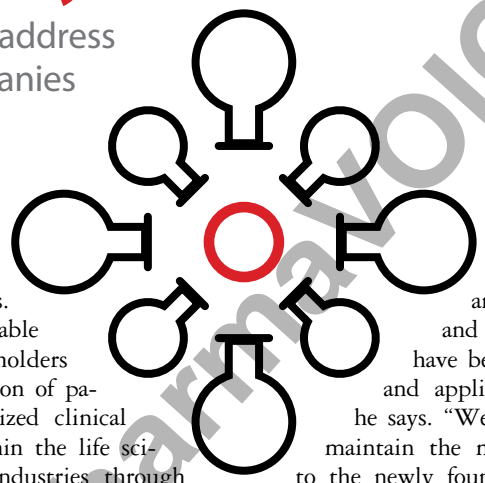
By Taren Grom

Decentralized Clinical Trials: The Way Forward

COVID-19 prompted the need for the industry to address patient needs in the clinical trial space, and companies along the drug development paradigm pivoted successfully to the benefit of patients.



Necessity is the mother of invention, and over the past 12 to 18 months because of the limitations necessitated by COVID-19, clinical trials have undergone somewhat of a revolution. Decentralized clinical trials, otherwise known as DCTs, which were being promoted as a promise of what could be just a few years ago, are front and center of nearly every clinical trial-related conversation today. DCTs offer some distinct advantages in terms of patient convenience and eligibility, but the big question that remains is whether the DCT movement is sustainable.

Organizations such as Decentralized Trials & Research Alliance (DTRA), which recently launched, are trying to create standards and a harmonized framework for life-sciences sponsors, contract research organizations, and other trial partners. DTRA's goal is to enable collaboration of stakeholders to accelerate the adoption of patient-focused, decentralized clinical trials and research within the life sciences and healthcare industries through education and research.

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DR. SY PRETORIUS
Parexel

With the global virtual clinical trial market value estimated to expand at a compound annual growth rate (CAGR) of 5.1% from 2020 to 2027 from a baseline of $7.0 billion in 2019, it's no surprise that DCTs are one of the hottest trends at the moment.

A New Future or Status Quo?

"The pandemic presented our industry with an opportunity to rapidly deploy patient-centric and decentralized trial approaches that had long been endorsed but never fully embraced," says Dr. Sy Pretorius, president, clinical development and chief medical officer, Parexel. "In the interest of safety, we quickly adapted traditional trials to decentralized or hybrid models to ensure patients continued to receive critically needed medications and to maintain clinical trial continuity, despite unprecedented challenges."

To date, Parexel has conducted more than 100 DCTs, including more than 200 remote patient engagement strategies, from telemedicine and digital sensors to home nurse visits and direct-to-patient drug shipments. "We are seeing tremendous interest from sponsors that have witnessed the benefits DCTs convey, and we've found that patients truly appreciate the increased flexibility and convenience. I see no signs of this trend slowing anytime soon. There is no going back — the future is now."

Nicholas Kenny, Ph.D., chief scientific officer at Syneos Health, sincerely hopes that DCTs are a new way of conducting research. "We cannot fall backward into the 'old ways' and lose the efficiencies, opportunities, and practical patient, site, and developer solutions that have been effectively advanced and applied to support DCTs," he says. "We have to capitalize and maintain the momentum that adapts to the newly founded constraints of the COVID-19 pandemic."

Conducting a trial remotely may have seemed unusual before, says Anthony Costello, president, Patient Cloud at Medidata, a Dassault Systèmes company, but COVID-19 has transformed the industry's viewpoint on how to run clinical trials and transformed patient expectations about participation. "Clinical trials that leverage digital connectivity between the patient and physician can lead to increased engagement and more consistent access to critical study data," Mr. Costello says. "With more sophisticated, patient-centric tools, DCTs have more potential than ever to provide a broader and deeper view of the patient. Patient insights and feedback need to be baked into each level of the clinical trial process, from study design and burden to the use of technology."

