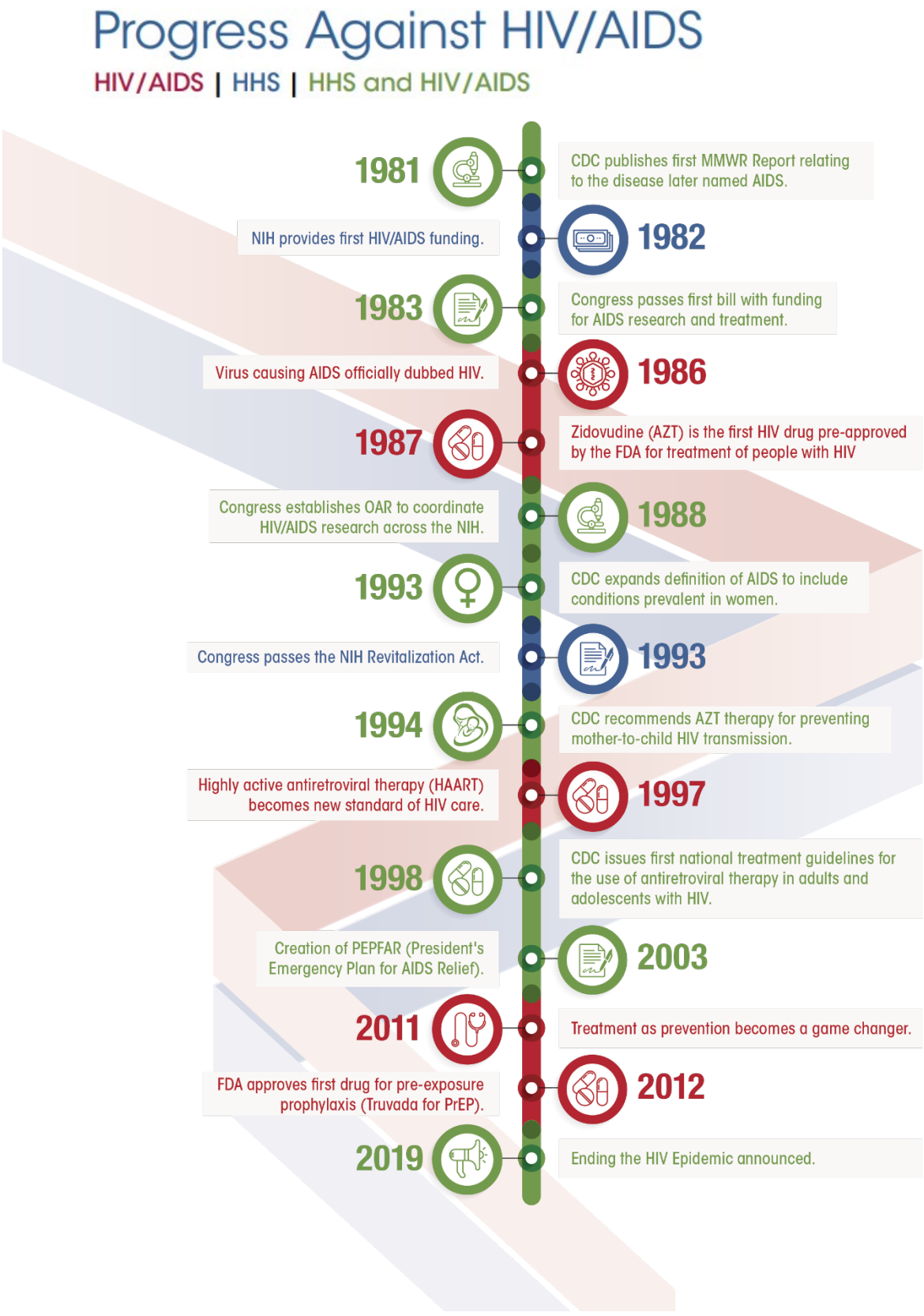
Specifically, NIH is committed to promoting opportunities for new researchers and enhancing training and mentorship programs to encourage successful, independent careers for ESIs in a way that enhances workforce diversity. Over the last several years, NIH has taken numerous steps to balance, strengthen, and stabilize the biomedical research workforce, but increased investments in supporting and expanding ESIs in the HIV field are needed. A priority for developing workforce diversity is to promote research on the engagement of community health workers as integral members of a multidisciplinary health care team to improve HIV care engagement, antiretroviral adherence, viral suppression, and ultimately, health outcomes.

Budget Policy: The FY 2022 President's Budget request to advance the critical framework of crosscutting areas of research to end the HIV pandemic is $1,292.4 million, an increase of $28.5 million or 2.3 percent compared to the FY 2021 Enacted level.

NIH- and HHS-wide Initiative

Ending the HIV Epidemic in the U.S. (EHE): OAR works with its NIH and HHS partners to continue to advance the goals of the EHE to: (1) reduce new HIV infections; (2) increase access to care and improve health outcomes for people with HIV; (3) reduce HIV-related health inequities; and (4) achieve a more coordinated national response to the HIV epidemic. NIH will expand upon its initial support of pilot implementation science projects funded through its CFARs and ARCs to leverage investments in these and other institutions that represent and are located among populations in U.S. states and territories most affected by the HIV epidemic.




