Monica M. Bertagnolli, M.D.
Director, National Institutes of Health

On behalf of the National Institutes of Health (NIH), I am transmitting the Congressional Justification of the NIH request for the fiscal year (FY) 2025 budget. This request for a total program level of $50.1 billion that will support NIH's mission to turn biomedical research discoveries into better health for all. This budget request encompasses investments in foundational research, which lay the groundwork for future health advances, as well as efforts to prevent disease and develop cures. Also included are NIH efforts to support and maintain a robust, talented, and diverse workforce of researchers at all career stages.

After being confirmed on a bipartisan basis by the U.S. Senate, I was honored to begin working as the 17th Director of NIH on November 9, 2023. On behalf of NIH, I extend my heartfelt gratitude to Dr. Lawrence Tabak for serving as Acting Director of NIH since December 2021 when Dr. Francis Collins stepped down as head of the agency.

From recent advances in gene therapies for sickle cell disease to new vaccines to protect against respiratory syncytial virus to exciting initiatives advancing artificial intelligence for health, NIH research has made significant contributions to improving the health of people in the United States and around the world. But we still have work to do: Families across the country are grappling with new cancer diagnoses, facing high rates of maternal mortality, struggling with ill health from Long COVID, losing loved ones to the opioid overdose crisis, and struggling to manage chronic diseases, among many other challenges. According to a 2021 consensus study from the National Academies of Sciences, Engineering, and Medicine, the United States is experiencing rising mortality rates among working-age adults. Biomedical research remains crucial to reversing this trend.

We will continue to foster research that is responsive to new and ongoing health issues. Importantly, NIH research occurs not only in the laboratory and the clinic but also in communities across the country. To tackle the most persistent and complex problems, and to restore trust in science and the value it brings to society, we need to bring more members of the public into the research enterprise as our partners in discovery. Income, age, race, ethnicity, geographic location, and disability status should not be barriers to participating in research or to benefitting from research advances.

Traditional clinical research networks primarily exist in academic medical centers and aim to recruit people with specific conditions. However, many people, especially those in rural and other underserved areas, do not have access to these types of trials and often do not benefit from the resulting knowledge. We envision connecting our research to communities of all types through the primary care setting. By meeting people where they already receive care and supporting efforts from those providing medical care, NIH could leverage the use of electronic health records infrastructure to gather data and conduct research securely. My hope is to integrate basic research with public health and clinical care data, and, crucially, more rapidly

disseminate evidence to guide patient and provider decisions, tracking progress for outcomes that matter to the people we serve.

As we look ahead, advanced scientific methods and new data analytics and technologies are unlocking possibilities to harness data in ways that achieve faster and more definitive results. As the growing rush of information comes in, we must work to convert that information to knowledge and connect what we learn to everyday life and clinical practice. For example, with advances in artificial intelligence, we can identify patterns in large, complex datasets and can evaluate the likely outcomes of different courses of treatment. We aim to harness the National Library of Medicine as a focal point to support multidisciplinary data sharing and use for biomedical research. By democratizing access to data and analytic tools, researchers and clinicians outside major medical centers could benefit from and contribute to knowledge generation more easily.

I believe in the power of science to bring us answers and of the research community to channel new knowledge in ways that transform lives. However, our efforts will only succeed if our programs are inclusive and participants diverse—across geography, demographics, and socioeconomics.

Our goal is to link the laboratory to the clinic and to communities that encompass the diversity of our country, and make sure that the information we collect is used safely and ethically to improve health for all people. This work will build on existing programs, structures, and technology at NIH. If we integrate crucial, fundamental knowledge with clinical practice and our everyday lives, I know we can find solutions to the health challenges facing our communities. After all, a guiding principle at NIH is that our work is not finished when we deliver scientific discoveries; our work is finished when all people are living long and healthy lives.

Monica M. Bertagnolli, M.D.

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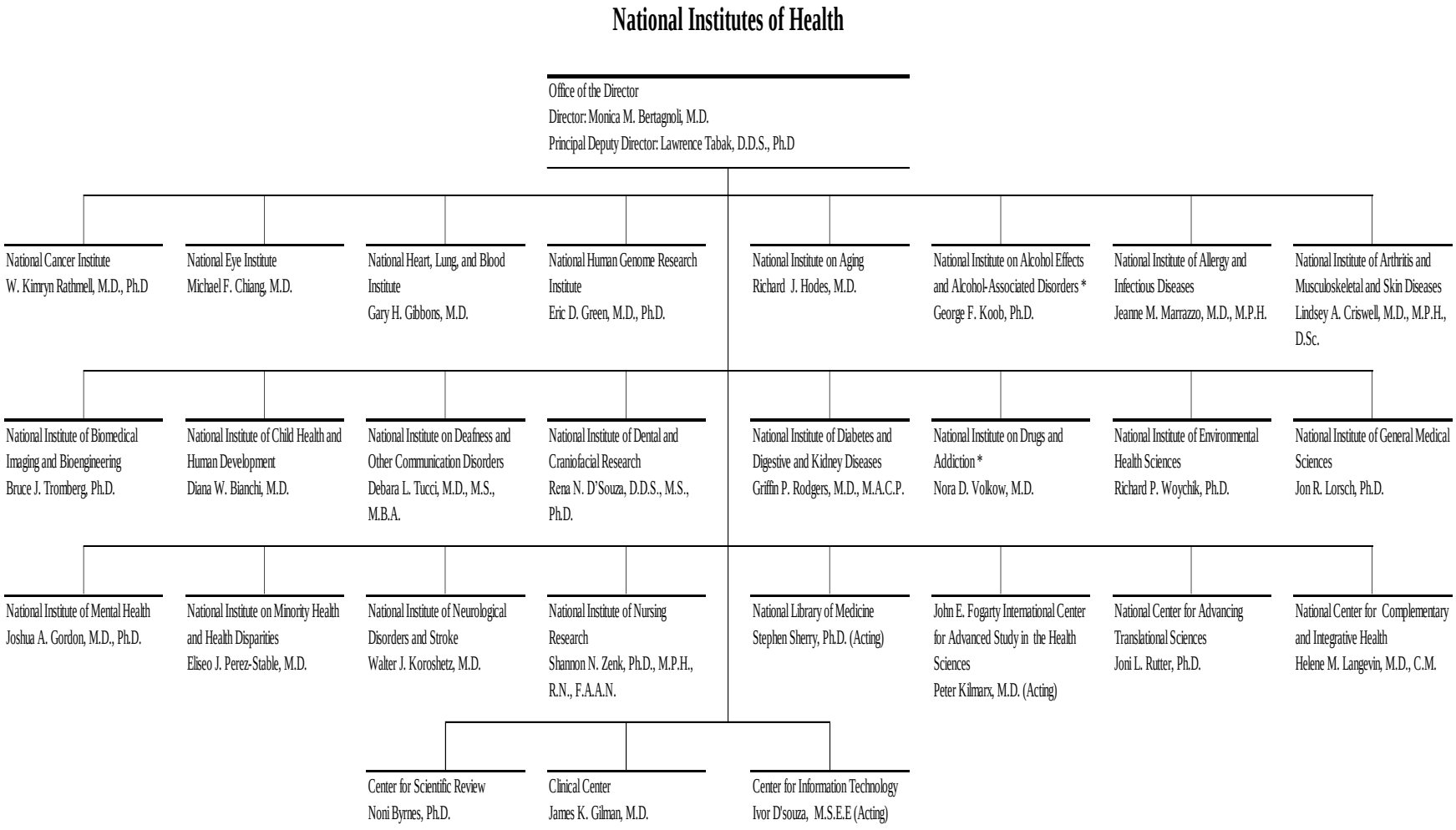
DRUG CONTROL PROGRAMS

General Notes

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

ORGANIZATION CHART



*The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction and to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.

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.[1] 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 largest 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 well-being. NIH works to develop, maintain, and renew scientific, human, and physical resources that will ensure the Nation's capability to address the public health concerns of the Nation as well as to treat and prevent disease and poor health. 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.

[1] In 2021, the Advisory Committee to the NIH Director (ACD) Working Group on Diversity, Subgroup on Individuals with Disabilities issued a report, including a recommendation to update the NIH mission statement to remove "reducing disability". A proposed revised mission statement was developed, and public feedback was requested through a Request for Information (RFI) (NOT-OD-23-163). NIH is currently reviewing the responses to inform its decision.

OVERVIEW OF BUDGET REQUEST

Introduction

For Fiscal Year (FY) 2025, the National Institutes of Health (NIH) requests a total program level of $50.1 billion, a $2.4 billion increase from the FY 2023 Final level.[2] The NIH budget level is intended to support critical research conducted in service to the agency's mission and support new and ambitious priority investments necessary for improving the health of the Nation.

NIH's investment in biomedical research is critical to advancing healthcare discovery that benefits the health and well-being of the Nation. The agency's primary goals are to facilitate important advances in biomedical research, ensure the accessibility of NIH-funded research, and maintain the highest levels of public trust in the biomedical research enterprise. NIH strives to produce translatable, transparent findings that result in robust, reproducible data, and to ensure the data is shared with the public in an accessible manner. NIH also continues to promote the principles of scientific integrity and rigor within the biomedical research community, to ensure that NIH-supported researchers and staff are held to the highest ethical standards to support the best science.

Key to the promotion of the best biomedical science is building and maintaining the biomedical workforce. NIH appreciates the importance of harnessing unique ideas from diverse perspectives, which in turn leads to diversity of thought and discovery. NIH seeks the brightest minds from every stage of the biomedical career trajectory, including early-stage, mid-career, and late-career scientists. This commitment underscores the critical importance of inspiring the next generation of biomedical researchers who will make the scientific discoveries of tomorrow.

Historically, NIH has been a leader in biomedical research worldwide, and discoveries made possible by NIH funding have saved countless lives and continue to have a positive impact on the health and well-being of the Nation. NIH intends to maintain this trajectory of discovery into the future. This will be accomplished through the continued development of a robust workforce with diverse perspectives, leveraging lessons learned from recent and ongoing public health challenges, and developing innovative science that will fuel the discoveries of tomorrow.

A History of Excellence: The Returns from Long-Term Investments in NIH Basic, Translational, and Clinical Research

Prior investments in NIH have saved lives and will continue to drive further discoveries. This can most easily be identified in advances in medical interventions resulting from clinical research – that is, research that directly studies the use of new diagnostic and treatment advances in people. However, these clinical advances would not be possible without decades of prior basic and translational research paving the way for clinical discovery. No greater testament of this can be found than the fact that NIH has supported a total of 169 researchers who have

[2] This program level excludes the Advanced Research Projects Agency for Health (ARPA-H). The FY 2025 Budget request for ARPA-H, which reports directly to the Secretary of Health and Human Services, is outlined in a separate Congressional Justification volume.

received or shared 101 Nobel Prizes. One of the latest additions to this legacy of excellence is the NIH-funded work that led to the award of the 2022 Nobel Prize for the development of a transformative scientific approach known as "click chemistry."[3] This form of chemistry has made it possible for researchers to snap together molecular building blocks to form hybrid biomolecules, often with easy-to-track imaging agents attached. Not only has click chemistry expanded our ability to explore the molecular underpinnings of a wide range of biological processes, but it has provided us with new tools for developing drugs, diagnostics, and a wide array of "smart" materials.[4]

NIH's lengthy history of biomedical excellence is measured not only in the awards received by the researchers it funds but also in the lasting impact that NIH research has had on people's lives – from major medical advances to simple everyday health choices. For example, NIH – in partnership with the Food and Drug Administration (FDA) – recently celebrated the 10th anniversary of the Tobacco Regulatory Science Program (TRSP), which aims to reduce the public health impact of tobacco use across the country. This unique partnership represents a new field of study called tobacco regulatory research, which informs proposed regulations for tobacco products through the continued development of strong scientific evidence. The TRSP brings together scientists from diverse fields, such as epidemiology, chemistry, toxicology, addiction, and psychology, to shed light on why people try and continue to use tobacco, how tobacco use affects health, and which policies might help reduce the risk of harm. This extremely productive partnership has resulted in more than 400 research grants,[5] all peer-reviewed and designed to increase our understanding of existing and emerging tobacco products and their associated health risks. These studies include research unpacking the impacts of menthol cigarettes on nicotine dependence and assessing how flavored tobacco products target socioeconomically disadvantaged populations.[6] The TRSP is a prime example of how NIH's long-term investments yield expansive, far-reaching data.

One of the most recent and noteworthy examples of NIH leveraging its long commitment to basic and translation research is its role in the development of vaccines for SARS-CoV-2. Decades of NIH-supported research, including investments in HIV research, revolutionized vaccine development, leading to the first two FDA-approved vaccines for COVID-19 and the 2023 Nobel Prize in Physiology or Medicine.[7] These vaccines use messenger RNA (mRNA) to train the body to recognize SARS-CoV-2, the virus that causes COVID-19. The development of these vaccines has led to countless lives being saved and has aided the Nation in the process of emerging from the COVID-19 pandemic.

[3] nobelprize.org/prizes/chemistry/2022/press-release/
[4] directorsblog.nih.gov/2022/10/11/the-chemistry-clicked-two-nih-supported-researchers-win-2022-nobel-prize-in-chemistry/
[5] prevention.nih.gov/tobacco-regulatory-science-program/funded-research-tobacco-regulatory-science-program
[6] directorsblog.nih.gov/2023/05/09/10-years-of-protecting-public-health-through-tobacco-regulatory-research/
[7] nobelprize.org/prizes/medicine/2023/press-release/

Addressing Today's Challenges: NIH Continues to Fund Biomedical Research That Saves Lives

While it is important to acknowledge the decades of previous biomedical advancements made possible by NIH investments, it is imperative to continue addressing the vast array of public health challenges that persist, which can affect health across the lifespan. NIH supports biomedical and behavioral research applicable to the full spectrum of public health challenges and needs, and NIH continues to invest in research that benefits the well-being of all individuals across their lifespan, regardless of their background, race, age, gender, sexual orientation, or health status.

Addressing Public Health Across the Lifespan

21st Century Cures Act

The FY 2025 request level provides $127.0 million in funding authorized under the 21st Century Cures Act (Cures Act) for the *All of Us* Research Program and the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, a decrease of -$742.0 million in Cures Act funding for these programs compared to FY 2023. The request proposes a corresponding increase of $742.0 million in non-Cures Act discretionary resources to hold *All of Us* and BRAIN flat to FY 2023, for a total of $1,221.4 million in Cures Act and non-Cures Act funding. In addition, NIH proposes to continue discretionary funding for the Cancer Moonshot – for which authorized Cures Act funding ended in FY 2023 – requesting non-Cures Act discretionary funding of $716.0 million in FY 2025, an increase of $500.0 million from the $216.0 million of Cures Act funding provided in FY 2023, while also adding $1,448.0 million in new mandatory funding.

All of Us. With a total request of $541.0 million in FY 2025, including $36.0 million in 21st Century Cures Act authorized funding and $505.0 million in non-Cures Act base funding to hold the program flat to the FY 2023 Final level, the *All of Us* Research Program will continue its mission to accelerate health research and medical breakthroughs to enable individualized prevention, treatment, and care. *All of Us* aims to deliver one of the largest and richest biomedical data sets that protects participant privacy while catalyzing an ecosystem of communities, researchers, and funders to make *All of Us* data an indispensable part of health research. *All of Us* is on its way to enrolling one million or more participants by the end of 2026, with nearly 758,000 participants from all 50 states, D.C., and Puerto Rico enrolled as of January 2024, of whom 520,000 have completed the initial steps of the program. More than 3,600 researchers across more than 435 institutions have registered to access *All of Us* data. Nearly half of the participants self-report being racial and ethnic minorities, and over 80 percent report being from communities historically underrepresented in biomedical research.

All of Us provides researchers with access to one of the world's largest and most diverse datasets of its kind, and this resource has the ability to inform thousands of studies across all sectors of the biomedical research ecosystem and influence a new era in which researchers, health care providers, technology experts, community partners, and the public work together toward the development of individualized health care. *All of Us* is

revolutionizing large genomic studies that have historically lacked diversity through a partnership with participants and diverse communities across the country. Participants share data about themselves, including physical measurements, survey responses, electronic health records, DNA samples, and data from wearable devices (e.g., Fitbits). Researchers have access to nearly 250,000 genome sequences, 313,000 genotyping arrays, and more than 1,000 detailed long-read sequenced genomes. Data accessible via the Researcher Workbench is broadly available to researchers from academic, nonprofit, or health care organizations with a signed agreement that helps ensure data is shared in a way that protects participant privacy and security concerns. The resource is also being used by both intramural and extramural labs, and more than 7,410 researchers have registered to use the data from in excess of 600 institutions, including 93 minority-serving institutions, to inform more than 7,100 ongoing research projects.

All of Us has a special focus on engaging American Indian/Alaska Native (AI/AN) communities interested in medical research, to close information gaps and help increase health equity. To support the participation of AI/AN individuals in the *All of Us* program, a series of virtual information sessions for Tribal communities and Urban Indian Organizations were conducted in partnership with the Tribal Health Research Office (THRO) in the NIH Office of the Director. In line with the March 2021 *All of Us* Tribal Consultation Report,[8] recruitment and engagement on Tribal lands is prohibited without approval from Tribal Nations, and the program developed a Tribal engagement plan to support program commitments to Tribes and incorporated Tribal priorities, such as Tribal data sovereignty, cultural sensitivity and awareness of AI/AN specific policies, training and education, data protections, research transparency, and the return of information to Tribal communities. In support of those efforts, *All of Us* also announced three awards in September 2023 totaling $1.5 million to institutions partnering with AI/AN and Indigenous communities to advance Tribally-led participation in precision medicine research and to enhance AI/AN workforce development.

Additional non-Cures funding as requested to maintain total *All of Us* funding at $541.0 million, will support enrollment of new participants, aiming to reach the 2026 enrollment goal and begin planned pediatric enrollment, while supporting activities to provide the program's robust and rich data to researchers.

NIH BRAIN Initiative®. 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. The NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative® is an ambitious program to develop and apply new tools and technologies to answer fundamental questions about the brain and ultimately to inspire new treatments for brain diseases. The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute of Mental Health (NIMH) are leading partners in the NIH BRAIN Initiative®, working with eight other NIH Institutes, Centers, and Offices (ICOs). The BRAIN Initiative® has invested over $3 billion in more than 1,300 research projects, engaging scientists from many areas of expertise as well as mathematicians, engineers, and physicians in individual labs and

[8] allofus.nih.gov/all-us-research-program-tribal-consultation-final-report

inter-disciplinary teams. The BRAIN Initiative® has also led to positive change in the culture of neuroscience research through its emphasis on neuroethics, diversity and inclusion, and promoting infrastructure and practices for sharing research data and tools.

With total funding requested at $680.4 million for FY 2025, including $91.0 million in 21st Century Cures Act authorized funding and $589.4 million in non-Cures Act base funding to hold the program flat to the FY 2023 Final level, the BRAIN Initiative® promotes scientific advances that provide opportunities to understand the structure and function of the brain at an unprecedented level of detail. Researchers throughout neuroscience are rapidly adopting these advances, and the BRAIN Initiative® is both dramatically enhancing existing methods and developing entirely new technologies to study and manipulate brain circuits. BRAIN Initiative® activities will continue to be guided by the three overarching priorities as recommended in the BRAIN® 2.0 Working Group reports published in 2019: (1) stay on course to accomplish the original goals set out in the BRAIN® 2025 report (published in 2014); (2) ensure sufficient funds for new projects each year to continue the pace of innovation of the Initiative and pursue emerging opportunities across all mission areas; and (3) launch large-scale transformative projects that will significantly change the trajectory of neuroscience research and the treatment of human brain disorders. The BRAIN Initiative® will also continue to work to shift the research culture within neuroscience through its emphasis on neuroethics, diversity and inclusion in the research community, and data-sharing practices to enable and enhance the scientific and technological advances from this initiative. Additional non-Cures funding as requested to maintain total BRAIN® funding at $680.4 million will support FY 2025 commitments for existing research projects and planned investments in new competing awards, including the launch of the large-scale transformative projects under BRAIN® 2.0.

Cancer Moonshot. The overall request for Biden Cancer Moonshot for FY 2025 is $2,164.0 million, supporting President Biden's ambitious but attainable goal of reducing age-adjusted cancer death rates by 50 percent over the next 25 years. The whole-of-government Cancer Moonshot approach to reach this goal must rest on a foundation of scientific research. The National Cancer Institute (NCI) is uniquely positioned to lead this research and offers this bold budget proposal to meet the President's goal and end cancer as we know it for all people. To support these objectives, the FY 2025 request level includes $716.0 million in discretionary funding, an increase of $500.0 million from the FY 2023 Final level. Because FY 2023 marks the final authorization of appropriations of Moonshot funding for NCI under the Cures Act, this funding will enable NCI to sustain research that will make vital scientific contributions to the seven pillars of Cancer Moonshot. As first proposed in the FY 2024 President's Budget (PB), the request also proposes to extend the Cures Act Cancer Moonshot authorization through 2026, providing $1,448.0 million in mandatory funding in each of FY 2025 and FY 2026.

Since 2015, overall cancer death rates have declined about 2 percent a year, but this progress is not fast enough to reach the goal of reducing cancer death rates by 50 percent over the next 25 years. A recently published study by NCI-supported researchers showed

that we must accelerate the decline in age-adjusted cancer death rates to reach the 50 percent goal by 2047.

This budget proposal includes six areas for investment to stimulate progress:

1. Innovate Cancer Prevention and Treatment
2. Transform Cancer Screening and Diagnosis
3. Revolutionize Cancer Clinical Trial Accrual and Completion Rates
4. Ensure Rapid Dissemination of Standards of Care
5. Sustain 21st Century Cures Act Progress and Fundamental Research
6. Support the Cancer Moonshot Scholars Program

These areas address needs across the entirety of cancer research to discover, develop, test, and deliver new approaches to prevent, detect, and treat cancer. The areas are interconnected and must be simultaneously supported and executed to deliver research findings and other evidence-based knowledge into clinical practice and change standards of care and outcomes for all people with cancer and those at risk for the disease.

Children and adolescent brain development

Led by the National Institute on Drugs and Addiction (NIDA),[9] the cross-NIH Adolescent Brain Cognitive Development (ABCD) study[10] is the largest long-term study of child health and development ever conducted in the United States. Following nearly 12,000 children, this study will help us understand how childhood and adolescent experiences such as drug use, sports, video games, social media, and unhealthy sleep patterns shape brain development and other outcomes. More than 600 scientific papers have been published utilizing data from the ABCD study. One analysis[11] utilizing brain imaging data of children aged 9-11 years found sex differences in brain connectivity and cognitive performance that likely reflect earlier brain development in girls than boys. The findings may help explain why young boys are more prone to substance use and other risky behaviors compared to girls. Another study found that children ages 9-10 years old who engaged in excessive non-school-related screen time showed structural brain changes that were associated with higher levels of internalizing symptoms. The structural changes were in brain regions linked to early initiation of alcohol use, suggesting possible shared neurobiological mechanisms between screen time addiction and drug/alcohol addiction.[12] In a separate study, researchers found that prenatal cannabis exposure was associated with a more than twofold increase in cannabis use initiation by early adolescence.[13]

Maternal Health

U.S. populations experience the highest rates of maternal deaths and severe maternal morbidity (SMM) relative to people living in other high-income nations. In 2021, the U.S. maternal mortality rate increased to 32.9 deaths per 100,000 live births from a rate of 23.8 in 2020 and 20.1 in 2019.[14] Disparities in maternal outcomes are particularly striking among marginalized

[9] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.
[10] abcdstudy.org/about/
[11] jamanetwork.com/journals/jamanetworkopen/fullarticle/2801653
[12] akjournals.com/view/journals/2006/12/1/article-p80.xml
[13] jamanetwork.com/journals/jamapediatrics/fullarticle/2806205
[14] cdc.gov/nchs/data/hestat/maternal-mortality/2021/maternal-mortality-rates-2021.pdf

groups such as African Americans, American Indians/Alaska Natives, Native Hawaiian/Pacific Islanders, and populations residing in rural maternity care deserts that lack providers offering obstetric care. NIH confronts the leading causes of SMM and maternal mortality (MM) with multifaceted, innovative research approaches to reduce preventable maternal deaths and improve maternal health before, during, and after delivery. Through the NIH-wide Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative, NIH supports research to mitigate preventable MM, decrease SMM, and promote health equity in the United States. In FY 2023, the IMPROVE initiative awarded $24.4 million to fund the first of seven years of the Maternal Health Research Centers of Excellence, which aim to develop and evaluate innovative approaches to reduce pregnancy-related complications and deaths and reduce health disparities in partnership with communities. IMPROVE emphasizes the importance of community involvement to improve maternal health outcomes through other program dimensions as well. The Connecting the Community for Maternal Health Challenge incentivizes local organization capacity building to perform research at the community level, and the IMPROVE Community Implementation Program works with local communities to implement evidence-based practices to improve maternal health outcomes in maternity care deserts. The RADx Tech for Maternal Health Challenge complements community-based work in underserved regions by awarding prizes for the development of remote and point-of-care technologies for assessment and care delivery that may improve access to and delivery of postpartum care. IMPROVE builds upon other NIH programs that explore facets of maternal morbidity, including prevention of perinatal depression, reducing intimate partner violence in populations of pregnant and postpartum people, detection of gestational diabetes and cardiovascular and other maternal health conditions, models for maternal recovery from opioid use disorder, and clinical trials with the potential to reduce maternal complications. NIH works to synergize these research efforts with interagency initiatives such as the HHS Maternal Health Action Plan, the White House Maternal Health Blueprint, the Maternal Mental Health Task Force, and the implementation of recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women with the aspiration that together we can make progress toward reducing MM and SMM, improve maternal health outcomes, and advance maternal health equity for all. The FY 2025 Budget request for IMPROVE is $43.4 million for the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), an increase of $13.4 million from NICHD's FY 2023 final funding level.

Alzheimer's Disease and Related Dementias

NIH continues to support a wide range of research on issues that primarily affect older adults. One area of major emphasis is research on Alzheimer's disease and related dementias. The National Institute on Aging (NIA) supports and conducts research to better understand the aging process, as well as the diseases, conditions, and needs associated with growing older. The Institute is also the primary federal agency supporting and conducting research into Alzheimer's disease and related dementias. NIA plays a lead role in the implementation of the National Alzheimer's Project Act's national plan to accelerate research on Alzheimer's disease and related dementias and to provide better clinical care and services for people living with dementia and their families.

With increased investment in research into Alzheimer's disease and related dementias, NIH has been able to spearhead incredible progress over the last decade. The 2023 NIH Scientific

Progress Report, *Advancements Build Momentum: 10 Years of Alzheimer's Disease and Related Dementias Research*, features a summary of the past 10 years of achievements made possible through NIH-funded intramural and extramural research. Through enhanced collaboration and innovative partnerships with industry, other agencies, and people living with dementia and their families, NIH has advanced understanding of the risk factors, genetics, and mechanisms of disease in dementia; diversified and de-risked the therapeutic pipeline for disease-modifying drugs; advanced drug repurposing and combination therapy development; discovered tools to detect, diagnose, and monitor dementia; advanced clinical research on lifestyle interventions; increased understanding of how social and physical environmental factors affect dementia risk and disparities; and expanded research on dementia care and care partner supports.[15]

Addressing Risk and Burden of Disease

Community Violence Interventions

Firearms deaths constitute an urgent and significant public health crisis. The overall death rate by firearms was up 21 percent and the rate of homicides by firearms was up 35 percent from 2019 to 2022. Additionally, firearm-related suicides increased to their highest ever recorded level in 2022, and firearms remain the leading cause of death for children and youth ages 1 to 19. Significant disparities by race, ethnicity, and poverty remain. NIH is committed to supporting scientific research to develop, evaluate, and implement effective public health interventions to better understand and prevent violence, including firearm violence, and the resulting trauma, injuries, and mortality. With $12.5 million in funding provided to NIH in FY 2023 to conduct research on firearm injury and mortality prevention, NIH released a Notice of Funding Opportunity (NOFO)[16] to add additional research sites to the Community Firearm Violence Prevention Network (CFVP) that was launched in FY 2022. The network now is comprised of six sites that are developing, implementing, and evaluating innovative structural interventions in partnership with communities to prevent firearm and related violence, injury, and mortality. In addition, NIH published two NOFOs[17,18] focused on advanced training and career development for established NIH investigators in related fields to obtain the necessary skills and expertise to integrate firearm injury prevention work into their research. These awards will be a critical first step to expanding the field of qualified researchers and building capacity for the future.

In addition to the Community Violence Interventions (CVI) focus in the CFVP network, several ongoing projects seek to develop or evaluate CVIs to reduce the risk of future firearm violence and identify barriers to the implementation of these interventions. These CVI projects include emergency department-based interventions at the point of care, place-based interventions that include vacant lot reuse and street lighting interventions, and comprehensive programs that focus on service provision and community engagement among particularly high-risk populations. One project is developing, implementing, and evaluating a burnout prevention program for CVI staff. This project recently completed the pilot phase and is moving on to complete the full intervention trial to determine the intervention's impact. If successful, this program to support

[15] nia.nih.gov/news/nih-releases-alzheimers-disease-and-related-dementias-research-progress-report-and-fiscal-year
[16] grants.nih.gov/grants/guide/pa-files/PAR-23-066.html
[17] grants.nih.gov/grants/guide/pa-files/PAR-23-107.html
[18] grants.nih.gov/grants/guide/pa-files/PAR-23-108.html

frontline violence intervention staff could have far-reaching implications for the long-term sustainability of effective CVI programs.[19]

The FY 2025 request for firearm research in the Office of the Director is $25.0 million, an increase of $12.5 million from the FY 2023 Final level.

Innovations in Mental Health Research and Treatment
Scientific and clinical advances are rapidly advancing mental health care in the United States. Progress in basic science has led to new tools and resources that enable investigators to gain significant insight into the complex interactions between the brain, environment, and disease. Intervention research continues to enhance the understanding and effectiveness of evidence-based care in a broad range of settings. NIMH supports innovative research to transform the understanding and treatment of mental illness to pave the way for prevention, recovery, and cure. In 2023, NIMH-funded investigators discovered a potential new target for developing improved treatments for mental disorders like anxiety and depression,[20] identified a new connection between the amygdala and the nucleus accumbens in the brains of mice that is sensitive to early life adversity and affects how mice respond to rewards,[21] and successfully reconstructed the firing of many neurons to get an in-depth look at how they fire together during neuronal avalanches to create order in the brain.[22] These and other innovations continue to improve mental health care for those in greatest need. Looking forward, NIMH hopes to change the game for precision medicine in psychiatry with a groundbreaking new initiative. NIMH's Individually Measured Phenotypes to Advance Computational Translation in Mental Health (IMPACT-MH) initiative will support research that tests new ways of adding data, such as performance on computerized behavioral tasks or information about activity levels, to traditional clinical information in ways that could help mental health providers and their patients make informed decisions about the future. Studies supported through the IMPACT-MH initiative will test whether combining these different kinds of data improves predictions about mental health treatment responses and outcomes, enabling a vision for precision psychiatry of the future.

In his Unity Agenda for mental health,[23] the President has emphasized strategies for addressing our national mental health crisis, including scalable approaches for prevention and early intervention. In alignment with this agenda, NIMH is focused on building and disseminating a robust evidence base for effective preventive and treatment interventions for mental and behavioral disorders, which requires investment in implementation science and collaboration with partner agencies. The Budget request includes a $200.0 million increase for mental health initiatives above the FY 2023 Final level for NIMH, including $10.0 million to support behavioral health prevention implementation science, focusing on sustainable prevention and early intervention approaches.

[19] news.northwestern.edu/stories/2022/03/harnessing-positive-emotions-to-prevent-burnout-among-gun-violence-interrupters/
[20] science.org/doi/10.1126/science.add7150
[21] nature.com/articles/s41467-023-36780-x
[22] nature.com/articles/s41467-023-37976-x
[23] whitehouse.gov/briefing-room/statements-releases/2023/05/18/fact-sheet-biden-harris-administration-announces-new-actions-to-tackle-nations-mental-health-crisis/

Research has yielded effective, evidence-based preventive interventions for people at high risk of mental and behavioral disorders, as well as interventions that, when delivered early in the course of illness, can significantly improve mental and behavioral health. For example, preventive and early interventions can be effective for alleviating depression, anxiety, schizophrenia, suicide risk, and substance use disorders, and for improving educational attainment. However, there is still a pressing need for research to validate which interventions work best. To address this need, NIMH supports targeted initiatives[24,25,26] that encourage:

1. Research focused on streamlining and optimizing evidence-based preventive and early interventions and services for mental and behavioral disorders, and evaluating their effectiveness when implemented in accessible settings (e.g., community clinics, schools, primary care); and
2. Implementation research focused on developing and testing strategies to promote the adoption and sustained use of research-informed, high-quality interventions and services, including strategies for training and supporting providers to ensure provider competency and sustained fidelity in the wide-scale delivery of effective preventive and early interventions.

In addition to these targeted initiatives, NIMH strives to incorporate evidence-based practices into service initiatives and programs spearheaded by collaborating with partner agencies, including the Substance Abuse and Mental Health Services Administration, the Administration for Children and Families, and the Department of Education. As an example of these cross-agency collaboration efforts, NIMH and NIDA are consulting with the Health Resources and Service Administration (HRSA) and the Agency for Healthcare Research and Quality to leverage the HRSA-administered Bright Futures program[27] to expand access to evidence-based behavioral health preventive services in community and pediatric primary care settings. Most recently, this cross-agency workgroup met to review potential formats, key questions, and associated costs for a scoping review of evidence-based programs.

By sustaining and expanding these targeted implementation science initiatives and cross-agency collaborations, NIMH aims to accelerate the identification and widespread adoption of sustainable, effective, evidence-based preventive and early interventions for a broad range of mental and behavioral disorders.

Opioid and Stimulant Misuse

The public health crisis of opioid misuse, addiction, and overdose in America continues to evolve rapidly and overlaps with other public health challenges, including that of untreated chronic pain and the national mental health crisis. The need for new treatments is real and urgent. Since early in the COVID-19 pandemic, studies have found increases in the use of many kinds of drugs, including fentanyl, cocaine, heroin, methamphetamine, cannabis, and alcohol. In

[24] grants.nih.gov/grants/guide/notice-files/NOT-MH-22-170.html
[25] nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/early-psychosis-intervention-network-epinet
[26] nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/practice-based-suicide-prevention-research-centers
[27] aap.org/en/practice-management/bright-futures

2022, there were over 110,000 drug overdose deaths in the United States.[28] More than 2 million Americans have opioid use disorder (OUD), and 10 million Americans misuse opioids. Additionally, more than 25 million Americans experience daily pain, putting them at increased risks for opioid use and misuse.[29] At the same time, rates of depression and anxiety continue to rise, and the grief, trauma, and physical isolation that many have experienced continue to drive these trends. One aspect of hope amid the tragedy is that the crisis has spurred unprecedented resources and human ingenuity toward finding novel scientific solutions that may one day make addiction a thing of the past.

NIH launched the Helping to End Addiction Long-term® (HEAL) Initiative in 2018 to provide scientific solutions to the opioid crisis and offer new hope for individuals, families, and communities affected by this devastating crisis. HEAL continues to address these evolving issues. This cross-cutting NIH effort spans basic, translational, clinical, and implementation science on opioid misuse, addiction, and pain. HEAL has funded over $3 billion in research, representing more than 1,000 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. In order to continue to respond to these evolving challenges, the FY 2025 request includes funding for the HEAL Initiative® of $635.6 million, maintaining the FY 2023 Final level. This HEAL funding is in addition to funding for opioid and pain research across the NIH ICOs, which is maintained at $1.2 billion, the same as the FY 2023 Final level.

Harm reduction is an evidence-based, often life-saving approach that directly engages people who use drugs to prevent overdose, disease transmission, and other harms. Through the HEAL Harm Reduction Research Network,[30] NIH is supporting a range of novel approaches to delivering harm reduction supplies, such as naloxone, a lifesaving medication to reverse overdose, and fentanyl test strips, which people can use to determine if drugs contain fentanyl. These include moving harm reduction services into communities via mobile vans, peer support specialists, smartphone-based tools, and other approaches. The network is also examining the impact of harm reduction policies and practices at state and local levels, such as policies that deter the use of mail-based delivery of harm reduction services.

Health Disparities

The FY 2025 budget request continues to place an emphasis on addressing the marked health disparities of the Nation's racial and ethnic minority, rural, low-income, and other underrepresented populations, as well as disparities within the biomedical research enterprise. The request sustains recent increases of $95.0 million for health disparities research by the National Institute on Minority Health and Health Disparities, National Institute of Nursing Research, National Institute of General Medical Sciences, and Fogarty International Center. NIH will also continue to support the following initiatives to advance health disparity research

[28] cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
[29] ncbi.nlm.nih.gov/pmc/articles/PMC6688196/pdf/collins-1536332.pdf
[30] nida.nih.gov/news-events/news-releases/2022/12/nih-launches-harm-reduction-research-network-to-prevent-overdose-fatalities

both in communities and address disparities within the biomedical research enterprise:

NIH UNITE Initiative
The NIH UNITE initiative has facilitated support for funding opportunities on the impact of structural racism on minority health (MH) and transformative research to address health disparities (HD). A UNITE recommendation led to the development of the Common Fund Transformative Research to Address Health Disparities and Advance Health Equity Initiative. This initiative supports research projects to prevent, reduce, or eliminate HD, advance health equity (HE), and expand HD research, including at minority-serving institutions (MSIs). UNITE recommendations have also led to the establishment of the Common Fund's Community Partnerships to Advance Science for Society (ComPASS), which aims to bolster funding for HD/MH research.[31]

Tribal Training Grants
Research is critically needed to address the health needs of urban American Indian and Alaska Native (AI/AN) communities, who comprise the majority (approximately 70 percent) of the AI/AN population and experience a significant and distinctive burden of socioeconomic and health disparities. At NIH, the Tribal Health Research Office (THRO) is the central point of contact at NIH for federally recognized AI/AN Tribes throughout the United States and the coordination hub for Tribal health research activities at NIH. NIH recently issued Supplemental Information on Responsible Management and Sharing of AI/AN Participant Data to complement the recently implemented NIH Policy for Data Management and Sharing. The Supplemental Information includes Considerations and Best Practices for NIH-sponsored researchers working with Tribal Nations, such as emphasizing the importance of respect for Tribal sovereignty, proactive engagement with Tribes, establishing mutual goals for data management and sharing, and addressing data management and sharing plans in the informed consent process. NIH expects that this will enhance the ability of Tribal Nations to participate in biomedical research. NIH is also developing supplemental information for the ethical conduct of research with American Indians and Alaska Natives residing in urban areas outside of the legal geographical jurisdiction of Tribal lands. This research raises important questions about Tribal sovereignty and governance that should be considered when conducting biomedical research. NIH remains committed to working with Tribal communities and Tribal Colleges and Universities to further develop educational and research opportunities for Native American students. NIH supports student research programs with Tribal Nations through regional training hubs. These programs are designed to prepare junior and senior high students for careers in science. Additionally, NINDS also supports the Health Disparities in Tribal Communities Summer Internship Program. This program is designed to prepare undergraduate and graduate students for careers in science by offering students the opportunity to work side by side with investigators.

NIH Advancing Prevention Research for Health Equity (ADVANCE)
The Office of Disease Prevention (ODP) within the Office of the Director launched ADVANCE in 2022. ADVANCE is an NIH-wide initiative to develop new preventive interventions and implement existing evidence-based interventions and preventive

[31] commonfund.nih.gov/healthdisparitiestransformation

services in populations that experience health disparities and inequities. ADVANCE emphasizes supporting research that specifically tests preventive intervention strategies that address social and structural determinants of health by integrating the latest knowledge and methodological advances in both prevention science and health disparities science. The ODP is facilitating and coordinating ADVANCE to solicit and support high-impact research that falls across the missions and subject areas of multiple NIH ICOs. Four NIH-wide ADVANCE workgroups are developing funding announcements on preventive intervention research to address long-standing health disparities and inequities.

Women's Health

The mission of the NIH Office of Research on Women's Health (ORWH) is to enhance research related to diseases, disorders, and conditions affecting women, help ensure that women are appropriately represented in NIH-supported biomedical research, and improve the advancement of women in biomedical careers. The ORWH FY 2025 budget request is $153.9 million, a $76.4 million increase over FY 2023. In FY 2025, ORWH plans to use the additional funds to support a range of new and ongoing activities to enhance research into women's health issues, including increasing the number of hubs in the Maternal and Pediatric Precision in Therapeutics Centers of Excellence (MPRINT) initiative to increase the knowledge, tools, and expertise in maternal therapeutics available to the broader research, regulatory science, and drug development communities; expanding trial capacity for the Maternal-Fetal Medicine Unit Network to advance specific treatment approaches to leading drivers of maternal morbidity and mortality, and establishing clinical trials to test technologies developed through the RADx-Tech Maternal Health Challenge based on levels of readiness of the technology in rural and remote locations. The funds will also support new research into important topics such as menopause and diabetes, opioid use disorder in pregnant women, and alcohol use during pregnancy, and will allow ORWH to support cross-NIH initiatives to promote sex and gender equity across all domains of research.

Climate Change

As climate change continues to be an ongoing crisis, the risks to human health will grow, exacerbating existing health threats and creating new public health challenges. Global climate change is already directly and indirectly affecting human health in the United States and around the world. Impacts occur through changes to climate systems such as temperature, air and water quality, and extreme weather events, as well as through changes to the geography and timing of exposures. Climate change contributes to or exacerbates a wide range of health impacts, including non-communicable diseases, injury and trauma, and infectious diseases. Although climate change affects everyone, certain populations are especially vulnerable to various impacts due to social determinants of health, including life stage, sex, underlying health status, access to health care, education, and economic, racial, and ethnically driven disparities. In this way, the climate change and health agenda are inextricably linked to health equity. Climate change impacts are the concern of NIH as a whole and are often at the intersection of multiple NIH ICOs. For this reason, NIH has developed an "all of NIH" approach to building a solutions-driven climate change and health strategic framework that will build on past research investments.[32] The NIH strategic framework will seek to understand the health impacts and

[32] nih.gov/climateandhealth

factors that contribute to individual and community susceptibility, strengthen capacity for needed research and the development of a transdisciplinary workforce, and promote community-engaged research, translation, and dissemination to maximize efforts and outcomes among the United States and global communities most urgently affected. The FY 2025 budget request of $40.0 million sustains the FY 2023 Final increase to boost research on the human health impacts of climate change.

Transforming Nutrition Science

Over the past several years, NIH has bolstered nutrition research, given the broad impact that nutrition has on health and disease. The Office of Nutrition Research (ONR) in the NIH Office of the Director (OD) accelerates progress in nutrition research by planning, coordinating, and tracking progress toward achieving the objectives of the 2020-2030 Strategic Plan for NIH Nutrition Research.[33] The FY 2025 request of $1.3 million for ONR sustains its level in FY 2023, enabling OD to support the objectives of the Strategic Plan.

The Food is Medicine Networks and Centers of Excellence Program is an NIH-wide, nutrition-focused initiative. A lack of good nutrition is the number one driver of poor health outcomes in the United States.[34] Rates of obesity and other diet-related diseases are skyrocketing, and poor diet quality is now the leading risk factor for death in the United States. Poor diets also exacerbate health inequities, as exemplified by individuals with lower incomes, living in rural communities, and from historically marginalized racial and ethnic groups being most affected. Moreover, poor diets are harming the United States economy in that the combined health care spending and lost productivity from poor diets cost over $1 trillion each year. Yet a focus on nutrition is currently missing in the health care system, which in large part explains the rising disease burdens, costs, and inequities in diet-related chronic diseases. The Food is Medicine Networks and Centers of Excellence Program will specifically address this gap by supporting programs that respond to the critical link between diet and health with the provision of healthy food, as well as having health care organizations as their nexus. The program will also address current barriers that exist both in communities and within health care systems that severely limit the ability to reduce obesity and other diet-related diseases (e.g., cardiovascular disease, cancer, and diabetes). Significantly, this innovative program will also support implementation science and intervention and health quality research on culturally sensitive Food is Medicine initiatives and other strategies to improve public health and address barriers to care.

Another timely nutrition-focused initiative is centered on the reciprocal relationship between climate and environmental changes and food systems and its impact on food/nutrition security and health. For example, heat, drought, and floods are having dramatic effects on the food supply, while greenhouse gas emissions, air and water pollution, and environmental toxins are altering the nutritional quality of food. Concurrently, the many components of the food system contribute to the changing climate and impact the availability of natural resources. Importantly, these relationships are related in that not only does the changing environment affect food systems, but food systems have important impacts on the environment in ways we are just

[33] dpcpsi.nih.gov/onr/strategic-plan
[34] cdc.gov/chronicdisease/about/costs/index.htm

beginning to understand. This initiative is centered on increasing our understanding of these reciprocal relationships to improve nutrition and human health.

Emerging from the COVID-19 Pandemic and Continuing to Study the Lingering Effects of SARS-CoV-2

Long COVID

Millions of Americans have recovered from SARS-CoV-2 infections, but unfortunately, many people are still dealing with the long-term effects, known as post-acute sequelae of SARS-CoV-2 (PASC, commonly known as Long COVID). Those who suffer from Long COVID continue to experience debilitating fatigue, shortness of breath, pain, difficulty sleeping, racing heart rate, exercise intolerance, gastrointestinal and other symptoms, as well as cognitive problems that make it difficult to perform at work or school. These symptoms persist long after the initial acute phase of COVID-19 infection has ended. To address this growing public health concern, NIH's National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Allergy and Infectious Diseases (NIAID), and NINDS, along with several other NIH Institutes and the OD, are leading NIH's Researching COVID to Enhance Recovery (RECOVER) initiative,[35] a national research program to understand PASC. The NIH RECOVER initiative, launched with $1.15 billion in COVID supplemental appropriations in FY 2021 and continued with an additional $515 million in funds from the Public Health and Social Services Emergency Fund, funds research aiming to understand how people recover from COVID-19 infection and why some people do not fully recover and develop Long COVID. The RECOVER initiative brings together patients, caregivers, clinicians, community leaders, and scientists from across the Nation to understand, prevent, and treat Long COVID.

In 2023, the NIH RECOVER initiative launched and opened enrollment for phase II clinical trials that will evaluate at least four potential treatments for Long COVID, with additional clinical trials to test at least seven more treatments expected in the coming months. Treatments will include drugs, biologics, medical devices, and other therapies. The trials are designed to evaluate multiple treatments simultaneously to identify more swiftly those that are effective. These trials were informed by findings from other RECOVER research over the past two years and focus on several of the symptoms described as most burdensome by people experiencing Long COVID. With its complementary research efforts, RECOVER has positioned NIH to design and conduct trials that have the potential to provide Long COVID patients who experience varying symptoms with relief sooner than any individual study can alone.

COVID-19 and Children's Health

Although most children infected with SARS-CoV-2 experience only mild illness, the impact that the pandemic has had on children cannot be underestimated. Many children experienced loss during the pandemic, be it the loss of a family member or loved one due to COVID-19, or the loss of economic, food, or housing security. A study co-sponsored by NIDA and published in a paper entitled *COVID-19-Associated Orphanhood and Caregiver Death in the United States* revealed that, as of June 2021, more than 140,000 children in the United States lost a parent or primary caregiver during the pandemic.[36] Sudden parental death can be traumatizing to children

[35] recovercovid.org/

[36] doi.org/10.1542/peds.2021-053760

and leave families unprepared to deal with the consequences. Studies on the mental health effects of COVID-19 indicate that children and adolescents experienced higher rates of anxiety and depression during the pandemic period than they did before it. Studies have also demonstrated that youth emergency department visits for mental health increased during the pandemic,[37] and that adolescents living through the pandemic experienced increased incidence of symptoms of anxiety and depression.[38] While it is not clear if these mental health effects are due to the pandemic itself (i.e., concern about themselves or loved ones being infected and becoming seriously ill), a reaction to instability that may have been caused by a death or a job loss in the family, or as an indirect consequence of public health measures, it is imperative that we learn from these experiences to properly support children and adolescents as early as possible. ICOs across NIH are funding research on exposures and risk factors from childhood trauma, interventions, pediatric intensive care, and long-term health effects. For example, NIMH is supporting research in children to clarify how, when, and for whom trauma exposure increases the risk for adverse physical and mental health outcomes. The FY 2025 budget request includes funding in NICHD to sustain the $10.0 million provided in FY 2023 for research into the effects of COVID-19 on children, including multisystem inflammatory syndrome in children (MIS-C), and the $3.0 million provided for research on mitigating the effects of COVID-19 on pregnancies, lactation, and postpartum health with a focus on individuals from racial and ethnic minority groups.

COVID-19 and Mental Illness

Children are not the only population dealing with the mental health impacts of the COVID-19 pandemic, as the issue affects people of all ages. Mental illnesses are the fifth leading cause of disability in the United States, accounting for 6.6 percent of all disability-adjusted life years in 2019,[39] and the pandemic only exacerbated this issue. NIH supports research on many facets of mental health including rapid interventions to reduce severe suicide risk, funding adaptive interventions to optimize adolescent mental health treatments, and aggregating data to address mental health disparities research gaps. In response to the pandemic, NIH launched a project to support research focused on the social, behavioral, and economic impacts of COVID-19, which supports research on the secondary effects of the pandemic, such as financial hardship, reduced access to health care, and school closures.[40] This initiative includes NIMH-supported research on the impact of COVID-19 mitigation efforts on socioeconomic disparities in mental health and health care utilization;[41] the effectiveness of digital health apps like Headspace as a just-in-time approach to immediate, personalized behavioral health care;[42] the effectiveness of a digital platform on depression/anxiety symptoms of healthcare workers during the COVID-19 pandemic;[43] and effectiveness, barriers, and facilitators to the implementation of a gold standard exposure treatment for post-traumatic stress disorder in healthcare system employee assistance programs serving frontline healthcare workers.[44] The FY 2025 request includes $25.0 million for research into the impact of COVID-19 on mental health, sustaining the FY 2023 Final

[37] doi.org/10.1001/jamapsychiatry.2023.2195
[38] doi.org/10.1016/j.bpsgos.2022.11.002.
[39] Institute of Health Metrics and Evaluation. ghdx.healthdata.org/gbd-results-tool accessed October 2021.
[40] covid19.nih.gov/news-and-stories/covid19-ripple-effects
[41] reporter.nih.gov/search/_E4VoHbiwU293-ndTNu8Kw/project-details/10490467
[42] reporter.nih.gov/search/nG0a0LRnBk2HZbig_DW6ew/project-details/10402904
[43] reporter.nih.gov/search/EMyREeTC3kan_rHKVyS6Fw/project-details/10451636
[44] reporter.nih.gov/search/Wz5OqrJM_keh6fQgmV9ZMg/project-details/10246656

funding level.

The Community Engagement Alliance (CEAL) Against COVID-19 Disparities
The Community Engagement Alliance (CEAL) works closely with the communities that were most impacted by COVID-19.[45] The CEAL research teams focus on COVID-19 awareness and education research, especially among African Americans, Hispanics/Latinos, and American Indians/Alaska Natives (AI/AN)—populations that account for over half of all reported cases in the United States. They also promote and facilitate the inclusion and participation of these groups in vaccine and therapeutic clinical trials to prevent and treat the disease. CEAL has made a significant impact since its launch; 21 CEAL teams across 21 states, the District of Columbia, and Puerto Rico have reached nearly 91 million people in 101 counties. These CEAL teams are collaborating with almost 1,000 organizations, including health care providers and hospital systems, academic and research organizations, schools, associations, and independent businesses. Most importantly, over half of those partners are community-service, faith-based, grassroots, nonprofit, social service, and civic community-based organizations. Working with these partners, CEAL research teams have held more than 3,000 local events, reaching over 600,000 participants. This includes vaccination events at which over 300,000 people received the COVID-19 vaccine. Over 2,600 people have signed up to participate in COVID-19-related clinical trials.

As the country shifts to an endemic phase of COVID-19, CEAL continues to be leveraged as a foundation and platform for addressing the host of health disparities that remain within CEAL communities. NHLBI is leveraging this platform for scientific initiatives addressing public health issues that have a disproportionate impact on the same communities that bore the brunt of COVID-19. While CEAL continues to operate with the principles of trust and partnership, it now broadens to include research focus areas of community interest like maternal health (MH-CIP),[46] the impact of climate on health,[47] and ensuring access to accurate and timely public health information. Additional upcoming initiatives are under development and include enriching research capacities within AI/AN communities, and the interests of other Institutes like NHGRI's work to increase the understanding of and participation in genomic research in diverse communities.

As CEAL expands, NIH is committed to continue reporting the accomplishments, lessons learned and promising practices in community engaged research to address these issues. The FY 2025 request level includes $30.0 million for CEAL, maintaining the FY 2023 Final level, to expand the program beyond COVID-19 to focus on other health issues in communities experiencing health disparity such as climate health, maternal health, gaps in public health knowledge, and more.

Pandemic Preparedness
The FY 2025 Budget provides $20.0 billion in mandatory funding through the Public Health and Social Services Emergency Fund (PHSSEF) to NIH, FDA, the Centers for Disease Control and Prevention (CDC), and the Administration for Strategic Preparedness and Response (ASPR) to

[45] nhlbi.nih.gov/news/2020/COVID-19-nih-funds-community-engagement-research-efforts-areas-hardest-hit
[46] maternalhealthcip.org/
[47] nih.gov/climateandhealth

prepare for and respond rapidly and effectively to future pandemics and other high-consequence biological threats. Within this total, $2.69 billion is allocated to NIH. These funds will allow NIH to conduct and support preclinical and clinical research on vaccines and therapeutics (including host-tissue-directed therapies) to provide protection against prototype or representative pathogens selected from a preliminary group of around 10 viral families of concern. It will invest in expanding laboratory capacity (including biosafety level 3 and 4 laboratories) and pilot lot manufacturing in compliance with FDA's Current Good Manufacturing Practice (cGMP) regulations, as well as its network of clinical trial sites that were so critical to addressing the COVID-19 pandemic. Finally, NIH will leverage the successful Rapid Acceleration of Diagnostics (RADx) initiative to develop next-generation diagnostics that fill critical gaps, such as the need for affordable and accessible at-home tests that are as reliable as lab-based PCR tests. For more information on the Department-wide pandemic preparedness mandatory proposal, please see the detailed narrative in the PHSSEF Congressional Justification.

The Future of Biomedical Research at NIH – New Approaches to Scientific Discovery

NIH continues to leverage scientific advances and innovative research methodologies of today to foster the discoveries of tomorrow. This scientific advancement requires a cadre of diverse minds ready to tackle complicated scientific problems. NIH supports the training and development of the next generation of scientists who will bring diverse perspectives, skillsets, and backgrounds. For this reason, NIH reaffirms its commitment to support diversity, equity, inclusion, and accessibility in its workforce and beyond.

Inspiring the Next Generation of Biomedical Researchers by Bolstering the NIH Biomedical Workforce

Working Group on Re-envisioning NIH-Supported Postdoctoral Training
Science, Technology, Engineering, and Math (STEM) doctorate holders are critical to the health of the national and global scientific ecosystem. Within the U.S. research enterprise, postdoctoral scholars, predominantly based in academic research labs, are a bellwether of its sustainability. These labs train postdoctoral scholars to pursue broad, intellectually curious questions, often underpinning innovation that precipitates new treatments or devices. However, the existing postdoctoral research system is not optimally supporting the current biomedical research ecosystem, nor is it building the best foundation for a diverse, inclusive, productive, successful, and sustainable future. Among other issues, postdoctoral scholars often receive low compensation and benefits relative to their education and work experience; they confront job insecurity, insufficient support for professional development, and uncertain career prospects; and they are subject to a power imbalance that favors the institutional establishment. Further, postdoctoral scholars from historically marginalized groups and international postdoctoral scholars face disproportionate structural and implicit barriers in academia, exacerbating the challenges experienced for these groups. Recognizing these complex issues, in January 2023 the Acting NIH Director charged a new NIH Advisory Committee to the Director (ACD) Working Group on *Re-envisioning NIH-Supported Postdoctoral Training*,[48] building upon work from

[48] acd.od.nih.gov/working-groups/postdocs.html

previous groups.[49,50] NIH hosted four public listening sessions[51] and posted a Request for Information[52] to engage the community on issues affecting and possible solutions to the challenges facing postdocs. Informed by this feedback, the Working Group's final report was published in December 2023,[53] and includes recommendations for improving the postdoctoral experience to optimize the effectiveness of postdoctoral training and professional development to benefit engaged individuals and the scientific enterprise as a whole. NIH is currently evaluating these recommendations and next steps for implementation.

UNITE: Inspiring the Next Generation of Scientists

To take on issues as pervasively entrenched in the scientific enterprise as structural and systemic racism, UNITE works across three domains—the internal NIH workforce, the external biomedical workforce, and advancing HD/MH research. Through the NIH Common Fund, UNITE launched the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program to enhance and maintain scientific environments that cultivate and benefit from a full range of talent. UNITE efforts have led to the expansion of the Science Education and Partnership Award program, with 17 NIH ICOs joining the National Institute of General Medical Sciences (NIGMS) in focusing on projects that generate resources to increase career opportunities for underrepresented groups from diverse backgrounds, including those underrepresented in biomedical research as well as outreach to these groups in the kindergarten through grade 12 (K-12) STEM community. Via UNITE efforts, NIH is also developing a DEIA prize competition to reward and recognize institutions of higher education for innovative interventions that enhance faculty and student DEIA. In 2022, UNITE released its inaugural Progress Report,[54] which describes the actions that NIH has taken to identify and address structural racism that may exist within the NIH and in the biomedical and behavioral research enterprise. Also, in April 2023, NIH launched the NIH Institutional Excellence in Diversity, Equity, Inclusion, and Accessibility in Biomedical and Behavioral Research Prize Competition,[55] administered by the Chief Officer for Scientific Workforce Diversity Office in close collaboration with UNITE and 24 Institutes and Centers. The prize competition aims to recognize transformative cultures, systems, projects, and processes developed by academic institutions to promote inclusive excellence and create environments that foster and value a culture of DEIA. The prize competition will also identify practices for enhancing DEIA within faculty, postdoctoral scholars, and student bodies that can be disseminated for adoption by other institutions.

STEM Education Training

NIGMS support for STEM education and training starts at the earliest stages of the career pathway. An effective means of helping youth imagine their future selves in a biomedical research career is to acquaint and involve them in the research process. Thus, NIGMS's Science Education Partnership Award (SEPA) supports projects that build interactive educational resources that both capture the imaginations of pre-K through grade 12 students and stimulate the

[49] acd.od.nih.gov/working-groups/nextgen.html
[50] acd.od.nih.gov/working-groups/bwf.html
[51] acd.od.nih.gov/documents/IMOD_Postdoc_Listening_Sessions_summary.pdf
[52] acd.od.nih.gov/documents/RFI_Postdocs_Report_2023.pdf
[53] acd.od.nih.gov/documents/presentations/12152023_Postdoc_Working_Group_Report.pdf
[54] nih.gov/sites/default/files/research-training/initiatives/ending-structural-racism/UNITE-progress-report-2022.pdf
[55] diversity.nih.gov/blog/2023-04-04-announcing-nih-institutional-excellence-deia-prize-competition

types of scientific curiosity and inquiry-based approaches used in biomedical research.[56] Many of these projects provide opportunities for students to be involved in citizen science projects that aim to understand and address issues that affect their individual communities. In addition, they provide opportunities to interact with current biomedical research professionals from diverse backgrounds as role models: one SEPA program, for instance, pairs veterinarians from a nationwide "superhero" League of VetaHumanz with local schools or community centers that support underserved students.[57] To help educators find free science education content, NIGMS recently launched a STEM teaching resources website. The website includes NIH-wide teaching materials as well as those from SEPA programs, categorized by different health and research topic areas.[58]

In addition to its early outreach efforts, NIGMS promotes access to research experiences by supporting training programs with a strong mentorship component across all educational stages. Research and career development programs at the undergraduate level, for instance, can help set the trajectory of a student's career by allowing them to succeed in the laboratory, thereby allowing individuals to visualize a potential future in scientific research. Participants in diversity-oriented programs like the Maximizing Access to Research Careers (MARC) and Undergraduate Research Training Initiative for Student Enhancement (U-RISE) programs often comment on how they were inspired seeing people from backgrounds like their own conducting—and succeeding in—science.[59,60]

Finally, achieving a diverse and productive workforce means supporting critical phases of the career development pathway, including key transition points between one stage of the pathway and the next. The Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program, which focuses on the transition from postdoctoral scholar to independent investigator, combines individual awards with a cohort-based mentoring program that has attracted and retained a diverse class of fellows.[61,62] Following the success of this program, NIGMS is developing a similar cohort-based program to support trainees during the transition from graduate school to postdoctoral training.

Short-Term Research Experience Program to Unlock Potential (STEP-UP)
The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) launched the STEP-UP program over two decades ago to make research opportunities accessible to high school and undergraduate students, with a focus on students from groups underrepresented in research careers. STEP-UP provides a hands-on summer research and mentoring experience, reaching students throughout the country and in U.S. territories in the Pacific and Caribbean. The program includes a symposium at which students present their research results and gain continued mentorship after the summer. With NIDDK grant support, academic and non-profit

[56] nigms.nih.gov/capacity-building/division-for-research-capacity-building/science-education-partnership-awards-(sepa)
[57] biobeat.nigms.nih.gov/2022/06/the-league-of-vetahumanz-encouraging-kids-to-use-their-powers-for-good/
[58] science.education.nih.gov/
[59] nigms.nih.gov/training/MARC/Pages/USTARAwards.aspx
[60] nigms.nih.gov/training/RISE/Pages/U-RISE-T34.aspx
[61] nigms.nih.gov/training/careerdev/Pages/MOSAIC.aspx
[62] In its first two years, the MOSAIC program supported 82 scholars, 76 percent of whom were women, and 71 percent from under-represented backgrounds.

institutions across the country serve as STEP-UP coordinating centers to identify mentors, coordinate student recruitment, help students find research sites close to their home or school, and manage other aspects of the program. Evaluation of STEP-UP's first two decades showed that many of the participants have pursued careers as researchers, physicians, and physician-scientists. Building on this success, NIDDK renewed the program in 2022[63] and expanded the undergraduate component to provide support for year-round research. NIDDK also plans to expand STEP-UP to include a coordinating center that will operate a high school program in the upper west to reach out to students from Wyoming, Utah, Montana, the Dakotas, and other states where there has been low participation in the STEP-UP program to date. STEP-UP is an important component of NIH's multifaceted efforts to develop a talented and diverse biomedical research workforce, where opportunity is defined by talent, not zip code.

DEIA Strategic Plan

In FY 2023, NIH released the Fiscal Years 2023–2027 NIH-Wide Strategic Plan for Diversity, Equity, Inclusion, and Accessibility (DEIA) to articulate NIH's vision for embracing, integrating, and strengthening DEIA across all NIH activities to achieve the NIH mission.[64] The Strategic Plan lays out the current and future NIH activities to meet that strategic vision and is organized around accomplishments, needs, opportunities, and challenges in addressing DEIA in the NIH intramural and extramural workforce, its structure and culture, and the research it supports. The Strategic Plan was developed in part as a response to directives included in the House FY 2022 appropriations report calling for a diversity strategic plan[65] and is responsive to *Executive Order 14035* and the *Government-Wide Strategic Plan to Advance Diversity, Equity, Inclusion, and Accessibility in the Federal Workforce*.[66] The Strategic Plan highlights NIH's efforts to foster DEIA within the biomedical, behavioral, and social sciences research enterprise, and NIH created a two-page overview that summarizes the content of the Strategic Plan.[67] NIH's implementation of the Strategic Plan is described in more detail in the OD chapter of the NIH Congressional Justification.

Fostering Scientific Innovation and Harnessing New Technologies

The NIH Director's Challenge Innovation Award

The NIH Director's Challenge Innovation Award is a program designed to identify and fund projects that foster NIH-wide collaborations across the NIH Intramural Research Program (IRP). The program seeks to fund innovative, high-impact projects that require the cooperation of researchers in more than one of NIH's Institutes and Centers. The award provides seed money from the NIH Office of Intramural Research (OIR) for innovative and high-impact research that shows significant benefit to a variety of research, infrastructure, and/or scientific endeavors throughout the IRP. In FY 2022, the program supported investigator-initiated, collaborative, and interdisciplinary projects that employ engineering and/or physical science approaches to

[63] grants.nih.gov/grants/guide/rfa-files/RFA-DK-22-510.html
[64] nih.gov/about-nih/nih-wide-strategic-plan-diversity-equity-inclusion-accessibility-deia
[65] congress.gov/116/crpt/hrpt450/CRPT-116hrpt450.pdf
[66] whitehouse.gov/briefing-room/presidential-actions/2021/06/25/executive-order-on-diversity-equity-inclusion-and-accessibility-in-the-federal-workforce/
[67] nih.gov/sites/default/files/about-nih/nih-wide-strategic-plan-deia-two-page-overview.pdf

problems in biology and medicine. The program made six two-year awards, ranging in amount from $194,000 to $250,000 per year.

