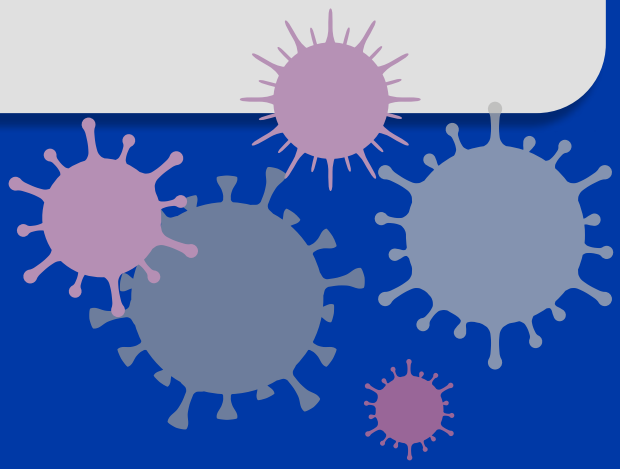
MILKEN INSTITUTE
CENTER FOR STRATEGIC PHILANTHROPY

A New Imperative for Private Research Funders



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GIVING SMARTER IN THE AGE OF COVID-19

ABOUT US

About the Milken Institute

The Milken Institute is a nonprofit, nonpartisan think tank.

For the past three decades, the Milken Institute has served as a catalyst for practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. Guided by a conviction that the best ideas, under-resourced, cannot succeed, we conduct research and analysis and convene top experts, innovators, and influencers from different backgrounds and competing viewpoints. We leverage this expertise and insight to construct programs and policy initiatives.

These activities are designed to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

About the Center for Strategic Philanthropy

The Milken Institute Center for Strategic Philanthropy advises philanthropists and foundations seeking to develop and implement transformative giving strategies.

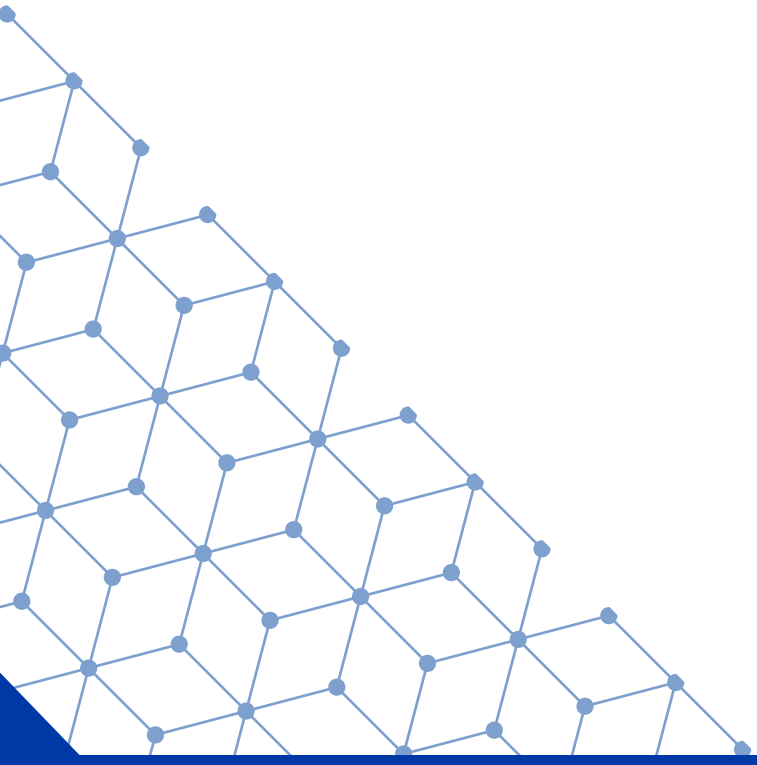


TABLE OF CONTENTS

EXECUTIVE SUMMARY

Quickly after the novel coronavirus ripped through the world, science and high-impact donors responded to accelerate COVID-19-relevant research at a pace never experienced before. While this unprecedented response to an unprecedented situation was urgent and necessary, in the background, other biomedical research efforts across many health conditions, including Alzheimer's disease, diabetes, and depression came to an almost immediate halt. Months later, we are now beginning to dig out from underneath a public health and economic burden that lobs new curveballs almost every day.

The Milken Institute Center for Strategic Philanthropy works with philanthropists and foundations to guide scientific strategy. Generally, our guidance focuses on deploying capital in new, discrete spaces where a donor has a specific interest. In this report, however, we take a broad look at the biomedical ecosystem to identify the specific ways that COVID has thrown it out of balance—ranging from time and resources lost to supply chain disruptions and economic turmoil.