Progress Against HIV/AIDS
HIV/AIDS | HHS | HHS and HIV/AIDS
1981
CDC publishes first MMWR Report relating to the disease later named AIDS.
NIH provides first HIV/AIDS funding.
1982
1983
Congress passes first bill with funding for AIDS research and treatment.
Virus causing AIDS officially dubbed HIV.
1986
1987
Zidovudine (AZT) is the first HIV drug pre-approved by the FDA for treatment of people with HIV
Congress establishes OAR to coordinate HIV/AIDS research across the NIH.
1988
1993
CDC expands definition of AIDS to include conditions prevalent in women.
Congress passes the NIH Revitalization Act.
1993
1994
CDC recommends AZT therapy for preventing mother-to-child HIV transmission.
Highly active antiretroviral therapy (HAART) becomes new standard of HIV care.
1997
1998
CDC issues first national treatment guidelines for the use of antiretroviral therapy in adults and adolescents with HIV.
Creation of PEPFAR (President's Emergency Plan for AIDS Relief).
2003
2011
Treatment as prevention becomes a game changer.
FDA approves first drug for pre-exposure prophylaxis (Truvada for PrEP).
2012
2019
Ending the HIV Epidemic announced.

DRUG CONTROL PROGRAMS

RESOURCE SUMMARY

	Budget Authority[1] (in millions)		
	FY 2020 Final	FY 2021 Enacted	FY 2022 Request
Drug Resources by Function			
Research and Development: Prevention	$488.462	$496.004	$609.092
Research and Development: Treatment	$1,029.853	$1,045.804	$1,306.604
Total, Drug Resources by Function	**$1,518.315**	**$1,541.808**	**$1,915.696**
Drug Resources by Decision Unit			
National Institute on Alcohol Abuse and Alcoholism (NIAAA)			
Research and Development: Prevention	$51.145	$51.911	$53.341
Research and Development: Treatment	$9.446	$9.588	$9.852
National Institute on Drug Abuse (NIDA)			
Research and Development: Prevention	$437.317	$444.093	$555.751
Research and Development: Treatment	$1,020.407	$1,036.216	$1,296.752
Total, Drug Resources by Decision Unit	**$1,518.315**	**$1,541.808**	**$1,915.696**
Drug Resources Personnel Summary			
Total FTEs (direct only)	363	388	388
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in Billions)	$40.3	$41.5	$50.5
Drug Resources percentage	3.77%	3.72%	3.79%

[1]Reflects regular appropriations for NIH drug control programs. These programs did not receive supplemental funding in FY 2020 or FY 2021.

PROGRAM SUMMARY

MISSION

The National Institute on Drug Abuse (NIDA) and the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two of the 27 Institutes and Centers of the National Institutes of Health (NIH), support research in pursuit of the objectives of the National Drug Control Strategy. NIDA is the lead federal agency supporting scientific research on drug use and its consequences. Its mission is to advance science on drug use and addiction and apply that knowledge to improve individual and public health. This includes basic and clinical research on drug use (including nicotine), addiction, and the underlying neurobiological, behavioral, and social mechanisms involved. NIDA also works to ensure the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorder (SUD) and to enhance public awareness of addiction as a brain disorder. While NIDA's mission broadly encompasses substance use, addressing opioid misuse and addiction is a top priority at NIDA.

NIAAA's mission is to generate and disseminate fundamental knowledge about the effects of alcohol on health and well-being, and apply that knowledge to improve diagnosis, prevention, and treatment of alcohol-related problems, including alcohol use disorder, across the lifespan. A major priority within NIAAA's mission is research on the prevention and treatment of underage drinking and its harmful consequences.

Substance use and SUD cost the U.S. more than $740 billion a year in healthcare, crime, and lost productivity;[261] but dollars cannot capture the devastating human cost of addiction to individuals, families, and communities. Drug overdose is now the leading cause of unintentional fatal injury in our nation. In 2019, more than 20 million Americans had SUD,[262] and drug overdose claimed more than 71,000 lives, about 70% of which were from illicit or prescription opioids.[263] For every fatal overdose it is estimated that there are 10 non-fatal overdoses and 20 opioid-related hospitalizations.[264]

The collision of the overdose crisis with the coronavirus disease 2019 (COVID-19) pandemic puts people with SUD at particular risk. Early data show increases in drug use and overdose since the pandemic began,[265] and the highest number of overdose deaths (over 90,000) ever recorded occurred in the 12 months ending in September 2020.[266] Individuals with SUD, especially Blacks/African Americans and those with opioid use disorder (OUD), are at higher risk for COVID-19 and its adverse outcomes.[267]

Alcohol misuse has profound effects on the health and well-being of individuals, families, and communities, costing the United States an estimated $249 billion per year. NIAAA is committed to reducing the burden of alcohol misuse for individuals at all stages of life and supports a diverse portfolio of research to accomplish this goal. Research areas include biological and behavioral mechanisms underlying alcohol misuse, alcohol use disorder (AUD), and alcohol-related health conditions; epidemiological assessments of patterns and trends in alcohol use; and the development and evaluation of interventions to identify, prevent, and treat alcohol misuse and its consequences, including among youth. NIAAA also supports efforts to translate research findings to improve prevention and treatment of alcohol-related problems and co-occurring conditions and to disseminate evidence-based information to health care providers, researchers, policy makers, and the public. These ongoing efforts have significantly broadened our understanding of alcohol misuse and AUD and have provided support for the integration of alcohol prevention and treatment services into mainstream health care.

METHODOLOGY

NIDA's entire budget is drug-related and classified as a part of the National Drug Control Budget.

[261] www.drugabuse.gov/related-topics/trends-statistics
[262] 2018 National Survey on Drug Use and Health, 2019. SAMHSA
[263] www.cdc.gov/drugoverdose/index.html#:~:text=The%20number%20of%20drug%20overdose
[264] Rudd, R. et al. MMWR Morb. Mortal. Wkly. Rep. 65, 1445-1452, (2016).
[265] emergency.cdc.gov/han/2020/han00438.asp
[266] www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
[267] pubmed.ncbi.nlm.nih.gov/32929211/

The prevention and treatment components of NIAAA's underage drinking research program are classified as a part of the National Drug Control Budget. Underage drinking research is defined as research that focuses on alcohol use by youth (individuals under the legal drinking age of 21), as well as the negative consequences of underage alcohol use (e.g., alcohol-related injuries, impact on adolescent development including on the developing brain, and risk for AUD). It includes basic biological and behavioral research, epidemiological research, screening studies, the development and testing of preventive and treatment interventions, and efforts to disseminate evidence-based information. NIAAA's methodology for developing budget estimates for the Budget and Performance Summary is a two-step process. First, NIAAA identifies its underage drinking projects using NIH's automated, electronic text mining system for research, condition, and disease categorization. Once these projects are verified as underage drinking projects, NIAAA conducts a manual review of the project listing and codes each verified project as relevant to prevention or treatment.