Undiagnosed Diseases Network (UDN)
The UDN, which builds on the success of the Undiagnosed Diseases Program at the NIH Clinical Center, is a nationwide network of clinicians and researchers who use both basic and clinical research to uncover the underlying disease mechanisms associated with rare and undiagnosed conditions. It has been estimated that approximately 25 million Americans suffer from a rare disorder. The UDN pioneered a new personalized medicine model for helping patients who have historically been the most difficult for the medical community to diagnose, taking advantage of cutting-edge technologies such as genomic sequencing, metabolomics and assessing patient variants in model organisms to give clinicians new, powerful information to help understand the cause of extremely rare diseases. The FY 2025 request includes $18.0 million in NINDS to continue these activities, an increase of $16.0 million in base funding in order to complete the transition of this program from the Common Fund.

Rare Diseases and Translational Science Research
When it comes to tackling the undiscovered and developing novel health interventions, one way we can accomplish this is by supporting innovative work to address many diseases at one time. The critical need for platform-based, multi-disease approaches is underscored when considering the collective impact of rare diseases. The public health need for applying innovation to rare diseases research is clear: there are over 7,000 different rare diseases, and 1 in 10 individuals has a rare disease. Recent reports estimate that this results in approximately $400 billion per year in medical costs for patients in the United States and upwards of $1 trillion in total costs.[68] Some of this economic burden reflects the long odyssey that many patients must take to receive a correct diagnosis, only to realize that 90 percent of rare diseases lack a treatment. As home to translational science and a leader in rare diseases research, the National Center for Advancing Translational Sciences (NCATS) is positioned to tackle many scientific opportunities of high public health need to address the significant challenges faced by patients, particularly those with rare diseases.

NCATS has already embarked on optimization of gene-directed therapies such as the Platform Vector for Gene Therapy (PaVe-GT) Program and the Accelerating Medicines Partnership® Bespoke Gene Therapy Consortium (BGTC). These programs seek to advance rare diseases research by expanding treatment development and interventions for diseases and include:

- Data-science and informatics, personalized medicine, and novel diagnostics;
- Clinical trial infrastructure innovations and increased integration and coordination of the Rare Diseases Clinical Research Network (RDCRN) and rare diseases research with the Clinical and Translational Science Awards (CTSA) program; and
- Shortening the diagnostic odyssey for rare disease patients by using real-world data and real-world evidence, such as leveraging and expanding the NCATS National COVID Cohort Collaborative, which bridges together clinical data from CTSA-affiliated clinics

[68] healthaffairs.org/do/10.1377/forefront.20220128.987667

and hospitals for research use and has demonstrated its ability to identify three different types of Long COVID.

Leveraging Discoveries and Lessons Learned to Combat Infectious Disease

The rapid successes and generational leaps that have occurred in the field of biomedical research throughout the course of the COVID-19 pandemic have placed us in a unique position to prepare for the future. We can leverage scientific advances developed during the pandemic, such as mRNA vaccine technology, to address current public health crises such as the HIV epidemic, and future potential pandemic pathogens.

Universal Flu Vaccine

The influenza virus remains a deadly and costly pathogen, placing a substantial health and economic burden on the United States and across the world each year. In the United States, the Centers for Disease Control and Prevention (CDC) estimates that the disease burden of influenza has resulted in between 9.2 million and 35.6 million illnesses, between 140,000 and 710,000 hospitalizations, and between 12,000 and 56,000 deaths annually since 2010, all of which results in an estimated $27 billion in health costs. Current influenza vaccination strategies rely on the development of an annual vaccine targeting the circulating strains that are anticipated to spread in the United States. NIH supports a research portfolio with the ultimate goal of developing a universal influenza vaccine to generate robust, long-lasting protection against multiple subtypes of influenza, eliminating the need to update the vaccine each year and protect against newly emerging strains with pandemic potential. NIH-funded researchers are making progress toward this goal by utilizing several novel approaches to develop vaccine candidates for clinical testing. Building upon the success of mRNA vaccines developed during the COVID-19 pandemic, NIH is working to expand this concept to the development of a universal influenza vaccine. Additionally, NIH-supported researchers are actively identifying and developing novel adjuvants for influenza vaccines to increase their immunogenicity and effectiveness. Earlier this year, scientists at NIAID's Vaccine Research Center (VRC) reported in two new studies that an experimental influenza vaccine designed to elicit immunity against a broad range of influenza viruses performed well in a small trial of volunteers.[69] In fact, the vaccine has advanced to a second trial led by scientists at Duke University through NIAID's Collaborative Influenza Vaccine Innovation Centers (CIVICs). Continued investment in this research will enable the development of universal influenza vaccines to protect millions of people from infection. The FY 2025 budget request includes $270.0 million for universal influenza vaccine research, the same as the FY 2023 Final level.

Ending the HIV Epidemic (EHE)

HIV disproportionately affects populations and geographic areas throughout the United States. In 2016 and 2017, 50 percent of newly diagnosed HIV infections in the United States occurred in 48 counties, some territories, and 7 states that have a significant and disproportionate occurrence of HIV in rural areas. The EHE initiative, announced in 2019, aims to reduce new HIV infections in the United States by 75 percent by 2025 and to end the HIV epidemic by 2030. As part of the initial EHE response, the NIH Centers for AIDS Research (CFARs) and the HIV/AIDS Research Centers (ARCs) built on existing relationships with local health authorities,

[69] niaid.nih.gov/news-events/vrc-uni-flu-vax

community-based groups, and other HHS agencies involved in the EHE initiative, including the CDC and HRSA.[70] With these partners, researchers have identified and evaluated 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 acquisition. These locally focused activities have used proven HIV treatment and prevention tools, including 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 3 days of exposure and taken for an additional 28 days. As the original halfway point of this initiative approaches, it is clear that an expanded, diversified response is required to reach communities and populations that continue to be disproportionately affected by the HIV epidemic. NIH's multi-institute response is centrally coordinated within the NIH OD in the Office of AIDS Research (OAR). The $26.0 million request sustains the level for EHE into FY 2025 and reflects plans to expand implementation research to additional types of awardees in order to broaden geographical coverage and build partnerships with unrepresented communities across the country.

Investing In Tomorrow's Discoveries by Supporting Robust Research Resources, Policies, and Infrastructure

As NIH continues to address the ongoing public health challenges that threaten the Nation while anticipating the potential threats of the future, it is imperative to continue supporting the infrastructure that underpins the NIH biomedical enterprise. This includes both the physical and digital infrastructure, as well as the policies that NIH promotes.

Impactful Policy to Shape Biomedical Research

Data

The lifeblood of a research-driven Agency is its data, and for NIH, this includes data spanning fundamental research (basic science) generated in laboratories, large health care systems, and individual communities. NIH seeks to reach the full potential of all biomedical, behavioral, and social sciences research and clinical care data to develop new treatments, prevention approaches, and health care delivery methods that improve the lives of all people. NIH will continue to work with grantees and across other HHS agencies to develop a modern infrastructure that optimally supports data sharing and use.

In January 2023, a new NIH Policy for Data Management and Sharing[71] went into effect. Newly funded research projects must add a description of how the researchers will produce data that can be used by others to uncover new insights and, when applicable, reproduce their research results.

[70] nih.gov/news-events/news-releases/nih-bolsters-funding-hiv-implementation-research-high-burden-us-areas
[71] grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html

NIH will support the 2023 - 2028 HHS Data Strategy,[72] to integrate data from basic and social sciences research, public health, and clinical care. Emphasis will be placed on obtaining inclusive, diverse, and secure data from all clinical care environments. The NIH OD is exploring options to expand clinical research capacity to reach communities of all types via a new NIH-wide network focused on primary care. In addition, the OD will partner with all HHS agencies to further develop the electronic health record as a vehicle for engaging the people who represent the full diversity of our society in biomedical research.

NIH envisions the National Library of Medicine (NLM) to serve as a focal point to support data sharing and use for biomedical, behavioral, and social sciences research across the Nation. In response to user community needs, the NIH Office of Data Science Strategy (ODSS) will work with NLM to increase capacity for data hosting, development of policies, programs, and infrastructure to deliver minimal cost access to open-industry data standards, support for broad access to advanced analytics and computational power, and support for education and workforce development, particularly for population groups not currently represented. The FY 2025 Budget requests a $30.0 million increase for NLM to support a new Clinical Data initiative to develop the tools, computational resources, and datasets necessary to extend NIH clinical research capabilities, including supporting artificial intelligence research and development.

Scientific Integrity

Promoting and integrating scientific integrity principles throughout the research enterprise helps ensure that science is conducted, managed, communicated, and used in ways that preserve its accuracy and objectivity and protect it from suppression, manipulation, and inappropriate influence. NIH has always sought to incorporate robust scientific integrity principles and practices throughout every level of its scientific enterprise. To provide an overarching framework for the agency's commitment to supporting scientific integrity, NIH has developed a Draft Scientific Integrity (SI) Policy.[73] The Draft Policy aligns with the January 2021 "Presidential Memorandum on Restoring Trust in Government Through Scientific Integrity and Evidence-Based Policymaking," which tasks NIH and other agencies to update their SI policies as appropriate to ensure agency alignment with the principles set forth in the January 2022 "Protecting the Integrity of Government Science" report from the National Science and Technology Council's Scientific Integrity Fast-Track Action Committee and the Draft HHS SI Policy. The Draft NIH Scientific Integrity Policy articulates the procedures and processes in place at NIH that aid in maintaining rigorous scientific integrity practices and proposes several new functions to further enhance scientific integrity at NIH and throughout the NIH-funded biomedical research enterprise. The draft policy includes a federal definition of SI that aligns across the federal government, establishes key roles and responsibilities for those who will lead the agency's scientific integrity program, and, as appropriate, establishes relevant reporting and evaluation mechanisms. The policy will be finalized in early 2024.

Modernizing Data Ecosystems and Maximizing Access to Publications and Data that Result from Research

[72] cdo.hhs.gov/s/hhs-data-strategy

[73] federalregister.gov/documents/2023/09/25/2023-20733/request-for-information-on-the-draft-scientific-integrity-policy-of-the-national-institutes-of

NIH's vision for a modernized, integrated biomedical data ecosystem, as outlined in the NIH Strategic Plan for Data Science[74] and the NIH Policy for Data Management and Sharing (DMS Policy)[75] aims to promote responsible sharing of and access to data collected from NIH-supported research. The DMS Policy, which took effect in January 2023, reflects NIH's longstanding commitment to making the results of the research it supports with public funds available to the public by expecting NIH-supported researchers to prospectively plan to maximize appropriate data sharing.

NIH has a longstanding Public Access Policy that expects the submission to PubMed Central of NIH-funded final, peer-reviewed manuscripts upon acceptance for publication. The manuscripts, or in some cases the final versions of record, are made publicly available after a maximum 12-month embargo from the official date of publication. In August 2022, the White House Office of Science and Technology Policy (OSTP) released a Memorandum on "Ensuring Free, Immediate, and Equitable Access to Federally Funded Research" that establishes new guidance for improving public access to scholarly publications and data resulting from Federally supported research.[76] In February 2023, NIH released its Plan to Enhance Public Access to the Results of NIH-Supported Research for public comment.[77] The Plan provides a roadmap for how NIH will update its existing Public Access Policy to align with the OSTP Memorandum, including by removing the allowable embargo period for publications. The public comment period closed on April 24, 2023, and NIH is using this input to inform a draft revised Public Access Policy that will be released for comment in 2024.

Data modernization activities include improving the AI-readiness of NIH-funded data,[78] enhancing researcher training, and enabling NIH-funded data repositories to adopt best practices to align with OSTP's May 2022 guidance, "Desirable Characteristics Of Data Repositories For Federally Funded Research."[79] Other examples include funding opportunities for data repositories and knowledge bases as well as strategic partnerships such as the Generalist Repository Ecosystem Initiative (GREI).[80] NIH will continue to support data interoperability to facilitate complex integrations of data including data analysis in the cloud. For example, CloudLab,[81] a cloud-based platform for learning and exploration of data, was established in the Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative.[82] To promote streamlining and standardizing processes for researchers to access NIH data, ODSS is developing strategies for updating existing data access systems and centralizing search capabilities and automation that will further the OSTP's 2022 Directive.[83] These examples of NIH-wide efforts to modernize data ecosystems and maximize

[74] datascience.nih.gov/sites/default/files/NIH_Strategic_Plan_for_Data_Science_Final_508.pdf
[75] sharing.nih.gov/data-management-and-sharing-policy
[76] whitehouse.gov/wp-content/uploads/2022/08/08-2022-OSTP-Public-Access-Memo.pdf
[77] grants.nih.gov/grants/guide/notice-files/NOT-OD-23-091.html
[78] datascience.nih.gov/artificial-intelligence/initiatives/Improving-AI-readiness-of-Existing-Data
[79] whitehouse.gov/wp-content/uploads/2022/05/05-2022-Desirable-Characteristics-of-Data-Repositories.pdf
[80] datascience.nih.gov/data-ecosystem/exploring-a-generalist-repository-for-nih-funded-data
[81] cloud.nih.gov/resources/cloudlab/
[82] datascience.nih.gov/strides
[83] whitehouse.gov/ostp/news-updates/2022/05/26/new-guidance-to-ensure-federally-funded-research-data-equitably-benefits-all-of-america/

access show that NIH is committed to ensuring data are in line with OSTP's guidance regarding equitable access to federally funded research.

Anti-Harassment Efforts

NIH is committed to promoting safe, respectful, and healthful work environments conducive to high-quality research. NIH is committed to creating and maintaining a work environment that is free of harassment and other inappropriate conduct and holding all NIH community members accountable for such behaviors regardless of position or status. For example, the NIH Civil program provides the entire NIH community with reporting tools and a process to review all allegations, identify inappropriate behaviors, and refer findings. The NIH-wide Anti-Harassment Steering Committee, chaired by the OD, is regularly informed of the NIH Civil work and findings, and responds by making recommendations on the implementation of new anti-harassment policies and updates to procedures for handling allegations and findings of harassment.

NIH will continue working towards ensuring safe and respectful workplaces, free from harassment and discrimination, wherever NIH-funded research is conducted. Over the past several years, NIH has taken many substantive actions within the extent of NIH's grant authorities to address harassment and discrimination in NIH extramural biomedical science, including the development and implementation of policies and processes. NIH expects recipient institutions to have policies and practices in place that foster an environment free from harassment, including sexual harassment, discrimination, and other forms of inappropriate conduct that can result in a hostile work environment.[84] Through regular outreach, notifications, and engagement with the recipient community, NIH conveys to institutions and researchers that such behaviors are not acceptable.[85,86] In December 2022, NIH revised the NIH Grants Policy Statement setting the expectation for recipients to establish codes of conduct, which define expectations of integrity and ethical values and criteria of competence of personnel involved in the work supported by NIH grant funds. This includes assuring work environments are free of harassment and are safe and conducive to the production of high-quality work. In May 2022, NIH published a guide notice informing recipients of their statutory obligation to notify NIH when an individual on an NIH award has been removed from their position or has been otherwise disciplined by the recipient institution due to concerns about harassment, bullying, retaliation, or hostile working conditions involving Senior/Key Personnel. Recognizing the support from Congress, the efforts of NIH staff, and enhanced institutional awareness, NIH is now much better positioned to prevent "passing the harasser." Allegations and notifications related to harassment (including sexual harassment), discrimination, and hostile work environments have increased substantially since NIH started tracking these in 2018.[87] This rise in numbers is likely due in part to the heightened awareness[88] and attention about harassment in the scientific workforce,

[84] grants.nih.gov/grants/policy/harassment/policy-requirement.htm
[85] grants.nih.gov/grants/policy/harassment/related-statements.htm
[86] nexus.od.nih.gov/all/2023/07/17/case-study-in-research-integrity-banned-from-supervising-cant-go-in-lab-but-no-impact-on-nih-funded-research/
[87] nexus.od.nih.gov/all/2023/03/22/trends-in-extramural-research-integrity-allegations-received-at-nih/
[88] nih.gov/about-nih/who-we-are/nih-director/statements/creating-meaningful-reforms-end-sexual-harassment-science

together with NIH's outreach efforts and strengthened recipient notification requirements.[89] NIH regularly updates the data publicly reported on harassment allegations and outcomes.[90]

Optimizing Levers to Transfer NIH-Funded Technologies into Private Sector Product Development

NIH funding is critical to stimulating new knowledge and discoveries driving innovation across sectors, and the agency is committed to thinking carefully about its role in making federally funded inventions accessible to the public. To that end, on July 31, 2023, NIH hosted a workshop titled *Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer*, focused on how NIH, as a research institution, approaches patenting and licensing of inventions.[91] The workshop panels tracked the path an invention can take from discovery to licensing, and panelists explored how NIH decides what to patent and license, who NIH partners with, and how NIH negotiates those agreements. Throughout the day, panelists shared perspectives on how NIH can best approach these questions to fulfill public health goals. NIH invited technology transfer professionals from inside and outside NIH, as well as patient advocates, academics, legal experts, and industry. There was also a separate oral public comment period and opportunities for written public comments.

Continuing to Promote Safe and Secure Research

NIH is committed to ensuring the safe and secure conduct of research to preserve critical advances while appropriately managing the potential risks. One example is a recent effort of the Novel and Exceptional Technology and Research Advisory Committee (NExTRAC), which is an advisory committee that provides recommendations to the NIH Director and provides a public forum for the discussion of the scientific, safety, and ethical issues associated with emerging biotechnologies. In 2020, NExTRAC was charged to consider issues associated with conducting research with gene drive modified organisms (GDMOs) safely and responsibly. During its deliberations, the Committee consulted with subject matter experts and held a public workshop. Ultimately, the NExTRAC produced key recommendations for strengthening NIH's existing policies and guidance which are outlined in its final report to NIH,[92] and which helped inform a proposed policy update to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*.[93] The proposed revisions would strengthen biosafety practices and incorporate specific considerations and requirements for NIH-supported research involving GDMOs in contained research settings. Furthermore, NIH continues to promote biomedical research that prioritizes biosecurity. For example, NIH supports the activities of the National Science Advisory Board for Biosecurity (NSABB),[94] a federal advisory committee chartered to provide advice and guidance to the U.S. Government on issues related to biosecurity and dual-use research, and any other issues as directed by the HHS Secretary. In 2023, NSABB provided

[89] nexus.od.nih.gov/all/2022/05/10/congress-strengthens-nihs-ability-to-address-harassment-in-nih-funded-activities/
[90] grants.nih.gov/grants/policy/harassment/data
[91] osp.od.nih.gov/events/workshop-on-transforming-discoveries-into-products-maximizing-nihs-levers-to-catalyze-technology-transfer/
[92] osp.od.nih.gov/wp-content/uploads/NExTRAC-Gene-Drives-Final-Report.pdf
[93] federalregister.gov/d/2023-17178
[94] osp.od.nih.gov/policies/national-science-advisory-board-for-biosecurity-nsabb#tab0/

several recommendations[95] in fulfillment of a charge delivered by NIH.[96] These recommendations are helping to inform U.S. Government revisions to two major U.S. biosecurity policy frameworks, which aim to effectively balance science and security while safely enabling critical, lifesaving research.

Enhancing Patient and Community Engagement

Key to NIH efforts to continue to promote responsible and effective research is engagement – not only with members of the broader biomedical sciences community to ensure that NIH policies are keeping pace as science evolves, but also addressing the needs of patients, caretakers, partners in patient advocacy groups, and the communities most impacted by NIH-supported research. In August 2023, the NExTRAC was charged to develop a harmonized and implementable vision and framework for including public voices in the design and planning of NIH-funded clinical research and to define pathways for widespread dissemination of study findings. This framework will outline approaches appropriate for the breadth and diversity of NIH-funded clinical research studies and assess the potential opportunities and challenges of varying levels of engagement activities for different types of clinical research studies, as well as the impact and value of engagement with patients, communities, and the broader public on clinical research. To address this charge, the NExTRAC will consult with the ACD and convene public consultations with a wide range of relevant parties. Through this framework and community convenings, the Committee will provide recommendations regarding different engagement methods, the optimal timing for meaningful engagement activities, and equitable and inclusive approaches for engagement.

Bolstering Infrastructure Needed to Tackle New Challenges

A critical aspect of NIH supporting the discovery of novel diagnostics, therapeutics, and cures to disease is having facilities, infrastructure, and ecosystems that can support state-of-the-art imaging, discover tumors at the earliest stage possible, develop safe and effective novel treatments such as cellular therapy, and more. Support for NIH's physical and digital infrastructure ensures that it can continue to produce the best biomedical products.

Buildings and Facilities

Facilities must co-evolve with science for NIH to achieve its full potential. NIH requests a funding level for Buildings and Facilities (B&F) of $350.0 million, equal to the FY 2023 Final level. This amount will assist in addressing the pressing campus-wide infrastructure needs identified in the independent review of the facility needs of NIH's main campus in 2019 by the National Academies of Sciences, Engineering, and Medicine. NIH's Backlog of Maintenance & Repair (BMAR) was approximately $3.8 billion at the end of FY 2023. Together, the B&F request, continued use of the appropriations general provision allowing use of IC funding for B&F purposes within certain limits, and the planned FY 2025 allocation of $120.6 million from the Nonrecurring Expenses Fund would enable NIH to improve the condition of its facilities and curtail the growth of the BMAR. The COVID-19 pandemic has made biomedical research and the facilities that support it more important than ever. Research facilities will play an important

[95] osp.od.nih.gov/wp-content/uploads/2023/03/NSABB-Final-Report-Proposed-Biosecurity-Oversight-Framework-for-the-Future-of-Science.pdf
[96] osp.od.nih.gov/wp-content/uploads/2022/06/Tabak_and_Jorgenson-2022_Charge_to_the_NSABB.pdf

role in NIH's ability to continue to respond to national and global health threats. This budget aims to adapt NIH buildings and infrastructure to a changing biomedical research landscape, while maintaining the safety and reliability of its buildings and infrastructure.

NIH is considering alternative means of stemming the deterioration of NIH facilities and providing the necessary infrastructure for cutting-edge science. One such strategy is to prioritize whole-building projects that replace outdated BMAR-intensive facilities and also create swing space to renovate facilities more efficiently while activities are relocated elsewhere, as discussed in the separate B&F Congressional Justification chapter.

Cybersecurity
NIH continues to promote cross-NIH multi-year activities to improve the overall cybersecurity posture of NIH and to meet the standards and requirements set forth in the President's Executive Order on Improving the Nation's Cybersecurity, issued on May 12, 2021, and subsequent memoranda and Department of Homeland Security/Cybersecurity and Infrastructure Security Agency (CISA) directives. Estimated cybersecurity funding of $251.4 million in FY 2025 will support pro-active, risk-based cybersecurity protections necessary to keep up with the increasing threats to NIH and the cybersecurity challenges and attacks that threaten the privacy and security of NIH's data and overall operations. Specific funding is needed to support NIH-wide cybersecurity investments and improvements to support NIH in three broad areas of requirements:

- Enable better prevention, detection, assessment, and remediation of cybersecurity threats. A high priority is NIH's multi-year initiative to implement a Zero Trust Architecture across the NIH network and operating environments, including on-premises and cloud platforms.
- Continue improvements in tools and capabilities to protect all NIH data, systems, and services, and reduce the cyber-attack surface.
- Expand, enhance, and deploy capabilities for NIH-wide continuous monitoring, risk mitigation, and incident response.

Research Resource Infrastructure
The National Primate Research Centers (NPRCs) and other nonhuman primate (NHP) facilities are national resources that serve NIH and federal investigators, as well as researchers in private biomedical research foundations and the biotechnology and pharmaceutical industries. NHPs are critical for understanding a wide range of human diseases and informing the development of vaccines and therapeutics. Beyond the need for NHPs in responding to emerging infectious diseases, these animal models have led to critical advances in metabolism, developmental biology, diabetes, obesity, aging, organ transplantation, and cardiovascular and neurologic diseases, among many others. More recent applications of NHP models have been in the fields of regenerative medicine and gene therapy.

The COVID-19 pandemic increased the demand for nonhuman primates,[97] because these preclinical models are the most relevant to disease and treatment in humans. The increased demand highlighted the already limited availability of research NHPs and the infrastructure

[97] nature.com/articles/s41684-021-00760-9

required to support them. Failing to adequately expand U.S. NHP resources and expertise available through NPRCs and other NHP research centers will adversely affect our Nation's ability to respond to emerging infectious disease threats and the development of new vaccines and therapeutics. In addition, with limited research resources, maintaining pandemic preparedness and ongoing SARS-CoV-2 research such as for post-COVID sequelae also slows research in other biomedical fields such as Alzheimer's disease, diabetes, or other illnesses.

During the COVID-19 pandemic, NIH rapidly recognized the need to increase domestic rhesus macaque colonies, improve infrastructure, provide biocontainment facilities, and ensure research and animal welfare expertise at the NPRCs.[98,99,100] NPRCs were awarded funds from the CARES Act to modernize and improve housing for rhesus macaque breeding colonies, improve animal care infrastructure support, purchase equipment, and renovate high-containment research facilities. Thus, these funds supported a necessary, but limited increase in the overall efficiency of breeding colonies and accessibility of Biosafety Level-3 laboratories, providing rapid support for COVID-19 research. CARES Act funds were a one-time investment and expired in FY 2024. Expanding support for NHP research infrastructure is needed to ensure that the Nation's critical biomedical research enterprise is improved and remains competitive worldwide.

The NIH Office of Research Infrastructure Programs (ORIP) supports a well-coordinated national consortium of seven NPRCs and five other NHP breeding colonies that collectively address current and emerging research needs, best husbandry practices, maintenance of genetic diversity, standardization of animal models, scientific rigor, and reproducibility. The FY 2025 NIH request includes $10.0 million for improvements to NHP infrastructure, as part of total support of $120.0 million for the NPRCs. This request would provide critical funding to improve facilities used to house NHPs, which require continual updates and maintenance. The funds would be distributed by soliciting applications from the existing NHP research centers to improve facilities. Several NHP facilities are over 60 years old, and housing enclosures require frequent repair and replacement. New construction for research facilities would include improvements to animal holding and animal care rooms, updated equipment – including centrifuges, ultrasound devices, clinical analyzers, veterinary clinical support, and psychological and environmental enrichment, which necessitates highly skilled technical staff and additional resources to provide proper care of the nonhuman primates. This FY 2025 request builds on earlier investments in these research centers to maximize their use for a broad range of NIH research.

Catalyzing the Use and Development of Novel Alternative Methods (NAMs)
From its foundation to the present day, NIH has funded research into the development and application of Novel Alternative Methods (NAMs, sometimes referred to as New Approach Methodologies, or non-animal models) as valuable tools in supporting its mission. These experiments *in chemico* (cell-free models), *in vitro* (cultured cells), and *in silico* (computational modeling and simulation) can complement and sometimes replace and refine the use of animal studies. NIH investment in NAMs has increased dramatically over the past 15 years alongside the agency's ever-expanding technological capabilities. By continuing to increase its portfolio

[98] orip.nih.gov/sites/default/files/ORIP_Nonhuman_Primate_Resources_Fact_Sheet.pdf
[99] orip.nih.gov/resource-directory/national-primate-research-centers
[100] nprcresearch.org

investment in NAMs, NIH aims to provide researchers with complementary tools to existing animal models that hold great promise in establishing more accurate and reliable research into human health and disease. In January 2023, the Acting NIH Director charged a new ACD Working Group on *Catalyzing the Use and Development of Novel Alternative Methods* (Working Group) to identify where NAMs are currently being used and to make recommendations on where NAMs are positioned to be most applicable or beneficial, especially in terms of advancing our understanding of human health.[101] This Working Group includes members with expertise in a wide range of technologies, scientific fields, and backgrounds, including members from academia, industry, and federal partners with *ex officio* members. The establishment of this Working Group follows on the recommendation included in the ACD Working Group on *Enhancing Rigor, Transparency, and Translatability in Animal Research's* June 2021 report.[102] The final report was published in December 2023 and identifies seven thematic clusters of high priority needs that should be addressed moving forward.[103] NIH is simultaneously conducting planning activities to inform a potential Common Fund research program called Complement Animal Research In Experimentation (Complement-ARIE) aimed at the development, standardization, validation, and use of NAMs that will more accurately model human biology.[104]

Conclusion

The Nation's investment in NIH is born from the recognition that a healthy population is a productive and thriving population. NIH seeks to foster a culture of scientific minds with diverse backgrounds and ideas; a culture that endeavors to conduct science with the highest standards of rigor and integrity to achieve the NIH mission of improving the health and well-being of all Americans. Each year, NIH awards over 60,000 grants that directly support more than 300,000 researchers at more than 2,500 different institutions. NIH investments in research stimulate increased private investment. A $1.00 increase in public basic research stimulates an estimated additional $8.38 of industry R&D investment in a particular research area after eight years. In rural states, each $1.00 of NIH spending generated an average $1.80 of total economic impact.[105] This economic activity then generates significant revenues for state and local governments, quantified by a 2019 study as an average of $22 million per state for applicable taxes and fees paid by businesses and employees.[106]

A healthier nation is a more productive and economically sound nation. As one example, NIH-supported research on drug development for eye diseases has saved $28.5 billion in health care costs over 10 years and reduced legal blindness due to wet age-related macular degeneration by 50 percent.[107] Each permanent one percent reduction in cancer deaths alone has been approximated to have a value of nearly $500 billion to current and future generations of

[101] acd.od.nih.gov/working-groups/novel-alternatives.html
[102] acd.od.nih.gov/documents/presentations/06112021_ACD_WorkingGroup_FinalReport.pdf
[103] acd.od.nih.gov/documents/presentations/12142023_NAMs_Working_Group_Report.pdf
[104] commonfund.nih.gov/complementarie/strategicplanning
[105] sciencepolicy.colorado.edu/students/envs_5100/Toole2007.pdf
[106] unitedformedicalresearch.org/wp-content/uploads/2019/03/NIH-Research-Rural-States-ExecutiveSummary-FINAL-3.13.19.pdf
[107] pubmed.ncbi.nlm.nih.gov/32681907/

Americans. A full cure could be worth more than three times today's Gross Domestic Product.[108] The benefits of NIH research can be felt in the near term through the 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.

[108] ucema.edu.ar/u/je49/capital_humano/Murphy_Topel_JPE.pdf

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 supporting research to translate and effectively disseminate that knowledge to advance the development and adoption of new diagnostics, therapeutics, and preventive measures to improve health.

The FY 2025 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 and well-being 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. As outlined in the *NIH-Wide Strategic Plan for FY 2021-2025*,[109] NIH supports a wide spectrum of biomedical and behavioral research and engages in a full range of activities that enable research. Because of this diversity and complexity, NIH uses a set of representative performance measures that reflects the priorities enumerated in the *Plan* and allows for tracking progress on the *Plan*. Collectively, NIH's measures reflect the Agency's objectives to: 1) advance biomedical and behavioral sciences; 2) develop, maintain, and renew scientific research capacity; and 3) exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science. Furthermore, the measures support the Administration's goal of protecting and improving the health and well-being of the American people. They reflect NIH's ongoing efforts to address a variety of public health challenges and to further the U.S. biomedical research enterprise, including the need to identify effective prevention interventions for substance use disorders, support the development of diagnostic technologies and antiviral drugs to enhance pandemic preparedness, leverage health information technologies to improve minority health and reduce health disparities, and diversify and foster the next generation of biomedical and behavioral scientists.

[109] www.nih.gov/about-nih/nih-wide-strategic-plan

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 research capacity-building programs and administrative management functions.

The NIH performance framework includes: 1) priority setting with input from key communities; 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-quality research is a process of adapting to new developments and newly identified barriers, and frequently involves 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.

All 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 the 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 NIH approach to performance management is undergirded by the NIH Governance Structure. That structure includes the NIH Steering Committee and standing Working Groups.[110, 111] 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.

[110] 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.

[111] The standing working groups are: Board of Scientific Directors; Clinical Center Governing Board; Data Science Policy Council; Diversity, Equity, Inclusion, and Accessibility Working Group; Extramural Activities Working Group; Enterprise Information Technology Council; Facilities Working Group; Management and Budget Working Group; Research Services Working Group; Scientific Data Council; and UNITE.

ALL PURPOSE TABLE

(Dollars in Millions)[1,2,3]	FY 2023	FY 2024	FY 2025	
	Final[7]	CR	President's Budget	+/- FY 2023 Final
Total, NIH Program Level	**$49,178.485**	**$48,609.035**	**$51,616.517**	**$2,438.032**
Less mandatory and funds allocated from different sources:				
PHS Program Evaluation	$1,412.482	$1,412.482	$2,018.482	$606.000
Mandatory Type 1 Diabetes Research – Baseline[4]	$141.450	$150.000	$0.000	-$141.450
Mandatory Type 1 Diabetes Research – Proposed	$0.000	$100.000	$260.000	$260.000
Mandatory Type 1 Diabetes Research Subtotal	$141.450	$250.000	$260.000	$118.550
Mandatory Cancer Moonshot	$0.000	$0.000	$1,448.000	$1,448.000
Total, NIH Discretionary Budget Authority	**$47,624.553**	**$46,946.553**	**$47,890.035**	**$265.482**
Interior Budget Authority	$83.035	$83.035	$83.035	$0.000
Total, NIH Labor/HHS Budget Authority	**$47,541.518**	**$46,863.518**	**$47,807.000**	**$265.482**
Total, NIH Program Level, excluding ARPA-H	**$47,678.485**	**$47,109.035**	**$50,116.517**	**$2,438.032**
Pandemic Preparedness Mandatory via PHSSEF (non-add)	*$0.000*	*$0.000*	*$2,690.000*	*$2,690.000*
Number of Competing RPGs	*11,106*	*9,739*	*10,273*	*-833*
Total Number of RPGs	*43,176*	*42,973*	*43,636*	*460*
FTE[5]	*19,180*	*20,942*	*21,256*	*2,076*
Nonrecurring Expenses Fund:[6]	*$63.140*	*$120.130*	*$120.555*	
ORF/ORS/NIAID Support Facilities, Rocky Mountain Laboratories, MT	*$40.650*			
Electrical Power Reliability, Building 10	*$22.490*	*$26.100*	*$30.000*	
Replace Steam & Chilled Water Lines from Vault 2 to Vault 31C		*$29.300*		
Replace Cooling Towers 18,19 and Chillers 17,18,19		*$40.000*		
Repair Parking Garages, Bethesda		*$13.360*		
Building 11 Provide Sprinkler Protection		*$11.370*		
Upgrade Existing Site Electrical Distribution System, Bethesda Campus			*$52.875*	
Research Triangle Park, Generator For Campus Emergency Chilled Water Service			*$37.680*	

1 Numbers may not add due to rounding.

2 Includes 21st Century Cures Act funding and ARPA-H.

3 All columns reflect a reduction by transfer of $5.0 million from OD to the HHS Office of Inspector General.

4 Amount in FY 2023 reflects a reduction of $8.550 million for Budget Control Act sequestration; baseline reflects assumed reauthorization at level of $150.0 million in FY 2024.

5 Includes 4 NIH FTEs funded by PHS trust funds in all years.

6 FY 2024 NEF project requests are currently under review and pending OMB approval. HHS has not yet notified for FY 2025.

7 Excludes emergency and supplemental funding of $27.5 million in the Disaster Relief Supplemental Appropriations Act (P.L. 117-328, Division N).

IMPACT OF BUDGET LEVEL ON PERFORMANCE

Programs and Measures (Dollars in Millions, except where noted)	**FY 2023 Final**	**FY 2024 CR**	**FY 2025 President's Budget**	**FY 2025 +/- FY 2023**
Research Project Grants	$26,580.896	$26,307.866	$27,141.249	2.1%
Competing Average Cost (in thousands)	$611	$579	$591	-3.3%
Number of Competing Awards (whole number)	11,106	9,739	10,273	-7.5%
Estimated Competing RPG Success Rate	21.4%	17.5%	18.4%	-3.0%
Research Centers	$2,881.155	$2,852.909	$2,931.206	1.7%
Other Research	$3,336.712	$3,189.658	$3,917.757	17.4%
Training	$984.331	$1,021.440	$1,034.208	5.1%
Research & Development Contracts	$4,032.891	$3,857.225	$4,582.467	13.6%
Intramural Research	$5,046.199	$5,133.445	$5,274.376	4.5%
Research Management and Support	$2,331.451	$2,442.336	$2,689.558	15.4%
Common Fund (non-add)	*$735.001*	*$735.001*	*$722.401*	*-1.7%*
Advanced Research Projects Agency for Health (ARPA-H)[1]	$1,500.000	$1,500.000	$1,500.000	0.0%
Buildings & Facilities Appropriation	$350.000	$350.000	$350.000	0.0%
Other Mechanisms[2,3]	$2,134.849	$1,954.155	$2,195.696	2.9%
Total, Program Level[4]	**$49,178.485**	**$48,609.035**	**$51,616.517**	**5.0%**
Total, Program Level excluding ARPA-H	$47,678.485	$47,109.035	$50,116.517	5.1%
Mandatory Pandemic Preparedness via PHSSEF (non-add)			*$2,690.000*	*N/A*

[1] FY 2023 and FY 2024 reflects the amount transferred from the HHS Office of the Secretary.

[2] 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.

[3] Amounts in each year reflect directive transfer of $5.0 million to the HHS Office of Inspector General.

[4] 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 for Type 1 Diabetes and Cancer Moonshot.

APPROPRIATIONS LANGUAGE

NATIONAL CANCER INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to cancer, $7,839,141,000, of which $716,000,000 shall remain available until expended, and of which up to $50,000,000 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, $3,997,086,000.

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, $521,695,000.

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, $2,309,991,000.

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, $2,788,327,000.

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, $6,581,291,000.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to general medical sciences, $3,249,375,000, of which $2,018,482,000 shall be from funds available under section 241 of the PHS Act: Provided, That not less than $427,231,000 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, $1,766,415,000.

NATIONAL EYE INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to eye diseases and visual disorders, $898,818,000.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

For carrying out section 301 and title IV of the PHS Act with respect to environmental health sciences, $916,791,000.

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, $83,035,000.

NATIONAL INSTITUTE ON AGING

For carrying out section 301 and title IV of the PHS Act with respect to aging, $4,425,295,000.

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, $689,697,000.

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, $535,929,000.

NATIONAL INSTITUTE OF NURSING RESEARCH

For carrying out section 301 and title IV of the PHS Act with respect to nursing research, $198,263,000.

NATIONAL INSTITUTE ON ALCOHOL EFFECTS AND ALCOHOL-ASSOCIATED DISORDERS

For carrying out section 301 and title IV of the PHS Act with respect to alcohol misuse, alcohol use disorder, and other alcohol-associated disorders, $598,903,000.

NATIONAL INSTITUTE ON DRUGS AND ADDICTION

For carrying out section 301 and title IV of the PHS Act with respect to drugs and addiction, $1,668,343,000.

NATIONAL INSTITUTE OF MENTAL HEALTH

For carrying out section 301 and title IV of the PHS Act with respect to mental health, $2,503,162,000.

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

For carrying out section 301 and title IV of the PHS Act with respect to human genome research, $663,660,000.

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, $441,944,000.

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, $170,894,000.

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, $526,710,000.

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), $95,415,000.

NATIONAL LIBRARY OF MEDICINE

For carrying out section 301 and title IV of the PHS Act with respect to health information communications, $526,796,000: Provided, That of the amounts available for improvement of information systems, $4,000,000 shall be available until September 30, 2026: Provided further, That in fiscal year 2025, 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, $926,086,000: Provided, That up to $70,000,000 shall be available to implement section 480 of the PHS Act, relating to the Cures Acceleration Network: Provided further, That at least $631,444,000 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, $3,000,855,000: 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 $722,401,000 shall be available for the Common Fund established under section 402A(c)(1) of the PHS Act: Provided further, That $153,909,000 shall be available for the Office of Research on Women's Health established under section 486 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 up to $10,000,000 shall be used to carry out section 404I of the PHS Act (42 U.S.C. 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 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 2025 and 2026 no later than 30 days after the date of

enactment of this Act: Provided further, That amounts made 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 Office of the Director, $12,600,000 is appropriated from the 10-year Pediatric Research Initiative Fund described in section 9008 of the Internal Revenue Code of 1986 (26 U.S.C. 9008), 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.

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, $350,000,000, to remain available through September 30, 2029.

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, $127,000,000, 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.

GENERAL PROVISIONS

SEC. 214. Not to exceed $100,000,000 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 $5,000,000 per project.

LANGUAGE ANALYSIS

Language Provision to be Changed[112]	Explanation/Justification
OFFICE OF THE DIRECTOR *Provided further, That $153,909,000 shall be available for the Office of Research on Women's Health established under section 486 of the PHS Act*	This revision specifically enumerates the funding for the Office of Research on Women's Health within the Office of the Director (OD).
OFFICE OF THE DIRECTOR *In addition to other funds appropriated for the Office of the Director, $12,600,000 is appropriated from the 10-year Pediatric Research Initiative Fund described in section 9008 of the Internal Revenue Code of 1986 (26 U.S.C. 9008), 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.*	This proposed revision removes references to the Common Fund within the Gabriella Miller section of the OD appropriations language since as of FY 2025 the Gabriella Miller Kids First Pediatric Research program will be funded within the OD Division of Program Coordination, Planning, and Strategic Initiatives rather than in the Common Fund.

[112] Language changes are relative to appropriations language proposed in the FY 2024 President's Budget.

BUDGET MECHANISM TABLE

(Dollars in Thousands)[1,2,3]	FY 2023 Final[9]		FY 2024 CR[9]		FY 2025 President's Budget[9]		FY 2025 +/- FY 2023 Final	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	30,177	$17,975,116	31,389	$19,039,410	31,481	$19,444,480	1,304	$1,469,365
Administrative Supplements[3]	*(3,793)*	535,090	*(3,048)*	368,151	*(2,999)*	351,610	*(-794)*	-183,480
Competing	11,106	$6,783,224	9,739	$5,643,337	10,273	$6,069,919	-833	-$713,305
Subtotal, RPGs	41,283	$25,293,430	41,128	$25,050,898	41,754	$25,866,009	471	$572,580
SBIR/STTR	1,893	1,287,467	1,845	1,256,967	1,882	1,275,239	-11	-12,227
Research Project Grants	43,176	$26,580,896	42,973	$26,307,866	43,636	$27,141,249	460	$560,352
Research Centers:								
Specialized/Comprehensive	1,045	$2,271,984	1,065	$2,317,655	1,119	$2,480,487	74	$208,504
Clinical Research	57	328,369	36	258,996	24	198,750	-33	-129,619
Biotechnology	40	64,909	40	65,869	30	42,739	-10	-22,171
Comparative Medicine	49	137,280	47	131,225	47	130,065	-2	-7,214
Research Centers in Minority Institutions	23	78,613	23	79,164	23	79,164	0	551
Research Centers	1,214	$2,881,155	1,211	$2,852,909	1,243	$2,931,206	29	$50,051
Other Research:								
Research Careers	5,043	$928,335	5,030	$935,151	5,048	$945,157	5	$16,822
Cancer Education	83	23,219	82	22,837	82	22,837	-1	-382
Cooperative Clinical Research	269	485,641	245	485,100	436	1,008,525	167	522,884
Biomedical Research Support	126	111,657	120	103,257	47	54,321	-79	-57,336
Minority Biomedical Research Support	154	55,759	86	37,745	30	25,523	-124	-30,236
Other	2,536	1,732,101	2,457	1,605,568	2,764	1,861,395	228	129,294
Other Research	8,211	$3,336,712	8,020	$3,189,658	8,407	$3,917,757	196	$581,046
Total Research Grants	52,601	$32,798,763	52,204	$32,350,433	53,286	$33,990,212	685	$1,191,449
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,968	$191,272	4,113	$200,800	4,122	$203,304	154	$12,032
Institutional Awards	13,469	793,060	13,812	820,640	13,800	830,904	331	37,844
Total Research Training	17,437	$984,331	17,925	$1,021,440	17,922	$1,034,208	485	$49,876
Research & Development Contracts	2,745	$4,032,891	2,623	$3,857,225	2,933	$4,582,467	188	$549,576
(SBIR/STTR) (non-add)[3]	*(101)*	*(75,193)*	*(79)*	*(61,364)*	*(166)*	*(130,942)*	*(65)*	*(55,750)*
Intramural Research		$5,046,199		$5,133,445		$5,274,376		$228,177
Research Management & Support		2,331,451		2,442,336		2,689,558		358,107
SBIR Admin (non-add)[3]		*(10,098)*		*(10,881)*		*(11,287)*		*(1,188)*
Office of the Director - Appropriation[3,4]		*(3,066,208)*		*(2,885,514)*		*(3,044,455)*		*(-21,753)*
Office of the Director - Other		2,021,814		1,841,120		2,062,661		40,847
ORIP (non-add)[3,4]		*(309,393)*		*(309,393)*		*(259,393)*		*(-50,000)*
Common Fund (non-add)[3,4]		*(735,001)*		*(735,001)*		*(722,401)*		*(-12,600)*
ARPA-H		1,500,000		1,500,000		1,500,000		0
Buildings and Facilities[5]		380,000		380,000		400,000		20,000
Appropriation[3]		*(350,000)*		*(350,000)*		*(350,000)*		*(0)*
Type 1 Diabetes[6,7]		-141,450		-250,000		-260,000		-118,550
Mandatory Cancer Moonshot[6]		0		0		-1,448,000		-1,448,000
Program Evaluation Financing[6]		-1,412,482		-1,412,482		-2,018,482		-606,000
Subtotal, Labor/HHS Budget Authority		**$47,541,518**		**$46,863,518**		**$47,807,000**		**$265,482**
Interior Appropriation for Superfund Research		83,035		83,035		83,035		0
Total, NIH Discretionary Budget Authority		**$47,624,553**		**$46,946,553**		**$47,890,035**		**$265,482**
Type 1 Diabetes[7]		141,450		250,000		260,000		118,550
Mandatory Cancer Moonshot		0		0		1,448,000		1,448,000
Total, NIH Budget Authority		**$47,766,003**		**$47,196,553**		**$49,598,035**		**$1,832,032**
Program Evaluation Financing		1,412,482		1,412,482		2,018,482		606,000
Total, Program Level		**$49,178,485**		**$48,609,035**		**$51,616,517**		**$2,438,032**
Pandemic Preparedness Mandatory via PHSSEF (non-add)[8]		*(0)*		*(0)*		*(2,690,000)*		*(2,690,000)*

See footnotes on following page.

Budget Mechanism Table Footnotes.

[1] Subtotal and Total numbers may not add due to rounding.

[2] Includes 21st Century Cures Act funding and excludes supplemental financing.

[3] 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), mandatory Cancer Moonshot, and 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] Amount in FY 2023 reflect a reduction of $8.550 million for Budget Control Act sequestration. FY2024 reflects annualized CR level of $150.0 million plus $100.0 million reauthorization proposal..

[8] The FY 2025 budget also provides $20 billion in mandatory funding across HHS for pandemic preparedness, which is reflected in the Public Health and Social Services Emergency Fund chapter. Of this total, NIH will receive $2,690 million.

[9] Reduced by a transfer of $5.0 million from OD to the HHS Office of Inspector General.

AUTHORIZING LEGISLATION

(Dollars in Thousands)	FY 2024 Amount Authorized	FY 2024 Amount Appropriated[1]	FY 2025 Amount Authorized	FY 2025 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[2]	TBD	46,361,400	TBD	48,190,882
Advanced Research Projects Agency-Health: Section 499A(s) of the PHS Act	500,000	1,500,000	500,000	1,500,000
Pediatric Research Initiative: Section 402A(a)(2) of the PHS Act[3]	TBD	12,600	TBD	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	83,035	Indefinite	83,035
3. 21st Century Cures Act:				
Precision Medicine: Section 1001(b)(4)(A)	235,000	235,000	36,000	36,000
BRAIN Initiative: Section 1001(b)(4)(B)	172,000	172,000	91,000	91,000
Cancer Moonshot: Section 1001(b)(4)(C)	0	0	0	0
4. Special Diabetes Programs: Section 330B(b) of the PHS Act[4]	65,753	65,753	TBD	260,000

[1]Reflects annualized amounts under the FY 2024 Continuing Resolution.

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

[3]The authorization of appropriations expired as of September 30, 2023.

[4]The amount for the Special Diabetes Programs in the FY 2024 Amount Appropriated column reflects the funding level enacted on January 19, 2024 in Public Law 118-35.

APPROPRIATIONS NOT AUTHORIZED BY LAW

	Last Year of Authorization	Authorization Level	Appropriations in Last Year of Authorization	Appropriations in FY 2024[1]
NIH Labor/HHS Budget Authority[2]	FY 2020	$36,472,442,775	$40,954,400,000	$46,361,400,000

[1]Reflects annualized levels under the FY 2024 Continuing Resolution.

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

NARRATIVE BY ACTIVITY TABLE/HEADER TABLE

(Dollars in Millions)	FY 2023 Final[3]	FY 2024 CR[3]	FY 2025 President's Budget[3]	FY 2025 +/- FY 2023
Program Level[1,2]	$49,178.5	$48,609.0	$51,616.5	$2,438.0
Program Level, excluding ARPA-H[1,2]	$47,678.5	$47,109.0	$50,116.5	$2,438.0
FTE	19,180	20,942	21,256	2,076

[1] All columns exclude supplemental funds.

[2] Includes 21st Century Cures Act funding, mandatory funding for Cancer Moonshot and Type 1 Diabetes, and Superfund; includes NIGMS Program Evaluation funding of (in thousands) $1,412,482 in FY 2023, $1,412,482 in FY 2024, and $2,018,482 in FY 2025.

[3] Reduced by transfer to the HHS Office of Inspector General ($5.0 million).

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 seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to improve the health of the Nation. To achieve these goals, NIH supports research on the causes, prevention, and treatments of human diseases and disorders; processes in healthy development and aging; and methods for collecting and disseminating data and health information. NIH invests over $45 billion annually in research programs to achieve its mission.

In FY 2023, NIH-funded scientists have continued to make paradigm-shifting contributions across the full spectrum of biomedical, behavioral, and social sciences research from groundbreaking basic science through pivotal clinical trials and implementation research. As the coronavirus disease 2019 (COVID-19) pandemic has shifted, NIH has continued adopting new approaches, learned during the pandemic, to enhance mission-critical scientific research and funding. The lessons learned continue to both inform other research areas and ensure preparedness for future public health emergencies. Examples of these critical efforts and scientific research areas are described below.

Looking beyond the COVID-19 Pandemic

With the COVID-19 Public Health Emergency ending, NIH has prioritized the overarching review of its response to the COVID-19 pandemic, including the assessment of NIH's management, operations, procedures, policies and resource allocations. In FY 2023, together with partner organizations, NIH leadership outlined NIH's COVID-19 research response and critical lessons learned, highlighting recent biomedical efforts and developments that will inform the public health research response to future pandemics. By building on decades of basic and applied research and engaging in highly collaborative public-private partnerships, NIH and the broader biomedical community were able to quickly develop safe and effective vaccines, therapeutics, and diagnostics in response to the fast-evolving COVID-19 pandemic. Lessons learned from the COVID-19 pandemic will be translated into actionable initiatives, policy changes, and other recommendations that will ensure NIH is prepared for the next pandemic and public health crisis. Efforts to prepare for the next emerging and re-emerging disease are already underway with NIH-funded research teams working to develop universal vaccines against diseases with pandemic potential and to support global surveillance of pathogens and advance response readiness.

A paramount focus of NIH's COVID-19 response was community engagement. In collaboration with the Administration for Strategic Preparedness and Response (ASPR) at the U.S. Department of Health and Human Services (HHS), NIH launched the Home Test to Treat program.[113] This virtual community health intervention provided free COVID-19 health services, including at-home rapid COVID-19 tests, telehealth sessions, and at-home treatments to communities across the country. As part of the RADx-Tech effort, NIH was also instrumental in working with biomedical device manufacturers to quickly develop home-based COVID-19 tests.[114] Building

[113] www.nih.gov/news-events/news-releases/nih-launches-home-test-treat-pilot-covid-19-telehealth-program

[114] www.nibib.nih.gov/covid-19/radx-tech-program/listening-session/agenda

on the important work and infrastructure developed to respond to the COVID-19 pandemic, NIH is more prepared than ever to respond to emerging and re-emerging pathogens and diseases.

While many people recover fully within a few days or weeks of being infected by SARS-CoV-2, the virus that causes COVID-19, others suffer from long-lasting symptoms. To better understand, treat, and prevent this condition, termed Long COVID, the NIH launched the NIH-wide Researching COVID to Enhance Recovery (RECOVER) initiative[115] in 2021. Led by the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Allergy and Infectious Diseases (NIAID), and the National Institute of Neurological Disorders and Stroke (NINDS), in coordination with the Office of the Director (OD) the RECOVER initiative addresses the widespread and diverse manifestations of Long COVID through a national research network that includes observational cohort studies, *in silico* studies of electronic health records, clinical trials, and studies on the underlying pathobiology. RECOVER's comprehensive research framework has provided the critical foundation for understanding and treating Long COVID and is already providing valuable insights into the condition. In FY 2023, NIH also launched and opened enrollment for Phase 2 clinical trials that will evaluate potential treatments for Long COVID, including drugs, biologics, medical devices, and other therapies. The trials are designed to evaluate multiple treatments simultaneously to identify more swiftly those that are safe and effective. The RECOVER-VITAL clinical protocol is looking at whether viral persistence is a cause of some Long COVID symptoms, and RECOVER-NEURO is examining interventions for cognitive dysfunction related to Long COVID, including brain fog, memory problems, and difficulty with attention, thinking clearly, and problem solving. Additional protocols are expected to launch in the coming months.

Addressing Health Disparities and Inequities in Biomedical Research and Supporting a Diverse Health Disparities and Biomedical Research Workforce

Health disparities, preventable differences in health status and outcomes that adversely impact certain populations,[116] are a key focus of NIH's mission to improve health in the United States. NIH is dedicated to improving minority health, reducing health disparities, and removing barriers to health disparities research. Only by researching the influence of environment, social determinants, and other underlying mechanisms which lead to differential health outcomes can disparities in health be prevented. Efforts across NIH are underway to study mechanisms and reduce disparities in all areas of health, with each IC supporting health disparities research and efforts to support a diverse biomedical research workforce as part of their overall portfolios.

At NIH, the National Institute on Minority Health and Health Disparities (NIMHD) leads the way on research to improve minority health and reduce health disparities, collaborating across NIH and the federal government to advance promising studies. NIMHD supports all aspects of this research ranging from genetic, molecular, and biologic science to clinical, behavioral, and translational research, as well as research on health systems, workforce development, and environmental justice. NIMHD recently awarded $60 million in grants through the John Lewis NIMHD Research Endowment Program.[117] These grants will create institutional endowments for the development and expansion of research capacity and infrastructure in recipient

[115] recovercovid.org/
[116] www.nih.gov/ending-structural-racism/minority-health-health-disparities-research
[117] www.nimhd.nih.gov/programs/extramural/research-endowment.html

institutions. This program also supports research education opportunities for students from diverse backgrounds and those from underrepresented groups.

In recognition of the fundamental importance of addressing health disparities in all aspects of the research enterprise, all of the NIH Institutes, Centers, and Offices (ICOs) lead efforts to advance health disparities research and address inequities within their scientific and medical areas of interest. For example, the NIH Common Fund addresses emerging scientific opportunities in biomedical research that no single NIH Institute or Center (IC) can address on its own. The programs within the Common Fund are considered high priority for NIH. One such program is the Community Partnerships to Advance Science for Society (ComPASS).[118] The ComPASS program aims to 1) develop, share, and evaluate community-led health equity structural interventions that leverage partnerships across multiple sectors to reduce health disparities, and 2) develop a new health equity research model for use across NIH and other federal agencies.[119] This first-of-its-kind community-led research program aims to redefine the culture at NIH-funded extramural institutions by implementing a cohort faculty recruitment model and building a community of scientists committed to diversity and inclusivity.

Diversity in the workforce is a key component of innovation and achievement in all areas of research, including health disparities research. The NIH UNITE Initiative was launched in 2021 as an NIH-wide effort committed to ending racial inequities across the biomedical research enterprise. It is composed of five committees, each with a specific, targeted focus: (U)nderstanding stakeholder experiences through listening and learning; (N)ew research on health disparities/minority health/health inequity; (I)mproving the NIH culture and structure for equity, inclusion, and excellence; (T)ransparency, communication, and accountability with NIH's internal and external stakeholders; and (E)xtramural research ecosystem and changing policy, culture, and structure to promote workforce diversity. To support research on health inequities the UNITE Initiative reviews NIH's research portfolio to identify and make recommendations for addressing research gaps, reviews systems for measuring and tracking health disparity research, and supports research on behavioral, biological, and social determinants of health, structural racism, and discrimination. The NIH UNITE Initiative has received considerable community input through a Request for Information (RFI) on how NIH might advance diversity within the biomedical and behavioral research workforce and expand research to eliminate or lessen health disparities and inequities with over 1,100 written responses and an audience of over 1,300 participants across 14 listening sessions. Community input received through the RFI is leading the way for future UNITE Initiative developments. Accountability and communication are a commitment for the UNITE Initiative which is tracking facts and figures regarding aggregated diversity, equity, and inclusion-related data and analyses related to funding, the internal NIH staff, and the external scientific workforce through a public Data Dashboard.[120]

The Chief Officer for Scientific Workforce Diversity (COSWD) Office in the NIH OD leads NIH's efforts in diversifying the national scientific workforce. In 2023, the COSWD Office announced a new initiative, the Diversity, Equity, Inclusion and Accessibility (DEIA) Prize

[118] commonfund.nih.gov/compass

[119] commonfund.nih.gov/first

[120] www.nih.gov/sites/default/files/research-training/initiatives/ending-structural-racism/UNITE-progress-report-2022.pdf

competition.[121] This competition was developed to recognize and reward institutions whose biomedical, social, and behavioral science departments, centers, programs or divisions have identified gaps/barriers towards addressing DEIA; as well as those institutions that, design, implement, and evaluate interventions to address gaps to successfully achieve sustained improvement in DEIA within their faculty, postdoctoral scholars, and student bodies.

In March 2023, NIH released the NIH-Wide Strategic plan for Diversity, Equity, Inclusion and Accessibility.[122] The five-year strategic plan articulates NIH's commitment to strengthen DEIA across the agency to enhance its operations, research, and the workforce. The DEIA Strategic Plan also includes approaches to advance DEIA within the broader biomedical, behavioral, and social sciences research enterprise, including within NIH's workforce and through the research it supports.

In September 2023, NIH designated people with disabilities as a population with health disparities for research support by NIH. People with disabilities often experience a broad and varying range of health conditions leading to poorer health and shorter lifespan. In addition, discrimination, inequality and exclusionary structural practices, programs and policies inhibit access to timely and comprehensive health care, which further results in poorer health outcomes.[123] This decision was made in consultation with the Agency for Healthcare Research and Quality and after careful consideration of a report[124] developed by an NIMHD advisory council, input from the disability community, and a review of the science and evidence. A report[125] issued in December 2022 by the Advisory Committee to the (NIH) Director (ACD), informed by the work of the Subgroup on Individuals with Disabilities, explored similar issues faced by people with disabilities. NIH has also issued a notice of funding announcement[126] calling for research applications focused on novel and innovative approaches and interventions that address the intersecting impact of disability, race and ethnicity, and socioeconomic status on healthcare access and health outcomes. These actions are among the important steps NIH is taking to address health disparities faced by people with disabilities and ensure their representation in NIH research.

NIH will continue to increase coordinated support for research on health disparities and approaches to reducing them and enhance opportunities for scientists and trainees from diverse backgrounds and life experiences. By supporting these goals, NIH will foster scientific innovation, improve the quality of research, and advance opportunities for populations facing health disparities to participate in and benefit from biomedical, behavioral, and social sciences research.

Reignite the Biden Cancer Moonshot

The Cancer Moonshot launched in 2016 with goals of accelerating scientific discovery in cancer, fostering greater collaboration, and improving the sharing of cancer research data. Since its

[121] www.nihdeiaprize.org/about
[122] NIH-Wide Strategic Plan for DEIA
[123] nih.gov/news-events/news-releases/nih-designates-people-disabilities-population-health-disparities
[124] nimhd.nih.gov/docs/advisory-council/nacmhd_workGrpOnHealthDisparitiesAndPeopleWithDisabilities_report_2023sept.pdf
[125] acd.od.nih.gov/documents/presentations/12092022_WGD_Disabilities_Subgroup_Report.pdf
[126] grants.nih.gov/grants/guide/pa-files/PAR-23-309.html

launch, the Cancer Moonshot has made significant progress, launched over 70 research programs and consortia, and supported more than 250 research projects, leading to more than 2,000 research publications and 49 clinical trials. Research advances resulting from the Cancer Moonshot have led to more precise cancer diagnostic tools, novel cancer treatment options, and new data sharing networks and collaborations. In 2022, the Biden Cancer Moonshot was announced with a new ambitious goal to reduce the cancer death rate by half in the next 25 years. To reach this goal, NIH is substantially increasing the number and diversity of people who participate in clinical trials, ensuring access to current and new standards of cancer care, enhancing diversity in the cancer research workforce, and increasing the pipeline of new cancer drugs.[127]

As an example of Cancer Moonshot activities, the Human Tumor Atlas Network supports research to construct three-dimensional atlases of the cellular, morphological, and molecular features of human cancers as they evolve from precancerous lesions to advanced disease.[128] Understanding the molecular features of a cancer cell or tumor can significantly inform diagnostic and treatment decisions by adding clarity to which treatment options a tumor may be most responsive to. A recently released colorectal cancer atlas gives researchers a new and highly detailed view of colorectal cancer tumors, leading to the discovery of previously unnoticed structural and molecular tumor features. The researchers leading the colorectal cancer atlas previously released a melanoma cancer atlas and will soon develop atlases for breast and brain cancer. In addition to their laboratory-based research, scientists are expanding their research methods and bringing their colorectal cancer atlas into the clinic to deliver improved cancer diagnostic and treatment tools to clinicians and patients.[129]

As examples of National Cancer Institute (NCI)-funded research which directly led to development of new therapeutics to make a real difference to patients, the Experimental Therapeutics Clinical Trials Network leverages NCI's relationships with academic institutions, pharmaceutical companies, and individual investigators to support a coordinated, collaborative, and inclusive team-based approach to early phase experimental therapeutic clinical trials. In December 2022, the first of these clinical trials resulted in an U.S. Food and Drug Administration (FDA) approval of an immunotherapy treatment for advanced alveolar soft part sarcoma (ASPS).[130] ASPS is a rare cancer that affects mostly adolescents and young adults. The approval of the ASPS immunotherapy drug, atezolizumab (Tecentriq) was the result of the largest study ever conducted on ASPS, which enabled sarcoma specialists at academic medical centers across North America to enroll patients in the trial. Nearly all of the patients in the clinical trial experienced stable disease and one-third of patients experienced tumor shrinkage as a result of the treatment.[131] In another recent NIH-funded study, patients with pancreatic ductal adenocarcinoma (PDAC), the most common type of pancreatic cancer and one of the deadliest cancer types, were treated with the same immunotherapy drug approved for ASPS in preparation for receiving a customized mRNA vaccine that was developed to specifically target each patient's tumors. Patients who exhibited a strong immune response to their customized mRNA vaccine had an excellent prognosis with no sign of cancer cells returning for a year and a half

[127] www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/progress
[128] humantumoratlas.org/
[129] directorsblog.nih.gov/2023/01/
[130] www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-approval-atezolizumab-alveolar-soft-part-sarcoma
[131] www.cancer.gov/news-events/press-releases/2022/nci-trial-atezolizumab-approval-alveolar-soft-part-sarcoma

after treatment.[132]

As another example of research addressing urgent needs, NIH launched in 2023 the Persistent Poverty Initiative to address the structural and institutional factors of persistent poverty in the context of cancer.[133] Specifically, those who live in areas where 20 percent or more of the population has lived below the federal poverty line for at least 30 years have a higher incidence of cancer, experience delays in cancer diagnosis and treatment, and are more likely to die from cancer than people living in other areas. Despite the known impact that poverty has on cancer diagnoses, care, and prognoses, there has been limited research on how to improve cancer outcomes in persistent poverty areas. This initiative will support five new Centers for Cancer Control Research in Persistent Poverty Areas, lowering barriers to entry and leading to an expansion in the number of people who participate in clinical trials, ensuring that new approaches to preventing and treating cancer work for everyone. The Biden Cancer Moonshot builds on the exceptional research progress since the launch of the Cancer Moonshot and focuses on areas of cancer research and prevention that are most likely to benefit the American people.

Increasing Participation and Representation in Artificial Intelligence and Machine Learning Research Through the AIM-AHEAD Program

Another example of how NIH-funded research is pushing the boundaries of research to benefit everyone is the launch of the Artificial Intelligence/Machine Learning Consortium to Advance Health Equity and Researcher Diversity, or AIM-AHEAD, program in 2021.[134] The artificial intelligence and machine learning (AI/ML) research field lacks diversity in its researchers as well as in the data sets that it uses. These gaps pose a risk of creating and continuing harmful biases in how AI/ML is used, how algorithms are developed and trained, and how findings are interpreted. Critically, these gaps can lead to continued health disparities and inequities for underrepresented communities.

