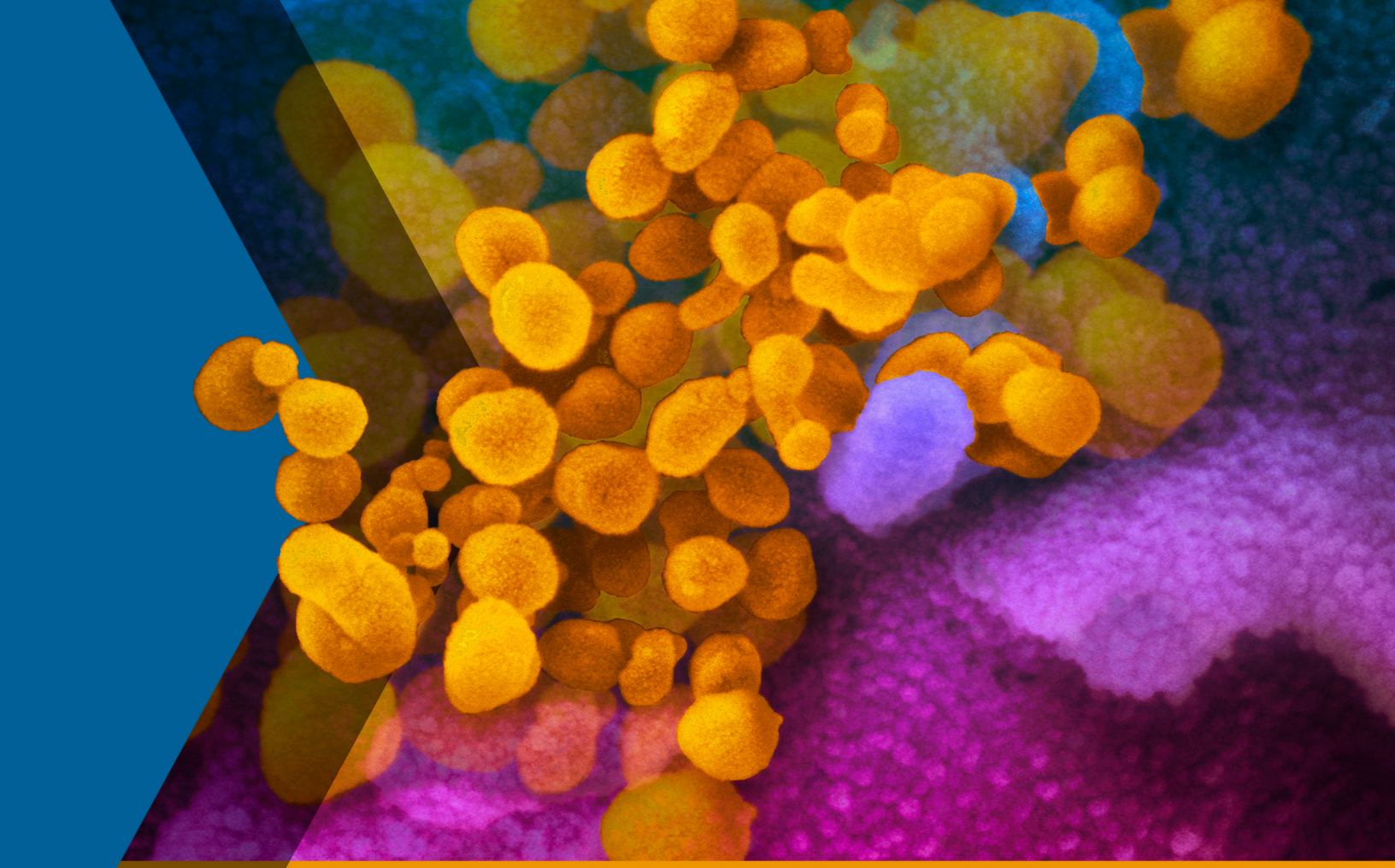


NIH-Wide Strategic Plan for

COVID-19 Research

2021

National Institutes of Health

Updated from July 2020

Cover Image

Coronavirus SARS-CoV-2

This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient in the United States, emerging from the surface of cells (blue/pink) cultured in the laboratory.

Credit: Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, NIH

FOREWORD

To the American People,

With the aim of turning discovery into better health for all, the National Institutes of Health (NIH) invests in biomedical research that spurs innovations in science and technology. NIH research has proven its value to the United States and the world over the years by rising to meet the challenges of polio, AIDS, and many other formidable health foes. Most recently, the critical importance of NIH research has been demonstrated by our response to what is likely the greatest public health crisis of our generation: the coronavirus disease 2019 (COVID-19) pandemic.

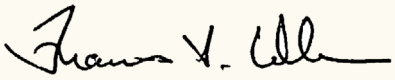
Over the past year, COVID-19 has inflicted a staggering toll on our Nation, claiming the lives of more than a half-million Americans. U.S. science has risen to this daunting challenge and made unprecedented progress in the fight against this swiftly spreading disease caused by the coronavirus SARS-CoV-2.

To address the challenges that COVID-19 poses to our health and economy, NIH has, from the pandemic's outset, worked with all sectors of society in unprecedented ways with unprecedented speed. Enabled by the strong support of Congress and other partners in the public and private sectors, the U.S. biomedical research enterprise has mounted a vigorous response that has given rise to increased testing capacity, innovative therapeutic strategies, and, perhaps most important, safe and effective vaccines. The breathtaking pace and scope of this progress has been made possible by decades of NIH-funded basic research, which built a robust foundation for our continuing efforts to combat COVID-19 and the emerging viral variants that threaten to extend the pandemic's tragic timeline.

Among the out-of-the-box initiatives now underway under NIH's leadership are the following: a highly innovative, competitive effort to expand the capacity and accuracy of testing; a pioneering public–private partnership to accelerate development of therapeutics and vaccines; and a major new push to understand and devise ways to treat or even prevent Post-Acute Sequelae of SARS-CoV-2, or "Long COVID." NIH research also is tackling the disturbing disparities seen in the COVID-19 response, with the aim of developing effective, evidence-based methods to ensure that tests, treatments, and vaccines reach all populations, particularly those disproportionately affected by this devastating disease.

In this updated strategic plan, NIH shares its framework for ensuring that no stone goes unturned in the scientific response to COVID-19. We will carry out this mission by supporting the collective efforts of NIH's researchers, collaborators, and diverse stakeholders to improve, advance, and optimize COVID-19-related research in five key areas: fundamental knowledge, detection and diagnosis, treatment, prevention, and health disparities.

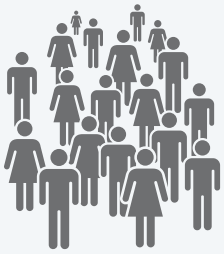
NIH acknowledges that the goals set forth in this plan are very ambitious. Yet we remain optimistic because of our agency's strong record of encouraging ingenuity and delivering biomedical breakthroughs, even in the most difficult of times. We are convinced that pulling together the best minds in science will continue to enable our Nation to meet the twin challenges of closing the door on the COVID-19 pandemic and opening the door to new strategies for confronting future pandemics.



Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

NIH-Wide Strategic Plan for COVID-19 Research

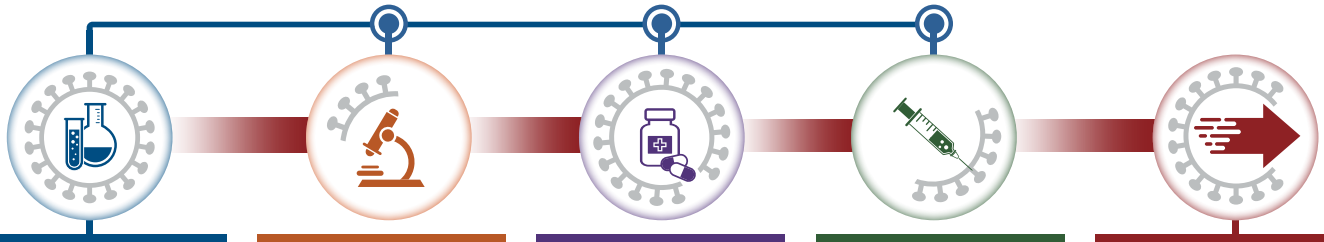
A BOLD COMMITMENT TO AN UNPRECEDENTED HEALTH CHALLENGE



GOALS

- **UNDERSTAND** SARS-CoV-2 and COVID-19
- **PREVENT** SARS-CoV-2 infection
- **DETECT and TREAT** COVID-19
- **MITIGATE** the threat of COVID-19

Guided by FIVE STRATEGIC PRIORITIES



PRIORITY 1

Improve Fundamental Knowledge

of SARS-CoV-2 and COVID-19 disease progression, outcomes, and recovery

PRIORITY 2

Advance Research To Improve Detection

by developing and validating new assays and retooling existing diagnostic platforms

PRIORITY 3

Support Research To Advance Treatment

by evaluating new or repurposing existing treatments and defining implementation strategies

PRIORITY 4

Accelerate Research To Improve Prevention

by developing vaccines, other methods to prevent transmission, and implementation models

PRIORITY 5

Prevent and Redress Poor COVID-19 Outcomes

in health disparity and vulnerable populations

CROSSCUTTING STRATEGIES

PARTNERING to promote collaborative science

SUPPORTING the research workforce and infrastructure

INVESTING in data science

ENGAGING and educating the public

NIH National Institutes of Health

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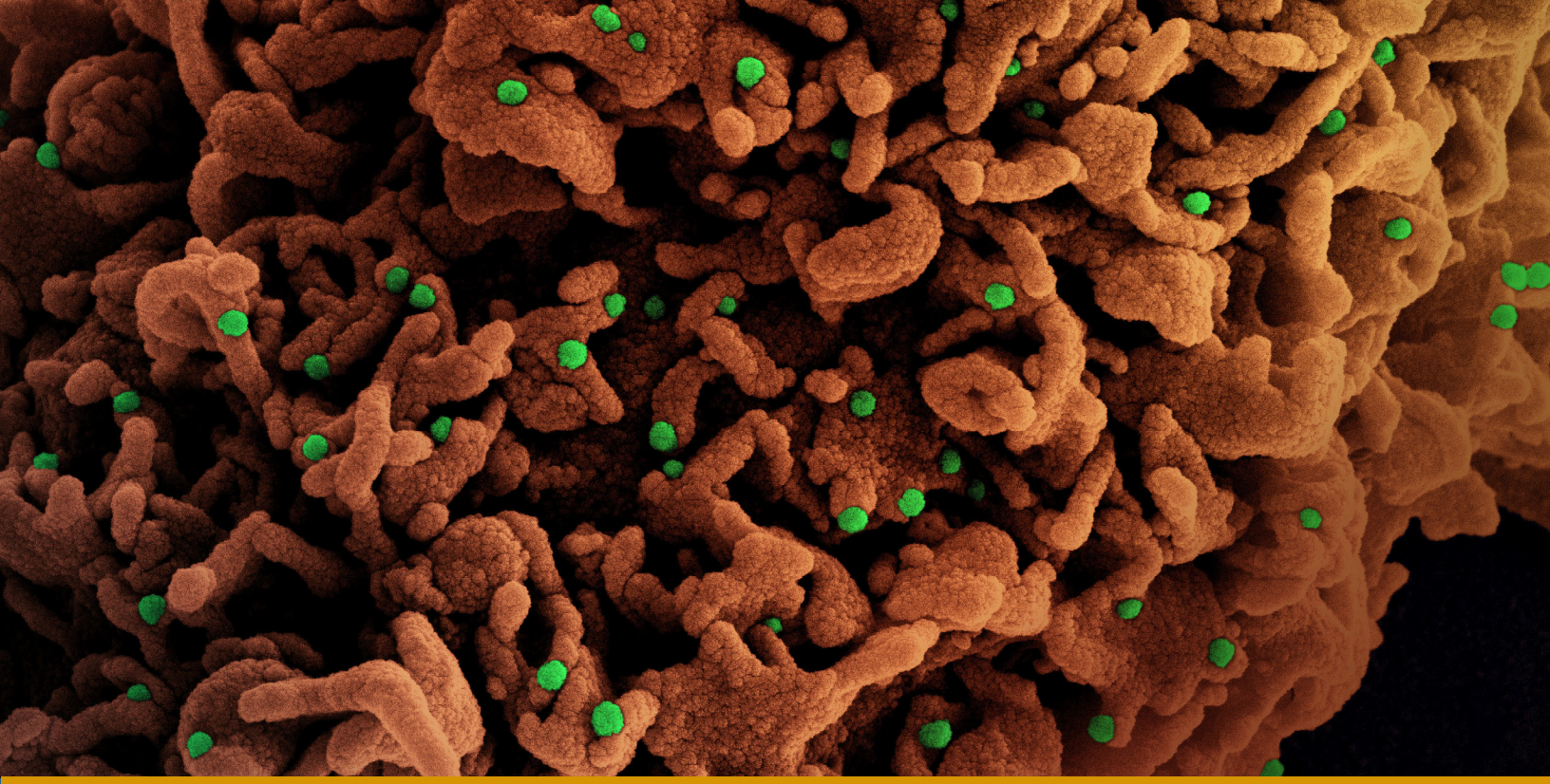


