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Building Community-Based Infrastructure for Inclusive Research:

Lessons from the Pandemic for Federal Action

Introduction: An Ecosystem of Excellence, Not Islands of Pilots

COVID-19 has focused the public's attention on the racial and ethnic disparities in health outcomes, unequal access to health care, and some communities' lack of trust and participation in medical research. These problems have been decades, if not centuries, in the making, and they cannot be quickly or easily solved. However, attention is a critical prerequisite to action, and FasterCures believes that we must seize this moment to make real change, particularly to transform the way that local institutions conduct clinical research so that it is representative of the diverse communities comprising the American population.

Examples certainly exist of clinical research networks that have succeeded in increasing the engagement and participation of underserved communities. Many local health-care institutions, however, lack the resources and infrastructure to engage in research, resulting in less robust trials for sponsors, lower access to innovation, and poorer outcomes across communities. COVID-19 revealed in stark terms the price to be paid for the lack of a comprehensive community-based research system that can generate evidence to answer a broad range of critical research questions, whether in the context of sponsor-driven product development trials, comparative effectiveness studies, or a fast-moving public health emergency (PHE).

Ideally, such a nationwide system would find participants in all the places they live and access their care, not just the large academic medical centers where much clinical research is currently conducted. Yet, who should be responsible for creating and maintaining such a system? What steps can the federal government take to build capacity at the local level—to create an "ecosystem of excellence" rather than "islands of pilots"?

Building on findings from FasterCures' "Lessons Learned from COVID-19: Are There Silver Linings for Biomedical Innovation?" report and a virtual leadership roundtable held in September 2021, this issue brief:

- Highlights best practices from organizations that are leading the way in community-based clinical research;
- Identifies common infrastructure gaps that exist at the community level and how we can build engaged, interoperable health systems in research moving forward; and
- Pinpoints national policies and resources needed to strengthen critical infrastructure at the community level to empower local institutions to participate in clinical research.

Case Studies: Leaders in Engaging Community Research Sites

Although the interest in addressing inequities in health care and health-care research has risen dramatically during the past two years, many individuals and organizations have been leaders in engaging more diverse and representative populations in research for many years—several coming to the fore during the pandemic in remarkable ways. Below we describe some of these organizations and the lessons they offer for future federal focus in these areas.

CASE STUDY

National Institutes of Health's Community Engagement Alliance (CEAL) and COVID-19 Prevention Network's (CoVPN) Clinical Trials: Leveraging Existing Investments to Engage Communities during COVID-19

When the COVID-19 pandemic hit, the National Institutes of Health (NIH) drew on existing investments and programs that connect physicians and researchers with community members to drive more effective and inclusive medical research. To engage the communities most impacted by the pandemic, CEAL leveraged the relationships cultivated and lessons learned from the *All of Us* Research Program, and CoVPN is built on the foundation of the HIV Trial networks that have a long and deep history of engaging local communities.

To date, CEAL includes 21 teams across the country that address misinformation around COVID-19, build and maintain community trust in science, and promote diverse participation in biomedical research. Across different mediums of digital and traditional channels, CEAL communications have realized more than 2 billion cumulative views. CEAL has also led to reductions in vaccine hesitancy, improvements in vaccination uptake, and increased participation of racial and ethnic minority populations in COVID-19 clinical trials in its catchment areas.

CoVPN aimed to enroll volunteers for Phase 3 clinical trials for COVID-19 medical countermeasures, with a focus on priority populations—including people with underlying medical conditions, people with greater chances of exposure at their jobs, and people from racial and ethnic groups that were disproportionately impacted by the pandemic. CoVPN also focused on building a foundation of knowledge among these groups to ensure uptake and acceptability of vaccines that would eventually be approved for COVID-19. The effort was ultimately successful, with 47 percent of participants recruited at CoVPN clinical research sites identifying as either Black, Indigenous, or a person of color (BIPOC), which is far more representative of the American population than most trials. CoVPN has also succeeded in improving the

process of designing, implementing, and analyzing vaccine trials; streamlining protocol development while maintaining input from diverse stakeholders; and setting new statistical standards for the field.

