

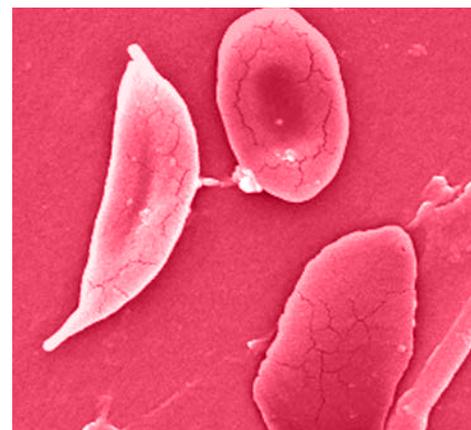
ADVANCING

Heart, Lung, Blood, and Sleep Research



National Heart, Lung,
and Blood Institute

January 2020 | WWW.NHLBI.NIH.GOV



In 2019, NIH's National Heart, Lung, and Blood Institute (NHLBI) remained steadfast in its commitment to fueling the scientific discoveries needed to improve the health of the nation. We value the partnerships we have with our constituents that enhance our efforts to understand human biology, reduce human disease, advance translational science, and develop and sustain the next generation of researchers to support the NHLBI mission.

We know that many health concerns within the NHLBI's heart, lung, blood, and sleep health portfolio disproportionately affect certain populations, and we have reaffirmed our commitment to addressing these disparities. Several cohort studies involving high-risk populations are helping us understand these disparities and reduce their impact. For example, in 2019, we launched the Risk Underlying Rural Areas Longitudinal (RURAL) Cohort Study to examine factors that might contribute to higher rates of cardiovascular, lung, and other chronic health conditions in rural communities. We also renewed our funding for the Strong Heart

Study—the largest, longest-running study of cardiovascular disease in American Indians—and met with Tribal leaders to lay the groundwork for community-led projects. We are leveraging these and other cohort studies to support discovery of genomic and other complex risk factors through our Trans-Omics for Precision Medicine (TOPMed) program. In addition, we are developing a new cloud-based data science platform—known as the BioData Catalyst—to support data mining, analysis, and collaboration among researchers.

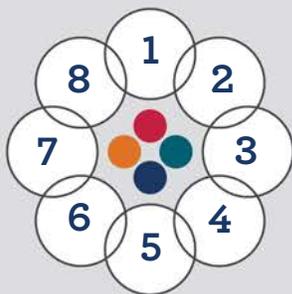
Along with our commitment to large-scale initiatives, we continue to prioritize investigator-initiated fundamental discovery science. These are the studies that often lead us to unanticipated findings and sometimes to entirely new lines of

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NHLBI STRATEGIC VISION

Eight Objectives to Advance Our Science



- 1** Understand normal biological function and resilience.
- 2** Investigate newly discovered pathobiological mechanisms important to the onset and progression of HLBS (heart, lung, blood, and sleep) diseases.
- 3** Investigate factors that account for differences in health among populations.
- 4** Identify factors that account for individual differences in pathobiology and in responses to treatments.
- 5** Develop and optimize novel diagnostic and therapeutic strategies to prevent, treat, and cure HLBS diseases.
- 6** Optimize clinical and implementation research to improve health and reduce disease.
- 7** Leverage emerging opportunities in data science to open new frontiers in HLBS research.
- 8** Further develop, diversify, and sustain a scientific workforce capable of accomplishing the NHLBI's mission.

www.nhlbi.nih.gov/about/strategic-vision

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inquiry. For instance, NHLBI grantee Dr. Gregg Semenza has spent decades conducting fundamental science to better understand the body's response to oxygen deprivation. His research revealed a molecular pathway that the body uses to sense oxygen levels and make appropriate adjustments to blood cell production and blood vessel remodeling. This work may lead to new therapies for heart disease, anemia, or even cancer, and it was recognized with the 2019 Nobel Prize in Physiology or Medicine.

