

ADVANCING

Heart, Lung, Blood, and Sleep Research



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National Heart, Lung,
and Blood Institute

Director's Message

Advancing Heart, Lung, Blood, and Sleep Research



NHLBI Director Gary H. Gibbons, M.D.

The National Heart, Lung, and Blood Institute (NHLBI), its partner organizations, and the biomedical community have responded to the COVID-19 pandemic with speed and dedication, yielding lifesaving vaccines and treatments that emerged at an unprecedented pace. Still, many continue to suffer severe illness and death, some are coping with loss, and others are coping with continued-ill health. As we enter a third year of the COVID-19 pandemic—with even more effective therapeutics and hope that we are through the worst of it—this is a time to reflect, recharge, refocus, and work together to plan our path forward. At the same time, we have reinforced efforts to sustain and grow research supporting the Institute's mission to reduce the burden of heart, lung, blood, and sleep disorders.

Mobilizing to Defeat COVID-19

As the pandemic unfolded, we quickly saw disparities in the impact of COVID-19, with rates of infection and severe outcomes highest in the same communities that experience higher rates of chronic heart, lung, blood, and sleep disorders. It also soon became clear that COVID-19 can have life-threatening effects not only on the lungs but also on the heart, blood, and blood vessels. For these reasons, NHLBI has been at the vanguard of the NIH response to COVID-19.

- With the National Institute on Minority Health and Health Disparities (NIMHD), NHLBI launched the Community Engagement Alliance (CEAL) Against COVID-19 Disparities. CEAL has forged partnerships between researchers and community organizations in more than 20 states. It has helped people in hard-hit communities engage in vaccine research, get vaccinated, and garner important, tailored resources on COVID-19.
- NHLBI's clinical research networks helped investigate potential therapies for acute COVID-19. One such trial found that the blood thinner, heparin, used in non-critically ill patients increased the probability of survival to hospital discharge as compared with usual-care; other trials found that treatments once considered promising were, in fact, not effective—including convalescent plasma in at-risk outpatients seeking emergency room care.

- In late 2020, as a growing number of COVID-19 survivors continued to experience debilitating illness, NHLBI was asked to co-lead the NIH Researching COVID to Enhance Recovery (RECOVER) initiative, which is investigating the causes of Long COVID and is expected to begin testing potential therapies in 2022.

Advancing Health Equity

COVID-19 reaffirmed NHLBI's ongoing commitment to community-based research to address health disparities. NHLBI's investments in this area have continued to grow from population health studies that seek to identify the causes of disparities to intervention studies seeking to reduce them. The latter includes DECIPHeR, a new community-based participatory research network that has researchers in several states testing new approaches to expand the use of evidence-based interventions for heart and lung diseases in high-risk communities.

Two other new programs focus on the high rates of maternal morbidity and mortality in women of color. Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH) will examine whether cardiovascular health modules delivered through federal home visiting programs can enhance maternal and early childhood heart health. And the Maternal Health Community Implementation Project will fund regional coalitions of organizations, researchers, and networks to test a variety of evidence-based interventions before and during pregnancy to reduce high maternal death rates in four U.S. regions.

Sustaining Investigator-Initiated Research

Despite the challenges of the past year, the Institute has maintained its support for investigator-initiated research, with success rates for R01 research project grants around 20 percent or better. By prioritizing support for early-stage investigators (ESIs), NHLBI increased the ESI RO1 success rate from 28.6 percent in fiscal year (FY) 2020 to 36.8 percent in FY 2021. In addition, to foster next-generation investigators,





we have adapted our training and career development programs and clinical trial networks. Ongoing efforts such as our Programs to Increase Diversity among Individuals Engaged in Health-Related Research (PRIDE) continue to successfully prepare junior faculty from underrepresented backgrounds for research careers. NHLBI also participates in trans-NIH efforts to boost inclusive excellence, such as the Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) and Faculty Institutional Recruitment for Sustainable Transformation (FIRST) programs, that work to increase the representation of faculty from groups underrepresented in biomedical science.

Lessons Learned and Looking Ahead

Although the COVID-19 pandemic is not yet firmly behind us, as a community, we've worked together to set a path forward. We've learned how frontline partnerships between NIH and community organizations can improve inclusion in research and access to results. We've gained experience in quickly mobilizing clinical research networks, and we've conceived new flexibilities to sustain researchers in times of crisis. Now it's time to build on these new insights and assets to address persistent challenges in heart, lung, blood, and sleep disorders—including the need to reduce health disparities and to develop therapies tailored to each patient's unique profile.