The key lesson learned from both initiatives is that consistent and continuous engagement with community members—not only those within the medical community but also faith leaders, local government leaders, representatives of community-based organizations, and other local influencers—fosters trust and shared goals. However, this trust must extend in all directions, and federal agencies must create efficient infrastructure (e.g., for payment and reimbursement) so that community partners will work alongside them. Ultimately, the hope is that this trust and engagement will be underpinned by clinical trials that have been carefully crafted and executed with local needs, concerns, and contexts in mind.

CASE STUDY

The Veterans Affairs Research Enterprise: A Ready-Made Community-Based Infrastructure

For decades, the Department of Veterans Affairs (VA) has been dedicated to health discovery and innovation with the mission of (1) increasing access to high-quality clinical trials; (2) increasing the real-world impact of VA-led research; (3) putting data to work for patients; (4) actively promoting diversity, equity, and inclusion; and (5) building community through VA research. The VA maintains 103 active research sites, and its research ecosystem and patient base are vast and diverse, making it an important asset to national biomedical research efforts. By one estimate, from 2019 to 2045, the projected proportion of veterans who are non-Hispanic Whites will decrease from 74 percent to 61 percent, emulating demographic changes in the broader US population. The VA ecosystem can serve as a potential model for stronger, more resilient research systems with both national and local reach, during both peacetime and times of crisis.

In response to the COVID-19 pandemic, the VA conducted a wide array of activities spanning biomedical research, therapeutics and vaccine trials, and data analyses that leveraged its rich electronic health record system. Throughout this process, the VA coordinated closely with internal and external partners, including the NIH and other federal agencies and pharmaceutical companies, to identify the localities and communities in which its research contributions could make the most impact.

A key learning for VA officials has been that VA research is best approached as an enterprise instead of fragmented. Vaccine and therapeutics trials ran more smoothly when there was a single point of contact within the VA versus when clinical research organizations and trial sponsors interacted directly with individual trial sites. A major challenge during the pandemic has been putting interagency agreements (IAA) in place rapidly, even in the midst of a crisis. (VA's IAA with the Biomedical Advanced Research and Development Authority was only executed in October 2021, more than 18 months into the PHE). Another challenge in working with partners outside the VA has been the lack of standardized data platforms and software tools used by public and private research sponsors. Finally, the VA was initially not allocated any federal resources directly for COVID-19 research until it linked up with the CoVPN network. The VA is an important national, community-based research infrastructure that should not be left on the sidelines.

CASE STUDY

Clinical Directors Network: The Power of Practice-Based Research Networks

Frequently invoked as potential community research partners are the Federally Qualified Health Centers (FQHCs), which are funded and administered by the US Department of Health and Human Services' (HHS) Health Resources and Services Administration (HRSA) and reach diverse communities across the country. Although the FQHCs' primary mission is care delivery, they have been involved in recruiting participants for NIH's *All of Us* Research Program, and they are key components of "practice-based research networks" (PBRNs) such as the Clinical Directors Network (CDN).

The Agency for Healthcare Research and Quality (AHRQ), also housed within HHS, defines PBRNs as "groups of primary care clinicians and practices working together to answer community-based health care questions and translate research findings into practice." CDN is a PBRN composed of informal networks of clinical leaders that practice as primary care providers in low-income and minority communities. They aim to translate clinical research into clinical practice to eliminate health disparities. CDN has enrolled almost 400,000 low-income, minority, medically underserved patients in clinical trials and observational studies. CDN is also an AHRQ-designated Center of Excellence (P30) for practice-based research and learning.

