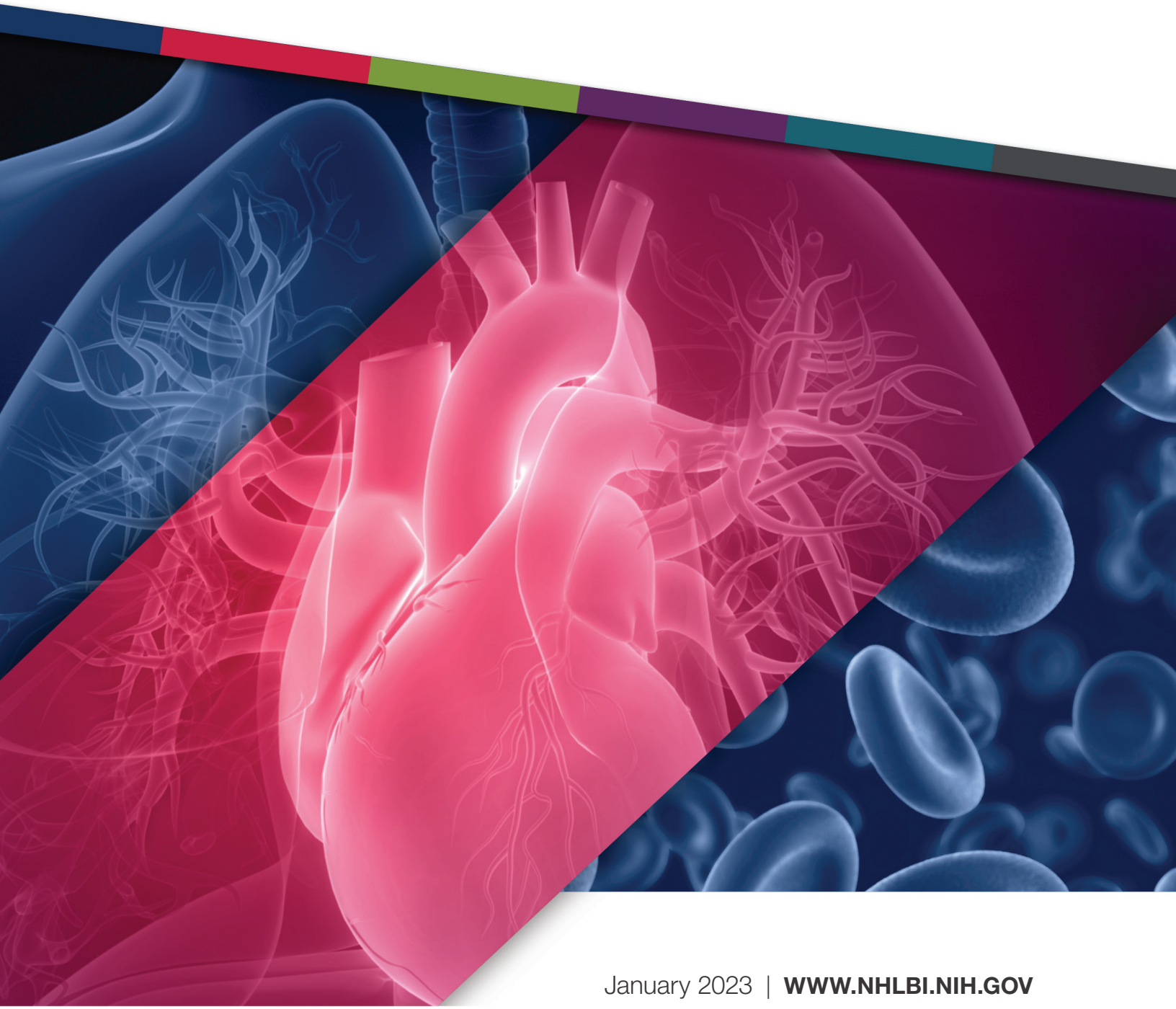
ADVANCING

Heart, Lung, Blood, and Sleep Research

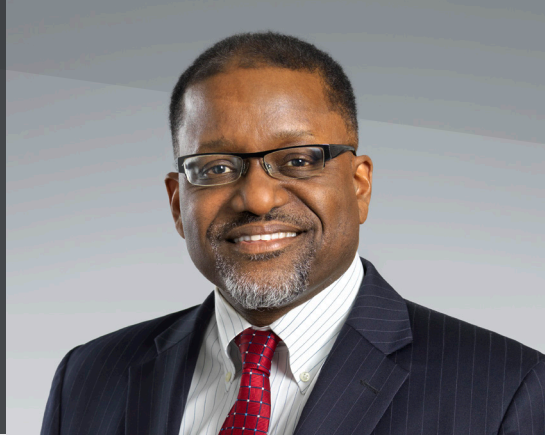


January 2023 | **WWW.NHLBI.NIH.GOV**

National Heart, Lung, and Blood Institute

Director's Message

Advancing Heart, Lung, Blood, and Sleep Research



NHLBI Director Gary H. Gibbons, M.D.