As we maintain our commitment to clinical and fundamental research, we also remain nimble enough to respond to emerging public health threats. This past year, we saw the unfolding of a crisis associated with the use of e-cigarettes, also known as vaping. In response, we have pivoted some of our resources toward enhanced support for research on the health effects of vaping.

In this brochure, we highlight research advances across the NHLBI portfolio over the past year, with a special focus on research that addresses one or more goals in the NHLBI Strategic Vision.



NHLBI grantee and Nobel Laureate Dr. Gregg Semenza's work helped reveal pathways controlling blood cell production and blood vessel growth.

HEART DISEASE RESEARCH



Maintaining Momentum for Pediatric Heart Disease Research

The NHLBI continues to support research on the causes of and treatments for congenital heart disease (CHD), the most common birth defect in the United States. The Pediatric Heart Network (PHN), established in 2001 and encompassing more than 30 children’s hospitals, has been working to improve evidence-based treatment for CHD. In a recent PHN study, known as the Fontan Udenafil Exercise Longitudinal (FUEL) Trial, teenagers born with a single working ventricle of the heart—a rare defect that cannot be completely corrected—showed a significant improvement in their ability to sustain moderate exercise after treatment with udenafil, a drug that helps improve blood flow.

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STRATEGIC VISION OBJECTIVES

Addressing health disparities in American Indians

The NHLBI is expanding its commitment to address the high burden of chronic disease among American Indians and other underserved populations. In February 2019, the NHLBI renewed its funding for the Strong Heart Study, which is the largest study of cardiovascular risk factors ever undertaken in American Indian communities and is conducted in partnership with 12 Tribal Nations in Arizona, Oklahoma, and the Dakotas. In the following months, NHLBI Director Gary Gibbons embarked on a listening tour with Tribal leaders to reaffirm and strengthen these partnerships.

- A recent analysis from the Strong Heart Study found that across two generations, cardiovascular disease incidence rates dropped among the participants, with decreased mortality for men, although not for women.
- In the next few years, funding will be made available for community-based projects driven by Tribal leaders and health officials. The study also continues to support biomedical training and career development for American Indian students and early-career investigators.

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The NHLBI is leveraging the PHN and other resources, including the Institute's Pediatric Cardiac Genomics Consortium (PCGC), as part of the trans-NIH project known as Investigation of Co-occurring Conditions Across the Lifespan to Understand Down syndrome (INCLUDE). Through INCLUDE, NHLBI-funded researchers are investigating the genetic factors that could link Down syndrome with CHD. In 2019, the PHN provided career development awards to four emerging clinician-scientists to help them gain expertise in treating patients with CHD and Down syndrome.

Linking Heart Health and Brain Health

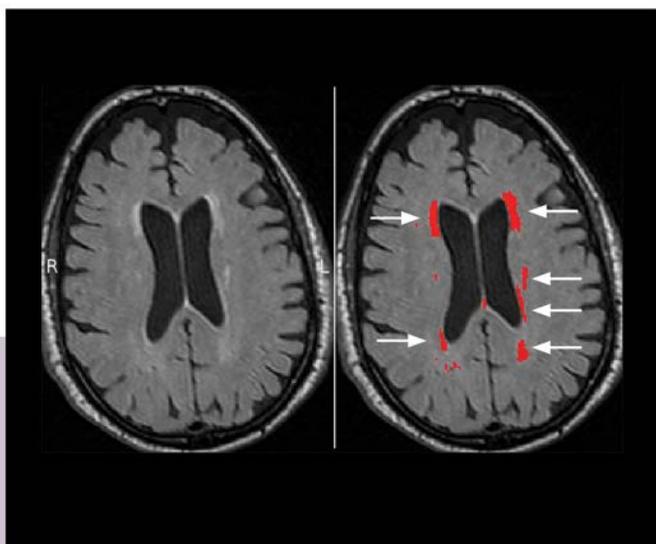
The NHLBI is increasing its investment to explore and better understand how heart health affects brain health. In 2020, the NHLBI's Jackson Heart Study, the largest longitudinal study of heart disease in African Americans, will begin to include detailed assessments of participants' cognitive function.