KEY UPDATES

NIH has made incredible progress toward understanding, diagnosing, treating, and preventing SARS-CoV-2 infection and COVID-19 in the past year. However, new challenges have come to light as the pandemic has evolved, necessitating a corresponding evolution in the NIH response, which is reflected in this *NIH-Wide Strategic Plan for COVID-19 Research* (hereafter referred to as the "Strategic Plan"). This second iteration of the Strategic Plan includes updates throughout the document to convey the progress made, new research studies planned, and NIH community outreach efforts. The most significant updates to the Strategic Plan are highlighted below:

- Investigating and treating the long-term health consequences of COVID-19, including Post-Acute Sequelae of SARS-CoV-2 Infection (PASC; also referred to as Long COVID) and pandemic-related impacts on the overall physical and mental health of Americans
- Understanding and responding to new SARS-CoV-2 variants that contain mutations in the spike protein of the virus that may impact the effectiveness of treatments and vaccines against SARS-CoV-2
- Highlighting progress on the development of diagnostic tests, vaccines, and treatments for SARS-CoV-2 infection and developing implementation strategies to determine efficient, effective methods of providing these resources

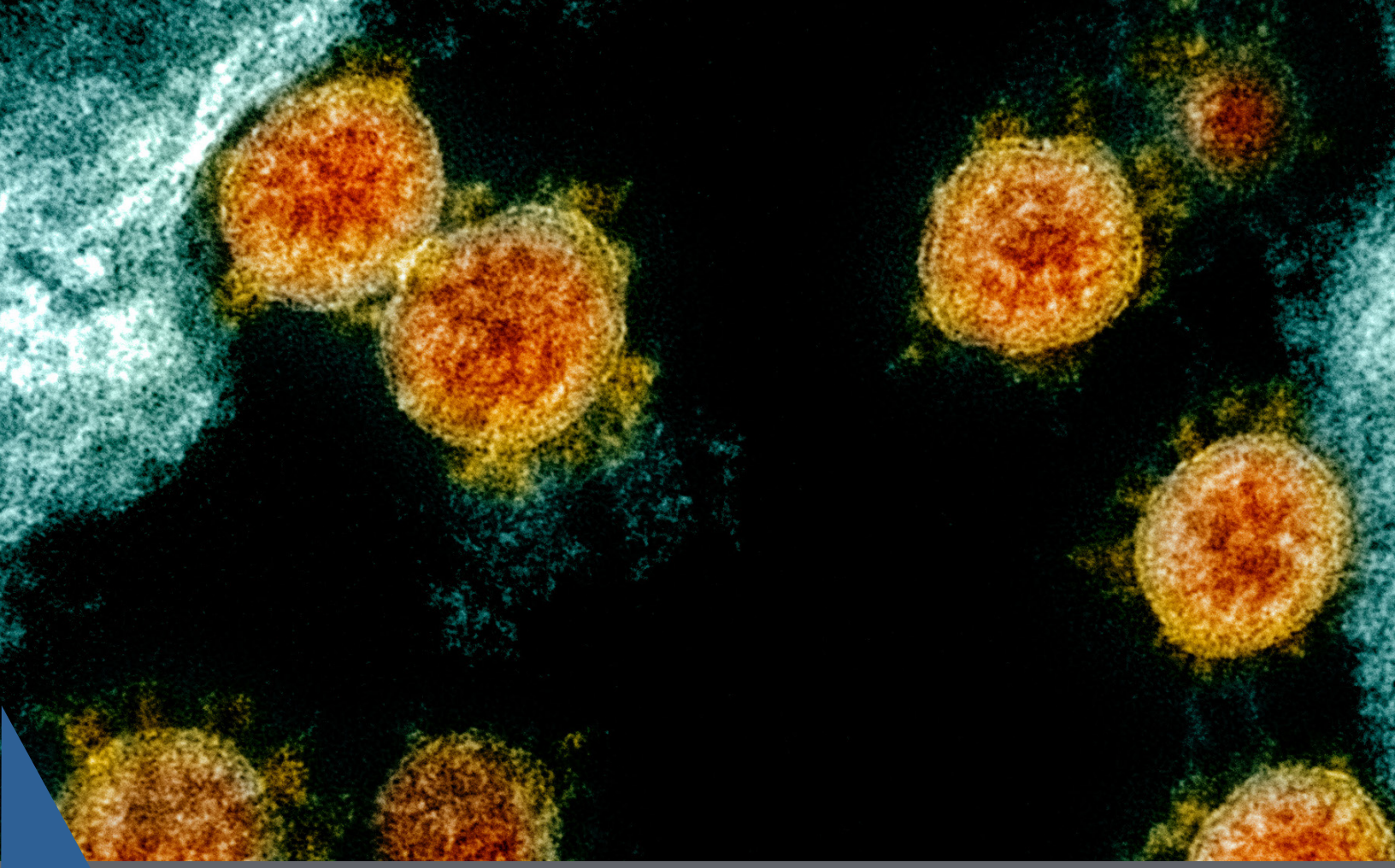
- Understanding and engaging disproportionately impacted and other populations at high risk of SARS-CoV-2 infection to ensure appropriate information, testing, treatments, and vaccines for SARS-CoV-2 and COVID-19 are available to all who need them

These updates and the trajectory of the NIH strategic response take into account input solicited from the public in the *Request for Information* on the *NIH-Wide Strategic Plan for COVID-19 Research* (NOT-OD-21-018). After an open submission period of 6 weeks, NIH staff analyzed and summarized all responses to inform the updates to the Strategic Plan described above. In all, 192 respondents submitted feedback, including respondents from the United States (162 responses), international locations (8), and unknown locations (22). Many of the respondents were from academic institutions (120), the private sector (19), or professional societies (13). The majority of respondents were students and trainees (82), with most of the remaining responses coming from mid-level (42) or senior level leaders (33) within an organization. Twelve responses were submitted anonymously and 51 were submitted on behalf of an organization.

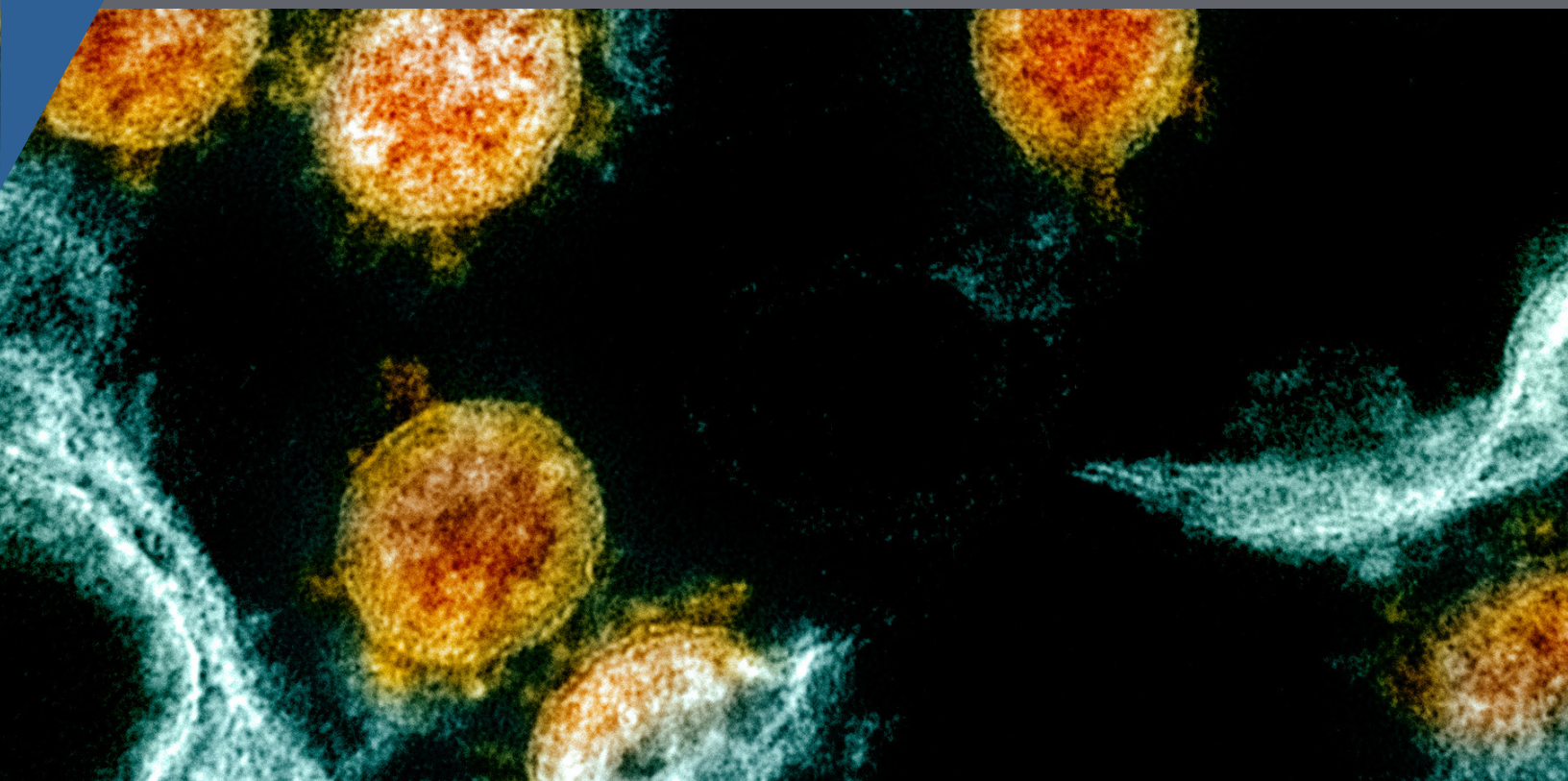
Respondents largely approved of the NIH research response to the COVID-19 pandemic and referenced the scientific initiatives NIH has supported as critical activities for combating the spread of SARS-CoV-2 and preventing COVID-19. They expressed a high level of interest in research included in Priority 1: Improve Fundamental Knowledge of SARS-CoV-2 Infection and COVID-19 (76), Priority 4: Improve Prevention of SARS-CoV-2 Infection (65), and Priority 5: Prevent and Redress Poor COVID-19 Outcomes in Health Disparity and Vulnerable Populations (83) of the Strategic Plan.

Respondents identified scientific gaps (158) and commented on scientific and medical accomplishments mentioned in (87) or missing from (45) the Strategic Plan, health disparities in research or implementation (68), additional resources required (39), and the conduct and stewardship of science (20). Key themes that emerged were the need for research on the long-term impacts of the pandemic and SARS-CoV-2 infection, greater and more inclusive research for at-risk and health disparities populations (including minorities, people with disabilities, and essential worker populations), as well as building research infrastructure and preparing for future pandemics or emergencies. Some responses also mentioned potential collaborations with private organizations and state-level government that could be beneficial to NIH research and tools developed by others to track viral transmission and vaccine uptake.

Some responses also provided input on the Strategic Plan's crosscutting strategies: investing in data science (20), partnering to promote collaborative science (19), and supporting the research workforce and infrastructure (17). Responses emphasized the importance of communicating clearly and effectively with the public to encourage preventive behaviors, like mask wearing and social distancing, and to address questions and concerns about COVID-19 vaccines. Suggestions for new areas of crosscutting focus included a greater emphasis on international collaboration, inclusion of affected populations in research planning processes, and increased support for early-career scientists and clinical care workers.



Goal: Improve basic understanding of SARS-CoV-2 and COVID-19 and develop the necessary tools and approaches to better diagnose, prevent, and treat this disease.



INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a naturally arising virus—the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus spreads easily from person to person through respiratory droplets, and infection typically causes fever, loss of taste or smell, shortness of breath, a dry cough, gastrointestinal symptoms, and other symptoms and complications. The ease with which the virus spreads and its ability to be transmitted by asymptomatic individuals have caused possibly the most severe worldwide infectious disease pandemic of the modern age. The COVID-19 pandemic was the third leading cause of death in the United States in 2020, resulting in approximately 375,000 deaths.

NIH is leading a swift, coordinated research response to this public health crisis. By leveraging existing funding mechanisms and establishing new programs, NIH is rapidly mobilizing the disbursement of emergency government funding to the biomedical research community while

still maintaining a scientifically and ethically rigorous review process and strong scientific stewardship to support the most promising and meritorious science in the face of a public health emergency.