This year, the National Heart, Lung, and Blood Institute (NHLBI) celebrates its 75th anniversary. Over the decades, NHLBI has supported groundbreaking research that has pushed the frontiers of fundamental science, epidemiological (population) studies, clinical research, and implementation science. It has also been bold and innovative in its health education and dissemination efforts. In a word, the Institute has been active. It launched initiatives in emergent fields such as community-engaged research, artificial intelligence (AI)/machine learning, and data science, and it has supported the development of new and curative therapies for common and rare diseases and conditions. NHLBI's research programs have helped improve longevity and quality of life for people in the United States and around the world, while increasing the focus on communities bearing a disproportionate burden of heart, lung, blood, and sleep disorders.

In observance of this anniversary, we reflect on NHLBI's long history of research accomplishments in improving public health. We renew our commitment to supporting cutting-edge basic and applied research aimed at finding effective ways to prevent, diagnose, and treat the diseases and disorders within NHLBI's purview.

Community-Engaged Research to Advance Public Health

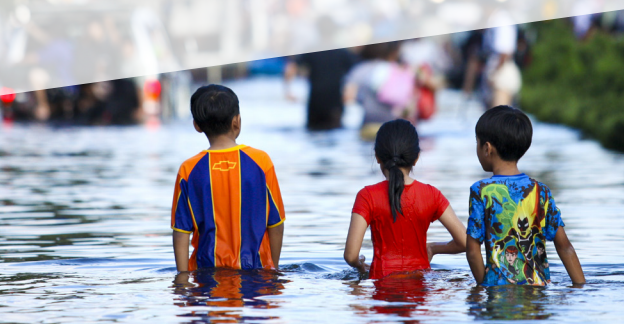
NHLBI continues to increase its commitment to community-based research that successfully addresses public health problems. NHLBI's investments in this area have continued to grow, from population health studies that seek to identify the causes of disparities, to intervention studies seeking to reduce them. Many of the diseases in NHLBI's portfolio have a disproportionate impact on people of color, people living in rural communities, and other underserved populations. Clinical researchers are now acknowledging the need to address the complex network of factors that influence health and disease, such as where people live; how they interact with their community, family, and friends; and what kind of health behaviors they have adopted. The road to discovery depends upon the trusting participation of these communities in the research enterprise. This requires re-envisioning the composition of a research team.

> "Over the decades, NHLBI has supported ground-breaking research that has pushed the frontiers of fundamental science, epidemiological studies, clinical research, and implementation science.

- In July 2020, NHLBI partnered with the National Institute on Minority Health and Health Disparities (NIMHD) to launch **Community Engagement Alliance (CEAL) Against COVID-19 Disparities**. CEAL brings together multidisciplinary teams of researchers and trusted community partners, including community- and faith-based organizations, minority professional societies, and others in communities affected by COVID-19.
- NHLBI is now leveraging the CEAL community engagement platform for other initiatives, including the **NHLBI Maternal Morbidity and Mortality Community Implementation Program (MH-CIP)**, the NIH **Implementing a Maternal health and PRegnancy Outcomes Vision for Everyone (IMPROVE) initiative**, and the **NIH Climate Change and Health Initiative**.
- NHLBI also co-leads the NIH **RECOVER (Researching COVID to Enhance Recovery) initiative**, launched in 2021, to better understand why some people develop long term symptoms of SARS-CoV-2 infection, or long COVID. Since its inception in 2021, RECOVER has depended on the input, support, and participation of those most affected by long COVID: the people living with the condition. Having this large-scale, diverse cohort ensures that the voices of those disproportionately affected by the disease are meaningfully represented in the research endeavor.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov



Supporting Diversity, Equity, Inclusion, and Access Across the Research Enterprise

Studies show teams that embrace diversity at every level of the research endeavor produce more — and more significant — scientific breakthroughs. NHLBI firmly believes this, which is why the Institute is working to fundamentally change the meaning of a multidisciplinary research team in all its work. This kind of diversity requires not only including people with different scientific expertise and skills but also collaborating with communities and affected populations at every phase of the research enterprise — from the formulation of research questions; through the planning, design, and implementation of research protocols; to the eventual interpretation and dissemination of findings. Exposing more communities to the research endeavor means opening doors to young people who might never have considered a career in biomedical research and inviting them to share their unique perspectives and knowledge.

By actively engaging communities, supporting diversity at all levels of the research enterprise, and fostering new and diverse types of partnerships — all while continuing to invest in critical research — the Institute continues to do its part to accelerate discoveries that enhance public health.

> Studies show teams that embrace diversity at every level of the research endeavor produce more — and more significant — scientific breakthroughs.

Responding to the Public Health Challenges of Climate Change

The World Health Organization describes climate change as the biggest threat to human health and well-being moving into the future. Both short- and long-term impacts will lead to increases in, and worsening of, chronic diseases such as cardiovascular disease, respiratory conditions, and sleep disorders. At every level, everyone will be affected, though in different ways, and public health strategies will have to be developed to take these differences into account. Community-engaged research will be center stage in these efforts.