BUDGET SUMMARY

The FY 2022 Request for drug-related activities at NIH is $1,915.7 million ($1,852.5 million for NIDA and $63.2 million for NIAAA), a 24.2 percent increase compared with the FY 2021 Enacted level.

NIH-supported research has provided and will continue to provide the scientific basis for drug control policy. For example, NIH continues to explore the many biological, behavioral, and environmental influences on substance misuse and addiction vulnerability, which will allow the development of more targeted and effective prevention approaches. Research reveals that universal prevention programs not only reduce drug use, underage drinking, and other risky behaviors that can lead to HIV and other adverse outcomes, but can also promote other positive outcomes, such as strengthening young people's sense of community or "connection" to school—key to reducing substance misuse, violence, and mental health problems.

Another top priority continues to be the development and deployment of therapeutic interventions to treat SUD, including medications, biologics, behavioral interventions, and non-pharmacological interventions such as transcranial magnetic stimulation or neurofeedback. NIH is now poised to capitalize on a greater understanding of the neurobiology underlying addiction, and of newly identified candidate molecules and brain circuits that show promise as potential targets for the treatment of SUD. However, discovering new therapies is not sufficient to combat SUD if these therapies do not reach the people who need them. In many cases, such as medications for the treatment of OUD (MOUD), studies suggest that effective treatments are under-utilized despite strong evidence of their effectiveness. To address this issue, NIH is also exploring ways of improving the dissemination and implementation of evidence-based practices (implementation science) in real world settings to improve the prevention and treatment of SUD and co-occurring conditions such as HIV and psychiatric disorders, thereby enhancing the public health impact of NIH-supported research.

In April 2018, NIH launched the HEAL Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. This Initiative will build on extensive, well-established NIH research, including basic science studying the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioral interventions with MOUD.

As part of the NIH HEAL Initiative, NIDA (and to a lesser extent, NIAAA) supports a variety of projects aimed at advancing our understanding of how to prevent and treat opioid misuse and addiction and reverse opioid overdose. This includes research studies focused on:

- Enhancing the NIDA Clinical Trials Network to Address Opioids[268]
- Focused Medication Development to Treat Opioid Use Disorder and Prevent/Reverse Overdose[269]
- Determining strategies to reduce opioid overdose in communities hardest hit by the opioid crisis (the HEALing Communities Study)[270]

[268] heal.nih.gov/research/research-to-practice/enhancing-clinical-trials-network
[269] heal.nih.gov/research/medication-options/focusing-development
[270] heal.nih.gov/research/research-to-practice/healing-communities

- Determining ways to improve the effectiveness and adoption of interventions within justice systems. (The Justice Community Opioid Innovation Network)[271]
- Preventing At-Risk Adolescents Transitioning into Adulthood from Developing Opioid Use Disorder[272]
- Prevention of Progression to Moderate or Severe Opioid Use Disorder [273]
- Optimizing the Duration, Retention, and Discontinuation of Medication Treatment for Opioid Use Disorder[274]
- Studying the effects of environmental factors, including opioids and other substance use, on early brain development from pregnancy through early childhood (HEALthy Brain and Child Development Study)[275]

Stimulants have also emerged as an overdose threat. From 2012 through 2019, the number of deaths involving methamphetamine increased more than 6-fold (from around 2,600 to more than 16,100), and the number involving cocaine more than tripled (from around 4,400 to nearly 16,000).[276] Given the urgent need to confront these dramatic increases, NIDA has prioritized the development of medications to treat stimulant use disorders.

National Institute on Drug Abuse
FY 2022 Request: $1,852.5 million
($372.2 million above the FY 2021 Enacted Level)

NIDA's efforts consist of Neuroscience and Behavioral Research; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; Clinical Trials Network; High-Tech Biomedical Product Development; Responding to the Opioid Crisis; Intramural Research Program (IRP); and Research Management and Support (RMS). The section entitled "Responding to the Opioid Crisis" details how NIDA is using dollars budgeted to the HEAL Initiative for the purpose of opioid research, but those dollars supplement base funding for opioid and pain research that are included within other NIDA program areas. Funding for both the HEAL initiative and other opioid and pain research will be increased from the FY 2021 Enacted level within NIDA's overall FY 2022 Request.

Neuroscience and Behavioral Research
FY 2022 Request: $603.8 million
($111.0 million above the FY 2021 Enacted Level)

NIDA's Division of Neuroscience and Behavior (DNB) advances knowledge of the basic biological mechanisms that underlie drug use and guide the development of novel prevention strategies and treatments for SUD. This includes identifying the effects of illicit substances on brain structure and function throughout the lifespan and across stages of drug use and SUD.