To close these gaps, the AIM-AHEAD program aims to increase the participation and representation of the researchers and communities that are currently underrepresented in AI/ML modeling and applications by creating mutually beneficial partnerships. Efforts are focused on four key areas: partnerships, research, infrastructure, and data science training. By creating a "network of networks" through regional, multi-disciplinary partnerships, AIM-AHEAD is working to integrate AI/ML-focused, data science research networks with community engagement and clinical research networks to form mutually beneficial collaborations and to engage underrepresented scientists across the career pipeline. These multi-disciplinary partners will use existing real-world data, such as electronic health records, image data, and social determinants of health research data to develop and enhance AI/ML algorithms and apply AI/ML approaches to address health inequities and disparities. AIM-AHEAD is also expanding capacity and infrastructure to support AI/ML research in minority-serving institutions (MSIs), through the AIM-AHEAD Program for AI Readiness (PAIR) program and Data and Infrastructure Capacity Building (DICB) program.[135,136]

[132] www.nih.gov/news-events/nih-research-matters/mrna-vaccine-treat-pancreatic-cancer
[133] www.cancer.gov/news-events/press-releases/2023/nci-launches-persistent-poverty-initiative
[134] datascience.nih.gov/artificial-intelligence/aim-ahead
[135] www.aim-ahead.net/call-for-proposals-year-2/hub-specific-pilot-grant-program/
[136] www.aim-ahead.net/call-for-proposals-year-2/consortium-development-projects/

Looking into the future, AIM-AHEAD is training a new generation of diverse researchers and leaders in AI/ML by supporting early-career researchers from underrepresented populations. The AIM-AHEAD Research Fellows program trains researchers in biomedical research to use novel and innovative data science to solve data-focused research problems.[137] A complementary program, the AIM-AHEAD Fellowship Program in Leadership, engages a diverse group of participants to acquire the skills and competencies necessary to become leaders who can advocate for the use of AI/ML as a tool to address health disparities in their communities.[138] AIM-AHEAD also supports training of AI/ML through efforts like the AIM-AHEAD Data Science Training Core Training Practicum (PRIME), which provides AI/ML training for graduate and undergraduate students, and the AIM-AHEAD Connect platform, which serves as a virtual hub to enhance collaboration and connect early-career researchers with mentors.[139,140] These efforts are part of a broader set of investments in training and career development programs across NIH to improve our future.

Research Across the Lifespan

NIH supports research across the human lifespan from screening newborns for fatal disease to better understanding the fundamental reasons why humans age and how healthy lifespan can be improved and even extended. For humans to live a long and healthy life, it is critical to identify disease early and to identify and understand any possible mitigating factors for disease onset and progression.

A study led by researchers at NIAID recently demonstrated just how important early disease detection can be. The NIH-funded Primary Immune Deficiency Treatment Consortium (PIDTC) led a study to measure how effective population-wide newborn screening for a disease called severe combined immunodeficiency (SCID) is at preventing health complications and death. Infants with SCID appear healthy at birth, but are highly susceptible to severe infections and death unless they receive immune-restoring treatment. Analyzing data from the PIDTC, researchers found that early detection using newborn screening and subsequent intervention of SCID led to a 5-year survival rate of 92.5 percent among children with no family history of the disease.[141]

Early intervention and prevention of disease onset is also essential for asthma, which affects over 4 million children in the United States and causes about 150 child deaths per year.[142] Research on mitigating asthma has largely been focused on urban environments and industrial regions where poor air quality contributes to asthma but little work has been done to investigate the impact of air pollutants on asthma in rural agricultural areas. The National Institute of Environmental Health Sciences (NIEHS) supported a study that worked with families and community partners to develop a small sensor that could measure the presence of known asthma irritants in homes and to overcome barriers related to rural agricultural communities' reluctance to participate in clinical studies. Researchers found that pairing the installation of HEPA

[137] www.aim-ahead.net/research-fellowship/
[138] www.aim-ahead.net/leadership-fellowship/
[139] www.aim-ahead.net/data-science-training-core/data-science-training-core-pilot-programs/aim-ahead-training-practicum-prime/
[140] connect.aim-ahead.net
[141] www.nih.gov/news-events/news-releases/screening-newborns-deadly-immune-disease-saves-lives
[142] www.cdc.gov/asthma/most_recent_national_asthma_data.htm

filtration systems in homes with community outreach and education greatly reduced exposure to agricultural irritants and reduced symptoms and biomarkers of asthma in children.[143]

Researchers are working to better understand the fundamental biological processes for why humans age, what factors contribute to aging, and how we might be able to slow down or mitigate risks that contribute to aging and age-related disease. A recent study supported by the National Human Genome Research Institute (NHGRI) contributed to our fundamental understanding of the biological process of senescence, a hallmark of human aging, where cells are in an arrested state, no longer growing or dividing. While studying tissue regeneration in *Hydractinia symbiolongicarpus*, a small, tube-like shaped animal that is related to both jellyfish and coral, researchers found senescent cells. This discovery that senescent cells are involved in regeneration in *Hydractinia* changes how researchers think of senescence, its role in aging, and how the function of senescence may have evolved over time.[144] In another surprising discovery, researchers who have long studied a role for hunger and fasting in aging and longevity found that genetically altering fruit flies to activate their brain's hunger response could increase lifespan, suggesting that activating the biological processes involved in hunger is sufficient to increase lifespan, even when animals are not actually fasting.[145]

NIH supports basic science and health research that promises to benefit all ages, from testing that saves the lives of newborns to research that provides insights on how to live longer, healthier lives.

Down Syndrome Research and the INCLUDE Project

The INCLUDE Project is a NIH-wide initiative, engaging 17 institutes across NIH, that aims to better understand critical health and quality-of-life needs for individuals with Down syndrome (DS). Now entering its fifth year, the INCLUDE Project continues to expand its research portfolio by releasing innovative funding opportunities and building the field of investigators by enhancing career pathways for trainees, early-stage investigators, and established investigators with expertise related to conditions commonly experienced by individuals with DS. Since its launch in FY 2018, the INCLUDE Project has funded approximately 200 research studies spanning all 3 components of the initiative: basic science studies on chromosome 21, large cohort development for individuals with DS, and the inclusion of individuals with DS in clinical trials.

The INCLUDE project touches the full spectrum of basic, translational, and clinical research to address the specific needs of the DS community. The studies supported by the INCLUDE Project are building on countless basic scientific discoveries to make promising contributions to the field and develop an understanding of both the biological and genetic underpinnings of DS and the conditions commonly experienced by individuals with DS. The goal of this NIH-wide program is to prevent these conditions from reducing the capacity of people with DS to lead healthy and optimal lives. To support basic science and foundational investigations on DS, the INCLUDE Project has already driven advances in data sharing and storage infrastructure to increase collaboration, rigor, and transparency in DS-related research. The INCLUDE Data

[143] www.nih.gov/sites/default/files/about-nih/impact/asthma-case-study.pdf

[144] www.nih.gov/news-events/news-releases/scientists-discover-clues-aging-healing-squishy-sea-creature

[145] www.nia.nih.gov/news/study-fruit-flies-finds-hunger-causes-brain-changes-slow-aging

Coordinating Center[146] offers free, accessible tools, including the INCLUDE Data Hub,[147] to bring together and share information and resources for researchers to study DS, a relatively rare condition difficult to study in large populations, more quickly. Basic science research and data tools will increase the potential for DS research to enhance the quality of life for individuals with DS and their families.

The INCLUDE Project also aims to establish needed knowledge and infrastructure for advancing treatments and other clinical therapies inclusive of people with DS. In FY 2021, the INCLUDE Project supported seven clinical studies investigating potential treatments for critical and co-occurring conditions associated with DS. These studies aim to assess treatments for sleep apnea and ADHD, and to evaluate the impact of hypoglossal nerve stimulation on cognition and language.[148] Early results show promise for each potential therapy, despite setbacks caused by the COVID-19 pandemic. NIH anticipates increasing its support for clinical trials in the coming years, including support for a trial to examine the effect of anti-amyloid drugs in individuals with DS. As the INCLUDE Project continues to support the highest quality, targeted research designed to address critical health and quality-of-life needs for individuals with DS and their families, the applications of such research will lead to even greater improvements to care.

The INCLUDE Project is also expanding the diversity of participants in study cohorts and clinical trials through dedicated outreach to underrepresented communities. The INCLUDE Project recently developed a Strategic Communication and Outreach plan. This plan outlines unique opportunities the INCLUDE Project will pursue to amplify communications, ensure representation and diversity in DS research by reaching new communities, and engage new and early-stage investigators through websites, workshops, and resources for scientists and clinicians. In Fall 2022, the INCLUDE Project held a virtual workshop[149] on diverse cohort recruitment for investigators, clinicians, self-advocates, and family members to identify barriers for research participation, and share effective strategies and best practices for expanding the diversity of DS research participants as well as researchers. INCLUDE has used the input from this workshop and listening sessions, as well as the strategies presented, to advance INCLUDE Project goals to improve diverse recruitment and support researchers.

In 2022, NICHD and the INCLUDE Project jointly published the next iteration of the NIH INCLUDE DS Research Plan,[150] detailing a vision for the goals and objectives for NIH-funded DS research until 2028. Importantly, the plan incorporates input from key partners including the public, collected through two RFIs. Approaches to address the need for greater diversity among DS research participants; a better understanding of health disparities among individuals with DS; and expanding the pipeline of new and early-stage investigators with a diversity of expertise and perspectives will be integrated throughout the plan. The DS Research Plan offers a broad overview of NIH-funded projects and summaries of some of the key DS research findings, identified from the projects' nearly 600 publications over the last 7 years while touching on 5 broad themes: basic research, cohort development and epidemiology, clinical research and co-occurring conditions, living and aging with DS services research, and research infrastructure and

[146] includedcc.org/
[147] portal.includedcc.org/
[148] www.nih.gov/include-project/include-project-down-syndrome-ds-research-plan
[149] videocast.nih.gov/watch=46235
[150] www.nih.gov/sites/default/files/research-training/initiatives/include/NIH_INCLUDE_DS_Research_Plan_Final2022.pdf

tools. The plan offers a roadmap for DS-related research, highlighting the continued importance of partnerships among researchers, clinicians, family members, other stakeholders, and most importantly, individuals with DS.

To continue robust support for research on DS, the INCLUDE Project is now both renewing previously successful funding opportunities for researchers and moving into new areas, expanding on what the project has learned and heard from the community to take the INCLUDE Project into the future.

All of Us

Launched in 2018, the *All of Us* Research Program is an ambitious effort to gather health data from one million or more people living in the United States to accelerate research that may improve health. As a longitudinal cohort study, *All of Us* aims to accelerate health and medical breakthroughs to enable individualized prevention, treatment, and care for all. *All of Us* is committed to recruiting a diverse participant pool that includes members of groups that have been left out of research in the past. Currently, more than 50 percent of *All of Us* participants who have completed initial steps of the program identify with a racial or ethnic minority group, and about 80 percent of participants are from populations underrepresented in biomedical research, including people over age 65, LGBTQ+ people, those who live in rural areas, people with low income or limited education, and people with disabilities.

With over half a million participants already enrolled, *All of Us* is building one of the largest, most diverse health databases of its kind, capable of informing thousands of studies on a variety of health conditions. Genomic data from *All of Us* can be used to identify genetic variants, which are genes that are slightly different across the population. Although most genetic variants are harmless, some have been linked to health problems and disease. Demonstrating the power of this resource, researchers have recently used *All of Us* data to identify genetic variants in a gene called *G6PD*, which can cause G6PD deficiency, sometimes leading to anemia, fatigue, trouble breathing, and dizziness. Researchers were able to identify 118 *G6PD* gene variants and distinguish which variants led to G6PD deficiency with or without anemia.[151] Discoveries like this are possible because of the diversity of *All of Us* participants and the amount of health data they share.

Along with identifying genetic variants, *All of Us* data can answer many other questions about human health. For example, researchers recently used *All of Us* data to explore how the COVID-19 pandemic affected the mental health of people who were blind or had low vision. Previous work has identified that half of people with blindness or low vision have anxiety or depression at rates twice as high as people with normal vision. During the pandemic, people with blindness or low vision were at a higher risk of developing new or worsening feelings of anxiety or depression than people with normal vision.[152] Data from *All of Us* allow researchers to explore the links between disability, mental health, and disease, giving insight into the experiences, health, and well-being of a specific population at a unique point in time.

[151] allofus.nih.gov/news-events/research-highlights/discovering-more-genetic-variants-thanks-to-all-of-us-data
[152] allofus.nih.gov/news-events/research-highlights/what-all-us-data-says-blindness-mental-health-covid-19

Maternal Health and Growth of the IMPROVE Initiative

The United States has a higher maternal mortality rate than any other developed nation and maternal health outcomes have only worsened in recent years. In 2021, the U.S. maternal mortality rate increased to 32.9 deaths per 100,000 live births from a rate of 23.8 in 2020 and 20.1 in 2019. Outcomes are significantly worse for certain groups, with non-Hispanic Black women experiencing the highest maternal mortality rate at 69.9 deaths per 100,000 live births.[153] NIH generates ground-breaking research that seeks to better understand the dynamics of maternal health in the United States.

Launched in 2019, the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE)[154] initiative supports research to reduce preventable causes of maternal deaths and to improve health for women before, during, and after delivery. IMPROVE places a special emphasis on health disparities and populations that are disproportionately affected by severe pregnancy complications and maternal death. In FY 2023, as part of this initiative, NIH distributed $8 million in awards to the winners of the Rapid Acceleration of Diagnostics Technology (RADx® Tech) for Maternal Health Challenge,[155] a prize competition aimed to accelerate the development of technologies to improve maternal health outcomes in "maternity care deserts." IMPROVE also sponsored the Connecting the Community for Maternal Health Challenge[156] to encourage and reward non-profit community-based or advocacy organizations to develop research capabilities and infrastructure to pursue research projects in the area of maternal health, inclusive of maternal morbidity and mortality. In FY 2023, NIH also supported the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (nuMoM2b) follow-up nuMoM2b Heart Health Study. Researchers supported by this study found that certain pregnancy complications are associated with increased risks for heart disease, such as developing high blood pressure, years after pregnancy.[157] Additionally, NIH awarded $24 million in first-year funding to establish Maternal Health Research Centers of Excellence in FY 2023, which are designed to develop and implement research projects to address the biological, behavioral, environmental, sociocultural, and structural factors that affect pregnancy-related complications and deaths. They will focus on populations that experience health disparities, including racial and ethnic minorities, socioeconomically disadvantaged populations, those living in underserved rural areas, sexual and gender minority populations and people with disabilities. Research centers will partner with community collaborators, such as state and local public health agencies, community health centers and faith-based organizations. Additionally, the research centers will support training and professional development of maternal health researchers, including those from backgrounds underrepresented in the biomedical research workforce.

In FY 2023, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) sponsored the NIH Technology Accelerator Challenge (NTAC) for Maternal Health,[158] a prize competition that awarded innovative diagnostic technologies for identifying maternal health conditions. This challenge aimed to spur the development of low-cost, point-of-care molecular, cellular, and/or metabolic sensing and diagnostic technologies integrated with a digital platform

[153] www.cdc.gov/nchs/data/hestat/maternal-mortality/2021/maternal-mortality-rates-2021.pdf
[154] www.nichd.nih.gov/research/supported/IMPROVE
[155] www.nichd.nih.gov/newsroom/news/040323-RadxTech-Deep-Dive
[156] www.challenge.gov/?challenge=community-maternal-health
[157] www.nhlbi.nih.gov/news/2023/moms-helping-moms-through-research
[158] www.nibib.nih.gov/research-program/NIH-Technology-Accelerator-Challenge

to guide rapid clinical decision-making, improve patient outcomes, and ultimately prevent maternal morbidity and mortality.

NIH-supported maternal health research has provided much-needed insight into causes of death or morbidity during pregnancy and postpartum. NIH's continued efforts to better understand social, structural, and genetic risk factors that increase maternal mortality rates will lead to more innovative technologies, earlier intervention, and better disease detection that will improve maternal health outcomes in the United States.

To align and support these and other collaborative maternal health initiatives, NIH remains actively engaged in coordinated efforts across the federal government, including the HHS Task Force on Research Specific to Pregnant Women and Lactating Women, the White House Blueprint for Addressing the Maternal Health Crisis and Maternal Health Interagency Policy Committee, and the establishment of HHS agency priority goals for maternal health.

Innovations in Mental Health Research and Treatment

Research shows that mental illnesses are common in the United States, affecting tens of millions of people each year, but estimates suggest that only half of people with mental illnesses receive treatment.[159] These acute needs were further brought to light during the rise of mental health condition incidence during the COVID-19 pandemic. Scientific and clinical advances are paving the way for improvement of mental health conditions. NIMH supports innovative research to transform the understanding and treatment of mental illness and to pave the way for prevention, recovery, and cure. Recent basic science advances include a new study showing that the G protein-coupled receptor GPR158 is capable of altering activity in an area of the brain important for understanding and treating mental disorders.[160] This discovery presents a potential new target for developing improved treatments for mental disorders like anxiety and depression.

Building on findings from the Recovery After an Initial Schizophrenia Episode (RAISE) initiative,[161] the Early Psychosis Intervention Network (EPINET)[162] is a broad clinical research initiative that aims to determine the best way to treat people experiencing symptoms of early psychosis. Psychosis refers to a collection of symptoms that affect the mind, where there has been some loss of contact with reality. During an episode of psychosis, a person's thoughts and perceptions are disrupted, and they may have difficulty recognizing what is real and what is not. Left untreated, psychotic symptoms can disrupt school and work activities, strain family relationships, lead to separation from friends, and make a person's mental health problems worse. Research from RAISE demonstrated that coordinated specialty care (CSC) was more effective for treating psychosis than typical care. CSC is a recovery-oriented, team approach to treating early psychosis that promotes easy access to care and shared decision-making among specialists, the person experiencing psychosis, and family members.[163] It involves individual or

[159] www.nimh.nih.gov/health/statistics
[160] doi.org/10.1126/science.add7150
[161] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/recovery-after-an-initial-schizophrenia-episode-raise
[162] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/early-psychosis-intervention-network-epinet
[163] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/recovery-after-an-initial-schizophrenia-episode-raise

group psychotherapy, family support and education programs, medication management, supported employment and education services, and case management. EPINET funded awards to establish regional scientific hubs connected to multiple CSC programs that provide early psychosis treatment and a national data coordinating center. The initiative has expanded to 8 regional hubs in 17 states with more than 100 clinics that provide coordinated specialty care.[164]

Mental health disorders are highly prevalent among youth and the rates of youth with moderate and severe depression have increased over the last 20 years. The increased prevalence of severe mental health disorders in youth has led to a devastating increase in suicide rates across all youth age groups (10-14 years; 15-19 years; 20-24 years) since 2001.[165] These rates are even more devastating when the data is disaggregated by race, revealing a disparity in suicide rates in Black and American Indian/Alaska Native youth compared to youth who identify with other races.[166] To respond to the need to increase the effectiveness of mental health interventions and to address disparities in the delivery and quality of mental health services for youth populations, NIMH launched the Advanced Laboratories for Accelerating the Reach and Impact of Treatments for Youth and Adults with Mental Illness (ALACRITY) Research Center program.[167] ALACRITY supports 14 mental health research centers across the country whose goals are to rapidly transform treatments for youth mental illness by providing a space to develop and test new mental health research and interventions in a clinical setting. NIH continues to support funding for ALACRITY and to renew resources for research in mental health disorders, test new mental health interventions, and support clinical trials at ALACRITY Research Centers; thereby, reducing barriers to access for cutting edge mental health treatment for youth across the country.

Additionally, NIH is investing in understanding the impacts of social media on the mental health of children and youth. The Adolescent Brain Cognitive Development (ABCD) Study[168] is the largest long-term study of brain development and child health in the United States. Approximately 12,000 children ages 9-10 years have joined the study and will be surveyed into young adulthood about digital media and technology use. Data can be correlated with other assessments, such as measures of mental health, cognition, and sleep. Current research explores the relation between technology and digital media use and children's executive functioning, language development, attention, and other health outcomes, as well as ways to promote healthy screen time usage. NIMH recently published a request for applications to study the Bidirectional Influences Between Adolescent Social Media Use and Mental Health, responding to the U.S. Surgeon General's Advisory on Youth Mental Health.[169,170]

[164] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/early-psychosis-intervention-network-epinet
[165] www.samhsa.gov/data/release/2021-national-survey-drug-use-and-health-nsduh-releases
[166] www.nimh.nih.gov/health/statistics
[167] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/advanced-laboratories-for-accelerating-the-reach-and-impact-of-treatments-for-youth-and-adults-with-mental-illness-alacrity
[168] www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/adolescent-brain-cognitive-developmentsm-study-abcd-studyr
[169] grants.nih.gov/grants/guide/rfa-files/RFA-MH-23-115.html
[170] www.hhs.gov/sites/default/files/surgeon-general-youth-mental-health-advisory.pdf

Understanding the BRAIN

The NIH *Brain Research Through Advancing Innovative Neurotechnologies*® (BRAIN) Initiative is an ambitious program to develop and apply new technologies to answer fundamental questions about the brain and ultimately to inspire new treatments for brain diseases.[171] The NIH BRAIN Initiative is managed by 10 ICs whose missions and current research portfolios complement the goals of the BRAIN Initiative, with primary funding provided by NINDS and NIMH.[172] The BRAIN Initiative is highly collaborative within NIH, across Federal agencies, and with private organizations and the international scientific community.

Within NIH, the BRAIN Initiative collaborates with the NIH Helping to End Addiction Long-term (HEAL) Initiative (see below). In a major scientific advance from this effort, researchers have recorded pain-related data from inside the brain of individuals with chronic pain disorders caused by stroke or phantom limb pain from amputation. A long sought-after goal has been to understand how pain is represented by brain activity and how to modulate that activity to relieve suffering from chronic pain. By collecting data from patients at home over the span of months and analyzing them using machine learning tools, researchers identified an area of the brain associated with chronic pain and objective biomarkers of chronic pain in individual patients. This study represents an initial step towards uncovering the patterns of brain activity that underlie our perception of pain. Identifying such a pain signature will enable the development of new therapies that can alter brain activity to relieve suffering due to chronic pain.[173] Additional research co-funded by BRAIN and HEAL showed that psychedelic drugs being tested as therapies for treatment-resistant depression activate receptors within brain cells that promote new brain cell connections.[174] A better understanding of these mechanisms could lead to related drugs that encourage new brain cell connections while avoiding hallucinogenic effects.

BRAIN Initiative advances bolstered by collaborations between NIH and other governmental agencies include the Machine Intelligence from Cortical Networks (MICrONS) program, supported by the Intelligence Advanced Research Projects Activity (IARPA), part of the Office of the Director of National Intelligence. The MICrONS program aims to better understand the brain's internal wiring and allows scientists to sift through reams of data from high-resolution electron microscopy imaging to masterfully reconstruct individual neurons and their connections. With this increased knowledge, researchers will develop more sophisticated machine learning algorithms for AI applications, which will in turn advance fundamental basic science discoveries and the practice of life-saving medicine.[175] For instance, these applications may help in the future to detect and evaluate a broad range of neural conditions, including those that affect the primary motor cortex.

The BRAIN Initiative is also improving understanding of brain structure, which allows for comprehensive knowledge of the cellular basis of brain function and dysfunction and helps pave the way for a new generation of precision therapeutics for people with mental disorders and other disorders of the brain. The BRAIN Initiative Cell Census Network (BICCN), a cooperative network to promote collaboration and coordination among the projects within the BRAIN

[171] officeofbudget.od.nih.gov/pdfs/FY23/br/Overview of FY 2023 Cross-cutting Initiatives.pdf
[172] braininitiative.nih.gov/about/overview
[173] www.ninds.nih.gov/news-events/press-releases/brain-signatures-chronic-pain-identified-small-group-individuals
[174] pubmed.ncbi.nlm.nih.gov/36795823/
[175] directorsblog.nih.gov/2022/12/

Initiative, aims to develop a comprehensive inventory of the cells in the brain, including where they are, how they develop, how they work together, and how they regulate their activity. In 2023, an international team of scientists supported by the BRAIN Initiative created the first-ever complete cell atlas of a whole mammalian brain,[176] describing the type, location, and molecular and functional information of more than 32 million mouse brain cells. Researchers also mapped the genetic, cellular, and structural makeup of both the human brain and the nonhuman primate brain with great detail.[177] Investigators collected cell census data and developed comprehensive 3D common reference brain cell atlases that integrate molecular, anatomical, and functional data for describing specific cell types. Research funded by the BRAIN Initiative continues to improve the scientific community's understanding of how brain disorders develop and progress and lays the foundation for the development of a new generation of precision therapeutics for people with mental and neurological disorders of the brain.

Opioid Use Disorder (OUD) and Pain Research

The HEAL Initiative is an NIH-wide effort to improve prevention and treatment strategies for opioid misuse and addiction and to enhance pain management. In 2018, NIH launched the HEAL Initiative®, to find scientific solutions for the opioid public health emergency. The lack of safe and effective treatments for pain continues to be a main driver of the national opioid and overdose crisis. HEAL has two main goals: improving the understanding, management, and treatment of pain, and improving the prevention and treatment of opioid misuse and addiction. HEAL research in pain and opioid misuse and addiction addresses urgent unmet needs across the lifespan – from infants exposed to opioids during pregnancy to teens treated with opioids after a routine medical procedure and adults living with chronic pain. HEAL research covers many areas of scientific promise and concrete strategies capable of providing rapid and lasting solutions to the opioid crisis.

The HEAL Initiative continues to respond to an evolving overdose crisis on several fronts. Today we are seeing the return on this investment with major new findings that will change clinical care.[178] HEAL researchers through the Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW)[179] research program found that using the Eat, Sleep, Console (ESC) care approach cut hospital stays by nearly seven days for babies experiencing extreme discomfort and withdrawal symptoms. The ESC care approach also reduced by 63 percent the infants' need for opioid medications to recover from withdrawal symptoms. ESC prioritizes non-opioid care as a first line of treatment – including involving mothers as therapy with skin-to-skin contact, holding, swaddling, and rocking in a low light and quiet environment. ACT NOW is a partnership between the IDeA States Pediatric Clinical Trials Network[180] (itself a part of the NIH Environmental influences on Child Health Outcomes program, or ECHO)[181] and the Neonatal Research Network,[182] funded by NICHD. The Eat, Sleep, Console clinical trial was conducted across 18 states and included 1,305 infants and their primary caregivers at more than

[176] www.nih.gov/news-events/news-releases/scientists-unveil-complete-cell-map-whole-mammalian-brain
[177] www.nih.gov/news-events/news-releases/scientists-unveil-detailed-cell-maps-human-brain-nonhuman-primate-brain
[178] www.nejm.org/doi/full/10.1056/NEJMoa2214470
[179] heal.nih.gov/research/infants-and-children/act-now
[180] www.nih.gov/echo/idea-states-pediatric-clinical-trials-network-clinical-sites-foa
[181] www.nih.gov/research-training/environmental-influences-child-health-outcomes-echo-program
[182] neonatal.rti.org/

2 dozen hospitals in urban and rural environments. This diversity enabled the research team to address the needs of communities that have been impacted especially hard by the opioid crisis. The research results are also more likely to be generalizable across the country. Conducted mostly during the height of the COVID-19 pandemic, the Eat, Sleep, Console research team faced many challenges; however, the team is significantly invested in improving care for this young population. The team trained about 5,000 nurses in the ESC care approach.[183]

Chronic pain and its companion crisis of opioid misuse have taken a terrible toll on Americans. The impact has been even greater on U.S. service members and veterans, who often deal with the compounded factors of service-related injuries and traumatic stress.[184] This disproportionate burden of chronic pain among veterans and service members led NIH's National Center for Complementary and Integrative Health (NCCIH) to forge a collaboration in 2017 across NIH, the U.S. Department of Defense (DoD), and the U.S. Department of Veteran's Affairs (VA) to establish the Pain Management Collaboratory (PMC).[185,186] The PMC's research focusing on the implementation and evaluation of non-drug approaches for the management of pain is urgently needed in the military and across our entire country. Non-drug approaches require a shift in thinking: rather than focusing solely on blocking pain temporarily using analgesics, non-drug approaches work with the mind and body to promote the resolution of chronic pain and the long-term restoration of health. This resolution comes through techniques and practices such as manual therapy, yoga, and mindfulness-based interventions. Addressing chronic pain in ways that do not only rely on drugs means addressing underlying issues, such as joints and connective tissue that lack adequate movement or training our brains to "turn down the volume" on pain signals. Using mind and body practices to reduce pain can help promote health in other ways. Possible additional benefits include better sleep, more energy for physical activity, a better mindset for making good nutritional choices, and/or improved mood. The PMC supports a shared resource center and 11 large-scale pragmatic clinical trials. Within this real-world health care setting, the clinical trials have enrolled more than 8,200 participants across 42 veteran and military health systems. These studies offer both significant numbers of participants and insights into what happens when learnings from controlled clinical trials collide with the realities of health care delivery and the complexities of daily life.

NIH research through the HEAL initiative seeks to bring tangible solutions to people with addiction and at risk for overdose. Recent studies led by the National Institute on Drugs and Addiction (NIDA)[187] aimed to improve access to and success of the medication buprenorphine, a lifesaving tool for the treatment of opioid use disorder. Although medications can prevent overdose and death and aid individuals on their path to long-term recovery, most individuals with an opioid use disorder are not prescribed medication. Recent NIH-supported findings[188] have demonstrated that providing patients with buprenorphine in the emergency room following

[183] heal.nih.gov/director/power-of-connection

[184] directorsblog.nih.gov/2023/03/28/a-whole-person-approach-to-lifting-the-burden-of-chronic-pain-among-service-members-and-veterans/

[185] www.nccih.nih.gov/news/press-releases/federal-agencies-partner-for-military-and-veteran-pain-management-research

[186] painmanagementcollaboratory.org/

[187] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.

[188] nida.nih.gov/news-events/news-releases/2023/03/Buprenorphine-initiation-in-ER-found-safe-and-effective-for-individuals-with-OUD-using-fentanyl

an overdose was safe and effective for individuals using fentanyl, a powerful synthetic opioid responsible for 75 percent of overdose deaths. Additional studies[189] found that higher doses of buprenorphine were associated with improved long-term retention in treatment for opioid use disorder. Together this research gives hospitals and clinicians vital tools to help people with addiction and prevent opioid overdose death.

In a continued commitment to elevating health in every community, NIH held Tribal Consultations in 2018 and 2022 to seek input on research needs for addressing opioid misuse and improving pain management in Native communities.[190,191] Many themes emerged, including the importance of Indigenous Knowledge and local expertise and the need to invest in research and data led by Tribes and Native American Serving Organizations (T/NASOs). In direct response to priorities identified in Tribal Consultations, the HEAL Initiative developed and launched the Native Collective Research Effort to Enhance Wellness (N CREW) Program, a highly collaborative partnership between NIH, T/NASOs, and ally organizations established to directly respond to the opioid/drug public health emergency.

The N CREW Program[192] will support T/NASOs to conduct locally prioritized research to address overdose, substance use, and pain, including related factors such as mental health and wellness. Research led by Native communities is essential for enhancing culturally grounded, strengths-based, effective, and sustainable intervention strategies, ultimately promoting healthy equity. The N CREW Program has three main goals including: 1) supporting T/NASOs to lead community-prioritized research projects, including research elevating and integrating Indigenous Knowledge and culture; 2) enhancing capacity within T/NASOs to conduct locally prioritized research by developing and providing novel, accessible, culturally grounded technical assistance and training, resources, and tools; and 3) improving access to and the quality of data on substance use, pain, and related health and wellbeing factors to maximize their potential for use in local decision-making. These and other efforts across NIH work together to steward NIH's investments in the best science to improve health and life in every community.

Scientific Breakthroughs Ushered by NIH

The NIH ICOs support basic, translational, and clinical research in specific areas of health, the human body, and disease to fulfill both their own unique missions and the broader NIH mission of enhancing public health and advancing scientific breakthroughs. The distinctive approaches to research taken by each ICO have led to critical scientific discoveries and work together to accomplish the NIH mission. Among the many examples of accomplishments supported by the ICOs this past year include:

- Building on ten years of major scientific breakthroughs at the NIAID Vaccine Research Center (VRC), FDA approval was granted to the first Respiratory Syncytial Virus (RSV) vaccine for adults 60 years and older. RSV can cause severe illness or death in elderly

[189] nida.nih.gov/news-events/news-releases/2023/09/higher-buprenorphine-doses-associated-with-improved-retention-in-treatment-for-opioid-use-disorder
[190] dpcpsi.nih.gov/thro/nih-tribal-consultation-opioid-crisis-indian-country
[191] dpcpsi.nih.gov/sites/default/files/HEAL-ConsultationReport2022.pdf
[192] heal.nih.gov/research/research-to-practice/native-collective-research-effort-enhance-wellness-overdose-substance-mental-health-pain

populations, young children, and those with existing heart, lung, or immune conditions. The vaccine, Arexvy, targets the prefusion F protein that was developed at NIAID and is more than 80 percent effective at preventing symptomatic RSV infection in those 60 years and older.[193] The decade-long dedication of NIAID researchers and clinical trial volunteers, along with collaborations with academic partners and the pharmaceutical industry, will prevent thousands of hospitalizations and deaths from RSV infections in older adults each year.

- The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) funded research through the Human Placenta Project that developed a same-day test to identify abnormal fetal chromosomes.[194] Using samples collected during prenatal testing, the Short-read Transpore Rapid Karyotyping (STORK) test, detects extra or missing chromosomes. STORK has shown an accuracy rate of 98 to 100 percent, which is comparable to standard clinical tests, and is faster, costs less, and does not require transporting samples to a clinical laboratory. This innovation may be particularly useful in identifying genetic causes of miscarriage and streamlining the in vitro fertilization (IVF) process.[195]

- The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) supported a clinical trial that showed an artificial pancreas improved blood glucose control in children ages 2 to 5 years with Type 1 Diabetes (T1D). During the trial, children with the artificial pancreas spent 12 percent more time within their target blood glucose range compared to children using traditional blood glucose management and a continuous glucose monitor. These findings are especially promising because, compared to adults and older children with T1D who are better able to understand and communicate their needs, young children with T1D tend to have blood glucose levels that are higher, or lower, than they should be.[196] In addition, much of this study was conducted virtually, suggesting the potential to integrate the technology into remote and underserved areas.

- Research studies funded by the National Institute of Mental Health (NIMH), National Institute on Aging (NIA), and NCI showed that blocking an enzyme involved in forming HIV particles stopped the virus from becoming infectious and points to a possible new target for treating HIV infection. The researchers investigated whether a newly developed compound was effective in blocking a cellular enzyme called nSMase2, which is vital to forming HIV particles. Researchers found that blocking nSMase2 disrupted the formation of the virus and prevented the processing of a protein required for the virus to mature and become infectious.[197] These research studies have introduced the potential of improved medications to treat HIV long-term or possibly lead to a cure for HIV infection.

These and other discoveries by NIH-funded investigators deliver new treatments, cures, and innovative prevention strategies to communities and patients around the world. In FY 2024, NIH

[193] www.niaid.nih.gov/news-events/nih-celebrates-fda-approval-rsv-vaccine-people-60-years-age-and-older
[194] www.nichd.nih.gov/research/supported/human-placenta-project/default
[195] www.nichd.nih.gov/newsroom/news/081722-STORK
[196] www.niddk.nih.gov/about-niddk/meet-director/directors-update/2023-summer/research-updates
[197] www.nimh.nih.gov/news/science-news/2023/blocking-hiv-enzyme-reduces-infectivity-and-slows-viral-rebound

continues to make bold investments in novel ideas and enable the scientific workforce with cutting-edge resources and opportunities.

FUNDING HISTORY (FIVE-YEAR FUNDING TABLE)

Fiscal Year	Amount[1, 2]
2021	$42,940,500,000
2022[3,4]	$46,182,990,000
2023[3,5]	$49,183,485,000
2024[6]	$48,514,035,000
2025 Budget Request[7]	$51,621,517,000

[1] Appropriated amounts include discretionary budget authority received from both Labor/HHS appropriations 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 and $1,448,000,000 in the FY 2025 request for Cancer Moonshot. Includes NIGMS Program Evaluation financing of $1,271,505,000 in FY 2021, $1,309,313,000 in FY 2022, $1,412,482,000 in FY 2023, $1,412,482,000 under the FY 2024 Continuing Resolution (CR), and $2,018,482,000 in the FY 2025 request. Includes CURES Act amounts of $404,000,000 in FY 2021, $496,000,000 in FY 2022, $1,085,000,000 in FY 2023, $407,000,000 under the FY 2024 CR and $127,000,000 in the FY 2025 request.

[2] Excludes supplemental appropriations and permissive and directive transfers unless otherwise noted.

[3] Reflects mandatory sequestration of $8,550,000 for the Special Type 1 Diabetes Research account.

[4] Reflects $1,000,000,000 for the Advanced Research Projects Agency for Health (ARPA-H) provided to NIH through transfer from HHS Office of the Secretary (OS).

[5] Reflects $1,500,000,000 for the ARPA-H provided to NIH through transfer from HHS OS.

[6] Reflects annualized levels under the FY 2024 CR, including $1,500,000,000 for ARPA-H.

[7] Reflects $1,500,000,000 for ARPA-H.

SUMMARY OF REQUEST NARRATIVE

The FY 2025 President's Budget (PB) request provides a program level of $50.1 billion for NIH, excluding the Advanced Research Projects Agency for Health (ARPA-H). This request is an increase of $2.4 billion, or 5.1 percent, over the FY 2023 Final level of $47.7 billion.

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 ($46.4 billion in FY 2025); discretionary budget authority in the Department of the Interior, Environment, and Related Agencies appropriations dedicated to the Superfund Research Program ($83.0 million in FY 2025); mandatory budget authority provided for Type 1 Diabetes research ($260.0 million in FY 2025) and Cancer Moonshot ($1.448 billion in FY 2025); and Program Evaluation Financing for the National Institute of General Medical Sciences (NIGMS) under Section 241 of the Public Health Service Act ($2.018 billion in FY 2025).

The FY 2025 Budget provides $20.0 billion in mandatory funding across HHS for pandemic preparedness, provided through the Public Health and Social Services Emergency Fund. Of this total, $2.69 billion is allocated to NIH. This allocation is not included in the program level total above.

The primary budget mechanisms discussed below include allocations by mechanism of Program Evaluation Financing, Type 1 Diabetes, and Cancer Moonshot funds. The Superfund Research Program and ARPA-H are a lump-sum amount within the NIH mechanism tables.

In FY 2025, 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.

Research Project Grants (RPGs)
The FY 2025 President's Budget provides $27.1 billion for RPGs, which is $0.6 billion more than the FY 2023 Final level. This amount would fund 10,273 Competing RPGs, or 833 fewer than the FY 2023 Final level. It would also support 31,481 Noncompeting RPGs, 1,304 more than the FY 2023 Final level. In addition, the projected average cost for Competing RPGs of

approximately $591,000 would be 3.3 percent below the FY 2023 Final level projected average cost of $611,000.

- **Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) RPGs.** The FY 2025 President's Budget provides $1,275.2 million for SBIR/STTR program grants, which is $12.2 million below the FY 2023 Final level. The statutory minimum set-aside requirement of 3.65 percent for NIH-wide SBIR/STTR support is achieved in FY 2025.

Research Centers
The FY 2025 President's Budget provides $2,931.2 million for Research Centers, which is $50.1 million more than the FY 2023 Final level. This amount would fund 1,243 grants, 29 more than the FY 2023 Final level. Resources for specialized/comprehensive research centers reflect allocations of a portion of the mandatory funding for the Cancer Moonshot into this submechanism line.

Other Research
The FY 2025 President's Budget provides $3,917.8 million for this mechanism, which is $581.0 million more than the FY 2023 Final level. This amount would fund 8,407 grants, which is 196 more than the number of awards projected in the FY 2023 Final level. Resources for cooperative clinical research and the "other research other" line reflect allocations of a portion of the mandatory funding for the Cancer Moonshot into these submechanism lines, and resources for biomedical research support reflect a proposed reduction of $50.0 million in grants for instrumentation that are located in this submechanism line.

Training
The FY 2025 President's Budget provides $1,034.2 million for research training, which is $49.9 million above the FY 2023 Final level. This amount would fund 17,922 Full-Time Trainee Positions (FTTPs), which is 485 more than in the FY 2023 Final level, and would reflect assumed stipend increases of 2.0 percent for FY 2024 and FY 2025.

Research & Development (R&D) Contracts
The FY 2025 President's Budget provides $4,582.5 million for R&D contracts, which is $549.6 million more than the FY 2023 Final level. Resources for R&D contracts reflect allocations of a portion of the mandatory funding for the Cancer Moonshot into this mechanism line. The requested amount would fund an estimated 2,933 contracts, or 188 more than the FY 2023 Final level.

- **SBIR/STTR R&D Contracts.** The FY 2025 President's Budget includes a $130.9 million set-aside within the R&D Contracts mechanism for support of qualified SBIR/STTR contracts.

Intramural Research (IR)
The FY 2025 President's Budget provides $5,274.4 million for IR, which is $228.2 million more than the FY 2023 Final level. This level would account for required pay cost increases for NIH employees in FY 2024 and FY 2025, including actual and proposed pay raises for civilian and military personnel and the estimated cost increase in the agency share for health insurance

premiums. It also incorporates an allocation of a portion of the mandatory Cancer Moonshot increase to the IR program within the National Cancer Institute (NCI).

Research Management and Support (RMS)
The FY 2025 President's Budget provides $2,689.6 million for RMS, which is $358.1 million more than the FY 2023 Final level. As with intramural research, the amount covers anticipated pay cost increases for military personnel as well as growth in health insurance premiums for civilian employees.

Office of the Director (OD)
The FY 2025 President's Budget provides $3,044.5 million for OD, which is $21.8 million less than the FY 2023 Final level.

- **Common Fund (CF)**
  Funding of $722.4 million is allocated for CF-supported programs, which is $12.6 million less than the FY 2023 Final level. The reduction is due to the shift of the Gabriella Miller Kids First Pediatric Research Program out of the Common Fund and into OD Other.

- **Office of Research Infrastructure Programs (ORIP)**
  Funding of $259.4 million is allocated for ORIP, which is $50.0 million less than the FY 2023 Final level. The reduction is due to proposed cuts in ORIP's instrumentation grant program.

- **Other**
  The $2,062.7 million allocated for OD components other than the Common Fund or ORIP is a net increase of $40.8 million from the FY 2023 Final level. The request for OD Other includes initiative increases of $76.4 million for the Office of Research on Women's Health and $12.5 million for firearms research, along with an increase of $12.6 million due to the shift of the Gabriella Miller Kids First Pediatric Research Program from the Common Fund. These increases are partially offset by a $70.0 million reduction in funding for grants for extramural facilities. This reduction reduces an existing $80.0 million appropriations set-aside for this purpose to $10.0 million, with the remaining funding repurposed to support facilities needs for non-human primate research centers.

Buildings & Facilities (B&F)
The FY 2025 President's Budget provides $400.0 million for infrastructure sustainment projects associated with the B&F program, which is $20.0 million above the FY 2023 Final level. This amount includes $350.0 million for NIH's Buildings and Facilities appropriation, unchanged from FY 2023, and $50.0 million within the appropriation for the National Cancer Institute (NCI) for facility repair and improvement activities at NCI's Frederick, Maryland, facility, an increase of $20.0 million.

Superfund Research Program
The FY 2025 President's Budget provides $83.0 million for the Superfund Research Program, which is equal to the FY 2023 Final level.

Program Evaluation Financing

The FY 2025 President's Budget provides $2,018.5 million for Program Evaluation Financing purposes in NIGMS, which is a $606.0 million increase over the FY 2023 Final level.

OUTPUTS AND OUTCOMES

NIH-Wide Strategic Plan Objective: Advancing Biomedical and Behavioral Sciences

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
SR-NCI-001 By 2027, address critical knowledge gaps and lack of representation in clinical data by enrolling 2,400 participants in the Participant Engagement and Cancer Genome Sequencing (PE-CGS) Network, including 40 percent from underrepresented and underserved populations, and increase the number of tumors sequenced from tumor types and populations that lack clinical data by sequencing 1,400 tumors from the enrolled patients. (Output)	FY 2023: The PE-CGS Network enrolled 890 participants (around 30 percent from underserved communities and about 70 percent with rare cancers) and sequenced 100 tumors (more than 90 percent from underserved communities and less than 10 percent from rare cancers). Target: Enroll 500 participants and sequence 50 tumors lacking clinical data, including rare cancers/subtypes, highly lethal cancers, cancers with an early age of onset, cancers with high disparities in incidence and/or mortality, or cancers in understudied populations. (Target Exceeded)	Enroll an additional 500 participants and sequence an additional 200 tumors lacking clinical data, including rare cancers/subtypes, highly lethal cancers, cancers with an early age of onset, cancers with high disparities in incidence and/or mortality, or cancers in understudied populations.	Enroll an additional 800 participants and sequence an additional 400 tumors lacking clinical data, including rare cancers/subtypes, highly lethal cancers, cancers with an early age of onset, cancers with high disparities in incidence and/or mortality, or cancers in understudied populations.	N/A
SR-NIA-001 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 2023: The Alzheimer's Disease Sequencing Project consortium identified risk and protective alleles suggesting two molecular pathways as candidates for drug target intervention against late-onset Alzheimer's disease. Two candidate drugs are currently in phase two and three clinical trials, respectively. One drug is targeting a molecular pathway (TREM2) in brain immune cells and another is targeting a fat metabolism molecular pathway (Apo-E) previously implicated in Alzheimer's disease.	N/A	N/A	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	Target: Identify risk and protective alleles that lead to one novel therapeutic approach, drug target, or pathway to prevention for late-onset Alzheimer's disease. (Target Exceeded)			
SR-NIA-002 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 one human studies. (Output)	FY 2023: Eleven new drug candidates for Alzheimer's disease (AD) or related dementias have been developed and have advanced into phase one human trials. These drug candidates are diverse in type of drug (e.g., vaccine, gene therapy, antibody, small molecule) and variety of biological target (e.g., inflammation, growth factors and hormones, brain receptors, brain proteins Tau and Amyloid beta previously implicated in AD). Target: Advance the development of three novel drug or biologic therapeutic candidates for AD or related dementias toward the point of entry into phase one human studies. (Target Exceeded)	N/A	N/A	N/A
SR-NIAAA-001 By 2025, develop, refine, and evaluate the effectiveness of evidence-based intervention strategies for facilitating treatment of alcohol misuse in underage populations. (Output)	FY 2023: Researchers conducted a study to evaluate the efficacy of a novel behavioral economic and wellness-based intervention for non-student emerging adults to reduce alcohol use. Target: Evaluate the effectiveness of an alcohol intervention in reducing alcohol misuse among emerging adults outside of	Continue a clinical trial to evaluate the effectiveness of screening and brief intervention in primary care for reducing alcohol misuse among underage populations.	Conduct research to develop and evaluate the effectiveness of mobile and telehealth interventions to address alcohol misuse in underage populations.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	college settings. (Target Met)			
SR-NIAAA-002 By 2025, identify neurobehavioral precursors or consequences of adolescent substance use or other childhood experiences. (Outcome)	FY 2023: In a clinical study, researchers examined whether risk factors (e.g., childhood trauma) during adolescence increased the risk for alcohol use among high school students. In a preclinical study using an animal model of adolescent alcohol consumption, researchers explored whether alcohol use during adolescence contributed to increased pain during adulthood. Target: Conduct preclinical and clinical studies to better understand the predictors and consequences associated with adolescent alcohol misuse. (Target Met)	Examine the neurobiological mechanisms that underlie the relationship between childhood trauma and increased risk of alcohol misuse during adolescence and adulthood.	Conduct research to identify or characterize neurobiological mechanisms underlying the relationship between sleep and adolescent alcohol misuse.	N/A
SR-NIAAA-003 By 2025, advance one to two new or repurposed compounds that act on neurobiological targets that may have the potential for treating alcohol or other substance use disorders. (Outcome)	FY 2023: NIH supported preclinical and clinical studies to evaluate the potential of repurposed, FDA-approved drugs in reducing alcohol consumption in individuals with alcohol use disorder (AUD). One study found that a high blood pressure medication reduced alcohol consumption in an animal model, and another study found that a psoriasis medication reduced drinks consumed per day in individuals with AUD. Target: Evaluate a candidate compound for the treatment of alcohol use disorder in a preclinical and/or clinical	Conduct a clinical study to evaluate a candidate compound for the treatment of alcohol use disorder in individuals with a co-occurring mental health condition.	Evaluate a repurposed candidate compound that acts on a neurobiological target for the treatment of alcohol use disorder in a preclinical and/or clinical study.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	study. (Target Met)			
SR-NIAAA-004 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 2023: Researchers tested a family-based intervention to decrease violence in families, promote wellness, and reduce/postpone alcohol and other drug use among Native Americans. Target: Evaluate a culturally appropriate family-based intervention to prevent and reduce underage drinking among an underserved population. (Target Met)	Develop and/or evaluate a preventive intervention to address alcohol use in underage populations.	Develop and/or evaluate an intervention to address alcohol misuse among college age individuals and disseminate these or other evidence-based intervention strategies for preventing substance misuse and its consequences in underage populations.	N/A
SR-NIAID-001 By 2026, advance the preclinical or clinical development of 10 antivirals for current or future infectious disease threats. (Outcome)	FY 2023: Researchers advanced the preclinical development of three antiviral therapeutic candidates and supported two phase three clinical studies that are evaluating antiviral therapeutics. Target: Advance preclinical or clinical development of two antiviral therapeutics. (Target Exceeded)	Advance preclinical or clinical development of two antiviral therapeutics.	Advance preclinical or clinical development of two antiviral therapeutics.	N/A
SR-NIBIB-001 By 2026, establish a formalized funding pathway for the development, validation, and regulatory review of diagnostic technologies to enhance surveillance and pandemic preparedness. (Outcome and Efficiency)	FY 2023: NIH supported the development of six at-home COVID-19 tests, one of which addresses the accessibility needs of people with disabilities, one point-of-care (POC) COVID-19 test, and two POC multiplex tests for COVID-19 and flu. All nine tests received an FDA emergency use authorization for marketability. Target: Receive FDA	Receive FDA authorization or approval (including updated authorization or approval) for at least two home, point-of-care, or lab-based diagnostics, at least one of which is more accessible to people with disabilities.	Submit for FDA authorization or approval two home, point-of-care, or lab-based diagnostics, at least one of which detects multiple pathogens.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	authorization or approvals for two home, point-of-care, or lab-based diagnostics, at least one of which addresses accessibility needs of people with disabilities. (Target Exceeded)			
SR-NIDA-001 By 2026, evaluate the efficacy of new or refined interventions to treat opioid use disorders (OUD). (Output)	FY 2023: Completion of a phase two clinical trial of a long-acting formulation of an opioid antagonist is delayed due to lingering effects of the COVID-19 pandemic and unanticipated delays in receiving FDA regulatory approval. The trial is expected to launch in FY 2024 and proceed as planned. Target: Complete a phase two trial of a long-acting formulation of an opioid antagonist. (Target Not Met)	Conduct phase one clinical trials of at least two anti-opioid vaccines.	File one New Drug Application with FDA for a new treatment for OUD.	N/A
SR-NIDA-002 By 2025, develop or evaluate the efficacy or effectiveness of new or adapted prevention interventions for substance use disorders (SUD). (Outcome)	FY 2023: Researchers conducted two clinical trials testing approaches to prevent opioid and other substance misuse by intervening on social determinants of health. Target: Launch one to two clinical trials testing approaches to prevent opioid and other substance misuse by intervening on social determinants of health. (Target Met)	Launch preliminary epidemiological research studies to inform pilot studies that will develop novel strategies to prevent substance use among youth and young adults.	Continue preliminary epidemiological research studies to inform pilot studies that will develop novel strategies to prevent substance use among youth and young adults.	N/A
SR-NIDA-003 By 2027, develop evidence on the effectiveness and implementation of new and existing harm reduction services and identify strategies to	FY 2023: Researchers launched nine clinical research studies to examine the effectiveness and/or implementation of new and existing harm reduction strategies, and began	Initiate steps of the dissemination and publication plan to ensure that findings from the clinical research studies will	Begin data analysis for clinical research studies and begin sharing data collected as part of these studies via the Helping to End	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
address barriers to implementing these services, through research studies and community engagement. (Outcome)	community engagement by convening the Community Engagement Council and Community Advisory Boards. Target: Launch nine clinical research studies to examine the effectiveness and/or implementation of new and existing harm reduction strategies, and begin community engagement by convening the Community Engagement Council and the Community Advisory Boards. (Target Met)	reach a broad audience.	Addiction Long-term (HEAL) Initiative® Data Ecosystem, a cloud-based platform for sharing and analyzing data collected through the HEAL Initiative®.	
SR-NIDA-004 By 2027, strengthen community-informed research on the effectiveness of recovery support services for persons taking medications for opioid use disorder (MOUD). (Outcome)	FY 2023: Researchers launched two pilot trials to assess the feasibility, acceptability, and preliminary effectiveness of interventions to retain individuals on MOUD but, due to unexpected delays, one survey to assess MOUD capacity in recovery homes was not completed. Target: Launch two pilot trials to assess the feasibility, acceptability, and preliminary effectiveness of interventions to retain individuals on MOUD, and one survey to assess MOUD capacity in recovery homes. (Target Not Met but Improved)	Launch a third pilot trial to test the feasibility, acceptability, and preliminary effectiveness of an intervention to link individuals taking MOUDs to recovery community centers.	Publicly report early results of the pilot studies and disseminate recovery research tools to other researchers via the Helping to End Addiction Long-term (HEAL) Initiative® data ecosystem.	N/A
SR-NIDCD-001 By 2025, increase the number of potential treatment options for communication disorders that are being tested in clinical trials by adding	FY 2023: NIH initiated a clinical trial testing one new treatment for a disorder affecting hearing. Target: Initiate testing one new treatment for a disorder	Initiate testing one new treatment for a disorder affecting balance.	Initiate testing one new treatment for a disorder affecting speech.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
one new treatment option per year. (Outcome)	affecting hearing. (Target Met)			
SR-NIDDK-001 By 2023, perform comparative effectiveness studies to test five therapies for prevention or treatment of type 2 diabetes. (Outcome)	FY 2023: The Alliance of Randomized Trials of Medicine vs. Metabolic Surgery in Type 2 Diabetes (ARMMS-T2D) study found that bariatric surgery results in a more sustained remission of type 2 diabetes compared to intensive medical/lifestyle management alone. Target: Determine the long-term durability of diabetes remission following bariatric surgery compared with medical/lifestyle intervention. (Target Met)	N/A	N/A	N/A
SR-NIGMS-001 By 2025, expand the use of program-focused versus target-focused award mechanisms by National Institute of General Medical Sciences (NIGMS) investigators. (Output)	FY 2023: Out of 4,389 investigators supported by R01 or MIRA/R35 grants, 2,414 were MIRA/R35 investigators (55 percent). This is an increase of 8 percentage points from 47 percent in FY 2022. Target: Expand NIGMS investigator participation in the Maximizing Investigators' Research Award (MIRA) program by two percentage points. (Target Exceeded)	Expand NIGMS investigator participation in the MIRA program by two percentage points.	Expand NIGMS investigator participation in the MIRA program by two percentage points.	N/A
SR-NIMHD-001 By 2026, enhance understanding of how five health information technologies can be applied effectively to improve minority health	FY 2023: Investigators leveraged natural language processing and informatics to build and pilot test the Rosie the Chatbot mobile app. The investigators assessed the application's ability to provide information that	Identify barriers and enhancers to adoption of health information technologies, such as clinical decision aids, from the perspective of	Identify barriers and enhancers to adoption of chronic disease self-management support enhanced by health IT, from the perspective of racial or ethnic minority,	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
or to reduce health disparities. (Output)	meets the maternal health and infant care needs of racial and ethnic minority mothers who experience health disparities. Target: Assess the feasibility of using data mining, natural language processing and/or other technological advances to improve health or healthcare for individuals who experience health disparities. (Target Met)	physicians who care for populations who experience health disparities.	rural, sexual and gender minority, or socioeconomically disadvantaged patients.	
SR-NINDS-001 By 2023, advance the development of one to two 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 2023: Thirteen therapeutic or device candidates for the treatment of neurological diseases have advanced to the point of preparedness for first-in-human studies. Target: Advance the development of one to two 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. (Target Exceeded)	N/A	N/A	N/A

NIH-Wide Strategic Plan Objective: Developing, Maintaining, and Renewing Scientific Research Capacity

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
RC-NIGMS-001 Maintain the yearly number of undergraduate students with mentored research experiences through the IDeA (Institutional 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)	FY 2023: More than 1,450 undergraduate students participated in mentored research experiences, consistent with FY 2022 level. Target: Sustain the number of undergraduate mentored research experiences from FY 2022 level. (Target Met)	Sustain the number of undergraduate mentored research experiences from FY 2023 level.	Sustain the number of undergraduate mentored research experiences from FY 2024 level.	N/A
RC-NIGMS-002 Increase the total number of National Research Service Award (NRSA) slots for high-quality research training awarded to Historically Black Colleges and Universities (HBCUs), Tribal Colleges and Universities (TCUs), Tribal Organizations (TOs), and institutions in Institutional Development Award (IDeA) states, to develop a diverse pool of well-trained scientists with the skills necessary to conduct rigorous, reproducible research and transition into careers in the biomedical research workforce. (Output)	FY 2023: Approximately 483 NRSAs were supported at HBCUs, TCUs, TOs, or institutions in IDeA states. Target: Support 424 NIGMS NRSAs at HBCUs, TCUs, TOs, or institutions in IDeA states. (Target Exceeded)	Support 498 NIGMS NRSAs at HBCUs, TCUs, TOs, or institutions in IDeA states.	Support 503 NIGMS NRSAs at HBCUs, TCUs, TOs, or institutions in IDeA states.	N/A
RC-NIMH-001 Collect and distribute human tissue samples and molecular and genetic data from human tissues to the scientific community with the purpose of supporting	FY 2023: Brain tissue from 40 new donors was obtained. Samples were distributed to 36 researchers. Target: Collect brain tissue from an additional 30 new donors and distribute tissue	Collect brain tissue from an additional 30 new donors and distribute tissue samples or data derived from tissue to 20 researchers	Collect brain tissue from an additional 30 new donors and distribute tissue samples or data derived from tissue to 25 researchers studying mental or	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
research on brain and behavior. (Output)	samples or data derived from tissue to 20 researchers studying mental or neurological disorders. (Target Exceeded)	studying mental or neurological disorders.	neurological disorders.	
RC-OER-001 Provide research training for predoctoral trainees and fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2023: Award rate to comparison group reached 15 percent. Target: N ≥ 10 percent (Target Exceeded)	N ≥ 10 percent	N ≥ 10 percent	N/A
RC-OER-002 Provide research training for postdoctoral fellows that promotes greater retention and long-term success in research careers. (Output)	FY 2023: Award rate to comparison group reached 18 percent. Target: N ≥ 10 percent (Target Exceeded)	N ≥ 10 percent	N ≥ 10 percent	N/A
RC-ORIP-001 Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation. (Output)	FY 2023: The NIH's Shared Instrumentation Grant (S10) Program awarded 128 grants in FY 2021. Of the 126 grant awards, 109 instruments (85 percent) were installed within 24 months of the Notice of Award date. Target: Verify 60 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 24 months after award. (Target Exceeded)	Verify 70 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 24 months after award.	Verify 75 percent of awarded state-of-the-art instruments are installed at NIH-supported research institutions across the nation 24 months after award.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
RC-OSC-001 By 2030, foster cultures of inclusive excellence (cultivating and benefiting from a full range of talent) in the biomedical research community by supporting diverse early-career faculty cohorts and institutional culture change, through the Faculty Institutional Recruitment for Sustainable Transformation (FIRST) program. (Outcome)	[Measure will begin reporting in FY 2024.]	Complete hiring and development of individual development plans (IDPs) for first set of faculty cohorts; implement tailored activities, interventions, and policies/practices to promote cultures of inclusive excellence at each awardee site.	Complete hiring and development of individual development plans (IDPs) for second set of faculty cohorts; implement tailored activities, interventions, and policies/practices to promote cultures of inclusive excellence at each awardee site.	N/A

NIH-Wide Strategic Plan Objective: Exemplifying and Promoting the Highest Level of Scientific Integrity, Public Accountability, and Social Responsibility in the Conduct of Science

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
OS-NBS-001 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 2023: NBS successfully implemented the federal mandate and transitioned to the Treasury G-Invoicing solution. Target: Identify or initiate development effort for the implementation of the G-Invoicing platform. (Target Met)	Transition NBS portfolio to a FedRAMP-certified cloud service provider.	Complete assessment and continue the enhancement of the NBS architecture.	N/A
OS-OALM-001 Utilize performance-based contracting (PBC). (ongoing) (Output)	FY 2023: NIH obligated 47 percent of eligible service contracting dollars to PBC. Target: Obligate the FY 2023 goal of eligible service contracting dollars to PBC.	Obligate the FY 2024 goal of eligible service contracting dollars to PBC.	Obligate the FY 2025 goal of eligible service contracting dollars to PBC.	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	(Target Met)			
OS-OHR-001 Address diverse workforce recruitment needs to ascertain highly qualified staff to conduct or support biomedical research. (Ongoing) (Output)	FY 2023: The use of industrial-organizational psychologists and advanced assessments has improved hiring outcomes for managers across NIH. Target: Examine key area to enhance recruitment: Examine use of advanced applicant assessments to help improve the quality of applicant pools for highly skilled positions at the NIH and determine whether or not there is an impact on hiring and retention. (Target Met)	Examine key area to enhance recruitment: Examine use of resources created specifically to assist HR Specialists with the promotion of vacancies to underrepresented groups, veterans, etc. in an effort to increase awareness of NIH opportunities among diverse populations and determine whether or not there is an impact on the diversity of NIH's applicant pools.	Examine key area to enhance recruitment: Examine the impact of the change in qualification requirements for the Scientist Administrator positions (e.g., Health Scientist Administrator, Social and Behavioral Scientist Administrator) at NIH to guide future approaches to filling vacancies.	N/A
OS-OIR-001 Reallocate laboratory resources based on external reviews by Boards of Scientific Counselors (BSC). (Output)	FY 2023: 25 percent of Principal Investigators were reviewed, resulting in $6,540,757 of resources recommended to be reallocated. Target: Conduct BSC reviews annually of 25 percent of Principal Investigators to assess quality of science and prioritize resources. (Target Met)	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
OS-ORF-001 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 2023: 20 of the 24 active projects were under construction. 4 projects were completed, with 2 above and 2 below the final approved project cost. Target: 24 Active Projects	27 Active Projects	27 Active Projects	N/A

Measure	Year and Most Recent Result / Target for Recent Result / (Summary of Result)	FY 2024 Target	FY 2025 Target	FY 2025 Target +/-FY 2024 Target
	(Target Not Met but Improved)			
OS-ORF-002 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 2023: The NIH Building and Facilities project portfolio was modified to include 27 projects due to the availability of funds. NIH managed the design and construction of 25 of the 27 funded projects within plus or minus 10 percent adjustment to the approved scope. Target: 24 Active Projects (Target Met)	27 Active Projects	27 Active Projects	N/A
OS-ORF-003 Reduce the footprint of office and warehouse space in NIH's owned and leased facilities portfolio by one percent annually to comply with guidelines in the Office of Management and Budget (OMB) Memorandum M-12-12, Promoting Efficient Spending to Support Agency Operations. (Output and Efficiency)	FY 2023: The usable square footage of rentable office and warehouse space was reduced by 0.2 percent. Target: Reduce one percent of FY 2022 usable square feet. (Target Not Met but Improved)	Reduce one percent of FY 2023 usable square feet.	Reduce one percent of FY 2024 usable square feet.	N/A

GRANT AWARDS TABLE

	FY 2023 Final[3,a]	FY 2024 CR[3,a]	FY 2025 President's Budget[3,a,b]
Number of Awards	52,601	52,204	53,286
Average Award (in Whole $s)	$623,539	$619,693	$637,883
Range of Awards (in Whole $s)[1,2]	$1,000 to $32,887,320	$1,000 to $35,295,545	$1,000 to $36,244,258

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

[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.

[a] Figures do not include any awards or funding related to ARPA-H.

[b] Figures include awards or funding related to the Cancer Moonshot.

NEF NARRATIVE

Budget Summary

(Dollars in Thousands)

	FY 2023[2]	FY 2024[3]	FY 2025[4]
Notification[1]	$63,140	$120,130	$120,555

[1] Pursuant to Section 223 of Division G of the Consolidated Appropriation Act, 2008, notification is required of planned use.
[2] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on September 23, 2022.
[3] Notification submitted to the Committees on Appropriations in the House of Representatives and the Senate on October 19, 2023.
[4] HHS has not yet notified for FY 2025.