- NHLBI understands the important role it has to play in this massive challenge and has provided significant funding to **NIH's Alliance for Community Engagement-Climate and Health (ACE-CH) initiative**.

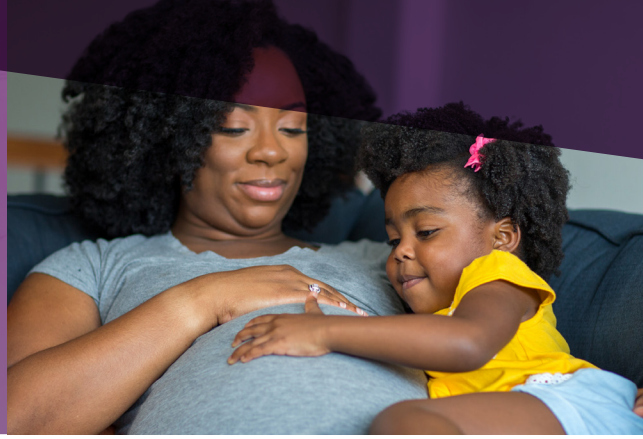
Cardiovascular Disease and Maternal Health

Each year, an estimated 700 women in the United States die from complications related to pregnancy, and more than 50,000 experience severe morbidity. Most cases of maternal morbidity and mortality (MMM) are related to underlying heart, lung, blood, and sleep conditions. Cardiovascular disease (CVD) is the leading cause of pregnancy-related deaths, accounting for more than one-third of these deaths annually. NHLBI supports research aimed at preventing or managing cardiovascular risk factors and CVD across a woman's entire lifespan.

- The **nuMoM2b Heart Health Study**, funded by NHLBI with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), is studying the effects of pregnancy complications on future cardiovascular health, including social factors that correlate with the future heart health of new parents, especially in communities of color.
- Results from the **Chronic Hypertension and Pregnancy** trial (discussed below) showed that targeting a blood pressure of less than 140/90 mmHg in pregnant women with mild chronic hypertension leads to better pregnancy outcomes.

Highlights in

Heart Health



Advancing Research in Heart Failure

- In September 2022, NHLBI and the Foundation for the National Institutes of Health (FNIH) tapped into the **Accelerating Medicines Partnership® (AMP®)**. AMP is a public-private partnership between NIH, the U.S. Food and Drug Administration (FDA), and biopharmaceutical and life science companies. It integrates the distinct resources and expertise of these entities on drug discovery and development to further support established NHLBI programs and initiatives. A new addition to this program, **AMP Heart Failure**, is forming working groups to systematically analyze data from **HeartShare**, **Trans-Omics for Precision Medicine (TOPMed)**, and other NHLBI resources. The goal is to turn discovery of novel therapeutic targets into safe and effective treatments.
- Patients and their clinicians want to know whether they are at high risk of sudden cardiac death. A recent study showed that a simple, inexpensive test for coronary artery calcium (CAC), in combination with the use of traditional risk factors, can identify individuals with a higher risk of sudden death. Patients and clinicians will find this information useful when they are deciding what preventive strategies to use. A second study found that even a small amount of CAC detected on a scan indicates that some young adults will be at higher risk of heart attacks and other cardiovascular events into mid-life, even though doctors assume their risks are low when assessed by traditional risk equations.

Improving Heart Health in Women Across the Lifespan

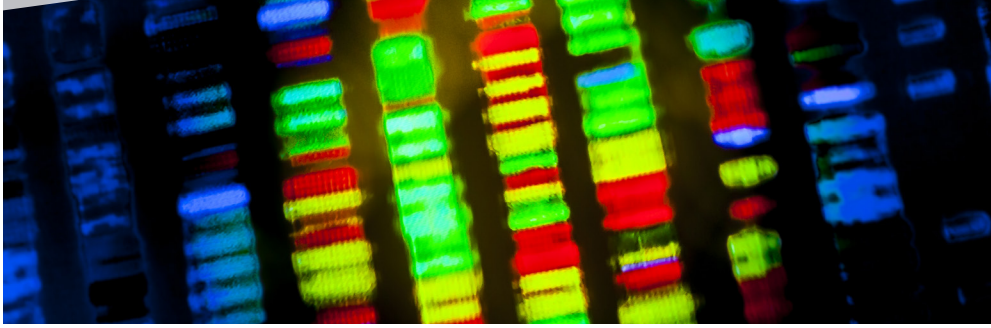
- NHLBI's **Chronic Hypertension and Pregnancy (CHAP)** trial seeks to prevent adverse pregnancy and fetal growth outcomes by focusing on interventions that safely control the cause of the problem: mild chronic hypertension during pregnancy. Recent results from this study have shown that a strategy of targeting a blood pressure of less than 140/90 mmHg in pregnant women with mild chronic hypertension leads to better pregnancy outcomes than a strategy of reserving treatment only for severe hypertension. The new strategy had no negative effect on fetal growth, a concern that had previously constrained interventions. This discovery has been so significant that it led to immediate changes in the American College of Obstetricians and Gynecologists' clinical practice guidelines for treatment of mild chronic hypertension during pregnancy.
- **IMPROVE**, an NIH-wide initiative, aims to reduce preventable causes of maternal morbidity and mortality and improve health for women before, during, and after delivery. Among developed nations, the United States has the highest prevalence of maternal mortality. Pre-pregnancy factors (e.g., hypertension, obesity, diabetes), age (e.g., women over age 40 have higher rates), and disparities in rural/urban areas and among racial/ethnic groups (e.g., African Americans and American Indians bear a greater burden) contribute to the country's high maternal mortality and morbidity rates. In addition, maternal cardiovascular health declines during the life course, a factor that underscores the need to start interventions during pre-pregnancy and early pregnancy periods. IMPROVE includes populations that have a high prevalence of maternal mortality, and its research focuses on the importance of early intervention and support, maternal mortality, disparities, and community engagement.