The long-term health of our world depends on robust research ecosystems, but because of the pandemic, progress toward multiple health issues that impact our daily lives is at great risk.

Philanthropic capital, when invested strategically, can keep innovation on track to reach patients. In this environment, philanthropy can be the driver that solves for short-term difficulties while laying the groundwork to create a better biomedical research ecosystem for the long-haul.

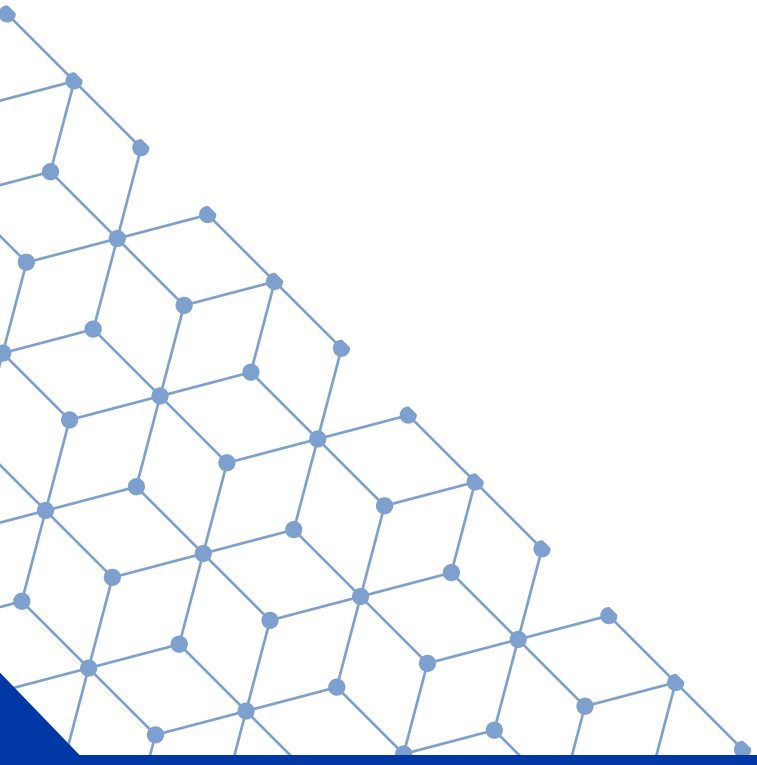
AREAS OF CONSIDERATION FOR BIOMEDICAL RESEARCH FUNDERS

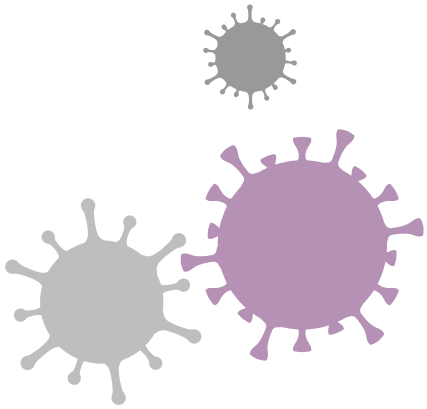
- Work with scientists to identify COVID-related shortfalls and increase budgets
- Focus on human talent
- Reevaluate the meaning of "productive" in the context of the pandemic
- Strengthen the biomedical nonprofit sector

INTRODUCTION

Like much of the world, research institutions have been forced to make dramatic changes to their daily activities to protect their staff, students, patients, and communities from the threat of COVID-19. Labs were shuttered, scientists lost work hours, and some years-long experiments were destroyed. After three months of severe closures, research institutions began to reopen partially in June 2020. Although some enterprises may be able to regain lost time, research and funding communities are concerned that lab closures and fundraising losses may lead to long-lasting delays in biomedical progress. In turn, progress toward treatment and cures for thousands of diseases will be delayed, and the biomedical workforce will be irreparably damaged.

The Milken Institute Center for Strategic Philanthropy spoke with approximately two dozen researchers and research funders to glean an understanding of how philanthropy can help restart progress. Broadly, we found that researchers and their institutions are facing challenges in two distinct areas: research setbacks caused by COVID-19 and compounded by related mitigation efforts, and an acute workforce crisis exacerbated by a system that was already in distress. In general, private funding through nonprofits, philanthropists, and endowments is a key source of capital to fill acute intermittent gaps. However, the ensuing and complex financial downturn has strained private research funders and has led to critical research shortfalls across the biomedical enterprise.





