

# COVID-19 and the Clinical Research Profession

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WHITE PAPER

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ACRP<sup>+</sup>



# INTRODUCTION

Much has already been written about the impact of COVID-19 on the clinical research landscape. In both academic journals and industry publications, numerous analyses have focused not only on the global effort to develop COVID-19 vaccines in record time, but also on the paradigm shift required to continue conducting routine clinical research in the midst of a pandemic. Alongside the urgent need for COVID-19-specific trials was an equally significant need to keep the wheels of clinical research turning in hundreds of other medical fields. **However, within this growing body of literature, very few authors have considered the impact of the pandemic on the clinical research profession itself.**

The drug discovery scientists who spearheaded the vaccine development mission—and the pharmaceutical industry decision-makers who negotiated with regulators on new imperatives for clinical trial design and operations—are not the only protagonists in this story.

When the pandemic hit, the need for ambitious new research plans to be implemented at speed landed with full force on those at the frontline—the people whose job it is to run and manage clinical trials on a daily basis. Those directly involved in the COVID-19 vaccine trials were all too aware that the entire world was waiting with bated breath for these studies to read out. At the same time, demand for decentralized clinical trials, which don't depend on face-to-face encounters between researchers and participants, skyrocketed, but almost no guidance or ground rules for how best to conduct them existed.

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**This paper spotlights the impact of COVID-19 on clinical research professionals at both an organizational and human level, examining their challenges, their insights, their successes, and the personal price many had to pay in the interests of their vocation.**

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# ACKNOWLEDGEMENTS

ACRP would like to acknowledge the significant contributions to this paper of:



**JENNIFER BYRNE**  
CEO, Javara Inc

"I believe this story is important as it captures several specific examples of teams of people coming together to make bold moves at a time of radical uncertainty, personal risk, and forging solutions to address the public health crisis of a pandemic in the absence of a playbook. No time, in the history of the clinical trials enterprise, has it been so evident that clinical research professionals, like patients, are true and valiant warriors. Additionally, this moment in our history provided much-needed perspective around driving innovation and adoption of new ways to re-imagining clinical trials in the 21st Century."

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**OTIS JOHNSON, PhD, MPA**  
Chief Diversity, Inclusion &  
Sustainability Officer, Clario

"COVID-19 shone a bright light on the serious health inequities that are still rampant in society. It has motivated corporations to use their position of privilege and power to reverse decades of systemic, unhealthy business practices to create irreversible, positive social change. Decentralized trial offerings, which COVID-19 accelerated, are the new clinical trial norm. They are widely recognized as a key medium to enable easier trial access for all, not just those who have traditionally been able to access clinical trials and the therapies that result from them."

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**DR. DAVID MORIN**  
Director of Research,  
Holston Medical Group

"In March 2020, the pandemic presented an existential threat to humanity, potentially affecting the integrity of thousands of clinical trials, and redirected our focus toward developing vaccines and therapeutics. Yet, this moment in history saw rapid changes to adapt and embrace processes that allowed research to continue. In addition, it initiated unprecedented collaboration among the scientific community, regulatory and governmental agencies, and those who stepped forward to volunteer as a participant in clinical trials to provide hope to millions. This paper documents the remarkable story of the fight against COVID and why it affects the future of research."



# CLINICAL TRIALS ON HOLD

March 18, 2020 marked the day the U.S. Food and Drug Administration (FDA) brought clinical research to a near stop in the United States, sending the life science industry into “an existential crisis,” in the words of one industry observer.<sup>1</sup>

Virtually all trials were stalled or put on hold as travel restrictions and governmental requirements for social distancing made it more and more difficult for patients and research teams to meet. Patient recruitment efforts suffered badly, but so did participant retention, data collection, and adherence to trial protocols. According to a Clario survey of 114 clinical research professionals with various roles at sponsors, contract research organizations (CROs), and sites,<sup>2</sup> participant screening/engagement and data capture were the issues of most concern to respondents (Figure 1). However, sites also began to face revenue shortages and loss of staff (due to sick leave, furlough, or co-optation to clinical care teams), while scarcity of personal protective equipment meant that those who continued to work—and those with whom they interacted—were exposed to the risk of infection. A team at the University of Kansas Medical Center produced a very detailed description of the stringent safety measures it implemented in the first wave of the pandemic to protect clinical trial participants and research staff, which was published in the *International Journal of Clinical Trials*.<sup>3</sup>