CDN has proven through its work that there is usually a standardized set of determining factors for trial success in this context. These factors include whether trials and other studies are well-aligned with the workflow and can be implemented with the current workforce; whether the trial is designed for delivery; whether there is a baseline level of trust in the organizations and individuals involved; and whether there has been multi-level, systems-thinking and design efforts incorporated into the trial. Addressing these factors will optimize the chances of trial success and sustainability, which is critical when trying to institutionalize and strengthen the clinical trials ecosystem at the community level. To take these best practices forward, CDN has collaborated with clinicians and research teams to build out training programs to help practicing clinicians gain proficiency in practice-based research methods and help academic investigators work with community-based clinicians.

CDN represents an important model for effective community-based research practices. CDN has identified several recommendations for improvements to community-based research infrastructure. These include (1) integrating global and local data streams with big data and artificial intelligence to identify patterns of disease in communities; (2) building a more diverse—and flexible—clinical trials workforce that includes practicing clinicians and staff, as well as patients; (3) increasing investment and efforts to embed research in care-based settings to enable the ongoing conduct of research and implementation of research findings back into those communities; and (4) increasing the use of registry-based and electronic health records-based trials.

CASE STUDY

The Role of Decentralized Trials and Remote Tools in Addressing Disparities

Since the pandemic began, decentralized trials—that is, trials in which activities are brought to patients, often through personal technology and strong community-based research infrastructure, rather than bringing patients to a trial site—have taken off. This offers significant promise to accelerate clinical development, enable more diversity in trials, advance patient-centric approaches that were otherwise impossible in traditional clinical trials, and improve care access.

Decentralized trials are not only here to stay but also likely to be formally regulated, based on a provision in the Cures 2.0 Act currently sitting with Congress. Regulation is especially important because, during the COVID-19 pandemic, patient access to clinical trial sites was reduced by 80 percent to prevent the spread of the virus, raising major concern of a similar situation during a future public health crisis. Apart from their usefulness during the pandemic, decentralized trials will likely become a mainstay because they enable researchers to meet patients where they are. Currently, about 70 percent of potential trial participants live more than two hours away from a trial site, and decentralization offers much broader reach.

However, care must be taken to ensure that efforts to advance the use of decentralized trials and remote tools do not further disenfranchise already underserved communities. The future must consist of remote tools and technologies that are fit for purpose in trials, creating more flexibility to meet the needs of patients in hybrid models that may include on-site components. Although this movement presents an opportunity to engage more patients than has been possible in the traditional model, we must be intentional to not inadvertently freeze out patients and providers who lack the technology required to participate. Building tools and systems *with* and *for* these communities will be critical.

The National Role and Interest in Supporting More Inclusive Research

As demonstrated by several of the cases described above, aspects of COVID-19 research and product development were expedited by clinical research infrastructure, funding, and partnerships built over years, as well as flexibilities introduced in response to the pandemic that should remain in place.

Among the elements that increased engagement of diverse sites and patients were the following:

- Identification of existing government-funded research infrastructure and community-engaged researchers to participate in initiatives such as CEAL and CoVPN,
- Federal action by agencies, including the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS), to enable and encourage the use of more decentralized and remote methods and tools to conduct trials during the pandemic (many of which will explicitly be terminated at the end of the PHE),

- Federal leadership in directing sponsors of COVID-19 vaccine trials to achieve greater diversity in the study population, and
- Leveraging an arm of the RADx program to accelerate innovation in COVID-19 diagnostics to focus specifically on understanding and addressing the needs of underserved populations.

The pandemic also revealed significant gaps in our clinical research ecosystem that must be addressed to bring research within reach of more communities nationwide. Janet Woodcock, former FDA acting commissioner, has repeatedly highlighted lessons that must be learned from the pandemic experience about the shortcomings in the clinical development of therapeutics (as distinct from vaccines). In an analysis conducted by Woodcock and colleague Kevin Bugin, during the first nine months of the pandemic, of the more than 2,500 COVID-19 trial arms launched with plans to enroll more than half a million participants, only five percent were randomized and adequately powered and therefore could be considered to have generated actionable evidence. Woodcock believes that this problem is not limited to COVID-19 therapeutic development; rather, it exists across the biomedical innovation ecosystem.