Addressing Heart Health Disparities

A recent 2022 paper from the **Multi-Ethnic Study of Atherosclerosis (MESA)** analyzed disparities in cardiovascular disease mortality across four race and ethnic groups, with adjustments for socioeconomic status, lifestyle, psychosocial factors, and immigration history. In another 2022 paper, investigators used two decades of U.S. mortality data from the Centers for Disease Control and Prevention (CDC) to evaluate demographic and regional trends in mortality from acute myocardial infarction (AMI). They report that, despite decreases in AMI mortality rates in all groups, disparities persisted. Higher mortality rates are seen in Black individuals, men, and people living in the South.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov



- The **Early Intervention to Promote Cardiovascular Health of Mothers and Children (ENRICH)** program will tap into existing federal home visiting programs that serve at-risk families. Its goal is to determine whether adding a cardiovascular intervention will enhance maternal and early childhood outcomes for approximately 3,000 mother-child pairs. This is especially important because adverse pregnancy outcomes — hypertensive disorders of pregnancy (HDP), preterm delivery, and low birth weight babies, for example — are associated with poor maternal and offspring cardiovascular health. Between 2007 and 2019, HDPs increased from 38.4 to 77.8 per 1,000 live births. The increase was higher in Black people and older age groups.
- A study from the **Women's Health Initiative (WHI) Memory Study (WHIMS)–Epidemiology of Cognitive Health Outcomes (WHIMS-ECHO)** found an association between air pollution and cognitive decline in older women. The study also showed that improving air quality (i.e., reducing exposure) reduced the rate of cognitive decline, which is considered a strong risk factor for dementia.

Dietary Interventions to Reduce Cardiovascular Disease

- In a study reported in November 2022, researchers compared the effects of three eating patterns on patients' risk of experiencing a cardiovascular event within the next 10 years: the Dietary Approaches to Stop Hypertension (DASH) diet; a diet rich in fruits and vegetables; and the Western diet, which is typically low in fruits and vegetables but high in fat and sodium. The team's findings suggest that while the DASH and fruit/vegetable diet each reduced risk scores by about 10 percent over an 8-week period, the DASH diet conferred additional benefits for women and Black adults.
- A recent NHLBI-supported study provides evidence that dietary changes — particularly replacement of margarine, butter, eggs, yogurt, cheese, or processed meats with avocado — are associated with a lower risk of cardiovascular disease.
- A study found that consuming more olive oil (versus butter, mayonnaise, dairy fat, etc.) was associated with a lower risk of mortality from cardiovascular and respiratory events. This study contributes to the body of evidence indicating the health benefits of olive oil.

Supporting Research to Identify Potential Therapeutic Targets

- NHLBI-supported scientists identified extensive molecular alterations in failing hearts at single-cell resolution. They did this by performing single-nucleus RNA sequencing of nearly 600,000 nuclei in left ventricle samples from 11 hearts with dilated cardiomyopathy. Understanding the landscape of genes in the human heart that are involved in health and disease may offer new potential therapeutic targets and biomarkers for heart failure.
- A recent study has identified 162 unique genes that exert their effects on up to seven disease-relevant tissues and cell types. The study was aimed at developing a comprehensive integrative genomics analysis pipeline for coronary artery disease (CAD) and to provide a prioritized list of causal CAD genes.
- Machine learning was recently used to improve patient stratification through the identification of phenotypic subtypes of dilated cardiomyopathy. These subtypes of disease have different clinical outcomes, which may reflect different underlying pathologies. This work is promising in identifying subtypes that, when further investigated, may lead to more targeted treatment approaches.

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 Health

Making Healthier Lives for People with 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 continue to make progress in implementing it.