The Atherosclerosis Risk in Communities Study (ARIC) is also expanding to learn more about vascular dementia and other cognitive issues through the ARIC Neurocognitive Study. ARIC



researchers found that after 17 years of follow-up, participants who engaged in regular moderate-to-high levels of physical activity in midlife had about a 40 percent reduced incidence of dementia than their less physically active peers.

In 2019, the Systolic Blood Pressure Intervention Trial Memory and Cognition in Decreased Hypertension (SPRINT MIND) found that aggressive treatment in midlife for high blood pressure—rather than standard treatment—may reduce the risk of vascular-related cognitive decline later in life. Magnetic resonance imaging (MRI) studies among a subgroup of SPRINT MIND participants found that the treatment helped slow the accumulation of white matter lesions in the brain, which are associated with cognitive



An MRI brain scan of a SPRINT MIND participant. The white blotches in the left side image, which have been enhanced on the right side (see arrows), are white matter lesions, which are associated with cognitive decline. *Image courtesy of R. Nick Bryan, M.D., Ph.D., University of Texas at Austin.*

decline. The NHLBI co-funds SPRINT MIND with the National Institute of Neurological Disorders and Stroke and the National Institute on Aging.

Addressing Rural Health Disparities

In 2019, the NHLBI stepped up its efforts to address health disparities experienced by people living in rural communities. For example, the newly funded RURAL Cohort Study aims to identify why cardiovascular, lung, and other chronic diseases occur in Southern rural communities at higher rates than in other areas. The NHLBI is also supporting increased enrollment of rural patients in northern New England into the Cardiothoracic Surgical Trials Network, as well as efforts to implement research findings in rural communities.

People who live in rural areas can also have difficulty accessing care. To address this issue, the NHLBI-supported Improved Cardiovascular Risk Reduction to Enhance Rural Primary Care (ICARE) study is testing whether telemedicine-based access to pharmacists can improve medication adherence and outcomes for patients in rural areas.



STRATEGIC VISION OBJECTIVES



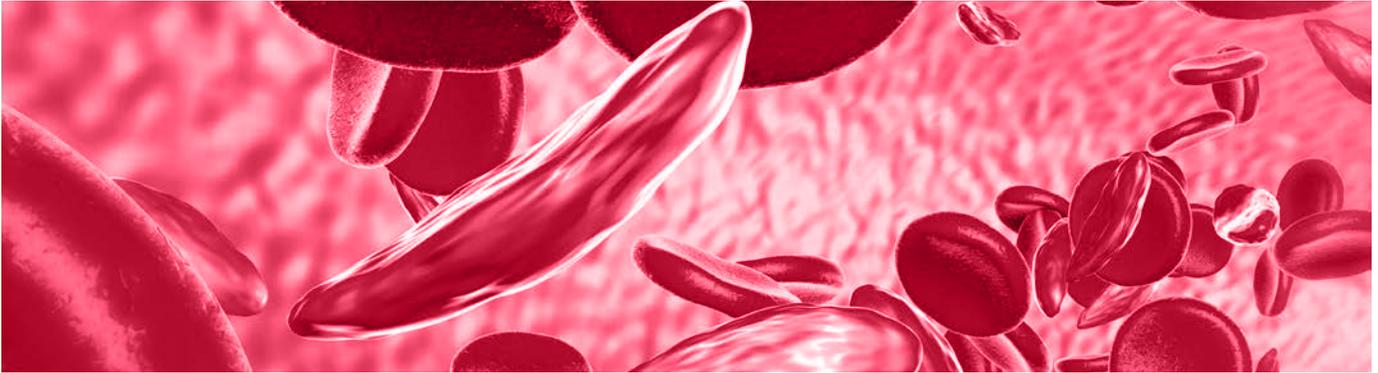
Addressing women's heart health before, during, and after pregnancy

Pregnancy can increase a woman's risk for future cardiovascular disease—and each year, hundreds of American women die from pregnancy- or delivery-related cardiovascular complications. In addition, with rising rates of obesity, diabetes, and high blood pressure among young people, many women come into their pregnancies already at higher risk for cardiovascular disease. The NHLBI supports research to understand and reduce women's risk of cardiovascular disease throughout their lifespan, including before, during, and after pregnancy.