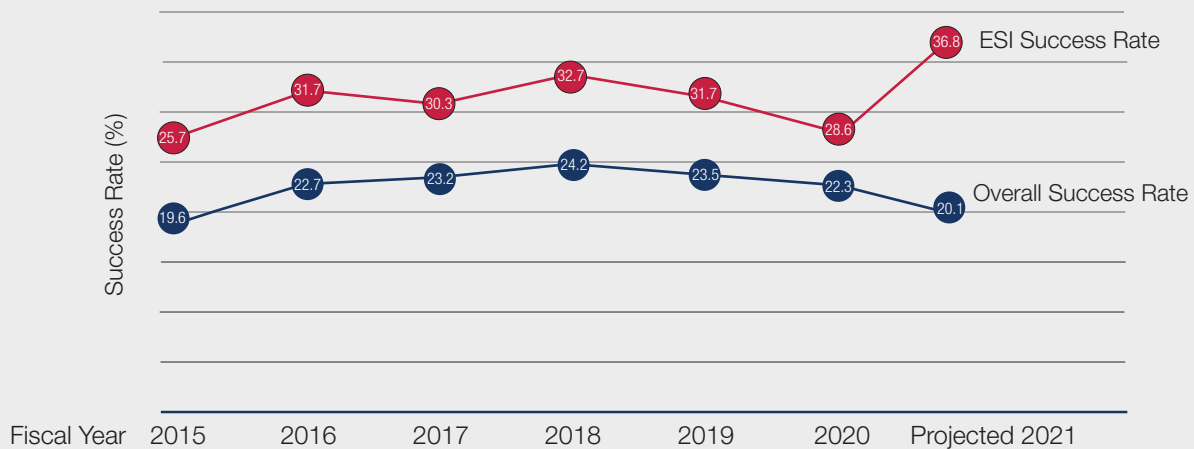
Meeting NHLBI Strategic Vision Objectives 1, 2, and 7

For a complete list of goals and objectives, visit www.nhlbi.nih.gov/about/strategic-vision.

Investing in Data Science to Drive Precision Medicine

The Institute continues to break new ground in data science, providing researchers with the tools they need to explore the biology of heart, lung, blood, and sleep disorders and set the stage for precision medicine. NHLBI's TOPMed program has supported collection and analysis of whole genome and other molecular and clinical data from more than 200,000 participants in 90 diverse cohort studies. NHLBI's BioData Catalyst platform houses TOPMed, other large datasets, and a suite of analytic tools, enabling researchers to explore potential new disease mechanisms and therapeutic targets. These programs also provide training opportunities for early-career investigators interested in using data science to solve public health problems.

Success Rates for NHLBI R01 Applications: 2015 to 2021



Highlights in Heart Health



Accelerating Our Efforts to Treat Complex Heart Failure

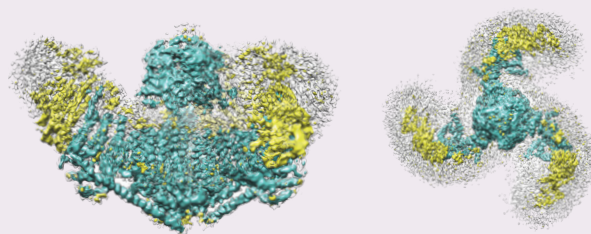
- Heart failure affects more than 6 million Americans, more than half of whom have heart failure with preserved ejection fraction (HFpEF). This complex condition, where the heart contracts normally but fills with blood too slowly, has limited treatment options. In 2021, NHLBI launched **HeartShare**, which will define mechanisms of HFpEF by analyzing clinical, laboratory, and imaging data from about 1,500 patients. NHLBI also anticipates working through the **Accelerated Medicines Partnership (AMP)**, a collaboration of NIH, the Food and Drug Administration (FDA), and industry to deconstruct HFpEF and identify therapeutic targets.
 - ◇ HeartShare will incorporate winning ideas from the recent **Big Data Analysis Challenge**, which sought new models and artificial intelligence tools to define different subtypes of heart failure.
 - ◇ Data from HeartShare are also being made available through the **BioData Catalyst**.

Supporting Clinical Studies to Improve Cardiovascular Care

- NHLBI's **Cardiothoracic Surgical Trials Network (CTSN)** moves research from the proof-of-concept stage into clinical trials. A recent CTSN trial offers hope for people with mitral and tricuspid valve regurgitation (**leaky heart valves**), which is typically treated with surgery to repair the mitral valve or, in severe cases, surgery to also repair the tricuspid. The new trial found that patients who had tricuspid and mitral repair at the same time were less likely to die or advance to severe tricuspid regurgitation 2 years out, compared with those who had mitral repair alone. However, patients who had both procedures were also more likely to need a pacemaker.
- NHLBI's CABANA trial is the largest trial to date comparing ablation (a procedure to destroy arrhythmic cardiac tissue) with drug therapy for patients with heart failure and **atrial fibrillation (AFib)**. The trial found that ablation was superior for survival, freedom from AFib recurrence, and quality of life.