COMPOUNDING RESEARCH SETBACKS

In his remarks to Congress in late April, Francis Collins, director of the National Institutes of Health (NIH), explained that the NIH projected roughly $10 billion in research losses due to the COVID-19 pandemic, which is more than one-quarter of the agency's annual budget. This estimate assumes that research losses are limited to a five-month crisis and are driven by reduced productivity. It is becoming clearer that COVID-19 will continue to cause severe disruptions to research through 2020 and will require precautions through some or all of 2021. Therefore, research infrastructure and teams will continue to suffer, and NIH budgetary losses will grow.

Thus far, Congress has provided $3.6 billion in emergency funding to NIH to respond to the COVID-19 pandemic. This funding is earmarked for critical research to accelerate the science for coronavirus testing, treatment, and vaccines.

However, funding has not been set aside for losses sustained in research not directly related to the nation's COVID response, including Alzheimer's disease, diabetes, and depression.

Sustained focus on these and many other chronic conditions exacerbated by COVID-19 is critical as well. Eric Nestler, director of the Friedman Brain Institute and dean for academic and scientific affairs at the Icahn School of Medicine at Mount Sinai, told us, "The effects of COVID-19 are compounded by many other diseases including heart disease, diabetes, and substance use disorder. Funding for COVID-19 cannot come at the expense of other fields." Below we outline the specific drivers of increased cost to the biomedical research system due to the COVID-19 pandemic.

Lost Time

As explained in NIH's justification for the $10 billion in research losses, the biomedical research system has sustained months of drastic slowdowns and shutdowns. Even though some research activities could be continued remotely (for example, data analysis or writing), most in-person research activities were abruptly halted. As labs reopen, social distancing and other precautions will necessitate rationed, "trickle back" uses of research facilities rather than a full restart. These slowdowns have been accompanied by a number of hard costs. Most personnel have been paid throughout the slowdown, despite a reduced ability to achieve defined goals within funded grants. In addition, some research has a baseline cost whether or not experiments are running. For example, most institutions use a daily charge system for housing research animals; these costs continue to accrue even if animals are not actively being used in experiments. In total, lost productivity and research funds have been substantial and will likely grow as the country navigates the evolving pandemic. Unfortunately, losses are presumably just the beginning; most institutions are bracing for more.

Lost Research Assets and Supply Chain Disruptions

Researchers have reported that key resources, such as animals and cell lines, were lost during extended closures. Resuming research activities will require reestablishing these resources, which will require more money and time. The processes to reestablish animal and cell lines vary but often require rebreeding and aging animals. For example, BrightFocus Foundation, which funds Alzheimer's research, reported that funded investigators lost animals that had been aged to model the brain of an 80-year-old human. Given the time needed for breeding and aging, these experiments will take more than a year to resume.

In addition, researchers have reported difficulties in accessing pharmaceutical compounds, ordering computers, and servicing equipment. Although they are seeking alternative approaches to conduct research, these inefficiencies are wasting valuable time and resources, and generally complicating the business of doing science.

Clinical Research Disruptions

Clinical research has also experienced dramatic losses for two key reasons: Patients have not been able or willing to assume the risk associated with an in-person assessment for clinical trials, and many clinical researchers who were working on testing therapies for other diseases have shifted priorities to focus on COVID trials.

Shutdowns have led to interruptions in non-COVID-related longitudinal studies and life-saving clinical trials, some of which have been running for years. These studies may not restart even after labs reopen because the necessary resources for experiments, such as therapeutic agents, are difficult to obtain, and participants, especially those who are at high risk for COVID-19, will likely remain reluctant to expose themselves to unnecessary risk. These disruptions may be temporary, but the timeline for restarting non-COVID clinical studies remains unclear.

Finally, nonprofit organizations have expressed concerns that the US Food and Drug Administration (FDA) may introduce new delays in the review of non-COVID therapies and medical products. Although FDA has not signaled this intent, pre-COVID reports revealed chronic understaffing at FDA. The need to focus resources on the pandemic may lengthen review timelines, which would slow the access of new therapeutics for a wide array of diseases.