- One ongoing trial is examining whether pregnant women with mild chronic high blood pressure will benefit from lowering their blood pressure to a target often used for nonpregnant adults (<140/90 mmHg) without affecting blood flow to the womb.

- The nuMoM2b Heart Health Study is looking at how sleep apnea and other pregnancy complications, such as preeclampsia and high blood pressure, affect a woman's long-term health.
- New studies are working to improve understanding and treatment of blood clots (thrombosis) in reproductive-age women. These studies will shed new light on long-standing data showing a higher risk of thrombosis during use of oral contraceptives, during pregnancy, and within the first several weeks after delivery.
- Researchers are also working to determine the most effective ways to improve pregnancy-related outcomes in obese and overweight pregnant women. A recent study found that lifestyle interventions can help.

BLOOD DISEASE RESEARCH



Working to Develop Cures and Deliver Better Care for Sickle Cell Disease

Now in its second year, the Cure Sickle Cell Initiative is making progress toward gene-based cures for sickle cell disease (SCD). For example, researchers have devised an approach that uses CRISPR gene-editing technology to repair disease-causing mutations in the hemoglobin gene. The team is now preparing for an early-phase clinical trial in adults with severe SCD. In related efforts, researchers in the NHLBI's Division of Intramural Research have developed a vector system to more efficiently deliver a normal hemoglobin gene to blood-forming stem cells.

Since data show that many patients with SCD do not receive guideline-based treatment, the SCD Implementation Consortium is testing new approaches to enhance care for SCD and improve health outcomes in eight geographically diverse areas. The first three protocols have begun, including one that focuses on improving emergency department care of patients in sickle cell crisis.

Sub-Saharan Africa is home to more than 75 percent of SCD births worldwide, and more than half of children with SCD in this region die before age 5. The NHLBI supports major programs in the region that are building research capacity and developing an infrastructure to enhance disease surveillance and delivery of care, including the Sickle Pan-African Research Consortium. The NHLBI is also part of a newly announced NIH collaboration

with the Bill & Melinda Gates Foundation that aims to develop affordable, gene-based cures for SCD that will be made available in low-resource communities globally. The collaboration is also addressing HIV/AIDS.

Thanks in part to NIH support, two new medications for SCD were approved by the U.S. Food and Drug Administration (FDA) late last year. An NHLBI-funded clinical trial found that Adakveo (crizanlizumab-tmca) reduced the frequency of sickle cell crises in patients age 16 and older. NIH funding for basic research also contributed to the development of Oxbryta (voxelotor). It reduced red blood cell sickling in an industry-funded trial.

Reducing Risk of Graft-Versus-Host Disease After Blood or Bone Marrow Transplants

Graft-versus-host disease (GVHD) can occur after a patient receives a blood or bone marrow transplant to treat conditions such as sickle cell disease or blood cancers. In GVHD, the tissue donor's cells attack the patient's organs or tissues. In a study in mice, NHLBI-supported researchers developed a promising strategy for potentially reducing the frequency of GVHD. They devised an injectable sponge-like gel that serves as a type of scaffold, allowing for enhanced regeneration of key immune cells known as T cells after a blood or bone marrow transplant, thus reviving the recipient's immune system faster and reducing the likelihood of developing GVHD.

LUNG DISEASE AND SLEEP RESEARCH



In 2019, the NHLBI’s Division of Lung Diseases celebrated its 50th year of advancing research on chronic obstructive pulmonary disease (COPD), asthma, and other lung conditions. In April, the American Thoracic Society organized a Capitol Hill reception to mark this milestone, featuring remarks and accolades by Congresswoman Rosa DeLauro (D-CT), Congressman Peter King (R-NY), and the co-chairs of the Congressional COPD Caucus, Senator Michael Crapo (R-ID) and Congressman Chris Stewart (R-UT).