- NHLBI is working to improve survival after **out-of-hospital cardiac arrest**, which has a 90 percent fatality rate. The ARREST trial examined the potential to treat such patients with extracorporeal membrane oxygenation (ECMO), which uses a machine outside the body to oxygenate and pump blood. Compared with patients given standard care, those given ECMO as soon as they arrived at the hospital had better survival rates and neurologic function at 6 months.
- NHLBI's **Pediatric Heart Network (PHN)** is celebrating 20 years at the forefront of pediatric cardiology research. With nine clinical hubs and affiliated sites across the country, the PHN is currently enrolling five clinical research studies that includes children and adults living with congenital heart disease (CHD), with two more studies nearing launch, including the PHN's first nurse-led clinical trial. The PHN tested udenafil, a drug that increases blood flow to the lungs, in teenagers who have only one working heart ventricle. The trial found that udenafil improved exercise capacity in such teens. The drug manufacturer has submitted these data to FDA to get the drug approved for use in this population.

Discovery Science Highlight



NHLBI grantee Dr. Ardem Patapoutian, along with Dr. David Julius, won the 2021 Nobel Prize in Physiology or Medicine for discovering the molecular bases for heat, cold, and touch perception. It turns out that these molecules are also involved in maintaining blood pressure and controlling iron levels in red blood cells. Patapoutian and his team discovered a cell-membrane protein that senses pressure, which they named Piezo1. The protein has a unique propeller shape; it is thought that the propeller “blades” become deformed when the cell membrane is deformed by pressure—providing part of the basis for pressure sensation.





Understanding Heart Disease in Diverse Populations

- NHLBI's **RURAL study** aims to better understand the high burden of heart and lung disease in the rural Southeast by following 4,000 people in this region. In 2021, the study began deploying a mobile exam unit equipped with the latest diagnostic technologies to collect medical data and uncover disease risk factors. The study will also collect socioeconomic and environmental data and is expected to inform disease prevention strategies for rural Americans.
- In 2021, the Institute announced Dr. April P. Carson as the new director of the **Jackson Heart Study**, the nation's longest-running study of **cardiovascular health in African Americans**. Carson, an epidemiologist, was

previously a key investigator with NHLBI's CARDIA study—investigating health disparities in cardiovascular disease—and brings significant experience in community-engaged research.

- For 33 years, the **Strong Heart Study** has partnered with tribal nations in Arizona, Oklahoma, and the Dakotas to understand the high rates of **heart disease among American Indians**. In 2021, the study launched its Strongheart Tribal Approach to Research (STAR) program, which will support community-driven projects to address the health priorities of the partner tribes.
- To advance health equity for **Asian Americans, Native Hawaiians, and Pacific Islanders**, the Institute is planning long-term research examining the burden of heart and lung diseases in these diverse populations.

Meeting NHLBI Strategic Vision Objectives 4, 5, and 6

For a complete list of goals and objectives, visit www.nhlbi.nih.gov/about/strategic-vision.

Preserving Cardiovascular Health Across the Life Course

Given that cardiovascular disease is the leading cause of pregnancy-related deaths, NHLBI has taken a lead role in working with others at NIH to support research to reduce the nation's alarming rates of maternal mortality and morbidity. NHLBI's programs take a life course approach that focuses on improving women's heart health before, during, and after reproductive age. These programs also focus on the significant disparities in maternal health that affect communities of color.

- The CHAP trial is examining the safety and effectiveness of using medication to treat mild **chronic hypertension in pregnancy**, which is typically deferred for severe hypertension.
- The Institute has extended funding for the **nuMoM2b Heart Health Study**, which is examining how pregnancy

affects a woman's future cardiovascular health in a large diverse cohort. The study has found that women who experience adverse pregnancy outcomes have worse cardiovascular outcomes, including higher risk for hypertension, as late as 2 to 7 years after delivery.

- Two new NHLBI programs aim to move evidence-based interventions for maternal health into broader practice.
 - ◇ The **Maternal Health Community Implementation Program** will fund several regional coalitions to pilot-test implementation of community-based interventions in areas where maternal death rates are high, particularly in the Southeast.
 - ◇ NHLBI's new **Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH)** program will tap into existing federal home health and wellness visiting programs that serve at-risk families to determine whether adding heart-healthy lifestyle interventions will enhance maternal and early childhood outcomes.

Dr. David Goff

@NHLBI_HEARTDir

NHLBI's Division of Cardiovascular Sciences (DCVS) supports research to advance understanding of and interventions for promoting heart and vascular health across the lifespan. It also supports research aimed at preventing and treating pediatric and adult cardiovascular diseases, including heart attack, heart failure, stroke, and congenital heart disease. DCVS is led by David Goff, M.D., Ph.D.



Highlights in Lung and Sleep Health



Reducing the Burden of COPD

Chronic obstructive pulmonary disease (COPD) is a leading cause of death and disability in the United States. NHLBI and its federal and nonfederal partners released the first-ever **COPD National Action Plan** in 2017 and are making progress in implementing it.