- Genetic testing allows people to better understand their genetic risks for certain diseases and health conditions. However, calculating these risks across racial and ethnic groups limits the accuracy of the tests. Researchers used data from **NHLBI's TOPMed** program to determine that, compared to using the standard "polygenic risk scores," a novel framework called a "polygenic transcriptome risk score" improved the accuracy of predictions regarding risk of COPD.
- In collaboration with the Respiratory Health Association, **NHLBI's Learn More Breathe Better® program** launched the COPD Caregiver's Toolkit in 2022. This resource addresses the top issues that COPD patients and caregivers face, including home management, physician visit preparation, and emergency preparedness.
- NHLBI has partnered with the COPD Foundation to support the **SPIROMICS Study of Early COPD Progression (SOURCE)**, which began recruiting in 2022. This observational study aims to define the nature of early COPD in younger, at-risk individuals. This is important because most of what we know about COPD comes from research about its later stages. However, many experts believe the best chance to slow or halt the progression of COPD involves targeting mechanisms at the earliest stages of the disease.

Using the LungMAP Consortium to Advance Cures

Researchers are using cutting-edge technology to create molecular and cellular maps of the human body. In 2022, the NHLBI-funded **LungMAP Consortium** synthesized current data into a comprehensive and practical cellular census of the lung. This flagship program will lead to novel therapeutic targets for lung diseases.

Developing Targeted Prevention and Cures

Idiopathic pulmonary fibrosis (IPF) is a serious chronic disease that affects the tissue surrounding the air sacs, or alveoli, in the lungs. Life expectancy after diagnosis is approximately three years. Repurposing drugs to treat conditions other than the one for which they were developed and/or approved can make effective, more affordable treatments available to patients sooner. NHLBI-supported translational researchers recently discovered that saracatinib, a drug initially developed to treat cancer, shows promise as an IPF therapeutic. It is currently being tested in a Phase 1b/2a clinical trial supported by the National Center for Advancing Translational Sciences (NCATS).

> "Repurposing drugs can make effective, more affordable treatments available to patients sooner.

Understanding Critical Illness Syndromes

NHLBI and the National Institute of General Medical Sciences (NIGMS) have partnered to form the **ARDS, Pneumonia, and Sepsis Phenotyping (APS) Consortium**. This group will support a longitudinal observational study to better understand the heterogeneity and underlying mechanisms of critical illness syndromes and recovery, specifically in adults with acute respiratory distress syndrome (ARDS), pneumonia, and/or sepsis. It also will explore the relationship and biological overlap among these syndromes. Awards that will establish the Consortium are expected to be made in fiscal year 2023.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov

Studying Climate Change and Lung Health

A 2022 NHLBI-funded study found that inhaled particles from air pollution accumulate in lung-associated lymph nodes and weaken immune defenses over time. Researchers found that lung-associated lymph nodes collected from younger donors were largely beige, while those collected from donors over age 30 were blackened and got darker with increasing age. The researchers found that the blackened lymph nodes of these older donors were clogged with particles from airborne pollutants. This study suggests that air pollution may contribute to why older people are more susceptible to respiratory infections.

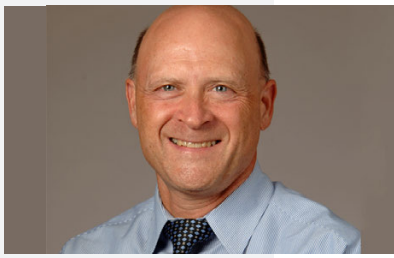
> This study suggests that air pollution may contribute to why older people are more susceptible to respiratory infections.

Improving Lung Transplantation Outcomes

The survival rate for lung transplantation is lower than the rate for transplantation of other organs. To coordinate research efforts and advance the field, NHLBI has created the **Lung Transplant Consortium (LTC)** that will coordinate research efforts. NHLBI launched the LTC in August 2022, funding seven projects and a data coordinating center to support a series of studies. These aim to understand the impact of site-specific lung transplant selection criteria and clinical management strategies on donor lung utilization and/or early post-transplant outcomes in recipients.

Dr. James Kiley
@NHLBI_LUNGDir

NHLBI's Division of Lung Diseases (DLD) supports research on the causes, diagnosis, prevention, and treatment of lung diseases, including asthma, COPD, cystic fibrosis, 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

Sleep Disorders Research

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. The impetus for this work has been well-established. Sleep and circadian rhythms profoundly influence the crucial functions of nearly every cell and organ in the body. NCSDR's mission areas are:

- Sleep and circadian research projects related to the regulation of sleep and sleep disorders and the etiology and treatment of heart, lung, and blood diseases.
- The diagnosis, treatment, and prevention of sleep disordered breathing.
- Studies to determine how the brain controls breathing during sleep.

Advancing Sleep and Circadian Research

- Studies have shown that elevated nighttime temperature lowers sleep quality, with the largest effects being felt by older adults and low-income individuals. There are also biological differences in sleep quality and its health impacts. For example, women report poorer sleep quality and have higher risk for insomnia than men do and may be affected by changes in sleep related to menstruation, pregnancy, post-childbirth, and menopause.
  - ◊ NHLBI research has revealed that exposure to even ambient light while sleeping was linked with obesity, diabetes, and high blood pressure in older adults.