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.

Budget Allocation FY 2025

NIH FY 2025 NEF-funded activities consist of the following three projects:

Electrical Power Reliability for the Clinical Center Complex (Phase 4)
One of NIH's highest facility-related priorities is to support the safety and reliability of the infrastructure that provides utility services to patient-related areas of the Clinical Center Complex (CCC) on the Bethesda Campus. The CCC is composed of three major structures including the original Building 10, Ambulatory Care Research Facility's (ACRF), and Clinical Research Center (CRC) built in 1952, 1980, and 2005, respectively. This four-phase project consists of three major initiatives to achieve electrical power reliability in the CCC, including: 1) new electrical risers and associated equipment; 2) electrical vault decommissioning; and 3) upgrades to existing vaults. This utility project will replace and upgrade aging services with safe, state-of-of the art, cost effective, contiguous, and secure electrical systems. The entire program (all three initiatives) will be executed in four phases. This FY 2025 NEF request is for Phase 4, which will consist of three elements:

Element 1 – Install New Electrical Risers and Associated Equipment: Provide 8 new normal and 13 new emergency electrical distribution risers (total of 21) of varying ampacity in the A, B, C, D, G, H, and J wings of Building 10 (B10) by extending the current installation from the perimeter of the building to full height of distal wings. Each riser will be adjacent to and usurp one of the East and West freight elevators and lobbies. This will enable each riser to reach the highest level of each wing and to house panel boards and switchgear necessary to complete the

system. These new risers will allow: 1) the transfer of all distribution equipment in old B10 for service by these new risers; 2) replacement of panel boards/distribution boards/switchboards/motor control centers that, after evaluation, were determined not suitable to function in the new distribution; 3) installation of new lighting panels and life safety panels on every floor of each distal wings; 4) provision of life safety panels 208V and 480V for egress requirements for the library wing; and 5) replacement of all 208V ballast as necessary in East and West distal wings of old B10 preparing the fixtures for 277V service from dedicated lighting panel boards.

Element 2 – Decommission Existing Vaults: Fully decommission and remove existing equipment in vaults 1, 2, 4, and 5 including environmental requirements for removal of Polychlorinated Biphenyl (PCB) contaminated transformers.

Element 3 – Perform Upgrades to Existing Vaults: Replace and upgrade electrical vaults V6, V7, V8, V9, and V10 one vault at a time while maintaining full functional service to the ACRF facility.

Upgrade Existing Site Electrical Distribution System (Phase 1)
The NIH mission is dependent upon the reliability of the campus electrical distribution system. To meet this demand, the existing electrical distribution system needs to be upgraded to provide resiliency, redundancy, capacity, and maintainability – the cornerstones of a reliable power system. Upgrading the existing distribution system to a power ring bus configuration by electrically connecting the campus' existing three substations and two switching stations together offers a viable solution to mitigate the impact of power outages and unexpected downtime on mission-critical research. This project is to design and install the interconnection of three existing substations and two existing switching stations in a power ring bus configuration at the NIH Bethesda Campus; these five stations make up the campus' medium voltage (15kV) electrical distribution system. The completed project will allow for any one of the three substations to serve as backup to any other substation and will provide redundant sources of power to the two switching stations. The work will be performed in four phases; this FY 2025 NEF planned project is for phase 1.

Generator for Campus Emergency Chilled Water Service, Building 105, North Electrical Plant, Research Triangle Park Campus
This project will design and construct a medium voltage standby power generating system in the North Electrical Plant Building 105 Central Utility Plant (CUP) on the Research Triangle Park (RTP), North Carolina campus to provide a critical power source for the campus chilled water service that is both redundant and on emergency power. Construction of an emergency power generating system will: 1) assure continuity of operations, 24 hours per day/7 days a week; 2) safeguard against disruptions to important research and/or loss of computer network equipment; 3) protect research animal welfare, 4) provide critical cooling to expensive research equipment and 5) ensure the future reliability and resiliency of the chilled water service to the RTP campus. This project will design and provide a modernized 13.8 kV Power Supply Yard, with standby power generation capability. Providing increased normal power switching capability for the south campus will strengthen the ability to support 24/7 facility operations and harden the campus power distribution system. The project will also provide the CUP with an emergency

power source sized to provide uninterruptable chilled water production during a power failure and will be expandable as campus needs change.

Budget Allocation FY 2024

$26.1 million of FY 2024 NEF funding was allocated to Phase 2 of the Electrical Power Reliability program for the CCC. The Electrical Power Reliability program to replace failing and unreliable electrical power systems in the CCC on the Bethesda campus consists of three major initiatives, to be completed in four phases. This funding is for Phase 2, which will replace Vault 9, rebuild Vault 6, remove the existing freight elevator, and create new floors and electrical rooms, extend the electrical busducts from the West vault to the newly created electrical rooms, and decommission Vault 4.

$40.0 million of FY 2024 NEF funding was allocated to the Building 11 Chiller & Cooling Tower Replacement Program– Electrical Upgrades. In all, there are six chillers that require replacement under the Building 11 Chiller and Cooling Tower Replacement Program – Chillers 16 through 21 and their associated Cooling Towers. Chillers 16 and 17 and Cooling Towers 16, 17 and 18 were replaced under FPAA Project N-15-007 – Replace R22 Refrigerant Chillers.

$11.4 million of FY 2024 NEF funding was allocated to Building 11 Provide Sprinkler Protection. This project will provide sprinkler protection in the NIH CUP, Building 11. The CUP is a nearly 70-year-old, 290,488 gross square feet (GSF) building that provides chilled water and steam to cool, heat, and humidify nearly 12 million GSF of space at the NIH Bethesda Campus. The current infrastructure is over 40 years old and is at the end of its useful life; the necessity for an overhaul to the CUP's current sprinkler system is based on the requirements of the National Fire Protection Association (NFPA) 101, Life Safety Code.

$29.3 million of FY 2024 NEF funding was allocated to Replace Steam and Chilled Water Lines from Vault 2 to Vault 31C. This project will design and replace failed, underground Steam, Chilled Water and Domestic Water piping from existing Valve Vault 2 (VV2) to existing Valve Vault 31C (VV31C) within a new, underground walkable utility tunnel on the Bethesda campus, Maryland. This repair will provide for the final "West" leg of a continuous tunnel, connecting to the ends of the existing Northeast tunnel between VV2 and VV31C.

$13.4 million of FY 2024 NEF funding was allocated to Repair Parking Garages, Bethesda. This project is a three-phase repair/restoration program of four multi-level parking (MLP) garages located on the NIH Bethesda campus. The MLP garages on the Bethesda campus were built at different times, so their condition and service life vary. However, all have common issues - the structures are deteriorating due to lack of maintenance and poor drainage. To correct and mitigate garage deterioration and safety issues, the NIH is proposing a garage repair/restoration program that will: 1) provide for a complete remediation of the parking structures (including stairs towers) to include concrete and drainage repairs, as well as any other repair necessary to ensure the safety and structure integrity of the parking garage system; and 2) provide a 25-year maintenance/repair plan for the expected service life of each garage. The plan will prioritize the preventative maintenance, repair, and rehabilitation needs for the entire garage system on a yearly basis.

Budget Allocation FY 2023

$22.5 million of FY 2023 NEF funding was allocated to Phase 3 of the Electrical Power Reliability program for the CCC. As noted above, this program consists of three major initiatives, to be completed in four phases. Phase 3 of this project will extend the life safety, emergency, and normal power bus ducts from the East Vault to the "A" Wing of Building 10. The project will provide a new tower on the south side of the "A" Wing for the bus duct risers and closets and offer distribution to all "A" Wing floors. Additionally, the work will upgrade Vault 8 to four 2000 kVA transformers and Vault 9 to four 2500 kVA transformers.

$40.7 million of FY 2023 NEF funding was allocated to the NIAID Support Facility (Building J), Rocky Mountain Laboratories (RML), Montana. Building J is a multistory addition to existing NIAID Building J for departmental functions including Microscopy, Intramural Administrative Management Branch, Acquisition Management and Operations Branch, Office of Cyber Infrastructure and Computational Biology, and NIH Police. The existing facilities housing the essential support functions of these programs have remained unchanged for many years, while the scientific structure being supported continues to expand. All areas of services have had additional demands placed on them and additional staff have been hired without adequate facilities available to house and support them. The current deficient facilities negatively affect the ability to provide the central support functions and consequently, negatively affect the scientific mission of NIH at RML.

Budget Allocation FY 2022 and prior

$212.4 million of FY 2020 and $225.0 million of FY 2021 NEF funding was allocated to the NIH for the development of enhanced bridging documents and the design build (D/B) construction of the Surgery, Radiology and Lab Medicine Building (SRLM) on the Bethesda campus. This project will construct a new addition and repurpose two floors of the west laboratory wing of the CRC. The project will include the Clinical Center's (CC) Surgical (Department of Perioperative Medicine and Interventional Radiology), Radiology (Radiology and Imaging Sciences), and Laboratory Medicine (Department of Laboratory Medicine) departments now located in the 1982-era ACRF wings S&T and the National Cancer Institute's (NCI) research laboratories located on floors 1W and 3W of the CRC West laboratory wing. These departments involve some of the most advanced and technology dependent cutting-edge programs supporting NIH's Translational Research initiatives. The project is focused on developing a facility that supports medical research initiatives to improve the nation's health and strengthen NIH's biomedical research capacity in close proximity to the CRC. Some of the major deficiencies include the following: 1) functional space inadequacies/inefficiencies; 2) routes of circulation are not efficient; 3) facility has numerous limitations restricting the flexibility/adaptability to address growth and change; 4) infrastructure systems are deficient and unreliable (major areas of concern include normal and emergency power, communication systems, heating, cooling, and ventilation); and 5) structural problems (light steel structure) result in unacceptable vibration levels in some areas of the building. The total project will consist of 630,000 GSF, including new construction of 527,000 GSF and 103,000 GSF of renovation. The new wing will be an eight-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 is located on the west end of the CRC-West Laboratory Wing. Once the new addition is completed, two floors of the West Lab wing (1W and

2W) will be renovated after the existing NCI Research Labs are moved to the new addition. The funds for the Enhanced Bridging Documents and D/B construction have been obligated.

$12.6 million of FY 2020 NEF funding was allocated to the NIH for the Building Automation System (BAS) Replacement, Building 10, Bethesda. The project is to upgrade and replace the obsolete Johnson Controls, Inc. Building Automation System (BAS) of NIH Bethesda campus Building 10 CRC with a new state-of-the-art, cost-effective, contiguous, simple, and secure system. The CRC is within the Building 10 CCC. 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.

$63.5 million of FY 2019 NEF funding was allocated to the NIH for construction of the Utility Vault and Patient Parking Garage on the Bethesda campus, providing a new, 330,000 GSF, Utility Vault and Multi-Level Parking Garage to serve the NIH Clinical Center. The project also included several 'enabling' tasks for the construction of the SRLM Building, being built as an addition to the CRC. The enabling tasks included a new 2MW generator and switchgear for the SRLM Building and the Clinical Data Center, replacement of electrical duct bank currently serving the CRC, which is in the footprint of the new SRLM building, 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 and 59A (emergency generators and switchgear) replacement. In all, the new Utility Vault and Parking Garage will: 1) ensure the reliability and long-term sustainability of the electrical power feeds to the 4.5 million square foot hospital and biomedical research complex; 2) mitigate the security risk, personal safety risk, and liability risk associated with the existing underground parking garage; and 3) enable the new SRLM Building addition. This project is complete.

$19.5 million of FY 2019 NEF funding was allocated to the NIH for Phase 1 of the Electrical Power Reliability program to replace failing and unreliable electrical power systems in the CCC on the Bethesda campus. As noted above, this program consists of three major initiatives, to be completed in four phases. Phase 1 will replace the most critical Vault 10 in the ACRF and provide critical immediate upgrades to Vaults 6 through 9. These funds have been obligated.

$35.3 million of FY 2017 NEF funding was allocated for the replacement of R22 Refrigerant Chillers. This project involves replacing two existing York 5,000-ton dual steam turbine/electric driven chillers (CH-21 FY 2016, CH-16 FY 2017) in Building 11 with four new 3,000-ton variable speed electric chillers. Due to the efficiency achieved in the current chilled water upgrades accomplished between 2013 and 2015 and the additional efficiency and capacity of the four new chillers, the remaining four R22 chillers 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. These funds have been obligated.

$16.5 million of FY 2017 NEF funding was allocated for Emergency Generators to support the CUP. The original scope of this project was to install three 2,500 KW emergency generators and associated electrical gear adjacent and within 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 of power to various substations on the Bethesda Campus, which in turn feeds the CUP. The new scope of work for this project was 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 utility (Pepco). In order to protect the critical mission of 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, through a sequence of electrical relays, 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. This project is complete.

$162.1 million of FY 2016 NEF funding was allocated for the Renovation of the E-Wing in the NIH Clinical Center (Building 10). Building 10 is a 70-year-old facility built over 2 years beginning in 1950 that provides clinical services, laboratories and supporting office space. With failing infrastructure, the condition of Building 10 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: 1) impacting accreditation by "The Joint Commission" and "College of Anatomical Pathologists" relating to the close proximity of the Anatomical Pathology area located in the adjoining F wing; 2) failing to provide the necessary functional adjacency to the existing Institutes and the Center’s outpatient clinics; and 3) causing the NIH to fail in fulfilling its mission. These funds have been obligated.

$10.0 million of FY 2015 NEF funding was allocated for National Institute of Environmental Health Sciences (NIEHS) Net-Zero Energy Warehouse in Research Triangle Park North Carolina. The government-owned warehouse facility is located on the NIEHS main campus and replaced an off-site leased facility. This eliminated the need to pay for a continuing lease and provided an increased level of security for the warehouse. The location of the warehouse also routes traffic away from the agency’s research and administrative staff facilities, therefore improving the continuity of operations. This project is complete.

Exhibit A

(In millions of dollars)

NIH Nonrecurring Expense Fund (NEF) Overview									
Project	FY2016 Received $M	FY2017 Received $M	FY2018 Received $M	FY2019 Received $M	FY2020 Received $M	FY2021 Received $M	FY2022 Received $M	FY2023 Received $M	FY2024 Received $M
E-Wing Renovation, Building 10, Bethesda, MD	$ 162.10								
R22 Refrigerant Chillers Replacement, Bethesda, MD		$ 35.27							
Emergency Power Generators to Assure Chilled Water, Bethesda		$ 16.48							
Surgery, Radiology and Lab Medicine Building (SRLM), Bethesda, MD					$ 212.40	$ 225.00			
ORF/ORS/NIAID Support Facilities, RML, MT								$ 40.65	
Electrical Power Reliability, Building 10, Bethesda. MD				$ 19.50				$ 22.49	$ 26.10
Building Automation System (BAS) Replacement, Bldg 10, Bethesda, MD					$ 12.60				
Utility Vault and Patient Parking Garage, Bethesda, MD				$ 63.54					
Replace Cooling Towers 18,19 and Chillers 17,18,19									$ 40.00
Building 11 Provide Sprinkler Protection									$ 11.37
Replace Steam & Chilled Water Lines from Vault 2 to Vault 31C									$ 29.30
Repair Parking Garages, Bethesda									$ 13.36
Upgrade Existing Site Electrical Distribution System (Connect SWS-B-48 to SS-B-46)									
Generator For Campus Emergency CW Service, Bldg 105, North Electrical Plant, RTP									
Totals:	$ 162.10	$ 51.75	$ -	$ 83.04	$ 225.00	$ 225.00	$ -	$ 63.14	$ 120.13

BUDGET REQUEST BY IC (SUMMARY TABLE)

(Dollars in Thousands)[1]	FY 2023 Final[6,7]	FY 2024 CR[7]	FY 2025 President's Budget[7]
NCI[2]	$7,317,241	$7,104,159	$9,287,141
NHLBI	$3,985,158	$3,982,345	$3,997,086
NIDCR	$520,138	$520,163	$521,695
NIDDK[3]	$2,444,548	$2,550,721	$2,569,991
NINDS	$2,809,418	$2,674,925	$2,833,827
NIAID	$6,561,652	$6,562,279	$6,581,291
NIGMS[4]	$3,239,679	$3,239,679	$3,249,375
NICHD	$1,747,784	$1,749,078	$1,766,415
NEI	$896,136	$896,549	$898,818
NIEHS[5]	$996,842	$997,014	$999,826
NIA	$4,412,090	$4,407,623	$4,425,295
NIAMS	$687,639	$685,465	$689,697
NIDCD	$534,330	$534,333	$535,929
NIMH	$2,341,653	$2,198,843	$2,548,662
NIDA	$1,663,365	$1,662,695	$1,668,343
NIAAA	$596,616	$595,318	$598,903
NINR	$197,671	$197,693	$198,263
NHGRI	$660,510	$663,200	$663,660
NIBIB	$440,625	$440,627	$441,944
NIMHD	$525,138	$524,395	$526,710
NCCIH	$170,277	$170,384	$170,894
NCATS	$923,323	$923,323	$926,086
FIC	$95,130	$95,162	$95,415
NLM	$495,314	$497,548	$526,796
OD	$3,066,208	$2,885,514	$3,044,455
ARPA-H	$1,500,000	$1,500,000	$1,500,000
B&F	$350,000	$350,000	$350,000
Total, NIH Program Level	**$49,178,485**	**$48,609,035**	**$51,616,517**
Special Type 1 Diabetes Research (mandatory)	-$141,450	-$250,000	-$260,000
Mandatory Cancer Moonshot	---	---	-$1,448,000
PHS Program Evaluation	-$1,412,482	-$1,412,482	-$2,018,482
Interior Appropriation (Superfund Research)	-$83,035	-$83,035	-$83,035
Total, NIH Labor/HHS Budget Authority	**$47,541,518**	**$46,863,518**	**$47,807,000**
Pandemic preparedness (mandatory) (non-add)	---	---	*$2,690,000*

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

[2] Includes mandatory Cancer Moonshot proposal as shown later in the table

[3] Includes Type 1 Diabetes mandatory funding with proposal as shown later in the table.

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

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

[6] Amounts reflect 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 TABLES (FY 2023)

(Dollars in Thousands)	FY 2023 Enacted	Type 1 Diabetes Sequestration	Permissive Transfer (NIH Innovation Account)[3]	OIG Transfer[4]	HIV/AIDS Transfer[5]	ARPA-H Transfer[6]	FY 2023 Final
NCI	$7,104,159		$216,000		-$2,918		$7,317,241
NHLBI	$3,982,345				$2,813		$3,985,158
NIDCR	$520,163				-$25		$520,138
NIDDK[1]	$2,450,721	-$8,550			$2,377		$2,444,548
NINDS	$2,588,925		$225,000		-$4,507		$2,809,418
NIAID	$6,562,279				-$627		$6,561,652
NIGMS	$3,239,679						$3,239,679
NICHD	$1,749,078				-$1,294		$1,747,784
NEI	$896,549				-$413		$896,136
NIEHS[2]	$997,014				-$172		$996,842
NIA	$4,407,623				$4,467		$4,412,090
NIAMS	$685,465				$2,174		$687,639
NIDCD	$534,333				-$3		$534,330
NIMH	$2,112,843		$225,000		$3,810		$2,341,653
NIDA	$1,662,695				$670		$1,663,365
NIAAA	$595,318				$1,298		$596,616
NINR	$197,693				-$22		$197,671
NHGRI	$663,200				-$2,690		$660,510
NIBIB	$440,627				-$2		$440,625
NIMHD	$524,395				$743		$525,138
NCCIH	$170,384				-$107		$170,277
NCATS	$923,323						$923,323
FIC	$95,162				-$32		$95,130
NLM	$497,548				-$2,234		$495,314
OD	$3,740,514		-$666,000	-$5,000	-$3,306		$3,066,208
B&F	$350,000						$350,000
ARPA-H	$0					$1,500,000	$1,500,000
Total, NIH Program Level	**$47,692,035**	**-$8,550**	**$0**	**-$5,000**	**$0**	**$1,500,000**	**$49,178,485**
Less funds allocated from different sources:							
Mandatory Type 1 Diabetes Research	-$150,000	$8,550					-$141,450
PHS Program Evaluation	-$1,412,482						-$1,412,482
Total, NIH Discretionary Budget Authority	**$46,129,553**	**$0**	**$0**	**-$5,000**	**$0**	**$1,500,000**	**$47,624,553**
Interior Budget Authority	-$83,035						-$83,035
Total, NIH Labor/HHS Budget Authority	**$46,046,518**	**$0**	**$0**	**-$5,000**	**$0**	**$1,500,000**	**$47,541,518**

[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.

[6]Reflects transfer of $1,500.0 million from HHS Office of the Secretary to NIH.

APPROPRIATIONS ADJUSTMENT TABLES (FY 2024)

(Dollars in Thousands)	FY 2024 CR Enacted	Type 1 Diabetes Proposed	Cures Innovation Account Limitation[3]	Permissive Transfer (NIH Innovation Account)[4]	OIG Transfer[5]	ARPA-H Transfer[6]	FY 2024 CR Operating
NCI	$7,104,159						$7,104,159
NHLBI	$3,982,345						$3,982,345
NIDCR	$520,163						$520,163
NIDDK[1]	$2,450,721	$100,000					$2,550,721
NINDS	$2,588,925			$86,000			$2,674,925
NIAID	$6,562,279						$6,562,279
NIGMS	$3,239,679						$3,239,679
NICHD	$1,749,078						$1,749,078
NEI	$896,549						$896,549
NIEHS[2]	$997,014						$997,014
NIA	$4,407,623						$4,407,623
NIAMS	$685,465						$685,465
NIDCD	$534,333						$534,333
NIMH	$2,112,843			$86,000			$2,198,843
NIDA	$1,662,695						$1,662,695
NIAAA	$595,318						$595,318
NINR	$197,693						$197,693
NHGRI	$663,200						$663,200
NIBIB	$440,627						$440,627
NIMHD	$524,395						$524,395
NCCIH	$170,384						$170,384
NCATS	$923,323						$923,323
FIC	$95,162						$95,162
NLM	$497,548						$497,548
OD	$3,740,514		-$678,000	-$172,000	-$5,000		$2,885,514
B&F	$350,000						$350,000
ARPA-H	$0					$1,500,000	$1,500,000
Total, NIH Program Level	**$47,692,035**	**$100,000**	**-$678,000**	**$0**	**-$5,000**	**$1,500,000**	**$48,609,035**
Less funds allocated from different sources:							
Mandatory Type 1 Diabetes Research[1]	-$150,000	-$100,000					-$250,000
PHS Program Evaluation	-$1,412,482						-$1,412,482
Total, NIH Discretionary Budget Authority	**$46,129,553**	**$0**	**-$678,000**	**$0**	**-$5,000**	**$1,500,000**	**$46,946,553**
Interior Budget Authority	-$83,035						-$83,035
Total, NIH Labor/HHS Budget Authority	**$46,046,518**	**$0**	**-$678,000**	**$0**	**-$5,000**	**$1,500,000**	**$46,863,518**

[1]Includes Type 1 Diabetes baseline and proposed.

[2]Includes Superfund Research activity.

[3]Reflects reduction in appropriation from the Cures Innovation Account as limited by fund balances.

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

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

[6]Reflects transfer of $1,500.0 million from HHS Office of the Secretary to NIH.

BUDGET MECHANISM TABLE

(Dollars in Thousands)[1,2,3]	FY 2023 Final[9]		FY 2024 CR[9]		FY 2025 President's Budget[9]		FY 2025 +/- FY 2023 Final	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	30,177	$17,975,116	31,389	$19,039,410	31,481	$19,444,480	1,304	$1,469,365
Administrative Supplements[3]	*(3,793)*	535,090	*(3,048)*	368,151	*(2,999)*	351,610	*(-794)*	-183,480
Competing	11,106	$6,783,224	9,739	$5,643,337	10,273	$6,069,919	-833	-$713,305
Subtotal, RPGs	41,283	$25,293,430	41,128	$25,050,898	41,754	$25,866,009	471	$572,580
SBIR/STTR	1,893	1,287,467	1,845	1,256,967	1,882	1,275,239	-11	-12,227
Research Project Grants	43,176	$26,580,896	42,973	$26,307,866	43,636	$27,141,249	460	$560,352
Research Centers:								
Specialized/Comprehensive	1,045	$2,271,984	1,065	$2,317,655	1,119	$2,480,487	74	$208,504
Clinical Research	57	328,369	36	258,996	24	198,750	-33	-129,619
Biotechnology	40	64,909	40	65,869	30	42,739	-10	-22,171
Comparative Medicine	49	137,280	47	131,225	47	130,065	-2	-7,214
Research Centers in Minority Institutions	23	78,613	23	79,164	23	79,164	0	551
Research Centers	1,214	$2,881,155	1,211	$2,852,909	1,243	$2,931,206	29	$50,051
Other Research:								
Research Careers	5,043	$928,335	5,030	$935,151	5,048	$945,157	5	$16,822
Cancer Education	83	23,219	82	22,837	82	22,837	-1	-382
Cooperative Clinical Research	269	485,641	245	485,100	436	1,008,525	167	522,884
Biomedical Research Support	126	111,657	120	103,257	47	54,321	-79	-57,336
Minority Biomedical Research Support	154	55,759	86	37,745	30	25,523	-124	-30,236
Other	2,536	1,732,101	2,457	1,605,568	2,764	1,861,395	228	129,294
Other Research	8,211	$3,336,712	8,020	$3,189,658	8,407	$3,917,757	196	$581,046
Total Research Grants	52,601	$32,798,763	52,204	$32,350,433	53,286	$33,990,212	685	$1,191,449
Ruth L Kirchstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	3,968	$191,272	4,113	$200,800	4,122	$203,304	154	$12,032
Institutional Awards	13,469	793,060	13,812	820,640	13,800	830,904	331	37,844
Total Research Training	17,437	$984,331	17,925	$1,021,440	17,922	$1,034,208	485	$49,876
Research & Development Contracts	2,745	$4,032,891	2,623	$3,857,225	2,933	$4,582,467	188	$549,576
(SBIR/STTR) (non-add)[3]	*(101)*	*(75,193)*	*(79)*	*(61,364)*	*(166)*	*(130,942)*	*(65)*	*(55,750)*
Intramural Research		$5,046,199		$5,133,445		$5,274,376		$228,177
Research Management & Support		2,331,451		2,442,336		2,689,558		358,107
SBIR Admin (non-add)[3]		*(10,098)*		*(10,881)*		*(11,287)*		*(1,188)*
Office of the Director - Appropriation[3,4]		*(3,066,208)*		*(2,885,514)*		*(3,044,455)*		*(-21,753)*
Office of the Director - Other		2,021,814		1,841,120		2,062,661		40,847
ORIP (non-add)[3,4]		*(309,393)*		*(309,393)*		*(259,393)*		*(-50,000)*
Common Fund (non-add)[3,4]		*(735,001)*		*(735,001)*		*(722,401)*		*(-12,600)*
ARPA-H		1,500,000		1,500,000		1,500,000		0
Buildings and Facilities[5]		380,000		380,000		400,000		20,000
Appropriation[3]		*(350,000)*		*(350,000)*		*(350,000)*		*(0)*
Type 1 Diabetes[6,7]		-141,450		-250,000		-260,000		-118,550
Mandatory Cancer Moonshot[6]		0		0		-1,448,000		-1,448,000
Program Evaluation Financing[6]		-1,412,482		-1,412,482		-2,018,482		-606,000
Subtotal, Labor/HHS Budget Authority		**$47,541,518**		**$46,863,518**		**$47,807,000**		**$265,482**
Interior Appropriation for Superfund Research		83,035		83,035		83,035		0
Total, NIH Discretionary Budget Authority		**$47,624,553**		**$46,946,553**		**$47,890,035**		**$265,482**
Type 1 Diabetes[7]		141,450		250,000		260,000		118,550
Mandatory Cancer Moonshot		0		0		1,448,000		1,448,000
Total, NIH Budget Authority		**$47,766,003**		**$47,196,553**		**$49,598,035**		**$1,832,032**
Program Evaluation Financing		1,412,482		1,412,482		2,018,482		606,000
Total, Program Level		**$49,178,485**		**$48,609,035**		**$51,616,517**		**$2,438,032**
Pandemic Preparedness Mandatory via PHSSEF (non-add)[8]		*(0)*		*(0)*		*(2,690,000)*		*(2,690,000)*

See footnotes on following page.

Budget Mechanism Table Footnotes.

[1] Subtotal and Total numbers may not add due to rounding.

[2] Includes 21st Century Cures Act funding and excludes supplemental financing.

[3] 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), mandatory Cancer Moonshot, and 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] Amount in FY 2023 reflect a reduction of $8.550 million for Budget Control Act sequestration. FY2024 reflects annualized CR level of $150.0 million plus $100.0 million reauthorization proposal..

[8] The FY 2025 budget also provides $20 billion in mandatory funding across HHS for pandemic preparedness, which is reflected in the Public Health and Social Services Emergency Fund chapter. Of this total, NIH will receive $2,690 million.

[9] Reduced by a transfer of $5.0 million from OD to the HHS Office of Inspector General.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING TYPE 1 DIABETES

FY 2025 Budget Authority by Object Class Including Type 1 Diabetes Funds[1]

(Dollars in Thousands)

Object Classes	FY 2024 CR[2]	FY 2025 President's Budget
Personnel Compensation		
Full-Time Permanent (11.1)	$1,425,949	$1,513,140
Other Than Full-Time Permanent (11.3)	$695,364	$721,376
Other Personnel Compensation (11.5)	$90,590	$94,566
Military Personnel (11.7)	$20,074	$21,093
Special Personnel Services Payments (11.8)	$267,072	$273,196
Subtotal, Personnel Compensation (11.9)	**$2,499,048**	**$2,623,372**
Civilian Personnel Benefits (12.1)	$843,784	$888,253
Military Personnel Benefits (12.2)	$4,051	$4,274
Benefits to Former Personnel (13.0)	$0	$0
Total Pay Costs	**$3,346,883**	**$3,515,899**
Travel & Transportation of Persons (21.0)	$49,278	$49,861
Transportation of Things (22.0)	$8,360	$8,484
Rental Payments to GSA (23.1)	$37,104	$42,791
Rental Payments to Others (23.2)	$4,756	$5,621
Communications, Utilities & Misc. Charges (23.3)	$11,763	$14,208
Printing & Reproduction (24.0)	$311	$322
Consultant Services (25.1)	$1,523,875	$1,601,937
Other Services (25.2)	$1,490,979	$1,546,434
Purchase of Goods and Services from Government Accounts (25.3)	$3,559,924	$3,702,055
Operation & Maintenance of Facilities (25.4)	$53,089	$54,720
R&D Contracts (25.5)	$2,891,558	$2,917,185
Medical Care (25.6)	$44,016	$45,753
Operation & Maintenance of Equipment (25.7)	$253,423	$263,191
Subsistence & Support of Persons (25.8)	$0	$0
Subtotal Other Contractual Services (25.0)	**$9,816,865**	**$10,131,275**
Supplies & Materials (26.0)	$260,592	$279,376
Equipment (31.0)	$156,519	$156,210
Land and Structures (32.0)	$330,762	$318,005
Investments & Loans (33.0)	$0	$0
Grants, Subsidies & Contributions (41.0)	$33,089,042	$33,543,660
Insurance Claims & Indemnities (42.0)	$0	$0
Interest & Dividends (43.0)	$1,284	$1,288
Refunds (44.0)	$0	$0
Subtotal Non-Pay Costs	**$43,766,635**	**$44,551,101**
Total Budget Authority	**$47,113,518**	**$48,067,000**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, Program Evaluation Financing, and Mandatory Cancer Moonshot. Includes Advanced Research Projects Agency for Health.

[2] FY 2024 amounts for Type 1 Diabetes program reflect annualized CR level of $150.0 million plus $100.0 million reauthorization proposal.

BUDGET AUTHORITY BY OBJECT CLASS INCLUDING SSF AND MF

FY 2025 Budget Authority by Object Class Including Service and Supply Fund and Management Fund[1]

(Dollars in Thousands)

Object Classes	FY 2024 CR[2]	FY 2025 President's Budget
Personnel Compensation		
Full-Time Permanent (11.1)	$1,922,096	$2,023,180
Other Than Full-Time Permanent (11.3)	$746,350	$773,790
Other Personnel Compensation (11.5)	$135,598	$140,835
Military Personnel (11.7)	$32,087	$33,668
Special Personnel Services Payments (11.8)	$276,654	$283,045
Subtotal, Personnel Compensation (11.9)	**$3,112,785**	**$3,254,518**
Civilian Personnel Benefits (12.1)	$1,060,037	$1,111,751
Military Personnel Benefits (12.2)	$4,919	$5,182
Benefits to Former Personnel (13.0)	$0	$0
Total Pay Costs	**$4,177,741**	**$4,371,452**
Travel & Transportation of Persons (21.0)	$53,026	$53,729
Transportation of Things (22.0)	$10,905	$11,118
Rental Payments to GSA (23.1)	$111,839	$119,993
Rental Payments to Others (23.2)	$71,907	$74,988
Communications, Utilities & Misc. Charges (23.3)	$131,998	$138,427
Printing & Reproduction (24.0)	$314	$326
Consultant Services (25.1)	$754,054	$807,072
Other Services (25.2)	$3,086,862	$3,196,993
Purchase of Goods and Services from Government Accounts (25.3)	$901,071	$956,725
Operation & Maintenance of Facilities (25.4)	$207,452	$214,125
R&D Contracts (25.5)	$2,892,633	$2,918,290
Medical Care (25.6)	$73,219	$75,475
Operation & Maintenance of Equipment (25.7)	$517,687	$536,375
Subsistence & Support of Persons (25.8)	$0	$0
Subtotal Other Contractual Services (25.0)	**$8,432,978**	**$8,705,055**
Supplies & Materials (26.0)	$468,163	$493,408
Equipment (31.0)	$215,400	$216,869
Land and Structures (32.0)	$348,803	$336,569
Investments & Loans (33.0)	$0	$0
Grants, Subsidies & Contributions (41.0)	$33,089,103	$33,543,721
Insurance Claims & Indemnities (42.0)	$0	$0
Interest & Dividends (43.0)	$1,341	$1,347
Refunds (44.0)	$0	$0
Subtotal Non-Pay Costs	**$42,935,777**	**$43,695,548**
Total Budget Authority	**$47,113,518**	**$48,067,000**

[1]Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee, Program Evaluation financing, supplemental appropriations, and mandatory Cancer Moonshot. Includes Advanced Research Projects Agency for Health.

[2] FY 2024 amounts for Type 1 Diabetes program reflect annualized CR level of $150.0 million plus $100.0 million reauthorization proposal.

SALARIES AND EXPENSES

FY 2025 Budget Authority by Object Class Including Type 1 Diabetes Funds[1]
Salaries and Expenses / Administrative Expenses
(Dollars in Thousands)

Object Classes	FY 2024 CR	FY 2025 President's Budget
Personnel Compensation		
Full-Time Permanent (11.1)	$1,425,949	$1,513,140
Other Than Full-Time Permanent (11.3)	$695,364	$721,376
Other Personnel Compensation (11.5)	$90,590	$94,566
Military Personnel (11.7)	$20,074	$21,093
Special Personnel Services Payments (11.8)	$267,072	$273,196
Subtotal, Personnel Compensation (11.9)	**$2,499,048**	**$2,623,372**
Civilian Personnel Benefits (12.1)	$843,784	$888,253
Military Personnel Benefits (12.2)	$4,051	$4,274
Benefits to Former Personnel (13.0)	$0	$0
Total Pay Costs	**$3,346,883**	**$3,515,899**
Travel & Transportation of Persons (21.0)	$49,278	$49,861
Transportation of Things (22.0)	$8,360	$8,484
Rental Payments to Others (23.2)	$4,756	$5,621
Communications, Utilities & Misc. Charges (23.3)	$11,763	$14,208
Printing & Reproduction (24.0)	$311	$322
Other Contractual Services		
Consultant Services (25.1)[2]	$1,364,419	$1,441,807
Other Services (25.2)	$1,490,979	$1,546,434
Purchase of Goods and Services from Government Accounts (25.3)[2]	$2,497,842	$2,610,118
Operation & Maintenance of Facilities (25.4)[2]	$53,089	$54,720
Operation & Maintenance of Equipment (25.7)	$253,423	$263,191
Subsistence & Support of Persons (25.8)	$0	$0
Subtotal Other Contractual Services	**$5,659,752**	**$5,916,270**
Supplies & Materials (26.0)	$260,592	$279,376
Subtotal Non-Pay Costs	**$5,994,812**	**$6,274,141**
Total Salaries and Expense / Administrative Costs	**$9,341,695**	**$9,790,040**

[1] Excludes the Superfund Research account under the jurisdiction of the Interior & Related Agencies Appropriations Subcommittee,, Program Evaluation Financing and Mandatory Cancer Moonshot. Includes Advanced Research Projects Agency for Health.

[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 2023 Actual	FY 2024 Estimate	FY 2025 Estimate
NCI	3,250	3,468	3,468
NHLBI	943	966	966
NIDCR	226	252	252
NIDDK	698	756	756
NINDS	650	713	729
NIAID	2,109	2,180	2,180
NIGMS	189	219	219
NICHD	561	602	624
NEI	272	291	300
NIEHS	634	685	685
NIA	584	650	800
NIAMS	241	250	258
NIDCD	134	140	140
NIMH	605	623	635
NIDA	419	445	470
NIAAA	204	238	238
NINR	84	106	106
NHGRI	356	385	385
NIBIB	123	160	160
FIC	54	61	61
NIMHD	94	210	210
NCCIH	94	110	115
NCATS	278	298	319
NLM	642	741	741
OD	1,134	1,217	1,241
ARPA-H	47	112	137
Central Services:			
OD - CS	871	911	916
CC	1,765	2,034	2,034
CSR	485	510	510
CIT	199	237	237
ORS	479	542	543
ORF	756	830	830
Subtotal Central Services[1]	**4,555**	**5,064**	**5,070**
PHS Trust Fund (non-add)[2]	*4*	*4*	*4*
CRADA (non-add)[3]	*4*	*4*	*4*
Total	**19,180**	**20,942**	**21,265**

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

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

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

PROGRAMS PROPOSED FOR ELIMINATION

The FY 2025 request for the National Institutes of Health does not propose any programs for elimination.

PHYSICIAN'S COMPARABILITY ALLOWANCE WORKSHEET

		FY 2022 Actual	FY 2023 Actual	FY 2024 Estimate[1]	FY 2025 Estimate
1) Number of Physicians Receiving PCAs		94	91	87	87
2) Number of Physicians with One-Year PCA		1	3	2	2
3) Number of Physicians with Multi-Year PCA		93	88	85	85
4) Average Annual Physician Pay (without PCA payment)		$172,520	$179,325	$177,227	$182,189
5) Average Annual PCA Payment		$21,996	$22,918	$24,400	$25,083
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position				
	Category II Research Position	93	91	87	87
	Category III Occupational Health				
	Category IV-A Disability Evaluation				
	Category IV-B Health and Medical Admin.	1	0	0	0

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

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 2023, there were a total of 91 PCA recipients across NIH. In FY 2024 and beyond, as indicated by the decrease 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 2024 data will be approved during the FY 2025 Budget cycle.

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 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]	$19,599,758	$7,481,452	72.4%	27.6%	10.1%	9.4%
FY 2019[1]	$20,544,931	$7,953,747	72.1%	27.9%	4.8%	6.3%
FY 2020[1]	$21,765,222	$8,406,459	72.2%	27.8%	5.9%	5.7%
FY 2021[1]	$22,363,606	$8,620,853	72.2%	27.8%	2.8%	2.6%
FY 2022[1,a]	$23,352,941	$8,993,865	72.2%	27.8%	4.4%	4.3%
FY 2023 Final[1,a]	$24,405,711	$9,377,383	72.2%	27.8%	4.5%	4.3%
FY 2024 CR[1,a]	$24,118,301	$9,253,572	72.3%	27.7%	-1.2%	-1.3%
FY 2025 President's Budget[1,a,b]	$25,376,479	$9,647,941	72.5%	27.6%	5.2%	4.3%

Note: Data for fiscal years 2024 and later represent estimates and will change as actual data are received.

[1] Includes 21st Century Cures Act funding.

[a] Figures do not include any funding related to ARPA-H.

[b] Figures include funding related to the Cancer Moonshot.

RPGS – TOTAL NUMBER OF AWARDS AND FUNDING

(Dollars in Thousands)	FY 2015	FY 2016	FY 2017 Actual[1]	FY 2018 Actual[1]	FY 2019 Actual[1]	FY 2020 Actual[1]	FY 2021 Actual[1]	FY 2022 Actual[1,a]	FY 2023 Final[1,a]	FY 2024 CR[1,a]	FY 2025 President's Budget[1,a,b]
No. of Awards:											
Competing	9,540	10,364	10,123	11,116	11,020	11,373	11,258	11,333	11,106	9,739	10,273
Noncompeting	23,261	23,528	24,638	25,780	27,624	28,366	28,492	29,423	30,177	31,389	31,481
Subtotal	32,801	33,892	34,761	36,896	38,644	39,739	39,750	40,756	41,283	41,128	41,754
SBIR/STTR	1,578	1,689	1,807	2,034	2,023	1,832	1,863	1,840	1,893	1,845	1,882
Total	**34,379**	**35,581**	**36,568**	**38,930**	**40,667**	**41,571**	**41,613**	**42,596**	**43,176**	**42,973**	**43,636**
Average Annual Cost:											
Competing RPGs	$452	$484	$522	$527	$573	$559	$599	$588	$611	$579	$591
Total RPGs[X]	479	502	523	546	552	571	583	594	613	609	619
Percent Change in Average Cost from Prior Year[Y]											
Competing RPGs	8.2%	7.2%	7.8%	1.0%	8.7%	-2.4%	7.2%	-1.8%	3.8%	-5.1%	2.0%
Total RPGs[X]	8.0%	4.8%	4.0%	4.4%	1.1%	3.5%	2.1%	2.0%	3.1%	-0.6%	1.7%
Average Length of Award in Years	**3.5**	**3.6**	**3.6**	**3.6**	**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.

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

[Y] Based on average costs in whole dollars.

[1] Includes 21st Century Cures Act funding.

[a] Figures do not include any awards or funding related to ARPA-H.

[b] Figures include awards or funding related to the Cancer Moonshot.

RPGS – SUCCESS RATES

INSTITUTES & CENTERS[+,1,2]	FY 2016	FY 2017 Final[3]	FY 2018 Final[3]	FY 2019 Final[3]	FY 2020 Final[3]	FY 2021 Final[3]	FY 2022 Final[3,a]	FY 2023 Final[3,a]	FY 2024 CR[3,a]	FY 2025 President's Budget[3,a,b]
NCI	12.0%	11.7%	11.3%	11.9%	12.9%	13.8%	15.4%	16.1%	13.5%	14.8%
NHLBI	24.2%	23.5%	25.1%	22.3%	22.2%	20.5%	21.3%	21.1%	20.1%	20.2%
NIDCR	19.9%	17.8%	22.2%	23.8%	21.7%	21.8%	21.0%	22.0%	18.6%	16.0%
NIDDK	20.1%	17.8%	21.6%	20.3%	24.4%	22.7%	22.1%	22.9%	21.5%	22.7%
NINDS	19.8%	17.7%	22.4%	20.4%	23.7%	20.2%	22.1%	21.6%	16.8%	15.4%
NIAID	23.8%	19.1%	22.9%	22.1%	23.9%	17.5%	17.3%	20.8%	20.4%	19.7%
NIGMS	29.6%	30.6%	29.2%	32.6%	32.3%	33.4%	35.8%	36.3%	28.7%	28.3%
NICHD	13.2%	16.1%	18.4%	19.5%	18.0%	18.4%	17.3%	18.8%	18.3%	19.1%
NEI	25.7%	24.9%	26.7%	28.4%	29.6%	24.8%	25.6%	26.2%	23.6%	23.6%
NIEHS	14.2%	15.0%	17.1%	14.8%	14.2%	14.4%	16.7%	15.1%	14.0%	21.5%
NIA	22.8%	26.6%	28.9%	29.2%	25.8%	24.2%	25.3%	24.0%	10.4%	10.4%
NIAMS	16.0%	17.0%	16.7%	17.1%	18.0%	17.6%	18.4%	17.8%	14.2%	12.6%
NIDCD	26.7%	24.4%	27.1%	25.2%	24.2%	24.0%	25.0%	26.9%	24.9%	24.8%
NIMH	22.9%	20.9%	22.2%	24.8%	22.5%	22.1%	24.3%	22.4%	17.8%	29.7%
NIDA	15.4%	19.7%	19.4%	17.5%	16.9%	14.7%	19.4%	22.1%	15.9%	17.5%
NIAAA	18.8%	22.0%	26.7%	20.9%	21.4%	17.1%	27.1%	30.5%	20.1%	22.7%
NINR	9.0%	8.9%	10.3%	9.3%	10.8%	12.6%	15.4%	16.9%	20.7%	19.2%
NHGRI	25.6%	23.9%	28.0%	19.2%	21.8%	24.7%	25.1%	22.0%	21.3%	20.3%
NIBIB	14.6%	13.0%	16.8%	18.3%	19.8%	17.2%	21.5%	17.7%	15.6%	16.3%
NIMHD	19.3%	21.5%	10.7%	7.5%	7.9%	11.2%	17.2%	18.8%	9.6%	16.2%
NCCIH	13.9%	16.7%	20.3%	12.5%	11.6%	11.1%	14.8%	14.4%	9.6%	9.2%
NCATS	27.7%	21.8%	36.4%	20.7%	25.2%	14.7%	20.4%	26.8%	20.4%	20.6%
FIC	29.5%	10.8%	19.5%	20.6%	19.7%	13.8%	20.9%	22.3%	14.6%	20.8%
NLM	13.0%	14.9%	17.7%	18.4%	13.4%	11.9%	15.3%	14.8%	14.0%	13.6%
ORIP & SEPA[A]	18.8%	16.5%	17.8%	34.2%	29.6%	25.9%	27.1%	34.0%	34.0%	34.0%
Common Fund	12.6%	11.8%	10.9%	11.0%	9.5%	8.8%	11.8%	14.6%	9.2%	9.8%
NIH	**19.1%**	**18.7%**	**20.3%**	**20.1%**	**20.7%**	**19.1%**	**20.8%**	**21.4%**	**17.5%**	**18.4%**

[+] Success Rates identified in FY 2024 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] Includes 21st Century Cures Act funding.

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

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

[b] Figures include awards related to the Cancer Moonshot.

TOTAL R01 EQUIVALENT DATA FOR FIRST-TIME AND ESTABLISHED INVESTIGATORS

R01 Equivalent Grants[1,2,3,4]	FY 2023 Final[5,a]	FY 2024 CR[5,a]	FY 2025 President's Budget[5,a,b]
Applications			
Received	35,072	37,819	38,441
Funded	**7,629**	**6,772**	**7,188**
Total Investigators			
Received	32,547	35,329	36,324
Funded	**9,702**	**8,734**	**9,394**
Established Investigators			
Received	20,454	22,126	22,849
Funded	**6,888**	**6,199**	**6,672**
First-time Investigators			
Received	12,093	13,203	13,475
Funded	**2,814**	**2,535**	**2,722**

[1] R01 Equivalent Grants form a subset of all RPG awards. In FY 2023 they comprised roughly 69% of Funded Applications, 72% of Funded Total Investigators, 78% of Funded Established Investigators and 61% of Funded First-time Applicants. The year-to-year variation of these figures is about 2%, plus or minus.

[2] The ratio of total and funded applicants to applications and the proportion of total and funded first-time applicants are based on linear extrapolation of five years of the latest actual data.

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

[4] Estimates for received applications reflect consolidations of Institute/Center validated refinements to linear extrapolation of five years of latest actual data. Funded application figures reflect the annual estimate identified in the New/Competing RPG line of mechanism budget table.

[5] Includes 21st Century Cures Act funding.

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

[b] Figures include awards related to the Cancer Moonshot.

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 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 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023 Final	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Clinical Center	1,765	$703,301	2,034	$730,047	2,034	$754,153	269	$50,853
Center for Scientific Review, SREA	485	$150,393	510	$156,128	510	$161,295	25	$10,903
Office of Research Services, and Administrative services, support		$30		$0		$0		-$30
TOTAL	**2,250**	**$853,723**	**2,544**	**$886,175**	**2,544**	**$915,449**	**294**	**$61,726**

MF BUDGET AUTHORITY BY OBJECT CLASS

		FY 2024 CR	FY 2025 President's Budget
Total compensable workyears:			
	Full-time equivalent	2,544	2,544
	Full-time equivalent of overtime and holiday hours	41	41
	Average ES salary	$220	$224
	Average GM/GS grade	11.6	11.6
	Average GM/GS salary	$127	$130
	Average salary, Commissioned Corps (42 U.S.C. 207)	$118	$123
	Average salary of ungraded positions	$134	$137
OBJECT CLASSES		**FY 2024 CR**	**FY 2025 President's Budget**
	Personnel Compensation		
11.1	Full-Time Permanent	229,533	235,960
11.3	Other Than Full-Time Permanent	42,160	43,340
11.5	Other Personnel Compensation	29,329	30,150
11.7	Military Personnel	7,639	7,997
11.8	Special Personnel Services Payments	9,424	9,688
11.9	**Subtotal Personnel Compensation**	**318,085**	**327,135**
12.1	Civilian Personnel Benefits	105,708	109,250
12.2	Military Personnel Benefits	862	902
13.0	Benefits to Former Personnel	0	0
	Subtotal Pay Costs	**424,656**	**437,288**
21.0	Travel & Transportation of Persons	2,308	2,373
22.0	Transportation of Things	804	827
23.1	Rental Payments to GSA	5	5
23.2	Rental Payments to Others	10	10
23.3	Communications, Utilities & Misc. Charges	2,272	2,363
24.0	Printing & Reproduction	0	0
25.1	Consulting Services	21,293	21,910
25.2	Other Services	125,534	130,806
25.3	Purchase of Goods and Services from Government Accounts	80,379	84,329
25.4	Operation & Maintenance of Facilities	6,480	6,642
25.5	R&D Contracts	347	353
25.6	Medical Care	24,707	25,078
25.7	Operation & Maintenance of Equipment	39,888	41,403
25.8	Subsistence & Support of Persons	0	0
25.0	**Subtotal Other Contractual Services**	**298,628**	**310,522**
26.0	Supplies & Materials	129,729	133,621
31.0	Equipment	23,691	24,307
32.0	Land and Structures	4,012	4,072
33.0	Investments & Loans	0	0
41.0	Grants, Subsidies & Contributions	61	62
42.0	Insurance Claims & Indemnities	0	0
43.0	Interest & Dividends	0	0
44.0	Refunds	0	0
	Subtotal Non-Pay Costs	**461,519**	**478,161**
	Total Budget Authority by Object Class	**886,175**	**915,449**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

MF DETAIL OF POSITIONS

GRADE	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Total, ES Positions	2	2	2
Total, ES Salary	$417,676	$439,395	$448,183
GM/GS-15	116	134	134
GM/GS-14	359	379	379
GM/GS-13	352	407	407
GS-12	529	613	613
GS-11	360	417	417
GS-10	33	38	38
GS-9	77	91	91
GS-8	73	81	81
GS-7	152	174	174
GS-6	38	42	42
GS-5	10	12	12
GS-4	5	6	6
GS-3	6	7	7
GS-2	3	4	4
GS-1	0	0	0
Subtotal	2,113	2,405	2,405
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	11	11	11
Senior Grade	9	9	9
Full Grade	11	11	11
Senior Assistant Grade	9	9	9
Assistant Grade	1	1	1
Junior Assistant Grade	0	0	0
Subtotal	41	41	41
Ungraded	220	220	220
Total permanent positions	2,131	2,421	2,421
Total positions, end of year	2,376	2,668	2,668
Total full-time equivalent (FTE) employment, end of year	2,250	2,544	2,544
Average ES salary	208,838	219,698	224,092
Average GM/GS grade	11.7	11.6	11.6
Average GM/GS salary	121,123	127,422	129,970

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 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023 Final	
Extramural Research	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**	**FTE**	**Amount**
Detail								
Research Support and Administrative, OD, CC-CIF	1,350	$1,613,795	1,453	$1,878,119	1,459	$1,936,998	109	$323,203
Office of Research Facilities, Development & Operations	756	$579,784	830	$697,569	830	$720,589	74	$140,805
Center for Information Technology	199	$527,929	237	$547,990	237	$566,107	38	$38,178
TOTAL	**2,305**	**$2,721,508**	**2,520**	**$3,123,678**	**2,526**	**$3,223,694**	**221**	**$502,186**

SSF BUDGET AUTHORITY BY OBJECT

Budget Authority by Object Class [1]

(Dollars in Thousands)

		FY 2024 CR	FY 2025 President's Budget
Total compensable workyears:			
	Full-time equivalent	2,520	2,526
	Full-time equivalent of overtime and holiday hours	57	57
	Average ES salary	$223	$228
	Average GM/GS grade	12.1	12.1
	Average GM/GS salary	$131	$134
	Average salary, Commissioned Corps (42 U.S.C. 207)	$127	$133
	Average salary of ungraded positions	$161	$164
OBJECT CLASSES		**FY 2024 CR**	**FY 2025 President's Budget**
	Personnel Compensation		
11.1	Full-Time Permanent	$266,614	$274,079
11.3	Other Than Full-Time Permanent	$8,827	$9,074
11.5	Other Personnel Compensation	$15,680	$16,119
11.7	Military Personnel	$4,374	$4,578
11.8	Special Personnel Services Payments	$157	$161
11.9	**Subtotal Personnel Compensation**	**$295,651**	**$304,011**
12.1	Civilian Personnel Benefits	$110,545	$114,248
12.2	Military Personnel Benefits	$6	$6
13.0	Benefits to Former Personnel	$0	$0
	Subtotal Pay Costs	**$406,201**	**$418,265**
21.0	Travel & Transportation of Persons	$1,440	$1,495
22.0	Transportation of Things	$1,742	$1,808
23.1	Rental Payments to GSA	$74,730	$77,196
23.2	Rental Payments to Others	$67,141	$69,357
23.3	Communications, Utilities & Misc. Charges	$117,963	$121,856
24.0	Printing & Reproduction	$3	$4
25.1	Consulting Services	$96,060	$98,673
25.2	Other Services	$1,470,349	$1,519,753
25.3	Purchase of Goods and Services from Government Accounts	$382,447	$394,034
25.4	Operation & Maintenance of Facilities	$148,883	$152,763
25.5	R&D Contracts	$728	$752
25.6	Medical Care	$4,496	$4,645
25.7	Operation & Maintenance of Equipment	$224,376	$231,781
25.8	Subsistence & Support of Persons	$0	$0
25.0	**Subtotal Other Contractual Services**	**$2,324,339**	**$2,402,400**
26.0	Supplies & Materials	$77,842	$80,411
31.0	Equipment	$35,191	$36,352
32.0	Land and Structures	$14,029	$14,492
33.0	Investments & Loans	$0	$0
41.0	Grants, Subsidies & Contributions	$0	$0
42.0	Insurance Claims & Indemnities	$0	$0
43.0	Interest & Dividends	$57	$59
44.0	Refunds	$0	$0
	Subtotal Non-Pay Costs	**$2,714,477**	**$2,805,428**
	Total Budget Authority by Object Class	**$3,123,678**	**$3,223,694**

[1] Includes FTEs whose payroll obligations are supported by the NIH Common Fund.

SSF DETAIL OF POSITIONS

GRADE	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
Total, ES Positions	6	7	8
Total, ES Salary	$1,272,600	$1,561,904	$1,820,734
GM/GS-15	119	130	131
GM/GS-14	362	378	379
GM/GS-13	758	803	805
GS-12	336	372	372
GS-11	131	144	144
GS-10	10	10	10
GS-9	101	126	126
GS-8	42	50	49
GS-7	99	110	112
GS-6	10	15	15
GS-5	7	11	13
GS-4	9	14	12
GS-3	12	11	11
GS-2	6	6	6
GS-1	4	7	7
Subtotal	2,006	2,187	2,192
Commissioned Corps (42 U.S.C. 207)			
Assistant Surgeon General	0	0	0
Director Grade	5	5	5
Senior Grade	5	5	5
Full Grade	8	8	8
Senior Assistant Grade	2	2	2
Assistant Grade	0	0	0
Junior Assistant Grade	0	0	0
Subtotal	20	20	20
Ungraded	323	352	352
Total permanent positions	2,305	2,481	2,502
Total positions, end of year	2,355	2,566	2,572
Total full-time equivalent (FTE) employment, end of year	2,305	2,520	2,526
Average ES salary	212,100	223,129	227,592
Average GM/GS grade	12.2	12.1	12.1
Average GM/GS salary	124,652	131,134	133,757

CYBERSECURITY

Cyber Category	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
Cyber Human Capital	0.155	0.155	0.155	--
Planning Roles and Responsibilities	--	--	--	--
Sector Risk Assessment, Management, and Operations	--	--	--	--
Sector Coordination	--	--	--	--
Other NIST CSF Capabilities:				
Detect	25.450	27.990	28.040	2.590
Identify	65.140	71.640	71.782	6.642
Protect	99.921	109.913	110.110	10.189
Recover	10.030	11.041	11.070	1.040
Respond	27.482	30.230	30.283	2.801
Total Cyber Request	**228.178**	**250.969**	**251.440**	**23.262**
Technology Ecosystems (non-add)	--	--	--	--
Zero Trust Implementation (non-add)	*0.042*	*0.042*	*0.023*	*-0.019*

LEGISLATIVE PROPOSALS

Discretionary Legislative Proposals

Expanding the Hiring Authorities for NIH Undergraduate Scholarship Program.
In an effort to improve equity in STEM (science, technology, engineering, and math) education, the NIH Undergraduate Scholarship Program (UGSP) offers competitive college scholarships to students from disadvantaged backgrounds. The program offers college scholarships, up to $20,000 annually, in return for two payback obligations in the form of service to NIH under 42 CFR § 68b.7. The proposal would allow for expanding the hiring authorities that may be used to appoint awardees in the Undergraduate Scholarship Program (UGSP), allowing the use of the more appropriate Intramural Research Training Award hiring authority to appoint all scholarship awardees during the summer payback and some award recipients during the full-year payback obligation. This would allow awardees to receive benefits and support provided to other NIH public health interns and trainees, and would streamline administration of the program compared to appointing awardees using the time-consuming Title 42 employee appointment authority.

Permit the Mailing of Electronic Nicotine Delivery Systems Through the United States Postal Service for Certain Research and Public Health Purposes.
The Prevent All Cigarette Trafficking Act of 2009 (PACT Act), Public Law 111–154, codified in 18 U.S.C. 1716E, imposes certain restrictions on the mailing of cigarettes and smokeless tobacco. Title VI of Division FF of the Consolidated Appropriations Act of 2021 instructed the U.S Postal Service (USPS) to apply the same restrictions to the mailing of electronic nicotine delivery systems (ENDS). The proposal would allow the mailing of ENDS for the purposes of conducting public health research, investigations, and surveillance. This would remove restrictions that are creating serious obstacles to the ability of NIH-funded researchers to obtain consistent ENDS products and to conduct research on the factors that contribute to ENDS use and addiction, and the potential long-term health consequences of ENDS.

Modify Statutory Requirements for the AIDS Research Advisory Committee (ARAC)
The AIDS Research Advisory Committee (ARAC) was established in 1988 in section 2304 of the Public Health Service Act (42 U.S.C. 300cc-3). The committee's membership was restricted to physicians whose clinical practice includes a significant number of patients with acquired immune deficiency syndrome (AIDS). The ARAC was directed to advise the Director of the National Institute of Allergy and Infectious Diseases (NIAID) or other NIH Institutes on the appropriate research activities to be taken with respect to clinical treatment of AIDS. The proposal would modify statutory requirements for the ARAC that are no longer in line with the current state of science, which recognizes that the advent of effective HIV antiretroviral therapies has enabled nearly all people living with HIV to avoid progressing to AIDS. The requirements of the ARAC limit NIH's ability to receive advice on the current and future directions of HIV/AIDS research. Given NIH's need to receive scientifically appropriate guidance, NIH proposes to modify the statutory requirements of ARAC to reflect the current status of HIV/AIDS science. The modified requirements would allow NIH to address the current and future needs of the research community, and to seek advice from a committee with relevant experience in basic virology, immunology, medicine, community engagement, and public health. The changes would include renaming the committee from the AIDS Research Advisory

Committee to the HIV Research Advisory Committee, revising membership standards to focus on those with basic and clinical research, clinical care, or other expertise as well as lived experience with HIV, and stating the committee's duties to advise NIH on matters relating to the full spectrum of HIV research rather than only AIDS.

Mandatory Legislative Proposals

Reauthorization of the Special Statutory Funding Program for Type 1 Diabetes Research. Codified in Section 330B of the PHS Act, this Program began in FY 1998 with a funding level of $30 million per year over 5 years. In December 2000, the Program was renewed to increase the FY 2001 and 2002 levels to $100 million and to extend the FY 2003 level at $100 million of mandatory funds. In December 2002, the Program was extended and increased to $150 million per year for FY 2004-2008. The Program has subsequently been extended multiple times at this annual level of $150 million. Most recently, the Program was extended at a level of $150 million per year for FY 2021-2023 and funded in the FY 2024 continuing resolutions at prorated amounts corresponding to the $150 million annual level. The proposal would reauthorize the NIH Special Diabetes Program for Type 1 Diabetes Research at an annual amount of $250 million in FY 2024, $260 million in FY 2025, and $270 million in FY 2026, as well as exempt this funding from mandatory sequestration. The three-year reauthorization would facilitate planning of long-term research projects, and the reauthorized funding level would restore the lost purchasing power of the program since it was last increased to the level of $150 million in FY 2004.

Provide Outyear Funding and Enhanced Operating Authorities to the National Cancer Institute to Conduct Initiatives to Deliver Cancer Moonshot Goals.
In February 2022, President Biden announced a reignition of the Cancer Moonshot, highlighting new goals: to reduce the cancer death rate by half within 25 years to improve the lives of people with cancer and cancer survivors, and to reduce cancer health disparities. The legislative proposal would provide $1.448 billion of mandatory funding in each of FY 2025 and FY 2026 to advance Cancer Moonshot priorities, including doubling cancer clinical trial accruals and establishing a comprehensive cancer data ecosystem to accelerate the pace of cancer discovery and speed the introduction of precision oncology into clinical practice.[198] The proposal would also grant NCI five key operating authorities – Other Transactions Authority, Management and Operating Authority, Strategic Partnership Authority, enhanced pay authority, and facilities improvement authorities -- to support these efforts.

Other Transaction (OT) Authority for Cancer Moonshot activities would enable NCI to scale up clinical trials and other National Cancer program activities to deliver Cancer Moonshot goals. Grants and contracts would remain the norm for many NCI awards, but OT Authority would enable accelerated progress toward cutting cancer deaths in half. OT Authority would permit NCI to take a more active, substantive role in managing the science of trials and would allow NCI to bring non-traditional partners, companies, and individuals into NCI's expanded and re-engineered clinical trial enterprise.

[198] For more information on the reignited Cancer Moonshot, see the NCI FY 2025 Congressional Justification.

Management and Operating (M&O) Authority would grant the NCI Frederick National Laboratory for Cancer (FNLCR) access to a valuable authority that other U.S. national laboratories enjoy, but FNLCR currently lacks. Unlike many of the other existing Federally Funded Research and Development Centers (FFRDCs) at national labs, the NCI FFRDC only has access to basic, limited FFRDC authorities under current law. M&O contracting, as defined by Federal Acquisition Regulations (FAR) subpart 17.6, would be especially beneficial to deliver rapid, creative solutions required for Cancer Moonshot success.

Strategic Partnership Authority would give FNLCR the flexibility to conduct research, development, commercialization, and training activities with or on behalf of other public or private research labs, allowing the labs to access the unique FNLCR facilities, services, and technical expertise to advance cancer science and Moonshot priorities. Another advantage of Strategic Partnerships is the possibility of establishing more flexible terms for intellectual property and licensing rights. This authority would include allowing NCI to accept, retain, and use funds and tangible and intangible property provided by others to support such activities. The authority also allows any funds received to support such activities to remain available until expended.

Enhanced hiring authority would allow NCI to use funds to make or rescind appointments of scientific, medical, and professional personnel without regard to any provision in Title 5 governing appointments and removals under the civil service laws, and may use funds to fix the compensation of such personnel at a rate to be determined by the Director of the NCI, up to the amount of annual compensation (excluding expenses) specified in Section 102 of Title 3, United States Code. The ability of NCI to deliver on the promise of the Cancer Moonshot will significantly depend on NCI's ability to compete with the private sector for top talent to lead Moonshot programs. Using this hiring authority, NCI can attract and hire top talent capable of driving progress in cancer discovery, reducing cancer deaths, and ensuring broad, equitable access to optimum standards of cancer care.