- NHLBI has established an online system for all partners to track and share their progress in meeting the plan's goals, including the goal to increase and sustain research on COPD. The following NHLBI programs and projects are helping make an impact.
 - ◇ Using **TOPMed** data, researchers recently sequenced the genomes of nearly 20,000 diverse people with COPD and found an association with 22 new genes.
 - ◇ To improve diagnosis and treatment of COPD, researchers are assessing the impact of a simple **COPD screening tool** called CAPTURE in primary care settings.
 - ◇ NHLBI has embarked on a new two-phase **Air You Wear Challenge** to stimulate the development of lighter, more portable oxygen devices for the more than 1.5 million Americans who use supplemental oxygen for COPD and other conditions. Phase I winners were announced in December 2021.
 - ◇ In 2021, the **Lung Health Cohort** study began recruiting 4,000 adults ages 25–35 from over 20 metropolitan regions across the U.S. to evaluate the impact of environment, lifestyle, and physical activity on respiratory health and improve early detection of lung disease.

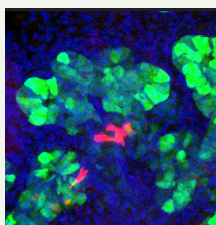
Precision Medicine for Lung Disease

- The PreciSE Network aims to develop precision medicine for **severe asthma**. PreciSE will test six therapies, including two immunotherapy drugs, that are tailored to each trial participant based on their unique biomarker profile. The network is enrolling 650 teens and adults with severe asthma at 30 sites nationally.
- NHLBI is supporting genomic research to better characterize and treat **sarcoidosis**. This disease develops when groups of immune cells form lumps in various organs, most often the lungs. The GRADS study recently identified four clusters of patients with unique gene expression profiles, suggesting that there are distinct subtypes of sarcoidosis that might respond to distinct therapies.
- PRECISIONS is the first clinical trial to explore the effectiveness of precision medicine for **idiopathic pulmonary fibrosis (IPF)**. The trial will examine whether the antioxidant N-acetylcysteine (NAC) is effective for patients with IPF who have undergone genetic screening. Past trial results have been mixed but suggest a potential benefit specific to patients who carry a gene variant that affects the lung's immune defenses.

Advancing Clinical Research in Lung Transplantation

- The survival rate for lung transplantation is lower than for other organs, but NHLBI is supporting research to advance the field. For example, researchers are conducting a Phase I clinical trial of the drug regadenoson for patients undergoing lung transplant. This drug is typically used in diagnostic testing for heart disease, but laboratory studies show that it also has anti-inflammatory effects that could help prevent lung graft failure. Another small trial has shown that patients given a high dose of the diabetes drug sitagliptin, in addition to standard medications, had lower rates of graft-versus-host disease. To build on this momentum, the Institute is assembling a **Lung Transplant Consortium** that will coordinate research efforts.

Discovery Science Highlight



An NHLBI-funded team recently charted key steps in the development of the alveoli, the tiny air sacs in the lungs required for gas exchange. They found that a subtype of alveolar cells act as a signaling hub during lung development, shedding light on potential approaches to repairing the lungs after injury or disease.





Fostering Sleep and Circadian Research

The **National Center on Sleep Disorders Research (NCSDR)**, housed within NHLBI, supports research on sleep and circadian biology and coordinates sleep research across federal agencies.

- In 2020, the Institute named a new NCSDR director, Marishka K. Brown, Ph.D., who worked across NIH and stakeholder communities to develop a new **NIH Sleep Research Plan**, released in December 2021.
- The goals of the Plan are to (1) elucidate sleep and circadian mechanisms underlying health and disease; (2) improve treatment of sleep and circadian disorders and reduce the risks associated with sleep deficiency; (3) accelerate the clinical implementation of sleep and circadian research and identify gaps and opportunities to protect the health of the public; (4) advance the understanding of sleep and circadian contributions to health disparities, populations, and public safety; and (5) foster the development of a strong and diverse workforce for sleep and circadian research.
- Recent studies supported by NCSDR focus on the **links connecting sleep disruptions, obesity, and chronic disease.**

- ◇ One study shows that the well-known association between lack of sleep and obesity seen in adults can begin in infancy; the study followed nearly 300 infants ages 1–6 months and found that those who slept less were more likely to be overweight.
- ◇ Another study offers an explanation and a potential solution for the higher risk of diabetes and heart disease faced by night shift workers. The study, which simulated night work conditions in a controlled setting, found that eating at night—as many shift workers do—can increase glucose levels, a risk factor for diabetes. Restricting meals to daytime prevented this effect.

Meeting NHLBI Strategic Vision Objectives 2, 3, and 7

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Climate Change and Health

Climate change and other environmental factors, such as air pollution and wildfires, increase the risk and severity of asthma and other lung diseases. For that reason, NHLBI supports efforts to reduce the health impacts of climate change, especially in low-income and underserved communities, which are more likely to be exposed to pollution. For example, the AIRHEALTH study is investigating how acute and chronic exposures to air pollution lead to cardiopulmonary disease. The Lung Health Cohort, the RURAL study, and other cohort studies include measures to investigate the impact of environmental health on personal health. NHLBI also participates in the Human Health Exposure Analysis Resource (HHEAR) program, which provides services for researchers to add or expand exposure analysis in their studies.