Researchers are continuing to build on an immense foundational knowledge base on viruses and their effects on humans drawn from decades of NIH-supported research. Leveraging the most modern technologies and techniques—as well as a rich reservoir of existing diagnostics, prevention strategies, and treatment options used to combat viruses—researchers are rapidly identifying characteristics of SARS-CoV-2 and its mutations of concern and human responses to infection to speed the development of sorely needed interventions to prevent and treat COVID-19. This work includes studying how people infected with COVID-19 develop Long COVID syndrome, clinically termed Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), in which symptoms caused by SARS-CoV-2 infection linger past the usual recovery time for a respiratory virus or emerge and persist after the acute phase of infection seems to be over (See Box 1).

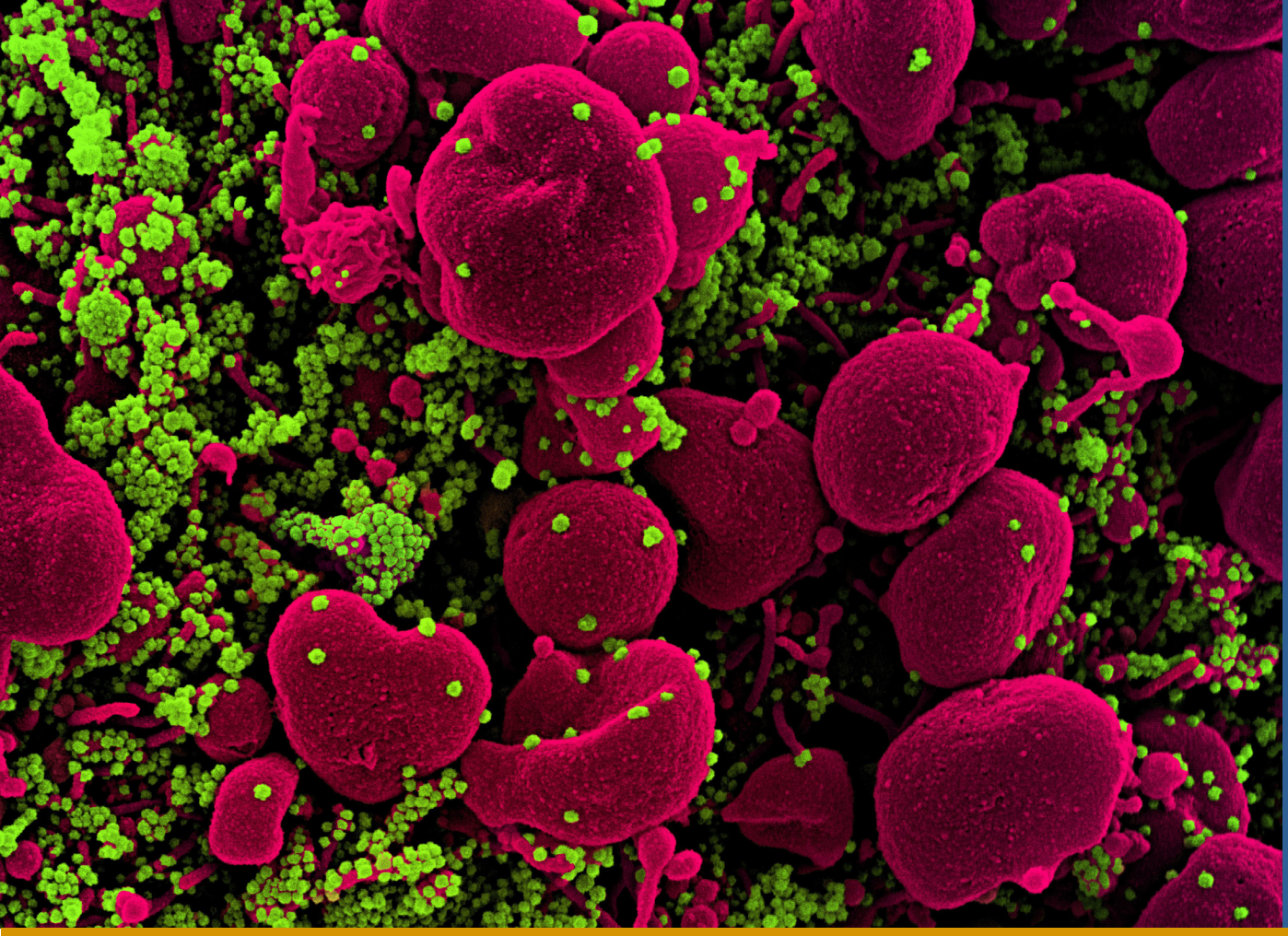
To hasten the development of interventions, NIH is capitalizing on the strengths of its extramural and intramural research infrastructure (domestic and international) and working in close collaboration with its partners in industry, academia, nonprofit organizations, the public, and other government agencies and offices. NIH's intramural scientists are engaging in fundamental studies, creating models, and identifying or screening existing therapeutic drugs against SARS-CoV-2, as well as developing and modifying existing vaccine and diagnostic platforms to prevent and detect the virus. Likewise, NIH's alignment and coordination with other Federal agencies as part of the *National Strategy for the COVID-19 Response and Pandemic Preparedness* (referred to as the National Strategy hereafter) are forging groundbreaking approaches to ramp up the identification, development, evaluation, and manufacture of promising candidate therapeutics and vaccines. The National Strategy also incorporates a plan for distribution of diagnostics, vaccines, and therapeutics proven accurate, safe, and effective.

Recognizing the disproportionate impact on health disparity and specific populations that are at high risk of COVID-19, NIH-funded researchers are working to identify the underlying factors and barriers that contribute to the staggering losses of life in these communities.

Inclusion of these populations in clinical trials for diagnostics and interventions is a critical part of NIH's pandemic response, as is exploring effective communication strategies and ways to reduce barriers and improve access to care and interventions for all populations, especially populations at a higher risk of developing COVID-19.

In keeping with the urgency of the pandemic, NIH is rapidly communicating findings to the scientific community, health care providers, and the public. For the scientific community, NIH is moving as quickly as possible to disseminate data in multiple data-sharing platforms. Preprint and peer-reviewed publications relevant to all aspects of the research effort are available, including literature compendiums and analysis tools, such as LitCovid and *iSearch* COVID-19 Portfolio. For health care providers, NIH continues to convene a panel of experts who develop treatment guidelines that continue to evolve as new data and clinical expertise become available. Last, NIH is providing the latest information about NIH efforts and research results to the public through the NIH COVID-19 website and also investing in research to identify the best methods for disseminating scientific findings to the communities and populations who need them most, especially underserved and other populations at high risk of SARS-CoV-2 infection and COVID-19.

NIH is responding to the COVID-19 pandemic by supporting research to understand SARS-CoV-2 and mitigate the threat of COVID-19 for the health of all people. NIH is building on existing research initiatives and accelerating the development of new ones that are focused on the five research priorities detailed in this strategic plan. Through its pursuit of research in these priority areas, NIH hopes to achieve the vision of a world safe from COVID-19 by improving basic understanding of SARS-CoV-2 and COVID-19 and developing the necessary tools and approaches to better diagnose, prevent, and treat this devastating disease.



PRIORITY 1

Improve Fundamental Knowledge of SARS-CoV-2 and COVID-19

NIH-supported researchers continue to work with their partners to understand the biology of SARS-CoV-2 infection, acute COVID-19, and PASC, as well as the impact that the infection and disease have on individuals, communities, and public health. As fundamental knowledge of SARS-CoV-2 and COVID-19 grows, it will be used to identify novel approaches and improvements to existing diagnostics, prevention strategies, and treatments. Importantly, it also will be leveraged to better prepare for future infectious disease outbreaks.

Objective 1.1: Advance fundamental research for SARS-CoV-2 and COVID-19

NIH-supported researchers are building on an already strong foundation of knowledge to understand SARS-CoV-2 infection and COVID-19, including the research priorities outlined

in the National Institute of Allergy and Infectious Diseases' *NIAID Strategic Plan for COVID-19 Research*. For example, researchers are working to understand essential host and SARS-CoV-2 proteins and host-virus interactions, including for SARS-CoV-2 variants, to understand how they mediate infection and disease. Researchers also are working to understand fundamental aspects of how host tissues—such as the heart, lung, blood, and blood vessel wall—respond to the virus. NIH will continue to support research to better understand the mechanisms of infection and how infection contributes to disease in different tissue and organ systems, including the eyes and mouth, the latter of which may play a role in transmitting SARS-CoV-2 to the lungs or digestive system. This knowledge of the virus and host tissue response will enable the development of more effective treatment and prevention strategies.

The immune system plays a critical role in preventing and fighting infections. Researchers are advancing knowledge of the body's immune response to SARS-CoV-2 infection through

Box 1. Addressing the Post-Acute Sequelae of SARS-CoV-2 Infection or "Long COVID"

A significant number of people sickened by COVID-19 report symptoms that may persist for several months or longer after the acute illness has passed, a condition often referred to as "Long COVID" and now clinically referred to as the Post-Acute Sequelae of SARS-CoV-2 infection (PASC). Examples of commonly reported symptoms include fatigue, shortness of breath, "brain fog," sleep disorders, fevers, gastrointestinal symptoms, anxiety, and depression. Symptoms may involve multiple organs and systems throughout the body and can significantly affect overall function and quality of life. The long-term public health implications and impact on Americans' lives of PASC are still unknown, but soon after the first reports arose, NIH began a **study** to track COVID-19 survivors and held a **workshop** to determine the best path forward, actions that informed the development of the **NIH PASC Initiative** launched in February 2021.

The goal of this initiative is to rapidly improve understanding of recovery after SARS-CoV-2 infection and to prevent and treat PASC. Studies will focus on characterizing the biological and clinical spectrum of recovery from SARS-CoV-2 infection, including the subset of patients who have symptoms of disease beyond the standard course, the impact of treatments for acute COVID-19 or for post-acute symptoms on the duration and severity of symptoms, and factors that affect outcomes for patients infected by SARS-CoV-2.

Key features of the initiative include the **SARS-CoV-2 Recovery Cohort and Investigator Consortium**, which will leverage existing and new clinical studies to chart recovery from infection and to assess the full range of PASC symptoms and findings in diverse adult and pediatric populations. The Initiative also will support a data science and biorepository core and leverage a variety of NIH clinical platforms, including large-scale electronic health records and other real-world data-based approaches, existing clinical studies and networks, COVID-19 clinics, registries, and observational studies.

efforts such as the Serological Sciences Network for COVID-19 (SeroNet), the Nation's largest coordinated effort to study immune responses to COVID-19 and the Immunophenotyping Assessment in a COVID-19 Cohort (IMPACC) study. Antibodies, blood proteins produced by the immune system to fight viruses, are a key component of the immune system and, in some cases, prevent future infection from the same virus. Recent studies have shown that patients with COVID-19 develop SARS-CoV-2-specific antibodies capable of neutralizing virus that can last for many months in the blood. Another immune system cell that plays a role in the immune response to viruses, the T cell, also may be beneficial in long-term protection against SARS-CoV-2. Additional research is needed to fully understand how the immune response to SARS-CoV-2 affects the wide range of symptoms and disease outcomes experienced by people with COVID-19. The immune system, although typically protective, sometimes can overreact and contribute to tissue and vascular damage, as observed in COVID-19. Thus, patients with severe COVID-19 may benefit from therapies that turn down the immune response or directly target the virus.

Understanding SARS-CoV-2 transmission—how the virus spreads—and why some individuals are more susceptible to severe disease or long-term effects is an important piece of the COVID-19 response. To gain new insight on these topics, NIH is supporting research to identify potential animal reservoirs, understand animal-to-human and human-to-human transmission, and characterize the genetic diversity of the virus. Studies to examine biological factors that influence individual susceptibility to infection—such as age, sex and gender, genetics, and environmental exposures—already are in progress. Through the COVID Human Genetic Effort, an international project spanning more than 50 genetic sequencing hubs and hundreds of hospitals, NIH researchers discovered that 10 percent of patients with life-threatening COVID-19 pneumonia had, at the start of their infection, autoantibodies that attack a vital component of the immune system, greatly impairing their ability to fight off the virus. Because 95 percent of these patients were men, the findings may provide the first explanation for why more men than women die from COVID-19. Researchers also are examining social and structural factors related to COVID-19, such as health disparities based on race and ethnicity, including their influence on biological factors. This information will be critical to understanding infection and disease progression and outcomes, and it may inform the development of interventions and vaccines.