> Sleep and circadian rhythms profoundly influence the crucial functions of nearly every cell and organ in the body.

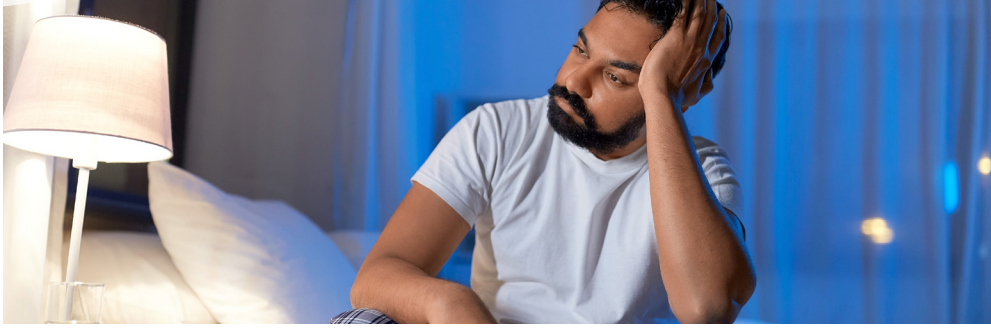
Research to Address Sleep Disparities

Appropriate sleep is key to the proper function of the human body. Unfortunately, some groups, such as racial and ethnic minorities and those of lower socioeconomic status, are disproportionately affected by poor sleep. Suboptimal sleep environments, including those burdened by climate change, also influence how and how well people sleep.

- Sleep dysfunction and insufficient sleep are associated with Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD). African Americans are disproportionately affected by higher rates and earlier onset of ADRDs relative to White Americans.
- In a study sample of predominantly African American older adults, both the amount of time spent awake while in bed (known as low sleep efficiency) and frequently waking up while sleeping (known as wakefulness after sleep onset, or WASO) were associated with poorer cognitive function. Improving sleep health may help prevent ADRD and reduce health disparities.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov



Sleep Health and Immune Function

A 2022 study supported by NHLBI and the NCATS found that getting a consistent good night's sleep supports normal production and programming of hematopoietic stem cells in humans and mice. Sleep has long been linked to immune function, but researchers discovered that getting enough of it influenced the environment where monocytes form, develop, and get primed to support immune function. They analyzed how sleep disruptions increased circulating levels of these immune cells and changed the environment in the bone marrow. Prior studies have identified genetic mutations that drive the proliferation of hematopoietic stem cells. However, this study found that putting pressure on the hematopoietic system, in this case through sleep restriction, produced similar results without the driver mutations. The findings underscore the importance of establishing sound sleep patterns early in life, which may reduce the severity of other inflammatory conditions.

Sleep and the Opioid Epidemic

The Helping to End Addiction Long-term® Initiative, or **NIH HEAL Initiative®**, is an aggressive, interagency effort to speed scientific solutions to stem the national opioid public health crisis. Almost every NIH Institute and Center is accelerating research to address this public health emergency from all angles. The initiative is funding hundreds of projects nationwide. Researchers are taking a variety of approaches to tackle the opioid epidemic through:

- Understanding, managing, and treating pain
- Improving prevention and treatment for opioid misuse and addiction

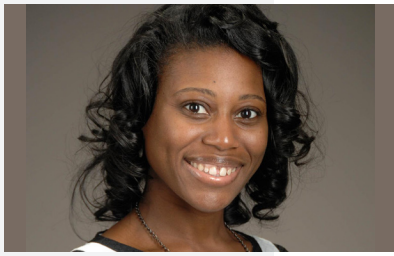
NIH Sleep Research Plan

In December 2021, the Institute released the **NIH Sleep Research Plan**. It is based on a set of research needs and opportunities identified with input from researchers, public representatives, NIH workshop participants, and NHLBI programmatic staff. The plan incorporates cross-cutting NIH priorities that address topics such as minority health and health disparities, sex/gender, sleep across the lifespan, the impact of opioid addiction, and how poor sleep may exacerbate the risk and outcome of infectious diseases such as COVID-19. The plan also covers the development of personalized treatments for sleep and circadian disorders.

NCSDR is contributing to the HEAL initiative by funding studies to examine how sleep and circadian rhythms affect opioid use disorder (OUD) and response to medication-assisted treatment. Some FDA-approved medications for other conditions are also potential treatments for OUD and pain. For example, the insomnia treatment suvorexant is being tested for its ability to improve sleep and address other withdrawal symptoms in people with OUD. HEAL scientists showed that suvorexant effectively treats sleep problems related to withdrawal, mitigates opioid craving, and has little potential for harmful use.

Dr. Marishka Brown

The National Center for Sleep Disorders Research supports research on the causes, diagnosis, prevention, and treatment of sleep disorders. The Center is led by Marishka Brown, Ph.D.