Near-term, the pandemic was devastatingly disruptive. About 80% of non-COVID-19 trials were either stopped or interrupted. As of January 2021, COVID-19 had

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stopped more than 2,000 clinical trials. A March 2020 article published by Fierce Biotech about a Clinical Research IO survey reported that 63% of responding sites were prohibiting onsite monitoring visits, and 24% of investigators were halting new enrollments due to patient safety concerns.<sup>4</sup> This was around the time



when the pandemic was gaining momentum. People were afraid of visiting healthcare institutions of any type, even for emergencies. As time went on, it also became clear that the pandemic was disproportionately affecting people of color—spotlighting a long-simmering concern about the poor representation of many demographic groups in clinical trials and the critical need for greater participant diversity. This concern is grounded with strong evidence and remains a challenge for our industry. Of the 371 drugs and biologics approved by the FDA between 2007 and 2017, only 37% of the trials supporting those submissions had ethnicity data. The Tufts Center for the Study of Drug Development (CSDD) described this situation as “dangerous.”<sup>5</sup>

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# THE RISE OF DECENTRALIZED CLINICAL TRIALS

For the clinical research world, the pandemic has also had a silver lining. The so-called “COVID-catalyst” has sparked new interest, receptivity, and regulatory acceptance of innovative new practices and technologies, most notably in terms of decentralized trials (DCTs) that enable patients to participate from home.

By utilizing digital technology such as telehealth and remote patient monitoring, DCTs effectively “bring the trial to the patient,” rather than expecting the patient to come to the trial.

This approach didn’t just provide a solution to conducting research within a pandemic. For years, patient advocates had been pushing for this sort of model, to make clinical trial participation more patient-centric, extend opportunities for participation to those who don’t live near sites, and increase participant diversity. Before the March 2020 lockdown, one company that supports DCTs said it had about a dozen calls a week from potential clients. By June, it was receiving hundreds of weekly inquiries. Having proven their mettle in the cauldron of COVID-19, most experts agree that DCTs are here to stay. As Esther Krofah, Executive Director of the Washington, D.C. thinktank FasterCures, notes, “We’re going to see decentralized trials as a new, normal part of clinical research. The cat is out of the bag.”<sup>6</sup>

The aforementioned 2020 Clario survey<sup>2</sup> among clinical research professionals established that at least 86% planned to jump on the DCT bandwagon, citing a variety of potential methodologies for remote data collection:

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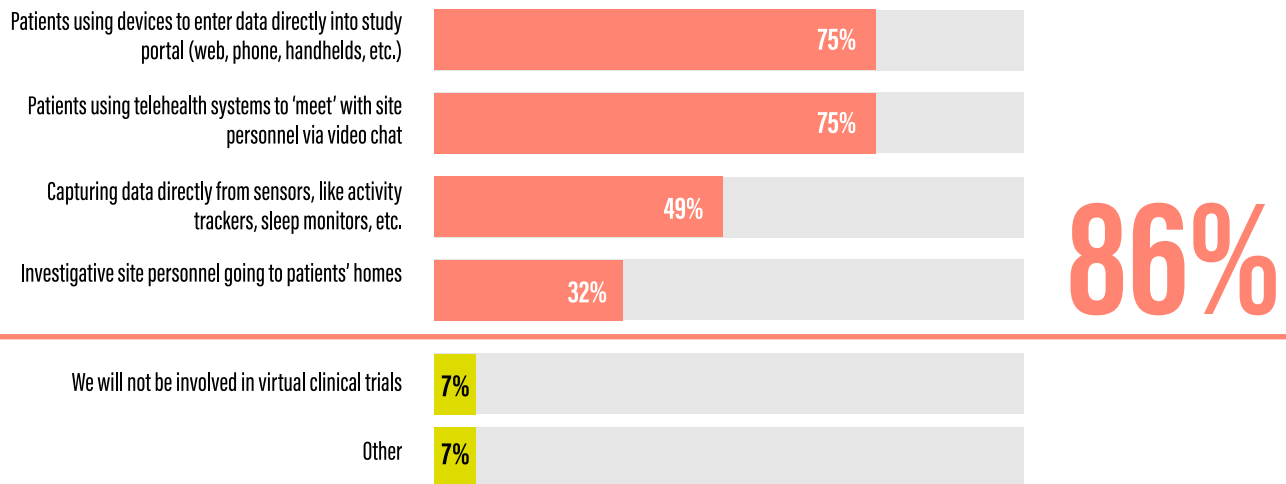