Enhanced facilities and improvement authority would allow NCI to use up to $50 million for alterations, repairs, improvements, and construction of laboratories and other facilities of the Institute (previous Appropriations acts set this authority at $30 million). This enhanced authority is particularly important to maintain and enhance research operations at NCI's facilities at Fort Detrick. Fifty years ago, when NCI received Fort Detrick laboratories and facilities from the Army, many were aging, substandard, and needed to be repaired or modernized. Over the years, despite NCI investment, these research facilities continued to age, wear, and degrade. To meet the needs of cancer patients and deliver on Cancer Moonshot goals, NCI must refurbish existing labs at Fort Detrick. This proviso would also support needed repair and improvements to certain NCI facilities at the Bethesda NIH campus.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Cross-Cutting Initiatives

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INTRODUCTION

As the Nation's premier biomedical research agency, the National Institutes of Health (NIH) is entrusted with leading scientific research and development for the United States with the ultimate goal of improving understanding of fundamental human biology and enhancing human health. The pace of biomedical research and development continues to accelerate in a constantly evolving global landscape, and the forthcoming years are poised to bring forth novel scientific opportunities as well as new and persistent challenges to human health. NIH strives to address the current and developing needs of biomedical science while setting the standard for high-caliber and ethical scientific research.

The NIH's more than 27 Institutes, Centers, and Offices (ICOs), which each have a specific research agenda and budget, pursue a host of collaborative efforts to address important scientific and clinical questions in areas such as emerging technologies, pain research, and scientific and workforce capacity building. These NIH-wide efforts allow NIH ICOs to leverage expertise and combine resources strategically to tackle complex challenges in broader and more impactful ways than they would be able to alone. Building strong research collaborations and partnerships across ICOs requires both a diverse scientific workforce and participant pool to develop thoughtful and innovative approaches to answering crucial questions about human health and disease. NIH-wide efforts continue to focus on gaining understanding of human biology, developing and testing interventions, therapeutics, and tools to enhance health, and promoting targeted research on tailored public health, clinical, and community preventive services in diverse settings and contexts.

The scope, scale, and complexity of many biomedical questions and health challenges requires multi-disciplinary and collaborative teams to address the wide variety of human health needs. For example, the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Allergy and Infectious Diseases (NIAID) co-lead the Researching COVID to Enhance Recovery (RECOVER) Initiative to understand, prevent, and treat the long-term effects of COVID-19, which can affect nearly all body systems. As a comprehensive, multi-faceted, and nationwide research program, RECOVER involves collaboration with several NIH ICOs and other agencies across the Department of Health and Human Services (HHS). Similarly, NIH ICOs are collaborating with other HHS agencies to address the growing maternal mortality and morbidity crisis through programs such as the Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative, an NIH-wide program that aims reduce preventable causes of maternal deaths and improve health for women before, during, and after delivery. Collaborative programs like the Helping to End Addiction Long-term (HEAL)^{SM} Initiative are also key parts of NIH's efforts to address the opioid misuse and overdose crisis by providing scientific solutions to the opioid crisis via research on prevention and treatment of opioid misuse, addiction, and overdose, as well as enhancing pain management. Nutrition impacts health in a myriad of ways, so multiple ICOs support research on how nutrition affects health and disease.

To stimulate scientific discovery and sustain progress also requires investment in innovative tools and research methodologies as well as in the next generation of scientists that can drive forward research. The NIH engages in efforts to enhance the development and use of emerging

technologies to catalyze scientific discovery; these “Novel Alternative Methods” provide a complementary approach to traditional models while offering tremendous promise for enhancing understanding of the human system and for more effectively treating human conditions. These methods, including techniques performed on cells outside the body like organoids and 3D tissue culture and methods using computing platforms or custom hardware that use various computational techniques, may transform how scientists study health and disease. Rapidly developing technologies like artificial intelligence (AI) and machine learning (ML) capabilities have become ubiquitous across biomedical and health research. NIH-wide collaborations allow for leveraging these technologies in tailored ways to meet the needs of the NIH mission and to ensure ethical and trustworthy AI development. Supported by several NIH ICOs, the Common Fund’s High Risk, High Reward initiative is designed to launch new science areas, refine our understanding of complex systems, and pioneer new therapies to produce rapid advancements in biomedicine with the potential for broad impact. The NIH Clinical Center has supported multidisciplined, ethical, and efficient clinical research since 1953 to translate laboratory discoveries into state-of-the-art diagnostic, preventive, and therapeutic interventions to improve the nation's health. The biomedical research enterprise also relies upon a talented, qualified, diverse group of investigators to bring new insights and translate fundamental research findings into improved health. NIH ICOs collaborate in several efforts to support the successful recruitment and retention of outstanding independent, early career researchers essential to the sustainable success of the biomedical research enterprise.

During FY 2025, NIH will continue to utilize multi-Institute, NIH-wide, and inter-agency collaborations and partnerships to leverage existing infrastructure, coalesce scientific expertise, and ultimately improve health and prevent disease through effective scientific discovery. Fostering new and existing collaborative relationships is critical to facilitate scientific and clinical research that improves human health. NIH will continue to learn and grow from these essential partnerships going forward. As the steward of medical and behavioral research for the United States, NIH will continue to rapidly respond to the American people’s urgent, evolving health needs, examine health disparities, and build upon previous discoveries and capabilities. While emphasizing diversity, equity, inclusion, and accessibility, NIH will remain a leader in biomedical research and development in FY 2025 and beyond.

ARTIFICIAL INTELLIGENCE

Program Overview

The use of artificial intelligence (AI) and machine learning (ML) capabilities is becoming ubiquitous across biomedical, behavioral, and health research. AI and ML have the potential to drive new research discoveries by finding patterns in very large datasets that are otherwise not apparent to human researchers and, through new generative AI techniques, to transform the way we capture data and create connections among data. NIH leverages and adapts these technologies to meet the unique needs of the NIH mission,[199] support business operations, and ensure ethical and trustworthy AI development. Bias in AI/ML models is a significant concern, particularly in applications for biomedicine, behavioral, and social sciences, and health. Potential sources of bias include under- or over-representation of racial and ethnic groups and underserved rural, low socio-economic status, or other demographic groups. NIH has made significant investments in making diverse, AI-ready datasets and analysis tools available to the research community, in supporting new collaborations among biomedical researchers and AI and ethics experts, and in developing and applying AI methods to speed discoveries and treatments, as well as improving NIH business operations. NIH has several overarching high-profile AI activities that address the agency's priorities in diverse AI-ready data, ethical AI, and development of new capabilities to address unique challenges in biomedicine.[200] This includes NIH-wide programs to support new training opportunities in AI, activities to bring new communities to biomedical-AI research, new research to develop social and advanced AI-technical solutions that will embed ethics across the lifecycle of AI applications, and support to make existing NIH funded data AI-ready while ensuring participant privacy protections. Furthermore, NIH initiatives in AI are aligned to the priorities by the implementation of the President's October 2023 Executive Order, "Executive Order on the Safe, Secure, and Trustworthy Development and Use of Artificial Intelligence."[201]

NIH Collaboration

NIH is committed to harnessing the power of AI/ML to advance research across diverse fields, diseases, and scientific communities. NIH has launched innovative and ambitious initiatives to propel fusion of biomedicine and AI/ML.

The NIH Common Fund supports several collaboratives, NIH-wide programs related to AI/ML. The *Nutrition for Precision Health, powered by the All of Us Research Program* (NPH)**[202]** aims to develop AI algorithms that predict individual responses to food and dietary patterns. NPH will leverage advances in AI, microbiome research, and the infrastructure of the large and diverse *All of Us* participant group. NPH is designed to implement some of the goals and objectives within the first Strategic Plan for NIH Nutrition Research[203] by leveraging the *All of Us* infrastructure to study how a range of factors, including genes, lifestyle, health history, the gut microbiome, and social determinants of health influence a person's response to diet. The

[199] nih.gov/about-nih/what-we-do/mission-goals
[200] datascience.nih.gov/artificial-intelligence/initiatives
[201] whitehouse.gov/briefing-room/presidential-actions/2023/10/30/executive-order-on-the-safe-secure-and-trustworthy-development-and-use-of-artificial-intelligence/
[202] commonfund.nih.gov/nutritionforprecisionhealth
[203] dpcpsi.nih.gov/onr/strategic-plan

NIH Bridge to Artificial Intelligence (Bridge2AI)[204] program will set the stage for widespread adoption of AI that addresses complex biomedical challenges beyond human intuition. The key deliverables are the generation of new "flagship" datasets and best practices for ML analysis. Bridge2AI will also produce tools, software, and standards to accelerate the creation of AI/ML-ready datasets and design training materials and activities for skills and workforce development.

NIH's Artificial Intelligence and Machine Learning Consortium to Advance Health Equity and Research Diversity (AIM-AHEAD)[205] supports projects that use or develop novel AI/ML algorithms to address health disparities and improve health outcomes in underrepresented and/or underserved communities and was highlighted in the Executive Order. The initiative was developed to redress the lack of diversity among AI/ML researchers and lack of representation in AI training data, including electronic health record data. These gaps contribute to harmful biases in how AI/ML is used, how algorithms are developed and trained, and how findings are interpreted, ultimately leading to continued health disparities and inequities. AIM-AHEAD initiated a range of training opportunities across the academic continuum to increase participation of underrepresented researchers and leaders in AI/ML biomedical research, like the PRIME training practicum,[206] the Research Fellowship,[207] and the Leadership Fellowship.[208] AIM-AHEAD collaborates with *All of Us* and the National Center for Advancing Translation Sciences (NCATS) National Covid Cohort Collaborative (N3C)[209] to increase researcher diversity in AI/ML by leveraging data, resources, and infrastructure.

The National Institute on Minority Health and Health Disparities' (NIMHD) Science Collaborative for Health disparities and Artificial Intelligence bias Reduction (ScHARe)[210] is a social science data repository and multidisciplinary research collaboration platform co-sponsored with the National Institute of Nursing Research. ScHARe is a cloud platform with population, social determinants of health, and other social science AI-ready datasets. It is a resource to test AI bias mitigation strategies and to advance health disparities research. An integral part of the program is the Think-a-Thons,[211] which prepare low resource institutions and researchers, students, and collaborators from populations with health disparities and are underrepresented in the AI field, to learn how to leverage the ScHARe platform for reducing health disparities, improving health care delivery, and conducting bias mitigation research.

The National Institute of Biomedical Imaging and Bioengineering's Medical Imaging and Data Resource Center (MIDRC)[212] is an imaging repository to develop methods to reliably diagnose COVID-19 from medical images. MIDRC fulfills the high priority need of researchers for large, high-quality image datasets to develop reliable AI/ML methods that identify disease. MIDRC has addressed this need by ingesting over 309,000 demographically diverse imaging datasets and releasing more than 135,000 images into the open commons for research use. The need for high-

[204] commonfund.nih.gov/bridge2ai
[205] aim-ahead.net/
[206] aim-ahead.net/p/prime
[207] aim-ahead.net/research-fellowship/
[208] aim-ahead.net/leadership-fellowship/
[209] ncats.nih.gov/n3c
[210] nimhd.nih.gov/resources/schare/
[211] nimhd.nih.gov/resources/schare/think-a-thons.html
[212] nibib.nih.gov/medical-imaging-and-data-resource-center

quality imaging datasets in AI/ML research extends to all diseases, so MIDRC plans to expand its repository to include other organs and diseases.

AI Programs to Address Specific Opportunities to Improve Health and Treat Disease

NIH invests in AI programs to address disease-specific challenges, while advancing trustworthy AI methods and socio-technical approaches to screen for, detect, and diagnose health conditions and predict disease trajectory.

National Heart, Lung, and Blood Institute (NHLBI) investigators are engaged in AI/ML-driven research and collaborations focusing on heart, lung, blood, and sleep (HLBS) disorders. The Integrative Omics Analysis of NHLBI TOPMed Data[213] effort aims to apply the power of AI/ML to the institute's TOPMed[214] resource to uncover biological function and disease pathobiology. NHLBI's IDEA2Health[215] stimulates HLBS research and advancement of data science methodologies of data science. Published by RADx-rad in partnership with RECOVER, the NIH Long COVID Computational Challenge (L3C) Prize competition focused on the prognostic problem by developing AI/ML models and algorithms that serve as open-source tools for using structured medical records to identify which patients infected with SARS-CoV-2 have a high likelihood of developing PASC/Long COVID.

The Center for Alzheimer's and Related Dementias,[216] a collaboration between the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke, uses AI/ML to extract insights on disease risk and protective factors from large networks of data and supports precision medicine applications like prediction of disease risk and progression. These efforts and others at NIA support the use of AI to identify genetic variants that contribute to or protect against the development of Alzheimer's Disease (AD), leading to new strategies for treatments or prevention. AI/ML in this space helps achieve insights faster, accelerating discovery and facilitating the growth of open science and precision medicine for AD and AD-related disorders.

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development supports research on Autism Spectrum Disorders (ASD) that uses AI research methods to optimize diagnosis and care for ASD patients. These techniques can expedite ASD screening in children and reach commonly overlooked individuals, thereby lowering many of the hurdles and access issues experienced by these underserved communities.

The National Institute on Drugs and Addiction[217] is developing and evaluating a machine-learning opioid prediction and risk-stratification e-platform[218] to assist healthcare providers and systems in safe opioid prescribing by identifying patients at high risk for opioid use disorder and overdose.

[213] grants.nih.gov/grants/guide/notice-files/NOT-HL-23-074.html
[214] topmed.nhlbi.nih.gov/
[215] grants.nih.gov/grants/guide/notice-files/NOT-HL-22-001.html
[216] card.nih.gov/
[217] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction
[218] reporter.nih.gov/project-details/10597698

The National Cancer Institute's interagency partnership with the U.S. Department of Energy[219] accelerates advances in precision oncology and scientific computing as part of the Cancer Moonshot℠ program. The program leverages AI and advanced computing to improve drug discovery and patient outcomes. Many AI/ML resources have been openly released[220] to the community, including software, datasets, and trained models.

The National Institute of Mental Health's Explainable AI for Decoding and Modulating Neural Circuit Activity Linked to Behavior[221] uses new AI/ML techniques to better understand the causal links between brain activity and complex behaviors, opening new avenues for clinical therapeutics.

The National Eye Institute is advancing the use of AI and clinical imaging data to advance telemedicine, diagnosis, and treatment decisions for eye diseases and disorders. The first U.S. Food and Drug Administration-approved AI system[222] detected eye-related complications of diabetes. Another new screening tool[223] was approved for use with multiple camera options increasing access to care while allowing clinics to use existing equipment. A patient-centric home-based system[224] allows doctors to manage age-related macular degeneration (AMD) through remote monitoring, and other new AI algorithms[225] predict progression to late AMD and patients with rapidly advancing disease.

The National Institute of Diabetes and Digestive and Kidney Diseases is supporting research on applications of AI/ML to advance diagnosis, treatment, and prevention of its mission diseases. This includes research using ML to identify[226] panels of biological markers that can predict development of early stages of type 1 diabetes months in advance and to develop[227] automated, more reliable measurement tools for kidney stone detection.

NCATS' Biomedical Data Translator[228] connects compartmentalized and disparate data across diseases and disciplines using AI-guided knowledge mapping for drug repurposing, disease classification, and identification of possible treatments for rare and difficult-to-treat diseases. NCATS' Challenge prize competition for Minimizing Bias and Maximizing Long-Term Accuracy, Utility and Generalizability of Predictive Algorithms in Health Care Challenge[229] aims to mitigate the risk of unwitting bias in algorithms used in clinical decisions. This challenge fosters "good algorithmic practices" and the creation of tools that increase the accuracy of AI/ML algorithms used in the healthcare setting.

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[219] datascience.cancer.gov/collaborations/nci-department-energy-collaborations
[220] datascience.cancer.gov/collaborations/nci-department-energy-collaborations/ai-ml-resources
[221] grants.nih.gov/grants/guide/notice-files/NOT-MH-23-110.html
[222] fda.gov/news-events/press-announcements/fda-permits-marketing-artificial-intelligence-based-device-detect-certain-diabetes-related-eye
[223] eyenuk.com/us-en/articles/news/eyenuk-fda-multiple-cameras/
[224] notalvision.com/assets/press-releases/Feb-22-2023-Clinical-trials-results-demonstrate-value-of-home-OCT-at-international-meetings.pdf
[225] nei.nih.gov/about/news-and-events/news/ai-based-systems-can-help-identify-rapidly-advancing-age-related-macular-degeneration
[226] pubmed.ncbi.nlm.nih.gov/37390828/
[227] pubmed.ncbi.nlm.nih.gov/35908740/
[228] ncats.nih.gov/translator
[229] ncats.nih.gov/funding/challenges/bias-detection-tools-in-health-care

The National Institute of General Medical Sciences supports AI/ML research in numerous areas that provide a foundation for improving diagnosis and treatment, including drug discovery, molecular modeling, -omics data analysis, image analysis, protein structure modeling and prediction, and sepsis risk prediction.

The National Library of Medicine (NLM) conducts and funds research to advance AI methods and approaches to enable discovery and improve health. NLM intramural researchers leverage AI techniques to develop computational tools to improve screening and diagnosis of conditions, like cervical cancer, and facilitate health and biomedical information retrieval by researchers, patients, and the public. NLM-funded extramural researchers across the United States are reimagining health care delivery with AI and are advancing AI methods and approaches and developing tools that support care across the care continuum. NLM-funded researchers have applied AI/ML to predict treatment effectiveness and inform personalized medicine approaches and have developed new AI methods for image and biomedical data analysis. The FY 2025 Budget includes $30.0 million within NLM to support a new Clinical Data Initiative to develop the tools, computational resources, and datasets necessary to extend NIH clinical capabilities, including supporting AI research and development.

The National Human Genome Research Institute is planning to solicit grant applications to spur the development of novel adaptive AI/ML tools within an Ethical, Legal, and Social Implications framework to explore their potential applicability and feasibility in using multi-modal data to help uncover novel relationships between genotypes and phenotypes.[230]

AI/ML to Support NIH Decision Making and Operations

NIH also leverages AI/ML to enhance data-driven decision making and ensure good stewardship – including using AI tools to inform research investments, improve business processes, and improve access to and retrieval of biomedical data. The Office of Portfolio Analysis has developed AI/ML approaches and tools to implement data-driven decision making across the NIH research community. NLM has developed and applied AI to provide PubMed® end users with new functionality that helps them efficiently find the most relevant and high-quality information they need across its biomedical literature services. NLM also continues to build on its automated indexing of medical literature by refining its indexing algorithm to incorporate new terms in the biomedical literature. Importantly, AI tools are also used to create and track standardized metrics to measure the productivity and impact of NIH research investments.

Next Steps and Goals

NIH will support activities aligned with the Executive Order on AI and will continue to support collaborations among biomedical, behavioral, and AI and ethics experts for research and the development of new AI tools. Human-derived data will be essential to these efforts. NIH will invest in privacy-preserving methods and opportunities to use synthetic data to advance these fields. In addition, federated or distributed learning capabilities will also be essential for implementing AI research with diverse and/or disparate data. NIH will continue to lead the development of ethical AI for biomedical and behavioral research. NIH has unique needs and

[230] genome.gov/sites/default/files/media/files/2023-09/ML_AI_Tools_to_Advance_Genomic_Translational_Reseach.pdf

responsibilities for ethical AI that require renewed attention to data governance, diversity, and equity of AI outcomes. NIH will focus on the development of social and technical solutions to ensure transparency across the data and AI model life cycle, participatory approaches to tool development for more equitable AI outcomes, explainable AI, and new methods for assessing AI performance. NIH will continue to play a critical role in interagency collaborations like the National Science Foundation's National AI Research Resource[231] by providing AI-ready high-impact data and secure analysis platforms, with expertise in data and system interoperability. NIH will invest in research and community engagements in support of responsible, safe, and effective use of important new technologies, such as generative AI, including Large Language Models.

[231] nsf.gov/cise/national-ai.jsp

CATALYZING THE USE AND DEVELOPMENT OF NOVEL ALTERNATIVE METHODS (NAMS)

Program Overview

From its foundation to the present day, NIH has funded research into the development and application of novel technologies and approaches. These efforts converge with NIH's commitment to the continual development of non-animal model alternative methods and to support efforts to replace, reduce, and refine the use of animals in studies (also referred to as the 3Rs).[232] In different contexts, methods that incorporate the 3Rs have been referred to as "Novel Alternative Methods," non-animal models, or New Approach Methodologies (NAMs). These experiments *in chemico* (cell-free models), *in vitro* (cultured cells), and *in silico* (computational modeling and simulation) can complement and sometimes replace and refine the use of animal studies. The development of effective NAMs may both increase the tools available to achieve the NIH mission and reduce and refine the future use of animals in some areas of research. However, for the foreseeable future, both approaches are necessary to establish rigorous evidence for translating research into clinical intervention.

The promise of the use of NAMs in research is recognized by researchers, Congress, and the public. In 2022, Congress directed the NIH to assess its current portfolio of NAMs. Accordingly, NIH established an internal working group to articulate how NAMs are currently advancing NIH-supported research, including the value and limitations of these approaches in biomedical research. Following from this assessment, in January 2023, the NIH Acting Director charged a new Advisory Committee to the Director (ACD) Working Group on *Catalyzing the Use and Development of Novel Alternative Methods* (Working Group) to identify how NAMs are currently being used and to make recommendations on where NAMs are positioned to be most applicable or beneficial, especially in terms of advancing our understanding of human health.[233] This Working Group included members with expertise in a wide range of technologies, scientific fields, and backgrounds including members from academia, industry, and federal partners with *ex officio* members from the U.S. Food and Drug Administration (FDA) and Environmental Protection Agency (EPA).

To inform these efforts, the NIH sought public input via a Request for Information (RFI) from June 12 through September 5, 2023, on challenges and opportunities for the further development and use of NAMs in biomedical research.[234] Additionally, the NIH held a public virtual workshop on August 21, 2023, on approaches, challenges, and opportunities relating to the development of NAMs.[235] The output from this workshop, along with the information received from the RFI, was used to inform the development of the ACD Working Group's recommendations on high-priority areas for future investment in NAMs. These recommendations hinge upon the importance of putting together diverse, multi-disciplinary teams with the right complementary knowledge. To break down silos between researchers in various disciplines, it is critical to set up collaborations between groups (e.g., disciplines, sectors), train scientists in a multi-disciplinary fashion, create standardized language to

[232] caat.jhsph.edu/principles/the-principles-of-humane-experimental-technique
[233] acd.od.nih.gov/working-groups/novel-alternatives.html
[234] grants.nih.gov/grants/guide/notice-files/NOT-OD-23-140.html
[235] osp.od.nih.gov/events/nih-workshop-on-catalyzing-the-development-of-novel-alternatives-methods/

communicate across specialties and sectors, and build and maintain an infrastructure to foster data interoperability and integrated models.

NIH's Longstanding Leadership in the Development and Use of NAMs

The recent activity to catalyze the development and use of NAMs builds on NIH's longstanding commitment to leadership in the field over the past two decades through programs like the National Toxicology Program (NTP) run out of the National Institute on Environmental Health Sciences (NIEHS) and the Tissue Chips for Drug Screening program run out of the National Center for Advancing Translational Science (NCATS).

Toxicology research and testing have been particular areas of focus and critique for the use of animal studies but have also been the focus of significant effort and progress in the development and adoption of alternative methods. The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM),[236] an office within NIH/NTP, evaluates alternatives to animal use for chemical safety testing with a focus on scientific publishing. Additionally, NICEATM runs the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), [237] formally established in 2000 by the ICCVAM Authorization Act (42 U.S.C. 285l-3). NICEATM has multiple initiatives to address diversity, equity, inclusion, and accessibility (DEIA) and environmental justice public health concerns by optimally leveraging and further developing NAMs to better represent the full variability of the U.S. population.

NIH has also been a leader in the development of tissue chips (also called organ-on chips), which are *in vitro* 3-D platforms engineered to support living human tissues and cells. In 2012, NIH partnered with the Defense Advanced Research Projects Agency (DARPA) and the FDA to lead the development of these tools to test safety and efficacy in drug development. Today, the Tissue Chip for Drug Screening program partners with 11 Institutes, Centers, and Offices (ICOs) and 3 federal agencies, including a partnership with the International Space Station U.S. National Laboratory on the Tissue Chips in Space program,[238] a research program to better understand the role of microgravity on human health and diseases and translate those findings to improve human health on Earth.

These and other efforts have led to a four-fold increase in use of NAMs in the past two decades. Researchers are adapting and building upon these tools to increase their use beyond toxicological testing and drug screening into broader biomedical research use.

Current NIH Investments in NAMs

The NAMs field itself has seen tremendous growth over the past 15 years alongside NIH's ever-expanding technological capabilities. NAMs are used in research by every ICO at NIH that funds and/or conducts research. Often, NIH-funded researchers use these methods to help guide animal studies and bolster evidence for their conclusions by going from simpler to more complex models. In many cases, NAMs allow scientists to control variables and establish clearer roles for the building blocks of biological systems, while research in animal models is critical to

[236] ntp.niehs.nih.gov/whatwestudy/niceatm/index.html
[237] ntp.niehs.nih.gov/whatwestudy/niceatm/iccvam/index.html
[238] ncats.nih.gov/research/research-activities/tissue-chip/projects/space

understanding just how these fundamental pieces interact in a living organism as it behaves over time in its environment. Researchers continue to apply and develop NAMs in a wide range of areas of basic and clinical research, including cancer, diabetes, cardiovascular disease, Alzheimer's disease, mental illness, infectious disease, and rare and genetic diseases.

In vitro models

NIH supports efforts to create and characterize *in vitro* models for research, which involves growing and using cells outside of the body. These models traditionally include two types of *in vitro* systems: 1) cell lines (i.e., cells established in culture that can continue to replicate indefinitely), and 2) primary cells from biopsies, which are grown as 2-D monolayer cell cultures and tissue explants. Advances in cell culture techniques and bioengineering have led to the advent of 3-D cell culture technologies that can better replicate the physiological complexity of tissues and organs than can traditional 2-D cell culture. 3-D cell culture systems, also called Microphysiological Systems (MPS), are rapidly increasing the ability to model complex biology and disease and should continue to serve as a valuable tool in reducing and refining the number of animals required for basic and preclinical research in the future. One type of MPS, bioprinted tissue constructs and tissue- and organs-on-chips called organoids, has become common in research. A subset of select programs and discoveries are outlined here to illustrate the wide-ranging applications of *in vitro* methods in NIH-supported research.

The Engineering Next-Generation Human Nervous System Microphysiological Systems program, supported by the National Eye Institute (NEI), National Institute on Mental Health (NIMH), National Institute on Aging (NIA), National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA),[239] and National Institute on Deafness and Other Communication Disorders (NIDCD), aims to develop 3-D human cell-based assays that replicate complex nervous system architectures and physiology with improved fidelity over current capabilities. Addressing this complex technical challenge requires the collaboration of experts from diverse fields, including developmental and stem cell biology, circuit and systems level neuroscience, materials science, engineering, and bioethics. The resulting assays are expected to have a multi-lineage, complex architecture representing the normal characteristics and functions of the relevant nervous system structure (e.g., sensory input systems, brain or spinal integrative systems, motor output systems). It is anticipated that they will substantially exceed the state of the art in cellular maturation and integration, allowing reproducible measurement of human-relevant circuit-level activity under physiological conditions over a long period. A similar program was also launched by the Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative.[240] These improved assays may enable complex studies of the development, function, and aging of nervous systems in healthy and disease states.

Investments in *in vitro* technologies led to an influx of exciting and influential findings in the past year. In a new study published in 2023, NIH-funded researchers used a chip to simulate repeated overdoses and treatments to study the effects on the chip's organs. The project was part of the Helping to End Addiction Long-term® Initiative (NIH HEAL Initiative®) in partnership with NCATS. In another study, NEI and NCATS co-developed 3-D bioprinted vascularized eye

[239] The FY 2025 President's Budget proposes to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.
[240] RFA-MH-20-140: grants.nih.gov/grants/guide/rfa-files/rfa-mh-20-140.html

tissue with native tissue-like properties and used it for drug testing.[241] NEI and NCATS performed drug screening using similar models, leading to the discovery of drug candidates to treat ciliopathy and macular degeneration.[242] NEI and the National Heart, Lung, and Blood Institute (NHLBI) used patient-specific human adult cell-derived induced pluripotent stem cells (iPSCs) to discover disease causing mechanisms in a 3-D bioprinted vascularized eye tissue that reproduced macular degeneration in a dish.

In silico models

NIH also supports the development and use of *in silico* models to advance biomedical research. In recent years, the increased use of computational models using artificial intelligence (AI), including machine learning (ML) and deep learning (DL), has been enabled by greater computer performance and the ability to collect, store, and process vast amounts of data. NIH has prioritized the development of transformative AI/ML-based systems, emerging tools, and modern technologies for diagnosing and recommending treatments for a broad range of human diseases. The section on Artificial Intelligence within this chapter on cross-cutting initiatives goes into greater detail about the many initiatives that NIH has launched to tackle complex biomedical challenges, including Bridge2AI[243] and AIM-Ahead[244] (Artificial Intelligence/Machine Learning Consortium to Advance Health Equity and Researcher Diversity).

These programs and initiatives further leverage existing data and discoveries by using *in silico* models in a broad array of applications and fields. For example, researchers funded by NIDCD are developing a machine learning model to diagnose inner ear conductive pathologies to improve surgical specificity, minimize unnecessary exploratory surgery and imaging, and provide an objective clinical means of postoperative monitoring. Meanwhile, researchers funded by the National Institute for Allergy and Infectious Disease (NIAID) are using *in silico* models to predict the activity of new antibiotic combinations to fight antimicrobial resistance. As the need for combinatorial antibiotic approaches grows, these methods allow researchers to optimize therapies for patients in the clinic.

In chemico models

NIH continues to support efforts to use and develop *in chemico* NAMs, or cell-free experiments in which biological molecules can be studied in isolation or in complexes separate from their native environment. These highly controlled experiments allow detailed observation of biochemical interactions such as the structure and function of DNA, RNA, or proteins in isolation or in combination, and how potential drugs interact with these biological molecules, including to help establish therapies. As one example, researchers funded by the National Center for Complementary and Integrative Health (NCCIH) are using high-throughput methods to help better understand the basic mechanisms of action of botanical natural products, which can in turn accelerate the process to advance natural product drug discovery.

[241] pubmed.ncbi.nlm.nih.gov/36550275/
[242] pubmed.ncbi.nlm.nih.gov/34911940/; pubmed.ncbi.nlm.nih.gov/36975211/
[243] bridge2ai.org/
[244] aim-ahead.net

Resources and Education to Support the Use of NAMs

To move these technologies into widespread use, there must be targeted efforts to broaden their reach. To this effect, NIH is working to develop and disseminate resources to researchers across the biomedical research enterprise. As one example, NIH is creating large scale resources of iPSCs and related data that will be shared broadly with the biomedical community. Human adult cell-derived iPSCs represent a significant improvement in reliable and reproducible use of human-derived biological material to model human biology. Their remarkable developmental potential and unlimited self-renewal capacity *in vitro* enables the generation of many cell types of the human body from a single individual in large quantities. The iPSC Neurodegenerative Disease Initiative[245] is the largest iPSC genome engineering project to date and will model more than 100 mutations associated with Alzheimer's disease and related dementias (ADRD) in isogenic iPSC lines. Similarly, the Molecular Phenotypes of Null Alleles in Cells (MorPhiC) program[246] aims to create a catalogue characterizing the impact on *in vitro* multicellular systems when genes do not produce functioning proteins. NIH supports the Scalable and Systematic Neurobiology of Psychiatric and Neurodevelopmental Disorder Risk Genes (SSPsyGene) program[247,248] that aims to functionally characterize phenotypes for more than a hundred risk genes for neurodevelopmental and psychiatric disorders.

In January 2023, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) launched the intramural Center for Biomedical Engineering and Technology Acceleration (BETA Center), a multi-institute NIH resource that accelerates the development, validation, and dissemination of high-impact biomedical technologies to address urgent national and global health needs.

The National Cancer Institute (NCI) is advancing resources for researchers to use patient-derived and next generation cancer models to understand unique characteristics of individual cancers, identify possible treatments, and test those treatments for efficacy. The Human Cancers Model Initiative is an international collaboration that has generated over 250 models from 27 different cancer types available to researchers through an online catalogue.[249] Similarly, NCI's Patient-Derived Models Repository has created over 1,800 various patient-derived models to date that it distributes to the cancer research community upon request.[250]

Likewise, computational models are an increasingly used tool in research, including the cancer field. NCI supports the development and use of computational models to understand how cancer develops, progresses, and may or may not respond to treatment. NCI-funded researchers recently used both mouse and computational models to understand the evolution of pancreatic cancers, including inflammatory events that can lead to tumor development in certain subpopulations of cells with a specific mutation. Having this roadmap for cancer development

[245] card.nih.gov/research-programs/ipsc-neurodegenerative-disease-initiative
[246] genome.gov/research-funding/Funded-Programs-Projects/Molecular-Phenotypes-of-Null-Alleles-in-Cells
[247] grants.nih.gov/grants/guide/rfa-files/RFA-MH-22-110.html
[248] grants.nih.gov/grants/guide/rfa-files/RFA-MH-22-111.html
[249] cancer.gov/ccg/research/functional-genomics/hcmi
[250] pdmr.cancer.gov/

can help with strategies to detect or even prevent pancreatic tumors before they reach an advanced stage.

The Office of Resource Infrastructure Programs (ORIP) supports research infrastructure and research-related resource programs. One such resource is BioGRID: Biological General Repository for Interaction Datasets,[251] a public database that archives and disseminates genetic and protein interaction data from model organisms and humans. BioGRID currently holds over 1,400,000 interactions curated from both high-throughput datasets and individual focused studies, as derived from over 57,000 publications in the primary literature.

NIH also collaborates with partners in the private and public sectors, including DARPA and FDA, on advancements for NAMs. Recently, the Validation Workgroup of ICCVAM, co-chaired by the National Institute of Science and Technology (NIST), FDA, and Consumer Product Safety Commission (CPSC), put out a draft report on Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies and is now reviewing and incorporating public comment it received in September 2023.[252] The report has been reviewed by the Scientific Advisory Committee on Alternative Test Methods and will be finalized by early 2024.

As part of the commitment to promote the use of the most appropriate models, NIH provides numerous trainings, programs, and resources to researchers to promote animal care and appropriate use of NAMs. NIH works directly with the research community to advance their understanding of the science underlying alternative methodologies, through podcasts (See NIH All About Grants Podcast on Alternatives to Animals)[253] and webinars.

Many educational programs are run by specific ICOs to focus on a disease- or system-specific use of NAMs. As one example, the National Institute on Diabetes and Digestive and Kidney Disease (NIDDK) held a workshop entitled "Microphysiological Systems for Studying Type 2 Diabetes, Obesity, and Their Complications" in September 2023.[254] Other educational programs are held to discuss overarching methods for catalyzing the development and use of NAMs across the biomedical research enterprise, such as the Office of Laboratory Welfare's (OLAW) annual support of the 3Rs Symposium in partnership with John Hopkins University and the U.S. Department of Agriculture (USDA). In May of 2023, the symposium celebrated its 10th anniversary, with the theme "The 3Rs in Action!"[255]

An Ambitious Path Forward: Spurring Scientific Advances with NAMs

In its final report, the ACD Working Group on NAMs identified seven bold, ambitious, and equitable high priority areas for future investment in NAMs: 1) combinatorial NAMs; 2) interoperable, reliable datasets; 3) effective technology dissemination and interconnection; 4) comprehensive training; 5) multidisciplinary teams; 6) socially responsible technologies; and 7)

[251] orip.nih.gov/resource-directory/biogrid-biological-general-repository-interaction-datasets-0; thebiogrid.org/
[252] ntp.niehs.nih.gov/sites/default/files/2023-08/VWG%20Report%20Draft_for%20public%20comment_08Aug2023.pdf
[253] nexus.od.nih.gov/all/2020/11/18/all-about-grants-podcast-alternatives-to-animals/
[254] niddk.nih.gov/news/meetings-workshops/2023/microphysiological-systems-for-studying-t2d-obesity-and-complications?agenda
[255] olaw.nih.gov/news/registration-open-10th-annual-3rs-symposium-3rs-action.html

coordinated infrastructure.[256] These areas highlight the power and opportunity of integrated work that brings together different disciplines, sectors, technologies, and data. The ACD Working Group's final report, which was accepted by the ACD and shared for consideration of the NIH Director in December 2023, provides a roadmap forward to catalyze the development and use of NAMs at NIH and beyond.

The implementation of these recommendations will be an NIH-wide effort that builds upon the ongoing projects described here. For example, the Common Fund, a funding entity within NIH that supports bold scientific programs that catalyze discovery across all biomedical and behavioral research, is planning a potential new program called Complement Animal Research in Experimentation (Complement-ARIE) that would bring together multiple ICOs to catalyze the development, standardization, validation, and use of human-based NAMs.[257] The NIH looks forward to using this collaborative and innovative funding model, along with other programs outlined above and new, nascent ideas inspired by the new ACD Working Group recommendations to expand the researcher toolkit and catalyze scientific advances using NAMs.

[256] acd.od.nih.gov/documents/presentations/12142023_NAMs_Working_Group_Report.pdf
[257] commonfund.nih.gov/complementarie/strategicplanning

CHRONIC PAIN AND SUBSTANCE USE DISORDER

Program Overview

NIH launched the Helping to End Addiction Long-term (HEAL)® Initiative to provide scientific solutions to the opioid crisis by accelerating research on prevention and treatment of opioid misuse, addiction, overdose, and non-addictive treatments for pain conditions. NIH has a crucial role in reducing overdose deaths through research aligned with the HHS overdose prevention strategy (primary prevention, evidence-based treatment, harm reduction, recovery support). Extensive overprescribing of opioid analgesics contributed to the opioid crisis, highlighting an urgent need for evidence-based, effective, and safe pain management to alleviate pain and mitigate need for opioids. Moreover, addressing the intersection of chronic pain and opioid use disorder (OUD) is an important part of HEAL research, as chronic pain often co-occurs in people with OUD, and people with chronic pain on long-term opioid therapy can be at risk for OUD.

The HEAL Initiative is led by the National Institute on Drugs and Addiction (NIDA)[258] and the National Institute of Neurological Disorders and Stroke (NINDS) in collaboration with other NIH Institutes, Centers, and Offices (ICOs), including the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), National Institute of Mental Health (NIMH), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Center for Complementary and Integrative Health (NCCIH), National Institute of Allergy and Infectious Diseases (NIAID), National Center for Advancing Translational Sciences (NCATS), National Cancer Institute (NCI), National Institute of Nursing Research (NINR), National Institute on Minority Health and Health Disparities (NIMHD), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Dental and Craniofacial Research (NIDCR), National Institute of General Medical Sciences (NIGMS), National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA),[259] National Heart, Lung, and Blood Institute (NHLBI), National Institute on Aging (NIA), National Institute of Biomedical Imaging and Bioengineering (NIBIB), NIH Clinical Center (CC), and the NIH Tribal Health Research Office. Appropriated funds for HEAL are split between NIDA for substance use disorder (SUD) research and NINDS for pain management research. ICO partners coordinate overarching research and related initiatives at the intersection of pain and addiction; diversity, equity, inclusion, and accessibility; health disparities; community engagement; data sharing; and dissemination of research results. HEAL research on SUD extends beyond the intersection of pain and OUD discussed in this chapter. (See the CJ chapters for NIDA and NINDS for more about other HEAL programs.) NINDS and other ICOs also support research on understanding, treating, and preventing chronic pain beyond the HEAL programs highlighted here.

HEAL Programs at the Intersection of Treatment for Pain and Opioid Use Disorder

Chronic pain often co-occurs in people with OUD, yet for these individuals, a lack of evidence-based guidelines for concurrent treatment of both conditions can lead to poor health outcomes.

[258] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.

[259] The FY 2025 President's Budget proposes to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.

HEAL addresses this problem with two related programs. The Integrative Management of chronic Pain and OUD for Whole Recovery (IMPOWR) network will develop and test patient-centered interventions for co-occurring chronic pain and OUD in healthcare settings including primary care, opioid treatment programs, and hospitals. IMPOWR research focuses on treatment of the whole person, recognizing the influence of stigma, health inequities, and co-occurring mental health disorders. Challenges and solutions related to treatment barriers are addressed through partnerships with patient and community partners to maximize benefits of interventions and embed effective practices into health care systems. IMPOWR is generating a comprehensive dataset on chronic pain and OUD that includes measures on co-occurring psychiatric conditions, social determinants of health, cost-effectiveness evaluations, and intervention implementation. Researchers also have run several pilot studies to understand how stigma toward these populations affects health service provision and outcomes.

The second program is the Multilevel Interventions to Reduce Harm and Improve Quality of Life for Patients on Long Term Opioid Therapy (MIRHIQL). This program enhances IMPOWR through research to develop and evaluate interventions to prevent SUD in people who are on long-term opioid therapy without access to safer, high-quality care for chronic pain and may be at risk for OUD. Harms of long-term opioid therapy can include tolerance development with reduced analgesic relief and increased risk for concurrent benzodiazepine or alcohol use. MIRHIQL supports effective, patient-centered protocols for decreasing opioid doses (tapering) for patients on long-term opioid therapy and is creating a risk-benefit assessment tool to assist providers in deciding when opioids should be continued as prescribed, tapered, or discontinued.

Health Disparities in OUD and Pain

Quality care for all people with OUD, pain, and other co-occurring conditions often is difficult to access, but this challenge is especially great for populations who experience health disparities, including racial/ethnic minorities, socioeconomically disadvantaged populations, underserved rural populations, and members of the LGBTQ+ minority community. The HEAL Advancing Health Equity in Management of Pain and Co-occurring Conditions program supports research on evidence-based interventions tailored to these populations, with a goal to improve health outcomes via culturally appropriate approaches. ICOs with interests in many pain conditions manage the program, including NCI, NCCIH, NIA, NICHD, NINR, and NIMHD. The research explores multi-level interventions—from single providers to communities to health care systems—that are scalable, sustainable, and can be implemented rapidly into health care. For example, one project is developing an interactive simulation to assess effects of a care provider's biases on treatment decisions for patients prescribed opioids for pain. The simulation allows the research team to evaluate the influence of race or income on the doctor's decision about continuing opioid therapy. Their data will help to design solutions to reduce treatment biases.

Quality Data Collection and Sharing

Data harmonization and sharing across all pain and OUD studies are needed to ensure that data can be compared and used to answer broader research questions. The HEAL Data Ecosystem provides a platform for scientists to securely share data so they can be reused and reanalyzed by the broad OUD and pain research community, providing a foundation for future research. HEAL Connections translates data to put results into practice, building a bridge between the research setting and patients, caregivers, care providers, and others who can benefit from the findings.

The Initiative also includes a suite of other programs to enhance data collection and examination. The HEAL Data2Action (HD2A) program is a network of research projects and resource centers to accelerate use and enhance quality of data on the epidemiology of the opioid crisis and guide health service improvements for OUD and pain management. HD2A projects link data systems and create dashboards to track care quality and treatment strategies that improve patient outcomes. Researchers work with health care partners to improve data infrastructure to identify and fill service delivery gaps. The HD2A Data Infrastructure Support Center developed the HEAL Initiative HD2A Addiction and Chronic Pain Template,[260] an open-source online application to help researchers create Data Management and Sharing plans that comply with data sharing policies. The tool helps in navigating sharing requirements and provides policy guidance to support overall HEAL goals to make data more FAIR (Findable, Accessible, Interoperable, and Reusable) and amplify use of research findings on pain and addiction. Another innovative program, the HEAL Data and Methods to Address Urgent Needs to Stem the Opioid Epidemic program,[261] is developing approaches to provide insights into patterns of opioid and other prescription drug use and misuse from data streams such as electronic health records, epidemiological surveillance, health claims data, pharmacy dispensing, and mortality records. These projects will facilitate rapid monitoring of the opioid crisis to advance prevention and treatment efforts and inform decision making and resource allocation in local jurisdictions.

Enhancing the Research Workforce

A collective effort across all HEAL ICOs aims to improve the quality of research on pain and OUD through training, mentoring, and networking experiences for early-stage career scientists. This includes programs to support diverse populations at different career stages and innovative strategies for learning and career development. One approach couples a nationwide networking and training platform for pain scientists with a national network of mentors to train scholars in clinical pain research. The PURPOSE Network—for Positively Uniting Researchers of Pain to Opine, Synthesize, & Engage—is the first online platform for connecting pain researchers, serving as a central facilitator to enhance career development, integrate training, and connect with mentors. The National K12 Clinical Pain Career Development Program is a nationwide network of mentors and scholars to provide research training for early-stage career clinicians. It works with PURPOSE to offer training tools and resources for both scholars and mentors. The program enrolled its first wave of scholars and developed guidelines for mentoring and career development to promote their successful transition into independent research careers. HEAL also provides early- and mid-career scientists pursuing pain or opioid misuse research with hands-on training in translational research aimed at therapeutics development in industry, academia, or government research laboratories. Trainees receive broad exposure to therapeutics development while institutions benefit from trainees' pain or addiction expertise.

Other HEAL Research on Non-Opioid Pain Management

HEAL pain research spans early discovery of therapeutic targets and implementation of evidence-based care. HEAL preclinical and translational research in pain management supports efforts to discover new medications and devices to treat pain. HEAL clinical pain research

[260] hd2arasc.org/resources/

[261] grants.nih.gov/grants/guide/rfa-files/RFA-DA-22-044.html

includes networks to run trials to test effectiveness of pharmacologic and non-pharmacologic treatments and studies approaches to embed quality pain care into health care systems. Examples described below show progress toward effective, non-opioid approaches to treating pain.

Finding New Targets for Non-Addictive Pain Treatments

A long sought-after goal has been to understand changes in brain activity related to pain. A recent HEAL study reported new findings on brain activity associated with pain that offer opportunities to modulate brain circuits to reduce chronic pain. For the first time researchers recorded pain-related data over several months from inside the brain of individuals with chronic pain disorders and analyzed the data with machine learning tools. They identified a brain area associated with chronic pain and objective biomarkers of chronic pain in individual patients.[262]

Another HEAL team set out to find brain regions in preclinical models that might be targets for non-opioid pain interventions. Their novel approach was to find a pain-relief center in the brain by exploring regions that are activated by surgical anesthetics that block pain. Through optogenetic technology they identified neurons in the amygdala that were activated when mice were exposed to anesthetics. This brain region did not previously have a known role in pain relief. Further studies showed that activating these neurons suppressed pain by inhibiting a network of pain-activating neurons in other regions of the brain.[263] These two sets of findings are important steps towards developing novel methods for assessing and treating chronic pain.

The Program to Reveal and Evaluate Cells-to-gene Information that Specify Intricacies, Origins, and the Nature of Human Pain (PRECISION Human Pain) network focuses on identifying mechanisms underlying the pain experience. It coordinates, harmonizes, and integrates comprehensive datasets generated from human tissue-based research by capitalizing on recent technological advances to study human tissues and cells involved in pain processing. It seeks to identify molecular signatures and cell types that underlie pain pathways, to enable future translational research leading to development of non-addictive pain therapies.

To address the shortage of promising treatments in the drug development pipeline, the Pain Therapeutics Development Program is providing funding that is propelling potential pain drugs closer to testing in human participants and helping small companies attract venture capital to support late-stage clinical trials. Eight potential new pain treatments have received the green-light from the Food and Drug Administration to proceed with Phase 1 clinical trials.

HEAL Pain Clinical Research

HEAL established clinical research networks for various stages of clinical trials. The Back Pain Consortium (BACPAC) is exploring biological, psychological, and social factors that contribute to chronic low back pain and has developed diagnostic tools and a data analysis platform for its various trials to leverage. One of those trials is studying the link between such factors and whether they influence the effectiveness of four different treatments. The evidence generated could help doctors and patients determine the best personal course of action for their back pain treatment. Through the Effectiveness Research Network, clinical trials are evaluating best

[262] nature.com/articles/s41593-023-01338-z
[263] pubmed.ncbi.nlm.nih.gov/32424286/

approaches for acute pain management to prevent onset of chronic pain, including one trial showing that shared treatment decision strategies and education about post operative pain care reduced post-operative prescription opioid use after cesarean section.

A trial supported through the Small Business Innovation Research Program showed that effective perioperative pain management improved post-surgical pain outcomes, including reduced use of opioids. This research team questioned the trend toward reducing opioids during surgery, a practice intended to reduce opioid prescribing that may actually lead to increased postoperative pain and subsequent increased need for postoperative opioid prescribing. The team showed that increasing fentanyl administration during surgery led to less uncontrolled pain, lower risk of chronic pain after surgery, and fewer opioid prescriptions up to six months after surgery.[264] Their findings suggest that optimizing opioid use during surgery may prevent chronic pain.

Future Directions for HEAL Research

As HEAL looks to the future, the newest funding opportunities will ensure that research being generated will reach all of those in need of quality care for chronic pain and OUD, particularly in populations where access or evidence is lacking, such as American Indian/Alaska Native communities, pediatric populations, and those requiring integrated care from multiple providers.

NIH held Tribal consultations on research needs to address opioid misuse and pain management in Native communities. These highlighted the importance of Indigenous knowledge and local expertise and the need to invest in community-prioritized research led by Tribes and Native American Serving Organizations (T/NASOs). In response, HEAL established the Native Collective Research Effort to Enhance Wellness (N CREW) as a partnership with American Indian/Alaska Native and Native Hawaiian communities. N CREW is a collaboration between NIDA, NINDS, and NCATS with other ICOs participating. It will support T/NASOs in leading community research projects with a focus on integrating Indigenous knowledge and culture. N CREW will enhance research capacity within T/NASOs through accessible, culturally grounded technical assistance and resources, as well as improved access to quality data on substance use, pain, and related health and well-being factors for use in local decision-making.

Children represent another population in urgent need of better pain management. Care for children is often challenging in part because of lack of evidenced-based pain treatment guidelines. They also are often at risk for OUD because they are opioid naïve and may be exposed to opioids without proper risk assessment. HEAL KIDS is a program led by NICHD and NIAMS that supports innovative clinical trials to test safe effective therapies and at the same time advance the understanding, assessment, measurement, and treatment of pain in infants, children, and adolescents, including those with disabilities and/or experiencing health disparities.

Future activities also will focus on integrated care models for chronic pain. The Coordinated Approaches to Pain Care in Health Care Systems program, led by NINDS with other ICO support, will support research projects to embed effective coordinated pain care into health care systems. The goal will be to improve pain and health outcomes through delivery of integrated

[264] jamanetwork.com/journals/jamasurgery/fullarticle/2806264

multidisciplinary care that includes appropriate medication, behavioral therapy, physical rehabilitation, and pain self-management. The coordinated care delivery will be centered in primary care settings with referrals to specialty care or delivered through specialty care settings in coordination with primary care.

CUTTING-EDGE CLINICAL RESEARCH AND INFRASTRUCTURE AT THE NIH CLINICAL CENTER

Program Overview

At the NIH Clinical Center, clinical research participants—more than 500,000 since the hospital opened in 1953—are active partners in medical discovery, a partnership that has resulted in a long list of medical milestones, including development of chemotherapy for cancer; the first use of an immunotoxin to treat a malignancy (hairy cell leukemia); identification of the genes that cause kidney cancer, leading to the development of six new, targeted treatments for advanced kidney cancer; the demonstration that lithium helps depression; the first gene therapy; the first treatment of Acquired Immunodeficiency Syndrome (AIDS) (with azidothymidine [AZT]); and the development of tests to detect AIDS/HIV and hepatitis viruses in blood, which led to a safer blood supply. Patients come from all 50 states and from around the world.

Currently, there are about 1,600 clinical research studies in progress at the Clinical Center. About half are studies of the natural history of disease, especially rare diseases, which often are not studied anywhere else. What researchers learn by studying rare diseases often adds to the basic understanding of common diseases. Most other studies are clinical trials, which often are the first tests of new drugs and therapies in people. The clinical trials at the Clinical Center are predominantly Phase I and Phase II, often first-in-human to test safety and efficacy.

The Clinical Center has been a leader in "bench-to-bedside" medicine. Its specialized hospital design places patient care units in close proximity to research laboratories, facilitating interaction and collaboration among clinical researchers. The Clinical Center also offers world-class training in clinical research for physicians, nurses, medical students, dentists, and other members of the medical research community. This environment, offering access to the most advanced techniques, equipment, and ideas, attracts a global network of top scientists.

The hospital has 200 inpatient beds, 11 operating rooms, 93 day-hospital stations, critical care services and research labs, an ambulatory care research facility for outpatient visits, two onsite pharmacies, a blood bank, and a complex array of imaging and diagnostic services. The Clinical Center's infrastructure allows for isolation capabilities for infection control while patients participate in clinical research studies.

The Clinical Center serves as a valuable resource to researchers, its patients, and biomedical research, and as such conducts a wide array of clinical research in conjunction with other Institutes and Centers at NIH. Due to its unique environment as a government research hospital, the Clinical Center also participates in a number of additional accrediting programs to ensure it is a world-class facility. For example, Clinical Center graduate medical education (GME) programs are accredited by the Accreditation Council for Graduate Medical Education (ACGME), and the Department of Laboratory Medicine (DLM) is accredited by the College of American Pathologists (CAP).

Furthermore, the Clinical Center is accredited as a whole by the Joint Commission, an independent, not-for-profit organization that accredits and certifies more than 20,500 health care organizations and programs in the United States. Joint Commission accreditation and

certification is recognized nationwide as a symbol of quality that reflects an organization's commitment to meeting certain performance standards. To maintain and earn accreditation, organizations must have an extensive onsite review by a team of Joint Commission healthcare professionals at least once every three years. The review's purpose is to evaluate the organization's performance in areas that affect patient care. The Clinical Center received full accreditation status in 2021.

Diversity, Equity, Inclusion and Accessibility Efforts

The Clinical Center is dependent on a diverse workforce with a culture of teamwork and collaboration. The hospital has developed a comprehensive DEIA program to combat racism and reduce disparities across its workforce. Efforts are focused on promoting diversity and inclusion by reducing disparities, promoting inclusivity and equity, and lifelong learning.

Importantly, one of the many benefits of this program is that it also supports the Clinical Center's emphasis on providing culturally sensitive care for its patients. The Clinical Center provided a video[265] to staff announcing the launch of the program.

The Clinical Center is committed to transparency in addressing Diversity, Equity, Inclusion and Accessibility (DEIA). Workforce demographics specifically of Clinical Center government employees are available on the NIH Office of Equity, Diversity, and Inclusion's Workforce Demographics webpage.[266]

The Clinical Center has made many strides in the last year in support of its DEIA program, including the hiring of a new Scientific Diversity Officer and implementation of multiple additional programs born out of its Racial and Ethnic Equity Plan, some of which are outlined below.

In striving to support more diverse representation in recognition, retention, and development programs, the Office of Workforce Management and Development (OWMD) works closely with the Clinical Center Executive Leadership team to apply the Racial and Ethnic Equity Lens (REEL) to all decisions relating to these programs. Additionally, the Clinical Center has created a written policy for hiring and advancement, initially focused on the Nursing Department. This policy is being implemented now, with nursing leadership engaging departmental Nurse Educators to train staff on the use of the policy, and the Nursing Diversity, Equity, and Inclusion Council assisting with communication and implementation of the policy and related recommendations. As potential candidates for promotion and/or hire are identified, this new policy will be utilized to help ensure equitable decision making in the selection process. As is standard practice, the policy will be reviewed regularly to assess the need for any changes or additions after implementation, and will be expanded to the entire hospital.

While the Clinical Center is a relatively diverse[267] organization overall, there is less representation at the senior levels of the organization. In order to communicate its commitment

[265] youtube.com/watch?v=HGL4ROH0NHw
[266] edi.nih.gov/data/demographics/ic-workforce-demographics#cc
[267] edi.nih.gov/data/demographics/ic-workforce-demographics#cc

to DEIA, the Clinical Center inserted additional language into USAJobs announcements for senior positions that underlines the importance of experience with racial and ethnic equity. The Clinical Center also, when related to the duties of Clinical Center positions, inserted a specific question about experience working on DEIA initiatives in the hiring questionnaire applicants must answer to be considered for vacancies.

Further, the Clinical Center has robust programs in place when assessing existing or designing new space or facilities, reviewing hiring practices, and developing technical solutions. However, there is still always opportunity for advancement and improvement. The Clinical Center will work to eliminate barriers related to the employment, promotion, and advancement of people with disabilities as well as any physical or structural barriers. The FY 2024 focus on enhancing accessibility within the Building 10 Complex and Clinical Center operations consists of two primary components: Education and Practical Measures.

NIH Collaboration

The Clinical Center serves as the physical location for almost all the clinical research performed as a component of the NIH Intramural Program. This includes providing essential infrastructure that is responsive to the needs of the other NIH Institutes and Centers, such as the newly upgraded pharmacy and enhanced pediatrics program.

In addition to providing essential support to the rest of the organization, the Clinical Center also has its own research program, which has produced many exciting developments in the last few years. This research program is also informed by the priorities of the other NIH Institutes and Centers, and thus reflects the overall focus of NIH. Below are a few examples of advances that have recently occurred at the Clinical Center.

Sickle Cell Disease Treatment Trial

In models of sickle cell disease, a Clinical Center team conducted a pre-clinical trial of mitapivat, a drug that activates a key enzyme in the pathway to break down glucose in red blood cells. They showed that mitapivat increases adenosine triphosphate (ATP), which provides energy to power red blood cells and decreases the ineffective production of red blood cells in the model. These findings provided preclinical support for the testing of the drug in clinical trials to treat sickle cell disease in humans, which are now ongoing. If successful, the use of glycolysis activators might bring about a paradigm shift for the treatment of sickle cell disease.

Neurorehabilitation and Biomechanics Research Advance

A Clinical Center laboratory designed and implemented a real-time Electroencephalography (EEG)-based neurofeedback system to train motor skills in children with cerebral palsy who have brain injuries early in development that impair their motor abilities. Traditional therapies fail to restore some lost motor skills. The developed neurofeedback system uses brain-computer interface and deep learning methodologies to detect the child's own brain signals to activate enhanced sensory feedback during active motor training that strengthens neural and motor pathways. In the first 3 children enrolled, the team has already observed positive changes in

function and brain activation from only 10 training sessions, highlighting the potential of this novel approach.

Fungal Infection Diagnosis

Fungal infection, an often-deadly complication in transplant patients, is very difficult to identify early enough to allow successful treatment. The Clinical Center has modified a naturally occurring sugar that can be used as an imaging marker of fungal infection. This development has the potential to significantly improve the prognosis and survival of this vulnerable patient population.

Interventions for Early Puberty

Children who experience early puberty are at risk for adult short stature. Medication that blocks and delays puberty can result in decreased bone strength with risk of bone fracture later in life. An Clinical Center team evaluated children with a genetic endocrine disorder (congenital adrenal hyperplasia, CAH) at risk for early puberty and found that pubertal blockade for an average of 4.5 years did not compromise bone health in adulthood and did result in improved adult height. This finding will likely improve the treatment of children with CAH who experience early puberty.

Cutting-Edge Ventilators and Pain Management

Patients with advanced cancer frequently have pain that responds poorly to medication and greatly impacts their quality of life. In an ongoing human clinical trial at the Clinical Center, researchers are treating cancer patients with a non-opioid, non-addictive small molecule, RTX, a natural plant product. The ongoing clinical trial has shown that a single dose of this drug provides long-term pain relief, decreases the need for other pain medications, and enables the patient to resume greater activity.

The COVID-19 pandemic highlighted the need for emergency ventilators to support the respiratory care of patients during a crisis. An international collaboration including the NIH Clinical Center was assembled, and their efforts resulted in the development of a miniature (size of a memory stick), inexpensive, easy to use, no-maintenance ventilator that can be rapidly produced with a 3D printer. The Clinical Center has demonstrated proof of principle in a large animal model and is preparing for a first-in-human trial at the NIH.

Next Steps and Goals

The Clinical Center endeavors to maintain a cutting-edge facility with world class medical staff to ensure the best possible clinical care and research support. A primary focus moving forward is to mindfully construct and renovate space to meet the future needs of the NIH clinical research program. For example, in May 2023, construction began on the Surgery, Radiology, and Laboratory Medicine wing that will provide cutting-edge space for many of the necessary functions of the Clinical Center that are currently housed in 1980s-era space with outdated mechanical, electrical, and plumbing infrastructure. The construction work will add 547,290

square feet to the Clinical Center and renovate approximately 82,000 square feet of existing space. Work is anticipated to last until 2029. NIH and the Department of Health and Human Services leaders support these changes to modernize hospital facilities to ensure that the Clinical Center can continue to provide high-quality patient care alongside cutting-edge biomedical research.

THE FUTURE OF THE BIOMEDICAL WORKFORCE

Program Overview

The biomedical research enterprise relies upon a talented, qualified, diverse group of investigators to bring new insights and translate fundamental research findings into improved health. The National Institutes of Health (NIH) has long recognized that the most critical components of the biomedical research enterprise are the scientists who comprise its workforce.

The pathway to a career in biomedical research is long and challenging but ultimately rewarding. While NIH supports programs at the earliest stages of career development, including K-12, undergraduate, and graduate school training,[268,269] a working group of the Advisory Committee to the Director recently highlighted the unique challenges faced by postdoctoral research scholars,[270] and approaches to re-envision the NIH-supported postdoctoral experience.[271] Concerns about the decreasing numbers of NIH-supported postdocs in recent years were also considered.[272] As part of this effort, a 2023 Request for Information[273] was issued and it received over 3,000 public comments on the role of the academic postdoc, fundamental factors influencing postdoctoral training, and possible solutions. The recommendations from this report[274] include increasing pay and benefits for all NIH-supported postdoctoral scholars, which aligns with its goal to better support the full and varied talent pool of scholars; improving training and professional development of postdoctoral scholars and facilitating the transition of scholars into their next career stages; and supporting safe and diverse perspectives and environments across research programs. These recommendations are currently being considered by the NIH Director for possible implementation.

NIH continues to make support of early-stage investigators (ESIs) a very high priority. This includes those within 10 years of completing postgraduate clinical training or their highest research degree who have not yet competed successfully for a substantial NIH independent research award. While age to first R01 has been continuously increasing for ESIs, the rate of increase has slowed over the last 10 years.[275] In 2023, the mean age was 42.6 for PhDs, 46 for MDs, and 45.7 for MD/PhDs, consistent with recent years.

NIH Institutes, Centers, and Offices (ICOs) oversee a variety of innovative cross-cutting initiatives aimed at supporting the next generation of the NIH-funded biomedical workforce. The following are some of these initiatives.

[268] researchtraining.nih.gov/career-path
[269] nigms.nih.gov/research-training/programs/high-school-and-undergraduate
[270] acd.od.nih.gov/documents/presentations/12152023_Postdoc_Working_Group_Report.pdf
[271] nexus.od.nih.gov/all/2023/02/14/share-your-thoughts-on-how-to-re-envision-nih-supported-postdoctoral-training/
[272] nexus.od.nih.gov/all/2023/03/02/number-of-postdoctoral-researchers-supported-by-nih-grant-awards-fy-2017-fy-2022/
[273] nexus.od.nih.gov/all/2023/02/14/share-your-thoughts-on-how-to-re-envision-nih-supported-postdoctoral-training/
[274] acd.od.nih.gov/documents/presentations/12152023_Postdoc_Working_Group_Report.pdf
[275] nexus.od.nih.gov/all/2021/11/18/long-term-trends-in-the-age-of-principal-investigators-supported-for-the-first-time-on-nih-r01-awards/

Program Descriptions and Accomplishments

Next Generation Researchers Initiative (NGRI) Focusing on Early-Stage Investigators

NIH has long been committed to expanding opportunities that support and prioritize researchers early in their career. The 21st Century Cures Act (P.L. 114-255) directed NIH to establish the NGRI in an effort to further cultivate and support talent entering the biomedical and behavioral research workforce.[276] NGRI promotes opportunities for new researchers and earlier research independence through policies that increase opportunities for new researchers to receive funding, enhance training and mentorship programs, and enhance workforce diversity. As an example, ESI applications are given special consideration during peer review as well as at the time of funding consideration. NIH also tracks the impact of ESI funding prioritization, including subsequent grant submission and success. As a result of this initiative, the number of NIH-funded ESIs has increased from 978 in FY 2016 (before NGRI was started) to 1,513 in FY 2021[277] and 1,609 in FY 2022, and 1,587 in FY 2023.[278,279]

The Stephen I. Katz ESI Research Project Grant Program

The Katz ESI Research Project Grant Program is an initiative with multiple participating NIH ICOs. This program encourages ESIs' innovative ideas by supporting their proposed research that is a change in direction from their past work and experience, and for which they have no preliminary data. All applications received are clustered and reviewed together in appropriate standing NIH study sections, in alignment with NGRI efforts.