Highlights in

Blood Health

Therapeutic Approaches to SCD

- Sickle cell disease (SCD) and beta-thalassemia are caused by certain mutations in a gene that creates hemoglobin. The gene, called beta-globin, is turned on in red blood cells (RBCs) around the time of birth as the fetal version, called gamma-globin, is turned off. However, under the stress condition of hypoxia (low oxygen), gamma-globin genes are turned on in adults, and adult expression of gamma-globin can alleviate symptoms in people with SCD and beta-thalassemia.
  - ◊ A recent NHLBI-supported study identified a new molecular pathway, which is sensitive to oxygen levels, that turns on the gamma-globin gene in adult RBCs. Hypoxia stabilizes hypoxia-inducible factor 1 (HIF1), which turns on the gamma-globin gene in adult RBCs.
  - ◊ Using young red blood cells from individuals with SCD and testing in vitro, researchers found that prolyl-hydroxylase inhibitors (PHIs) can stabilize HIF1, leading to increased fetal hemoglobin and significantly less sickling of cells. This important finding could lead to new therapeutic approaches for reversing disease progression in people with these conditions.
- Developing and improving treatments for the severe pain episodes that people with SCD endure has been front and center for NHLBI.
  - ◊ This year, a proof-of-concept clinical study by NHLBI scientists showed that the pyruvate kinase activator mitapivat (AG-348) improved molecular hallmarks of SCD, increased blood oxygen levels, and reduced sickling in patients with sickle cell anemia.
  - ◊ Another SCD study identified 20 compounds in existing FDA-approved drugs that may be repurposed to treat SCD pain.
  - ◊ Should some of these therapies become available, millions of people around the world could have improved access to safe, affordable treatments.

CureSC: Moving Promising Genetic Therapies Safely into Clinical Trials

The **NHLBI Cure Sickle Cell Initiative (CureSC)** focuses on curative gene therapies while further examining the total effects of sickle cell disease (SCD) on a person's life — from their mental health to their work and finances.

- CureSC is funding two clinical trials in conjunction with the California Institute of Regenerative Medicine (CIRM). It is also funding data collection to allow for a comparative, contemporaneous cohort of patients who have not received curative therapies. This will provide comparator data to the investigators as well as to the FDA to demonstrate the effects of these genetically based curative therapies.
- NHLBI is conducting clinical trials for potential curative therapies. NHLBI researchers are now using the **ReFRAME drug repurposing library**, which looks at drugs that are already FDA-approved and have the potential to treat SCD pain in a cost-effective way.

> "The NHLBI Cure Sickle Cell Initiative focuses on curative gene therapies while further examining the total effects of sickle cell disease on a person's life — from their mental health to their work and finances.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov

Advancing Research in Bone Marrow Transfers and Aplastic Anemia

- Results from a recent NHLBI-supported study showed that adult blood cells are derived not just from blood stem cells (hematopoietic stem cells) as previously believed but also from long-lived embryonic blood progenitors. These findings could spark new strategies for developing treatments for blood disorders and cancers, as well as improve outcomes of bone marrow transplants.
- In early 2023, NHLBI is starting a new clinical trial that will study a potential new curative therapy for aplastic anemia, a rare autoimmune condition resulting in anemia.
  - ◊ The therapy, ruxolitinib, is currently FDA-approved for myeloproliferative neoplasms and graft-versus-host disease. In a recent animal trial, ruxolitinib treatment resulted in prolonged overall survival and alleviated T-cell–mediated immune destruction.

Understanding VEXAS

VEXAS syndrome is a disease that causes inflammatory and hematologic (blood) manifestations. The syndrome, first described by NIH researchers in 2020, is caused by somatic mutations in the *UBA1* gene of blood cells and acquired later in life.

- NHLBI researchers found that patients with VEXAS syndrome are at high risk of thrombosis, mainly venous, which can be recurrent despite use of blood thinners.
- A small study showed that an increase in white blood cell count may be the first sign of VEXAS in some patients. Researchers suggested *UBA1* mutation testing, particularly in older men with other blood count abnormalities.
- Researchers are conducting a clinical trial to understand whether stem cell transplants may be a curative therapy for VEXAS.

> A recent NHLBI-supported study showed that adult blood cells are derived not just from blood stem cells, but also from long-lived embryonic blood progenitors. These findings could spark new strategies for developing treatments for blood disorders and cancers, as well as improve outcomes of bone marrow transplants.

Dr. Keith Hoots

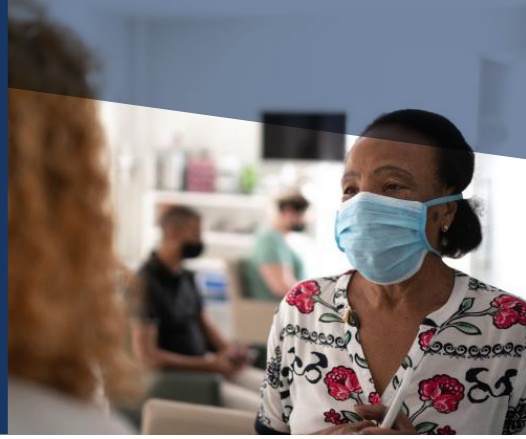
Dr. Keith Hoots, former director of NHLBI's Division of Blood Diseases and Resources, received the American Society of Hematology's 2022 Outstanding Service Award for his tireless advocacy in hematology research. Dr. Hoots retired in April 2022.