Dr. James Kiley

@NHLBI_LUNGDir

NHLBI's Division of Lung Diseases (DLD) supports research on the causes, diagnosis, prevention, and treatment of lung diseases and sleep disorders, including asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, sleep-disordered breathing, acute lung injury, pulmonary complications of HIV/AIDS, pediatric lung diseases, and pulmonary fibrosis and other rare lung disorders. DLD is led by James Kiley, Ph.D.



Highlights in Blood Health



Advancing Treatments and Cures for Sickle Cell Disease

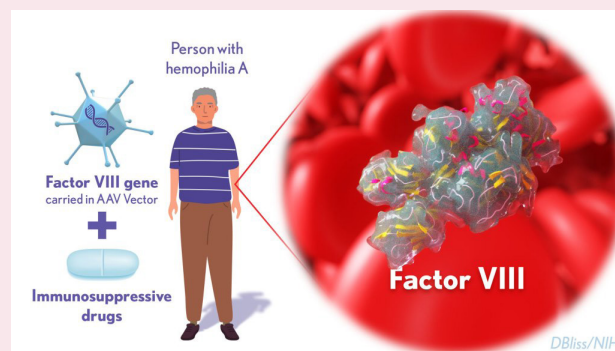
- Recent progress in **gene therapy** is allowing researchers to tackle sickle cell disease (SCD) at its molecular roots—inherited mutations in the gene that encodes adult hemoglobin (Hb), which is needed for red blood cells to transport oxygen. **NHLBI's Cure Sickle Cell Initiative (CureSCi)** and other programs are supporting clinical trials to replace, repair, or compensate for the adult Hb gene, and early results are promising.
 - ◇ A pilot trial funded by CureSCi found that gene therapy to reactivate a fetal form of Hb reduced the number of pain crises and the need for transfusions among six patients with severe SCD who were followed for six months.
 - ◇ NHLBI's **intramural program** is one of 11 sites in the U.S. participating in a clinical trial of LentiGlobin, a gene therapy that provides a working copy of the Hb gene. Interim results in 35 patients show that a one-time treatment with this therapy eliminated severe pain crises out to 18 months.
 - ◇ Risks of gene therapy for SCD include cell abnormalities that could lead to blood cancers—and even without gene therapy, research suggests that people with SCD may be at an increased risk of blood cancers. NHLBI has been working closely with researchers to identify patients at high risk, provide updated information on these risks, and implement closer patient monitoring after gene therapy.
 - ◇ In 2021, CureSCi also released a set of data standards for gene therapy trials—a toolkit that will help investigators collect the same kinds of data, using the same methods, so that results are easier to compare across trials.
 - ◇ The **Blood and Marrow Transplant Clinical Trial Network**, a research program supported by NHLBI and the National Cancer Institute (NCI) is conducting clinical trials in patients with SCD who undergo hematopoietic stem cell transplantation to evaluate how best to implement this curative therapy.

Meeting NHLBI Strategic Vision Objectives 1, 4, and 5

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Promising Gene Therapy Findings for Hemophilia A

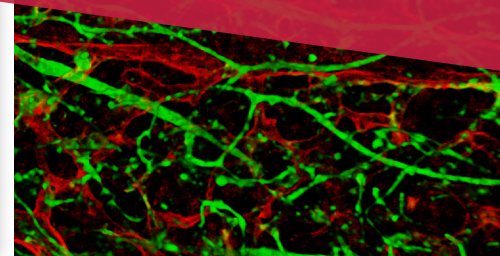
Hemophilia is a rare genetic disorder that can cause severe bleeding from a minor cut. About 20,000 people in the U.S., mostly men, suffer from hemophilia A because their genes do not make enough of a blood-clotting protein called factor VIII (FVIII). A common and often effective treatment is to provide intravenous infusion of FVIII concentrate, but this needs to be repeated often, and some patients develop antibodies to FVIII that render it ineffective. In 2018, NHLBI launched a 5-year multicenter program to understand how these antibodies arise and to develop work-arounds. In a recent clinical trial, researchers tested a gene therapy approach intended to restore FVIII. A single dose of this gene therapy restored the missing FVIII protein and nearly eliminated bleeding episodes for up to 2 years in all but 2 of 18 participants. All participants are enrolled in a 4-year follow-up trial.



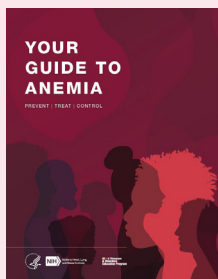


Blood Health Network

A Partnership of the Blood Diseases & Disorders Education Program



- NHLBI is leveraging the NIH **Helping to End Addiction Long-term (HEAL)** initiative, which supports research on pain and development of nonaddictive pain therapeutics, to develop more effective approaches to manage SCD pain. For example, a new program seeks to improve training for healthcare providers in SCD pain management, and to use telemedicine to extend the reach of care by SCD specialists.
- **The SCD Implementation Consortium**, a 7-year program launched in 2015, focused on strategies to improve delivery of evidence-based care for SCD. With a range of projects on issues such as widening the use of the drug hydroxyurea and improving how emergency departments treat patients in sickle cell crisis, the consortium built a community of practice combining expertise in implementation science and SCD. It also built a registry of 2,400 patients with SCD that will continue to be accessible and maintained by CureSCi. These accomplishments laid a foundation for investigators to design new multipronged projects to overcome barriers to care for SCD patients.