The NIH Director's Early Independence Award

The NIH Director's Early Independence Award is a Common Fund initiative coordinated with multiple NIH ICOs. This award supports outstanding junior scientists with the intellect, scientific creativity, drive, and maturity to bypass the traditional postdoctoral training period to accelerate the launch of their independent research careers. The Early Independence Award supported 13 investigators in FY 2023.[280]

The NIH Director's New Innovator Award

The NIH Director's New Innovator Award, a component of the High-Risk, High-Reward Program of the Common Fund, is coordinated with multiple NIH ICOs. The award supports exceptionally creative ESIs who propose innovative, high-impact projects in the biomedical, behavioral, or social sciences within the NIH mission. This award is different from traditional NIH grants as it specifically supports unusually creative investigators with highly innovative research ideas at an early stage of their career when they may lack the preliminary data required for a conventional R01 grant application. The New Innovator Award supported 58 investigators in FY 2023.[281]

[276] grants.nih.gov/ngri.htm
[277] nexus.od.nih.gov/all/2021/07/12/data-on-implementing-nihs-next-generation-researchers-initiative/
[278] report.nih.gov/nihdatabook/category/15
[279] report.nih.gov/nihdatabook/report/304
[280] commonfund.nih.gov/earlyindependence/fundedresearch
[281] commonfund.nih.gov/newinnovator/fundedresearch

The NIH Pathway to Independence Award

The Pathway to Independence Award offers an opportunity for highly promising postdoctoral scientists to receive both mentored and independent research support from the same award. The award is intended to foster the development of a creative, independent research program that will be competitive for subsequent independent funding and that will help advance the NIH mission.

Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC)

The MOSAIC program supports talented investigators from diverse backgrounds as they transition from postdoctoral scholars to independent early-stage faculty. The National Institute of General Medical Sciences (NIGMS) leads MOSAIC in coordination with multiple NIH ICOs. The program innovates on the design of individual postdoctoral career transition awards via a cohort-based program that not only builds a community of talented early-career researchers, but also engages scientific professional societies and academic institutions to provide the necessary mentorship, networking, and professional development activities required to successfully achieve this career transition. As of FY 2023, 17 NIH Institutes and Centers have funded a diverse pool of 137 MOSAIC scholars.[282] Forty-two scholars have already found faculty positions, with more expected to transition as they progress through the program.

The Medical Scientist Training Program (MSTP)

The NIGMS-led MSTP supports eligible domestic institutions that implement effective and evidence-based approaches for dual degree (e.g., MD-PhD, DO-PhD, DDS-PhD) training leading to the award of both a clinical degree and a research doctorate degree. In FY 2022, the MSTP supported over 1,100 trainees. In FY 2023, NIGMS, in coordination with the National Institute of Mental Health, launched the Leading Equity and Diversity MSTP, a second branch of the program. This program seeks to broaden the institutional and regional diversity of dual-degree clinician scientist training by supporting programs at Historically Black Colleges and Universities, Tribal Colleges and Universities, and institutions in Institutional Development Award (IDeA) states.

Other Efforts to Support Early-Career Researchers

The following initiatives provide additional opportunities to enhance training, retention, and diversification of the broader research community.

The Early-Career Reviewer (ECR) program

The Center for Scientific Review created the ECR program to enrich NIH review panels and develop well-trained peer reviewers. The ECR program provides first-hand experience at grant review to early-career scientists who tend to be more diverse than the applicant pool and reviewers on the whole.[283] As of 2023, 8,032 researchers have served as ECRs and 1,061 ECRs have been or are now members of standing study sections.

Biomedical Informatics and Data Science Training programs

Through this program, the National Library of Medicine supports PhD-level research training in biomedical informatics and data science at 18 universities across the United States, enrolling

[282] nigms.nih.gov/training/careerdev/Pages/mosaic-scholars.aspx
[283] public.csr.nih.gov/AboutCSR/Evaluations#reviewer_demographics

approximately 200 trainees per year.[284] It offers graduate and postdoctoral training and research experiences in a wide range of areas focused on biomedical data science concepts and methods, helping trainees to develop skills needed to lead independent future research.

The NIH Loan Repayment Program (LRP)

The LRP aims to recruit and retain highly qualified health professionals to careers in biomedical or biobehavioral research. LRPs can repay up to $100,000 of qualified educational debt over two years for those who are eligible and agree to perform NIH mission-relevant research. A total of 1,323 LRP awards totaling $92.5 million were made in FY 2023.[285]

Childcare Supplements for Ruth L. Kirschstein National Research Service Awards (NRSAs)

Recognizing the high cost of childcare, in 2021 NIH began allowing full-time NRSA fellows and trainees to request support for childcare costs. NIH issued fellows 224 childcare cost awards in FY 2021, 313 awards in FY 2022, and 328 awards in FY 2023.[286]

ESI Extensions

NIH recognizes that some researchers may have lapses in their research or research training or have experienced periods of less than full-time effort. Therefore, NIH offers support for ESIs with high potential to re-enter an active research career after an interruption for family responsibilities or other qualifying circumstances. Reasons such extension requests may be granted include: childbirth, medical concerns, disability, family care responsibilities, natural disasters, and active duty military service.

Administrative Supplements

- **Research Supplements to Promote Diversity in Health-Related Research** have supported eligible individuals from diverse backgrounds, including those from groups that have been shown to be underrepresented in health-related research and researchers with disabilities. NIH renewed its support of these administrative supplements in June 2023 and expanded eligibility to three new grant types.

- The **Research Continuity and Retention Supplements** program assists early-career investigators experiencing crucial life events. Applicants who are mentored career development awardees or first-time recipients of research project grants are eligible for this continuity and retention supplement program. The supplemental funds may be used for additional personnel, computational services, supplies and equipment, or other resources needed to sustain the investigator's research. Critical life events that qualify for consideration include high-risk pregnancy; childbirth; adoption; serious personal health issues such as illnesses and/or debilitating conditions; and primary caregiving responsibilities for an ailing spouse, child, partner, parent, or other member of the

[284] nlm.nih.gov/ep/GrantTrainInstitute.html
[285] report.nih.gov/nihdatabook/category/29
[286] nexus.od.nih.gov/all/2022/08/10/preliminary-data-on-childcare-cost-support-for-national-research-service-award-nrsa-individual-fellows/

immediate family. During the first two fiscal years of the program (2020–2021) the most cited reason for requesting a supplement was childbirth (77 percent).[287]

- The **Research Supplements to Promote Re-entry and Re-integration into, and Retraining in Health-Related Research Careers** set of programs provide provides administrative supplements to existing NIH research grants to support full- or part-time research by researchers returning to the scientific workforce or those wishing to expand their skill set. The Re-entry Supplements Program provides mentored research training opportunities for a minimum of one year to scientists who have had at least six months of interruption in their careers for family responsibilities or other qualifying circumstances. The Reintegration program addresses the critical need to enable researchers, including predoctoral students, who are adversely affected by unsafe or discriminatory environments resulting from unlawful harassment, to rapidly transition into new safer, and more supportive research environments. The Retraining/Retooling program provides support and protected time for a mentored research experience that allows an early or mid-career candidate to obtain new skills and permits the candidate to move to a new research environment while augmenting the parent grant. The supplements are designed to enhance existing research skills and knowledge to prepare applicants to apply for independent research support.[288]

Diversity, Equity, Inclusion, and Accessibility (DEIA)-Focused Initiatives and Awards

The one-time NIH DEIA Prize Competition coordinated by the Chief Officer for Scientific Workforce Diversity rewards effective strategies for enhancing DEIA in research environments. It aims to recognize transformative cultures, systems, projects, and processes developed by academic institutions to promote inclusive excellence and create environments that foster and value a culture of DEIA. NIH awards up to 10 prizes of $100,000 each through the competition with up to half of the prizes set aside for consideration of limited-resource institutions. Awardees will be announced in 2024.

Advisory Committee to the Director (ACD) Working Group (WG) on Diversity, Subgroup on Individuals with Disabilities

The ACD WG on Diversity subgroup on Individuals with Disabilities released a report in 2022[289] proposing detailed and actionable suggestions to support the inclusion of individuals with disabilities in the scientific workforce.[290] Some key changes the WG suggested include expanding efforts to include the perspectives of disability communities including researchers with disabilities in NIH initiatives. In response, an ad hoc group was formed to re-examine the NIH mission statement in response to a recommendation that it be made more inclusive of people with disabilities. Furthermore, the DEIA working group of the NIH Steering Committee established a Disabilities Subgroup to address recommendations without a clear owner, such as changing culture, addressing ableism, and examining research gaps.

[287] orwh.od.nih.gov/career-development-education/research-continuity-retention-supplements
[288] grants.nih.gov/grants/guide/notice-files/NOT-OD-23-170.html
[289] acd.od.nih.gov/documents/presentations/12092022_WGD_Disabilities_Subgroup_Report.pdf
[290] nexus.od.nih.gov/all/2023/06/05/more-early-stage-investigators-supported-in-fy-2022/

Simplified Peer Review Framework for Research Project Grants

NIH is implementing a simplified peer review framework for research project grants across the agency for grant receipt deadlines of January 2025 and beyond.[291] Amongst other things, the new framework changes the evaluation of investigator and environment from scored criteria to a binary assessment of sufficiency. This will focus reviewers on expertise and resources in the context of the proposed work, thus mitigating the undue influence of the reputation of the institution or investigator. These changes will help to better focus reviewers on the scientific merit of proposed research and deemphasize the career stage and institutional record of the investigator. This change is intended to give less established investigators a better chance of securing NIH funding.

Faculty Institutional Recruitment for Sustainable Transformation (FIRST)

The Common Fund's FIRST program aims to enhance and maintain cultures of inclusive excellence in the biomedical research community. "Inclusive excellence" refers to cultures that establish and sustain scientific environments that cultivate and benefit from a full range of talent. NIH aims to facilitate institutions in their building a self-reinforcing community of scientists, through recruitment of a critical mass of early-career faculty who have a demonstrated commitment to inclusive excellence. The program also seeks to have a positive impact on faculty development, retention, progression, and eventual promotion, as well as to develop inclusive environments that are sustainable.[292] The program supports a total of 15 cohorts.[293]

Implementing UNITE Efforts to Address Structural Issues Impacting Career Progression for Investigators from Diverse Backgrounds

The UNITE program acts as a think tank to promote equity, generate bold ideas, and catalyze new actions. UNITE is committed to identifying and addressing any racial and ethnic inequities in the greater scientific community via strategic, short- and long-term actions and funding initiatives that will result in significant, lasting change. UNITE focuses on health disparities and minority health research, the internal NIH workforce, and the external research workforce—topics that intersect and enable greater transparency, accountability, and communication across NIH and the biomedical and behavioral research community. UNITE released a progress report on data-driven efforts and developing initiatives in 2022.[294] To support the overall diversity in the biomedical workforce, UNITE has released a funding opportunity called the **Research With Activities Related to Diversity** program. The program's overarching goal is to enhance the breadth and geographical location of research and research-related activities supported by NIH by providing support for the health-related research of scientists who are making a significant contribution to DEIA and who have no current NIH research project grant funding.[295]

Conclusion

NIH recognizes that researchers are the foundation of the biomedical research enterprise. To ensure a sustainable, diverse workforce of the future, NIH is supporting many efforts to support

[291] nexus.od.nih.gov/all/2023/10/19/announcing-a-simplified-review-framework-for-nih-research-project-grant-applications/
[292] commonfund.nih.gov/FIRST
[293] commonfund.nih.gov/first/fundedresearch
[294] nih.gov/sites/default/files/research-training/initiatives/ending-structural-racism/UNITE-progress-report-2022.pdf
[295] grants.nih.gov/grants/guide/pa-files/PAR-23-122.html

individuals throughout the research career continuum. Moving forward, NIH is committed to the continued support of early career researchers through these and other targeted initiatives.

HIGH-RISK, HIGH-REWARD RESEARCH

Program Overview

Scientific progress often advances in modest steps, building on 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 pursue surprising and fortuitous discoveries. Such research is often referred to as "high-risk, high-reward" research.[296] 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 scientifically risky.

High-risk, high-reward research is often categorized as "person-based" or "project-based." In person-based awards, the emphasis of the award is on supporting individuals who have demonstrated high levels of creativity, innovation, and scientific ability. These awards may allow researchers to flexibly pursue new lines of inquiry or launch independent research careers. Project-based awards emphasize the innovative nature and potential for impact of the proposed research project.

The Common Fund provides an avenue for NIH to experiment with funding processes that explore new ways to better achieve agency R&D missions. A major source of support for high-risk, high-reward research at NIH is the Common Fund's High-Risk, High-Reward (HRHR) program.[297] The HRHR program supports exceptionally creative scientists pursuing highly innovative research with the potential for broad impact in biomedical, behavioral, or social sciences within the NIH mission. The HRHR program consists of four complementary initiatives that provide opportunities across various career stages:

Person-based:

- NIH Director's Pioneer Award: supports individual scientists with outstanding records of creatively pursuing pioneering approaches to major research challenges
- NIH Director's New Innovator Award: supports exceptionally creative early career scientists proposing innovative, high-impact projects
- NIH Director's Early Independence Award: supports exceptional junior scientists bypassing postdoctoral training to launch independent research careers as quickly as possible

Project-based:

- NIH Director's Transformative Research Award: supports individual investigators or teams proposing groundbreaking, unconventional research with the potential to create new scientific paradigms

[296] "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.

[297] commonfund.nih.gov/highrisk

HRHR awards often break new ground, providing foundations on which future research can build and supporting 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 with light (optogenetics) and expand the contents of tissue samples to allow detailed viewing of fine subcellular structures (expansion microscopy).[298,299] HRHR awardees are also addressing pressing public health issues, such as identifying racial/ethnic disparities in exposure to harmful contaminants in public drinking water.[300] The flexible nature of HRHR awards and the creativity of awardees enable rapid pivots to address emerging challenges that profoundly affect human health, such as defining the origin and genetic evolution of the 2014 Ebola outbreak in West Africa and exploring novel therapeutic approaches to treat and reduce transmission of SARS-CoV-2, the virus that causes COVID-19.[301,302]

The Common Fund has supported objective evaluations of several HRHR award initiatives.[303] Independent evaluations of the Pioneer, New Innovator, and Early Independence Awards concluded that these awards support research that is more innovative and impactful compared to traditional NIH research awards, based on expert assessment and bibliometric analyses. Additionally, evaluations of the New Innovator and Early Independence Awards demonstrated that these non-traditional awards for scientifically risky projects do not negatively impact early-career professional advancement.

NIH Collaboration

The Common Fund's HRHR program is a NIH-wide endeavor, managed by a Working Group that includes members from 28 Institutes, Centers, and Offices (ICOs) across NIH. These Working Group members work collaboratively to coordinate and oversee the program. ICOs may also support HRHR awards that address exciting scientific projects relevant to their missions. In FY 2023, 18 New Innovator awards were funded by ICOs. Additionally, one Pioneer Award, one Transformative Research Award, and two Early Independence Awards were co-funded by the Common Fund and ICOs.

In addition to participating in the Common Fund's HRHR program, several Institutes and Centers (ICs) support awards that target exceptionally creative and innovative researchers and high-risk projects within the IC's mission.

NIH IC Person-Based Awards

The National Institute of Dental and Craniofacial Research (NIDCR) Award for Sustaining Outstanding Achievement in Research (SOAR) provides support to mid-career NIDCR-funded investigators who have outstanding records of research productivity, mentorship, and professional service to the research community.[304] This award provides longer-term grant

[298] eurekalert.org/news-releases/878709
[299] directorsblog.nih.gov/2015/03/26/diaper-compound-brings-change-to-cell-microscopy/
[300] pubmed.ncbi.nlm.nih.gov/36460659/
[301] nih.gov/news-events/news-releases/single-animal-human-transmission-event-responsible-2014-ebola-outbreak
[302] pubmed.ncbi.nlm.nih.gov/36074824/
[303] commonfund.nih.gov/assessment/reports
[304] nidcr.nih.gov/grants-funding/funding-priorities/future-research-initiatives/nidcr-award-soar-r35

support, allowing researchers to have freedom to perform high-risk, high-reward research that has the potential to break new ground or expand previous discoveries in new directions. One SOAR awardee is creating new tools and strategies to unravel the molecular pathways underlying craniofacial birth defects, including a novel platform for rapid detection of key signaling pathway changes in fluorescent zebrafish embryos exposed to environmental toxins.[305] They also designed a way to test the effects of nicotine exposure during embryonic zebrafish development, which not only disrupted formation of the craniofacial skeleton, but also modified social behavior and caused hyperactivity in adults. This will be a useful new model for the study of nicotine-related craniofacial and behavioral outcomes.[306] Another SOAR awardee is leading a research team to help develop novel approaches to reverse salivary gland damage caused by aging, autoimmune disease, or cancer treatments. Through sustained local delivery of a hydrogel loaded with a nerve-boosting drug (cevimeline) to damaged salivary glands in a mouse model, the research team has shown that it is possible to restore and maintain salivary gland structure and function for months after radiation treatment.[307] This novel approach could help inform new treatment strategies for patients living with salivary gland dysfunction.

The National Institute of Mental Health (NIMH) Biobehavioral Research Awards for Innovative New Scientists (BRAINS) award is intended to support the research and career advancement of outstanding, exceptionally productive scientists in the early, formative stages of their careers who plan to make a long-term career commitment to research in specific mission areas of the Institute.[308] This award seeks to assist these individuals in launching an innovative basic, translational, clinical, or services research program that holds the potential to profoundly transform the understanding, diagnosis, treatment, or prevention of mental illness. The BRAINS initiative can be distinguished from most other research grants in that these projects emphasize career goals relevant to the Institute's mission, active participation of an external advisory committee, and a commitment from the institution to actively support research program development. Research projects proposed in response to this initiative are expected to directly address the goals and objectives of the NIMH Strategic Plan for Research and to have a defined impact on the understanding of the pathophysiology, trajectories, effective treatment, and/or prevention of mental illnesses.[309]

The National Institute of General Medical Sciences (NIGMS) Maximizing Investigators' Research Award (MIRA) encourages innovative research by supporting a cohesive scientific program of study within an investigator's laboratory rather than a series of individual projects.[310] MIRA provides investigators with flexibility to change research directions to pursue novel scientific insights, along with enhanced stability of support to allow researchers to take on more ambitious and creative scientific questions and studies.

MIRA has two separate components: one for early-stage investigators (ESIs) and one for more established investigators (EIs). The ESI-focused program shares certain characteristics with

[305] pubmed.ncbi.nlm.nih.gov/36369674/
[306] pubmed.ncbi.nlm.nih.gov/36287892/
[307] pubmed.ncbi.nlm.nih.gov/36542703/
[308] nimh.nih.gov/funding/grant-writing-and-application-process/concept-clearances/2021/nimh-biobehavioral-research-awards-for-innovative-new-scientists-nimh-brains
[309] nimh.nih.gov/about/strategic-planning-reports
[310] nigms.nih.gov/Research/mechanisms/MIRA

high-risk, high-reward programs in that ESIs applying for MIRA awards are neither expected nor required to include preliminary data in their applications. Applications from ESIs are also reviewed independently from those submitted by more established investigators, focusing on evaluating an ESI's scientific potential. Together, these unique characteristics of MIRA have catalyzed the ESI community to pursue ambitious research programs at an earlier stage in their scientific careers, as evidenced by both the tripling of the number of ESIs supported by NIGMS over the last decade and the lower average age at which ESIs obtain their first MIRA award relative to ESIs getting R01 awards. In FY 2023, several ESI MIRA awardees have taken advantage of the program's flexibilities to take their research in unexpected and innovative directions. For example, a researcher originally studying the molecular mechanisms of how bacterial growth responds to environmental stress was able to shift research directions into the metabolism and behavior of an infectious pathogen commonly contracted by hospitalized patients, which could inform future development of antibiotic treatments.[311]

NIH IC Project-Based Awards

The National Institute on Drugs and Addiction (NIDA)[312] supports two awards focused on high-risk, high-reward research. The NIDA Avant-Garde Award Program for HIV and Substance Use Disorder Research supports individual scientists of exceptional creativity at all career levels who propose high-impact research that will open new areas of HIV research and/or lead to new avenues for prevention and treatment of HIV among people who use drugs.[313] A recent Avant-Garde project identified genes that are down-regulated during HIV-related brain inflammation, suggesting a potential early step in HIV-associated neurocognitive disorder, which affects up to 50 percent of people with HIV.[314]

NIDA's Avenir Awards provide grants to ESIs who propose highly innovative studies. These awards represent NIDA's commitment to supporting researchers who represent the future of addiction science. NIDA has two Avenir award programs, one for HIV/AIDS and another on the genetics and epigenetics of substance use.[315,316] Examples of innovative research conducted by Avenir awardees include: leveraging machine learning to elucidate multiple social and spatial drivers of HIV transmission among people who inject drugs, determining that injection venue was most associated with HIV incidence and therefore a prime target for intervention; and identification of a previously undiscovered X-linked gene X-chromosome inactivation (XCI) escaper that will aid future research aimed at understanding the contribution of XCI escape to known sex disparities in rapid substance use escalation and negative withdrawal symptoms that disproportionately affect females.[317,318]

[311] pubmed.ncbi.nlm.nih.gov/36321838/
[312] The FY 2024 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.
[313] nida.nih.gov/about-nida/organization/offices/hiv-research-program-hrp/avant-garde-award-hivaids-research
[314] pubmed.ncbi.nlm.nih.gov/36525955/
[315] nida.nih.gov/about-nida/organization/offices/hiv-research-program-hrp/avenir-awards-hivaids-research
[316] nida.nih.gov/about-nida/organization/divisions/division-neuroscience-behavior-dnb/genetics-molecular-neurobiology-research-branch-gmnrb/avenir-award-winners
[317] pubmed.ncbi.nlm.nih.gov/36260674/
[318] pubmed.ncbi.nlm.nih.gov/37207894/

Next Steps

High-risk, high-reward projects are a fundamental component of the NIH portfolio of investments designed to launch new scientific areas, refine our understanding of complex biological systems, and pioneer new therapies. NIH is committed to supporting high-risk research with the potential for exceptionally large impact, balanced with support for more traditional, yet extremely important, research that also advances our understanding of human health and disease.

The most recent cohort of Common Fund HRHR awardees is just beginning to undertake exciting and innovative research projects. These include: investigating novel approaches to unlock the potential of chemotherapy-induced immune system modulation to treat the most aggressive form of breast cancer; exploring how odors may be used to diagnose a variety of diseases; leveraging advances in artificial intelligence technology to automate documentation from doctor-patient interactions; and harnessing naturally occurring electromagnetic sensing mechanisms to precisely tune metabolism to treat diseases such as diabetes.[319,320,321,322] Advances made possible by these awards, as well as other NIH high-risk, high-reward research investments, are expected to transform our understanding of biological processes and lead to breakthroughs in the treatment of a broad range of diseases and health conditions.

Enhancing Diversity, Equity, Inclusion, and Accessibility

The Common Fund's HRHR program is undertaking R&D and applying technology advances to ameliorate inequities and create opportunity in ways that strengthen the program's values. To ensure that diverse perspectives contribute to scientific discoveries that benefit all groups, the HRHR program encourages applications from researchers from diverse backgrounds (including individuals underrepresented in the biomedical research workforce), from the full range of eligible institutions (including emerging research institutions and historically underserved communities), and from all research areas broadly relevant to NIH's mission. Based on recommendations from the Advisory Committee to the Director Working Group on High-Risk, High-Reward Programs and input from the scientific community, the HRHR program is applying a four-pronged approach to enhance applicant diversity: (1) increasing outreach to meet underrepresented researchers where they are and ensuring these efforts are strategic and effective, (2) bolstering language in funding opportunities and on public websites to encourage applicants from the full range of backgrounds, institutions, and research areas, (3) taking steps to mitigate potential bias against some scientific topics, and (4) piloting anonymized review within the Transformative Research Award initiative to reduce inappropriate influence of investigator or institutional reputation.[323,324] NIH is evaluating these efforts and will continue to modify them as needed to support diversity across the HRHR program.

[319] reporter.nih.gov/project-details/10695288
[320] reporter.nih.gov/project-details/10695420
[321] reporter.nih.gov/project-details/10701364
[322] reporter.nih.gov/project-details/10687635
[323] acd.od.nih.gov/working-groups/hrhr.html
[324] grants.nih.gov/grants/guide/notice-files/NOT-RM-20-002.html

MATERNAL MORTALITY

Program Overview

The United States has the highest rate of maternal mortality among high-resource countries, and the number and rate of pregnancy-related deaths has risen over the past several years.[325] In 2021, as many as 1,200 women died from a pregnancy-related health issue or an existing condition exacerbated by pregnancy, either during pregnancy or in the first 42 days after giving birth.[326] The maternal mortality rate increases from 2020 to 2021 for all race and Hispanic-origin groups were significant.[2] Some populations are disproportionately affected by maternal morbidity and mortality (MMM). Maternal mortality rates for African American/Black women are 2.6 times higher than mortality rates for White women, and American Indian/Alaska Native women are about two times more likely to die from pregnancy-related complications compared to White women, according to the most recent data for each group.[327] Risk of death during pregnancy and up to one year postpartum is also significantly elevated among women residing in maternity care deserts, which are counties that lack hospitals with obstetric care or midwives.[328] Leading causes of pregnancy-related deaths up to one year after pregnancy include mental health conditions (including deaths due to suicide and overdose/poisoning related to substance use), excessive bleeding (hemorrhage), cardiac and coronary conditions, infection, blood clots, and hypertensive disorders of pregnancy.[329] Additional research showed that in 2020, pregnant or postpartum women had a 35 percent higher risk of homicide compared to their nonpregnant peers.[330] Black women were the most likely to die by pregnancy-associated homicide. Overall, more than 80 percent of pregnancy-related deaths may be preventable,[331] confirming the need for the ongoing NIH-wide research response to develop solutions for this crisis.

NIH coordinates maternal health research across all its Institutes, Centers, and Offices (ICOs) as well as with other HHS and government agencies. For example, NIH is part of the HHS Action Plan to Improve Maternal Health in America[332] and the White House Blueprint for Addressing the Maternal Health Crisis.[333] NIH's Office of Research on Women's Health (ORWH) maintains the NIH Maternal Morbidity and Mortality Web Portal, a central information hub for funding opportunities and research efforts at NIH and other HHS agencies.[334] The NIH Office of Disease Prevention (ODP) addressed maternal health through its **Pathways to Prevention (P2P) Program,** holding a workshop that brought together participants from across NIH and other federal agencies, researchers, and community members to understand the current state of the science, identify gaps, and suggest a research agenda and action plan to move the field

[325] cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm
[326] cdc.gov/nchs/data/hestat/maternal-mortality/2021/maternal-mortality-rates-2021.htm
[3] cdc.gov/reproductivehealth/maternal-mortality/pregnancy-mortality-surveillance-system.htm
[328] marchofdimes.org/maternity-care-deserts-report
[329] cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html
[330] nichd.nih.gov/newsroom/news/091622-pregnancy-associated-homicide#:~:text=Results,deaths%20per%20100%2C000%20live%20births.
[331] cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html
[332] aspe.hhs.gov/sites/default/files/private/aspe-files/264076/healthy-women-healthy-pregnancies-healthy-future-action-plan_0.pdf
[333] whitehouse.gov/wp-content/uploads/2022/06/Maternal-Health-Blueprint.pdf
[334] orwh.od.nih.gov/mmm-portal

forward.[335] The NIH-wide **Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) Initiative**[336] is led by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute of Nursing Research (NINR), and ORWH. Launched in 2019, IMPROVE's goals are to reduce preventable causes of maternal deaths and improve health for women before, during, and after delivery. In FY 2023, $43.4 million in IMPROVE funds ($30 million in NICHD appropriations and $13.4 million in other ICO funding) contributed to a robust NIH maternal health research portfolio.

The IMPROVE Initiative weaves together basic, clinical, social, training, and technological program components to address the leading causes of pregnancy-related MMM with an emphasis on incorporating community perspectives and inclusion of disproportionately affected populations (e.g., racial and ethnic minorities, very young women and women of advanced maternal age, and people with disabilities), as well as those who experience health disparities or limits in access to care (e.g., residents of maternity care deserts). Established in FY 2023, the **IMPROVE Maternal Health Research Centers of Excellence (COEs)** will develop, implement, and evaluate community-tailored interventions to address health disparities in maternal health and risk factors and mechanisms of the leading causes of MMM. The ten COEs are geographically diverse and include projects that will work with Tribal populations, rural populations, and Historically Black Colleges and Universities, among others. COEs will also support training and professional development of maternal health researchers, including those from backgrounds underrepresented in the biomedical research workforce, and work with a data innovation and coordination hub and an implementation science hub. The COEs received $24.4 million in first-year funding and are expected to operate for seven years and total an estimated $168 million, pending the availability of funds.

Community involvement and empowerment in addressing the factors affecting women in the communities where they live is one of the cornerstones of the IMPROVE initiative. The IMPROVE **Connecting the Community for Maternal Health Challenge**[337] (CCMH) encourages and rewards non-profit community-based or advocacy organizations to develop sustainable research capabilities and infrastructure to pursue research projects in maternal health, inclusive of MMM. In addition to $3 million in cash prize awards planned to be awarded in 2024, CCMH provides expert guidance and consultation on maternal health research project design, implementation, and evaluation. Organizations that advanced to the final phase of the competition are testing programs that include doula services, nutrition to reduce gestational diabetes, and maternal mental health care (e.g., depression, post-traumatic stress), among others. Another community-engaged effort, the IMPROVE **Community Implementation Program (CIP),** supports three coalitions that will build strategies to adopt and integrate evidence-based interventions into community settings to improve maternal health outcomes before, during, and after pregnancy, particularly among populations experiencing health disparities and in maternity care deserts. The program will include community partners engaged in every level of the project, including shared leadership. The IMPROVE-CIP program complements the **Maternal**

[335] prevention.nih.gov/research-priorities/research-needs-and-gaps/pathways-prevention/identifying-risks-and-interventions-optimize-postpartum-health
[336] nichd.nih.gov/research/supported/IMPROVE
[337] nichd.nih.gov/research/supported/challenges/community-maternal-health

Health-CIP[338] supported by the National Heart, Lung, and Blood Institute (NHLBI), which has established four coalitions to engage communities and pilot test the implementation of proven interventions in at-risk populations.

Improving maternal health in the communities that need it most requires technologies and tools that increase access to care and enable earlier diagnosis and intervention. The IMPROVE-funded **Rapid Acceleration of Diagnostics Technology (RADx Tech) for Maternal Health Challenge**[339] aims to accelerate development and commercialization of home-based or point-of-care diagnostic devices, wearables, or other remote-sensing technologies to extend postpartum care to improve maternal health outcomes in maternity care deserts. Prototype devices have the potential to identify women at risk and enable timely intervention. The initiative plans to award up to $8 million in FY 2024. Expanding on the need for technology-based solutions, in FY 2023, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) led the **NIH Technology Accelerator Challenge for Maternal Health** to award prizes for innovative diagnostic technologies integrated with a digital platform to identify maternal health conditions during and after pregnancy and to guide clinical decision-making, improve patient outcomes, and ultimately prevent MMM. Winning technologies included a mobile health monitoring tool for community health workers to detect postpartum surgical-site infections and anemia, as well as devices and wearables to detect fetal distress during labor, preeclampsia, maternal sepsis, and hemorrhage.[340]

Beyond the work of IMPROVE and the other programs already mentioned, NIH ICOs support a broad research portfolio to promote maternal health and address causes of and risk factors for MMM. For instance, 23 percent of pregnancy-related deaths in 2022 were due to mental health conditions.[341] Recognizing the ongoing struggle with these issues, the National Institute of Mental Health (NIMH) funded awards supporting research to improve intervention delivery to at-risk individuals to **prevent perinatal depression,**[342] and the National Institute on Drugs and Addiction (NIDA)[343] launched a funding opportunity to support research to identify barriers to opioid use disorder (OUD) treatment among pregnant and postpartum people and models for recovery-oriented, family-centered care.[344] NIDA also supports research to optimize the efficacy and safety of OUD medications for pregnant people through the **Medication Treatment for Opioid-dependent Expecting Mothers (MOMs)** study.[345]

Preexisting diabetes can cause pregnancy complications, maternal morbidity, and health consequences in the child. The development of gestational diabetes can also lead to short- and long-term health risks for mother and child. The National Institute of Diabetes and Digestive and Kidney Diseases launched the **Glycemic Observation and Metabolic Outcomes in**

[338] maternalhealthcip.org/
[339] nichd.nih.gov/research/supported/challenges/radx-tech-maternal-health
[340] nibib.nih.gov/news-events/newsroom/nih-announces-prize-winners-maternal-health-diagnostics-challenge
[341] cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html
[342] grants.nih.gov/grants/guide/rfa-files/RFA-MH-21-240.html
[343] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction.
[344] grants.nih.gov/grants/guide/notice-files/NOT-DA-24-008.html
[345] nida.nih.gov/about-nida/organization/cctn/ctn/research-studies/medication-treatment-opioid-dependent-expecting-mothers-moms-pragmatic-randomized-trial-comparing

Mothers and Offspring (GO MOMS) study[346] to better understand what happens to a mother's metabolism during pregnancy. Researchers at nine clinical sites are enrolling participants without preexisting diabetes to monitor glucose changes during pregnancy with the hope to develop a better way to detect gestational diabetes and enable earlier intervention and better health outcomes.

Cardiac and coronary conditions are other leading underlying causes of pregnancy-related complications and deaths, particularly among non-Hispanic Black people.[347] Building on NICHD's Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (nuMoM2B), NHLBI supported the **nuMoM2b Heart Health Study**,[348] which found that certain pregnancy complications are associated with increased long-term risks for heart disease, such as developing high blood pressure, years after pregnancy. Additional NHLBI research showed that treatment of mild chronic hypertension during pregnancy was associated with better pregnancy outcomes than reserving treatment only for severe hypertension.[349] These findings impacted treatment guidelines from the American College of Obstetricians and Gynecologists and the Society for Maternal Fetal Medicine. Further research supported by NHLBI indicated that early pregnancy blood pressure patterns can predict preeclampsia and gestational hypertension.[350]

Placental complications can also lead to maternal morbidity. The NICHD-supported Human Placenta Project[351] stimulated a robust research effort directed at safe, non-invasive, real-time assessment of placenta development and function across pregnancy. These efforts have led to new imaging approaches, both magnetic resonance imaging (MRI) and ultrasound, that show promise for early prediction of placenta-mediated pregnancy complications such as preeclampsia.[352] The National Institute of Allergy and Infectious Diseases (NIAID) supports research to investigate the factors and mechanisms that control interactions between the maternal immune system and the developing fetus as well as immune cells that support pregnancy and enable optimal placental development and function.[353] The importance of the interaction between the maternal immune system and the developing fetus was highlighted during the COVID-19 pandemic. NICHD-supported research showed that COVID-19 vaccination was safe and effective for pregnant people,[354] and NIAID-supported research showed that pregnant people who received a COVID-19 vaccine produced antibodies in their own blood and the umbilical cord blood, indicating protection for both mother and fetus.[355] The NICHD-supported **Maternal-Fetal Medicine Units (MFMU) Network**, consisting of 14 research centers focused on improving obstetric care, pregnancy health, and outcomes for lactating people and their babies, also pivoted to address unanswered questions for these populations during the COVID-19 pandemic. The MFMU conducted a clinical trial to assess the impact of COVID-19 infection during pregnancy and found that SARS-CoV-2 infection was associated with an increased risk

[346] gomomsstudy.org/
[347] cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html
[348] nhlbi.nih.gov/news/2023/moms-helping-moms-through-research
[349] nejm.org/doi/full/10.1056/NEJMoa2201295
[350] ahajournals.org/doi/full/10.1161/JAHA.123.029617
[351] nichd.nih.gov/research/supported/human-placenta-project/default
[352] ncbi.nlm.nih.gov/pmc/articles/PMC9295947/
[353] grants.nih.gov/grants/guide/rfa-files/RFA-AI-23-027.html
[354] nichd.nih.gov/newsroom/news/032921-COVID-vaccine-pregnancy
[355] covid19.nih.gov/news-and-stories/covid-19-vaccination-pregnancy-likely-benefits-moms-babies

for MMM.[356] Other ongoing studies through the MFMU are addressing the long-term impacts of COVID-19 on women, children, and families.[357]

Other infectious diseases and bacterial infections can increase the risk for MMM. Nine percent of maternal deaths in 2022 were associated with infections that can be prevented or treated with timely intervention.[358] For example, the NICHD-supported **Global Network (Global Network) for Women's and Children's Health**, co-funded by the Bill and Melinda Gates Foundation, found that a single oral dose of the antibiotic azithromycin during labor can reduce the risk of postpartum sepsis and death by one-third among women who deliver vaginally.[359] This result will likely change clinical practice and help prevent MMM worldwide. Pregnant people with HIV have a higher risk of dying during pregnancy and the postpartum period than nonpregnant people. NIAID (along with NICHD and NIMH) supports the **International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network**,[360] a global collaboration to advance the prevention and treatment of HIV and its complications for pediatric and pregnant/postpartum populations. The IMPAACT Network is prioritizing research to evaluate safety and dosing of antiretroviral therapies in pregnant people, which have not been thoroughly studied in that population despite 30 years of use.

Although 9 in 10 pregnant people take medication during pregnancy and about 70 percent take at least 1 prescription medication, little is known about the effects of taking most medicines during pregnancy because pregnant people are often not included in studies that determine the safety of the medication.[361] In 2016, Congress established the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) to advise the HHS Secretary regarding gaps in knowledge and research on safe and effective therapies for pregnant and lactating people.[362] To address some of the recommendations put forward by this group, NICHD established the **Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub**, which serves as a national resource to collect and expand the knowledge and expertise in this area. MPRINT also supports Centers of Excellence in Therapeutics (CETs). Current CETs are evaluating the effectiveness of maternal pharmacotherapy for opioid use disorder on "real world" outcomes for pregnant women and infants[363] and investigating how maternal antibiotics alter breast milk composition and impact infant outcomes.[364]

NIH also plans to fund new studies in FY 2024 on **Translational Research in Maternal and Pediatric Pharmacology and Therapeutics,**[365] focusing on improving precision medicine in pregnant and lactating people, neonates, and children through advancements in tools, methodology and technology development; understanding drug action in these populations; and developing novel therapeutics or enhancing the use of existing therapeutics. Precision medicine

[356] pubmed.ncbi.nlm.nih.gov/35129581/
[357] mfmunetwork.bsc.gwu.edu/web/mfmunetwork/research-projects
[358] cdc.gov/media/releases/2022/p0919-pregnancy-related-deaths.html
[359] nichd.nih.gov/newsroom/news/020923-azithromycin-postpartum-sepsis
[360] impaactnetwork.org/
[361] cdc.gov/pregnancy/meds/treatingfortwo/facts.html
[362] nichd.nih.gov/about/advisory/PRGLAC
[363] mprint.org/research/centers/vanderbilt-cet.html
[364] mprint.org/research/centers/ucsd-cet.html
[365] grants.nih.gov/grants/guide/pa-files/PAR-23-130.html

aims to provide disease treatments tailored to an individual's unique genes and environment. The **Trans-Omics for Precision Medicine (TOPMed)** program, sponsored by NHLBI, for example, integrates whole-genome sequencing (WGS) and other omics data (e.g., metabolic profiles, epigenomics, protein and RNA expression patterns) with molecular, behavioral, imaging, environmental, and clinical data.[366] Multiple studies/cohorts included in TOPMed include pregnant people, facilitating opportunities for future insights into conditions that co-occur with and contribute to pregnancy complications.

NIH-supported research has highlighted many facets of health disparities in MMM. For example, NHLBI-supported research showed that Black women with sickle cell disease (SCD) have worse maternal health outcomes than those without SCD.[367] NINR-supported researchers found that historical redlining, a tool of structural racism that influenced the trajectory of neighborhood social and material conditions, is associated with increased risk of experiencing severe maternal morbidity among Black and Hispanic birthing people in California.[368] NIH ICOs are supporting a range of research to address these disparities, including the IMPROVE initiative noted above. NINR's **Advancing Integrated Models (AIM) of Care** projects intend to stimulate research to develop or evaluate supportive care models that address healthcare access or healthcare quality, together with structural or social inequities, in efforts to prevent adverse pregnancy outcomes among racial and ethnic minority women.[369] The National Institute on Minority Health and Health Disparities (NIMHD) is supporting studies to address racial disparities in MMM, testing the efficacy and/or effectiveness of interventions or research strategies to deliver proven-effective prevention and treatment interventions to reduce these disparities.[370] The National Institute of Environmental Health Sciences, NICHD, and NIMHD support the Centers of Excellence on Environmental Health Disparities Research.[371] Two of these Centers conduct research with pregnant women. One assesses factors that contribute to environmental health disparities and the other explores the relationship among prenatal exposures, maternal social stressors, and maternal depression and cardiovascular health in the years after childbirth. The Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH) program supported by NHLBI aims to test the effectiveness of an implementation-ready intervention, delivered in the context of early childhood home visiting, to promote and address disparities in maternal and early childhood cardiovascular health.[372]

NIH will continue to invest in research and technology to prevent MMM and improve maternal health outcomes. The IMPROVE COEs and IMPROVE-CIP coalitions will conduct research through 2029, and NIH will encourage collaboration among investigators to explore potential new or augmented research projects, pending availability of funds. Innovators in the RADx Tech for Maternal Health and CCMH Challenges may be able to connect and collaborate with IMPROVE COE and IMPROVE-CIP investigators to further test and implement their technologies or community-based interventions. NIH will continually seek opportunities for IMPROVE components to collaborate with other maternal health research efforts throughout

[366] topmed.nhlbi.nih.gov/
[367] onlinelibrary.wiley.com/doi/10.1002/ajh.26818
[368] pubmed.ncbi.nlm.nih.gov/36420897/
[369] grants.nih.gov/grants/guide/rfa-files/RFA-NR-23-002.html
[370] grants.nih.gov/grants/guide/rfa-files/RFA-MD-20-008.html
[371] niehs.nih.gov/research/supported/centers/ehd/index.cfm
[372] hvenrich.org/ENRICH_about.asp

NIH and across HHS. The IMPROVE Initiative also plans to support new awards in FY 2024 for an initiative developed by NIH's Office of Behavioral and Social Sciences Research to address the interrelation of intimate partner violence and MMM.[373,374] Across NIH, ICOs will remain agile and work with Federal partners and other collaborators to respond to the crisis and reduce MMM.

[373] grants.nih.gov/grants/guide/rfa-files/RFA-OD-24-001.html
[374] grants.nih.gov/grants/guide/rfa-files/RFA-OD-24-002.html

PRECISION 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.[375] What should we eat to stay healthy? The answer to this question is not as simple as one might expect and there is no such thing as a perfect, one-size-fits-all diet. Precision nutrition aims to predict and account for differences in the way people respond to food based on a combination of genetic, environmental, and social factors to optimize their diets. Given the promise of precision nutrition to promote health and address diet-related chronic diseases, NIH has been bolstering the coordination of nutrition research and has placed a high priority on precision nutrition initiatives to accelerate its development.

The NIH initiatives described below aim to advance precision nutrition through diverse interdisciplinary teams of nutrition scientists and data scientists collecting and analyzing multi-dimensional datasets with the goal of creating predictive nutrition algorithms to support healthy living for individuals from every walk of life. Some of the research projects supported by these initiatives will utilize artficial intelligence (AI) and machine learning (ML) to untangle the various roles of whole foods, individual nutrients, sociocultural impacts on eating and lifestyle, and societal infrastructure on the health of individuals and populations.

One important component of NIH's precision nutrition efforts is the *Nutrition for Precision Health (NPH), powered by the All of Us Research Program*.[376] The goal of NPH is to describe and better understand variations in how different people respond to diet, with the aim of developing algorithms that predict individual responses to food and dietary patterns. NPH is building on recent advances in biomedical science, including AI and microbiome research, as well as the infrastructure and large, diverse groups of participants from the *All of Us* Research Program. These advances provide unprecedented opportunities to generate new data to provide insight into precision nutrition, and the scale and diversity of the participant population sets NPH apart from other nutrition studies. NPH launched in FY 2022, with awards to support clinical centers, data modeling and bioinformatics, multiple biological assays, and coordination efforts. The study began enrolling participants in 2023 from 14 sites across the United States, with the goal of engaging 10,000 participants from diverse backgrounds. NPH aims to develop and validate algorithms that predict individual responses to food and dietary patterns. The study's findings may allow health care providers to offer more customized nutrition guidance to improve individuals' overall health. Recruitment for clinical studies is ongoing. Over the next several years, NPH will conduct nutrition studies involving large numbers of diverse participants, perform analyses on biological specimens collected from individuals in response to various foods and dietary patterns, develop computational modeling and algorithms, and share data with the research community. NIH anticipates that these efforts will lead to more personalized nutrition guidance and improved health. NPH is supported by the NIH Common Fund and managed as a partnership with the *All of Us* Research Program, Office of Nutrition Research (ONR), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), *Eunice Kennedy Shriver*

[375] cdc.gov/chronicdisease/about/costs/index.htm
[376] commonfund.nih.gov/nutritionforprecisionhealth

National Institute of Child Health and Human Development (NICHD), National Heart, Lung, and Blood Institute (NHLBI), and National Cancer Institute (NCI). Multiple NIH institutes, centers, and offices (ICOs) participate in the NIH-wide Working Group that provides oversight of the program.

Another important precision nutrition initiative is the Advanced Training in Artificial Intelligence for Precision Nutrition (AIPrN) Science Research—Institutional Research Training Programs. These programs aim to diversify and expand the nutrition science workforce by equipping it to apply AL/ML to analyze large and complex datasets, such as those within the *All of Us* Researcher Workbench.[377] The ultimate goal is to tackle challenges in biomedical science to reduce diet-related diseases and health disparities. These training programs provide graduate students and postdoctoral fellows interdisciplinary research training in AI and precision nutrition that includes ML, systems biology, systems science, big data, and computational analytics. These programs support and emphasize NIH diversity, equity, inclusion, and accessibility (DEIA) goals and interest in diversity by emphasizing the importance of inclusive research environments, diverse backgrounds of trainees and mentors, and the research topics being pursued by trainees. Four AIPrN awards were made in FY 2023 to four different universities, supported by NIDDK, NICHD, Office of Dietary Supplements (ODS), Office of Data Science Strategy (ODSS), and ONR.

One of the main challenges in nutrition research is the ability to verify dietary adherence in clinical studies to establish dietary intake with high accuracy. This is in part due to a lack of valid biomarkers that would allow for independent verification of the dietary adherence during a clinical study. The Dietary Biomarkers Development Consortium (DBDC) will explore, identify, and validate metabolomics-based dietary intake biomarkers by comparing them with existing dietary assessment methodologies. The goal is to develop a database of validated biomarkers that are readily available to the research community. The consortium sites include representative study populations from underserved and underrepresented groups to develop the biomarkers that provide objective measures to inform individualized healthy dietary patterns. The dietary biomarkers identified through the DBDC will enable advancement of precision nutrition research by allowing accurate measurement of dietary intake in clinical studies with higher accuracy. The DBDC is supported by NIDDK and the U.S. Department of Agriculture's National Institute of Food and Agriculture. Seven awards were made in FY 2023 to establish the consortium and the clinicial studies are currently recruiting research participants.

Obesity affects approximately 20 percent of children and 42 percent of adults in the U.S., putting them at risk of chronic diseases such as type 2 diabetes, heart disease, and some cancers. Obesity costs the U.S. health care system nearly $173 billion a year.[378] Precision nutrition studies can help us better understand the causes and risks for obesity in children. An NIDDK-supported initiative "Pediatric Obesity Discovery Science Research to Improve Understanding of Risk and Causal Mechanisms for Obesity in Early Life" will support innovative, longitudinal, and discovery-based research studies to better characterize early-life risk factors for obesity development during infancy and early childhood, as well as to elucidate underlying causal mechanisms, including those that mediate behavioral and/or metabolic risk and how risk can be

[377] researchallofus.org/data-tools/workbench/
[378] ncbi.nlm.nih.gov/pmc/articles/PMC7990296/

modified by psychosocial, contextual, and/or environmental contributors. One study is testing the association of the "emotion-attachment-nutritive intake-system" in infancy with maternal feeding behavior, child eating behavior, child dietary intake, and child percent body fat at age 3 years. A total of three awards were made in FY 2023 to support clinical studies which are currently recruiting research participants.

These four initiatives will advance precision nutrition science by leveraging AI/ML and other technological advances, large diverse participant datasets, and an expanded scientific workforce to better inform dietary guidance for a healthier America.

RESEARCHING COVID TO ENHANCE RECOVERY (RECOVER)

Program Overview

The NIH Researching COVID to Enhance Recovery (RECOVER) Initiative, launched in 2021 with a $1.15 billion supplemental appropriation in the Consolidated Appropriations Act of 2021,[379] is a nationwide research program designed to understand, treat, and prevent Long COVID. Long COVID describes long-term symptoms following infection by SARS-CoV-2, the virus that causes COVID-19. More than 200 symptoms are associated with Long COVID, and the condition can cause problems throughout the body, affecting nearly all body systems including the nervous, cardiovascular, gastrointestinal, pulmonary, autonomic, and immune systems. RECOVER is a comprehensive and multi-faceted research initiative that includes longitudinal observational studies, electronic health record (EHR) studies, pathobiology and tissue pathology studies, a mobile health platform, and clinical trials.[380] Importantly, RECOVER is designed to be an inclusive, diverse, and patient-centered study of Long COVID across the lifespan. Clinical hubs and networks are selected for their capacity to reach disproportionately affected communities across the country. Patients have, since day one, been integral to the RECOVER initiative. Patient and community representatives serve alongside researchers in RECOVER and their input has been invaluable to the design of the various studies.

RECOVER is answering a number of important questions about Long COVID, including:[381]

- What are the various forms of Long COVID?
- How long do symptoms of Long COVID last? Can there be effects later in life?
- What effect(s) does Long COVID have on other diseases or health problems?
- What are the risk factors for developing Long COVID?
- What effects do different COVID-19 virus variants, SARS-CoV-2 re-infections, or COVID vaccination have on Long COVID?
- What happens inside the body that leads to Long COVID?
- What happens inside the body that protects some people from Long COVID?
- What treatments are effective for treating or preventing Long COVID?

NIH RECOVER has partnered with government entities, industry, and the investigator community to rapidly launch studies of Long COVID. While RECOVER is an NIH initiative, other agencies and Offices within the Department of Health and Human Services (HHS) also play key roles through participation on governance committees, consultations, and collaborations, including the Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and the Center for Medicaid and Medicare Services (CMS). Additionally, RECOVER funds hundreds of investigators across the country, including working with teams at New York University Langone Health, Duke Clinical Research Institute, Massachusetts General Hospital, Mayo Clinic, and RTI International to provide core functions for RECOVER investigators and studies.

[379] www.congress.gov/116/plaws/publ260/PLAW-116publ260.pdf
[380] recovercovid.org/research-components
[381] recovercovid.org/research#researchQuestions

NIH Collaboration

Within NIH, RECOVER is co-led by the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Allergy and Infectious Diseases (NIAID). RECOVER is truly a trans-NIH effort. Many NIH Institutes and Centers contribute substantively to scientific programmatic oversight of key RECOVER components such as the observational studies, clinical trials, and mobile health platform. For instance, Institutes and Centers whose expertise and missions are highly relevant to RECOVER provide programmatic subject matter experts who consult on RECOVER projects and lead expert working groups, including, for example: NHLBI, NIAID, NINDS, the NIH Office of the Director, the *All of Us* Research Program, the National Center for Advancing Translational Sciences (NCATS), the National Institute on Drugs and Addiction (NIDA),[382] the National Cancer Institute (NCI), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and the National Center for Complementary and Integrative Health (NCCIH).

Recent Findings/Key Progress

RECOVER's comprehensive research framework has provided the critical foundation for understanding and treating Long COVID and is already providing valuable insights into the condition. RECOVER studies have, for example, developed computable phenotypes (definitions based on computer analysis of electronic health record data) of Long COVID in adults and children,[383,384,385,386,387] determined that pre-COVID vaccination reduces risk of Long COVID,[388,389] determined prevalence of Long COVID in children (3.7 percent of children with SARS-CoV-2 develop Long COVID),[390,391,392] identified risk factors for Long COVID in adults[393,394,395] (severity of acute COVID, comorbidities,[396,397] female sex,[398] racial/ethnic minority[399,400]) and children[401,402] (< 5 years old, Intensive Care Unit (ICU) admission for acute infection, complex chronic conditions[403]); found that COVID-19 vaccination is safe for children

[382] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction
[383] www.nature.com/articles/s41591-022-02116-3
[384] jamanetwork.com/journals/jamanetworkopen/fullarticle/2788641
[385] www.medrxiv.org/content/10.1101/2022.04.18.22273968v2
[386] www.medrxiv.org/content/10.1101/2022.12.18.22283646v1
[387] www.sciencedirect.com/science/article/pii/S2589750022000486?via%3Dihub
[388] www.medrxiv.org/content/10.1101/2022.10.06.22280795v1
[389] www.cdc.gov/mmwr/volumes/71/wr/mm7114e1.htm
[390] jamanetwork.com/journals/jamapediatrics/fullarticle/2795569
[391] jamanetwork.com/journals/jamanetworkopen/fullarticle/2788641
[392] www.medrxiv.org/content/10.1101/2022.09.26.22280364v1
[393] www.medrxiv.org/content/10.1101/2022.08.15.22278603v1
[394] pubmed.ncbi.nlm.nih.gov/36785842/
[395] ieeexplore.ieee.org/document/9994851
[396] www.medrxiv.org/content/10.1101/2022.08.15.22278603v1
[397] elifesciences.org/articles/86002
[398] www.medrxiv.org/content/10.1101/2022.04.18.22273968v2
[399] link.springer.com/article/10.1007/s11606-022-07997-1
[400] www.medrxiv.org/content/10.1101/2022.12.02.22282944v1
[401] academic.oup.com/jamiaopen/article/6/1/ooad016/7071577
[402] www.medrxiv.org/content/10.1101/2022.12.22.22283791v1
[403] www.medrxiv.org/content/10.1101/2022.07.08.22276768v1

who have had MIS-C;[404] and identified an increased risk of new-onset conditions in Long COVID patients (type 2 diabetes,[405,406] anxiety, ataxia, myoneural disorders[407]). In addition, the first manuscript highlighting analyses of data from the RECOVER enrolling adult clinical cohort was recently published,[408] identifying sub-phenotypes and specific symptom criteria of Long COVID; characterizing impacts of different variants and vaccination; and defining Long COVID prevalence in adults. Researchers also recently found that severe COVID-19 may lead to long-term innate immune system changes; this may explain why COVID-19 damages so many organs and why some people with Long COVID have high levels of inflammation throughout the body.[409] As of December 4, 2023, 63 scientific papers have been published, posted as preprints, or submitted to journals and more than 60 others are in preparation.

Next Steps

In late July 2023, RECOVER launched and opened enrollment for Phase 2 clinical trials that will evaluate at least four potential treatments for Long COVID, with additional clinical trials to test at least seven more treatments expected in the coming months. This portfolio of clinical trials will explore treatments to address some of the proposed underlying causes of Long COVID as well as some of the major symptom clusters that have the greatest impact on patients' quality of life. Treatments will include drugs, biologics, medical devices, and other therapies. These trials are designed using platform protocols, which can evaluate multiple treatments simultaneously to identify more swiftly those that are effective. The trials are also adaptive, which allows potential therapies to be added or dropped quickly based on emerging findings and without the need to develop and implement entirely new protocols, which is a time-consuming process. Testing is performed at various key locations across the country and each site in a clinical trial will follow the same protocols and use common data elements, so data can be combined from many different locations to generate conclusive results. RECOVER researchers developed the portfolio of RECOVER trials with extensive input from patient representatives as well as experts in the symptom areas, proposed interventions, and clinical trial design. These platform trials are complex undertakings that require significant planning and effective coordination between multiple locations but are well-suited to studying the complexities of Long COVID.

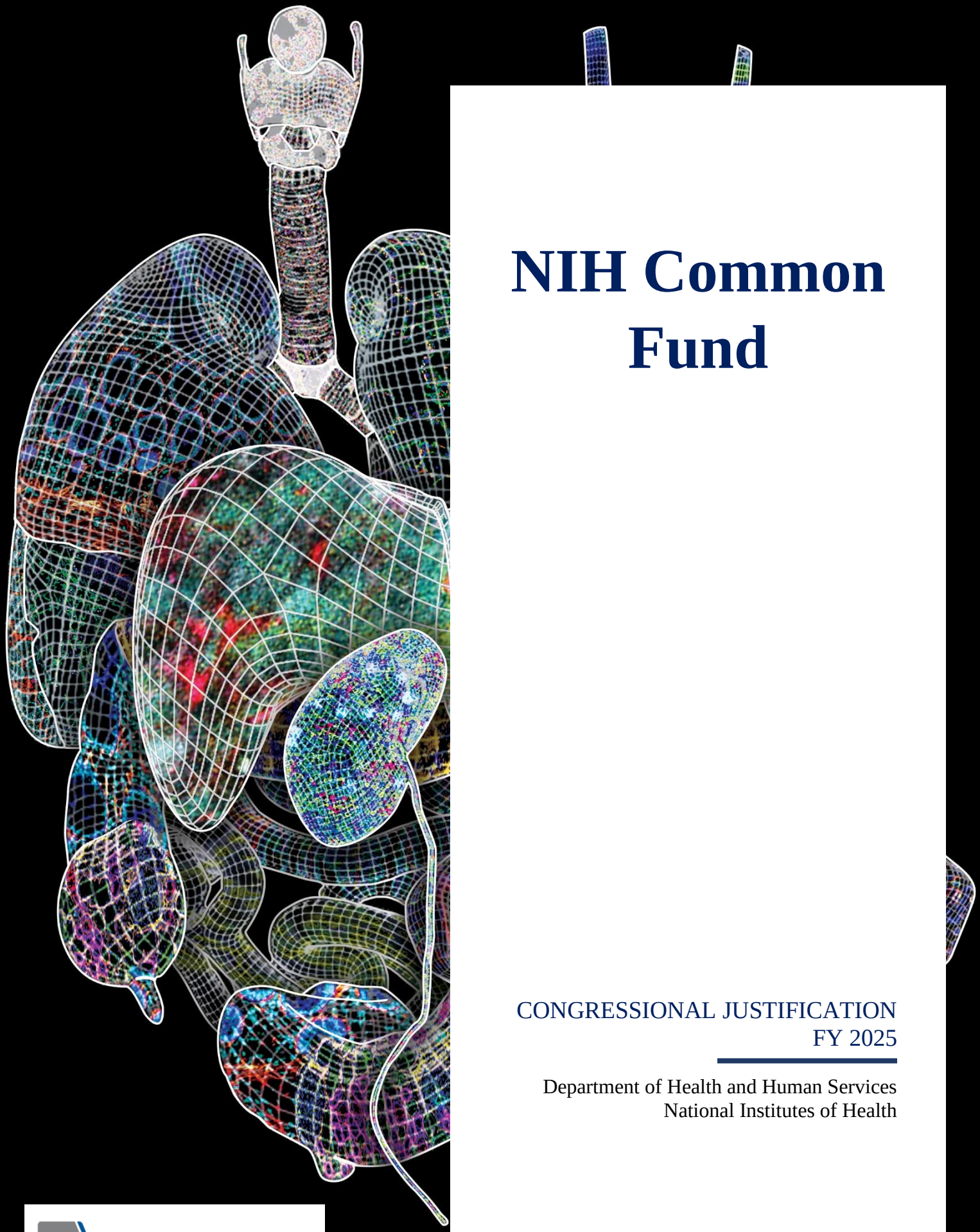
- The first two clinical protocols launched were:
    - **RECOVER-VITAL** studies whether viral persistence, which could occur if SARS-CoV-2 stays in the body and causes the immune system to not function properly and/or causes damage to organs, is a cause of some Long COVID symptoms.
    - **RECOVER-NEURO** examines interventions for cognitive dysfunction related to Long COVID, including brain fog, memory problems, as well as difficulty with attention, thinking clearly, and problem solving.
- The following additional protocols will launch in the coming months:
    - **RECOVER-SLEEP** will test interventions for changes in sleep patterns or ability to sleep after having COVID-19.

[404] www.nih.gov/news-events/news-releases/covid-19-vaccine-children-after-mis-c-appears-safe#:~:text=The%20researchers%20have%20routinely%20treated,is%20safe%20to%20do%20so.
[405] www.medrxiv.org/content/10.1101/2022.12.02.22283029v1
[406] www.medrxiv.org/content/10.1101/2022.11.03.22281916v1
[407] www.medrxiv.org/content/10.1101/2022.07.08.22277388v2
[408] jamanetwork.com/journals/jama/fullarticle/2805540
[409] pubmed.ncbi.nlm.nih.gov/37597510/

- **RECOVER-AUTONOMIC** will examine interventions to help treat symptoms associated with problems in the autonomic nervous system, which controls a range of critical bodily functions without our awareness including heart rate, breathing, and digestive system activity.
- **RECOVER-ENERGIZE** will focus on exercise intolerance and fatigue as well as post-exertional malaise.

Trials will continue to launch and enroll participants on a rolling basis. Enrollment will take place at clinical research sites located throughout the United States. A track record for enrolling diverse participants was a key criterion for site selection.

Continuation of ongoing RECOVER studies and the launch of new studies are necessary to capitalize on current momentum, build an evidence base for treating Long COVID, and significantly enhance the return on Congress' original investment. Given the very broad range of symptoms seen in Long COVID and the importance of developing treatments for children, additional clinical trials are needed. RECOVER studies of the pathobiology of Long COVID are aimed at elucidating the underlying mechanisms of disease and the associated therapeutic targets and biomarkers. Such findings will inform the selection of new interventions to be tested based on their ability to more precisely target underlying causes of specific symptoms and/or the root causes of Long COVID. In addition, given the development of new onset disorders and exacerbation of pre-existing conditions seen in patients with Long COVID, longer-term follow-up of patients is needed to understand and address longer-term health outcomes.



NIH Common Fund

CONGRESSIONAL JUSTIFICATION
FY 2025

Department of Health and Human Services
National Institutes of Health

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NIH Common Fund

FY 2025 Budget Table of Contents

General Notes

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

Cover Page

Nature cover image depicting progress made by the Human BioMolecular Atlas Program (HuBMAP) in mapping how cell types are arranged in the human body. The program is both developing and then deploying the necessary technology to create maps of organs at single-cell resolution. Image credit: Heidi Schlehlein

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DIRECTOR'S OVERVIEW

Director's Overview

Douglas Sheeley, Sc.D., Acting Director, Office of Strategic Coordination

The NIH Common Fund (CF) is a unique and exciting component of NIH, specifically designed to address challenges and opportunities that are high priority for the agency as a whole.[410] In order to enhance the basic and applied research that has been a hallmark of the American innovation enterprise and the envy of the world, we support research in areas of emerging scientific opportunities, public health challenges, and knowledge gaps that deserve special emphasis; that would benefit from strategic coordination and planning across NIH Institutes and Centers; and are designed to achieve specific, high-impact goals and milestones within a 5- to 10-year timeframe. Many Common Fund programs are strategically designed to produce specific deliverables, such as data sets, tools, technologies, or fundamental scientific paradigms, that fill a significant need across multiple fields of biomedical and behavioral research. We intend for these deliverables to spur subsequent scientific advances that would not be possible without our catalytic investment. The Common Fund provides an avenue for NIH to experiment with funding processes to better achieve its R&D mission by designing, trying, and assessing new approaches, such as engaging new R&D performers, exploring new R&D methods, and forging new partnerships. The Common Fund is managed by the Office of Strategic Coordination (OSC) in the NIH Office of the Director, in partnership with NIH Institutes, Centers, and Offices.

Since Common Fund programs are designed with clearly defined goals and milestones, it is important to rigorously monitor ongoing progress to ensure programs are on track, and to adjust if needed. Additionally, as Common Fund programs are intended to produce valuable resources and knowledge to spur subsequent research advances, it is also important to assess the impact of each program and its deliverables on the broad biomedical research landscape. We thoroughly evaluate Common Fund programs during their lifetime, and outcomes are assessed as programs end. Continuous, ongoing 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.