Dr. Julie Panepinto
@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 Julie Panepinto, M.D., M.S.P.H.

Highlights in

Translation Research and Implementation Science



Research to Reduce Maternal Mortality and Morbidity

In 2020, NHLBI established the **Maternal Health Community Implementation Project (MH-CIP)**. MH-CIP is a community-based approach to addressing health disparities in vulnerable populations over the life course. Addressing disparities is fundamental to identifying and implementing sustainable strategies to prevent maternal mortality and morbidity in the women most affected. NHLBI is supporting four community research coalitions, which are composed of research organizations, patient advocacy groups, and community partners, to pilot test the implementation of proven interventions in these at-risk populations.

Leveraging Local-Level Data to Advance Health Disparities Research

The **Global Burden of Diseases, Injuries, and Risk Factors Study (GBD)**–U.S. Health Disparities Collaboration is a strategic partnership of several NIH Institutes, Centers, and Offices (including NHLBI) and CDC, working closely with the Institute of Health Metrics and Evaluation at the University of Washington. The partnership was launched to examine local data on morbidity, mortality, life expectancy, and other measures of health and their links to socioeconomic markers, as well as structural and behavioral markers of risk. A recent report from the Collaboration confirmed that disparities in life expectancy among racial/ethnic groups are widespread and enduring and that local-level data are crucial to addressing the root causes of poor health and early death among disadvantaged groups. Importantly, for all racial/ethnic groups, improvements in life expectancy were more widespread across counties and larger from 2000 to 2010 than from 2010 to 2019.

> A recent report confirmed that disparities in life expectancy among racial/ethnic groups are widespread and enduring and that local-level data are crucial to addressing the root causes of poor health and early death among disadvantaged groups.

Mitigating the Health Effects of Climate Change

A collaborative, cross-disciplinary approach is needed to address the urgent issue of climate change, which is one of the greatest existential threats to the health of the planet and to human health. Extreme weather, rising sea levels, rising temperatures, and increases in carbon dioxide levels disproportionately affect the most vulnerable communities. Some of these adverse health outcomes may be short-lived, but others lead to chronic cardiovascular or respiratory illnesses. NHLBI is working closely with the National Institute of Environmental Health Sciences (NIEHS) to fund climate change–related research, including community outreach efforts. The **Alliance for Community Engagement-Climate and Health**'s goal is to reduce health threats across the lifespan and build health resilience in individuals, communities, and nations around the world, especially among those at highest risk. NHLBI will work with climate scientists, citizen scientists, and decision-makers to develop, monitor, and evaluate programs to control sensitivity (e.g., age, access to green space), control exposure (e.g., wildfires, outdoor activities in extreme heat), and create adaptive environments (e.g., cooling centers, heat warnings). NHLBI is also targeting sleep research to improve the negative health impacts of climate change on heart, lung, and blood health.

National Heart, Lung, and Blood Institute

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute
www.nhlbi.nih.gov

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 collaborated with NIMHD to establish the **NIH Community Engagement Alliance (CEAL) Against COVID-19 Disparities initiative**.

- CEAL connects researchers to community-based organizations and local leaders to help the hardest-hit communities get accurate, up-to-date information about COVID-19; facilitate COVID-19 testing and prevention (including face masks and vaccination); and ensure opportunities to participate in and benefit from COVID-19 research.
- CEAL has focused on communities that have experienced high rates of COVID-19 cases and poor outcomes, as well as barriers to prevention and treatment. These groups include underserved African American, Hispanic/Latino, American Indian/Alaska Native, and Asian American/Pacific Islander communities.
- The CEAL network is now active in more than 21 states, the District of Columbia, and Puerto Rico, with the potential to reach nearly 91 million people in 102 counties. Early in the pandemic, the network helped people in hard-hit communities 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 for addressing other long-standing disparities in chronic heart and lung diseases.
- The **Community Engagement Alliance Consultative Resource (CEACR)** was established to elevate best practices throughout CEAL and provide customized expertise to optimize inclusive participation across the research ecosystem.
- CEAL research teams are collaborating with nearly 1,000 organizations, including health care providers and hospital systems, academic and research organizations, schools, associations, and independent businesses. Most importantly, the partners include nearly 550 community service, faith-based, grassroots, nonprofit, social service, and civic community-based organizations. Working with these partners, CEAL research teams have held more than 1,500 local events reaching more than half a million participants. This includes nearly 750 vaccination events at which nearly 200,000 people received a COVID-19 vaccine. More than 600 people have signed up to participate in COVID-19–related clinical trials.

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.

January 2023 | **www.nhlbi.nih.gov**
Twitter: **twitter.com/nih_nhlbi** | Facebook: facebook.com/nhlbi

National Heart, Lung, and Blood Institute