Figure 1 (Source: Clario)

The same survey suggested that only 5% to 10% of clinical trials will be completely virtual. The remainder will still have some site involvement, with hybrid models likely to dominate. While elements of the DCT model can be integrated into any clinical trial, this approach is especially suitable for studies that collect physiological data from devices in the patients' home. According to some experts, a new opportunity also exists for traditional brick-and-mortar sites to evolve into "trusted hubs" which proactively reach out to their surrounding communities to provide education on the value of clinical trials in improving human health, while simultaneously supporting evolving trial delivery models.

An exciting future vision began to crystallize but, in the pressure cooker of the pandemic, the absence of best-practice guidance on DCTs was palpable. Authors at Bryn Mawr Hospital and the Sidney Kimmel Medical College in Philadelphia described with great transparency their experience of trying to set up a DCT early in the pandemic and the challenges they faced.<sup>7</sup>

However, know-how soon began to pick up and, the following year, Rutgers University in New Jersey successfully pioneered a model for conducting DCTs

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that has cut implementation and patient recruitment times by 50%. "We're also now reaching people who were previously challenging to recruit and have enhanced retention of study participants since they no longer need to travel. Added to this, the elimination of brick-and-mortar facilities has lowered our costs," explains Reynold Panettieri Jr., Director of the Rutgers Institute for Translational Medicine.<sup>8</sup> Alethea Wieland, President of Clinical Research Strategies, predicts that the meteoric rise of DCTs will soon necessitate new clinical research associate training to gain the required skills.<sup>9</sup>

# DELIVERING COVID-19 RESEARCH

Getting back to the fight against COVID-19 itself, the stunning speed with which effective COVID-19 vaccines were delivered was testament not only to cutting-edge discovery science, but also to the immensely expedited clinical trial program, in which thousands of U.S. clinical research professionals rose to the challenge at both an organizational and personal level.

By the end of June 2021, the COVID-19 vaccination program had prevented nearly 280,000 additional deaths and up to 1.25 million hospitalizations, according to a report from the Commonwealth Fund.<sup>10</sup> “If there had been no vaccination program, daily deaths from COVID-19 potentially would have jumped to nearly 4,500 deaths per day during a second ‘2021 spring surge’—eclipsing the observed daily peak of 4,000 during the first 2021 winter surge,” the report estimates.

Beyond the vaccines, there was a simultaneous urgent need for COVID-19 treatments. This proved to be more challenging for the U.S. clinical research industry: of the nearly 30 million individuals who developed COVID-19 in the U.S., only a few thousand participated in clinical trials. A 2021 JAMA Editorial<sup>11</sup> explains that the problem was not lack of intent, effort, or resources. Hundreds of trials were designed and registered, and multiple multi-institutional clinical trial networks quickly mobilized to develop study protocols. Funding was made available from several governmental agencies, pharmaceutical companies, and non-profit foundations. In addition, the FDA and institutional review boards across the U.S. offered accelerated review and support of modifications to existing procedures. Nonetheless, the structure of the U.S. clinical research enterprise, which is set up like a marketplace, became a key barrier. In normal

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– COMMONWEALTH FUND

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times, competition between research groups for funding and participants may foster meritocracy but—in a pandemic—the lack of a central body to prioritize research questions and pool resources for the greater good proved to be a challenge. A second challenge was the interface between clinical research and clinical





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care. Just as no single entity oversees the clinical research enterprise, there is no integrated coordination between research and routine care, so clinical colleagues approached to refer patients into trials during the pandemic may have seen this as distracting and counter to the priorities of clinical care.