[271] heal.nih.gov/research/research-to-practice/jcoin
[272] heal.nih.gov/research/new-strategies/at-risk-adolescents
[273] heal.nih.gov/research/new-strategies/prevent-progression
[274] heal.nih.gov/research/new-strategies/duration-retention-discontinuation
[275] heal.nih.gov/research/infants-and-children/healthy-brain
[276] www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

Areas of support include studies to identify genetic variants and epigenetic modifications that influence vulnerability to SUD, the effects of drugs on gene expression and brain development and function; the interaction of genes with environmental conditions, including how they influence brain development; and basic processes underlying vulnerability and resilience to SUD. DNB supports research to elucidate the pharmacology of drugs and to leverage this knowledge towards the development of therapeutics to treat SUD, the adverse consequences of illicit drugs, and pain. One recent DNB-supported study found that prenatal exposure to cannabinoids altered the ways the brains of male, but not female, adolescent rats respond to cannabis, and identified a drug that could normalize those responses.[277] The DNB portfolio also includes research on non-pharmacological SUD treatments including transcranial magnetic stimulation, transcranial direct current stimulation, deep brain stimulation, and neurofeedback. Research on the interactions of complex neural circuits that underlie substance use, aversive responses to drugs that can inhibit drug-seeking, and interactions between neural and non-neuronal cells in these circuits is also supported in this portfolio. DNB funds technology development that enables studies of the functional organization of the living brain from cells to circuits to networks, and advanced computational approaches including theoretical modeling and novel methods for analyzing large, diverse data sets. One recent study found that activity in two different brain regions is linked with nicotine addiction severity and nicotine withdrawal, which is of particular interest because current smoking cessation treatments only affect one of those areas.[278] Such studies can help inform the creation of new and improved treatments with basic data on neural circuits. Finally, DNB supports mechanistic research to address real-world challenges faced in clinical care of SUD, such as polysubstance use, co-occurring conditions, and sex and gender differences in the development of SUDs.

One of NIDA's flagship basic science projects is the Adolescent Brain Cognitive Development (ABCD) study, which will follow children over 10 years, beginning at ages 9-10. Scientists are using techniques such as advanced brain imaging, interviews, and behavioral testing to determine how childhood experiences interact to affect brain development and—ultimately—social, behavioral, academic, and health outcomes, including substance use. Understanding how drugs interact with individual genetic, neurobiological, environmental, social, and developmental factors is essential to understanding what puts a person at risk for or confers resilience to addiction. Enrollment is complete with a total of 11,878 youth and their families participating. The study has already released baseline and one-year follow-up data from the full cohort, and more than 70 research papers have been published using these data, leading to a better understanding of the association between certain traits and experiences and brain structure and function, cognitive ability, and mental health. For example, a recent study has found that certain measures of obesity correlate with measurements of the density of an area of the brain responsible for motivation and reward, suggesting a possible neural mechanism for behavioral changes that lead to obesity.[279]

[277] pubmed.ncbi.nlm.nih.gov/31611707/
[278] europepmc.org/article/med/22493758
[279] pubmed.ncbi.nlm.nih.gov/31816020/

Epidemiology, Services, and Prevention Research
FY 2022 Request: $418.0 million
($76.9 million above the FY 2021 Enacted Level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR) supports integrated approaches to understanding and addressing the interactions between individuals and environments that contribute to drug use, addiction, and related health problems. Through Monitoring the Future, the Population Assessment of Tobacco and Health study, and other studies, DESPR monitors trends in drug use, including marijuana, vaping/e-cigarettes, and other drugs, as well as the potential risks and health outcomes related to these behaviors.

Preventing the initiation of substance use to minimize risks of harmful consequences is an essential part of addressing SUD. To this end, DESPR funds a portfolio of prevention research to understand and intervene upon mechanisms that underlie risk for and resilience to addiction and common comorbidities. This includes studies on how biological, psychosocial, and environmental factors operate to enhance or mitigate an individual's propensity to initiate substance use or to escalate from use to misuse to SUD across different developmental stages. This information, along with rapidly growing knowledge about substance use and addiction, is helping to inform the development of evidence-based prevention strategies.

DESPR also supports research on integrating prevention and treatment services into healthcare and community systems to reduce the burden of drug problems across the lifespan. For example, ongoing research is examining efforts to implement evidence-based SUD treatment in jails and prisons, expand the use of effective medications for OUD in primary care settings, develop strategies to reduce transmission of viral infections related to substance use (e.g., HIV and Hepatitis C), and increase uptake and retention in treatment for SUD and HIV. DESPR also funds research into the efficacy of screening, brief intervention, and referral to treatment in primary care settings for reducing drug use and SUD.

Therapeutics and Medical Consequences
FY 2022 Request: $142.3 million
($26.2 million above the FY 2021 Enacted Level)

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports research to evaluate the safety and efficacy of pharmacotherapies and devices to treat SUD. This work spans all phases of medical product development including synthesis and preclinical evaluation of potential therapeutics, clinical trial design and execution, and preparing regulatory submissions. Through these investments, NIDA helps to mitigate risks of developing new treatments for SUD. For example, in collaboration with US WorldMeds, DTMC supported clinical trials on LUCEMYRA™, the first medication targeted specifically to treat the physical symptoms associated with opioid withdrawal,[280] which was approved by the FDA in May 2018.

[280] http://www.drugabuse.gov/about-nida/noras-blog/2018/05/nida-supported-science-leads-to-first-fda-approved-medication-opioid-withdrawal

NIDA also supports research to identify promising compounds and make them more feasible for pharmaceutical companies to complete costly clinical studies for SUD indications. As part of the HEAL Initiative[SM], described below, DTMC leads efforts to develop new and repurposed medications to treat OUD.

NIDA is also prioritizing the development of pharmacological treatments for stimulant use disorders. This portfolio includes approaches from repurposing approved medications for other SUDs, to developing a novel monoclonal antibody that could prevent or reduce methamphetamine intoxication (see program portrait "Medications Development for Stimulant Use Disorder").