NHLBI's "[Your Guide to Anemia](#)" provides an overview of anemia for health consumers, covering risk factors, diagnosis and treatment.

Improving Transfusion Medicine


The **Recipient Epidemiology and Donor Evaluation Study (REDS)**, launched in 1989 in response to the AIDS crisis, seeks to improve blood safety and availability. The current **REDS-IV-Pediatric** program supports studies involving adults, newborns and children to improve blood donor safety and transfusion outcomes across the lifespan.

- A new genome-wide study supported by REDS identified 27 genetic variables in donated blood samples that could influence the shelf life of stored blood. Further research on these variables could advance donor screening and storage policies and improve transfusion outcomes.
- In early 2020, as part of the federal response to COVID-19, REDS conducted repeated testing for SARS-CoV-2 antibodies in six U.S. metropolitan regions to estimate infection rates over time. This provided a foundation for a national seroprevalence program run by the Centers for Disease Control and Prevention (CDC).

Supporting Public Education on Blood Science

In September 2021, NHLBI launched the Blood Diseases and Disorders Education Program, which aims to improve public knowledge about blood safety, as well as the diagnosis, management, and treatment of blood diseases and disorders. The program also launched the [Blood Health Network](#), a coalition of public and private organizations working to improve awareness of and education about SCD.

Dr. Keith Hoots

 @NHLBI_BLOODDir

NHLBI's Division of Blood Diseases and Resources (DBDR) leads research on the causes, prevention, and treatment of congenital and acquired blood diseases. The program also helps ensure the safety of the world's blood supply and supports stem cell biology and new gene- and cell-based therapies to repair and regenerate human tissues. DBDR is led by Keith Hoots, M.D.



Highlights in Translation Research and Implementation Science



Testing Community-Driven Interventions

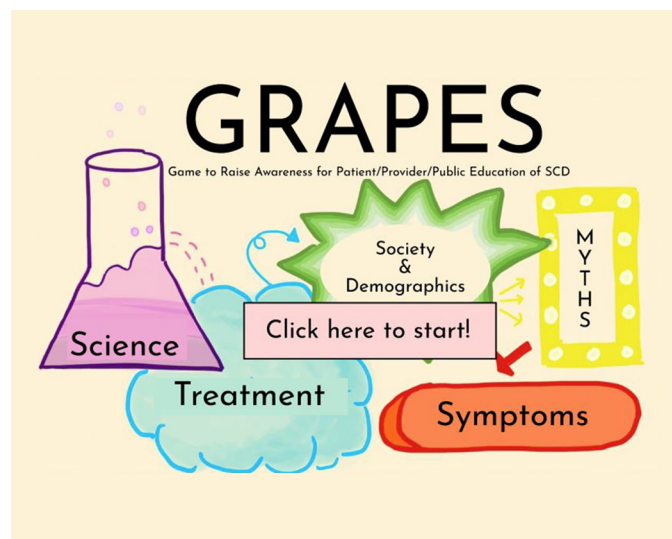
NHLBI's **DECIPHeR** program addresses health disparities through implementation science. Implementation science aims to improve health outcomes by studying how to deliver the best available interventions in a way that overcomes barriers and leverages individual, system, and community assets. Community members are at the forefront of these efforts. In 2020, the program began funding seven implementation research centers and a coordinating center to test new ways of delivering proven interventions for heart and lung disease to high-risk communities.

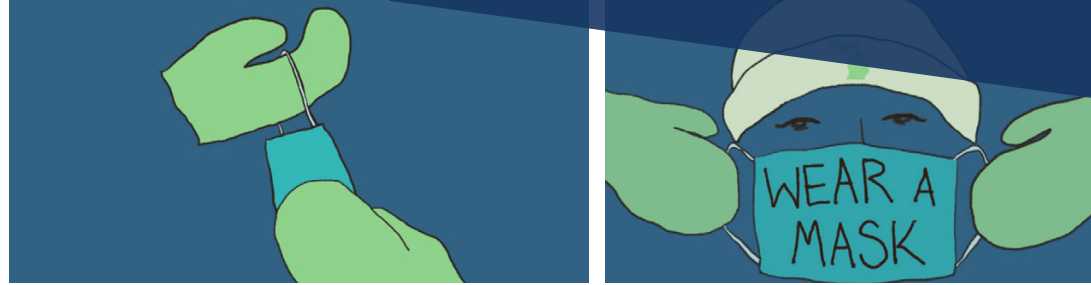
- In Michigan and Maryland, researchers are working with 24 community mental health program sites to test evidence-based cardiovascular disease (CVD) interventions in people with **serious mental illness** (SMI). People with SMI make up 5 percent of the U.S. population, and as a group, they experience a mortality rate two times higher, dying 10 to 20 years earlier, than the national average.
- In Chicago, researchers are trying to help low-income smokers quit by using a multipronged **smoking** cessation program that combines an online patient portal, a smokers' quit line, and messaging tailored for low health literacy.
- Another project in Chicago is testing strategies to bring evidence-based interventions for heart disease to predominantly Black communities with high rates of **hypertension, heart disease, and stroke**. The project will use an intervention model delivered successfully by a large healthcare system, but will be adapted for delivery by community health workers and church leaders.
- In Los Angeles, 51 adult primary care clinics will implement culturally tailored, multilevel, evidence-based strategies to improve **hypertension** control in this large and diverse county. Pharmacy-directed care and healthy lifestyle practices are key.
- In New York City, researchers are implementing three evidence-based interventions to improve **hypertension** control among Black patients in primary care practices. Nurse care management, home blood pressure monitoring, and community healthcare workers are all part of the integrated model being tested.