Some patients who had been participating in clinical trials either did not wish to continue to access sites due to increased infection risk, or they were blocked from accessing those sites due to government travel or site healthcare restrictions. "As a result, DCT techniques became a high priority for sponsors looking to rescue ongoing trials or design new trials that could be successful during the uncertainty of a pandemic," says Niklas Morton, senior VP, PPD Digital. "Perhaps one of the most consequential actions was the swift issuance of new guidance by global regulatory authorities that encouraged the decentralization of trials and the specific solutions therein. As for what's on the horizon, data continues to show an increased appetite for and adoption of DCTs."

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NIKLAS MORTON
PPD Digital

by PPD, the majority of key decision-makers across both biopharma and biotech believe the effect of the pandemic on research to be permanent.

"Study teams have not only built risk mitigation tactics into current research plans but also intend to proactively include DCT and digital strategies in future protocols," Mr. Morton says. "The message is clear: rather than revert back to traditional clinical trial designs the industry is considering decentralized trial approaches as a valuable asset in the design and execution of future clinical trials."

The increased popularity of DCTs during the COVID-19 pandemic provides the industry with proof points for what should be an important option when designing clinical trials now and in the future. "Our research shows that specific patient profiles rely on, and prefer, direct engagement with their HCP," says April Lewis, executive VP and general manager, Hu. "Our research also shows that for patient cohorts that tend to be more convenience-seeking and attracted to DCT design, retention risk can be elevated. The operationalization of DCTs needs to balance consumer demand with flexibility, keeping the patients' needs in mind. Real success will be achieved when we look at DCTs as a balanced approach to move away from site-centric and toward patient-centric approaches. Otherwise, we run the risk of ostracizing large patient cohorts with fully digital and remote approaches that are not grounded in insights about what will work best for patients."

Greg Licholai, M.D., chief medical information officer at PRA Health Sciences, notes

The digitization of trials will help enhance the diversity of patients participating in studies by expanding the reach and access of trials. Sponsors can help spearhead this effort toward greater diversity by specifically seeking out research sites in underrepresented geographies, while CROs invest in more support for investigators in areas with minority populations.

HENRY LEVY
Veeva Systems

that the use of digital health, telemedicine, and remote patient monitoring has been accelerated by COVID-19. "By providing digital health options to patients, we are lessening the burden on patients to participate in clinical research," he says. "DCTs take advantage of technological advances in connected devices, mobile communications platforms, and integrated electronic medical records (EMRs) with the goals of addressing costs, enrollment, and diversity issues. These technologies can help make drug development more efficient by increasing the speed of enrollment, distributing information, and getting more patients to participate."

There is little doubt that the realities of the pandemic have forced a faster pace of change and proven that clinical trials can be conducted successfully in a decentralized way. "Specifically, technology use, such as mobile apps and ambient monitoring devices, will likely continue to lower the burden of participation for people and expand availability while maintaining scientific rigor," says Lauren Lawhon, chief operating officer, Health Union.

Even though the COVID pandemic has driven very high adoption of DCTs in a very short period of time, Geoffrey Gill, president of Shimmer Americas, warns as COVID subsides, there will likely be some backsliding as some people return to their old and comfortable habits. "However, many people are committed to moving to DCTs and the recent experience has shown how effective they can be," he says. "We will not go all the way back to where we were, but only part of the way, and the overall trend to DCTs will accelerate."

DCTs and Patients

Health consumerism is at an all-time high, Ms. Lewis says, and the demand for hybrid models of care is leading the way. "Patients want access to HCPs on demand, and want to define what warrants an in-person visit," she says. "The trend overall is toward patients demanding more control over their treatment journey. DCTs or hybrid trials support these patient needs in ways that traditional clinical trials have not been able to meet. What we are looking at is the democratization of a clinical trial, allowing these often life-saving solutions to be viable care options irrespective of a patient's zip code or his or her local physician knowing how to connect a patient to a clinical trial."

Experts agree that a patient-centric approach via DCTs reduces the burden on patients to participate in clinical trials. "It also broadens the geographical reach of the study, enabling clinical research to be a potentially valuable healthcare option for individuals facing the historical limitations of the time and travel involved in accessing an often distant investigational site," Mr. Morton says.