One reason for trials falling short of expectations is the ecosystem's inability to run trials close to communities in order to rapidly and efficiently engage large and diverse groups of patients in clinical research. Although the COVID-19 vaccine trials did boost minority enrollment expeditiously, this outcome is not representative of most therapeutics trials.

Among the lessons Woodcock and others have taken from this experience are the following:

- Inadequately designed and powered trials waste time, resources, and patients—the most critical resource.
- Activating trial networks and partnerships during a PHE is difficult.
- Many established academic and commercial trial networks lack outreach into diverse communities.
- The ecosystem must have a broader, more diverse network of clinical research sites in place before the next PHE; however, sites must be resourced and engaged in other research opportunities (preferably ones that matter to those communities) for training and sustainability between PHEs.
- A governing body must be created that secures funding for and prioritizes such research and the training needed to conduct it.

In Woodcock's view, infrastructure for more community-based research offers many benefits:

- It creates opportunities to study conditions that disproportionately impact underserved communities.
- It enables trial results to reflect outcomes in populations that will use medical products after approval.
- It enhances diversity among trial staff, investigators, and key opinion leaders.
- It increases trial efficiency, brings a focus on real-world evidence, and gives affected communities the ability to shape and prioritize clinical trials.

Common Infrastructure Gaps

The medical research ecosystem's ability to meet potential research participants where they are—whether at an academic research hospital, a community health center, a local pharmacy, or at home—is limited by a wide range of factors, including:

- **Administrative and regulatory burdens on sites and investigators are cumbersome.** Contracting, Institutional Review Board (IRB) processes, consent requirements, and more are complicated and time-consuming and not fit-for-purpose to enable rapid site activation and efficient trial conduct. Even experienced government research entities such as the VA faced slow execution of interagency agreements, despite the existence of a PHE. Further complicating factors are differing state and institutional requirements for research conduct and administration.

- **Information technology/data systems are not available and/or interoperable.** Sponsors and contract research organizations do not use a consistent set of software tools. Federal agency requirements for data collection are not aligned. Trials are not regularly embedded in electronic health record systems or routine care workflow.
- **The clinical research workforce itself is not diverse.** The people powering clinical research are themselves not racially/ethnically diverse, including investigators, clinicians, research staff, and nurses. Health-care providers who are not full-time academics also often do not have the tools or capacity to engage in research studies—constraining our ability not only to conduct research in more places but also to gain insights from clinicians on the ground in these communities.
- **Financial and other resources are not widely available for training and conduct of research studies.** Even if training is available or dedicated research staff are in place, meaningful and appropriate research studies must be deployed to build and sustain research skills and provide incentives for maintaining research capacity.

Federal Priorities

- **Leadership.** The ability to deploy clinical trials more broadly, rapidly, and efficiently is an important national priority—for reasons of pandemic preparedness, more equitable access to the benefits of research, and more effective clinical research across the board. Accordingly, one authority at the federal level should set priorities and direct funding and collaborations—whether an existing entity within HHS or a new one.

  The US Congress is a key player and should be educated about the importance of supporting more community-based research infrastructure—and, in fact, could help drive needed change.

  - ***Coordination of government-funded networks and sites.*** As we have seen, the federal government already supports a number of trial networks and sites across a variety of federal agencies that have actual or potential reach into diverse communities and populations. In addition to NIH, other agencies fund networks including the Department of Defense, the Veterans Health Administration (including its Million Veterans Program), HRSA's Health Center Program (which is already supporting NIH's *All of Us* Research initiative), and the CMS Minority Research Grant Program (which develops capacity at minority-serving institutions to do research).

    A better view across and coordination of this existing infrastructure is needed and could be realized now through a federated approach that could also link to other private health-care systems and networks.