Implementing the COPD National Action Plan

Through the COPD National Action Plan, the NHLBI continues to work with its federal and nonfederal partners to intensify research and outreach to address the national burden of COPD, especially in underserved communities. For example, the NHLBI is looking for new ways to increase

the use of pulmonary rehabilitation (PR) for COPD patients. PR can be highly effective but is often difficult to access, especially in rural areas. To help address this problem, NHLBI-supported researchers are testing the effectiveness of a home-based PR program, alleviating the need for patients to travel for care.

In 2019, the NHLBI funded the first national adult cohort study that will help address the burden of COPD and other lung diseases—the American Lung Association Lung Health Cohort. The study will follow 4,000 healthy young adults (ages 25–35) over six years to identify early risk factors for lung disease—including the use of nicotine products and e-cigarettes. The study aims to detect lung diseases in their earliest stages, to allow for earlier intervention.

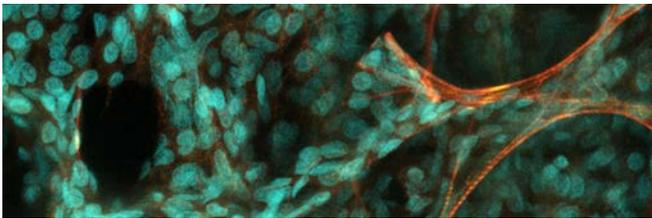
On hand at the Division of Lung Diseases (DLD) 50th anniversary scientific symposium were (from L) Drs. Adrienne Campbell-Washburn, James Crapo, James Kiley (DLD Director), Scott Fraser, Sanjay Jain, Gary H. Gibbons (NHLBI Director), Marcus Chen, Carmen Priolo, R. Graham Barr, and Gail Weinmann (DLD Deputy Director).



Tackling Asthma

The NHLBI is leading the effort to update the 2007 national asthma guidelines for adults and children. The new guidelines were released for public comment and are expected to be completed by fall 2020.

The Precision Interventions for Severe and/or Exacerbation-Prone Asthma Network (PrecISE) has begun to enroll patients with severe asthma at 30 locations nationwide. PrecISE will evaluate novel and approved treatments for asthma by targeting



The cells that make up tiny air sacs in the lung known as alveoli (green) are seen through a multi-photon microscope. The image was produced through the NHLBI LungMAP, a project to understand the molecular and cellular architecture of the human lung. *Source: Gloria Pryhuber, M.D., Cory Poole, University of Rochester Medical Center.*

them to groups of patients who share certain characteristics, such as genetic factors or biomarkers.

Recent NHLBI-funded research illustrates the benefits of tailoring asthma interventions based on patient characteristics.

- One study found that patients with high levels of eosinophils—a type of cell that can contribute to airway inflammation—are more likely to respond to inhaled corticosteroid medications than are patients with fewer eosinophils.
- Another recent study examined how African Americans with poorly controlled asthma respond to more intensive treatment options—either a higher corticosteroid dose or addition of a bronchodilator (a drug to open the airway). The latter option tends to work best for most African Americans older than 12 and for white children. But in this study, the two options were about equally likely to work for African-American children younger than 12.

STRATEGIC VISION OBJECTIVES



Addressing the vaping public health crisis

In 2019, we saw a rising number of cases of severe lung illness as well as deaths associated with e-cigarette use, or vaping. As part of a collaborative response by multiple federal health agencies, the NHLBI is expanding its research on e-cigarettes to better understand their effects on the heart and lungs. A recent NHLBI-funded study suggests that just one vaping session can damage the lungs of young adults. Other data reveal how daily vaping may prime the lungs for chronic disease.

In November 2019, the NHLBI joined several other NIH Institutes to announce a Notice of Special Interest to



address the increasing incidence of acute lung injuries related to vaping. The notice invites NIH-funded researchers to apply for additional funding specifically to study vaping-related illness and to better understand the roles of vaping devices, flavorings, aerosols, and behaviors in vaping-related illness and its outcomes.