Clinical Trials Network
FY 2022 Request: $48.6 million
($8.9 million above the FY 2021 Enacted Level)

The overarching mission of the NIDA Clinical Trials Network (CTN) is to allow medical and specialty treatment providers, treatment researchers, patients, and NIDA to cooperatively develop, validate, refine, and deliver new treatment options to patients. The CTN comprises: 16 research nodes with 31 principal investigators affiliated with academic medical centers and large health care networks; two research coordinating centers; and more than 240 community-anchored treatment programs. This unique partnership enables the CTN to conduct studies of behavioral, pharmacological, and integrated treatment interventions in multisite clinical trials to determine effectiveness across a broad range of settings and populations. It also allows the CTN to ensure the transfer of research results to providers and patients. The network evaluates interventions, implementation strategies, and health system approaches to addressing SUD and co-occurring conditions such as mental illnesses and HIV. Using support from HEAL, the CTN has been able to expand its geographical reach, adding 5 new nodes in 2020 that can develop and test interventions in new populations.

The CTN is conducting studies to evaluate strategies for integrating OUD screening and treatment into emergency departments, primary care clinics, and American Indian/Alaska Native communities. The CTN is also conducting a study to examine the effects of medications for OUD in pregnant women. It has supported studies to capture important data for research on SUD in electronic health record (EHR) systems in primary care and emergency departments, and is currently developing and testing a clinical decision support tool that integrates with EHR systems to help doctors diagnose OUD and provide treatment or refer patients to appropriate care. Complementing the work supported through NIDA's DTMC, CTN studies are investigating the effectiveness and safety of pharmacotherapies (e.g., ADAPT-2), and transcranial magnetic stimulation for methamphetamine and cocaine use disorders.

High-Tech Biomedical Product Development
FY 2022 Request: $55.9 million
($10.3 million above the FY 2021 Enacted Level)

NIDA's Office of Translational Initiatives and Program Innovations (OTIPI) takes research discoveries in prevention, detection, and treatment of SUD into candidate health applications for commercialization. OTIPI manages NIDA's Small Business Innovation Research/Small Business Technology Transfer Programs to advance health applications. It also uses novel fit-for-purpose funding authorities, such as Prizes and Open Competitions, and establishes teaching programs that equip scientists with the competence to translate advances in addiction research into products.

Many of these efforts take the form of innovative new technology applications, from mobile apps that help patients find open beds in addiction treatment facilities or connect to support communities, to more sophisticated medical devices. Among OTIPI-funded technologies are hospital bassinets delivering calming signals to infants with neonatal abstinence syndrome; alarms for detecting the early signs of a drug overdose; and virtual reality systems to manage pain and reduce opioid analgesic use.

Responding to the Opioid Crisis
FY 2022 Request: $405.4 million
($135.1 million above the FY 2021 Enacted Level)

Through the HEAL Initiative[SM], NIDA continues to expand its support for research to combat opioid addiction. For example, NIDA is supporting a study to prevent the high rate of opioid misuse initiation associated with the transition from adolescence to adulthood. HEAL funds are also being used to accelerate the availability of novel treatments for OUD and overdose, including to develop longer-acting formulations of existing OUD drugs like buprenorphine, repurpose approved drugs for other indications for OUD, and develop novel antibodies to prevent the action of opioids in the brain.

The HEAL Initiative[SM] leveraged NIDA's existing CTN to expand the network by adding 5 new nodes that are supporting the development of 26 new research protocols. Two large projects address knowledge gaps around treatment initiation and retention. The first is a study of the efficacy of prevention interventions to halt the progression from risky opioid use to OUD. Researchers will test the efficacy of a Subthreshold Opioid Use Disorder Prevention (STOP) intervention in primary care settings to identify and address early-stage opioid misuse. The second is a study to test strategies to improve retention in medication treatment for OUD, as well as strategies to improve outcomes for patients stabilized on OUD medications who want to stop taking them. This will be the first study of medications to treat OUD to follow prospectively a large sample of patients through discontinuation.

HEAL also supports studies that are developing effective implementation strategies for evidence-based interventions. The Justice Community Opioid Innovation Network (JCOIN) is testing strategies to expand effective OUD treatment and care for people in justice settings in partnership with local and state justice systems and community-based treatment providers, which will fully launch as clinical trials in early 2021. The HEALing Communities Study, a multisite implementation research study, is investigating coordinated approaches for deploying evidence-

based strategies to prevent and treat opioid misuse and OUD tailored to the needs of local communities. The goal of the study is to reduce opioid-related overdose deaths by 40 percent over 3 years. Research sites are partnering with 67 communities highly affected by the opioid crisis in 4 states to measure the impact of these efforts.

Finally, the HEALthy Brain and Child Development Study is a NIDA and HEAL-led, trans-NIH effort to add to our understanding of early brain development trajectories. This study will establish a cohort of pregnant women and follow their children through the first decade of their lives to determine how environmental factors, including maternal drug exposure and genetics, influence early brain development and behavioral and clinical outcomes such as mental illnesses and addiction.

Intramural Research Program
FY 2022 Request: $105.2 million
($3.1 million above the FY 2021 Enacted Level)

NIDA conducts research in high priority areas through its Intramural Research Program (IRP). The IRP portfolio includes research to: 1) elucidate the mechanisms underlying the development of SUDs; 2) evaluate potential new therapies for SUDs, including pharmacological and non-pharmacological interventions; and 3) identify and characterize emerging drugs such as synthetic opioids, stimulants, and cannabinoids.

One example of treatment evaluation at the IRP is a bench-to-bedside project in which IRP investigators are testing a novel compound to treat OUD that activates the same receptors as traditional opioids but has only a subset of their cellular actions. IRP investigators are testing whether the compound reduces self-administration of opioids in animal models and people with OUD, and whether it prevents opioid withdrawal with fewer side effects than medications in current use. If successful, this compound could be a new medication for OUD.