Given the existence of these systemic, infrastructural barriers, it is all the more impressive that clinical trial professionals across the country were able to collectively raise their game and deliver a number of regional successes. Clinical research teams at the University of Utah succeeded in launching COVID-19-related trials in under two weeks, citing the importance of “networking with the right resources to assemble a highly experienced team” and “open, frequent and streamlined communication among all team members to foster trust.”<sup>12</sup>

In New Hampshire, Dartmouth-Hitchcock Health helped launch two Phase III COVID-19-related therapeutic studies in only six business days. The Gilead-sponsored studies aimed to evaluate the safety and antiviral activity of Remdesivir (GS-5734™) in both moderate and severe cases of COVID-19. The swift launch represents “a true team effort on every level,” says Leigh A. Burgess, Vice President for Research Operations at Dartmouth-Hitchcock Health.<sup>13</sup>

Further, despite the odds, a Clinipace team succeeded in meeting enrollment goals for a COVID-19 inpatient trial within five months. Reflecting on conducting a trial under intense conditions with condensed timelines, team lead Jessica Thurmond comments, “We try to fit trials into a box, but what happens when the box no longer exists?” In this case, loss of the box meant it was time to think outside it. The trial was intended to utilize ten sites but ultimately Thurmond and team worked with over three times that number, including many smaller sites in less densely populated regions, in order to boost recruitment. The first patients were enrolled in May 2020 and, by September, enrollment was complete.<sup>14</sup>

In an article published in an academic journal, Katherine Tuttle, a nephrologist at the Providence St Joseph Health Hospitals in Washington, described the specific adaptations to clinical research—necessitated by the pandemic—that were implemented at her center. Perhaps most significantly, she stated that “our multi-specialty team of COVID-19 investigators meets in a daily huddle to review all hospital admissions for COVID-19 with the goal of finding a study option for every patient.”<sup>15</sup>



In addition to innovative approaches to interventional COVID-19 studies, other bold new initiatives and collaborations sprang up across the country. Early in the pandemic, Wake Forest Baptist Health joined forces with clinical research organization Javara Inc. to conduct a community-based research study of the novel coronavirus. The goal of the study, which employed extensive online data-gathering from local populations and at-home rapid diagnostic kits, was to help the medical community better understand regional infection patterns, track the disease in real time, and establish a framework for answering epidemiological questions. Atrium Health (one of the largest health systems in the Southeast) and MedStar Health (the largest healthcare system in the Maryland and Washington, D.C. region) later joined the project and planned to extend participation to additional health systems across the country. Data from the study have been shared with government agencies, such as the federal Centers for Disease Control and Prevention, National Institutes of Health, and state and local public health departments.<sup>16</sup>

Further, in North Carolina, a team at the Duke Clinical Research Institute (DCRI) spearheaded the HERO program, which invited healthcare workers to come on board and share information on what it was like to work and live during the pandemic, creating a research-ready registry. As of June 2021, they'd enrolled more than 35,000 healthcare workers and those who support them, including family members and friends. "We leveraged existing relationships to turn people into clinical trial champions," says Patty McAdams, communications project manager at DCRI.<sup>17</sup>

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— SUSAN LANDIS, Executive Director, Association of Clinical Research Professionals

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“Clinical trial practitioners should be very proud of the pivotal role they played in the COVID-19 vaccine development effort and in expediting trials for COVID therapies,” said Susan Landis, Executive Director of the Association of Clinical Research Professionals (ACRP). “Our members have helped to accelerate and advance the response to the pandemic every step of the way—from recruiting and running interventional trials to designing state-of-the-art population health studies that will evaluate the long-term effects of COVID-19 infection.”<sup>18</sup>

# NON-COVID-19 TRIALS BOUNCE BACK

The intense focus on COVID-19 research didn't stop clinical trials in other medical fields from quickly regaining their impetus. A study by the SWOG Cancer Research Network reports that, following an initial precipitous drop during the first wave of the pandemic, oncology trial enrollment recovered in the summer of 2020 to normal levels and only suffered comparatively minor setbacks in the second wave.