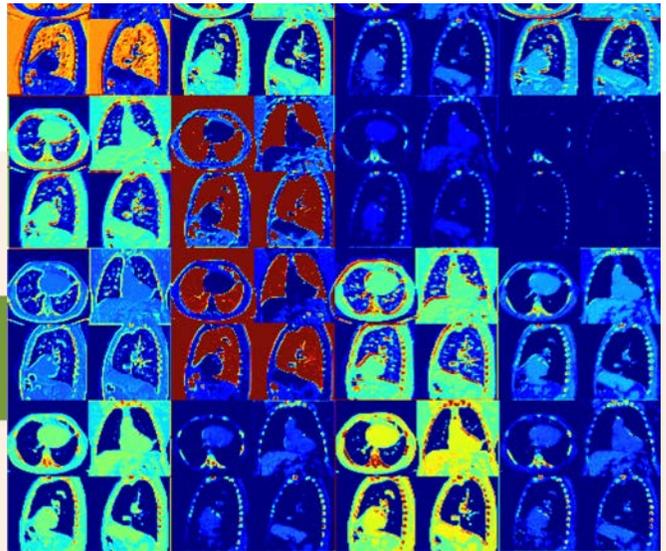


STRATEGIC VISION OBJECTIVES

Leveraging data science to help predict and prevent disease

The NHLBI launched a new cloud-based data science platform in 2019, the BioData Catalyst. In tandem with the NIH Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative, the BioData Catalyst will help researchers securely find, access, share, cross-link, and analyze large datasets, while also ensuring patient privacy. It includes more than 20,000 chest images from the COPDGene study and more than 150,000 whole genome sequences collected through the TOPMed program, which includes data from more than 80 diverse cohort studies.

In addition, the NHLBI is supporting development of artificial intelligence (AI) tools that can rapidly sift through



Composite chest images of COPDGene study participants using filters to enhance visualization of the lungs, chest wall, and bone structures. *Source: Gonzalez G, et al. Am J Respir Crit Care Med. 2018.*

vast amounts of biomedical data to identify patterns that can help detect disease. For example, the COPDGene study used AI principles to predict acute breathing problems in smokers with COPD, and another study used AI to distinguish between malignant and benign lung nodules (swellings).

Researching Sleep and Sleep Disorders

The NHLBI continues to support science on the biology of sleep, circadian rhythms, and sleep disorders, as well as their contributions to heart, lung, and blood health.

Years of NHLBI-supported basic research have established that the brain regulates sleep and wakefulness in part by releasing a hormone called hypocretin. In 2019, a study in mice found



that undisturbed sleep maintains the brain's proper release of hypocretin, which in turn helps quiet inflammation that can contribute to atherosclerosis. Sleep-deprived mice had lower levels of circulating hypocretin and higher rates of atherosclerosis, which could be prevented by giving them infusions of hypocretin. We may be able to leverage this pathway to develop new therapies for atherosclerosis.

We also know that not getting enough sleep can negatively affect heart health. A 2019 study found that people who slept fewer than seven hours per night had lower levels of certain microRNAs (a type of gene-regulating molecule) that help reduce inflammation and support blood vessel health. Another new study found that people who sleep fewer than six hours a night may be at increased risk of abnormal heart rhythm (atrial fibrillation).