The IRP is also working with the National Center for Advancing Translational Sciences on a dopamine D3 receptor antagonist that could be taken together with opioid pain relievers to reduce the chance of developing OUD. Preliminary animal studies suggest that the compound reduces opioid self-administration and drug-seeking behavior without reducing the pain-relieving effects of opioids. This compound holds promise as an adjunct to opioid treatment for pain and potentially for OUD.

Non-pharmacological addiction treatments are also being developed in NIDA's IRP. The on-site treatment-research clinic includes efforts to develop a smartphone app that uses machine learning to detect or predict stress, craving, and drug use within hours—and a parallel project to develop content that the app could deliver "just in time." Because current apps purporting to serve these functions do not meet scientific standards of evidence, IRP is addressing a major gap in mobile health. Using passive measurement and digital phenotyping techniques, the IRP is also developing interventions and big data methodologies to prevent HIV transmission associated with unprotected sex in the context of substance use.

Research Management and Support
FY 2022 Request: $73.3 million
($0.7 million above the FY 2021 Enacted Level)

Research Management and Support activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Additionally, the functions of RMS encompass strategic planning, coordination, and evaluation of NIDA's programs, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. RMS staff at NIDA play leadership roles in helping to coordinate NIDA's involvement in the NIH HEAL Initiative℠, spearheading NIH's response to the opioid overdose epidemic.

In addition to the infrastructure required to support research and training, NIDA strives to provide evidence-based resources and educational materials about substance use and addiction, including information about timely public health topics such as opioid overdose prevention, marijuana research, use and consequences of vaping, synthetic drug trends, and medications for treatment of SUD, including OUD. To this end, the RMS portfolio incorporates education and outreach activities to inform public health policy and practice with the goal of ensuring that NIDA is the primary trusted source for scientific information on drug use and addiction. Staff supported by NIDA's RMS budget coordinate key activities that help to train the next generation of addiction scientists. In addition, NIDA's RMS portfolio includes the NIDAMED initiative,[281] which is aimed at engaging and educating clinicians in training and in practice in the latest science related to drug use and addiction.

National Institute on Alcohol Abuse and Alcoholism
FY 2022 Request: $63.2 million
($1.7 million above the FY 2021 Enacted Level)

Although the prevalence of alcohol consumption among 8th, 10th, and 12th graders has declined by one-third over the past decade, alcohol remains the most widely used substance among U.S. youth. Binge drinking[282] and high intensity drinking (i.e., two or more times the gender-specific binge drinking thresholds) among young people remain significant concerns. These drinking patterns are particularly troubling as they increase risks for poor academic performance, alcohol-related blackouts, injuries, overdoses, sexual assault, unsafe sexual behavior, AUD, and other detrimental consequences.

Characterizing the effects of alcohol exposure on the developing adolescent brain

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. NIAAA's Neurobiology of Adolescent Drinking in Adulthood

[281] www.drugabuse.gov/nidamed-medical-health-professionals
[282] NIAAA defines binge drinking as a pattern of drinking that increases an individual's blood alcohol concentration to 0.08 percent or higher. This typically occurs after 4 drinks for women and 5 drinks for men – in about 2 hours. Research suggests that fewer drinks in the same timeframe result in the same blood alcohol centration in youth.

(NADIA) consortium enables investigators to examine, using animal models, the mechanisms by which adolescent drinking leads to changes in brain structure and function that persist into adulthood. For example, preclinical research conducted through NADIA established a link between adolescent alcohol exposure and specific molecular changes in the brain that contribute to increased anxiety in adulthood. Building on basic research, NIAAA funds collaborative research to assess the impact of adolescent drinking on brain development in longitudinal studies in humans. The National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a longitudinal study of approximately 800 youth ages 12-21, was designed to identify brain characteristics that may predict alcohol misuse and to elucidate the neurodevelopmental effects that occur as a consequence of alcohol exposure. NCANDA research has characterized the alterations in brain development that occur after adolescent alcohol exposure, including weakened connections between brain networks involved in the regulation of emotional and cognitive functioning. Recent studies have linked childhood trauma with future alcohol misuse in adolescence, suggesting potential benefits of targeted alcohol interventions among trauma-exposed youth. NCANDA laid the methodological foundation for NIH's ABCD study, the largest longitudinal study of brain development and child health in the United States.

Preventing underage drinking

NIAAA's underage drinking portfolio includes studies to develop, evaluate, and implement evidence-based prevention programs for youth. These programs include individual-, family-, school-, community-, and environmental-level interventions for underage individuals at large, as well as those designed or adapted for underserved populations and specific settings, including the college setting. The college environment remains a high priority target for reducing underage drinking. NIAAA developed the College Alcohol Intervention Matrix (CollegeAIM) to assist college and university officials in addressing alcohol misuse on their campuses. CollegeAIM is a user-friendly guide and website that rates over 60 evidence-based alcohol interventions in terms of effectiveness, cost, and other factors, allowing school officials to select among the many potential interventions to address harmful and underage student drinking. NIAAA is also interested in addressing alcohol misuse in young adults who are not enrolled in college, and challenges remain for targeting this population.

Promoting implementation of alcohol screening and brief intervention among youth and young adult populations

Increasing implementation of alcohol screening and brief intervention among youth and young adult populations in health care and other appropriate settings is a priority area for NIAAA. Alcohol screening and brief intervention in primary care has been recognized as a leading preventive service for reducing alcohol misuse in adults, and a growing body of evidence demonstrates its effectiveness in preventing and reducing alcohol misuse in youth. NIAAA-supported research has found that, relative to usual care, adolescent patients (ages 12-18) subjected to screening, brief intervention, and referral to treatment in pediatric primary care settings had improved substance use, mental health, and health outcomes over a three-year follow up period. To facilitate the integration of screening and brief intervention into primary care, NIAAA developed a youth alcohol screening tool, Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide, to enable pediatric and adolescent health

practitioners to identify patients at risk for underage drinking and associated problems. This screening tool has been validated among youth in pediatric emergency room settings, in school settings, in primary care settings (including among racially and ethnically diverse youth), and among youth with chronic health conditions.