Objective 1.2: Support research to develop preclinical models of SARS-CoV-2 infection and COVID-19

Animal models, particularly those that replicate human disease, are essential to understanding the basic biology of coronaviruses, including transmission, incubation periods, and host immune responses to infection. Such models also are critical to testing potential preventive and therapeutic strategies. Researchers are using mice, hamsters, ferrets, and

other animal models to study responses to experimental therapeutics and vaccines. NIH has established resources to leverage existing animal models of infection with other coronaviruses to develop preclinical models to study and understand SARS-CoV-2 infection and COVID-19. Given the major impact of underlying cardiovascular, pulmonary, and hematologic conditions on morbidity and mortality among patients with COVID-19, NIH is supporting research to develop model systems to rapidly test and advance the development of innovative therapeutics to prevent damage to critical host tissues and organs.

Previous experience with related coronavirus diseases suggests that replicating COVID-19 in animal models may be challenging. Thus, researchers are exploring new ways to increase access to validated animal models and enhance the comparison of approaches to identify informative assays. NIH is developing and validating human microphysiological systems—engineered 3D platforms that support living human cells and tissues—that can be used to study viral infections in relevant human tissue models—such as the lung, kidney, gut, or brain—and more clinically predictive assay systems to test new treatments. Systems biology and computational techniques are being used to complement preclinical models and aid in evaluation of therapeutic effects against SARS-CoV-2 and COVID-19. Scientists have accelerated COVID-19 modeling research by creating computer-generated maps and models of SARS-CoV-2 biological pathways throughout the infection cycle and are pursuing strategies to ensure the widespread discovery and use of such data to address the pandemic with novel computation modeling efforts.

Objective 1.3: Advance the understanding of SARS-CoV-2 infection risk and COVID-19 dynamics at the population level

Gaps exist in our understanding of the dynamics of virus transmission in different populations over time and the factors that influence a population's susceptibility to severe disease. Researchers continue to work toward understanding the progression of SARS-CoV-2 infection through natural history studies. These studies may reveal why some groups, such as older adults and people with preexisting conditions, are at higher risk of severe COVID-19 than others. NIH is supporting studies and online dashboards to describe the extent to which SARS-CoV-2 has spread throughout the United States and to provide insights into which communities and populations are most affected, including racial and ethnic minorities, underserved rural populations, socioeconomically disadvantaged populations, and sexual and gender minorities. For example, one study is leveraging an existing program that monitors threats to the U.S. blood supply to analyze the prevalence of SARS-CoV-2 antibodies in blood donors in six cities with high incidence of COVID-19.

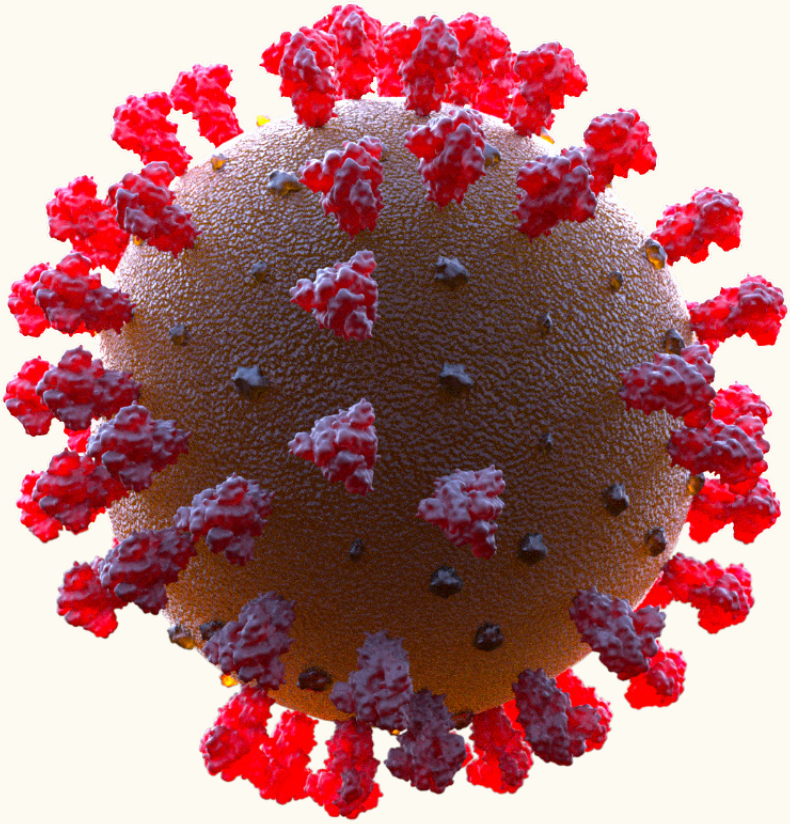
NIH also is supporting research to understand and address the behavioral and social factors that affect the spread of the virus. NIH-supported clinical epidemiology programs are leveraging existing clinical and community-based research platforms to characterize the clinical features and disease course of COVID-19. Population-level studies are being used to explain the role of different factors in driving disease severity and outcomes—including, but not limited to, older age; sex; social and structural determinants of health; and such comorbidities as diabetes, cancer, cardiovascular disease, kidney and digestive diseases, rare diseases, pain, substance use, and substance use disorders. For example, the Collaborative Cohort of Cohorts for COVID-19 Research (C4R) study combines existing diverse cohort studies—such as the Framingham Heart Study (HS), Jackson HS, and Strong HS—to examine COVID-19-related outcomes and factors that affect resilience and risk. Studies are ongoing to monitor mortality trends across the United States to better understand the patterns of death over part of 2020—those from COVID-19 and other causes.

Objective 1.4: Understand the short- and long-term health consequences of SARS-CoV-2 infection and COVID-19

As the United States and countries around the world respond to the COVID-19 pandemic, the negative impact of social, behavioral, and economic factors on people and their health is becoming clearer. Studies have shown that the pandemic has taken a disproportionate toll on people with intellectual and developmental disabilities and populations facing existing health disparities. Researchers are working to understand the pandemic's effect in additional populations, such as the rare diseases community, adults with fetal alcohol spectrum disorders, people with HIV, and health care workers. Studies aim to understand the effects of the COVID-19 pandemic across the lifespan and in different populations, especially populations that are at higher risk for the disease itself or who may experience complications related to measures taken to contain the pandemic.

NIH is supporting research to understand and address the impacts of the virus and public health measures used to prevent its spread—such as physical distancing, shelter-in-place orders, quarantining, school closures, and mask mandates—on social epigenomic pathways (how social experiences affect genes and biology); mental and physical health; child development; pregnancy; substance use; and well-being, illness, and recovery. In addition, studies are exploring the health consequences from delayed care, not only for COVID-19, but also for routine preventive practices (e.g., vaccinations) and detection and treatment of diseases and conditions (e.g., cancer).

Researchers also are investigating the long-term effects of SARS-CoV-2 infection, with or without acute COVID-19, as well as the influence of physical, environmental, neurobiological, social, and behavioral factors. Studies are underway to understand COVID-19's effects on various parts of the nervous system, such as the brain and eyes, and how the effects of COVID-19 on physical and mental health are influenced by alcohol, tobacco, and other substance use. A new NIH-wide initiative was launched recently to understand, treat, and prevent PASC. Additionally, because many of the lingering effects of infection are neurological in nature—such as the common complaint of "brain fog"—NIH has established a database and biobank specifically to collect information on the neurological symptoms, complications, and outcomes of COVID-19 across the lifespan, including pregnancy and old age.



PRIORITY 2

Advance Detection of SARS-CoV-2 Infection and Diagnosis of COVID-19

As Americans return to public spaces, a vital component of the National Strategy is detecting, diagnosing, and surveilling the population to identify and quarantine COVID-19 cases and track the spread of the virus. Although NIH has made significant contributions to increase the number of tests available, current testing capacity is insufficient to meet the Nation's needs—both in terms of the number of tests available and their ability to deliver answers in a timely manner at the point of care. Additionally, as the pandemic has evolved, new testing challenges have surfaced in the form of new viral variants, reinforcing the continued need for tests that can help accurately detect and track SARS-CoV-2, including variants of concern as they arise. To develop more accurate, rapid, scalable, affordable, and accessible tests, NIH is aggressively accelerating the development, validation, and commercialization of innovative SARS-CoV-2 testing technologies, focusing efforts both on viral tests—which indicate whether a person

has a current infection—and on antibody, or serological, tests—which indicate if a person has had a previous infection. To this end, NIH is advancing a wide range of initiatives to improve or repurpose current technologies and advance new ones.

Objective 2.1: Support research to develop and validate new diagnostic technologies

NIH is supporting the development and validation of new diagnostics, including nucleic acid tests and viral antigen detection tests, that can identify the presence of the virus in biospecimens. Most current testing for the virus depends on detection of the viral RNA using a polymerase chain reaction (PCR) test. These tests are accurate, but generally require a laboratory with expert technical staff and specialized equipment. Newer alternatives may be able to carry out this kind of nucleic acid detection with a simple point-of-care device.

Another alternative that NIH-supported researchers are pursuing is called viral antigen testing, which detects the virus protein capsule. Antigen tests are traditionally less sensitive, but new approaches for at-home use enable easier and more frequent testing, which may help maintain overall accuracy. Preliminary findings suggest that screening using rapid antigen tests on a regular cadence every two to three days achieves sensitivity comparable to reverse transcription–PCR tests. In February 2021, NIH launched a study to assess the performance and usability of the smartphone app, MyDataHelps, paired with the Quidel QuickVue At-Home OTC COVID-19 Test, which has now been authorized by the U.S. Food and Drug Administration (FDA) for over-the-counter use without a prescription.

To address the need for better diagnostics, NIH launched the Rapid Acceleration of Diagnostics (RADx℠) initiative to speed innovation in SARS-CoV-2 testing technologies, with the potential of delivering widely accessible, rapid testing strategies to the public (see Box 2). The RADx Tech arm of RADx aims to speed the development, validation, and commercialization of innovative point-of-care and home-based tests (including the Quidel QuickVue test referenced above), as well as improve clinical laboratory tests that can detect the virus directly. RADx Tech expanded the existing Point-of-Care Technology Research Network and is using a flexible approach to infuse funding and enhance technology designs at key stages of development. New technologies may employ less invasive sampling techniques, such as saliva collection, or other approaches, such as viral antigen testing to detect the virus protein capsule, and are designed to meet the needs of various settings, such as hospitals, schools, and places of business. Together with RADx Advanced Technology Platforms (RADx ATP), which focuses on scaling up promising technologies, RADx Tech supported more than 150 companies and contributed more than 180 million tests to the national testing capacity through April 2021 with additional capacity being added monthly. As of April 2021, the FDA has authorized 17 tests supported by RADx Tech/ATP for emergency use, including a rapid antigen home test that provides results in 15 minutes, point-of-care molecular tests that provide results in

Box 2. RADx℠: Rising to the Challenge of Widespread Testing

Over the last century, advances in biotechnology have improved medical treatment and saved lives. As the United States continues to fight a devastating public health threat, the **Rapid Acceleration of Diagnostics** (RADx℠) initiative calls on scientists and engineers to put forward their most promising biomedical technologies and implementation strategies to answer the pressing need for SARS-CoV-2 testing. The RADx initiative is a nationwide program aimed at speeding the development and commercialization of rapid, easy-to-use diagnostic tests. The program supports innovative approaches for implementation, expansion, accessibility, and acceptance of existing diagnostic testing. The initiative consists of five key components:

- **RADx Tech and RADx Advanced Technology Platforms (RADx-ATP)** use a phased approach to support the early development of point-of-care SARS-CoV-2 diagnostics and improved laboratory-based tests via RADx Tech. RADx-ATP focuses on reducing barriers for scaling up advanced technologies to increase the capacity for rapid, high-throughput testing infrastructure. As of April 2021, these programs have supported more than 150 companies, and 31 projects have been scaled up for manufacturing, with 27 still active. Seventeen tests have been authorized by the FDA for emergency use. Combined, these programs have increased testing capacity by more than 180 million tests through April 2021.
- **RADx Radical (RADx-rad)** advances nontraditional, but potentially transformational, approaches and repurposing of existing approaches for SARS-CoV-2 testing. With longer development timelines, 49 RADx-rad projects are addressing gaps in SARS-CoV-2 testing through technology platforms that can be used in future outbreaks of COVID-19 and that could be applicable to other, as yet unknown, infectious organisms.
- **RADx Underserved Populations (RADx-UP)** leverages existing community partnerships to build community-engaged demonstration projects focused on identifying effective implementation strategies to enable and enhance testing for populations at high risk of SARS-CoV-2 infection and address the unique needs of different communities. In Phase 1, RADx-UP provided 70 awards to 55 institutions across 33 states, including a Coordination and Data Collection Center, a collaborative network of clinical research centers across the country, and a program studying the social, ethical, and behavioral implications of testing.
- **RADx At-Home Testing** is supporting an innovative community health initiative called "**Say Yes! COVID Test**" to improve testing accessibility by providing communities with access to free, rapid antigen tests that individuals can administer to themselves at home. The study will use such technologies as the RADx Tech/ATP-supported Quidel QuickVue At-Home COVID-19 Test recently tested in a **pilot at-home study** and evaluate if frequent self-administered COVID-19 testing helps residents reduce community transmission of SARS-CoV-2.
- **RADx Data Management** supports researchers in their studies to develop new and novel testing devices and collects, standardizes, and harmonizes the resulting data. The data management team interfaces with coordinating centers across the RADx program to develop and implement common data elements and models, to facilitate harmonized data sharing in a secure cloud-based data platform, and to provide a research data repository of curated and de-identified RADx COVID-19 data.