    During the pandemic, NIH created a Clinical Trial Capacity Inventory and geotracking tool to enable more rapid and efficient deployment of COVID-related clinical trials. As a first step, this inventory should be maintained and expanded to include other government-funded health systems such as those of Veterans Affairs, the Department of Defense, and the FQHCs, along with other resources such as the Agency for Healthcare Research and Quality's registry of Practice-Based Research Networks.

  - ***Alignment of federal requirements.*** There must be an effort to align NIH, FDA, CMS, HRSA, and other US government data definitions and data collection tools so that there is one common approach. The current lack of alignment leads to differing expectations, difficult reporting, and challenging data aggregation and interoperability for many sites.

- ***Priority-setting.*** A national authority should seek to identify the most useful networks, policies, and resources activated during the PHE and enable their deployment against select public health priorities without the need to declare a formal emergency. A cross-agency working group should be convened—guided by representatives of diverse communities and researchers—to develop and execute a plan to train and keep community-based research sites engaged. Research prioritization can also be informed by more and better data monitoring and advanced analytics to identify patterns of disease in communities.

  What else might be deemed a PHE—cancer, opioids, suicide? Can we deploy existing resources and infrastructure to solve these problems in the way we did with the COVID-19 pandemic? Congress should ensure that agencies are directing funding toward such research priorities.

- ***Funding.*** Adequate and predictable funding must be available to support high-priority research studies deployed in community-based sites and networks to help build and sustain capacity for such work. Community practitioners face enormous time and financial pressures and must be compensated for participating in studies and discussing them with their patients. During the pandemic, Medicare provided (in addition to coverage of routine costs in approved trials) small payment bonuses to providers who participated in COVID trials through its quality incentive payments program. Such incentives should continue outside the context of the PHE, strengthening the linkage between clinical research and care quality improvement.

- **Modernizing regulation and use of technology to engage more patients.** Decentralized trials and remote tools reveal pathways for remote principal investigators to pair with community physicians to unlock the scale of and access to research opportunities. However, definitions of "sites" and "investigators" must be updated to reflect the current realities of technology-enabled trials and the importance of more inclusive research engagement.

  For example, to engage retail pharmacies, local imaging and diagnostics labs, and mobile nurses, we must clarify and modernize regulations, such as FDA's Form 1572, which governs the definition and responsibilities of investigators in investigational trials to reflect new research roles and locations.

  The widespread use of decentralized trials and remote tools during the pandemic relied significantly on flexibilities put in place temporarily in response to the PHE; specific actions will be required to preserve progress in the use of these tools, whether for care or research.

  Any research utilizing digital tools must ensure equitable access to the tools themselves and the broadband infrastructure needed to support them; all research involving any digital tool must provide support to provision and train participants and researchers to use them.

- **Building trust.** Trust is foundational to any infrastructure, whether a trial network or a skyscraper or a bridge. Much has been said about the need to build trust of research among individuals and communities that have suffered from discrimination and neglect. Trusted and trusting relationships are also critical at the level of community partners and practitioners. Trust is built through sustained consultation, support, and a commitment to communicating and implementing the results of research at the community level so that everyone may benefit.

Conclusion: Not New Challenges, But a New Moment

The legacy of mistrust of research within minority communities and the challenges to engaging more diverse participants in trials is decades-old and not easily addressed by policy changes alone. Despite an NIH mandate in 1993 to increase the inclusion of more racial and minority participants in federally funded research, little progress has been made.

This new moment of broad societal focus on diversity, equity, and inclusion in all aspects of American life has brought a surge of attention and resources to make good on that 20-year-old promise. Pilots, collaborations, and infrastructures are being created to show what can be done, although often without incorporating the lessons learned by researchers who have come before, or with an eye toward scaling and sustaining infrastructure that achieves the greatest impact and longevity. Commitment to the funding and other resources necessary to build that infrastructure and collaborations is needed from all entities comprising the clinical trials ecosystem, including federal agencies and the private sector, among others.

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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 FasterCures

FasterCures, a center of the Milken Institute, is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.

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