PERFORMANCE

Information regarding the performance of the drug control efforts of NIH is based on agency documents related to the Government Performance and Results Modernization Act and other information that measures the agency's contribution to the *Strategy*. NIH's performance measures are representative of Institute and Center contributions to NIH's priorities regarding specific scientific opportunities, identified public health needs, and Presidential priorities. Such measures, reflecting NIH's broad and balanced research portfolio, are not Institute- or Center-specific. Some measures are trans-NIH, encompassing lead and contributing Institutes and Centers. This approach reflects NIH's commitment to supporting the best possible research and coordination of research efforts across its Institutes and Centers.

NIDA and NIAAA lead and support a number of trans-NIH measures in the Scientific Research Outcome (SRO) functional area. While NIDA and NIAAA engage in many research and related activities, four measures best reflect the breadth of their efforts in the prevention and treatment of substance use, misuse, addiction, and its consequences.

One of these measures, created by NIDA, is SRO-5.2: "By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders." This new measure, which began reporting in FY 2020, is indicative of NIDA's portfolio of efforts to support the development and testing of prevention interventions for SUD. The annual targets for this goal reflect targeted investments in particular areas of need or opportunity, including vulnerable periods during critical life transitions for OUD, and reduction of vaping in teens. This measure replaces NIDA's reporting for SRO-5.15, which focused on SUD and prescription misuse in adolescent populations. NIDA's contribution to SRO-5.15 ended in FY 2019 as planned.

NIDA also created SRO-4.9: "By 2023, evaluate the efficacy of new or refined interventions to treat opioid use disorders." This measure began in FY 2018 and reflects NIDA's increasing focus on finding solutions to the current crisis of opioid overdose and addiction. As part of the NIH HEAL Initiative, NIDA has been supporting a variety of focused medications development research at varying stages of the clinical pipeline. Originally scheduled to be discontinued beginning in FY 2021, this measure has been extended through FY 2023 to reflect the five-year time horizon of FY 2018 investments in the development and evaluation of OUD interventions within HEAL.

SRO-5.15, created by NIAAA, aims to: "By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and substance use disorders and their consequences in underage populations." This measure, which began in FY 2014, is indicative of NIAAA's efforts to support research to foster the development and implementation of prevention-based strategies for reducing substance misuse and addiction. NIH's prevention portfolio encompasses a broad range of research on the efficacy and cost effectiveness of primary prevention programs—designed to prevent substance use before it starts, or prevent escalation to misuse or addiction—and how these programs can be enhanced by targeting prevention efforts toward populations with specific vulnerabilities (genetic, psychosocial, or environmental) that affect their likelihood of substance use or SUDs.

In addition to SRO-5.15, NIAAA created SRO-4.15: "By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations." This measure began in FY 2019 and reflects NIH's ongoing commitment to research on the development of interventions to improve treatment of alcohol-related problems among youth.

National Institute on Drug Abuse		
Selected Measures of Performance	**FY 2020 Target**	**FY 2020 Achieved**
Scientific Research Outcome-5.2: By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders (SUD).	Conduct 3-5 pilot studies to test the efficacy of promising prevention interventions for SUD.	Nine prevention pilot studies were conducted as part of the Helping to End Addiction Long-term (HEAL[SM]) Initiative.
Scientific Research Outcome-4.9: By 2023, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD).	Conduct 1 pre-clinical and 1 clinical study of a longer acting formulation of a medication for the treatment of opioid use disorders or opioid overdose.	NIH conducted a pre-clinical development study of a novel long-acting formulation of nalmefene for treating OUD, and a clinical study of a novel long-acting implant that delivers naltrexone, an effective treatment for OUD.

Prevention – Scientific Research Outcome-5.2
The FY 2020 target was met. NIH funded nine prevention pilot studies that were conducted in FY 2020, under the auspices of the Helping to End Addiction Long-term (HEAL[SM]) Initiative. These grants used the two-phase, milestone-based UG3-UH3 grant mechanism, which allows for grants that successfully complete pilot-study progress milestones to apply to advance into larger clinical studies. Of those nine pilot studies, seven completed their pilots and were eligible for transition. (Two of the studies had planned for two-year pilot phases, so were not eligible for transition.) Three of the seven transitioning studies are highlighted as examples below.

One transitioning study involves modifying an existing alcohol and drug prevention intervention designed for American Indian/Alaska Native youth to be appropriate for opioid prevention in young adults. The study conducted focus groups to determine how best to engage the target population, adapted and enhanced the intervention to specifically address opioid use, and pilot-tested the intervention. The scaled-up study will test the intervention in larger groups over a 12-month period, examine the mechanisms by which it produces change, and explore approaches to making it sustainable over time.

Another transitioning study is focused on preventing OUD among adolescents/young adults ages 18-24 years experiencing homelessness and explores whether providing housing in addition to opioid and related risk reduction services could improve outcomes. The pilot study demonstrated feasibility of recruitment, locating housing and placement into housing, and delivery of prevention services through strengths-based outreach and advocacy. Partnerships with community-based homeless youth service providers and landlords have been established for the post-pilot phase, housing has been identified, and Institutional Review Board (IRB) approval has been obtained. The scaled-up study will compare individuals randomly assigned to receive housing alongside opioid and related risk prevention services to individuals who receive those services alone.

A third study developed a plan to leverage technology that is appealing to adolescents and young adults to facilitate delivery of an emergency department-based intervention via health coaches. In their transitioning pilot, researchers were able to adapt promising health coach-delivered intervention and pilot test feasibility/acceptability in adolescents and young adults, as well as actively engage hospital administration leadership in the study. As the project transitions to the next phase, it will begin testing the intervention in a sample of over 1,000 adolescents and young adults in emergency department settings.