Box 2. Continued

The RADx initiative supports innovative technologies and, since its inception, has enabled the development of millions of additional rapid, easy-to-use, diagnostic tests for the United States. RADx identifies and employs evidence-based implementation strategies to increase accessibility and acceptance in those populations most affected by this deadly pandemic. By calling on the ingenuity and inventiveness of U.S. scientists and engineers, NIH will continue to advance diagnostic tools to prevent the spread of SARS-CoV-2, improve health, and save lives.

30 minutes, and technologies to increase the throughput of laboratory-based molecular tests. Through the RADx initiative, NIH is now assessing testing technologies for their ability to detect SARS-CoV-2 variants.

The RADx Radical (RADx-rad) arm of RADx is supporting new and nontraditional approaches that address gaps in COVID-19 testing, as well as adapting applications of existing approaches to make them more usable, accessible, or accurate. RADx-rad projects include a diagnostic breathalyzer, smell and taste tests, biosensors for the skin and mouth, community wastewater detection, and artificial intelligence applications for various diagnostic uses, such as predicting long-term risk of disease severity in children.

Other NIH intramural and extramural activities are focusing on the development of diagnostic approaches that include wearable, implantable, and remote sensors; medical imaging technologies combined with informatics solutions and artificial intelligence for detection and monitoring; and noncontact sensing and imaging for rapid mass screening and vital sign assessment. To characterize the different approaches to diagnostics, NIH data scientists developed the COVID-19 Portfolio Tool, using artificial intelligence and machine learning methodologies to provide a curated source of publications coupled with a user-friendly portfolio analysis interface for querying the contents of these publications.

Objective 2.2: Support research to retool existing diagnostic technologies

In addition to catalyzing the development of novel COVID-19 diagnostic technologies, NIH is supporting efforts by scientists to repurpose, modify, or improve diagnostic tools currently available or under development. Researchers are shifting their focus to repurpose diagnostic technologies and improve the speed, sensitivity, accuracy, and utility of available tests, including the use of imaging technologies for early detection of COVID-19 in the lungs and the use of artificial intelligence to improve image-based diagnosis. To further this approach, NIH launched the Medical Imaging and Data Resource Center (MIDRC), an ambitious effort that unites expertise from academia, professional societies, industry, and government. The first data set of images is now available for researchers to use.

Objective 2.3: Support research to develop and validate serological assays

Serology tests—also called antibody tests—detect the presence of antibodies in a person's blood. Someone who has antibodies to a virus, such as SARS-CoV-2, was infected at some point in time. However, because antibody tests do not look for components of the virus itself, they cannot be used to diagnose SARS-CoV-2 infection or determine if someone is infectious. Currently, the extent to which the presence of SARS-CoV-2 antibodies correlates with lasting immunity is unclear, as is how durable and protective these antibodies might be. Serology tests are crucial for determining the efficacy of promising therapeutic or vaccine candidates and for studies of disease prevalence and virus spread through communities.

NIH's focus on accelerating the availability of high-quality serology tests is a key part of its response to the pandemic. To address this need, NIH is supporting the SeroNet, which will study immune responses to COVID-19, establish a U.S. SARS-CoV-2 serology standard, develop new serological tests, collaborate with Federal partners to assess tests developed by industry and academic organizations, and expand the national serological testing capacity. The Recipient Epidemiology and Donor Evaluation Study (REDS) Program also is establishing a repository for sharing blood samples and data with government, academic, and industry scientists to advance serological testing and vaccine development. As part of the REDS Program, the REDS RESPONSE study is leveraging access to the blood supply and blood donors to help evaluate new serology tests. Other efforts underway by NIH-supported and intramural investigators are adapting platforms used to test for antibodies resulting from other infections to detect SARS-CoV-2 and identifying SARS-CoV-2 antibodies that may be able to be detected sooner after infection.

Objective 2.4: Support research on scale-up and implementation of testing

Widespread, frequent, and timely testing leading to early identification and quarantine of infected individuals is a critical facet of the National Strategy to stop the spread of SARS-CoV-2 infection. To help ensure that the national testing capacity scales to meet the demand of testing needs, NIH implemented RADx-ATP as part of the RADx program (see Box 2). RADx-ATP seeks to scale up existing technologies, such as high-throughput platforms; expand the use of platforms suitable for testing centers providing access to underserved populations; further develop point-of-care tests for at-home test use; and identify next-generation diagnostic testing platforms that could be scaled to population-level testing. NIH also is leveraging intramural research resources to help alleviate potential supply chain issues. For example, to address potential shortages in swabs used for testing, the NIH intramural program is developing and evaluating several variations of 3D-printed swabs.

NIH is committed to supporting research on dissemination and implementation models of testing that are effective, accessible, and inclusive. RADx-Underserved Populations (RADx-UP) is supporting community-engaged research on implementation of testing in underserved and other communities at high risk of COVID-19, including projects to support research on approaches to enable safe return to schools in these communities. RADx Tech supported the development of the COVID-19 Testing Impact Calculator, a free online resource that shows how different approaches to testing and other mitigation measures can curb the spread of the virus in schools and businesses. The website also provides a playbook for K–12 education to help guide schools on implementing testing strategies and a step-by-step Implementation Guide to help business leaders plan and implement a testing strategy to meet their organizations' needs. Researchers planning studies of in-home testing as an intervention also are using NIH-supported online platforms, such as the COVID-19 Pandemic Vulnerability Index (PVI) Dashboard, to help select local communities to study.

Because research indicates that transmission may be happening through contact with individuals who are not showing symptoms, traditional containment strategies—testing of only people with symptoms, contact tracing, quarantine—may not be enough to stop the spread. NIH is supporting research into alternative strategies that harness digital health solutions using such tools as smartphone apps, wearable devices, and software that can identify and trace contacts of infected individuals, keep track of verified SARS-CoV-2 test results, and monitor the health status of infected and potentially infected individuals, while still protecting personal privacy. In March 2021, NIH announced the launch of "Say Yes! COVID Test," a collaboration with the Centers for Disease Control and Prevention (CDC) to provide up to 160,000 residents of Pitt County, North Carolina, and Hamilton County, Tennessee, with free, rapid antigen tests to evaluate the effectiveness of self-administered testing.

PRIORITY 3

Advance the Treatment of COVID-19

When the COVID-19 pandemic began, FDA-approved treatments for coronaviruses did not exist. Normally, the discovery and development of a new therapeutic is a years-long process. The unprecedented need brought on by the COVID-19 pandemic has compelled a paradigm shift in the process to enhance the sharing of knowledge, resources, and infrastructure among academics, Federal agencies, and industry. Through such a shift, NIH was able to expedite the selection and testing of interventions to treat COVID-19, while continuing to apply rigorous standards to ensure safety and efficacy. To this end, NIH assembled the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership (see Box 3) and continues to work closely with other government agencies organized through the National Strategy.

NIH has made great strides in treating COVID-19 in a short amount of time, and the chances of surviving this disease have significantly improved since the beginning of the pandemic.

Box 3. ACTIV: An Unprecedented Partnership for Unprecedented Times

The rapid spread of COVID-19 and limited resources highlighted the need to coordinate and streamline research processes to optimize biomedical research and testing of potential therapeutic and vaccine candidates. In April 2020, NIH launched the Accelerating COVID-19 Therapeutic Interventions and Vaccines (**ACTIV**) public–private partnership to develop a coordinated research strategy for prioritizing and speeding the clinical evaluation of the most promising treatments and vaccines. Led by expert working groups, ACTIV is pursuing four fast-track focus areas that are most ripe for opportunity: (1) developing a collaborative, streamlined forum to standardize and share evaluation methods and testing of preclinical therapeutics and vaccines; (2) prioritizing and accelerating clinical testing of the most promising treatments for all stages of the disease; (3) leveraging clinical trial capacity and effectiveness; and (4) accelerating the evaluation of vaccine candidates to enable rapid authorization or approval. The coordinated efforts of the working groups have fed into six clinical trials:

ACTIV-1: Tests promising immune modulator compounds, a class of drugs that help minimize the negative effects of an overactive immune response to SARS-CoV-2 infection.

ACTIV-2: Evaluates the safety and efficacy of monoclonal antibodies and other therapies in outpatient settings. The trial tests if treatments can reduce the duration of symptoms and increase the proportion of participants with undetectable virus.

ACTIV-3: Examines the safety and efficacy of monoclonal antibodies and other therapies for hospitalized patients. The trial evaluates if investigational treatments can reduce the time to recovery and studies treatment effects on complications associated with COVID-19 and lung function.

ACTIV-4: Evaluates the safety and efficacy of different types of blood thinners to treat adults with COVID-19. The trial seeks to prevent and treat the effects of COVID-19-associated clotting and understand its effects in hospitalized, outpatient, and convalescing individuals.

ACTIV-5: Assesses if approved therapies or investigational drugs in late-stage clinical development show promise against COVID-19. Compounds that do not demonstrate efficacy based on interim evaluations are dropped, whereas those that demonstrate efficacy move forward into additional clinical trials.

ACTIV-6: Evaluates prescription and over-the-counter medications previously approved for other indications for people to self-administer to treat symptoms of COVID-19. The trial aims to provide evidence-based treatment options for the majority of adult patients with COVID-19 who have mild to moderate symptoms and are not sick enough to be hospitalized.

See the ACTIV website for a list of **therapeutics currently under investigation** in ACTIV clinical trials. In addition to trials conducted under the ACTIV partnership, NIH has prioritized and tested additional therapeutics in ACTIV-associated trials. These are **NIH-funded, randomized, placebo-controlled clinical trials** with one or more industry partners. NIH and its ACTIV partners will continue to work intensively to develop new and better treatments with the ultimate goal of ending the pandemic as soon as possible.

However, much work remains to improve the treatment of this disease. Orally administered drugs are needed for use as early-intervention strategies in primary care and outpatient settings that could potentially lessen the severity and duration of disease, as Tamiflu® does for influenza. Host-targeted treatments also are needed to prevent and address symptoms associated with COVID-19 that can cause lasting injury to the body and overall health of people with COVID-19. Candidates for such treatments include antivirals, host-targeted immune modulators, monoclonal antibodies (mAb), and symptomatic/supportive agents, including anticoagulants.

Treatment scenarios likely will become more complex and require additional studies as the pandemic continues to evolve, vaccines become more available, and viral variants continue to arise (e.g., treatments for reinfected people, immunocompromised individuals, vaccinated people who become infected, people whose symptoms persist longer than is typical for recovery from a respiratory virus). Through continued NIH-wide efforts and Federal, academic, and industry partnerships—such as ACTIV and ACTIV-associated trials—NIH is continuing to prioritize and test therapeutics to meet the changing needs of COVID-19 treatment and expand the populations eligible for treatment.

Objective 3.1: Identify and develop new or repurposed treatments for COVID-19

NIH has established a multipronged approach to discover or repurpose promising candidate therapies for COVID-19 using advanced screening methods—such as human cell–based models and animal models—to identify promising therapies that may interfere with the production of the virus or its ability to infect cells. These efforts will remain essential even in the context of vaccine availability as new viral variants arise that may be resistant to the currently available vaccines and therapeutics.

NIH-supported researchers are continuing to seek out and characterize candidate therapeutics that target the viral and host proteins that play an important biological role in SARS-CoV-2 infection, including candidates that inhibit viral replication or that block binding to ACE-2, the receptor through which the virus enters human cells. Data science tools are critical to this endeavor; NIH intramural and NIH-supported researchers already are creating complex computer-generated models of SARS-CoV-2 and its biological processes to determine key interactions and pathways to target for therapeutics development, as well as to predict resistance of newly arising virus mutants to currently available therapeutics.

Other therapeutic approaches under investigation involve passively boosting the immunity of people infected with SARS-CoV-2 by infusing convalescent plasma from patients recovered from COVID-19, pooling such blood products into hyperimmune blood proteins (alone or in combination with antiviral drugs), and using monoclonal antibodies designed to target and

neutralize the virus. NIH researchers and partners around the globe are continuing to develop and test new monoclonal antibodies for mild to moderate COVID-19 and hospitalized COVID-19 patients, and clinicians have begun treating patients in outpatient settings with monoclonal antibodies that already have demonstrated beneficial effects for mild to moderate COVID-19, including bamlanivimab (note that this treatment is not effective against some SARS-CoV-2 variants) and the combination antibody treatments casirivimab/imdevimab and bamlanivimab/etesevimab. In related work, NIH intramural scientists are exploring the potential use of nanobodies, a special type of antibody naturally produced by camelids (a group of animals that includes camels, llamas, and alpacas) to prevent or treat COVID-19.