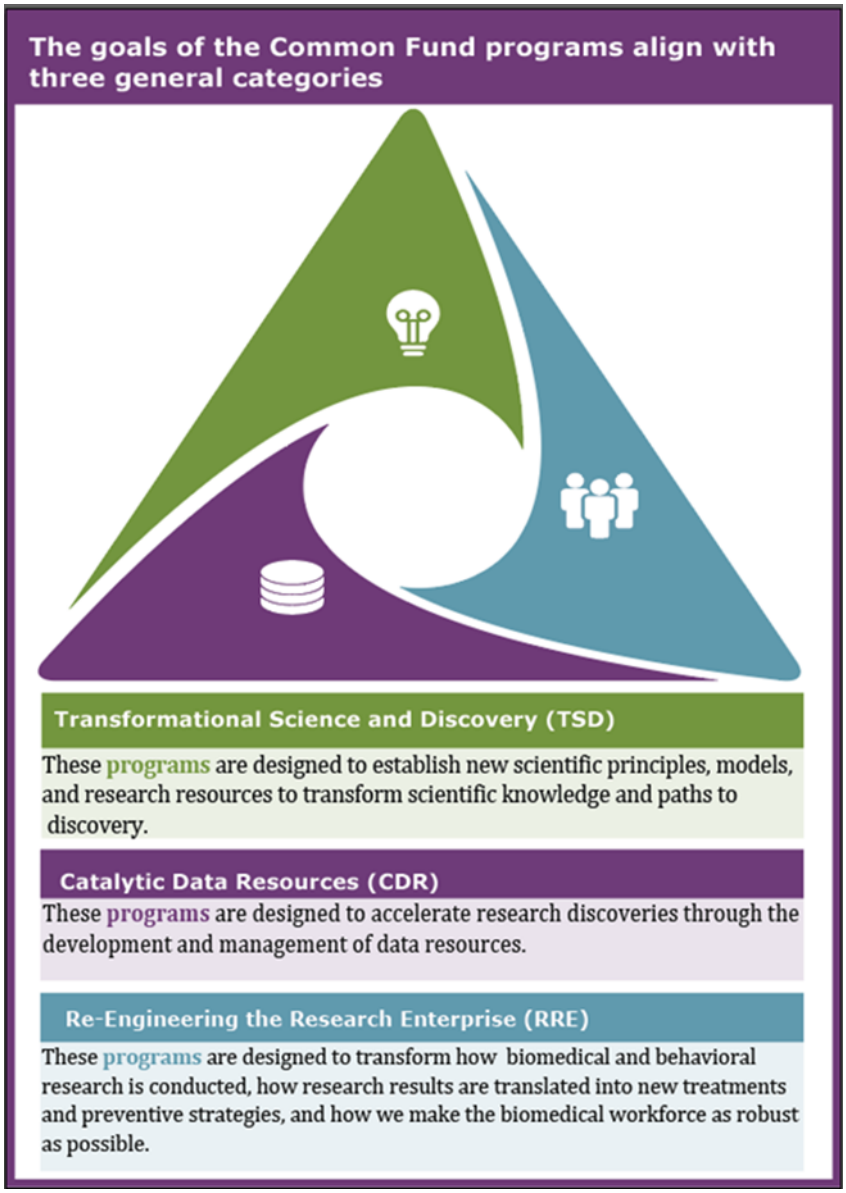
The responsive nature of Common Fund programs has enabled a highly strategic approach to leveraging budget increases over the past several fiscal years. High priority activities have been rapidly identified and implemented, including an accelerated launch of the Human Virome Project in FY 2024, support for additional clinical studies and data analysis to explore the molecular pathways underlying the benefits of physical activity, enhancement of activities to

[410] commonfund.nih.gov/

support use of Common Fund data resources, and support for additional early-stage investigators through the New Innovator Awards.

Common Fund programs are broad-reaching and span the entire NIH mission. As a general framework, they can be grouped into three categories:

- **Transformational Science and Discovery**: programs designed to establish new scientific principles, models, and research resources to transform scientific knowledge and paths to discovery.
- **Catalytic Data Resources**: programs designed to accelerate research discoveries through the development and management of data resources.
- **Re-Engineering the Research Enterprise**: programs designed to transform how biomedical and behavioral research is conducted, how research results are translated into new treatments and preventive strategies, and how we make the biomedical workforce as robust as possible.



The Common Fund: Past, Present, and Future

The Common Fund has its roots in the NIH Roadmap for Medical Research, initiated in 2004. The goal of the Roadmap was to transform biomedical research by identifying and addressing significant opportunities and challenges that no single or small group of NIH Institutes and Centers (ICs) could or should take on alone, but that the NIH as a whole must address.

In 2006, the NIH Reform Act provided continued support for Roadmap programs through a new entity called the NIH Common Fund. The Common Fund has continued to support innovative, high-impact programs that advance research across many biomedical and behavioral research fields. Although support for programs within the Common Fund is time-limited, the far-reaching impact of many programs often lasts beyond their Common Fund lifespan, exemplifying the catalytic nature of these programs to spur subsequent discovery that would not be possible without Common Fund investment. Notable examples include:

- **Large datasets developed by programs such as the Genotype-Tissue Expression (GTEx) program.**[411] GTEx data transformed our understanding of how genetic variants influence gene expression across multiple tissues and across individuals. GTEx data remains available to the biomedical research community and has recently been used to elucidate mechanisms of genetic susceptibility to COVID-19-related severe lung disease, identify genetic risk factors and gene expression patterns in migraines, and identify expression patterns for genetic variants associated with tobacco and alcohol use.[412,413,414]
- **New paradigms for how clinical research information is collected, used, and reported.** The Patient-Reported Outcomes Measurement Information System (PROMIS) program developed a rigorously tested measurement tool to quantify patient outcomes that have major impacts on quality of life, such as pain, fatigue, and emotional distress. PROMIS measures continue to be expanded and utilized in clinical research and practice and are integrated into the HealthMeasures suite of measurement tools along with other NIH-supported clinical measurement systems.[415,416]
- **Novel technologies that enable additional research discoveries**. Development of novel technologies is a hallmark of many Common Fund programs, and the High-Risk, High-Reward (HRHR) program has been particularly fruitful in generating groundbreaking new tools.[417] For example, HRHR awardees developed optogenetics, a technique used to precisely control the activity of genetically selected cells using light. This technique has become widespread in biomedical research, with over 8,000 scientific publications, 300 awarded patents, and 8 clinical trials related to optogenetics.[418]
- **Expanded research capacity around the globe.** Through programs like Human Health and Heredity in Africa (H3Africa), the Common Fund has expanded research capacity to enable scientists in more African regions to contribute to innovative discoveries.[419,420] H3Africa generated rich data resources on hereditary and environmental contributions to health and disease that remain available for future studies, as well as providing robust

[411] commonfund.nih.gov/GTEx
[412] ncbi.nlm.nih.gov/pmc/articles/PMC9259496/
[413] ncbi.nlm.nih.gov/pmc/articles/PMC8837554/
[414] ncbi.nlm.nih.gov/pmc/articles/PMC9771818/
[415] healthmeasures.net/index.php
[416] healthmeasures.net/explore-measurement-systems/promis
[417] commonfund.nih.gov/highrisk
[418] iSearch query for publications with the MeSH term "optogenetics"; USPTO patent public search for keyword "optogenetic"; iSearch query for clinical trials with keyword "optogenetic". All queries conducted Sept/Oct 2023.
[419] commonfund.nih.gov/global-health
[420] h3africa.org/

training experiences to build informatics capacity for African scientists who are now pursuing additional research projects.

Current Common Fund programs span the NIH mission, encompassing basic, translational, clinical, and behavioral research. These programs improve health and save lives through development of fundamental knowledge and resources that lead to new understanding of the basic biological processes that influence human health and disease, establishment of innovative approaches to translate novel therapeutics into the clinic, testing and evaluation of novel models to support the biomedical research workforce, and clinical research to improve health for diverse populations.

Several Common Fund programs are addressing urgent challenges that have a substantial impact on the health and well-being of our nation in order to ameliorate inequities and create opportunity in ways that strengthen our values. The Community Partnerships to Advance Science for Society (ComPASS) program is developing and testing multi-level structural interventions to reduce health disparities and advance health equity, so that all populations can achieve optimal health.[421] These interventions include innovative projects to support access to healthy food in underserved rural areas, explore whether early childcare improves mental health for children and parents, and create culturally appropriate and inclusive health resources for older adults from sexual and gender minority populations. The Acute to Chronic Pain Signatures (A2CPS) program is addressing the issue of chronic pain, which has contributed, in part, to the current opioid epidemic.[422] A2CPS is developing a set of objective biomarkers that provide "signatures" to predict if pain is likely to resolve or become chronic after an incident of acute pain, potentially leading to new pain therapies and prevention strategies.

Common Fund programs also leverage cutting-edge technologies to speed novel therapies to the clinic. The first stage of the Somatic Cell Genome Editing (SCGE) program developed novel genome editing tools with improved efficacy and specificity, enabling researchers to precisely target disease-causing genes even in tissues that have traditionally been difficult to reach, such as the brain, ear, heart, and lung. In the second phase, the program is now accelerating the translation of genome editing therapies into the clinic by developing and disseminating resources to enable genome editing clinical trials. These include technologies and assays for safety and efficacy studies, optimizing therapeutic leads to support advancement toward clinical trials, and supporting novel genome editing clinical trials for more than one disease.

The Common Fund is well-poised to address emerging scientific opportunities and research challenges of the future. As programs end, funds are available to address new challenges and opportunities. Through a robust strategic planning process involving broad input and prioritization by NIH senior leadership, the Common Fund identifies new program concepts that are high priority across NIH.

Upcoming programs include the Human Virome Program (launching in FY 2024) and Complement Animal Research in Experimentation (Complement-ARIE, potentially launching in FY 2025). The Human Virome program will explore the largely understudied collection of

[421] commonfund.nih.gov/compass
[422] commonfund.nih.gov/pain

viruses that live in the human body without causing obvious clinical disease.[423] Complement-ARIE will leverage new and emerging technologies to catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) to better model human biology, complementing, or in some cases possibly replacing, traditional model studies. Another exciting activity on the horizon is the development of a new Common Fund Venture Program to support high-risk, short-term initiatives, introducing additional flexibility and a more nimble approach to tackle a wider variety of research topics.

[423] commonfund.nih.gov/humanvirome

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The Common Fund

Bold science, catalyzing discoveries

The NIH Common Fund provides a dedicated source of support for scientific programs that are high-priority for NIH as a whole

SUPPORTING multi-disciplinary research efforts

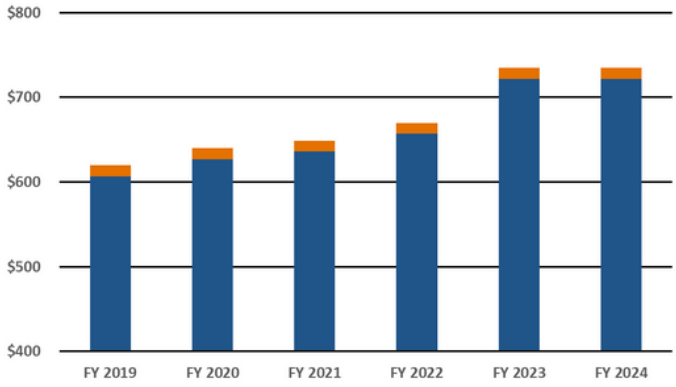
INVESTING in time-limited, goal-driven programs

ACCELERATING emerging science

REMOVING research roadblocks

FUNDING HISTORY

Dollars in millions



The FY 2025 President's Budget request is $722.4 million.

Blue = Common Fund base appropriation
*Orange = Gabriella Miller Kids First Pediatric Research**
**FY 2025 request does not include Gabrilla Miller funding due to transfer of program out of Common Fund*

FACTS AND FIGURES

23 Scientific Programs in FY 2023

544 Principal Investigators (PIs)*

188 High-Risk, High-Reward (HRHR) PIs*

102 Early-Career HRHR PIs*

142 Competing Research Project Grants*

23 NIH Institutes, Centers, and Offices Co-Leading Programs in FY 2023

**yearly averages FY 2019 - FY 2023*

COMMON FUND LEADERSHIP

Douglas Sheeley, Sc.D.

Dr. Sheeley became the Deputy Director of the Office of Strategic Coordination (OSC) in 2022 and the Acting Director of OSC in 2023.

COMMON FUND VENTURE PROGRAM

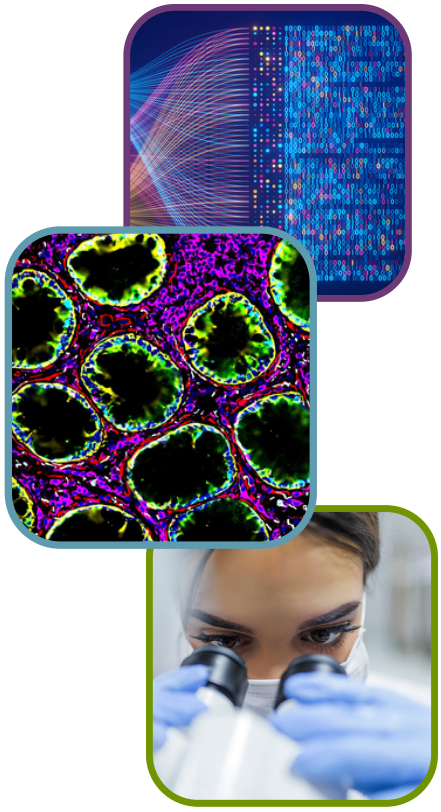
Amazing Things with Modest Funding

The new Common Fund Venture Program will support high-risk, short-term initiatives with potential to have a major impact in biomedical and behavioral research.

Venture projects will be:

- Highly innovative
- Responsive to the shared interests of NIH Institutes, Centers, and Offices
- Goal-driven and focused on a specific outcome

RESEARCH ACCOMPLISHMENTS



Common Fund Data Ecosystem (CFDE)

CFDE is supporting collaborative projects to develop resources and tools to enable discoveries across multiple CF data sets. As an example, researchers have developed a tool to map potential connections between parental exposure to drugs and birth defects, leveraging data from four CF programs.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP has published a collection of articles bringing together data on RNA, proteins, and metabolites in human organs at single-cell resolution to generate an open-access data platform for researchers to study the inner workings of the cells and how they affect health.

Transformative High-Resolution Cryoelectron Microscopy (CryoEM)

The CryoEM program has broadened access to cutting-edge microscopy techniques, leading to new discoveries such as the structure of tau fibrils bound to RNA (implicated in Alzheimer's disease) and the interactions between Substance P and neurokinin 1 receptor (implicated in conditions such as pain, inflammation, and mood disorders).

CURRENT ACTIVITIES

Community Partnerships to Advance Science for Society (ComPASS)

ComPASS is advancing health equity research by supporting community-driven, structural intervention research projects in areas such as health care access and quality, nutrition and access to healthy food, and neighborhood characteristics.

Human Virome Program

New in FY 2024, the Human Virome Program aims to transform our understanding of viruses that live in the human body and their impact on human health by identifying and characterizing a broad range of viruses and developing novel technologies.

Nutrition for Precision Health (NPH)

NPH is developing algorithms that predict individual responses to food and dietary patterns, leveraging the size and diversity of the NIH's All of Us Research cohort. Enrollment for this unprecedented study launched in FY 2023.

PLANNING FOR THE FUTURE

An NIH-wide strategic planning process led to the identification of a potential new program concept for FY 2025.

Complement Animal Research in Experimentation (Complement-ARIE)

This potential program would catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) to transform the way we do basic, translational, and clinical sciences by complementing, or in some cases possibly replacing, traditional models.

MAJOR CHANGES

Major Changes in the Budget Request

Major changes by budget mechanism and/or budget activity detail are briefly described below. Note there may be some overlap between budget mechanisms and activity detail, and these highlights will not sum to the total for the FY 2025 President's Budget request for the Common Fund, which is $722.4 million, a decrease of $12.6 million or 1.7 percent compared with the FY 2023 Final level.

Research Project Grants (RPGs) (+$27.1 million; total $354.2 million): The Common Fund expects to support a total of 352 RPG awards in FY 2025, 23 RPGs less than in FY 2023. Estimated awards for FY 2025 include 254 Noncompeting RPGs and 98 Competing RPGs.

Research Centers (-$21.5 million; total $136.4 million): The Common Fund expects to support a total of 61 Research Centers in FY 2025, 12 awards less than in FY 2023. This decrease reflects the planned completion of support for Clinical Research Centers within the Enhancing the Diversity of the NIH-Funded Workforce program, Biotechnology Centers within the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program, and Comparative Medicine Centers within the Somatic Cell Genome Editing program.

Other Research (-$7.4 million; total $197.0 million): The Common Fund expects to support a total of 109 Other Research awards in FY 2025, 5 awards less than in FY 2023. Within this category, the Common Fund will continue to prioritize Other Transaction (OT) awards in several programs. Several new or expanded activities, including Venture Program and Complement Animal Research in Experimentation (Complement-ARIE) will support OT awards in FY 2025.

Research Training (-$3.7 million; total $0.6 million): The Common Fund expects to support a total of eight full time training positions (FTTPs) as new Research Training Individual Awards within the Common Fund Data Ecosystem. The decrease in support for Research Training overall reflects the planned completion of Research Training Institutional Awards within the Enhancing the Diversity of the NIH-Funded Workforce program.

BUDGET MECHANISM TABLE

Budget Mechanism Table

Mechanism	FY 2023 Final		FY 2024 CR		FY 2025 President's Budget		FY 2025 +/- FY 2023	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Research Projects:								
Noncompeting	209	$155,874	277	$256,338	254	$252,341	45	$96,467
Administrative Supplements	*(39)*	$8,004	*(29)*	$5,988	*(25)*	$5,194	*-(14)*	-$2,810
Competing:								
Renewal	17	$18,684	0	$0	0	$0	-17	-$18,684
New	149	$144,546	99	$97,322	98	$96,669	-51	-$47,877
Supplements	0	$0	0	$0	0	$0	0	$0
Subtotal, Competing	**166**	**$163,230**	**99**	**$97,322**	**98**	**$96,669**	**-68**	**-$66,561**
Subtotal, RPGs	375	$327,108	376	$359,648	352	$354,204	-23	$27,096
SBIR/STTR	0	$0	0	$0	0	$0	0	$0
Research Project Grants	375	$327,108	376	$359,648	352	$354,204	-23	$27,096
Research Centers								
Specialized/Comprehensive	59	$131,825	74	$166,039	61	$136,417	2	$4,592
Clinical Research	10	$12,540	0	$0	0	$0	-10	-$12,540
Biotechnology	2	$9,094	3	$12,487	0	$0	-2	-$9,094
Comparative Medicine	2	$4,422	0	$0	0	$0	-2	-$4,422
Research Centers in Minority Institutions	0	$0	0	$0	0	$0	0	$0
Research Centers	**73**	**$157,882**	**77**	**$178,526**	**61**	**$136,417**	**-12**	**-$21,465**
Other Research:								
Research Careers	0	$100	0	$0	0	$0	0	-$100
Cancer Education	0	$0	0	$0	0	$0	0	$0
Cooperative Clinical Research	6	$14,455	6	$15,226	6	$15,027	0	$572
Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Minority Biomedical Research Support	0	$0	0	$0	0	$0	0	$0
Other	108	$189,877	76	$133,642	103	$181,961	-5	-$7,916
Other Research	**114**	**$204,432**	**82**	**$148,868**	**109**	**$196,988**	**-5**	**-$7,444**
Total Research Grants	562	$689,422	535	$687,042	522	$687,609	-40	-$1,813
Ruth L Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs		FTTPs	
Individual Awards	0	$0	0	$0	8	$600	8	$600
Institutional Awards	156	$4,329	0	$0	0	$0	-156	-$4,329
Total Research Training	**156**	**$4,329**	**0**	**$0**	**8**	**$600**	**-148**	**-$3,729**
Research & Develop. Contracts	3	$8,168	5	$15,008	1	$1,026	-2	-$7,142
SBIR/STTR (non-add)	*(0)*	*($0)*	*(0)*	*($0)*	*(0)*	*($0)*	*(0)*	*($0)*
Intramural Research	0	$690	0	$383	0	$383	0	-$307
Res. Management & Support	0	$32,392	0	$32,568	0	$32,783	0	$391
SBIR Admin. (non-add)		*($0)*		*($0)*		*($0)*		*($0)*
								0
Construction		$0		$0		$0		$0
Buildings and Facilities		$0		$0		$0		$0
Total, Common Fund	**0**	**$735,001**	**0**	**$735,001**	**0**	**$722,401**	**0**	**-$12,600**

* All items in italics and brackets are non-add entries.

BUDGET BY INITIATIVE

Common Fund Budget by Initiative

Common Fund Program (Dollars in Thousands)	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget
4D Nucleome	$27,931	$28,378	$245
Acute to Chronic Pain Signatures	1,281	3,338	3,138
Bridge to Artificial Intelligence (Bridge2AI)	35,391	20,589	32,394
Cellular Senescence Network (SenNET)	42,833	43,850	38,850
Common Fund Data Ecosystem	4,757	18,900	22,750
Community Partnerships to Advance Science for Society (ComPASS) Program	32,731	17,707	52,674
Enhancing the Diversity of the NIH-Funded Workforce	36,718	120	0
Extracellular RNA Communication	313	113	0
Faculty Institutional Recruitment for Sustainable Transformation (FIRST)	53,025	72,688	50,295
Gabriella Miller Kids First Pediatric Research	13,070	12,983	0
Global Health	90	0	0
Harnessing Data Science for Health Discovery and Innovation in Africa (DSI-Africa)	16,434	16,418	16,748
High-Risk Research	171,157	198,958	193,300
NIH Director's Pioneer Award	*44,607*	*42,515*	*39,413*
NIH Director's New Innovator Award Program	*58,401*	*88,551*	*86,790*
Transformative Research Award	*44,452*	*42,932*	*41,124*
NIH Director's Early Independence Award Program	*23,697*	*24,961*	*25,973*
Human BioMolecular Atlas Project (HuBMAP)	44,211	34,586	18,275
Human Virome Program (HVP)	0	42,259	46,357
Illuminating the Druggable Genome	7,168	390	0
Molecular Transducers of Physical Activity	19,019	15,783	8,420
Nutrition for Precision Health	42,399	42,404	46,955
Somatic Cell Genome Editing	47,445	46,254	47,501
Somatic Mosaicism across Human Tissues (SMaHT)	22,852	25,913	30,927
S.P.A.R.C. - Stimulating Peripheral Activity to Relieve Conditions	32,100	39,277	463
Transformative High Resolution Cryo-Electron Microscopy (CryoEM)	25,907	4,255	4,055
Transformative Research to Address Health Disparities	16,239	17,540	17,440
Undiagnosed Diseases Network	11,493	0	0
Venture Space	0	10,000	25,000
Strategic Planning, Evaluation, and Infrastructure	30,436	22,300	22,300
Subtotal Common Fund	735,001	735,001	678,086
New Initiatives in Common Fund	0	0	44,315
Total Common Fund	$735,001	$735,001	$722,401

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 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
BA	$735,001,000	$735,001,000	$722,401,000	-$12,600,000
FTE	0	0	0	0

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

Overall Budget Policy: The FY 2025 President's Budget request for the Common Fund is $722.4 million, a decrease of $12.6 million or 1.7 percent compared with the FY 2023 Final level. This decrease reflects the planned transfer of the Gabriella Miller Kids First Pediatric Research program from the Common Fund to the Division of Program Coordination, Planning, and Strategic Initiative within the NIH Office of the Director, in accordance with long-standing policy that Common Fund programs are supported for a maximum of 10 years. This funding level will support high priority activities within existing program and support the launch of exciting new activities, as described below.

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 that can be achieved within 5 to 10 years. Planned activities and budgets for CF programs are strategically developed, with clear milestones defined throughout the lifetime of the program to enable measurement of progress towards pre-defined goals. Therefore, CF programs often undergo planned budget shifts driven by the needs and activities for each program. New scientific challenges and opportunities will be addressed in FY 2025 from funds made available as current programs end, move to other sources of support, or require decreased support as indicated by evaluative data.

Several CF programs will receive their last year of support in FY 2024; funds are therefore not requested in FY 2025 for these programs. These include Enhancing the Diversity of the NIH-Funded Workforce, Extracellular RNA Communication, Gabriella Miller Kids First Pediatric

Research, and Illuminating the Druggable Genome.[424,425,426,427] In accordance with long-standing policy that Common Fund programs are supported for a maximum of 10 years, funds for the Gabriella Miller Kids First Pediatric Research program are requested within the NIH Office of the Director, rather than the Common Fund, starting in FY 2025. Additionally, the Global Health and Undiagnosed Diseases Network programs received their last year of support in FY 2023; funds are therefore not requested in FY 2024 or FY 2025.[428,429] Information on these programs and their accomplishments can be found on the program websites.

Highlighted below are programs that exemplify the high priority science to be supported in FY 2025, and/or which are undergoing significant programmatic changes in FY 2025.

4D Nucleome

The 4D Nucleome program aims to develop a fundamentally new understanding of how genetic material is organized in the cell in space and time, and how this organization influences human development, health, and disease.[430] Each human cell contains approximately 6.5 feet of DNA within the cell's microscopic nucleus. The arrangement of DNA in the nucleus is not random – it is carefully organized and packaged, and this arrangement dynamically changes to modulate which genes are turned on and off. However, the process of nuclear arrangement and re-arrangement is not well-understood. The 4D Nucleome program is producing tools and resources for the research community to explore the health effects of nuclear organization, including identification of new targets for human diseases that are caused by abnormal nuclear organization. To date, the 4D Nucleome program has developed and made available nearly 2,000 data sets, 52 software packages, and 23 protocols and reagents.

Budget Policy: The FY 2025 President's Budget request is $0.2 million, a decrease of $27.7 million or 99.1 percent compared with the FY 2023 Final level. The budget reflects the planned completion of the program, having achieved its goals of developing new datasets, tools, and technologies to enable to study of genetic organization over space and time. Requested funds will be used to support the final closing out of program activities.

Bridge to Artificial Intelligence (Bridge2AI)

Bridge2AI aims to set the stage for widespread adoption of AI that addresses complex biomedical challenges beyond human intuition.[431] A key deliverable for this program is the generation of new "flagship" data sets and best practices for machine learning (ML) analysis. These flagship data sets include voice and other data to identify abnormal changes in the body, data to make connections between genetic pathways and changes in cell shape and function, data to improve decision-making in critical care settings, and data to uncover biological processes underlying recovery from illness. Bridge2AI will also produce tools, software, and standards to accelerate the creation of AI/ML-ready data sets and design training materials and

[424] commonfund.nih.gov/diversity
[425] commonfund.nih.gov/Exrna
[426] commonfund.nih.gov/KidsFirst
[427] commonfund.nih.gov/IDG
[428] commonfund.nih.gov/globalhealth
[429] commonfund.nih.gov/Diseases
[430] commonfund.nih.gov/4Dnucleome
[431] commonfund.nih.gov/bridge2ai

activities for skills and workforce development. Additionally, Bridge2AI will foster a culture change for the community to embrace data preparation for AI/ML analysis and expand the interdisciplinary community between AI and biomedical and behavioral research.

Budget Policy: The FY 2025 President's Budget request is $32.4 million, a decrease of $3.0 million or 8.5 percent compared with the FY 2023 Final level. Funds in FY 2025 will continue to support generation of flagship data sets, tools, software, and standards, along with coordination and integration activities. Bridge2AI will leverage the flexibility of the Other Transactions funding mechanism to shift funds from FY 2024 to FY 2025, to optimally align with the scientific and budgetary needs of these highly dynamic projects and resulting in a temporarily lower level of funding for FY 2024.

Cellular Senescence Network (SenNet)

As we age, tissues throughout the body accumulate small numbers of specialized cells that no longer divide, yet they remain active and develop specialized characteristics that are different from other non-dividing cells. These specialized cells are called senescent cells. There are many unanswered questions about how, when, why, and where senescent cells form and what impact they have on human health and disease. 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.[432] SenNet researchers are mapping senescent cells in 18 human tissues and additional body fluids across the lifespan, in addition to 19 tissues from multiple mouse strains.

Budget Policy: The FY 2025 President's Budget request is $38.9 million, a decrease of $4.0 million or 9.3 percent compared with the FY 2023 Final level. The FY 2025 request reflects a planned decrease in technology application and development projects, while maintaining support for tissue mapping centers and a data coordination and organization center.

Common Fund Data Ecosystem

As data-intensive strategies are increasingly undertaken to achieve the goals of Common Fund programs, infrastructure to address challenges facing all data management centers has become necessary. This infrastructure, referred to as the Common Fund Data Ecosystem (CFDE), is enabling researchers to query across and use multiple Common Fund data sets, 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 Common Fund programs by enabling researchers to interrogate multiple disparate data sets, and thereby make new kinds of scientific discoveries that were not possible before. Prior to FY 2023, support for the CFDE was included within the Strategic Planning, Evaluation, and Infrastructure budget line. With the launch of a new stage in FY 2023, support for the new CFDE activities appears as a stand-alone line in the budget by initiative table. Ongoing FY 2023 activities from the first stage remain within the Strategic Planning, Evaluation, and Infrastructure item.

Budget Policy: The FY 2054 President's Budget request is $22.8 million, an increase of $3.1 million or 16.0 percent compared with the FY 2023 Final level (consisting of total support of

[432] commonfund.nih.gov/senescence

$4.8 million from the FY 2023 CFDE budget line as well as the FY 2023 amount for CFDE of $14.9 million within Strategic Planning, Evaluation, and Infrastructure). The new stage of CFDE will continue to engage with many Common Fund data generating programs and coordinate across the entire data ecosystem, enhancing the findability and accessibility of data and increasing emphasis on training and outreach to develop a diverse user base for Common Fund data resources.

Community Partnerships to Advance Science for Society (ComPASS)

The ComPASS program aims to accelerate the science of health disparities and advance health equity research.[433] The goals of ComPASS are to: 1) develop, share, and evaluate community-driven structural health equity interventions that leverage partnerships across multiple sectors to reduce health disparities; and 2) develop a new health equity research model for community-led, multisectoral structural intervention research across NIH and other federal agencies. These interventions will include ambitious projects to address underlying conditions and environments that influence health outcomes, such as economic development, social and community context, neighborhood characteristics, health care access and quality, and nutrition and access to healthy food.

Budget Policy: The FY 2025 President's Budget request is $52.7 million, an increase of $19.9 million or 60.9 percent compared with the FY 2023 Final level. The budget will support the scaling up of this program as it moves from development to implementation of health equity structural intervention research projects and coordinates cross-program activities.

Faculty Institutional Recruitment for Sustainable Transformation (FIRST)

While progress has been made to increase participation of historically underrepresented groups in biomedical research training stages, members of these groups are still less likely to be hired in positions as independently funded faculty researchers. 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.[434] Based on early successes of other cohort-based recruitment programs, FIRST employs a faculty cohort model for hiring, mentoring, and professional development; integrated, institution-wide approaches to address bias, faculty equity, mentoring, and work/life issues; and a coordination and evaluation center to conduct independent evaluations of program impacts.

Budget Policy: The FY 2025 President's Budget request is $50.3 million, a decrease of $2.7 million or 5.2 percent compared with the FY 2023 Final level. The budget reflects the planned decrease in support for the first faculty cohort as they transition to other funding sources, while continuing to support the second and third faculty cohorts, launched in FY 2022 and FY 2023, respectively, as well as program-wide coordination and evaluation efforts.

High-Risk, High-Reward Research (HRHR)

The HRHR program supports exceptionally creative scientists proposing innovative and transformative research with the potential for broad impact in any scientific area within the NIH

[433] commonfund.nih.gov/compass
[434] commonfund.nih.gov/first

mission.[435] This program supports four complementary initiatives: the Pioneer Award, New Innovator Award, Transformative Research Award, and Early Independence Award. These awards are intended to support research that is designed for unusual impact, but may be inherently difficult and scientifically risky, often because the project is exceptionally novel or is in an early stage of development. However, investment in high-risk research is an important approach to accelerate the pace of scientific discovery and advance human health.

Budget Policy: The FY 2025 President's Budget request is $193.3 million, an increase of $22.1 million or 12.9 percent compared with the FY 2023 Final level. Funds requested in FY 2025 will be used to support additional innovative projects with the potential for extraordinary impact.

Human BioMolecular Atlas Program (HuBMAP)

HuBMAP 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.[436] In complex, multicellular organisms like humans, the proper functioning of organs and tissues is dependent on the organization, specialization, and interaction of individual cells. However, determining the functions of and relationships between the estimated 37 trillion cells in the human body is a monumental undertaking. HuBMAP is developing an open and global platform to map healthy cells in the human body, generating foundational tissue maps, and developing tools, technologies, and resources for broad dissemination to the entire biomedical research community. To date, HuBMAP has generated over 2,000 datasets representing 31 human organs. HuBMAP researchers are also developing sophisticated ways to visualize this rich spatial and biomolecular information, including through development of a user-friendly virtual reality platform that enables researchers to explore HuBMAP data in a three-dimensional space.

Budget Policy: The FY 2025 President's Budget request is $18.3 million, a decrease of $25.9 million or 58.7 percent compared with the FY 2023 Final level. This funding level reflects the planned reduction in the final year of the program.

Molecular Transducers of Physical Activity in Humans (MoTrPAC)

Physical activity promotes health in a wide variety of ways, and lack of physical activity is a contributing factor to many common chronic health problems. However, we have a limited understanding of the molecular mechanisms that underlie how physical activity provides health benefits. 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. MoTrPAC is cataloging the biological molecules affected by physical activity in humans, identifying some of the key molecules that underlie the systemic effects of physical activity and characterizing their function.[437] Initial results from MoTrPAC's complementary animal studies are revealing exciting new insights into the effects of physical activity, including strong effects on biological pathways related to metabolism and the new discovery that a significant number of responses

[435] commonfund.nih.gov/highrisk
[436] commonfund.nih.gov/HuBMAP
[437] commonfund.nih.gov/MolecularTransducers

demonstrate sex-specific differences. Human studies and subsequent analyses are currently ongoing.

Budget Policy: The FY 2025 President's Budget request is $8.4 million, a decrease of $10.6 million or 55.7 percent compared with the FY 2023 Final level. The budget reflects the planned winding down of human clinical studies and associated coordination activities, while continuing support for sample analysis, animal studies, and data management.

Human Virome Program

The viruses that exist in the human body are large in number and very diverse, but research has predominantly focused on the relatively small number of viruses that cause obvious clinical disease. The vast majority of the human virome is not well-studied, and the impact of these viruses on human health is unknown. However, there is growing evidence that these viruses may play underappreciated roles in human health, including influencing the immune system, altering susceptibility to some diseases, or affecting metabolic processes. For example, recent research has shown that changes in components of the gut virome are linked to obesity and metabolic syndrome in children. Launching in FY 2024, the Human Virome Program aims to characterize the many viruses that reside inside humans and to improve our understanding of how these viruses impact human health.[1] This program will characterize the "healthy" human virome in diverse cohorts across the lifespan, remove technological roadblocks to studying these viruses, and define the virome's role in health and disease. Funds requested in FY 2025 will support these activities.

[1] commonfund.nih.gov/humanvirome

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 perfect, "one size fits all" diet. The goal of NPH is to describe and understand variations in how different people respond to diet, with the aim of developing algorithms that predict individual responses to food and dietary patterns.[438] 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. NPH will leverage the *All of Us* infrastructure and recent advances in biomedical science, such as artificial intelligence (AI) and microbiome research, to provide unprecedented opportunities to examine associations between nutrition and a variety of long-term outcomes.[439] Additionally, this program is closely coordinated with activities of the Office of Nutrition Research, to ensure NIH-wide nutrition efforts are complementary, not duplicative. NPH achieved an exciting milestone in spring 2023, opening enrollment for clinical nutrition studies at 14 sites nationwide.

Budget Policy: The FY 2025 President's Budget request is $47.0 million, an increase of $4.6 million or 10.7 percent compared with the FY 2023 Final level. Increased funds requested in FY 2025 will support increases in data and study coordination and biobanking, while supporting ongoing clinical nutrition studies, data generation, and AI and data modeling.

[438] commonfund.nih.gov/nutritionforprecisionhealth
[439] allofus.nih.gov/

Somatic Mosaicism across Human Tissues (SMaHT)
Over time, different cells within the body accumulate changes to the inherited DNA sequence, resulting in genetically distinct cells within an individual. There is mounting evidence that this genetic variation, called somatic mosaicism, plays important roles in biological processes such as development, aging, and disease. However, technical challenges in detecting rare somatic variations mean this phenomenon is understudied. The SMaHT program aims to transform our understanding of how somatic mosaicism influences biology and disease.[440] SMaHT will catalog somatic variants in 10-15 sets of tissues from diverse human donors at different life stages, develop innovative sequencing tools and analysis methods, and create a workbench to integrate analysis of somatic variation with the human genome.

Budget Policy: The FY 2025 President's Budget request is $30.9 million, an increase of $8.1 million or 35.3 percent compared with the FY 2023 Final level. Increased funds requested in FY 2025 will be used to support planned increases in support for generation of somatic variant catalogs, development of tools and methods, and creation of an integrative data workbench..

Stimulating Peripheral Activity to Relieve Conditions (SPARC)
The SPARC program is accelerating the development of novel neuromodulatory therapeutic devices to advance bioelectronic medicine through provision of foundational data and tools.[441] SPARC is addressing this need by generating maps and tools to precisely 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 2 diabetes, inflammatory disorders, and more. The first stage of the SPARC program developed new tools and technologies, mapped connections among a variety of different nerves and organ systems and created a public resource providing data and tools for advancing bioelectronic medicine. Now in its second stage, SPARC is investigating the anatomy and functional connectivity of the human vagus nerve, developing open-source neural engineering technologies, and supporting prize competitions for innovators to demonstrate proof of principle neuromodulation therapeutic benefits.

Budget Policy: The FY 2025 President's Budget request is $0.5 million, a decrease of $31.6 million or 98.6 percent compared with the FY 2023 Final level. Decreased funds requested in FY 2025 reflect the planned closing out of the program.

Transformative High-Resolution Cryoelectron Microscopy (CryoEM)
The CryoEM program is enabling novel discoveries in structural biology by broadening access to cutting-edge cryoelectron microscopy and cryoelectron tomography techniques and training.[442] These approaches enable researchers to determine the structure of biological molecules with unprecedented detail and accuracy. However, the high cost of required equipment and a lack of training mean that many researchers cannot leverage these critical approaches, and therefore opportunities for novel discoveries are missed. By providing increased access, the CryoEM program is anticipated to catalyze fundamental biological discoveries, as well as accelerate

[440] commonfund.nih.gov/smaht/
[441] commonfund.nih.gov/sparc
[442] commonfund.nih.gov/CryoEM

development of vaccines and therapeutics. Projects supported through the CryoEM program have made new discoveries about proteins that play roles in neurodegenerative and neuropsychiatric diseases, COVID-19, and antibiotic resistance.

Budget Policy: The FY 2025 President's Budget request is $4.1 million, a decrease of $21.9 million or 84.4 percent compared with the FY 2023 Final level. The funding level reflects the planned completion of support for cryoelectron microscopy efforts, while supporting the final year of the cryoelectron tomography network.

Venture Program

The Venture Program is a new approach within the Common Fund to support high-risk, short-term initiatives with the potential for high impact. These cross-cutting initiatives will be highly responsive to the shared interests of the NIH Institutes, Centers, and Offices, and will explore flexible ways of supporting innovative research projects that can be implemented quickly in response to emerging opportunities. Venture initiatives will have clear goals focused on a specific outcome, in the form of new knowledge, methods, or technologies. Similar to the HRHR program, Venture is anticipated to be an ongoing investment, in which new science is continually being supported through a series of short-term investments. Venture will launch as a pilot in FY 2024 with a small number of initial projects and will expand in FY 2025 to support additional innovative initiatives identified through an NIH-wide planning process.

Strategic Planning, Evaluation, and Infrastructure

CF management requires that certain activities be undertaken for the stewardship of the CF as a whole. These include activities related to strategic planning, evaluation, and infrastructure.

Strategic planning is undertaken every year to identify new scientific challenges and opportunities that may be ready for dedicated investment via a CF program. CF strategic planning first identifies broad scientific areas that are priorities for NIH as a whole and then establishes a focused strategy for investments that will catalyze research progress in those areas. The initial idea (or concept) gathering phase of strategic planning often involves input from interested parties with diverse expertise as well as internal discussions about shared challenges and emerging opportunities. The strategy development phase of 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 biomedical 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 adopt 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 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 2025 Common Fund programs leveraged the wide-ranging expertise of NIH's senior leadership and scientific staff, combined with public input through a Request for Information. Planning efforts led to the identification of one potential program idea for active exploration and further development, **Complement Animal Research in Experimentation (Complement-ARIE**). The purpose of this potential program is to catalyze the development, standardization, validation, and use of human-based new approach methodologies (NAMs) that will transform the way the biomedical research community conducts basic, translational, and clinical research by complementing, or in some cases possibly replacing, traditional models. This program is anticipated to lead to a new understanding of health and disease across diverse populations, support standardization and regulatory use of NAMs, and make all research more efficient and effective by adding validated new approaches for researchers to leverage. Planning for this program will leverage an innovative ideation challenge and robust listening sessions to gather input from the broad biomedical community, supported in FY 2024 via funds reserved for strategic planning activities. These planning activities will help to determine whether to proceed with the potential program, as well as define its possible scope and direction. Additionally, NIH is exploring potential opportunities to support a new approach for support of clinical research across a range of sites that will engage primary care providers to reach underserved communities. Plans for this activity are in very early stages of development but may leverage Common Fund support.

Office of AIDS Research

CONGRESSIONAL JUSTIFICATION
FY 2025

Department of Health and Human Services
National Institutes of Health

NIH National Institutes of Health
Office of AIDS Research

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research (OAR)

FY 2025 Budget Table of Contents

General Note

1. FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
2. Detail in this document may not sum to the subtotals and totals due to rounding.

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DIRECTOR'S OVERVIEW

Director's Overview

Diana Finzi, Ph.D.

NIH Acting Associate Director for AIDS Research and

Acting Director, Office of

The Office of AIDS Research (OAR) was established by the Health Omnibus Program Extension (HOPE) Act of 1988 to coordinate HIV/AIDS research across NIH. Subsequently, the NIH Revitalization Act of 1993 authorized OAR to establish HIV/AIDS research priorities, develop a strategic plan for HIV/AIDS research, and allocate the HIV/AIDS budget across NIH. OAR's mission is to ensure that HIV/AIDS research funding is directed at the highest priority research areas and to facilitate maximal return on the investment. In pursuit of this mission, OAR activities are guided by the *NIH Strategic Plan for HIV and HIV-Related Research (2021–2025)*. Furthermore, OAR works with the White House Office of National AIDS Policy to align NIH and other federal agency goals and to facilitate implementation of the National HIV/AIDS Strategy, 2022-2025.

NIH research contributions to life-saving advances in HIV prevention, treatment, and care

At the beginning of the HIV/AIDS pandemic in the 1980s, AIDS was a fatal condition with no effective treatment. In the 1990s, NIH research led to the development of several antiretroviral therapy (ART) regimens to prevent people with HIV from developing AIDS. These breakthrough medical advances changed the course of the pandemic, drastically reducing the number of AIDS-related deaths.

Over the last four decades, sustained investment in HIV/AIDS research at NIH has enabled progressive scientific advances that have led to improved ART with fewer side effects and better adherence which has transformed HIV infection into a manageable chronic condition. Today, people with HIV can anticipate near-normal life expectancy. These advances have also spurred the development and implementation of safe and effective tools to prevent HIV acquisition and transmission. When taken as prescribed, pre-exposure prophylaxis (PrEP), in various formulations, is highly effective at preventing HIV acquisition from anal and vaginal sex, and from injection drug use.[443] By 2018, NIH-supported research had demonstrated that ART taken by people with HIV effectively prevents sexual transmission of HIV to others when the virus reaches undetectable levels in the blood. This research provided the scientific basis for the "Undetectable = Untransmittable," or "U = U," public health campaign.

The benefits of HIV scientific discoveries extend beyond HIV. For example, technologies and resources initially developed in the quest for an HIV vaccine provided a critical platform for the rapid development of mRNA-based COVID-19 vaccines, resulting in major global health impact. In the United States alone, COVID-19 vaccines have helped avert an estimated 120,000 deaths and saved $7.0 billion in preventable hospitalizations.[444]

[443] cdc.gov/hiv/risk/estimates/preventionstrategies.html
[444] pubmed.ncbi.nlm.nih.gov/37098043/

NIH-sponsored HIV/AIDS research had a worldwide impact on public health when ART was introduced globally. Global availability of ART was bolstered by the President's Emergency Plan for AIDS Relief (PEPFAR), launched in 2003. PEPFAR is helping control the global HIV/AIDS pandemic in over 50 countries and has saved over 25 million lives since its launch.[445] Prevention of HIV transmission has averted an estimated 5.5 million infections in babies globally since 2004.[446] The number of new HIV infections worldwide decreased by 38 percent overall between 2010 and 2022.[447]

Responding to evolving HIV/AIDS research needs

Early HIV/AIDS research focused on epidemiologic surveillance to contain the epidemic; later, studies on the mechanisms of HIV pathogenesis were essential for drug discovery. Over time, HIV/AIDS research has developed safe and effective methods of HIV diagnosis, treatment, and prevention for universal implementation, as well as approaches tailored for various populations and settings. Development of a safe and effective HIV vaccine has proven to be more challenging than anticipated because of high rates of viral mutation and variability. Development of a safe, effective and scalable cure for HIV is a global public health priority but is hampered by the unique ability of HIV to persist hidden from the immune system and ART in certain cell types. While substantial progress in HIV vaccine and cure research has been achieved, a safe and effective HIV vaccine and an HIV cure will require continued investment in this critical area.

NIH has increased its attention to addressing the specific needs of different populations, such as sexual and gender minorities, minoritized racial and ethnic groups, and populations with behavioral risks and substance use. Additionally, OAR engages with scientists, clinicians, and members of the community affected by HIV to identify emerging research priorities and unmet scientific needs. Multisectoral outreach aims to ensure that the NIH HIV/AIDS research program is responsive to the needs of the HIV community, while focusing on scientific discoveries needed to prevent, treat, and cure HIV. In response, OAR is expanding its four Signature Programs that foster collaborative and multidisciplinary research initiatives:

- *HIV & Aging:* In 2021, more than half of all people with HIV in the United States were age 50 or older.[448] People with HIV experience age-related comorbidities, some of which are exacerbated by long-term use of ART. They are more likely than their peers without HIV to experience certain age-related conditions—such as frailty, neurocognitive decline, cardiovascular disease, metabolic disorders, and some cancers—and some at younger ages than those without HIV.[449] NIH supports basic, translational, and clinical research to increase understanding, prevention, and management of comorbidities in people aging with HIV. OAR organized two events to increase further research on HIV and Aging in 2023, including a multisectoral panel discussion as part of the U.S. Conference on HIV/AIDS. OAR also is currently working with NIH Institutes, Centers, and Offices (ICOs) to develop a coordinated agency-wide HIV and aging research agenda.

[445] state.gov/pepfar-latest-global-results-factsheet-dec-2023/
[446] state.gov/pepfar-latest-global-results-factsheet-dec-2023/
[447] unaids.org/en/resources/documents/2023/global-aids-update-2023
[448] cdc.gov/hiv/library/reports/hiv-surveillance/vol-34/
[449] clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/hiv-and-older-person

- *HIV & Women:* Women—particularly women of color, young women, and transgender women—remain disproportionately affected by HIV.[450] OAR has partnered with the Office of Research on Women's Health to promote the inclusion of women's health issues throughout the lifespan of all women with or impacted by HIV in the HIV/AIDS research agenda. NIH also supports career development for women in HIV/AIDS research, as described in the program portrait below.

- *Advancing Technologies to Improve HIV Diagnosis and Care:* There is a significant need for affordable, self-administered, and easy to use U.S. Food and Drug Administration (FDA)-approved diagnostics for HIV testing and monitoring of HIV viral load (level of virus in blood). These products could facilitate earlier diagnosis and lead to faster treatment initiation. They also could allow ongoing monitoring of treatment effectiveness to foster better adherence to ART that would improve the health of people with HIV and help reduce transmission of HIV to others. This signature program, which leverages lessons learned from the COVID-19 pandemic and NIH's Rapid Acceleration of Diagnostics (RADx) initiative,[451] may lead to fast-track development and delivery of diagnostic and self-monitoring tools that ultimately could help increase autonomy, mitigate stigma, reduce costs, improve the health of people with HIV, and save lives. In November 2023, OAR organized a workshop to solicit community, regulatory, academic, and industry input in identifying cutting-edge opportunities to advance the next generation of HIV diagnostic technologies.

- *Early Career HIV Investigators:* NIH is committed to supporting a diverse early career workforce. Since 2022, OAR has collaborated with other ICOs to host an annual professional development workshop for early career investigators interested in HIV/AIDS research. The workshops provide an opportunity to establish mentorship and networking connections and to share information about the NIH HIV/AIDS research program, funding opportunities, and the grant application process. Resources are available on OAR's Early Career Investigator Resources webpage.[452]

Addressing HIV-related health disparities

Disparities by race, ethnicity, gender, and sexual orientation operate in conjunction with other social and structural factors that increase the risk of HIV acquisition and adverse health outcomes for people with HIV. These social determinants of health interact to create syndemics (synergistic epidemics) of HIV, substance use disorder, sexually transmitted infections, viral hepatitis, violence, and mental health issues. A syndemic approach can facilitate the study of co-occurring conditions and the social factors that amplify morbidity and perpetuate health disparities to inform the development of safe, effective, and equitable, combination and multilevel HIV prevention, treatment, and care interventions.

Many new HIV infections in the United States occur in men who have sex with men and bisexual Black or African American and Hispanic or Latino men, particularly those living in

[450] unaids.org/en/resources/fact-sheet
[451] nih.gov/research-training/medical-research-initiatives/radx
[452] oar.nih.gov/nih-hiv-research-program/hiv-early-career-resources

high HIV prevalence areas in the U.S. South.[453] In combination, social justice and structural issues, including systemic racism and racialized stigma, create inequities that limit access to care. In Appalachia, the spread of the opioid epidemic during the last two decades has led to an increase in use of injected drugs and in transmission of HIV and hepatitis B and C viruses among people who inject drugs. To improve the health and well-being of all people with HIV and those vulnerable to acquiring it, OAR encourages a combination of biomedical, behavioral, and social sciences research to address the multiple interrelated factors at the individual, relational, community, and societal levels affecting people's ability to prevent, diagnose, and treat HIV.

In the United States, more than half of new HIV diagnoses are concentrated in 50 local areas and jurisdictions (48 counties; Washington, D.C.; and San Juan, Puerto Rico).[12] Focusing on these areas and the 7 states with a substantial rural burden, the *Ending the HIV Epidemic* (EHE) *in the U.S.* initiative was launched in 2019 to reduce new HIV infections by 75 percent by 2025 and 90 percent by 2030.[454] NIH supports the EHE initiative by funding implementation research in geographic areas disproportionately affected by HIV, often focusing on minoritized populations who are at highest risk of HIV acquisition. Specifically, OAR coordinates across NIH to fund new research projects at existing Centers for AIDS Research (CFARs) and AIDS Research Centers (ARCs). Some of these Centers now serve as regional hubs supporting implementation research. These EHE-related projects involve collaborations with local groups and institutions to explore which interventions are most effective. This work at the community level is founded on the four pillars of the EHE strategy—diagnose, treat, prevent, and respond—to end the HIV epidemic in the United States.

For almost four decades, OAR has built strong partnerships with other government agencies, academia, and communities affected by HIV to catalyze, coordinate, and communicate HIV/AIDS research. These vital partnerships have facilitated the translation of biomedical, behavioral, and social sciences research into HIV prevention, treatment, and care strategies and have stimulated innovation in the global fight against the HIV/AIDS pandemic. Although signs of progress are evident, steadfast support will be critical to sustain current gains and continue to save lives globally. Continued investment will be vital for NIH to achieve our aspirational goals to eliminate HIV transmission in areas of high incidence and prevalence, to revolutionize the care of people with HIV—including finding a safe and scalable cure from lifelong infection—and to bring an end to the HIV/AIDS pandemic.

[453] cdc.gov/hiv/group/index.html
[454] cdc.gov/endhiv/about-ehe/index.html

National Institutes of Health
Office of AIDS Research

Mission: The mission of the Office of AIDS Research (OAR) is to ensure that NIH HIV/AIDS funding is directed at the highest priority research areas and to facilitate maximal return on the investment.

Background and History

NIH provides the largest public investment in HIV/AIDS research in the world. The program spans nearly every area of medicine and scientific investigation. NIH HIV/AIDS research has helped turn HIV from a once-fatal disease into a manageable chronic condition with effective treatment.

In 1988, Congress authorized OAR to oversee, coordinate, and manage the NIH HIV/AIDS research portfolio. A component of the Office of the NIH Director, OAR coordinates NIH funding for HIV research. OAR collaborates across the U.S. government and with researchers, community groups, and global partners to identify priorities for HIV and HIV-related research.

Diana Finzi, Ph.D., M.P.H.
Acting Associate Director for AIDS Research and Acting Director of the Office of AIDS Research, NIH

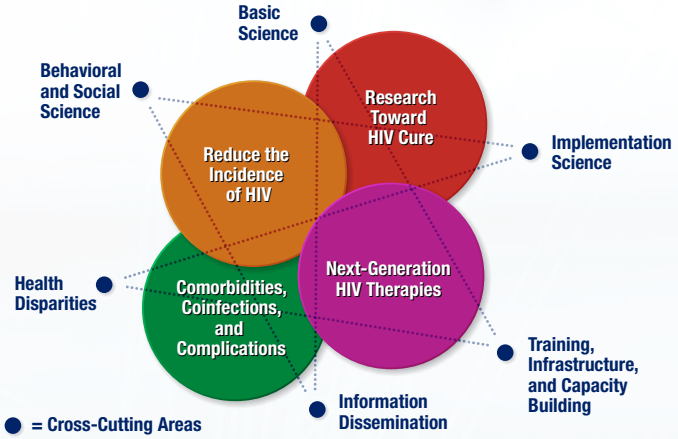
Facts & Figures

- An estimated **1.2 million** people in the United States had HIV at the end of 2021, with more than 50% over the age of 50.
- **6.9%** of the FY 2023 NIH budget was directed at HIV/AIDS funding, supporting around **3,800** HIV/AIDS research projects.
- **23** NIH Institutes, Centers, and Offices received HIV/AIDS funding in FY 2023.
- NIH HIV/AIDS research has informed efforts to reduce the burden of cancer, hepatitis, COVID-19, and many other diseases and conditions.

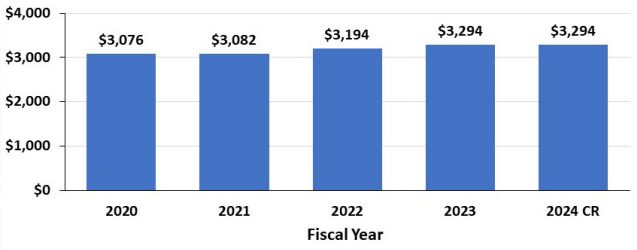
Research Highlights

- Daily statin medication reduces heart disease risk among adults with HIV by 35%.
- Long-acting antiretroviral therapy is safe and effective for people experiencing unstable housing, mental illnesses, substance use disorders, and those who encounter many barriers to treatment.
- Neurocognitive decline in people with HIV is linked to comorbidities, not HIV itself.
- The dapivirine vaginal ring protects women from HIV infection and offers a discreet, long-acting alternative to oral PrEP.
- Newly developed technology identified a profile of cells harboring latent HIV, further enhancing development of HIV cure strategies.

NIH Priorities for HIV and HIV-Related Research



NIH HIV/AIDS Funding: FY 2020–2024



The FY 2025 President's Budget request for the NIH HIV/AIDS research program is $3.294 billion, as was the FY2023 Final Level.

Recent Accomplishments

HIV Clinical Practice Guidelines: OAR coordinates development of federally approved treatment guidelines for HIV and AIDS. Posted on Clinicalinfo.HIV.gov, the guidelines provide current evidence-based standards of care for use by U.S. health care practitioners and inform audiences around the world. An important update this year clarified how to minimize risk from breastfeeding for people with HIV.

Early Career Investigators (ECI) Workshop: As part of OAR's ongoing efforts to increase the number and diversity of young investigators in the field, OAR hosted its second virtual workshop for ECIs with interests in HIV/AIDS research to enhance skills and knowledge for career development and identify funding opportunities in 2023. More than 200 people from 59 institutions across 20 countries attended.

OAR Data Hub: OAR launched the NIH OAR Data Hub, a public resource that leverages and synthesizes publicly available data to promote greater understanding of HIV/AIDS research at NIH and to enable public audiences to identify relevant awards.

Current Activities

HIV & Aging Signature Program: OAR launched a signature program on HIV & Aging to address the unique needs of a population aging with HIV and to catalyze interdisciplinary research and training at the intersection of HIV and aging. Events, resources, and funding opportunities are available on OAR's website.

HIV & Women Signature Program: OAR partnered with the Office of Research on Women's Health to launch the HIV and Women Signature Program. The program will stimulate research to address the disproportionate impact of HIV on women and girls. Events, resources, and funding opportunities are available on OAR's website.

Future Initiatives

Strategic Planning: OAR is preparing to update the *NIH Strategic Plan for HIV and HIV-Related Research* for a release in FY 2026. This update offers the opportunity to review current HIV/AIDS research priorities and ensure that resources are optimized to meet emerging needs.

Advancing Technologies for HIV Diagnosis and Care Signature Program: Affordable and accessible HIV testing and viral load monitoring are critical to prevent, care for, and treat HIV and AIDS. OAR is establishing a new program to accelerate the development of HIV diagnostics and health monitoring technologies. As a first step, OAR organized a workshop in November 2023 to gather public input on the best path forward.

Pharmacy-based HIV Care: The *National HIV/AIDS Strategy for the United States (2022–2025)* recognizes the importance of pharmacies and pharmacists in making HIV care more accessible and improving population health. OAR is exploring opportunities to facilitate effective pharmacy-based delivery and support of HIV-related prevention, testing, and treatment services.

HIVinfo.NIH.gov

OAR manages HIV Info, an online resource offering up-to-date HIV/AIDS information to the general consumer, people with HIV and AIDS, people recently diagnosed and those who care for them.

CLINICAL INFO HIV.gov

OAR manages Clinical Info, which offers access to the latest, federally approved HIV/AIDS medical practice guidelines, an HIV drug database, a glossary of HIV-related terms, and resources related to HIV-related research for health care providers, researchers, people affected by HIV/AIDS, and the general public.

BUDGET POLICY STATEMENT

Budget Policy Statement

The FY 2025 President's Budget request for the NIH-wide HIV/AIDS research program is $3,294.0 million, equal to the FY 2023 Final level. Funding at this level will expedite NIH efforts to end the HIV epidemic in the United States and globally; expand HIV prevention, treatment and cure strategies; and address the consequences of aging with HIV. NIH will continue to leverage HIV research and infrastructure to respond to public health needs, engage with early-career investigators (ECIs), as well as established investigators, to develop effective approaches for diversifying the HIV research workforce, and prioritize research training and development across the NIH Institutes, Centers, and Offices to expand the pool of ECIs in HIV research. NIH will capitalize on the use of new technologies and platforms and will continue the critical examination of health disparities in research and medicine. NIH will continue to advance dissemination and implementation research and strategies to identify efforts to optimize effective HIV prevention and treatment strategies to develop and implement effective community outreach and communication strategies.

BUDGET AUTHORITY BY INSTITUTE, CENTER, AND OFFICE

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NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Institute, Center, and Office
(Budget Authority in Thousands of Dollars)

Institute, Center, and Office	FY 2023 Final[1]	FY 2024 Continuing Resolution	FY 2025 President's Budget	FY 2025 +/- FY 2023
NCI	$256,734	$259,652	$256,734	$0
NHLBI	92,953	90,140	92,953	0
NIDCR	20,174	20,199	20,174	0
NIDDK	38,699	36,322	38,699	0
NINDS	41,206	45,713	41,206	0
NIAID	1,911,364	1,911,991	1,911,364	0
NICHD	152,881	154,175	152,881	0
NEI	-	413	-	0
NIEHS	5,512	5,684	5,512	0
NIA	28,538	24,071	28,538	0
NIAMS	4,875	2,701	4,875	0
NIDCD	2,262	2,265	2,262	0
NIMH	199,584	195,774	199,584	0
NIDA	278,533	277,863	278,533	0
NIAAA	35,219	33,921	35,719	500
NINR	17,375	17,397	17,375	0
NHGRI	824	3,514	-	-824
NIBIB	1,954	1,956	1,954	0
NIMHD	24,982	24,239	24,982	0
NCCIH	689	796	796	107
FIC	25,919	25,951	25,919	0
NLM	7,685	9,919	7,685	0
OD	146,038	149,344	146,255	217
OAR	*67,589*	*66,243*	*67,806*	*217*
ORIP	*78,449*	*83,101*	*78,449*	*0*
TOTAL, NIH	**$3,294,000**	**$3,294,000**	**$3,294,000**	**$0**

[1]Reflects HIV/AIDS transfers under the authority of Section 213 of the Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Act, 2023

BUDGET MECHANISM TABLE

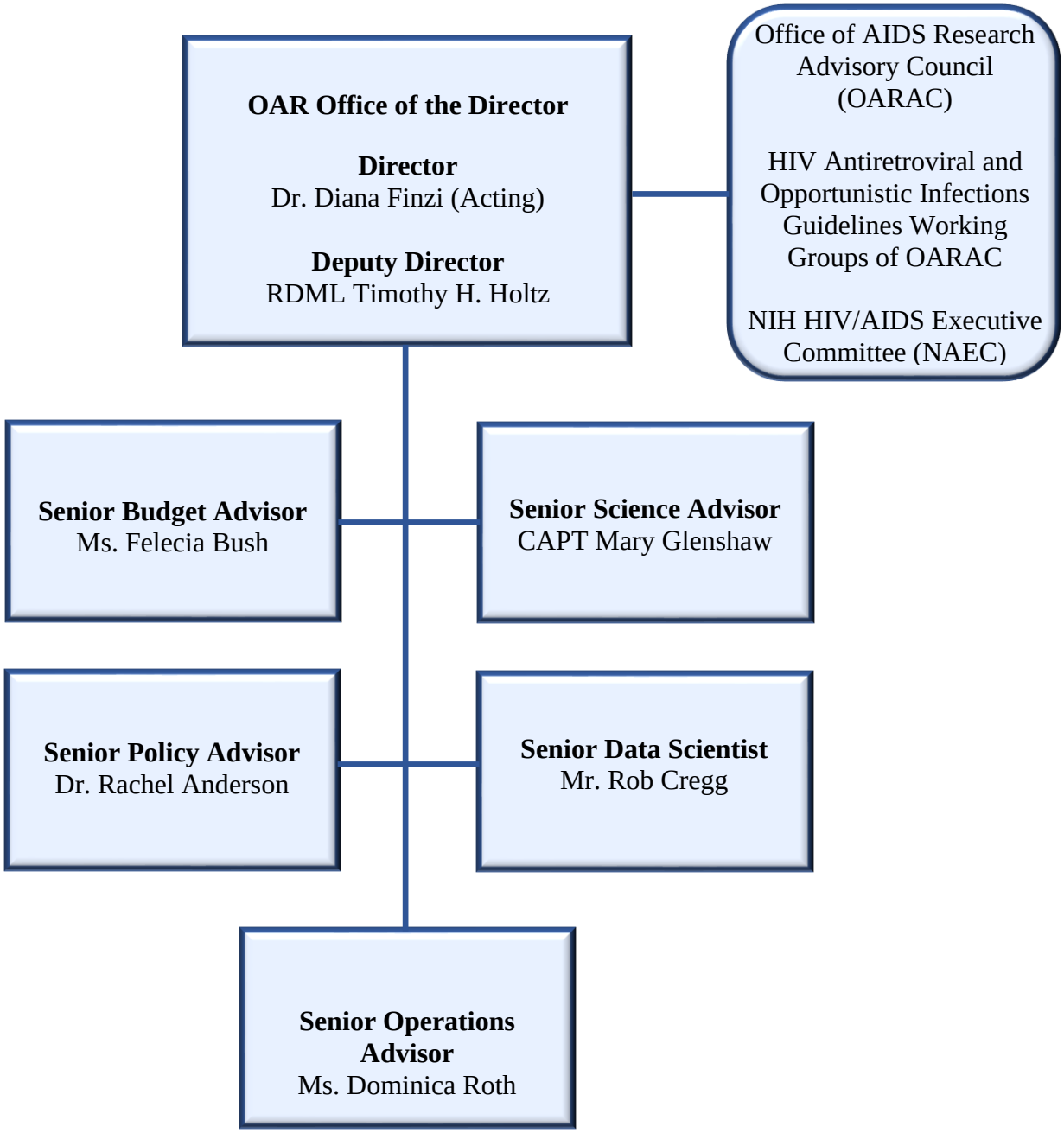
NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Mechanism - AIDS[1]
(Dollars in Thousands)

Mechanism	FY 2023 Final		FY 2024 C.R.		FY 2025 President's Budget		FY 2025 +/- FY 2023	
	No.	Amount	No.	Amount	No.	Amount	No.	Amount
Research Projects:								
Noncompeting	1,403	$1,496,895	1,402	$1,489,520	1,301	$1,405,577	-101	-$91,318
Administrative Supplements	*124*	25,051	*78*	15,678	*88*	17,594	*(10)*	-7,457
Competing	457	296,982	436	287,588	542	364,457	106	67,475
Subtotal, RPGs	1,860	$1,818,928	1,838	$1,792,786	1,843	$1,787,628	5	-$31,300
SBIR/STTR	21	12,650	24	15,018	24	15,173	0	2,523
Research Project Grants	1,881	$1,831,578	1,862	$1,807,804	1,867	$1,802,801	5	-$28,777
Research Centers:								
Specialized/Comprehensive	68	$160,945	65	$160,414	64	$154,416	-1	-$6,529
Clinical Research	0	0	0	0	0	0	0	0
Biotechnology	0	0	1	1,500	0	0	-1	0
Comparative Medicine	36	70,023	19	72,399	19	70,142	0	119
Research Centers in Minority Institutions	0	0					0	0
Research Centers	104	$230,968	85	$234,313	83	$224,558	-2	-$6,410
Other Research:								
Research Careers	252	$43,499	236	$41,672	237	$41,202	1	-$2,297
Cancer Education	0	0	0	0	0	0	0	0
Cooperative Clinical Research	20	13,443	20	13,283	20	12,802	0	-641
Biomedical Research Support	0	1,904		2,500		2,001	0	97
Minority Biomedical Research Support	0	0	0	0	0	0	0	0
Other	124	62,723	130	61,384	135	65,270	5	2,547
Other Research	396	$121,569	386	$118,839	392	$121,275	6	-$294
Total Research Grants	2,381	$2,184,115	2,333	$2,160,956	2,342	$2,148,634	9	-$35,481
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs			
Individual Awards	81	$3,588	66	$3,130	77	$3,644	11	$56
Institutional Awards	254	15,251	236	16,144	242	16,680	6	1,429
Total Research Training	335	$18,839	302	$19,274	319	$20,324	17	$1,485
Research & Develop. Contracts	85	$474,713	119	$492,745	119	$498,610	0	$23,897
(SBIR/STTR) (non-add)	*7*	*3,932*	*7*	*4,226*	*7*	*4,226*	*(0)*	*294*
Intramural Research		$362,982		$364,358		$366,113		$3,131
Res. Management and Support		185,762		190,424		192,513		6,751
Res. Management & Support (SBIR Admin) (non-add)		*0*		*0*		*0*		0
Office of the Director - Appropriation [2]		*146,038*		*149,344*		*146,255*		217
Office of the Director - Other		67,589		66,243		*67,806*		217
ORIP (non-add) [2]		*78,449*		*83,101*		*78,449*		0
Total, NIH Discretionary B.A.		**$3,294,000**		**$3,294,000**		**$3,294,000**		**$0**

[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.