Treatment – Scientific Research Outcome-4.9
The FY 2020 target was met. NIH funded the pre-clinical development of a new implant that will deliver nalmefene, a drug that blocks opioid signaling, over a six-month period. The goal is to advance this compound to be tested in humans for the prevention of relapse to opioid addiction in patients following opioid detoxification. This long-acting formulation will use the Proneura® technology that has been successful in an FDA-approved long-acting formulation of buprenorphine. This long-acting nalmefene is completing the necessary nonclinical safety, toxicology, pharmacokinetic and manufacturing activities to start studies in humans (clinical trials) and begin the process of applying for FDA approval.

In FY 2020, NIH also funded a clinical trial to evaluate the safety and efficacy of GM0017, an implant that delivers the opioid antagonist naltrexone for six months. This compound is being developed for prevention of opioid relapse in individuals with OUD who have been detoxified. Recruitment for this study has been delayed due to the COVID-19 pandemic, but it is expected that clinical results will soon be presented to the FDA.

National Institute on Alcohol Abuse and Alcoholism		
Selected Measures of Performance	**FY 2020 Target**	**FY 2020 Achieved**
Scientific Research Outcome 5.15: By 2025, develop, refine and evaluate evidence-based intervention strategies and promote their use to prevent substance misuse and SUDs and their	Develop a digital technology-based intervention to prevent or reduce alcohol misuse in underage individuals.	Researchers developed and tested technology-based interventions to prevent and reduce underage drinking.

consequences in underage populations.		
Scientific Research Outcome 4.15: By 2021, evaluate three interventions for facilitating treatment of alcohol misuse in underage populations.	Test a behavioral therapy for intervening with alcohol misuse in an underage population.	Researchers tested the effectiveness of multiple behavioral interventions for reducing alcohol use and other harmful behaviors in underaged incarcerated and homeless youth.

Prevention – Scientific Research Outcome-5.15
The FY 2020 target was met. NIAAA-funded investigators developed and evaluated digital technology-based interventions to prevent or reduce alcohol misuse among underage college and high school students.

Research indicates that perceived norms about alcohol use are a strong correlate of alcohol misuse that predict alcohol consumption over time. Perceived norms among college students tend to be exaggerated relative to actual drinking norms and may have adverse effects on both individuals and the community. NIAAA-supported researchers recently created a text messaging intervention for heavy drinking, underage college students that was designed to realign perceived drinking norms with actual drinking norms of their campus peers. Heavy drinking in the study was defined as more than four drinks per day or more than 14 drinks per week for males, and more than three drinks per day or more than seven drinks per week for females in the past 30 days. Participants were assigned to either an experimental or control condition. The experimental group received text messages containing information about campus-specific drinking norms while the control group received text messages containing unique facts unrelated to alcohol. Text messages were sent daily to participants over a period of 10 weeks. The intervention was shown to be effective at reducing peak alcohol consumption and alcohol-related consequences three months after the beginning of the study. These intervention effects, however, were not maintained another three months later. This study demonstrates the feasibility of text-based norms interventions in reducing alcohol use and its consequences around the time of engagement with the intervention.

In FY 2020, NIAAA also supported research to develop and test digital, school-based interventions aimed at preventing and reducing alcohol use among high school students. One ongoing study focuses on developing and testing the efficacy of an e-learning intervention to improve school staff's knowledge, skills, and self-efficacy in supporting sexual minority youth and protecting them from bullying victimization. Prior research has demonstrated that sexual minority youth have an increased risk of future alcohol and other substance use and supportive school environments can help reduce substance use.

Another school-based study recently demonstrated that eCHECKUP TO GO is effective in reducing alcohol-related cognitive risk factors and alcohol use in both male and female high school seniors. eCHECKUP TO GO is a brief, web-based personalized feedback intervention

designed to reduce alcohol use by targeting cognitive risk factors (e.g., perceived drinking norms among peers) and protective behavioral strategies (e.g., behaviors that minimize the risk of alcohol-related consequences).

In combination with the FY 2019 actual performance which demonstrated the efficacy of interventions designed to prevent alcohol misuse among college-age individuals, the digital interventions described above contribute to the Institute's goal of evaluating and promoting evidence-based intervention strategies to prevent substance misuse in underage populations.

Treatment – Scientific Research Outcome-4.15
The FY 2020 target was met. NIAAA-supported investigators evaluated a treatment invention in an underage, incarcerated population. Research suggests that combining evidence-based behavioral interventions – e.g., motivational interviewing plus cognitive behavior therapy (MI/CBT) – that focus on motivation, problem-solving, communication, mental health, and substance use may be useful in improving outcomes for incarcerated youth. In the current study, NIH-supported researchers conducted a randomized controlled clinical trial to evaluate the effectiveness of MI/CBT in mitigating alcohol and marijuana use and aggression among incarcerated youth. The control condition, RT/SET, was a combined intervention consisting of relaxation training (a mindfulness approach) and treatment as usual (substance-education and twelve step programming). Eligibility criteria included using alcohol or marijuana at least monthly; heavy drinking (defined as more than five standard drinks for boys, more than four standard drinks for girls) at least once; or alcohol or marijuana use in the four weeks before either the offense for which they were incarcerated, or before they were incarcerated. The researchers found RT/SET to be slightly more effective than MI/CBT in reducing percent of heavy drinking days and significantly more effective in reducing alcohol-related aggression after the youths' release from incarceration. RT/SET and MI/CBT both reduced aggression after release but neither showed significant effects on marijuana-related behavioral outcomes. These results suggest that RT/SET may be a viable, lower-cost intervention for delivery in youth correctional settings; however, additional research on RT/SET is needed.