The increased access granted by digital tools or decentralizing options allows biopharma, biotech, and government organizations to more easily recruit and retain patients in their trials. "We have seen recruitment rates much higher than the traditional site — 10 times in a recent study — resulting in significant reductions in recruitment timelines and in some cases making a trial viable that was otherwise not," Mr. Morton says. "In addition, we are observing strong patient retention rates of 90% in decentralized trials, a 20% reduction in patient dropout compared with traditional studies. In the current pandemic, decentralized trials also allow investigators, sponsors, and patients to continue engaging with clinical trial research in a manner that minimizes unnecessary risk of COVID-19 infections and maximizes the chances of trial success."

Patient feedback from a multitude of surveys and research studies has clearly demonstrated that logistical and financial burdens such as lost wages, childcare constraints, and transportation costs and travel time to and from study sites are common barriers to trial participation. "Research also has established that the majority of patients participating in clinical trials live more than two hours away from the clinical trial research site," Dr. Preto-

COVID-19 will hopefully serve as an inflection point in how clinical trials are conducted from this point forward, because the realities of the pandemic have forced a faster pace of change and proven that clinical trials can be conducted successfully in a decentralized way.

LAUREN LAWHON
Health Union

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ANTHONY COSTELLO
Medidata, a Dassault Systèmes Company

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DR. NICHOLAS KENNY
Syneos Health

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APRIL LEWIS
Huū

rius says. "As a result, up to 50% of sites enroll only one or no patients, and 85% of trials fail to retain enough patients for the duration of the study.

"DCTs significantly reduce these burdens by offering telehealth visits from home, wearable devices that transmit data to the cloud, smartphone apps with medication reminders and study-specific educational information, direct-to-patient drug delivery, and much more," he continues. "With these tools, patients can more easily integrate trial participation into their own lives and their families' lives. Lastly, DCTs are pushing the industry to streamline siloed electronic data systems so that data reporting and analyses happen more efficiently, more quickly, and with greater accuracy. Improving how we handle data limits data variance and increases accuracy, which are both critical to ensuring data integrity when results are ready to submit to regulatory authorities."

And regulatory agencies are also embracing virtual solutions, particularly remote monitoring, e-consent, telemedicine, and direct shipment of investigational products to patients. "About one-third of all clinical trials have already incorporated some form of virtualization, and the number of patients involved has more than doubled in the past few years," Mr. Costello says. "All in all, these trends indicate that DCTs and expanded use of technology could quickly become commonplace across the industry."

Ms. Lawhon says decentralized trials that use home health, apps, and virtual telehealth visits can reduce the burden of participation for patients. "They essentially expand the geographic availability of clinical trials for people who live in rural or underserved areas, or maybe don't live close to research centers that are conducting trials," she adds. "As a result, decentralized trials can empower people to consider clinical trials as treatment options while reducing the need to disrupt their daily lives for treatment and follow-up visits."

Dr. Kenny agrees that DCTs further accessibility and promote more practical solutions to accommodate people's lives. "The key advantage is DCTs allow us to take the trial to the patient as opposed to taking the patient to the site," he says.

Henry Levy, general manager, Vault CDMS, site, and patient solutions, at Veeva Systems, expects that clinical trials will continue to advance to better serve the needs of patients. "Whether through an electronic consent process, remote data collection, or virtual visits made possible in decentralized trials, there are numerous ways we'll see sponsors, CROs, and sites make it easier for patients to participate in trials while improving stakeholder collaboration throughout a study," he says. "Traditionally, patients that participate in clinical trials are required to attend multiple visits for check-ups and treatment. The extensive travel and time commitment can take a heavy toll on patients. Decentralized trials can significantly reduce that burden. By bringing the study into the home with virtual visits and solutions such as eConsent, patients have the option to complete trial activities without ever leaving their home. If less travel to sites is required, patients in rural areas gain access to more trials, broadening the reach of studies."

DCTs in the U.S. also have been shown to help with delivering a more diverse patient population than traditional trials — in some instances, double or triple that of a conventional model. "This is key to ensuring trials are generating evidence that is representative of and relevant to the full patient population," Mr. Morton says.

Dr. Pretorius agrees, adding that DCTs are expanding access to more people — and more diverse people — who might not have had the option of participating in the past.