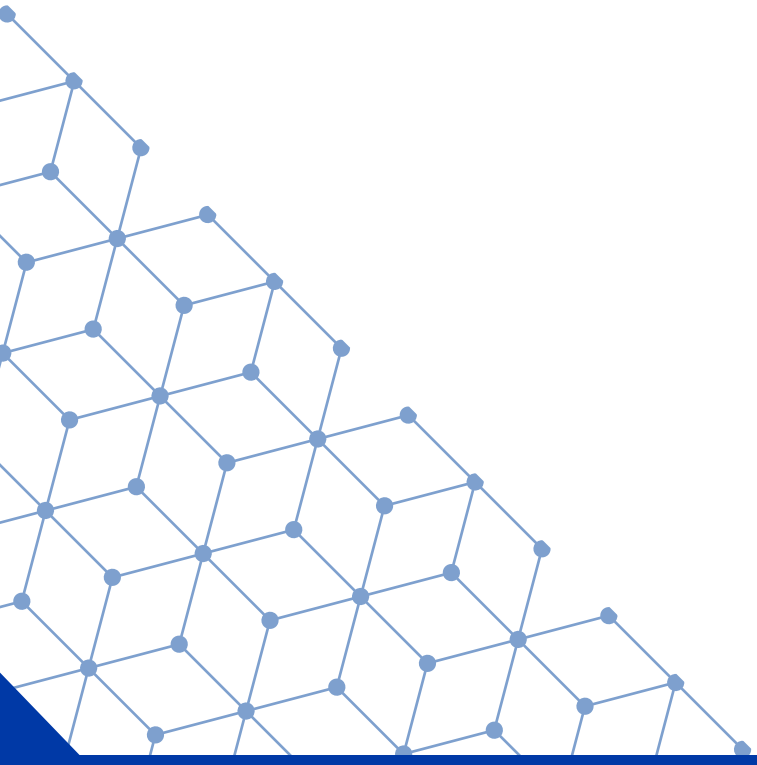
High Restart Costs and Prolonged Inefficiencies

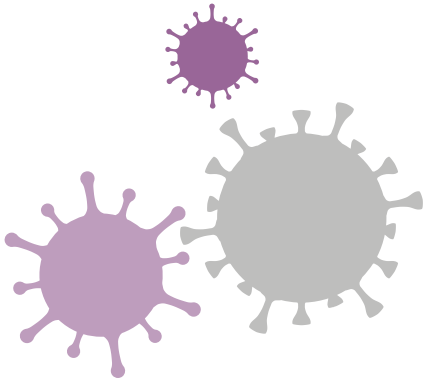
The reopening of labs is revealing the near-term costs of returning to bench research. For example, researchers will need personal protective equipment (PPE), such as gloves, masks, gowns, and face shields, which are in high demand in clinical settings and, therefore, more expensive. One professor at a state university told us in an interview for this report that decisions to continue undergraduate research lab closures into the fall semester are being made simply because of the inability to obtain PPE.

While needed to ensure researcher safety, new infrastructure and procedures, such as plastic partitions and enhanced cleaning protocols, add to the costs and time to conduct scientific research. Further, to comply with social distancing requirements, labs are operating at greatly reduced capacity by splitting or staggering researchers' schedules.

Scientific research is a highly collaborative process that relies on shared equipment and resources, and the lack of in-person interaction is limiting productivity.

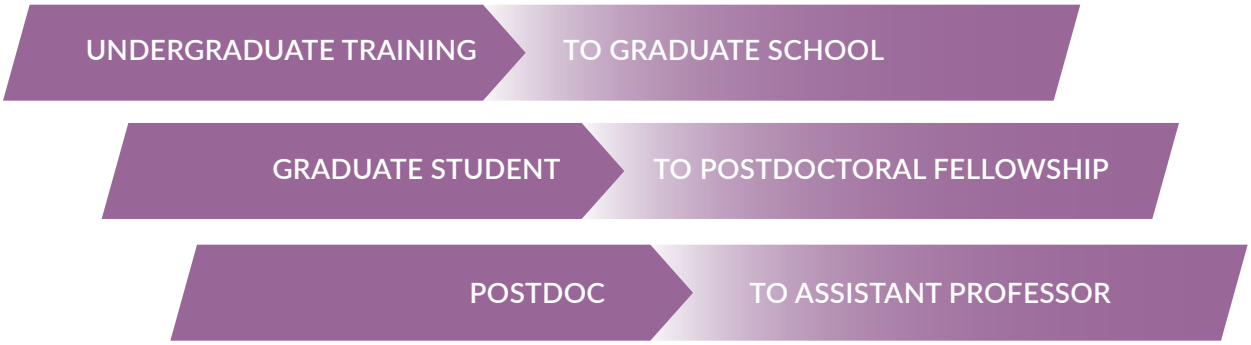
For example, a lab may need to purchase multiple software licenses to analyze data because team members cannot share a common computer in the lab. Further, the ability to learn new methods and procedures has been curtailed because the training process requires close contact and shared equipment. Research teams are developing creative solutions to these problems, such as the use of video conferencing software or head-mounted GoPro cameras to film or live-stream procedures and thus instruct lab members virtually. While ingenious, these virtual solutions impact constrained budgets and are inefficient, which further reduces researchers' productivity.