Joseph Unger, a SWOG health services researcher and biostatistician, explains that, early in the pandemic, the National Cancer Institute and FDA had released guidance allowing research sites more flexibility in enrolling and following patients on trials, including remote consent of patients, home visits, and virtual visits, all of which enabled trial operations to get back on track. In some cases, arrangements with primary care also enabled trial participants to visit their local doctor for basic procedures and assessments, rather than having to travel to a study site.<sup>19</sup>

A report from IQVIA<sup>20</sup> revealed that, although monthly trial starts fell significantly in the first quarter of 2020, they recovered from mid-year to higher levels than in 2019, even without counting COVID-19 studies.

Not only has the engine of clinical research regained its momentum, but the shock to the system that the pandemic represented has sparked a major new effort to modernize trial execution. According to the 2021 Veeva Unified Clinical Operations Survey: Annual CRO Report, the "COVID-Catalyst" is the real deal among CROs and sponsors. As many as 90% of CROs have taken decisive action to streamline trial execution by adopting new digital strategies and technologies to replace manual processes, unify clinical operations, and eliminate information siloes, enabling efficient information-sharing between sponsors, CROs and sites.<sup>21</sup>

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— 2021 Veeva Unified Clinical Operations Survey:  
Annual CRO Report

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# PRESERVING DATA INTEGRITY

In the battle against the pandemic, “clinical trials are critical,” Amy Abernethy, Principal Deputy Commissioner and Acting CIO of the FDA, told attendees at the Veeva R&D and Quality Summit in October 2020. While COVID-19 has also been a catalyst for adoption of new tools, technologies, and techniques in clinical research, it’s fair to say that some were adopted in haste and may have undermined data quality.<sup>22</sup>

Others have echoed this concern. Writing in JAMA, a trio of biostatisticians warned that methodological shortcuts in clinical research taken during the pandemic—while understandable—could have affected integrity and generalizability of data.<sup>23</sup> This was reiterated by the authors of a paper in The Lancet Global Health, which additionally highlighted the need for greater coordination and collaboration among research teams, with appropriate oversight and governance.<sup>24</sup>

Acknowledging that the clinical trial landscape has changed forever, Abernethy cautioned that the healthcare industry and its regulators will have to regroup in due course to recalibrate the critical balance between operational agility and scientific integrity.

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## BURNOUT

Running clinical trials is often a demanding activity, with sponsors and clinical stakeholders all eager for outcomes that are both speedy and robust. However, the strain of working under pandemic conditions was unprecedented.

According to a study led by the Tufts CSDD,<sup>25</sup> more than half (55%) of members of clinical research teams involved in interventional research reported feeling more professionally burned out since the pandemic forced most operations in a remote direction.

Nearly as many (42%) were concerned about “deteriorated connections” with colleagues.

Mary Jo Lamberti, Associate Director at Tufts CSDD and a lead author of the study, cited frequency of virtual meetings (“Zoom fatigue”) as a possible culprit.

Burnout was also attributed to added work responsibilities, unfamiliar operating models, and workload unpredictability.

Nonetheless, 43% of respondents reported that productivity was unchanged since the pandemic began and 35% reported that their productivity had increased.

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# LESSONS FOR THE FUTURE

The clinical research industry faced an extraordinary challenge when COVID-19 arrived in early 2020. Developing at least three effective vaccines in record time, clinical trial professionals successfully banded together with a common purpose.

However, as the worst of the pandemic recedes, some experts worry that key lessons will be forgotten. “We must never forget how hard COVID-19 hit the clinical research ecosystem,” says David Morin, Director of Research at Holston Medical Group. “It’s barely in our rearview mirror and I’m concerned some are already forgetting how bad it really was, and how much worse it could have been if we hadn’t united so powerfully.”

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**However, the pandemic has also shone a spotlight on pre-existing fissures in the system:**

**FIRST**, the industry must do a much better job to achieve diversity among clinical trial participants, reaching out especially to underserved ethnic subpopulations. This long-recognized challenge—so critical for data quality and generalizability—is in turn dependent on achieving greater diversity among the clinical research workforce itself.

**SECOND**, clinical trials must be made more patient-centric and more accessible to better represent and protect the entire population. DCTs are a paradigm shift in this regard.

**THIRD**, greater collaboration between individual research teams with common goals, central oversight, and sharing of best practices should be encouraged and facilitated.

**FINALLY**, clear career paths, standards, and infrastructures should be established to stem burnout and optimize the many rewards of the profession.

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