- In Louisiana, community health workers are partnering with local churches to reduce **CVD risk in African Americans** by promoting healthy lifestyle interventions that align with current CVD guidelines (e.g., healthy diet, physical activity, smoking cessation, weight loss).
- In rural and small metropolitan areas of Colorado, researchers are working with school-based asthma care navigators and nurses to test a team approach to reduce flare-ups in **underserved schoolchildren with asthma**.

Engaging Students in Sickle Cell Disease Education

NHLBI supports programs to train early-career researchers in community engagement and implementation science while delivering real benefits to patients. For example, the **Hope for Sickle Cell Disease Challenge** called for college teams to work together to come up with innovative solutions—such as digital tools, video games, and mobile devices—to help people with sickle cell disease live longer, healthier lives. One of the winning concepts, a trivia game about the disease, called GRAPES, is now being tested to see how well it improves knowledge among patients, caregivers, and healthcare providers.





Addressing COVID-19 in Communities with Significant Health Disparities

The COVID-19 pandemic provided a stark reminder of how social determinants of health can contribute to health disparities; for example, demographic groups that tend to have large numbers of essential workers, higher-density housing, and less access to health care saw the worst infection rates and outcomes. To reach those Americans hit hardest by the pandemic, NHLBI, in partnership with the National Institute on Minority Health and Health Disparities (NIMHD), established the NIH **CEAL** initiative.

- CEAL connects researchers to community-based organizations and local leaders to help underserved and vulnerable communities get accurate, up-to-date information about COVID-19; to facilitate COVID-19 testing and prevention (including face masks and vaccination); and to ensure opportunities to participate in and benefit from COVID-19 research.
- CEAL has focused on communities that have experienced high rates of COVID-19 infection and poor outcomes—as well as barriers to prevention and treatment—especially underserved African American, Hispanic/Latino, American Indian/Alaska Native, and Asian American/Pacific Islander communities.
- **The CEAL network is now active in more than 20 states.** Early in the pandemic, it helped people in hard-hit communities address misinformation, get tested for COVID-19, and find vaccine clinical trials; later, it set up local vaccination clinics. Nationally, CEAL continues to help people stay abreast of COVID-19 research, available vaccines, and preventive practices through information written in lay terms, in both English and Spanish. It provides a model and lessons learned to address other long-standing disparities in chronic heart and lung diseases.
- CEAL research teams developed a variety of innovative approaches to engage communities in reducing the spread of COVID-19. For example, teams in Michigan and North Carolina held contests that invited community members to develop poems, songs, graphics, and videos encouraging their neighbors to mask up and get vaccinated.

Meeting NHLBI Strategic Vision Objectives 3 and 6


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NHLBI and NIMHD Directors receive 2021 Service to America Medals



NHLBI Director Gary H. Gibbons and NIMHD Director Eliseo Pérez-Stable were recognized with 2021 Service to America Medals, or Sammies, for their leadership of the CEAL initiative. NIH Director Dr. Francis Collins (right) joined Dr. Gibbons (center) and Dr. Pérez-Stable as they received their awards, which are sponsored by the Partnership for Public Service and considered the Oscars for public servants.

Dr. George Mensah

 @NHLBI_Translate

NHLBI's Center for Translation Research and Implementation Science (CTRIS) supports research addressing both domestic and global health disparities and inequities and provides training and career development opportunities in these areas. CTRIS is led by George Mensah, M.D., FACC.



NHLBI's COVID-19 Response at a Glance

COVID-19 can have severe effects on heart, lung, blood, and sleep systems and poses a higher risk for people with preexisting heart, lung, blood, and sleep conditions. For these reasons, NHLBI has played a significant role in the nation's COVID-19 response, especially in research to understand COVID-19's short- and long-term effects on the body and to develop lifesaving treatments for people who get sick.

To mobilize quickly, NHLBI leveraged a variety of prior investments and resources already in place before the pandemic, including clinical trials networks and community-based studies. For example, NHLBI's trial networks have focused on treatments for moderate to severe COVID-19 and its effects on the respiratory and cardiovascular systems, including life-threatening blood clots. Several networks contributed to the NIH **Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)** initiative, a partnership of government agencies, academic research institutions, and pharmaceutical companies to conduct rigorous placebo-controlled trials. Taken together, these trials have been critical to identifying treatments that work for slowing acute COVID-19, as well as potential treatments that do not work.