In addition to new therapeutics, researchers are looking for ways to repurpose drugs approved for other indications and use them to treat COVID-19. NIH-supported and intramural researchers and their partners are screening existing FDA-approved therapeutics for activity against SARS-CoV-2, strategically targeting pathways identified in foundational coronavirus research studies as essential to virus production or infection. Within a few months of the pandemic's beginning, NIH collaborated with industry partners to show that the antiviral remdesivir, a drug formerly tested for the treatment of Ebola, accelerates the recovery of hospitalized, oxygen-supplemented patients with severe COVID-19. NIH now is testing remdesivir in combination with other new or repurposed drugs for treatment of patients with severe COVID-19. One combination treatment of remdesivir with a drug used to treat rheumatoid arthritis, baricitinib, reduces the time to recovery for people hospitalized with COVID-19 and now is being used to treat patients. Additional clinical trials are planned or are underway to evaluate the efficacy of other repurposed drugs through ACTIV and ACTIV-associated clinical trials or by leveraging ongoing NIH therapeutic clinical trials for other diseases to add measures to evaluate the efficacy of their target therapeutic against COVID-19 (see Box 3). NIH has taken steps to ensure that information about COVID-19 related clinical trials is swiftly shared through its ClinicalTrials.gov platform.

Objective 3.2: Evaluate new or repurposed treatments and treatment strategies for COVID-19

The multiorgan, multisystem involvement of moderate to severe COVID-19 prompts critical questions about its immediate and long-term impact, particularly in people with preexisting conditions. The severity of COVID-19 varies widely and can involve a number of different systems, including the cardiovascular, nervous, renal, and respiratory systems. NIH is supporting clinical trials to investigate whether existing antiviral drugs can be repurposed for early treatment of COVID-19 with a hope of preventing progression to severe disease and longer-term effects, but therapies to treat various COVID-19 complications are still needed.

The multifaceted nature of the impact of COVID-19 on multiple body systems necessitates evaluating a wide range of therapies that target disease processes resulting from SARS-CoV-2

infection. As part of this broad approach to therapy, NIH is evaluating treatment strategies that target the body's response to the virus, as well as evidence-based integrative health approaches. Clinical trials in progress include approaches to address disease processes resulting from SARS-CoV-2 infection, such as tissue injury, blood clotting, overreaction of the immune system, and inflammation. Some of these therapeutics under investigation have already demonstrated benefits in clinical trials.

To facilitate the testing of both antiviral and disease process-targeted treatments for COVID-19 and its complications, NIH created new research networks and is leveraging other clinical trial networks supported by Institutes, Centers, and Offices across NIH, including the Clinical Center. These networks are conducting a variety of flexible, adaptive clinical trials and support clinical trials designed in real-world hospital settings, called pragmatic clinical trials. NIH is collaborating with Federal, industry, and academic organizations through such partnerships as ACTIV to increase the capacity to conduct clinical trials across all phases, from pilot studies to large safety and efficacy trials. These partnerships are helping streamline recruitment and hasten the collection of data needed for FDA authorization to ensure that new or repurposed interventions will be advanced as quickly as possible.

Objective 3.3: Identify and evaluate new or repurposed treatments for the long-term effects of SARS-CoV-2 infection

Recovery from SARS-CoV-2 infection is extremely variable, with many patients recovering quickly but others experiencing longer-term illness. A significant number of COVID-19 survivors develop PASC (See Box 1). The magnitude of the public health impact of PASC is currently unknown but potentially profound, given the numbers of individuals across the age spectrum who have been and will be infected with SARS-CoV-2. It is imperative that we better understand and develop strategies to prevent and treat PASC and learn how to differentiate the general psychosocial impacts of the pandemic from the biological effects of the virus on cognitive function and mental health. Developing treatment strategies for all of these scenarios will be key to improving the well-being and functioning of the American people.

NIH has announced a research initiative to learn about the clinical spectrum of and biology underlying recovery from acute SARS-CoV-2 infection over time, across diverse populations, and throughout the lifespan. Through clinical and laboratory studies, including analyses of electronic health records, these research opportunities will help provide understanding of why most patients recover quickly but others have lasting or develop new symptoms after SARS-CoV-2 infection. This research will lay the foundation for clinical trials to identify safe and effective treatments to enhance the recovery of patients with persistent and new symptoms and identify interventions which, if initiated early, could prevent end-organ and systems damage and other symptoms. NIH also will evaluate medical care strategies that seek to improve COVID-19 outcomes, recognizing that individuals who receive critical care interventions, in particular, may require ongoing rehabilitation during recovery.

Objective 3.4: Investigate strategies for access to and implementation of COVID-19 treatment

The resolution of the COVID-19 pandemic will depend on the expeditious and broad dissemination of treatment strategies and care practices for use by health care practitioners and acceptance of these practices and strategies by communities to ensure that all members of the public have access to appropriate COVID-19 treatment. Delays in the adoption of up-to-date clinical practices could result in unnecessary prolongation of the pandemic, additional lives lost, and increased economic burden.

NIH is building on existing dissemination and implementation science research, both by testing the adaptation of strategies that have been successful in other disease areas, such as HIV and tuberculosis treatment, and by supporting new studies that examine methods to disseminate, provide access to, and facilitate uptake of interventions for COVID-19. Community-engaged research strategies and sex- and gender-focused approaches are essential to the success of implementing interventions, particularly for underserved and other populations at high risk of SARS-CoV-2 infection. These populations are disproportionately affected by COVID-19, experiencing the highest infection rates and risks for complications or poor outcomes. Equitable access to and uptake of treatments among these populations is of the utmost importance and critical to resolution of the COVID-19 pandemic. Community-engaged research seeks to use local communication channels, resources, and social infrastructure that can aid the design of tailored, local strategies to mitigate implementation barriers for underserved populations, such as barriers resulting from social determinants of health.

Essential to these goals is the consideration of cultural, ethical, social, behavioral, historical, and economic factors in the collection, storage, and dissemination of health-related data, as well as in evaluation of interventions. NIH is supporting in-depth examinations of factors that relate to barriers to and implications of treatment; stigma and financial burden associated with COVID-19 treatment and follow-up care; and issues of privacy, confidentiality, and data sharing.

PRIORITY 4

Improve Prevention of SARS-CoV-2 Infection

Critical to resolving the current COVID-19 pandemic and preventing future outbreaks is the development of countermeasures to stop transmission of the virus and prevent new infections. By supporting the development of new vaccines, behavioral and community interventions, and effective strategies for implementing these countermeasures, NIH is creating preventive interventions with the potential to reduce the incidence of new SARS-CoV-2 infections across the country. The NIH approach leverages existing knowledge, tools, networks, and infrastructure—in addition to developing and implementing novel approaches—to prevent new SARS-CoV-2 infections.

Objective 4.1: Develop novel vaccines for the prevention of COVID-19

To prevent outbreaks of COVID-19, safe and effective vaccines for SARS-CoV-2 needed to be developed and distributed as quickly as possible. The NIH intramural program played an important role in the early testing and development of several vaccine candidates, including the Moderna mRNA vaccine, developed by NIH and ModernaTX, Inc., (see Box 4) and the AstraZeneca vaccine, developed in a partnership between NIH and Oxford University. As of April 2021, the Moderna vaccine and another mRNA vaccine developed by Pfizer and BioNTech—as well as a recombinant vector vaccine developed by Johnson & Johnson's Janssen Pharmaceuticals—have received FDA emergency use authorization for administration in adults. Two additional vaccines developed by AstraZeneca and Novavax have ongoing Phase 3 clinical trials. NIH is continuing to support research and development of effective COVID-19 vaccines, including novel vaccine platforms such as a cage of sticky nanoparticles, which are ultrafine particles sized between 1 and 100 nanometers that have the potential to combat multiple strains of coronaviruses. NIH also is pursuing research on a universal coronavirus vaccine that would offer protection from multiple coronavirus strains and variants in an effort to prevent future outbreaks from occurring, as well as a clinical trial for the SARS-CoV-2 B.1.351 variant.

Similar to its role for therapeutics, ACTIV (see Box 3) has played a critical role in coordinating research efforts and clinical trials for vaccines across the NIH, FDA, and industry. To coordinate and accelerate clinical testing, NIH and its partners are leveraging existing clinical trial networks, such as the HIV Vaccine Trials Network; the HIV Prevention Trials Network; the Infectious Diseases Clinical Research Consortium; and the Prevention and Early Treatment of Acute Lung Injury Network (PETAL Network), which conducts trials to improve prevention and treatment of acute respiratory distress syndrome. NIH created the COVID-19 Prevention Network (CoVPN), which is coordinating clinical research sites for Phase 3 efficacy trials and providing centralized data coordination and novel epidemiological disease tracking tools to speed the evaluation of vaccine candidates. These data help inform the decision-making process for expanding vaccine testing to new populations, including groups at higher risk of SARS-CoV-2 infection. For example, based on the success and safety of vaccines in healthy adults, clinical studies to test the safety and efficacy of COVID-19 vaccines in children, adolescents, and pregnant individuals are now underway.

Objective 4.2: Develop and study other methods to prevent SARS-CoV-2 transmission

Until COVID-19 vaccines are widely available and we know more about how effective they are against newly arising variants of SARS-CoV-2, alternative methods to slow the spread of

the virus will continue to be necessary. NIH is supporting studies on preventive treatments, behavioral and community prevention practices, and policies to rigorously study and determine the most effective approaches to promote individual and community safety. These approaches are informed by NIH basic research into the mechanisms of viral survival, infection, and transmission.

Antibody treatments, in addition to their potential therapeutic use, hold promise as a method to prevent COVID-19 in individuals exposed to SARS-CoV-2 and those who are at high risk of serious illness. Clinical trials supported by NIH demonstrated that the monoclonal antibody bamlanivimab can prevent COVID-19 symptoms in SARS-CoV-2 positive patients and reduce the risk of SARS-CoV-2 infections in nursing home residents by up to 80 percent. Additional studies for the use of other monoclonal antibodies as preventive treatments are underway.

Research into the survival of SARS-CoV-2 in the environment and its transmission through respiratory droplets has guided the understanding of how physical distancing and personal protective equipment (PPE) can be applied to prevent viral spread. Modifiable risk factors, such as environment and nutrition, and interactions with preexisting biological mechanisms, such as epigenetics and metabolomics, that may contribute to a person's susceptibility to SARS-CoV-2 infection are being studied to better understand a broad range of prevention methods. The Community Prevalence of SARS-CoV-2 Study (COMPASS) will inform the development of future SARS-CoV-2 prevention research and provide valuable information on the effectiveness of prevention practices by assessing knowledge, attitudes, behaviors, and beliefs about the COVID-19 pandemic and modeling the potential impact of prevention strategies.

NIH also is supporting research into effective practices for PPE use and reuse, as well as the development of new PPE to protect health care workers, caregivers, and the public. NIH prioritizes the safety of health care workers and caregivers and seeks to build scientific knowledge of the best decontamination methods and other safety measures specific to the needs of health care environments, such as nursing homes, dental practices, and hospitals. The NIH Worker Training Program has supported 31 grants to create virtual trainings for COVID-19 essential and returning workers. As of April 2021, more than 8,200 health care workers, first responders, community-based organization staff, death care industry professionals, and other essential workers have completed these online trainings. NIH also supported research into the development of practices and innovative decontamination technologies and procedures—such as the use of ultraviolet light, heat, and chemical procedures—to decontaminate and reuse N95 respirator masks.

Objective 4.3: Develop effective implementation models for preventive measures

NIH and its funded scientists are leveraging existing and new collaborations to determine the best possible methods for developing, implementing, and distributing vaccines and behavioral prevention methods against SARS-CoV-2. As vaccines are becoming widely available, rigorous research is needed to answer critical questions about the most effective distribution practices. Ensuring vaccines are delivered equitably to at-risk individuals in high-need areas, with proper access and administration techniques, is critical to preventing further outbreaks. Key to this research is identifying methods to address social, ethical, and behavioral factors likely to influence the use of vaccines and other prevention practices. Implementing effective

Box 4. Groundbreaking Vaccine Development to End the Pandemic

The development of multiple safe and effective vaccines against COVID-19 is critical to ending the pandemic. As soon as the SARS-CoV-2 genetic sequence became public in January 2020, NIH-funded scientists began working at an unprecedented pace to identify, develop, and test promising vaccine candidates. Previously, new vaccines took, on average, longer than 10 years to develop, and many candidates were ultimately unsuccessful. Building on previous coronavirus vaccine research at NIH and the intense collaboration and dedication of NIH-supported and intramural scientists and its industry and Federal partners, several vaccine candidates have successfully been developed and deployed in one year without sacrificing standards for safety or scientific rigor. This extraordinary effort and record-breaking pace represent countless scientific and logistical advances in vaccine development made both before and during the current pandemic; these advances—and others to come—will help us better prepare for the rapid creation and testing of vaccines against future emergent viruses.