WORKFORCE CRISIS

Several transitions mark progression through the US academic research system:



These transitions are notoriously difficult even during periods of strong funding, but they have become more challenging during the past decade—the National Science Foundation reports that just 23 percent of biomedical PhDs are becoming tenure track faculty at universities. The pandemic has made it even more difficult for individuals to reach critical career milestones on the track to tenure. Further, the typical metrics used to evaluate researchers' productivity and the quality of their research for grantmaking and tenure decisions are heavily biased by age and research group size, giving well-resourced senior researchers a significant advantage and further entrenching systemic inequities. During interviews with the research community and funders, we heard that these pre-existing systems are stressed, and the additional pressures of COVID-19 may cause young and disadvantaged researchers to depart the experimental research field in unprecedented numbers.

Trainee Workforce

Scientists are considered "trainees" in academic research from their entrance into formal educational programs (generally graduate school) until their appointment to an independent faculty position or departure from the academic system. This progression enables scientists to develop skills and demonstrate their contributions to science, which facilitates movement to the next position.

University administrators reported that they have assured graduate students that their positions are secure. Nonetheless, graduate students in biomedical research, a field with a heavy emphasis on in-person mentorship, are navigating new remote learning environments for both scientific content and laboratory techniques.

Postdoctoral fellowships are the bridge from graduate studies to a junior faculty position, and senior graduate students who seek these positions are experiencing a different type of challenge. Such students reported that institutions have slowed hiring because they cannot guarantee

financial security for the new hires. The challenge is even greater for international students, who must obtain or renew work visas under the specter of the recent executive order that bans visas that allow people from other countries to work and study in the United States. As of 2015, the last year for which data exist, 55 percent of postdocs in the United States were temporary visa holders, and further immigration restrictions place this large research community in jeopardy. Broadly, the scientific community's concern that postdoctoral fellows will struggle to initiate and retain fellowships is growing.

Unstable Transitions

Postdoctoral fellows hoping to transition to permanent faculty positions are experiencing delayed or rescinded job offers as universities and medical centers navigate dramatic budget shortfalls. These losses are devastating to early-career investigators and initiate a domino effect. When trainees cannot transition out of the lab as planned, the lab faces financial strain because it may not have budgeted for that sustained salary support. Further, the lab may be precluded from bringing on new postdocs because their predecessors cannot leave.

NIH developed the K99 award to support the transition of postdocs to junior faculty. It has identified the temporary extension of K99 career development awards as a strategic, targeted mechanism to help postdoctoral fellows during the pandemic. However, relatively few trainees are funded directly through these mechanisms. Most are funded through traditional research grants awarded to the lab's principal investigator. As of 2016, just over 5 percent of K99 award applicants were funded, equating to less than 1 percent of the postdoctoral population. The loss of independent research opportunities in academia, however temporary, could push early-career scientists out of the lab, leading to the loss of a generation of academic researchers.

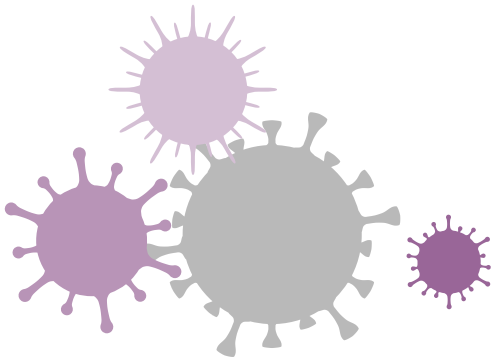
Scientists who have recently reopened their labs and were planning to apply for external funding can no longer perform the experiments necessary for a competitive application. The initial reaction to this concern may be that all faculty across the biomedical research enterprise are experiencing the same challenge; however, junior faculty generally operate their laboratories with start-up funds from the departments they joined. These start-up funds allow for early build-out of a research team and equipment able to collect sufficient data to compete for NIH funding. Although research institutions appear to be adjusting tenure timelines, they have not been able to recharge the institutional funds that allow a new faculty member to establish a new lab.

Exacerbation of Inequitable Circumstances

Like many other workers around the world, researchers with children have to provide child care while performing research activities, affecting their ability to be as productive as their colleagues who do not have caregiving demands.