ORGANIZATION CHART



BUDGET AUTHORITY BY ACTIVITY TABLE

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research
Budget Authority by Activity
(Dollars in Thousands)

[1]/ Reflects effects of Secretary's transfer

Research Priorities	FY 2021 Actual [1]	FY 2022 Final	FY 2023 Enacted	FY 2024 C.R.	FY 2025 President's Budget	FY 2025 +/- FY 2023
Reduce the Incidence of HIV	$684,570	$689,324	$690,815	$674,410	$674,410	-$16,405
Develop Next-Generation HIV Therapies	331,927	348,034	355,904	363,467	363,467	$7,563
Research Toward a Cure for HIV	224,737	223,450	229,925	230,732	230,732	$807
Address HIV-Associated Comorbidities, Coinfections, and Complications	560,766	630,948	664,765	665,668	665,668	$903
Cross-Cutting Areas	1,279,897	1,302,244	1,352,591	1,359,723	1,359,723	$7,132
Total	**$3,081,897**	**$3,194,000**	**$3,294,000**	**$3,294,000**	**$3,294,000**	**$0**

Office of AIDS Research

Budget Authority (BA):

	FY 2023 Final	FY 2024 CR	FY 2025 President's Budget	FY 2025 +/- FY 2023
BA	$3,294,000,000	$3,294,000,000	$3,294,000,000	$0

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

Overall Budget Policy: The FY 2025 President's Budget request for the Office of AIDS Research (OAR) is $3.294 billion, which is equal to the FY 2023 Final level. This level of funding will support the priorities of the NIH HIV research agenda, as described below, namely to reduce the incidence of HIV; develop next-generation HIV therapies; support research toward a cure; address HIV-associated comorbidities, coinfections, and complications; and advance cross-cutting areas of research in the basic sciences, behavioral and social sciences, epidemiology, implementation science, information dissemination, and research training.

Program Descriptions

Reduce the Incidence of HIV

Despite the available tools to prevent HIV transmission, more than one million people acquire HIV each year worldwide. In the United States and its dependent areas, 36,136 people received an HIV diagnosis in 2021.[455] Individuals from sexual and gender minority communities have the highest rates of infection. Both access and adherence to a daily medication for pre-exposure prophylaxis (PrEP) remains an issue for many in the United States and globally. To address these challenges, NIH is supporting research to develop more convenient HIV prevention approaches that can be long-acting or used intermittently when needed.

Using a syndemic framework is crucial to develop better prevention approaches adapted to the needs of each community. Ongoing research continues to investigate novel antiretroviral formulations and to identify barriers to successful implementation of HIV prevention and treatment in communities that urgently need these tools. For example, a vaginal ring that releases the antiretroviral drug dapivirine for 28 days can protect women from HIV acquisition. It offers a discreet, long-acting alternative to oral PrEP. Recent NIH-supported research showed the ring is safe and effective during late pregnancy and breastfeeding.[456] The HIV Prevention

[455] cdc.gov/hiv/basics/statistics.html
[456] pubmed.ncbi.nlm.nih.gov/37432541/

Trials Network is studying the long-acting injectable PrEP formulation containing the antiretroviral cabotegravir, which reduces the risk of sexually acquired HIV with injections every other month.[457] The recent Food and Drug Administration (FDA) approval of this long-acting PrEP is critical to address the global HIV/AIDS pandemic, protecting people for whom access or adherence to a daily medication is a major challenge.

NIH supports research to better understand the barriers to HIV prevention uptake in various communities. The NIH-supported International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) and the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) evaluate interventions to prevent and treat HIV in infants, children, adolescents, and pregnant/postpartum people, including the elimination of perinatal transmission. They conduct independent and collaborative research exploring promising prophylactic, behavioral, microbicidal, and vaccine modalities. The Prevention And Treatment through a Comprehensive Care Continuum for HIV-affected Adolescents in Resource Constrained Settings ($PATC^3H$) consortium was expanded to strengthen the scientific innovation that will yield effective public health interventions for adolescents and young adults in low-to-middle income countries. To address the disproportionate burden of HIV infection on sexual and gender minority populations, NIH is launching a new initiative[458] to support epidemiologic, intervention, and implementation research to identify focused approaches to reduce the number of new HIV infections among these groups. NIH continues to encourage research to develop innovative multipurpose prevention technologies (MPT) that simultaneously prevent HIV and pregnancy or sexually transmitted infections in cis and trans men and women of all ages.[459] To optimize uptake, MPT will have to be convenient and as safe and effective as each of its component medicines.

Ultimately, ending the global HIV/AIDS pandemic likely will require a safe and effective HIV vaccine. Vaccines work by inducing the immune system to make antibodies that can neutralize (kill) a particular pathogen. The ability of HIV to mutate rapidly has been challenging, and the immune system only rarely makes broadly neutralizing antibodies (bNAbs) that are effective in protecting against a wide range of HIV variants. Recent studies[460] have established the safety of an experimental HIV vaccine candidate that stimulates a rare type of immune B cell that is capable of producing bNAbs. This vaccine is intended to be the first part of a multistep vaccination regimen. A different vaccine candidate, called VIR-1388, is being tested in one of the NIH-supported clinical trial networks. This Phase 1 trial[461] will examine the safety of VIR-1388 and its ability to induce an immune response against HIV in people in the United States and South Africa. In addition, NIH is interested in projects that examine how to develop immunity to HIV early in life to harness young children's more adaptable and efficient immune systems.

Budget Policy: The FY 2025 President's Budget request to promote research to reduce HIV incidence is $674.4 million, a decrease of $16.4 million or -2.4 percent compared to the FY 2023 Final level.

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[457] pubmed.ncbi.nlm.nih.gov/34379922/; pubmed.ncbi.nlm.nih.gov/35378077/
[458] grants.nih.gov/grants/guide/rfa-files/RFA-DA-25-002.html
[459] grants.nih.gov/grants/guide/pa-files/PAR-22-222.html
[460] hiv.gov/blog/encouraging-first-in-human-results-for-a-promising-hiv-vaccine/; nih.gov/news-events/nih-research-matters/progress-toward-eventual-hiv-vaccine
[461] nih.gov/news-events/news-releases/clinical-trial-hiv-vaccine-begins-united-states-south-africa

Advancing Research on HIV and Women

Notwithstanding tremendous advances in HIV research over the last 40 years, women—particularly women of color, young women, and transgender women—remain disproportionately affected by HIV. Focused research initiatives are critical to better understanding optimal ways to prevent, treat, and cure HIV and associated comorbidities across women's lifespans.

In February 2023, OAR, and the Office of Research on Women's Health (ORWH) launched the HIV and Women Signature Program to advance research on HIV and women's health. The program contributes to achieving the NIH vision of a world in which all women—including cisgender, transgender, and gender-diverse women, as well as people assigned female at birth—receive evidence-based prevention, and treatment tailored to their unique needs, circumstances, and goals.

OAR and ORWH organized multiple research and community engagement events in FY 2023. A research symposium highlighted innovative, multidisciplinary research to address the health of women with or affected by HIV to identify the highest research priorities and the most impactful ways for NIH to advance women-centered HIV/AIDS research. To gather additional feedback from community members and federal partners, OAR and ORWH organized a workshop on HIV and Women at the 2023 U.S. Conference on HIV/AIDS. A recent funding opportunity announcement encourages research to improve uptake and equitable implementation of HIV prevention for women.

Ongoing activities of the Signature Program will inform women-centered HIV/AIDS research and be incorporated in the next NIH Strategic Plan for HIV and HIV-Related Research to ensure that research will improve the lives of all women and girls with or affected by HIV worldwide.

Develop Next Generation HIV Therapies

NIH continues to support research on new long-acting HIV treatments with fewer side effects, as well as novel formulations and delivery methods to improve efficacy of and support adherence to HIV medications. Innovative biological products, such as bNAbs engineered to destroy HIV-infected cells, could revolutionize HIV treatment and prevention strategies. Clinical trials have established that bNAbs are safe and can prevent infection and maintain viral suppression in people with different strains of HIV that are sensitive to these bNAbs.[462] NIH is supporting projects to design and evaluate bNAbs or similar antibody-like agents that could treat a broad range of HIV strains.

Injections of two existing antivirals, cabotegravir and rilpivirine, are the only long-acting antiretroviral therapy (ART) FDA-approved for people with HIV. NIH-supported research showed[463] that these novel therapeutics can be helpful to engage adults with HIV with high rates of unstable housing, mental illness, and substance use—people who historically have had challenges accessing effective treatment. Overall, nearly 98 percent of individuals in the study achieved viral suppression, a rate similar to that in more controlled clinical trials.

New products and delivery platforms are being tested to facilitate use in specific populations, such as children, adolescents, or pregnant and postpartum people. A recent study demonstrated the promise of dissolving patches[464] for intradermal delivery of long-acting ART for pediatric HIV. This approach would be less painful and safer than intramuscular injections, enabling the use of long-acting ART in children. A new type of antiretroviral, lenacapavir, is in development as a

[462] pubmed.ncbi.nlm.nih.gov/33730454/; pubmed.ncbi.nlm.nih.gov/35650437/; pubmed.ncbi.nlm.nih.gov/35418681/
[463] pubmed.ncbi.nlm.nih.gov/37399555/
[464] pubmed.ncbi.nlm.nih.gov/36224503/

long-acting agent to treat or prevent HIV. As lenacapavir acts via a different mechanism from existing ART, a trial[465] demonstrated that adding lencapavir to an optimized ART regimen was safe and effectively treated people with multidrug-resistant HIV.

Budget Policy: The FY 2025 President's Budget request to support research to develop next-generation HIV therapies is $363.5 million, an increase of $7.6 million or 2.1 percent compared to the FY 2023 Final level.

Research Toward HIV Cure

Groundbreaking research advances in HIV treatment have helped turn HIV into a manageable condition. These advances, however, do not obviate the need for a cure, which, while theoretically feasible, is not yet available. To work towards a cure for HIV, NIH supports studies to develop novel approaches and treatments that target HIV reservoirs. HIV can hide from the immune system by staying dormant in certain cells to constitute a latent viral reservoir. These cells, infected with HIV but not actively producing new virus, are usually located in areas such as the nervous system, which are protected from the immune system and ART.

The initiation of ART within the first few weeks of HIV infection has been associated with the development of a smaller latent reservoir. Accordingly, NIH is encouraging research to explore novel strategies designed to limit the establishment of the HIV reservoir around the time of ART initiation.[466] NIH-supported research continues to investigate the nature of HIV reservoirs and viral remission. For example, NIH is aiming to stimulate research[467] into more efficient bNAbs and other products that can seek out and destroy sufficient numbers of HIV-infected cells to reduce the existing HIV reservoir. This approach could enable people to maintain viral suppression without ongoing treatment, leading to a functional cure.

Current scientific findings suggest that the first step toward a potential HIV cure may require viral remission (a state in which the virus is suppressed without ART), also known as a functional cure. Potential cure-inducing treatments must be as safe, effective, and available for widespread use as today's ART regimens. Viral eradication, or elimination of the virus entirely, is a more challenging, longer-term goal. Integration of real-time, rapid viral load monitoring with analytical treatment interruption may also enable clinical evaluation of promising new approaches to achieving a functional cure for HIV.

NIH also supports studies that investigate the social, behavioral, and bioethical issues associated with HIV cure research. Current studies focus on topics such as study participant representation and diversity in HIV cure research, attitudes toward analytical treatment interruption, partner protection from HIV acquisition in cure trials, and other ethical considerations.

Budget Policy: The FY 2025 President's Budget request to promote research toward an HIV cure is $230.7 million, an increase of $0.8 million or 0.4 percent compared to the FY 2023 Final level.

[465] pubmed.ncbi.nlm.nih.gov/37451297/
[466] grants.nih.gov/grants/guide/pa-files/PAR-23-296.html
[467] niaid.nih.gov/grants-contracts/june-2023-daids-council-approved-concepts#engineering

Address HIV-Associated Comorbidities, Coinfections, and Complications

People with HIV are more likely to experience comorbidities, coinfections, and other complications across their lifespan that affect their health, well-being, and quality of life. NIH supports multiple longitudinal research cohorts that provide crucial sources of data and facilitate the long-term investigation of health conditions that impact people with HIV. For example, the Multicenter AIDS Cohort Study/Women's Interagency HIV Study Combined Cohort Study (MACS/WIHS-CSS)[468] is a collaborative research effort that focuses on the chronic health conditions—including heart, lung, blood, and sleep disorders—that affect people with HIV. The Veterans Aging Cohort Study[469] similarly examines the overall impact of HIV, HIV treatment, and comorbid conditions on morbidity and mortality. The central nervous system (CNS) HIV Anti-Retroviral Therapy Effects Research (CHARTER) cohort studies have produced a key repository containing data on neuro-medical conditions, neuropsychological assessments, psychiatric and drug use variables, treatment, neuroimaging, and viral and host genetics.

Comorbidities

People with HIV experience accelerated aging, altered metabolism, and chronic immune activation that converge and contribute to the development of several comorbidities. Comorbid conditions that disproportionately affect people with HIV include cardiovascular disease, chronic kidney disease, liver disease, frailty and reduced bone density, and cancers. Neuropsychiatric conditions, such as depression and neurocognitive disorders, also are significantly more prevalent among people with HIV than those without HIV and are associated with poor ART adherence. NIH supports multidisciplinary research to better understand and identify targets for intervention to mitigate multiple HIV-associated comorbidities.[470] For example, NIH currently is funding research projects that investigate the role of chronic immune activation and the gut microbiome in cardiovascular conditions and HIV.

The median age of people with HIV has increased in recent decades as a result of advances in HIV treatment. The increasing number of older adults with HIV poses challenges and opportunities for the treatment of HIV and HIV-associated comorbidities, coinfections, and complications across the lifespan. Similarly, people born with HIV have unique needs and challenges as they age with the virus.

Research on HIV and aging represents an active area of collaboration across NIH. NIH currently supports a number of projects through a research program for multidisciplinary studies of HIV and aging.[471] In FY 2023, increases in HIV/AIDS funding enabled expanded support for supplements for research on HIV and aging.[472] As a result, 14 awards from 6 NIH ICs were funded to expand emphasis on HIV and aging, including studies on co-occurring conditions such as neuroinflammation, cardiovascular disease, alcohol and substance use, and cognitive impairment.

[468] statepi.jhsph.edu/mwccs/about-mwccs/
[469] medicine.yale.edu/intmed/vacs/cohorts/vacsresources/
[470] grants.nih.gov/grants/guide/pa-files/PAR-21-027.html
[471] grants.nih.gov/grants/guide/pa-files/par-21-068.html
[472] grants.nih.gov/grants/guide/notice-files/NOT-AG-23-008.html

Recent advances highlight progress in addressing comorbidities in people with HIV. An NIH-supported clinical trial found that statins, a class of cholesterol-lowering medications, may offset the high risk of cardiovascular disease in people with HIV by more than a third, potentially preventing one in five major cardiovascular events or premature deaths in this population. Notably, the study population included people with low-to-moderate risk of cardiovascular disease who typically would not be prescribed statins.[473] These results will inform clinical care guidelines for people with HIV.

Results from another NIH-supported study indicated that neurocognitive decline in people with HIV may be unrelated to HIV infection, but significantly linked to comorbidities such as diabetes, hypertension, chronic pulmonary disease, frailty, and others. These findings demonstrate exacerbating indirect effects of multiple comorbidities that disproportionately affect people with HIV and underscore the importance of managing these (often treatable) conditions.[474]

Coinfections

Tuberculosis (TB), hepatitis, and sexually transmitted infections are common coinfections that affect the health and well-being of people with HIV of all ages.[475] Globally, TB is the leading cause of death for people with HIV.[476] In the United States, an estimated 10 percent of people with HIV have hepatitis B, and approximately 21 percent have hepatitis C. Hepatitis B and C progress faster and cause higher rates of mortality in people with HIV than in those without HIV.[477]

To improve the health of people with HIV and coinfections, NIH continues to support research on the mechanisms of and interventions for HIV-associated coinfections. NIH is soliciting research proposals to develop safe and effective treatments for TB specifically for people with HIV, as well as proposals to address the unique challenge of curing hepatitis B in people with HIV.[478] NIH is also encouraging research to develop and evaluate new models of care that integrate HIV, hepatitis B and C, addiction, and primary care services.[479]

Among people with HIV who also have TB and/or hepatitis, successful completion of prolonged multidrug regimens for each condition is significantly linked to improved health. Accordingly, NIH supports research to develop sustained release/long-acting drug delivery systems that require less frequent administration, potentially supporting improved adherence to the treatment regimens.[480]

Understanding how comorbidities and coinfections that are prevalent in people with HIV interact with HIV viral reservoirs represents another area for future investigation. Due to emerging evidence that co-occurring conditions impact the HIV reservoir in ways that may interact with

[473] nhlbi.nih.gov/news/2023/daily-statin-reduces-heart-disease-risk-among-adults-living-hiv
[474] pubmed.ncbi.nlm.nih.gov/36477867/
[475] aidsinfo.unaids.org/
[476] pubmed.ncbi.nlm.nih.gov/30897077/
[477] hiv.gov/hiv-basics/staying-in-hiv-care/other-related-health-issues/hepatitis-b-and-c/
[478] grants.nih.gov/grants/guide/notice-files/NOT-AI-22-043.html
[479] grants.nih.gov/grants/guide/rfa-files/RFA-DA-25-020.html
[480] grants.nih.gov/grants/guide/notice-files/NOT-AI-22-042.html

potential cure strategies,[481] future research on HIV reservoirs will need to investigate the impact of inflammation, altered metabolism, or other biological processes associated with prevalent comorbidities or coinfections.

Health conditions that co-occur with HIV interact with behavioral, economic, and environmental factors that influence the HIV/AIDS pandemic. Current NIH-supported projects are investigating interactions between HIV, co-occurring conditions, and other mitigating factors including substance use, polypharmacy, violence, sleep disruptions, and several social and structural determinants of health related to HIV prevention and treatment. Continued investment is needed to advance HIV/AIDS research on co-occurring conditions using a syndemic approach.[482]

Budget Policy: The FY 2025 President's Budget request to support research to address HIV-associated comorbidities, coinfections, and complications is $665.7 million, an increase of $0.9 million or 0.1 percent compared to the FY 2023 Final level.

Cross-Cutting Areas

NIH supports basic, foundational science to drive the discovery, development, and evaluation of novel HIV prevention, treatment, and cure strategies. The HIV/AIDS basic research agenda promotes advances in virology, immunology, and mechanisms of viral persistence. Basic research on the structural biology of the HIV capsid protein core provided the foundation for development of lenacapavir, the first capsid inhibitor approved by the FDA for treatment of HIV infection. A recent preclinical study showed that blocking an enzyme involved in forming HIV particles stopped the virus from becoming infectious, suggesting a possible new target for treating HIV infection.[483]

NIH supports behavioral and social sciences research to better understand and address the behavioral factors and social contexts that have an impact on HIV prevention, care, treatment, and cure. A recent study conducted in young adults with perinatally acquired HIV found that individuals who reported average or high levels of social support were more likely to maintain viral suppression than those with limited social support.[484] Behavioral and social sciences research also investigates the social determinants of health that influence well-being and quality of life. Recent research demonstrated that intersectional stigma and discrimination are factors that can discourage HIV testing, reduce engagement and retention in HIV prevention and care services, and result in worse health outcomes for women with HIV.[485] NIH continues to support research that investigates the mechanisms and pathways by which intersectional stigma and discrimination, or other social and structural determinants of health interact to affect HIV prevention and treatment outcomes.

[481] niddk.nih.gov/about-niddk/advisory-coordinating-committees/national-diabetes-digestive-kidney-diseases-advisory-council/concept-clearances/may-2023/impact-comorbidities-co-infections-hiv-reservoirs
[482] grants.nih.gov/grants/guide/rfa-files/RFA-HL-21-018.html; grants.nih.gov/grants/guide/rfa-files/RFA-DA-25-002.html; grants.nih.gov/grants/guide/pa-files/PAS-23-172.html
[483] nimh.nih.gov/news/science-news/2023/blocking-hiv-enzyme-reduces-infectivity-and-slows-viral-rebound
[484] nichd.nih.gov/newsroom/news/071723-HIV-social-support
[485] pubmed.ncbi.nlm.nih.gov/35876640/

To optimize the public health impact of HIV/AIDS research, scientific findings must be implemented in clinical and community practice and disseminated to people affected by HIV. NIH encourages research on information dissemination and health communication strategies to promote public understanding, acceptance, and uptake of effective HIV-related interventions. NIH also supports research to identify and address HIV service gaps, reduce HIV-related health disparities, and contain HIV outbreaks in defined populations or geographic regions. Implementation science can identify strategies to increase real-world adoption of evidence-based interventions to close the science-to-service gap. A recent NIH-funded study found that mobile integrated harm reduction services (i.e., provision of PrEP, medications for opioid use disorder, and syringe exchange within a mobile unit) represent an acceptable venue to deliver HIV prevention services to African American/Black people who inject drugs.[486]

NIH is currently developing a new implementation science network to build on the success of the PATC^{3}H research program.[487] The Network will expand the achievements of PATC^{3}H to new geographic settings, stimulating implementation science research to prevent HIV acquisition among at-risk adolescent populations, and to promote long-term viral suppression among youth with HIV in low-to-middle income countries. The first group of awards for this network were funded in FY 2023.

NIH also addresses HIV health care service gaps through a new initiative to stimulate research on decentralizing these services to increase access to and capacity for routine delivery of HIV testing, prevention, and care services through pharmacies. Pharmacies are often seen as places where people can go for health care without feeling judged or stigmatized, and they offer more convenient access through longer hours and more locations in communities affected by HIV. NIH convened a meeting in July 2023 to identify barriers to delivering HIV-related services in pharmacies to generate research questions, and efforts are underway to develop new implementation science funding opportunities in this research area.

Capacity-building and strengthening activities represent another cross-cutting area within the HIV/AIDS research portfolio. NIH supports the development, recruitment, and retention of a diverse, multidisciplinary HIV research workforce. OAR works with Institutes, Centers, and Offices (ICOs) to support initiatives for HIV researchers who are early in their careers, including those from underrepresented groups, through a variety of funding mechanisms. The NIH-funded Visiting Professors program, a career development program for scientists conducting research to reduce health disparities in HIV and sexually transmitted infections, reports that program alumni have been awarded nearly $300 million in grant funding since the program's inception in 1997.[488]

NIH also supports research infrastructure by funding renovation, equipment, and resources for facilities conducting HIV/AIDS research. OAR collaborates with ICOs to offer funding opportunities for institutions to support development or renovation of HIV/AIDS research facilities that serve underrepresented and underserved populations or are in states with historically low levels of NIH funding. These awards expand the diversity of researchers

[486] pubmed.ncbi.nlm.nih.gov/36463183/
[487] nichd.nih.gov/research/supported/PATC3H
[488] prevention.ucsf.edu/education/visiting-professor-program/accomplishments

contributing to scientific discoveries and ensure significant long-term institution-wide support for HIV/AIDS research.

Budget Policy: The FY 2025 President's Budget request to support research to address HIV/AIDS research in cross-cutting areas is $1,359.7 million, an increase of $7.1 million or 0.5 percent compared to the FY 2023 Final level.

RESOURCE SUMMARY

Drug Control Program
Department of Health and Human Services
NATIONAL INSTITUTES OF HEALTH (NIH)[1]

(Dollars in millions)

	Budget Authority		
	FY 2023 Final[2]	FY 2024 CR[3]	FY 2025 Request
Drug Resources by Function			
Research and Development: Prevention	$492.167	$492.009	$498.300
Research and Development: Harm Reduction	$187.960	$187.730	$190.253
Research and Development: Treatment	$954.055	$954.100	$951.443
Research and Development: Recovery	$104.792	$104.301	$104.246
Total, Drug Resources by Function	**$1,738.974**	**$1,738.140**	**$1,744.241**
Drug Resources by Decision Unit			
National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA)[4]			
Research and Development: Prevention	$64.682	$64.542	$64.930
Research and Development: Treatment	$10.927	$10.903	$10.969
Total, NIAAA	**$75.609**	**$75.445**	**$75.898**
National Institute on Drugs and Addiction (NIDA)[4]			
Research and Development: Prevention	$427.485	$427.467	$433.370
Research and Development: Harm Reduction	$187.960	$187.730	$190.253
Research and Development: Treatment	$943.128	$943.197	$940.474
Research and Development: Recovery	$104.792	$104.301	$104.246
Total, NIDA	**$1,663.365**	**$1,662.695**	**$1,668.343**
Total, Drug Resources by Decision Unit	**$1,738.974**	**$1,738.140**	**$1,744.241**
Drug Resources Personnel Summary			
Total FTEs (direct only)	419	445	470
Drug Resources as a Percent of Budget			
Total Agency Discretionary Budget (in Billions)[5]	$46.125	$45.447	$46.390
Drug Resources Percentage	3.77%	3.82%	3.76%

[1] Detail in this document may not sum to the subtotals and totals due to rounding.
[2] FY 2023 funding levels include HIV/AIDS transfers.
[3] FY 2024 funding levels cited in this document are based on the Continuing Resolution in effect at the time of budget preparation (Public Law 118-35) and do not include HIV/AIDS transfers.
[4] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction and to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.
[5] Excludes funding for Advanced Research Projects Agency for Health.

PROGRAM SUMMARY

MISSION

The National Institute on Drugs and Addiction (NIDA) and the National Institute on Alcohol Effects and Alcohol-Associated Disorders (NIAAA), 2 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.[489]

NIDA is the lead federal agency supporting scientific research on drug use and addiction, with the mission to apply that knowledge to improve individual and public health. NIDA supports and conducts basic and clinical research on drug use (including nicotine), addiction, overdose, and the neurobiological, behavioral, and social factors that influence drug use patterns and outcomes. 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 overdose, enhance public awareness of addiction as a brain disorder, and reduce stigma toward people with SUD.

In 2022, more than 110,000 Americans died from drug overdoses, driven in large part by synthetic opioids, stimulants, and combination drug use. While these are sobering developments, NIDA-funded research has led to life-saving treatments for SUD. For example, NIDA supported development of the first naloxone nasal spray, approved by the Food and Drug Administration (FDA) in 2015 as an effective medication to reverse opioid overdose. More recent NIDA investments helped lead to a nasal spray formulation of nalmefene, a longer-lasting opioid overdose medication, which received FDA approval in 2023. NIDA's research also has helped establish the safety and efficacy of medications that target the body's opioid signaling pathways to treat opioid use disorder (OUD).

NIDA continues to lead research advances toward additional, wider-reaching therapies for OUD and other types of SUD, and toward primary prevention of harmful substance use. The Institute is also increasing its research investments in harm reduction approaches such as community naloxone distribution, syringe services programs, and drug checking tools; and in recovery services such as residential and school-based programs. Importantly, NIDA also funds a variety of training and career development programs to support an addiction science workforce cross-trained in state-of-the-art disciplines such as data science and artificial intelligence (AI). NIDA also supports a growing number of research programs to leverage AI for understanding addiction, such as programs to characterize how neuronal ensembles encode the rewarding effects of addictive substances and to help identify potential targets for new SUD medications.

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 (AUD), across the lifespan. A major priority within NIAAA's mission is research on the prevention and treatment of underage drinking and its harmful consequences.

[489] The FY 2025 President's Budget proposes to rename the National Institute on Drug Abuse to the National Institute on Drugs and Addiction and to rename the National Institute on Alcohol Abuse and Alcoholism to the National Institute on Alcohol Effects and Alcohol-Associated Disorders.

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, 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.

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 estimates for the drug control budget 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 2025 Request for drug-related activities at NIH is $1,744.2 million ($1,668.3 million for NIDA and $75.9 million for NIAAA), $6.1 million above the FY 2024 CR level.

National Institute on Drugs and Addiction
FY 2025 Request: $1,668.3 million
($5.6 million above the FY 2024 CR level)

According to provisional data through March 2023, more than 110,000 Americans are dying from drug overdoses each year. While there are effective treatments that could have prevented many of these deaths, delivering these treatments remains a challenge. Of the 46 million people who had SUD in 2021, only about 6 percent received any treatment.[490] Another challenge is that existing treatments do not work for all people or all types of SUD; in particular, there is a need for effective medications to reduce stimulant use, which plays an increasing role in overdose deaths. Overall, these data speak to the persistent need to improve and disseminate evidence-based treatments for SUD and overdose, and to prevent SUD and harmful substance use from occurring in the first place. To that end, in the coming years, NIDA will strengthen its research investments in prevention, treatment, harm reduction, and recovery services related to substance use, in alignment with the priorities of the Office of National Drug Control Policy and with additional funding made available through the NIH Helping to End Addiction Long-term® (HEAL) Initiative.

In the prevention area, NIDA will continue working to understand risk and protective factors for substance misuse and SUD, which will enable more targeted and effective prevention programs. Research shows that adverse early childhood experiences are associated with early substance misuse, which may in turn alter brain development in ways that increase the risk of SUD in adulthood.[491] Yet, much remains to be learned about how a vast constellation of early-life experiences, combined with a person's genetic makeup, affects vulnerability to SUD and other psychiatric disorders. Led by NIDA, NIAAA, and the National Cancer Institute, the Adolescent Brain Cognitive Development (ABCD) Study is collecting brain imaging, genetic, and environmental data from more than 12,000 children aged 9-10 and following them through adulthood to help fill this knowledge gap. More recently, with funding from various Institutes and the HEAL Initiative®, the HEALthy Brain and Child Development (HBCD) Study was launched to complement the ABCD study by following brain development in thousands of children from birth through their first decade of life.

In the treatment area, it is critical to improve the reach of existing evidence-based treatments for SUD, such as medications for opioid use disorder (MOUD) including methadone, buprenorphine, and naltrexone. While MOUD can reduce opioid craving, use, and risk of overdose, they are vastly under-prescribed, especially among people of color.[492] NIDA-funded research has helped identify barriers to MOUD—such as lack of integration between primary

[490] samhsa.gov/data/release/2022-national-survey-drug-use-and-health-nsduh-releases
[491] pubmed.ncbi.nlm.nih.gov/29690790/
[492] pubmed.ncbi.nlm.nih.gov/31066881; cdc.gov/mmwr/volumes/71/wr/mm7129e2.htm

care and specialized addiction services—and is investigating approaches to overcome them and improve MOUD access. At the same time, saving lives from overdose will also require novel medications. MOUD may be less effective in treating addiction to fentanyl (which is 100 times stronger than morphine)[493] and there are no effective medications to reduce stimulant use, which is now implicated in 50 times as many fentanyl-related deaths as it was in 2010.[494] For this reason, NIDA continues to support development of novel treatments, including long-acting drug formulations, neuromodulation therapies, immunotherapies, and sequestrants designed to stop drugs from entering the brain. Since September 2019, NIDA-supported research has led to more than 50 Investigational New Drug applications and 2 Investigational Device Exemptions submitted to the FDA for evaluation in clinical trials.

NIDA also prioritizes research in harm reduction, which aims to reduce the risk of overdose and other drug-related harms—including transmission of HIV and hepatitis C virus, and risk of infections that can damage the heart. Harm reduction approaches such as syringe service programs and community naloxone distribution have been shown to reduce morbidity and mortality from substance use; drug checking tools can help people detect adulterants in drugs and take safety precautions.[495] Yet, because most harm reduction studies have focused on urban areas hit hard by the opioid crisis, there is a need to investigate these approaches in rural areas and to target unique harms from stimulants. With HEAL Initiative funding in FY 2022, NIDA launched a new research network that focuses on testing new harm reduction strategies, evaluating new ways to deliver existing strategies, and reaching underserved populations. In addition to opioids, the network is examining harm reduction strategies related to other drugs, including stimulants and xylazine—an increasingly common adulterant in fentanyl that the Administration has designated as an emerging drug threat. The network is also funding an observational study of overdose prevention centers, which allow people to consume pre-obtained drugs under the supervision of staff who are trained in addiction and overdose treatment.

Because drug combinations play an increasing role in overdose deaths, NIDA is leading several research efforts to better understand drivers for polysubstance use and to develop multi-pronged effective interventions for it. For example, a HEAL-funded program supports research to define polysubstance use patterns and outcomes, and to improve their prevention and treatment. One project is examining how changes in housing status and other factors affect patterns of combined fentanyl and stimulant use among people experiencing homelessness. Clinical trials funded through the program will investigate interventions for co-use of opioids and stimulants. For example, two trials will focus on contingency management, which typically provides small financial incentives for abstinence or treatment attendance and is the only intervention proven to reduce stimulant use. The trials will examine whether smartphone-based contingency management can be integrated into MOUD treatment programs to reduce polysubstance use and improve MOUD adherence.

Finally, given that addiction is a chronic relapsing disorder, NIDA is prioritizing research to identify best practices in addiction recovery and relapse prevention. There are a variety of recovery service models—including peer-based mutual aid groups, recovery housing, and youth

[493] pubmed.ncbi.nlm.nih.gov/36055727
[494] pubmed.ncbi.nlm.nih.gov/37705148
[495] pubmed.ncbi.nlm.nih.gov/34686281; pubmed.ncbi.nlm.nih.gov/28061909; pubmed.ncbi.nlm.nih.gov/35255392

programs—but there is little evidence regarding which kind of program works best for different people. Moreover, many such programs focus on short-term medical treatments and may lack support for participants to receive long-term MOUD.[496] In 2020, NIDA established a recovery research networks program to develop tools, resources, and training to grow this area of research. With additional support from the HEAL Initiative®, this program has expanded and is testing new and existing recovery models through clinical trials.

NIDA's research efforts are organized into the following programmatic areas: Neuroscience and Behavior; Epidemiology, Services and Prevention Research; Therapeutics and Medical Consequences; the NIDA Clinical Trials Network; Translational Initiatives and Program Innovations; HEAL Initiative® programs; Intramural Research Program (IRP); and Research Management and Support (RMS). Dollars budgeted to the HEAL Initiative® for the purpose of opioid research are used to supplement base funding for opioid and pain research that are included within other NIDA program areas. Funding for the HEAL Initiative® in NIDA will remain equal to the FY 2024 CR level.

Division of Neuroscience and Behavior
FY 2025 Request: $532.2 million
($44,059 below the FY 2024 CR level)

NIDA's Division of Neuroscience and Behavior (DNB) supports research to understand the biological mechanisms that underlie drug use and addiction, and to inform the development of novel prevention and treatment strategies for SUD. This includes identifying the effects of illicit drugs on brain structure and function throughout the lifespan; and how genes, the environment, and other factors such as sex and gender influence the risk of SUD and its outcomes. DNB also supports research on pharmacology of drugs with addiction potential; data science; foundations of neuromodulation technology; and technology that enables study of the living brain from cells to circuits to networks.

A recent study exemplifies DNB support for research on the genetics of addiction. In that study, researchers combed through genomic data from over 1 million people, including ABCD study participants, and found nearly 20 gene variants associated with SUD, regardless of the substance involved. The researchers then developed a genetic risk score that was able to discern between healthy individuals and people with an SUD diagnosis, with the highest accuracy for those who had polysubstance use disorder.[497] Although genetic approaches like this cannot fully predict who will develop SUD, they could someday aid in SUD risk assessment, lead to more personalized interventions, and inform potential targets for new SUD therapeutics.

Because people who use drugs are at higher risk for HIV infection, DNB also supports fundamental research on HIV. With funding through a data science program, one recent study investigated how HIV manages to persist in some people despite antiretroviral therapy, and found that HIV-infected cells sometimes multiply and continue producing the virus, acting as a viral reservoir.[498] With funding through the NIDA Avante-Garde program, another study

[496] pubmed.ncbi.nlm.nih.gov/34700201
[497] pubmed.ncbi.nlm.nih.gov/37250466
[498] pubmed.ncbi.nlm.nih.gov/35320704

identified genes that are down-regulated during HIV-related brain inflammation, suggesting a potential early step in HIV-associated neurocognitive disorder, which affects up to half of people with HIV.[499] Both of these programs were renewed in FY 2023.

DNB also supports research focused on the intersection of SUD and sleep disorders, which have a strong bidirectional association. Substance use can lead to sleep disturbances, and sleep disturbances can increase the risk of drug withdrawal, craving, and relapse. In fact, a recent DNB-funded study found that SUD and sleep disturbances are linked at a molecular level; compared to healthy individuals, people with OUD had unique daily rhythmic patterns of gene activity in the brain, specifically in brain regions involved in addiction.[500] In FY 2023, DNB announced new funding to explore the mechanisms that link sleep, circadian rhythms, and SUDs.

Division of Epidemiology, Services, and Prevention Research
FY 2025 Request: $391.1 million
($32,380 below the FY 2024 CR level)

NIDA's Division of Epidemiology, Services, and Prevention Research (DESPR) supports studies to understand and address the interactions between individuals and environments that contribute to drug use, addiction, and related health problems. DESPR supports a broad portfolio that informs evidence-based strategies to support prevention, harm reduction, treatment, and recovery for people at risk or with SUDs. This includes two nationally representative studies—the Monitoring the Future (MTF) survey, which measures substance use and related attitudes among adolescents, and the Population Assessment of Tobacco and Health (PATH) Study, which focuses on tobacco use, attitudes, and health outcomes of people aged 12 and older.

DESPR's research is shedding light on e-cigarette use among youth and its relation to smoking and other substance use. For example, many studies suggest that e-cigarette use, or vaping, in adolescence is a gateway to smoking later. New PATH data suggest that vaping also entrenches smoking among teens who have already tried it.[501] Meanwhile, MTF has found that compared to teens who do not use nicotine, odds of cannabis use are higher among those who vape nicotine—about 40 times higher among those who both vape and smoke nicotine.[502] Even accounting for smoking and cannabis use, youth who use e-cigarettes are more likely to experience wheezing, bronchitis, and shortness of breath.[503] These findings highlight the need for interventions to address the health risks of vaping during youth.

DESPR also supports the ABCD study, which is advancing knowledge about the impacts of social determinants of health on brain development. In one analysis, researchers found that Black children ages 9-10 faced greater adversity than white children—including lower parental education and income, living in disadvantaged neighborhoods, and more exposure to trauma such as vehicle accidents and assault—and that this adversity was associated with differences in brain structure. When the differences in adversity were controlled statistically, the brain

[499] pubmed.ncbi.nlm.nih.gov/36525955
[500] pubmed.ncbi.nlm.nih.gov/35347109
[501] pubmed.ncbi.nlm.nih.gov/37072167
[502] pubmed.ncbi.nlm.nih.gov/37198725
[503] pubmed.ncbi.nlm.nih.gov/37582630

differences largely evaporated.[504] Another analysis found that compared to children from high-income families, those from low-income families were likely to have structural brain differences as well as symptoms of anxiety and depression. More importantly, those disparities narrowed significantly among children living in states with robust antipoverty programs.[505] These studies provide real-world evidence that intervening on social determinants of health can help ensure healthy brain development.

DESPR also supports implementation science to identify and address gaps in translating evidence-based interventions into practice. For instance, a study of national Medicare data found that adults who received buprenorphine (BUP) following an overdose had a 62 percent lower risk of fatal overdose over the next year. However, fewer than 1 in 20 patients received it, and most recipients waited more than 30 days.[506] DESPR is funding research on innovative solutions to this challenge, such as collaborative care models that bring together BUP providers and pharmacists. A pilot trial in which the pharmacist handled BUP management including adjustments for withdrawal, in consultation with the provider, found that this model significantly boosts retention in treatment compared to usual provider-based care.[507]

Division of Therapeutics and Medical Consequences
FY 2025 Request: $109.8 million
($9,095 below the FY 2024 CR level)

NIDA's Division of Therapeutics and Medical Consequences (DTMC) supports research to evaluate the safety and efficacy of pharmacotherapies, behavioral interventions, and medical devices to prevent and treat SUDs and drug overdose. 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.

DTMC supports research on a diverse array of pharmacotherapies, including repurposing of drugs used for other conditions and developing new compounds with novel molecular targets. For example, diabetes drugs like semaglutide, which are based on the hormone glucagon-like peptide-1 (GLP-1), may hold potential for treating SUD. GLP-1 analogs help control food cravings, and anecdotal reports from people taking these drugs for diabetes or weight loss suggest they might help reduce drug cravings, too. NIDA is supporting preclinical studies of GLP-1 analogs for alcohol and opioid addiction and a small clinical trial for smoking cessation. While stimulants generally work by increasing dopamine signals in the brain, methamphetamine and cocaine use disorder (MtUD and CcUD) also involve changes in glutamate signaling. A phase I clinical trial is underway to investigate treating CcUD with a small-molecule inhibitor of the glutamate receptor mGluR5.

DTMC also supports research on therapies involving psychedelic and dissociative drugs. For example, a large randomized controlled trial is investigating whether psilocybin in combination

[504] pubmed.ncbi.nlm.nih.gov/36722118
[505] pubmed.ncbi.nlm.nih.gov/37130880
[506] pubmed.ncbi.nlm.nih.gov/36906496
[507] pubmed.ncbi.nlm.nih.gov/36630629

with psychotherapy can improve smoking cessation. Other trials are investigating ketamine-assisted therapy for CcUD and MtUD, and as a bridge to start MOUD.

Another focus of DTMC's portfolio is neuromodulation, which involves stimulating the brain to reset the circuitry underlying brain disorders. Deep brain stimulation— which involves inserting electrodes into the brain and is FDA-approved for treating Parkinson's disease and epilepsy—is in clinical trials for refractory OUD. DTMC also supports research on non-invasive neuromodulation therapies, including low-intensity focused ultrasound and transcranial magnetic stimulation (TMS). TMS is FDA-approved as an adjunct therapy for smoking cessation, in part due to NIDA-funded research, and is now being investigated for other SUDs.

DTMC has a growing portfolio of research to address OUD and other co-occurring mental health disorders. For example, 40-60 percent of people with OUD suffer from chronic pain and depression, which can increase their risk of opioid misuse. To improve health outcomes for these patients, researchers are evaluating an approach in which primary providers and behavioral health specialists provide collaborative care. In FY 2023, DTMC announced new funding to develop pharmacotherapies, behavioral therapies, and devices for co-occurring OUD and mental illness.

Center for Clinical Trials Network
FY 2025 Request: $35.7 million
($2,955 below the FY 2024 CR level)

The Center for Clinical Trials Network (CCTN) manages NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN), which provides a collaborative framework for healthcare providers, researchers, and patients to conduct clinical trials on the safety and efficacy of SUD interventions. The CTN includes 16 research nodes across the country and more than 240 community-anchored treatment programs. This unique structure enables the CTN to investigate behavioral, pharmacological, and integrated therapies across diverse settings and populations, and to develop implementation strategies that help bring research results into practice. Active protocols focus on a variety of areas, including primary prevention of SUD; increasing patient access and adherence to MOUD, especially in rural and underserved populations; evaluating potential medications for stimulant use disorder; and addressing stigma and other barriers to SUD treatment. Some examples are highlighted below.

Because adolescence is a critical time for susceptibility to SUD and responsiveness to interventions, the CTN prioritizes development and testing of screening tools tailored to this age range. A recent study tested three brief SUD screening tools in a large, diverse adolescent population and found that they performed well compared to an in-depth diagnostic interview.[508] Through the ongoing Subthreshold OUD Prevention (STOP) trial, the CTN seeks to determine if screening and intervention for low-severity OUD in primary care can reduce OUD progression and overdose risk.

The CTN is also testing strategies to identify OUD patients and start MOUD treatment in emergency departments (EDs)—at the frontline of the overdose epidemic. In one approach, the

[508] pubmed.ncbi.nlm.nih.gov/37213103

CTN designated champions to educate ED and community clinicians on BUP treatment and how to overcome stigma and other barriers to its use. Implementing this approach for six months led to higher rates of standard oral BUP initiation in the ED and referral to ongoing OUD treatment in the community, and was feasible even in rural and low-resource EDs.[509] The CTN is now conducting a similar implementation trial, called ED-INNOVATION, to compare initiation with oral BUP vs. a longer-lasting injectable form, which could help keep patients stable while providers address any barriers to referral.

The CTN also recently leveraged the ED-INNOVATION trial to address concerns about precipitated withdrawal—debilitating withdrawal symptoms that can occur within hours of receiving BUP. For patients who use potent opioids such as fentanyl, some clinicians prescribe BUP at lower doses to avoid precipitated withdrawal, but that practice may not adequately curb opioid craving and subsequent relapse. An interim analysis of trial data found that while most patients had used fentanyl, only one percent experienced precipitated withdrawal after BUP initiation, similar to rates seen for patients using less potent opioids.[510]

The CTN is developing and evaluating potential treatments for MtUD and CcUD, for which there are no FDA-approved therapies. A recent CTN trial found that a combination of injectable naltrexone and oral bupropion, a commonly prescribed medication for depression and nicotine cessation, was effective in helping people with MtUD reduce their use. A secondary analysis focused on men who have sex with men—who are at higher risk for MtUD and harmful outcomes, including HIV infection—and found they had higher response rates to this treatment than heterosexual men.[511] Two other CTN trials will examine whether patients with MtUD or CcUD and opioid co-use will benefit from injectable naltrexone and monthly injectable BUP.

Office of Translational Initiatives and Program Innovations
FY 2025 Request: $43.2 million
($3,580 below the FY 2024 CR level)

NIDA's Office of Translational Initiatives and Program Innovations (OTIPI) translates discoveries in addiction research into candidate health applications. OTIPI supports translational research through NIDA's Small Business Innovation Research/Technology Transfer (SBIR/STTR) programs, as well as Challenge competitions. OTIPI also develops training programs that help scientists move their discoveries from the lab to the real world.

In FY 2023, OTIPI issued a Primary Care Challenge competition to propose models for how primary care providers can more effectively identify people at risk for substance use and deliver interventions to reduce this risk. Three winning projects were selected. One project will focus on recently incarcerated adults, who are at high risk for drug use and overdose, with community health workers leading patient outreach, substance use screening, and linkages to preventive care. Another project will screen teens with a mental health diagnosis for substance use risk, and the third will use AI to identify high-risk pre-teens based on their electronic health records.

[509] pubmed.ncbi.nlm.nih.gov/37017967; pubmed.ncbi.nlm.nih.gov/37140493
[510] pubmed.ncbi.nlm.nih.gov/36995717
[511] pubmed.ncbi.nlm.nih.gov/33497547; pubmed.ncbi.nlm.nih.gov/37478502

OTIPI supports medical device development, including devices to treat neonatal opioid withdrawal syndrome (NOWS), which can affect infants exposed to opioids in the womb. For example, an SBIR project has developed a vibrating crib mattress to soothe infants with NOWS. In a large trial, infants who slept on this mattress needed less medication to manage withdrawal symptoms and left the hospital three days earlier on average than infants who received only usual care.[512] Another SBIR project focuses on treating NOWS by retooling an FDA-approved technology for opioid withdrawal in adults, called transcutaneous auricular neurostimulation. This technology uses an earpiece to painlessly stimulate nerves near the ears, transmitting signals that are believed to cause release of the brain's own endogenous opioids and help control withdrawal. A safety trial found that this technology was well-tolerated by infants with NOWS, and efficacy trials are planned.[513]

OTIPI also supports development of SUD treatment modalities that are powered by AI. One example is Woebot, a conversational smartphone app originally designed to help people struggling with depression. SBIR-funded researchers have modified Woebot to help people with SUD track their mood and drug cravings, and to provide coaching in behavior change. In a pilot study, after using Woebot-SUD for eight weeks, participants reported increased ability to resist craving and had improved scores on SUD screening tests.[514] Results from a larger trial are expected soon. Other researchers are working on a wrist-worn device for MOUD patients that would record biometric data, including mobility and skin temperature; use AI to read those data for signs of opioid withdrawal or relapse; and alert providers so that they can adjust treatment.

OTIPI is also supporting the development of tools to remove barriers to methadone treatment for OUD, which is available only from federally regulated opioid treatment programs (OTPs). Continuing flexibilities implemented during the COVID-19 pandemic allow OTPs to dispense up to 28 days of take-home methadone for stable patients, but clinicians have significant discretion—and difficult decisions—regarding take-home doses for less stable patients. In a pilot study, an OTP in Washington enabled patients to submit video confirmation that they were using their take-home methadone as prescribed. Compared to regular OTP clients, pilot participants had more days of observed dosing and were more often approved for increased take-home doses.[515] Other researchers are developing a wearable biosensor to remotely monitor patients' adherence to their take-home methadone, and a new OTIPI-led program calls for further research on low-cost point-of-need approaches to lower barriers to SUD care.

NIH HEAL Initiative®
FY 2025 Request: $355.3 million[516]
(Equal to the FY 2024 CR level)

The HEAL Initiative, which is co-led by NIDA and the National Institute of Neurological Disorders and Stroke (NINDS), aims to accelerate scientific solutions to the opioid crisis. One of its major focus areas has been research on how to implement effective prevention and

[512] pubmed.ncbi.nlm.nih.gov/37184872
[513] pubmed.ncbi.nlm.nih.gov/33762918
[514] pubmed.ncbi.nlm.nih.gov/33755028
[515] pubmed.ncbi.nlm.nih.gov/36215911
[516] Includes funding for RMS to support the HEAL Initiative.

treatment interventions for OUD and overdose across healthcare and non-healthcare settings. The HEALing Communities Study (HCS), led by NIDA in collaboration with the Substance Abuse and Mental Health Services Administration (SAMHSA), is testing the impact of integrating evidence-based interventions for OUD and overdose in 67 communities spanning 4 states. HCS communities have deployed over 1,000 evidence-based strategies to expand access to MOUD, implement overdose education and naloxone distribution, and reduce high risk prescribing. Lessons learned from the HCS have been captured in two practice guides to help providers, public health agencies, and others assemble community coalitions and implement effective approaches to reduce overdose deaths.

The Justice Community Opioid Innovation Network (JCOIN) is studying approaches to improve evidence-based treatment for people with OUD in criminal-legal settings. JCOIN has found that MOUD access during incarceration not only saves lives but is also associated with 32 percent lower recidivism after release.[517] JCOIN recently disseminated a first-of-its-kind MOUD Budget Impact tool to helps jail and prison administrators estimate the cost of providing MOUD services.[518] NIDA plans to extend JCOIN through at least FY 2030, with a focus on research to scale up MOUD and other evidence-based interventions across justice settings and where they intersect with community-based treatment.

The HEAL Harm Reduction Research Network is developing and testing strategies to prevent overdose, transmission of HIV and hepatitis C virus, and other harms associated with drug use. Current projects are studying delivery of harm reduction services during emergency care, and via mobile vans and smartphones for hard-to-reach patients. The network is also examining the impact of state and local harm reduction policies. In the first study of its kind in the United States, the network is examining outcomes associated with overdose prevention centers that are operating in New York and Rhode Island.

With HEAL funding, NIDA's Recovery Research Networks are working to build an evidence base for effective recovery support services. While such services have strong foundations in the lived experiences of people with SUD, most have not been formally evaluated. These networks are engaging recovery service providers and people with lived experience in research to examine what types of recovery services work best for different people and to help link recovery services with established standards of care including MOUD.

A new HEAL program funded in FY 2023—Research to Foster an OUD Treatment System Patients Can Count On—is supporting four projects in which researchers are working with providers, patients, payors, and public health agencies to develop quality measures to improve patient outcomes in OTPs and other settings.

Intramural Research Program
FY 2025 Request: $120.9 million
($2.4 million above the FY 2024 CR level)

[517] pubmed.ncbi.nlm.nih.gov/35063323
[518] pubmed.ncbi.nlm.nih.gov/36880906; www.jcoinctc.org/resources/budget-impact-tool

The NIDA Intramural Research Program (IRP) conducts research to inform strategies for prevention and treatment of SUD and related health outcomes. The IRP portfolio includes research to elucidate the mechanisms underlying development of SUDs, evaluate potential new therapies, and identify and characterize emerging drugs such as synthetic opioids, stimulants, and cannabinoids.

IRP researchers who study how opioids affect brain and respiratory functions were able to pivot quickly to study the additive effects of xylazine. In preclinical studies, they found that fentanyl exposure causes respiratory suppression, which produces a rapid, robust decrease in oxygen flow to the brain, followed by a gradual rebound. Adding xylazine to fentanyl eliminated this rebound, prolonging the brain's oxygen deficit—which could contribute to the increasing involvement of xylazine in opioid overdose deaths.[519]

The IRP Designer Drug Research Unit focuses on emerging synthetic drugs with addiction potential, including stimulants called synthetic cathinones. Like other stimulants, cathinones increase dopamine levels at synapses, sometimes by blocking the activity of transporters that clean up excess dopamine. Illicit synthetic cathinones, also called "bath salts," can be extremely potent, with longer lasting effects than cocaine. IRP researchers found that this is due to unusually long-lasting inhibition of dopamine transporters.[520] These researchers are also investigating cathinone derivatives that act preferentially on serotonin transporters as an alternative to selective serotonin reuptake inhibitors (like Prozac) for depression and anxiety.[521]

IRP researchers also are examining the neurobiological basis for opioid withdrawal symptoms, which contribute to relapse risk. One recent study investigated brain pathways responsible for increased pain sensitivity (or hyperalgesia) during opioid withdrawal. Through a combination of brain imaging and chemogenetics—the use of designer drugs and receptors to control neuronal activity—researchers identified a cell type in the mouse brainstem that contributes to hyperalgesia (see cover image).[522] Future neuromodulation therapies or other approaches could target those cells to reduce hyperalgesia and relapse risk.

Other IRP researchers are studying the addiction potential of S-ketamine. While S-ketamine is FDA-approved for treating severe depression, it has addiction potential that is thought to occur through opioid signaling. IRP researchers with expertise in functional brain imaging partnered with other NIH researchers to investigate this idea. They found that in rats, S-ketamine acts on opioid receptors to stimulate activity in the nucleus accumbens—a brain region associated with addiction—and that self-administration of S-ketamine leads to opioid tolerance.[523] Those findings have implications for monitoring the safety of S-ketamine therapy—both its current use for depression and emergent uses for opioid and stimulant addiction.

[519] pubmed.ncbi.nlm.nih.gov/37340247
[520] pubmed.ncbi.nlm.nih.gov/36730201
[521] pubmed.ncbi.nlm.nih.gov/36352123
[522] pubmed.ncbi.nlm.nih.gov/35728954
[523] pubmed.ncbi.nlm.nih.gov/36841701

Research Management and Support
FY 2025 Request: $80.1 million[524]
($3.4 million above the FY 2024 CR level)

NIDA Research Management and Support (RMS) activities provide administrative, budgetary, logistical, and scientific support in the review, award, and monitoring of research grants, training awards, and research and development contracts. Staff supported by NIDA's RMS budget also coordinate training and career development programs to sustain a talented, diverse workforce of addiction scientists. Other RMS functions include strategic planning, coordination, dissemination of latest research findings and funding opportunities, program evaluation, regulatory compliance, international coordination, and liaison with other Federal agencies, Congress, and the public. NIDA RMS funding also supports evidence-based education and outreach about substance use and addiction to inform public health policy, and to provide the public with timely, accessible, trustworthy information about drug research in English and Spanish.

National Institute on Alcohol Effects and Alcohol-Associated Disorders
FY 2025 Request: $75.9 million
($0.5 million above the FY 2024 CR level)

Although the rate of underage drinking in the United States has declined over the past several decades, alcohol remains the most widely used substance among youth. Binge drinking[525] and high intensity drinking[526] 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, alcohol use disorder (AUD), and other detrimental consequences. NIAAA supports a broad range of basic, translational, and clinical research to improve our understanding of the impact of alcohol exposure on adolescent health and to improve interventions for alcohol-related problems among youth in community and healthcare settings. NIAAA also disseminates information about evidence-based interventions through the development of resources for the public.

Basic research is key to informing the development of innovative prevention and treatment strategies for underage drinking. A key initiative within NIAAA's adolescent brain research portfolio is the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a multi-site longitudinal study to identify brain characteristics in humans that may predict alcohol misuse or occur because of adolescent alcohol exposure. Established in 2012, NCANDA investigators are now following the initial adolescent cohort into young adulthood and examining the sex-specific relationships between brain maturation, alcohol misuse, mental health, and sleep. Data from NCANDA, for example, has demonstrated that adolescent binge drinking is associated with accelerated decline of gray matter volume in the brain, with the most significant effects observed in the frontal regions that are important for executive functioning, such as performing complex tasks and decision-making. Using NCANDA data, a recent study

[524] Excludes funding for RMS to support the HEAL Initiative.
[525] 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 concentration in youth.
[526] NIAAA defines high intensity drinking two or more times the gender-specific binge drinking thresholds.

showed that alcohol use in adolescence was negatively associated with the volumes of subcortical (deep) regions of the brain, including structures that are important in movement, learning, memory, emotion, and motivation and reward. Both males and females showed a negative association between alcohol use and volume of the hippocampus. However, in females alcohol use was negatively associated with the volumes of two additional regions (caudate and thalamus). These findings suggest a potential vulnerability to alcohol use in females based on brain structure and morphometry.[527]

Another major program within NIAAA's portfolio on adolescent brain research is the Neurobiology of Adolescent Drinking in Adulthood (NADIA) consortium to examine, using animal models, the mechanisms by which adolescent drinking leads to changes in brain structure and function that persist into adulthood. NADIA researchers recently tested the effects of chronic adolescent alcohol exposure on pain-related behavior and brain function. They found that chronic adolescent alcohol exposure caused an abnormally heightened sensitivity to pain during adolescence and into adulthood, even after abstinence, in males but not females. In addition, chronic adolescent alcohol exposure resulted in alterations in a pain-related brain neurocircuit in adult males, but not adult females. This study suggests that there are sex-dependent effects of chronic adolescent alcohol exposure on pain-related behaviors and neurocircuitry that persist into adulthood.[528] These results are important given previous research demonstrating that alcohol consumption and coping with pain are linked, and that chronic alcohol misuse increases pain sensitivity and makes pain worse over the long-term.

Prevention of underage drinking has long been one of NIAAA's top priorities. NIAAA's portfolio in this area 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. NIAAA also supports research to better understand trends in alcohol use among youth to improve interventions based on that knowledge. For example, researchers recently found that students who begin high-intensity drinking, defined as 10 or more drinks on a single occasion, by grade 11 instead of later on are more likely to have a higher average weekly alcohol consumption, a higher frequency of high-intensity drinking, and an increased risk for AUD at age 20 years.[529] These findings emphasize the importance of prevention strategies that specifically prevent or delay high-intensity drinking among young people. For college settings, NIAAA provides the College Alcohol Intervention Matrix (CollegeAIM), an online resource 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 also supports research to address alcohol misuse among young adults outside of college settings. In an ongoing clinical study, NIAAA-funded researchers are testing the efficacy of two intervention approaches for non-college emerging adults that report heavy drinking.[530] One approach is a combined multi-session brief alcohol intervention (BAI) with a Substance Free

[527] www.sciencedirect.com/science/article/pii/S1878929323000993?via%3Dihub
[528] pubmed.ncbi.nlm.nih.gov/37717844/
[529] pubmed.ncbi.nlm.nih.gov/36716022/
[530] reporter.nih.gov/search/VqssJkar4k68M5kN23V5Mw/project-details/10157726

Activity Session (SFAS) to reduce drinking. The SFAS attempts to increase engagement in goal-directed activities that might provide alternatives to alcohol use. It also provides tools to reduce stress and develop mood-enhancing behavioral substitutes to drinking (or substance use). The researchers are also testing a second intervention, Relaxation Training (RT), in combination with SFAS to determine if this intervention approach better addresses risk factors for alcohol misuse by enhancing wellness, managing stress, and increasing positive activities with the goal of increasing effectiveness of intervention and the potential for dissemination.

Prevention interventions tailored for underserved youth is another important area within NIAAA's prevention research portfolio. For example, NIAAA-funded researchers conducted a pilot study of the Chukka Auchaffi' Natana: the Weaving Healthy Families (WHF) Program, a culturally-informed, family-based program designed to promote parenting practices, family resilience, and wellness, and as a result, prevent substance misuse among Native American families.[531] The researchers found that participation in the WHF program was associated with improvements in parenting quality, family resilience, community resilience that have been shown to serve as primary factors against substance misuse.

Increasing implementation of alcohol screening and brief intervention in primary care and developing evidence-based behavioral therapies to reduce underage drinking is another priority area for NIAAA. For example, NIAAA developed the Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide to assist pediatric and adolescent health practitioners in identifying patients at risk for underage drinking and associated problems. This screening resource has been validated among youth in pediatric emergency room settings, school settings, primary care settings (including among racially and ethnically diverse youth), and among youth with chronic health conditions.

Equity

Equity is a vital consideration in NIDA and NIAAA efforts to support the objectives of the National Drug Control Strategy. Both NIDA and NIAAA support the NIH UNITE initiative that was established to identify and address structural racism within the NIH-supported and greater scientific community. Both Institutes are also part of NIH's broader efforts to advance health equity research by improving minority health, reducing health disparities, and removing barriers to advancing health disparities research, as well as the agency's efforts to expand, sustain, and promote scientific workforce diversity.

NIDA's Racial Equity Initiative (REI) aligns with NIH's UNITE Initiative by promoting racial equity in NIDA's workplace, workforce, and research portfolio. In FY 2022, the REI released a suite of nine funding opportunities that are supporting research and research training efforts focused on increasing equity in the addiction science community, addressing racial-ethnic health disparities in substance use and addiction outcomes, and understanding how structural racism affects the risk of substance use and SUD. With HEAL funding and in close partnership with other NIH Institutes, Centers, and Offices, NIDA and NINDS are also supporting a new program focused on American Indian, Alaska Native, and Native Hawaiian health called the Native Collective Research Effort to Enhance Wellness (N CREW). N CREW researchers will work in

[531] pubmed.ncbi.nlm.nih.gov/36710265/

partnership with Tribes and Native American-serving organizations to identify community-based priorities related to overdose, substance use, mental health, and pain in Native communities; collaborate in research toward culturally grounded interventions; and build local capacity as needed for this research. The initiative has the potential to slow the rate of overdose deaths in American Indian and Alaska Native communities, which is higher than for any other racial-ethnic group.[532]

NIAAA supports a range of efforts aimed at reducing health disparities and promoting health equity. One area of interest is the social determinants of health that influence the initiation of underage alcohol use. Underserved populations bear a greater burden of alcohol misuse and its adverse effects. Current studies are exploring factors that drive alcohol misuse—including sleep quality, adverse childhood experiences, and family or peer stress—among underserved adolescent populations. Understanding the social and environmental factors that influence alcohol misuse can inform targeted prevention approaches. NIAAA also supports the development of culturally adapted interventions to reduce underage drinking.

[532] www.cdc.gov/nchs/products/databriefs/db457.htm