By giving patients an easier way to participate in clinical trials through virtual visits and electronic consent processes, and showing them their commitment to diversity in the coming years, life-sciences companies will be able to improve study outcomes and drive more effective drug development. "The digitization of trials will help enhance the diversity of patients participating in studies by expanding the reach and access of trials," Mr. Levy says. "Sponsors can help spearhead this ef-

fort toward greater diversity by specifically seeking out research sites in underrepresented geographies, while CROs invest in more support for investigators in areas with minority populations."

Adding the Patient Voice to the Clinical Process

"We've learned that patient input is vital at every step of the drug development process," Dr. Pretorius says. "Incorporating patient and caregiver insights early in trial design ensures that the endpoints being measured are relevant to real patients and truly reflect the way patients experience the disease. For example, if a study seeks to measure an outcome that doesn't significantly affect the most troublesome symptoms from the patient's point of view, then the real-world benefits of the drug won't be fully realized. Similarly, if the patient isn't consulted early in the protocol design, then particularly burdensome procedures or study requirements may preclude patients from enrolling. If we know ahead of time what's meaningful to patients, we can design the trials around their needs."

The use of DCTs as a care option will continue to expand across the industry even after COVID-19 has been better contained.

DR. GREG LICHOLAI
PRA Health Sciences

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MARI WELKE
Synchrogenix

Dr. Kenny says patient involvement should start at the very beginning. "There are so many good examples — notably the charge led by our colleagues in rare disease drug development — where intentional planning and engagement with patients leads to more appropriate and practical trial designs," he says. "It's also very encouraging to see regulatory support for this with the FDA's new patient-focused drug development initiatives."

Patient input should be considered early and often throughout the entire clinical development process, which starts with target product profiles, including understanding various patient pain points and identifying any opportunities for therapeutic intervention beyond the typical signs and symptoms, Ms. Lawhon says.

"Patient input throughout study design can ensure there is a clear balance between scientific study requirements with the realities of patient burden," she says. "And this input should continue through to recruitment to make sure patient materials can be understood and patient recruitment strategies are appropriate."

Mari Welke, director of safety and innovation at Synchrogenix, Certara's regulatory science division, says it's important to factor patient insights and experience into all phases of clinical trial design and execution.

"This will maximize the involvement of all patient populations and increase diversity," she says. "Without listening to patients, how can sponsors learn what barriers would prevent them from joining a trial or what issues might cause them to drop out? How can they define an acceptable risk or an unacceptable burden, without asking patients directly? Today, there are technologies available to help engage with patients and gather their input throughout the process."

The Path Forward

Advancements in digital health offerings will continue in 2021 and for years to come, Dr. Licholai predicts.

"We will continue to see companies inventing new, innovative ways for patients to monitor their health virtually," he says. "The use of DCTs as a care option will continue to expand across the industry even after COVID-19 has been better contained. Most importantly, DCTs are advantageous to patients. Patients are able to participate in clinical trials from the comfort of their own homes, without having to travel long distances to visit a site. Additionally, breaking down barriers to research expands access possibilities to enroll more diverse groups that are more representative of the medications' target therapeutic population in the real world."

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GEOFFREY GILL
Shimmer Americas

The next 12 to 24 months will see a dramatic increase in the use of wearables to support DCTs, enabling improved quantification of the patient experience, Mr. Gill says.

Ms. Lawhon also believes the continued use and evolution of health tracking apps, ambient devices, and other mobile app technologies are likely going to significantly impact clinical trials over the next few years.

"They will greatly reduce the need for many in-clinic aspects of the clinical trial process," she says. "Specifically, they will allow for remote monitoring of patient activity and compliance, as well as self-reporting of symptoms through e-diaries and other functions.

"Moreover, the increasing use of technology, either through mobile apps or telehealth, can enable the expansion of quality of life metrics and patient-reported outcomes as secondary endpoints in clinical trials," Ms. Lawhon adds.

As pharmaceutical companies continue to increase their investment in artificial intelligence (AI) and machine learning (ML) as part of their R&D processes, Ms. Lewis believes this presents an opportunity to remove the burden from the patients.

"Today, patients are still expected to shoulder unrealistic, rigid, and strict schedule requirements, from trial matching and eligibility assessment to rigor in data quality through collection," she says. "With the ability to apply more real-world design and digitally transforming mHealth and DCT solutions, the heavy lifting can be absorbed by data science. Clinical trials have the best chance of being attractive to patients when patients are at the center of the process." PV