

The Impact of COVID-19 on Heart, Lung, and Blood Systems

The NHLBI's Research Strategy to Understand and Treat COVID-19

The COVID-19 pandemic touches nearly all aspects of the National Heart, Lung, and Blood Institute's (NHLBI) research portfolio. People with chronic diseases such as certain lung conditions, cardiovascular disease, obesity, sickle cell disease, or diabetes are known to be at higher risk for severe outcomes from infection with SARS-CoV-2, the virus that causes COVID-19. Moreover, COVID-19 affects multiple organs, with potentially life-threatening effects on the heart, lungs, and blood/blood vessels.

A Responsive, Robust Research Strategy

Bolstered by \$103.4 million in additional support from the Coronavirus Aid, Relief, and Economic Security (CARES) Act, the NHLBI rapidly mobilized to support research on COVID-19 by leveraging existing NIH-funded studies and infrastructure.

The NHLBI's COVID-19 response has focused on research aiming to:

- Understand the factors that influence risk and resilience for infection and for severe illness
- Understand how COVID-19 attacks the body's vital organs
- Develop therapies to stop the disease and reduce the potential for long-term health effects
- Test behavioral, social, and community-based interventions to improve disease prevention and recovery
- Examine the prevalence of SARS-CoV-2 antibodies in the blood, their ability to protect against future infection, and their utility as a therapeutic

Integral to the NHLBI's approach is the **Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies (CONNECTS)**, which brings together more than 30 clinical trial networks to identify potential therapies for COVID-19. CONNECTS allows researchers to test a variety of interventions simultaneously, easily share their data, and quickly identify the most promising treatments.

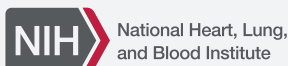
Masthead: A highly magnified image of SARS-CoV-2 virions (red) produced by human airway epithelial cells in the lungs. Credit: Camille Ehre, Ph.D., University of North Carolina School of Medicine.

COVID-19 Clinical Trials

- **The Outcomes Related to COVID-19 treated with hydroxychloroquine among In-patients with symptomatic Disease (ORCHID) Study** evaluated an anti-malaria drug in hospitalized COVID-19 patients. There was no evidence of benefit.
- **The Colchicine Coronavirus SARS-CoV-2 (COLCORONA) trial** is evaluating the gout drug colchicine to see whether it limits inflammation in the heart and lungs in patients with COVID-19.
- **The Clinical Trial of COVID-19 Convalescent Plasma of Outpatients (C3PO)** is evaluating the use of convalescent plasma to treat nonhospitalized patients with mild COVID-19.
- **The Accelerating COVID-19 Therapeutic Interventions and Vaccines 3 (ACTIV-3) trial** is evaluating whether monoclonal antibodies and other immune-modulating therapies can improve recovery in hospitalized patients.
- **ACTIV-4** includes three trials evaluating whether anticoagulants or antiplatelet drugs can reduce life-threatening blood clots in patients with various stages of COVID-19.
- **The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE)** is evaluating complications of SARS-CoV-2 infection among people living with HIV and whether statins can help.

COVID-19 Observational Studies

- **The COVID-19 Observational Study (CORAL)** is examining the pathobiology and outcomes among more than 3,000 adults hospitalized with COVID-19 for up to six months after discharge.
- **The Collaborative Cohort of Cohorts for COVID-19 Research (C4R)** is combining existing diverse population studies to look at long-term COVID-19-related outcomes and factors that affect risk and resilience.
- **The Recipient Epidemiology and Donor Evaluation Study (REDS)**, an NHLBI program that monitors threats to the U.S. blood supply, is analyzing the prevalence of SARS-CoV-2 antibodies (seroprevalence) among blood donors in six cities with high COVID-19 rates, setting up a framework for a nationwide seroprevalence survey.





Establishing Partnerships to Address Health Disparities

COVID-19 has taken its toll on almost every community, but some groups have been hit especially hard. Compared with whites, there are higher rates of COVID-19 among Asian Americans, Blacks, Latinos, American Indians/Alaska Natives, and Pacific Islanders. These groups also tend to be at higher risk for severe illness. Research increasingly shows that **social determinants of health** — conditions in the places where people live, work, and play — have a large impact on these disparities.

Building on their history of engaging communities in research, the NHLBI and the National Institute on Minority Health and Health Disparities (NIMHD) are co-leading the NIH **Community Engagement Alliance (CEAL) Against COVID-19 Disparities Initiative**. CEAL connects researchers to trusted community-based organizations, minority professional societies, and faith-based organizations in communities impacted by COVID-19. Together, they will address misinformation, work to increase preventive practices (e.g., wearing face masks, hand washing), and ensure the inclusion of people of color in trials of vaccines and new treatments. More information and resources are at <https://covid19community.nih.gov>.

In addition, the NHLBI participates in the **NIH Rapid Acceleration of Diagnostics in Underserved Populations (RADx-UP) initiative**, which is developing community-based projects to increase reach, access, uptake, and impact of COVID-19 testing among hard-hit populations.

Evolving Data, Evolving Research

The NHLBI remains poised to adapt and shift its focus as new information about the virus emerges. For example, we now know that some children infected with COVID-19 later develop a severe inflammatory response that requires hospitalization, with most experiencing cardiovascular complications.

In response, the NHLBI is partnering with other NIH Institutes to leverage multiple networks, such as the NHLBI's 29-hospital Pediatric Heart Network, to gain a better understanding of this rare **multisystem inflammatory syndrome in children (MIS-C)**. Through the 5-year **Long-Term Outcomes after the Multisystem Inflammatory Syndrome In Children (MUSIC)** study, clinicians will collect data from pediatric hospitalizations and medical visits to guide diagnoses and treatment. This aggregated information will support long-term evidence-based management guidelines for MIS-C.

In addition, some people who have had COVID-19 — and even asymptomatic SARS-CoV-2 infection — have continued to struggle with symptoms months later. Those with post-acute COVID-19 have developed serious conditions such as heart failure or myocarditis (heart inflammation), stroke, progressive lung disease such as pulmonary fibrosis, or kidney failure. Contingent on sufficient resources, the NHLBI plans to leverage the C4R study, as well as our data science platforms, to understand what causes these lingering health impacts of COVID-19 and to intervene early to prevent them.

The NIH is also developing a COVID-19 clinical trial data hub, which is integrating existing databases — including those housed within the NHLBI's BioData Catalyst — that contain clinical, lab, and imaging data from COVID-19 patients. The data hub will enable more rapid responses to COVID-19 surges, as well as to subsequent emerging threats.