SUSTAINING A DIVERSE AND DYNAMIC WORKFORCE FOR THE FUTURE

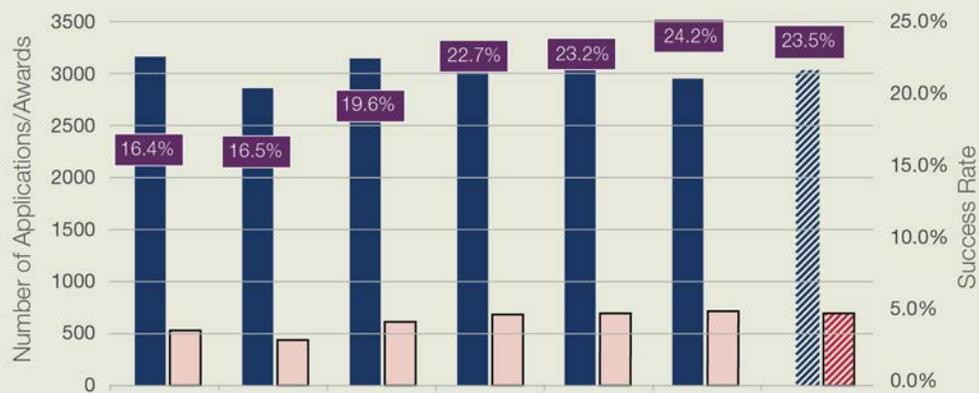
STRATEGIC VISION OBJECTIVE



The NHLBI continues to prioritize investigator-initiated science and support for early-stage investigators (ESIs). In fact, over the past five years, the award success rate for NHLBI ESIs improved by 78 percent. The Institute has also invested in programs to build and sustain a diverse

workforce. For example, supplemental awards can be made to grantees who diversify their research team. Moreover, the NHLBI's Programs to Increase Diversity Among Individuals Engaged in Health-Related Research (PRIDE) prepares junior faculty from underrepresented backgrounds for

Overall Success Rates for NHLBI R01 Applications from 2013 to 2019



Fiscal Year	2013	2014	2015	2016	2017	2018	2019
#Applications	3168	2839	3164	3129	3055	2942	3041
# Awards	518	468	619	730	708	711	716
Overall Success Rate	16.4%	16.5%	19.6%	22.7%	23.2%	24.2%	23.5%
ESI Success Rate	22.4%	18.0%	25.7%	31.7%	30.3%	32.7%	29.2%

of Applications # of Awards Overall Success Rate

Fiscal Year 2019 data is preliminary. Only non-AIDS applications and awards are included.

STRATEGIC VISION OBJECTIVE



Improving translation and implementation science

The NHLBI's Center for Translation Research and Implementation Science works to move evidence-based interventions into clinical practice for patients with heart, lung, blood, and sleep disorders.

The Center is supporting a new area called Simulation Modeling and Systems Science (SMSS), which examines how a new or emerging intervention might work in different settings or among different populations. With this understanding, SMSS allows researchers to adjust and refine the intervention as needed to ensure its success, before implementing it in the real world. A current project is using SMSS to project the 10- and 30-year impact of six evidence-based obesity interventions at the national level and in six socioeconomically diverse states.



NHLBI-supported implementation science is also being applied to help people living with HIV, who are at higher risk of developing chronic heart, lung, blood, and sleep disorders, compared to people who are HIV-negative. The Heart, Lung, and Blood Co-morbidities Implementation Models in People Living with HIV (HLB-SIMPLe) initiative funds research to understand the risk factors for HIV-associated disorders (comorbidities) in low- and middle-income countries. This research is expected to lead to methods for earlier detection and prevention of these comorbidities, which could also benefit Americans living with HIV.

successful research careers. From 2006 to 2018, graduates from PRIDE's cardiovascular research programs had a 63 percent success rate for NIH grant applications, compared with 19 percent for NIH applications overall.

Ensuring the long-term stability of an inclusive workforce is also a priority. NHLBI leadership and program staff make every effort to identify, grow, and retain tomorrow's scientific leaders; support them on a path to independence; and prepare them to train the next generation. For example, one type of training award, the NHLBI Midcareer Investigator Award in Patient-Oriented

Research (K24), currently supports 43 midcareer investigators. This award ensures mid-career physician researchers can mentor and guide early-career research trainees or junior faculty by providing them with 25 percent protected time for five years, allowing for a meaningful period of guidance and mentorship.

The NHLBI will continue its commitment to supporting talented scientists throughout their careers, helping them succeed not only as investigators but also as teachers and mentors for a future globally competitive workforce.