NIH ensured needed resources and supplies were available for researchers and vaccine developers, **leveraged existing clinical trial networks** to rapidly advance the testing of vaccine candidates, and coordinated across the U.S. Department of Health and Human Services to focus resources and standards on vaccine candidates moving through the development pipeline. Advancing candidates through preclinical study, clinical testing, and regulatory approvals required extraordinary coordination of Federal and industry partners via collaborations and partnerships, such as ACTIV (**see Box 3**). In one collaboration, ModernaTX, Inc., and the Biomedical Advanced Research and Development Authority developed the **mRNA-1273 vaccine** (called the Moderna vaccine). NIH provided funding and technical support for the Phase 3 efficacy trial that enrolled more 30,000 participants at 100 research sites across the country. As one of the first vaccines to receive **FDA emergency use authorization** in the United States, it is being delivered to millions of Americans daily. NIH and ModernaTX already have pivoted to address emerging SARS-CoV-2 variants and now are testing a **vaccine targeted toward the B.1.351 variant**.

and responsive prevention strategies in populations at high risk of SARS-CoV-2 infection is a principal priority for NIH (see Priority 5).

Leveraging testing technology and new knowledge of SARS-CoV-2 transmission is critical to preventing the spread of the virus. The COVID-19 Testing Impact Calculator (see description in Priority 2) provides clear guidance for schools and businesses to promote risk-reducing behaviors and navigate evolving conditions on a local level. NIH is using the SAFER COVID app—which tracks symptoms, assesses risky activities, and assists with at-home testing and reporting—to inform its own employees' safe return to work. A pilot study to determine if frequent at-home testing can reduce viral transmission began in March 2021.

NIH recognizes the need to communicate and partner with the public to help increase uptake of preventive measures, including vaccines, and address vaccine hesitancy. To help ensure development of vaccines that would work for all Americans, NIH worked to achieve diversity in vaccine clinical trial participants through the Community Engagement Alliance (CEAL) Against COVID-19 Disparities initiative. The initiative provides trustworthy information through active community engagement and outreach in disproportionately affected communities. In another effort, partners across NIH compiled evidence-informed communication strategies for prevention measures tailorable to the needs and concerns of diverse communities. NIH also has solicited research proposals for community-engaged research to evaluate strategies to increase vaccine uptake and address barriers to increasing vaccinations among populations experiencing health disparities and vaccine hesitancy.

PRIORITY 5

Prevent and Redress COVID-19 Outcomes in Health Disparity and Other Populations at High Risk of SARS-CoV-2 Infection

The impact of COVID-19 on populations that are underserved and experiencing health disparities[1] must be urgently addressed. There are consistent differences in COVID-19 prevalence and mortality across different age, racial, and ethnic groups, and among specific populations (e.g., people with asthma or diabetes).[2] The underlying causes are complex and include social

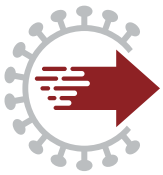
[1] Health disparity populations include Black/African American populations, Hispanics/Latinos, American Indians/Alaska Natives, Asian Americans, Native Hawaiians and other Pacific Islanders, socioeconomically disadvantaged populations, underserved rural populations, and sexual and gender minorities.

[2] Populations with increased risk of COVID-19 include residents of chronic care and assisted living facilities; community-dwelling older adults; individuals with rare diseases; individuals with cognitive impairment or dementia; homeless populations; incarcerated populations and those involved with the criminal justice system; adults with medical comorbidities; pregnant individuals; children and adolescents; individuals with substance use disorders or severe mental illness; those living in congregate housing; persons who are deaf or with disabilities, including visual, hearing, communication, or mobility impairment; detainees in immigration centers; migrant communities; individuals living on Tribal lands or reservations; and communities that are exposed to high rates of air pollution or other toxic exposures. Individuals who are on the frontlines of health care during the COVID-19 pandemic and those working in essential business operations also are at higher risk for COVID-19.

and structural determinants of health—such as social, economic, and political mechanisms that generate inequalities in society (e.g., discrimination, economic and educational disadvantages) and differences in health care access and quality. These concerns are amplified in densely populated urban areas where physical distancing is not possible; rural areas where access to testing and vaccines may be delayed or inadequate due to limited transportation networks and access to hospital and specialty care; communities with high rates of chronic health conditions; and lower- and middle-income countries with fragile health care systems. An in-depth understanding of the underlying causes that may exacerbate the spread and morbidity or mortality of COVID-19 in the United States, as well as different countries around the globe, allows the scientific, public health, and clinical communities to efficiently implement interventions to mitigate negative outcomes through better prevention, testing, and treatment of COVID-19. NIH aims to address key questions related to the differential impacts of the COVID-19 pandemic, including the long-term health consequences. These include understanding barriers to adherence to different mitigation strategies, including vaccine misinformation, distrust, and hesitancy among populations; and differences in risk and resilience based on biological factors, gender, race and ethnicity, socioeconomic status, disability, and other social and structural determinants of health. Ultimately, the United States cannot control the pandemic alone. NIH will continue to collaborate with the global scientific community, such organizations as the World Health Organization, and foundations, partnerships, and nongovernmental organizations engaged in research response not only to understand the spread of SARS-CoV-2, but also to develop and distribute the diagnostics, treatments, and vaccines needed to control the COVID-19 pandemic on a global scale.

Objective 5.1: Understand and address COVID-19 as it relates to health disparities and populations at higher risk for COVID-19 in the United States

As part of the RADx initiative (see Box 2), NIH is funding a series of interlinked community-engaged projects to enhance SARS-CoV-2 testing in underserved, under resourced, and rural populations across the United States. This initiative has developed infrastructure to assess and expand evidence-based testing capacity and address the social, cultural, ethical, and behavioral implications associated with SARS-CoV-2 testing for those populations that are most at risk for infection and adverse outcomes from contracting the virus. RADx Underserved Populations (RADx-UP) projects are conducting pragmatic and traditional clinical trials at multiple sites across the country to investigate a variety of testing methods and approaches to better understand the uptake, acceptance, and effectiveness of testing in specific populations. These projects are undertaken in partnership with community health centers (e.g., Tribal health centers, Health Resources and Services Administration–funded community health centers, Federally Qualified Health Centers), medical libraries, houses of worship, homeless shelters,



group care homes, jails and prison systems, and other community resources to address the unique needs of different communities. The implementation and evaluation of new community interventions to prevent SARS-CoV-2 transmission and its immediate and long-term adverse psychosocial, behavioral, and socioeconomic consequences on health disparity populations is crucial. In April 2021, NIH released funding opportunities to expand testing efforts in underserved communities and schools; address testing and vaccine hesitancy and social, ethical, and behavioral factors associated with testing and vaccination; and build partnerships with CEAL to ensure that communities have access to the best strategies to increase vaccine and testing uptake and address COVID-19.

The CEAL initiative also works to address the disproportionate burden of COVID-19 in underserved populations. CEAL connects researchers with trusted local leaders and organizations in hard hit communities to provide accurate, accessible information about COVID-19, preventive measures (including vaccines), and opportunities to participate in research. The initiative also develops and disseminates free culturally tailored educational resources in English and Spanish about ongoing clinical trials and emerging vaccines and treatments in the United States. Continued dialogue and engagement with communities at high risk of SARS-CoV-2 infection through RADx-UP, CEAL, and other NIH programs will be critical to the success of the national vaccination campaign. Vaccine hesitancy and mistrust are prevalent in underserved communities and could slow vaccination efforts in the communities that would benefit from vaccines the most. To that end, NIH launched a research initiative to promote vaccine acceptance, uptake, and implementation among populations that experience health disparities. Related efforts include holding an NIH Tribal Consultation on COVID-19 Research to seek input from Tribes about programs focused on enhancing testing capacity to better understand the best strategies for effectively addressing the COVID-19 pandemic in these populations. NIH will continue engagement efforts with Tribal leaders to assist the national vaccination campaign.

Multiple factors determine vulnerability and case fatality rates, including preexisting conditions, disabilities, and sex and gender disparities. This pandemic underscores the imperative to consider the entirety of the American population and social determinants of health to strengthen our collective capacity to respond equitably to COVID-19 and ensure study findings are relevant to everyone. NIH will fund mechanistic studies on the interaction between SARS-CoV-2 infection susceptibility, routes of infection, the course of COVID-19, and morbidity and mortality in people with preexisting conditions (e.g., obesity). Equitable distribution of resources, access to care, and accommodations related to disabilities and other transportation and mobility issues will be critical to ensure health care and resources are available to all who need them. NIH is supporting the development of tools that provide access to COVID-19 incidence information and help people with visual impairments plan their travel activities. With the goals of promoting scientific rigor and enhancing health equity, NIH developed guiding principles to

urge systematic examinations of sex and gender influences in COVID-19 research. The guidance addressed how NIH policies on sex as a biological variable and inclusion could inform study designs, analysis, and result reporting to improve health outcomes amid the COVID-19 crisis and public health emergency.

NIH is committed to including individuals who have been traditionally underrepresented in biomedical research in clinical trials for treatments and vaccines to understand how interventions may affect these populations differently and ensure the applicability of findings to all. For example, the trans-NIH INCLUDE (INvestigation of Co-occurring conditions across the Lifespan to Understand Down syndromE) initiative is supporting research that explores the effects of COVID-19 on individuals with Down syndrome. Similarly, the RADx-UP and NIH's Helping to End Addiction Long-term℠ (HEAL) programs are supporting research into the best implementation strategies to test for SARS-CoV-2 infection in children with intellectual and developmental disabilities and communities most heavily affected by the opioid epidemic, respectively.

Objective 5.2: Understand and address COVID-19 maternal health and pregnancy outcomes

Pregnancy is associated with alterations in the immune system—resulting in increased susceptibility to certain viral, bacterial, and parasitic infections—which may adversely impact maternal health, preterm birth, and infant health. More specifically, other respiratory viral infections, such as influenza, are associated with more severe disease outcomes in pregnant individuals and an increased risk of pregnancy-related and neonatal complications. Yet, information about SARS-CoV-2 infection and disease in pregnant individuals is scarce. Independent of COVID-19, individuals in the United States from underserved populations face substantially higher rates of pregnancy-related complications (i.e., severe maternal morbidity) and pregnancy-related death than non-Hispanic white women. Up to 60 percent of pregnancy-related deaths are preventable, highlighting inequities in health care access and quality-of-care factors that contribute to racial disparities in maternal mortality and severe morbidity. NIH will leverage existing research on maternal morbidity and mortality to investigate questions related to

pregnancy and COVID-19, including the effects of SARS-CoV-2 infection and treatment of COVID-19 on maternal and fetal health during pregnancy, as well as pregnancy outcomes. Populations at higher risk for COVID-19, including pregnant individuals, also are included in RADx-UP programs, to coordinate improved strategies for diagnostic testing.

NIH has initiated large-scale studies to investigate the effects of COVID-19 on such factors as pre-, peri- and postnatal care; rate of Cesarean section delivery; and maternal and infant health outcomes. Early results from the Maternal Fetal Medicines Unit Network's Gestational Research Assessments for COVID-19 (GRAVID) show that pregnant individuals who experienced severe symptoms of COVID-19 had a higher risk of complications during and after pregnancy, but women in the third trimester are unlikely to pass the infection on to their infants. Additional studies will examine neurodevelopmental issues in children whose mothers were infected with SARS-CoV-2 during pregnancy, while others will address neurological complications of COVID-19 in pregnant individuals, children, and newborns exposed to the virus. NIH-supported researchers also have created a repository of recent peer-reviewed journal articles on COVID-19, breastfeeding, infant feeding, and breast milk. NIH recognizes the need to determine the safety and efficacy of COVID-19 therapeutics for pregnant and breast-feeding individuals—a clinical trial to evaluate the use of remdesivir during pregnancy launched in February 2021.

Objective 5.3: Understand and address age-specific factors in COVID-19

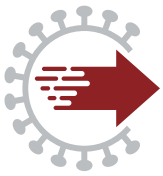
Certain age groups are at higher risk for serious complications from SARS-CoV-2 infection, such as older adults (65 years and older). NIH is supporting studies of neurological and neurocognitive symptoms in COVID-19 and complications associated with SARS-CoV-2 infection in older adults. In addition, NIH is funding research to explore the role of inflammation in older populations with COVID-19 and subsequent progression to more severe disease, including lung pathology. NIH also is developing aged animal or *in vitro* models suitable for studies on pathogenesis of the virus or preclinical testing of investigational therapeutics and vaccines against SARS-CoV-2.