- The **ACTIV-3** trials showed that monoclonal antibodies neither helped nor harmed hospitalized patients.
- The **ACTIV-4 Antithrombotics** trials include three adaptive platform trials evaluating whether anticoagulants or antiplatelet drugs can reduce the life-threatening blood clots in three different groups of patients: those who do not need hospitalization (outpatient), hospitalized patients, and those recovering after hospital discharge.
 - ◇ The ACTIV-4 inpatient protocols found that a 2-week regimen of the blood thinner heparin reduced the need for organ support, such as mechanical ventilation, for moderately ill hospitalized patients but not for critically ill patients in intensive care.

- ◇ An ACTIV-4 outpatient protocol involving non-hospitalized patients with COVID-19 found that treatment with aspirin or the blood thinner apixaban did not reduce rates of cardiopulmonary hospitalization compared with a placebo.
- ◇ The ACTIV-4 convalescent protocol is testing the safety and efficacy of anticoagulants and/or antiplatelets for patients discharged or recovering from hospitalization for COVID-19.
- ◇ A fourth ACTIV-4 protocol consists of “blockade studies” to evaluate novel drugs that may prevent tissue and organ damage in patients hospitalized for COVID-19.
- NHLBI's **ORCHID** trial found that hydroxychloroquine neither helped nor harmed hospitalized COVID-19 patients, a result confirmed by other trials internationally.
- Another trial examined whether high-risk outpatients with COVID-19 benefitted from **convalescent plasma**, which is derived from patients who have recovered from the disease. This approach did not prevent disease progression when administered within the first week of symptoms.



CEAL teams work with communities to address vaccine hesitancy. Placing vaccine vans near community food pantries has helped residents get vaccinated. Photo credit: New York Common Food Pantry

Masthead image: A highly magnified image of SARS-CoV-2 virions (red) produced by human airway epithelial cells in the lungs. Credit: Camille Ehre, Ph.D., University of North Carolina School of Medicine.



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NHLBI has also taken a leadership role in NIH initiatives to address COVID-19 disparities, long-term effects of COVID-19, and COVID-19 in children.

- To address high rates of COVID-19 hospitalization and death in underserved and racial/ethnic minority communities, NHLBI partnered with the National Institute on Minority Health and Health Disparities (NIMHD) to mobilize and expand existing community-based research partnerships through the **CEAL** initiative. Now active in more than 20 states, CEAL has connected researchers with trusted community leaders across the country to reach the people hit hardest by the pandemic, ensure research inclusion, address misinformation, and improve testing and vaccine uptake and access.
- Due to NHLBI's leading role in understanding how acute COVID-19 damages the body's organs and tissues, NHLBI also co-leads an initiative to understand—and ultimately treat and prevent—its potential long-term effects, often called Long COVID. The NIH **RECOVER** Initiative will follow tens of thousands of adults and children

to help us understand Long COVID and other persistent complications that can follow SARS-CoV-2 infection. In addition to clinical exams and laboratory tests, RECOVER will collect data through electronic health records and mobile health technologies to help reduce the burden on participants and enable the analysis of real-world data. To ensure a diverse cohort, CEAL teams are helping to engage and enroll patients into RECOVER. The initiative is expected to begin testing potential therapies for Long COVID in 2022.

- NHLBI also co-leads the **CARING for Children with COVID** initiative and is leveraging the Pediatric Heart Network to conduct a long-term observational study of **multisystem inflammatory syndrome in children (MIS-C)**. This rare condition follows SARS-CoV-2 infection in some children and often has cardiac complications. The study has enrolled more than 1,000 children (about 20 percent of affected children nationally), who will be followed for 5 years to gain insights into MIS-C, its risk factors, and potential interventions.



Meeting NHLBI Strategic Vision Objective 8

For a complete list of goals and objectives, visit www.nhlbi.nih.gov/about/strategic-vision.

Supporting the Next-Generation Workforce Through the Pandemic

The COVID-19 pandemic reinforced the need for a talented diverse cadre of **clinician-scientists** who can balance their efforts between research and clinical practice. To increase this pool, NHLBI supports the Stimulating Access to Research in Residency (**StARR**) and Transition Scholar (**StARRTS**) programs, which provide in-depth research opportunities to clinicians during residency. We also supported new clinician-

scientists in their transition from training (K) awards to a first R01 by providing a limited-competition K-R03 award or bridge award. Additional flexibilities during the pandemic included grant supplements to cover unanticipated study costs, such as temporary lab and clinic closures, as well as extended deadlines to meet study milestones. Other programs, such as the **Jackson Heart Study Scholars** program, created opportunities for students to become ambassadors in their communities to help fight misinformation about COVID-19 and build trust in NIH research while preparing them to enter the biomedical workforce.