Researchers who cannot write papers or grant applications while working remotely will fall behind their peers who have fewer competing demands.

These inequities could be exacerbated by institutions and funding agencies that continue to use traditional metrics such as publications to make funding decisions. In fact, *Nature Magazine* recently reported a decrease in publications from women and decreased participation in COVID-19-relevant submissions. To cite a close-to-home example, in a small number of programs managed by the Center for Strategic Philanthropy, we found that some parents could not meet grant deadlines, which effectively reduces participation in future research from this critical demographic.



TROUBLE IN THE NONPROFIT SECTOR

GuideStar estimates that nearly 20,000 nonprofit organizations are disease-focused, and many of them play a pivotal role in facilitating biomedical research that has a direct impact on patients. Nonprofit organizations are valuable for their ability to attract private funding to a scientific field and flexibly direct funding to specific research areas. For example, some organizations support particular initiatives to drive early-phase research to generate preliminary data, launch young investigators' careers, or diversify therapeutic pipelines. Many nonprofits employ and engage scientists on their management teams to ensure that funding drives meaningful and rigorous research forward.

Nonprofits also provide infrastructure for rare diseases that receive limited funding from the public sector. For example, the Barth Syndrome Foundation hosts an annual meeting that brings together researchers and patient families. During this meeting, these participants discuss scientific developments and make connections to facilitate sample collection as a means to accelerate research progress. The 2020 meeting has been canceled, which will prevent these important connections from occurring and, therefore, will slow sample collection.

Decreases in Fundraising

Revenue loss is already affecting the internal staffing and external functioning (e.g., grant making and conference development) of biomedical-focused nonprofits. The budgets of these nonprofits depend on a variety of funding sources, including events, direct-mail advertisements, and large-donor philanthropy. Those that have relied on events such as galas, sponsored walks, and annual meetings are experiencing record drops in revenue. In addition, instability in the financial markets makes large donors skittish, which has impacted the operations of larger programs that rely on them. Because the health crisis affects individual donors and funding streams differently, nonprofit leaders expect that some organizations may not survive the economic downturn caused by the pandemic.

Lost Expert Workforce

At foundations, program staff are often the heart of the organization, managing relationships across sectors and offering invaluable institutional knowledge of the field and research community. The foundation teams interviewed for this report indicate that they are prioritizing funding to ensure that researchers can perform their experiments. However, this prioritization has led to furloughs of program staff, with the expectation of deeper cuts, leading to an irreplaceable loss of expertise and experience.

Lost Flexibility in Supporting Research

As fundraising gaps grow, many organizations expect to cut back on research funding. These cuts will equate to lost preliminary data for new disease-focused research studies, and perhaps more importantly, will prevent nonprofits from working with scientific communities to navigate solutions to the direct COVID setbacks as well as the expanding scientific workforce crisis.

PHILANTHROPISTS' GUIDE TO SUPPORTING BIOMEDICAL RESEARCH IN A PANDEMIC

One small but important silver lining to the current crisis is that the world has become acutely aware of the grave importance of a biomedical research system that spans drug and test development, epidemiology, clinical trials, and vaccine development. Biomedical research leads to discoveries, which in turn lead to societal and economic benefits through invention and innovation. Philanthropists can play a pivotal role in moving the biomedical research system toward meaningful therapies for 10,000 known diseases.

Funders of scientific research should focus on several broad areas. A small but dedicated cohort already focuses on biomedical research, but the field must recruit new funders. There has never been a more crucial time.

OPPORTUNITIES FOR BIOMEDICAL PHILANTHROPY

Work with scientists to identify COVID-related shortfalls and increase budgets

Focus on human talent

Reevaluate what it means to be "productive" in the context of the pandemic

Strengthen the biomedical nonprofit sector

Targeted Budget Increases for Lost Resources

Biomedical research funders already engaged with a research community are well-positioned to work with scientists to identify the specific shortfalls caused by the pandemic. We have heard from foundations that they are helping researchers address these problems by encouraging no-cost extensions or modifications within existing budgets. Still, it is more likely that researchers will need supplemental awards to fill these gaps adequately. We recommend working with research teams to modify budgets to account for increased personnel time, additional materials, and rebuilding of critical resources. In conversations with funders, we often heard that providing extra support to current investigators is equivalent to "robbing Peter to pay Paul." In other words, nonprofit funders must use funding that was earmarked for future research to help those who need it now. To solve this, funders must take time to assess what researchers need to achieve results in experiments that were in progress but now are at risk.