Although the majority of children and young adults have mild, moderate, or asymptomatic cases of COVID-19 compared with adults, studies are needed to address the dynamics of the virus and the immune response in children and adolescents, as well as short- and long-term outcomes. For example, the NIH Human Epidemiology and Response to SARS-CoV-2 (HEROS) study will help determine what percentage of children infected with SARS-CoV-2 develop symptoms of the disease. Data also suggest that undiagnosed infections in children may present later as a pediatric inflammatory syndrome similar to Kawasaki disease called multisystem inflammatory syndrome in children (MIS-C). It is known that many children with MIS-C either were infected with SARS-CoV-2 or were exposed to someone with COVID-19. Trans-NIH efforts known as the Collaboration to Assess Risk and Identify Long-term Outcomes for Children with COVID (or CARING initiative) and the RADx-rad Predicting Viral-Associated Inflammatory Disease Severity in Children with Laboratory Diagnostics and Artificial Intelligence (or PreVAIL kIds) studies are part of a research plan to investigate MIS-C. These and other studies aim to describe the spectrum of pediatric SARS-CoV-2 infection and why some children are more likely to get infected, understand long-term outcomes for patients, identify MIS-C risk factors, and define other critical research questions to impact patient health. In another effort, the Pediatric Trials Network is using more than 50 established research sites to evaluate drugs given to children diagnosed with COVID-19. Researchers are analyzing blood samples collected from routine medical procedures to understand how these drugs act in children, refine dosing, and improve safety.

The long-term socioeconomic and health impacts of the COVID-19 pandemic on children remain to be seen, but the potential exists for profound and lasting detrimental consequences for the well-being, education, and mental health of children, particularly among underserved populations. Researchers funded by the Environmental influences on Child Health Outcomes (ECHO) program rapidly developed parent- and child-specific COVID-19 questions to study the impact of changes in environmental exposures resulting from the COVID-19 pandemic on child health outcomes. These tools are now available to researchers and clinicians through the NIH Public Health Emergency and Disaster Research Response COVID-19 Collection Tools and the PhenX Toolkit COVID-19 Protocol Library. Additionally, the RADx-UP program is supporting the study of school-based COVID-19 diagnostic testing approaches in high-risk communities to facilitate a return to in-person school for disproportionately affected and underserved populations, including racial and ethnic minorities and students with disabilities.

Objective 5.4: Address global health research needs revealed by COVID-19

NIH recognizes that a global pandemic requires a global response and is working with international partners to improve fundamental knowledge of SARS-CoV-2 and COVID-19, as well as optimize the development and delivery of diagnostic tests, treatments, and vaccines



to populations most in need. Much of the initial knowledge regarding the basic science, epidemiology, and disease characteristics of COVID-19 was gained from or developed in collaboration with the international scientific and medical communities. Collaborations with scientists around the globe have been essential to piecing together the emergence and spread of SARS-CoV-2, and they have helped identify the populations most severely affected. Critical to these efforts are open lines of communication and a collaborative approach among the international biomedical community. NIH continues to foster international collaborations to address the COVID-19 public health response on a global level, drawing on a worldwide network of grantees and former trainees, many of whom have leadership roles in global and national responses.

Robust international scientific collaboration is critical to the development and distribution of diagnostics, treatments, and vaccines needed to control COVID-19 on the global scale necessary for full social and economic recovery. NIH is coordinating efforts with other international COVID-19 product development accelerators to share best practices and information about clinical trials and the advancement of promising new medical countermeasures. For example, the NIH-supported Global Network for Women's and Children's Health Research is examining antibody testing at delivery to compare maternal, fetal, and neonatal outcomes of women infected with SARS-CoV-2 with those of noninfected women in different countries. Academic and industry collaborations outside the United States are providing critical perspective on SARS-CoV-2 transmission, tracking molecular changes in the virus, establishing epidemiological tools to help monitor outbreaks and new infection patterns, and developing countermeasures against the virus. Fogarty International Center in-house researchers have been collaborating with partners in Asia and Africa to use mathematical modeling to study the disease dynamics of COVID-19 in the United States and abroad. Fogarty scientists also have trained international partners in Africa, Asia, and South America to use genomic epidemiology to track local emergence of SARS-CoV-2 variants of concern. By applying lessons learned from implementation and dissemination science studies in low- and middle-income countries, NIH is employing its international clinical infrastructure to create new collaborations that ensure timely distribution of these diagnostics and interventions to the populations that would benefit from them the most.

Partnering to promote collaborative science

Supporting the research workforce and infrastructure

Investing in data science

Engaging and educating the public

CROSSCUTTING STRATEGIES

To support the five strategic priorities, NIH is pursuing crosscutting strategies that build on its existing strengths as the Nation's premier biomedical research agency. Specific examples of these strategies have been provided throughout this plan.

Partnering to promote collaborative science

NIH will continue fostering collaborative efforts to build an interactive, multidisciplinary scientific workforce in the United States and internationally to accelerate research on COVID-19. By leveraging existing NIH-funded global research networks, coordinating closely with its Federal partners, and creating new public–private partnerships, NIH continues to employ every opportunity to deepen the understanding of and develop interventions for COVID-19.

Many NIH-funded research networks already have been mobilized to address COVID-19—including those focused on specific practice areas, particular demographics, or otherwise at-risk populations—such as the PETAL Network.

NIH continues to expand collaborations with its fellow agencies and offices within the U.S. Department of Health and Human Services (HHS) (e.g., Biomedical Advanced Research and Development Authority, CDC, FDA) and beyond (e.g., U.S. Department of Defense) to ensure efficient and rapid dissemination of diagnostics, treatments, and vaccines to the public. Furthermore, NIH and its Federal partners are working closely and recognize the importance of collaboration with the private sector, scientific societies, nonprofit organizations, patient communities, and health care providers.

Supporting the research workforce and infrastructure

The COVID-19 pandemic has the potential to have a substantial negative impact on the livelihood and diversity of the scientific workforce, particularly for women and underrepresented groups, such as racial and ethnic, sexual, and gender minority populations. NIH has assessed the effects of COVID-19 on the scientific workforce at NIH and the extramural community at an individual and institutional level, including underrepresented groups, and is using these preliminary survey results to inform the best course forward for promoting a diverse and inclusive scientific community. Already, NIH has specified opportunities for extending fellowship and career development awards impacted by COVID-19, and investigators adversely impacted by COVID-19 can request an extension of their early-stage investigator status via the electronic Research Administration (eRA) Commons. NIH also provides substantial administrative flexibilities for researchers who have been adversely affected by the COVID-19 pandemic.

Despite challenges presented by the pandemic and measures put in place to limit its spread, NIH is working with the scientific community to advance SARS-CoV-2 and COVID-19 research. By adapting its processes to work within the physical distancing constraints of the pandemic, NIH continues to process proposals and fund research projects in a timely manner. For example, NIH has expanded its use of virtual meetings to conduct peer reviews to protect the health of reviewers and NIH staff while facilitating the funding of COVID-19 and other research.

NIH continues to support researchers by providing such resources as tools, reagents, and sequencing tools. For example, NIH provides validated biosamples and access to animal models of SARS-CoV-2 infection. Furthermore, NIH is continuing to solicit innovative ideas to aid the COVID-19 response, potentially from investigators outside of infectious disease or virology research, through such mechanisms as the NIH Common Fund High-Risk, High-Reward Program.

In addition to funding COVID-19 research in the extramural community, NIH continues to mobilize its Intramural Research Program and the Clinical Center in support of COVID-19 research. Talented investigators are using NIH's specialized infrastructure that provides access to unique patient cohorts and clinical trials networks, as well as its state-of-the-art equipment, to deliver one-of-a-kind services relevant to COVID-19. These efforts take advantage of a unique and wide range of research and technological expertise, as well as partnerships and collaborations with extramural investigators. Projects are underway to evaluate and validate serology tests, design and assess PPE, and complete onsite clinical trials and basic science research. NIH continues to maximize the capacity and use of its vaccine treatment and evaluation units to enroll participants rapidly and evaluate vaccine response in a safe and effective manner.

Investing in data science

The ability of researchers to rapidly access and use pandemic-related data, from viral sequences to infection rates, has been critical to the ground-breaking speed of the U.S. response. NIH supports multiple data science efforts to ensure that COVID-19 research data are findable, accessible, interoperable, and reusable (the FAIR principles). Artificial intelligence and machine learning approaches are being incorporated into studies across the spectrum of research to support data-driven decision-making and improve scientific stewardship. By enhancing

existing and creating new data science resources and analytical tools, NIH is facilitating the use of COVID-19 data to the greatest extent possible, both by those generating the data and by other researchers. These investments support the development of diagnostic tools, survey instruments, risk assessment models, public health surveillance tools, and portals to share data (e.g., National COVID Cohort Collaborative (N3C), NIH Repository of COVID-19 Research Tools, OpenData Portal, PhenX, Systemic Harmonization and Interoperability Enhancement for Laboratory Data Collaborative (SHIELD), SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance, and the COVID-19 SeroHub). NIH's investments in these and other tools and infrastructure continue to grow as the pandemic progresses, signaling NIH's commitment to the development of shared metrics and terminologies across research projects to facilitate and maximize the use of a wide breadth of data, from chemical structures to clinical trial results.

Through these approaches, NIH continues to explore and implement innovative ways to leverage its domestic and global infrastructure to address the needs of the COVID-19 pandemic and speed its resolution. Looking forward, NIH will build on the lessons learned regarding strategic data and information assets and data sharing infrastructure from this pandemic for use in streamlining future responses to health-related emergencies.

Engaging and educating the public

NIH has made considerable advances in the detection, treatment, and prevention of SARS-CoV-2 in the first year of the COVID-19 pandemic. To truly capitalize on these research advances, NIH must also focus on ensuring that the public is aware of and engaged in NIH research. This will help secure equitable impact across the Nation, as outlined by the National Strategy. To work toward reaching as many different audiences as possible, NIH is placing an emphasis on communication through different mediums—from television to social media to print. The NIH COVID-19 public website is serving as a central hub for the public to learn about and participate in COVID-19 research across all of NIH. NIH COVID-19-focused initiatives also have developed informative, engaging websites to communicate with the public, including specific audiences. For example, NIH has created the Women, Science, and the Impact of COVID-19 webpage and established a virtual speaker series on this topic. NIH's new Spanish COVID-19 website brings health information to the Spanish-speaking public. NIH also has collaborated on the HHS Combat COVID website, also available in Spanish.

Community engagement efforts are needed to foster public confidence in science and cultivate an informed public equipped to prevent the spread of SARS-CoV-2, particularly within communities hardest hit by the COVID-19 pandemic. CEAL has been instrumental to this endeavor, providing trustworthy information about vaccines and clinical trials through active community engagement and outreach to communities at high risk of SARS-CoV-2 infection (see description in Priority 5). These efforts are already beginning to pay off, with 37 percent of the volunteers in the NIH-Moderna vaccine trial coming from communities of color.

CONCLUSION

At the start of the COVID-19 pandemic, NIH and the biomedical community launched an unprecedented effort to diagnose, prevent, and treat this rapidly spreading disease. NIH has collected innovative and creative ideas from across the country, built new partnerships, and undertaken a bold and ambitious plan for protecting the American people from the novel coronavirus. These efforts already have shed light on the virus and its biology and have led to a number of approaches to save lives and mitigate the pandemic. Building on this knowledge and research infrastructure will prepare the world for future epidemics, and enhancing response capacity will be a vital legacy of this work.

The discoveries made by NIH scientists and NIH-funded investigators have built on countless scientific and technological advances in biomedical science. Genome sequencing, imaging technologies, data science and bioinformatics, and implementation science all have contributed to our knowledge of SARS-CoV-2 and COVID-19. To meet current needs, the approach to biomedical research has shifted in groundbreaking ways. By bringing together teams across a range of sectors and scientific disciplines and building on discoveries of the past, NIH will continue to take a crosscutting, integrative view of public health to put forward creative and bold strategies to end the COVID-19 pandemic.

The COVID-19 pandemic is the latest reminder of the constant threat to the health of the American people of emerging and reemerging infectious diseases. These pathogens require constant surveillance as they evolve and adapt to environmental pressures. Likewise, NIH must maintain a flexible, adaptable infrastructure to support research programs that aim to understand the foundational biology of new organisms and emerging diseases, the role of behavioral and social factors, and their potential impact on human health. These efforts will prepare scientific groundwork to protecting life from this and future public health threats. Under these extraordinary circumstances, NIH will continue to act swiftly to turn discoveries into health.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