Otherwise, inefficiency will impact progress for years to come as failed projects are repeated, or potentially worse, promising directions are assumed failed and dropped. These activities may require budget supplements, but they will ensure that the research supported by these foundations is sustainable.

Experiments must not be classified as "failures" because the research was not completed—rather, research must be completed so that conclusions can be deduced, even if completion comes at additional expense.

New Funding Opportunities Focused on Good People

Many funders recognize that good science happens when great scientists have time and space to explore and test ideas. In fact, Howard Hughes Medical Institute famously uses a "people, not projects" philosophy when making funding decisions. In a moment of high global uncertainty, funders should remain engaged to ensure that talented scientists can pursue research. Funders should look to policy and programmatic changes in the near- and mid-term to support trainees and early-career scientists, or those who are otherwise at risk of leaving the field.

Granting Policy and Practice Levers

Many policy and practice levers can be pulled to support good scientists. For example, timelines for funding eligibility of grant programs that target young and transitioning scientists, which are typically capped, can be extended in upcoming years to provide greater flexibility to individuals who experience career delays due to university closures or rescinded job offers.

Similarly, in future funding cycles, funders can screen for extenuating circumstances imposed by COVID-19, and scale requirements and expectations to ensure a level playing field. Although the specific conditions leading to reduced productivity will vary across individual circumstances, geographies, and research types, many researchers will likely be affected.

Finally, the metrics used to determine productivity should be modified in light of these evolving and unprecedented circumstances. Standard publication-based metrics are known to be biased to benefit well-resourced senior investigators; this bias, in turn, drives an increased concentration of scientific resources. Rather, funders should assess potential impact via their peer-review process and should make funding decisions to build a portfolio that spans a range of hypotheses and methodologies.

Targeted Funding Programs

In addition to addressing human capital stressors through policy, funders can reconsider their programmatic activities to strengthen the pool and diversity of investigators further. Recent data reveal that women and underrepresented minorities in academia already show significant attrition

throughout the stages of academic career-building, and the additional strain of COVID-19 could intensify this troubling trend.

Funders may not believe they have an immediate role to play in combatting inequities furthered by caregiving demands or differential abilities to accelerate research during a crisis. However, the myriad of institutions supporting science must track and counter these issues to ensure that diverse perspectives remain and have a place within the scientific ecosystem.

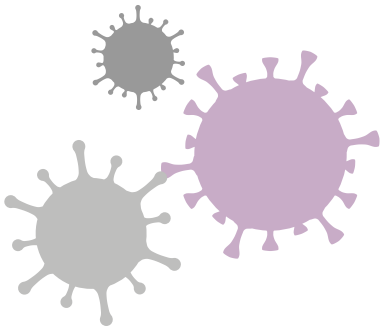
Funders can use specific initiatives to increase diversity in scientific research. Recent studies have found that diverse participation in research breeds innovation and improves therapy development; therefore, greater emphasis on the workforce in any issue area will have a lasting impact on a field's potential for innovation.

Strengthen the Nonprofit Sector

Philanthropists steeped in biomedical investment, as well as those just beginning their journey, can look to the nonprofit community as a key partner in keeping the focus on disease-specific funding during and beyond the pandemic. We recommend working with nonprofit partners to ensure that critical resources are sustained in the short term and that immediate and mid-term research funding can shift to address the specific needs arising in the relevant research field.

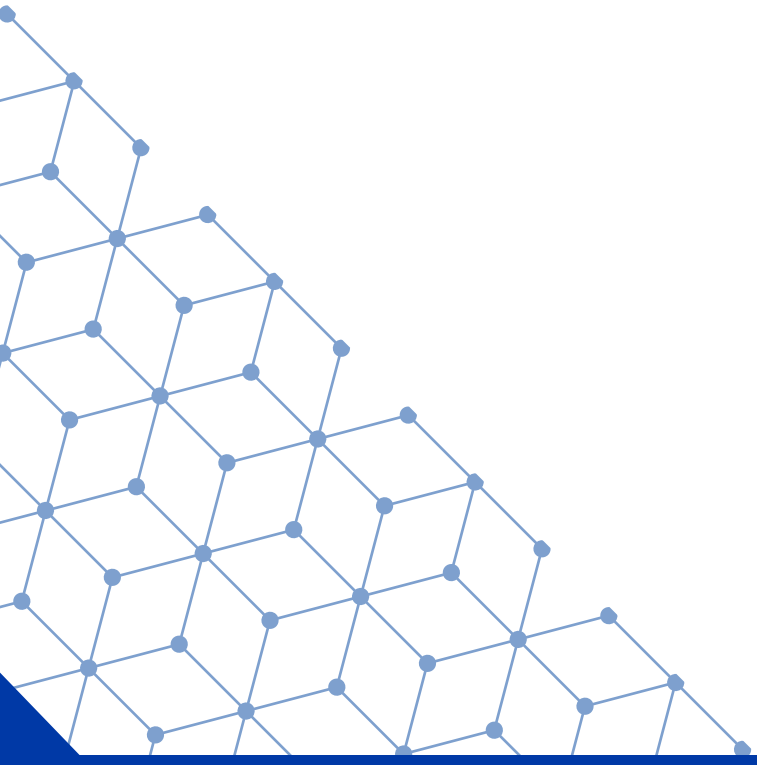
In addition, funding for organizational overhead allows nonprofits to keep critical programmatic and administrative staff in place. These individuals are often at the heart of the organization, providing invaluable institutional knowledge of the research community.

Increased funding for research and for overhead expenses will allow nonprofit organizations to deliver help where it is most needed, whether through supplement awards, "people, not project" approaches, or new awards so that they can ultimately lead to positive change for the research communities that they shepherd.



A CALL TO ACTION FOR THE PHILANTHROPIC COMMUNITY

The biomedical research system drives innovation to allow people to live healthy, meaningful lives. While COVID-19 has affected nearly every industry, its impact on biomedical science could have devastating effects on human health for decades to come as key research is interrupted and scientists leave the field to seek more stable careers. Philanthropic capital is a lever that leads to better treatments and cures in many biomedical research areas. Donors wanting to leave a lasting, positive effect on science, and indeed on the world, have provided risk capital to test new scientific hypotheses, fill gaps in the translational "valley of death," and invest in scientists, the very people whose knowledge advances progress. Today, biomedical research needs philanthropy to redouble these efforts in partnership with research communities and the nonprofits that serve them. Philanthropists are poised to lead—turning innovative research into treatments and cures that make a difference in patients' lives—even during a global situation that has placed years of hard-earned progress at risk.



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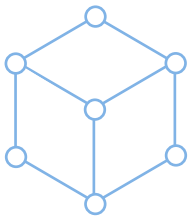
With more than a decade of experience in neuroscience research, including neurological devices, psychiatric illness, learning, and memory, as well as sleep and circadian rhythms, Altimus has led Center projects ranging from the development of a philanthropic drug development program for neurodegenerative disease to a large patient-perspectives study for depression and bipolar research.

Prior to joining the Institute, Altimus worked at the Food and Drug Administration, leading the Neural Interfaces Laboratory, which evaluates the safety and effectiveness of electrical stimulation methods in the brain. In addition to her research experience, she serves as the chair for the Trainee Advisory Committee for the Society for Neuroscience, is an advisor to the Ontario Brain Institute, and spent a year as an AAAS Science and Technology Policy Fellow developing a neuroscience research portfolio at the Department of Justice. Altimus holds a bachelor's degree in genetics from the University of Georgia and a doctorate in biology from Johns Hopkins University. She works at the Institute's Washington, DC, office.

Quinton Banks is an associate at the Milken Institute Center for Strategic Philanthropy. His extensive scientific background includes research into chronic pain, taste perception, and muscle physiology. Banks has training in biological sciences and psychology, providing him with a unique perspective on the human impact of high-net-worth giving. His work revolves around analyzing biomedical research fields and working with philanthropists to help identify where and how their resources can best be utilized to further the goals of health sciences and advance the well-being of our society. Banks received his bachelors' degree from Grinnell College, and his doctorate from the University of Maryland School of Medicine. He works at the Institute's Washington, DC, office.

Sylvie Raver is an associate director at the Milken Institute Center for Strategic Philanthropy. She applies her expertise in neuroscience, mental health, biomedical research, and higher education to identify opportunities where philanthropic investments can have a transformative impact on medical research and health. In her role, Raver provides analysis and advice to individual philanthropists, families, and foundations and implements strategies to deploy philanthropic capital to advance research and health priorities. Previously, Raver worked for the Society for Neuroscience and led the Society's global programming and policy efforts around neuroscience training for individual scientists and members engaged in biomedical workforce education and training. Raver received her bachelor's degree from Lafayette College, her doctorate from the University of Maryland School of Medicine, and conducted her postdoctoral training at the National Institute on Aging. She works at the Institute's Washington, DC, office.



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