Building a Collaborative Alliance for Decentralized Trials

When COVID-19 forced clinical trials across the world to shut down due to the risk it posed to patients and an overloaded healthcare system, it brought decentralized trials to the fore.

Decentralized clinical trials (DCTs) have been gaining impetus for several years, supported by mobile technologies and new innovations that have made trial activities that were once only possible through face-to-face methods both efficient and effective in a decentralized model.

Several industry leaders have led the charge to enable decentralized trials, recognizing that decentralizing makes it possible for more patients to participate in clinical research. Multiple conferences have been held on the topic of DCTs, discussing how digital technologies have the potential to transform clinical research and drive greater patient-centricity as well as patient recruitment and retention.

Recognizing the need to propel action on decentralized clinical trials, two of the industry's most respected names — Amir Kalali, M.D., and Craig Lipset — established a historic alliance of life-sciences and healthcare organizations to accelerate the adoption of such trials. The Decentralized Trials & Research Alliance (DTRA) is a nonprofit organization that brings together healthcare companies, regulators, patient groups, and research organizations to advance policies, research practices, and new technologies in support of decentralized clinical research.

"As Amir and I started to talk about this a little over a year ago, there was significant interest in the community for a sustaining entity that brought deliberate focus and attention around what's needed to make decentralized clinical trials really stick," Mr. Lipset says. "The work around DTRA began before COVID-19. Today, that need and urgency are greater than ever before."

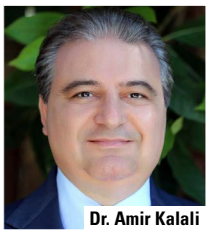
What sets DTRA apart from other initiatives focused on decentralized clinical research is that it brings together a diverse group of stakeholders, which Mr. Lipset says is both a blessing and a challenge.

"When an alliance is homogeneous, it's certainly easier to achieve agreement, but it's harder to build consensus around everything that's needed to make change happen," he says. "DTRA is already showing that it is well-positioned for collaboration across the ecosystem and across different initiatives."

DTRA is eager to work with and amplify the efforts of organizations that are devoting resources to the issue of DCTs.

"However, none of these entities are fully focused on decentralized clinical trials, whereas we are akin to a clearinghouse that is able to amplify what these organizations are doing, we can identify gaps in a holistic fashion, and bring together the whole ecosystem," Dr.

A Vision of Trial Accessibility


Dr. Amir Kalali


Craig Lipset

The Decentralized Trials & Research Alliance (DTRA) was convened in December 2020 based on a vision of making research participation accessible to everyone. The stated mission of DTRA, which was established by Amir Kalali, M.D., and Craig Lipset, is to "enable collaboration of stakeholders to accelerate the adoption of patient-focused, decentralized clinical trials and research within life sciences and healthcare through education and research."

Dr. Kalali is a physician scientist who leads at the intersection of the life-sciences and technology. A 2014 PharmaVOICE Red Jacket honoree, Dr. Kalali has been responsible for numerous successful drug development programs that have led to new treatments for patients. He is also chief curator and chairman of the CNS Summit, which was created to advance clinical development, with a focus on collaboration, innovation, and technology.

Mr. Lipset, a 2019 PharmaVOICE Red Jacket honoree, is a recognized leader at the forefront of innovation in clinical research and medicine development. He has long been committed to revolutionizing the role patients play in clinical research, making them true collaborators in uncovering new medical breakthroughs. He drove clinical innovation while at Pfizer, leading it to become the first pharmaceutical company to attempt a fully decentralized, blinded/randomized digital clinical trial. He also spearheaded Pfizer mClinical, a comprehensive mobile platform for clinical trial participants.

Mr. Lipset also served on the founding operations committee of TransCelerate that brings together subject matter experts from different companies to engage on specific projects and work with their peers at other companies who were facing the same day-to-day challenges.

Key Considerations for A Successful Decentralized Trial

Decentralization has the primary goal of making clinical trial participation as easy as possible, enabling participants to continue with their day-to-day lives with minimal disruption. Studies have revealed:

- 70% of patients live more than two hours from a research site
- In 50% of clinical trials, participants find it difficult to stay enrolled due to poor health
- 85% of trials fail to retain enough patients

Patients aren't just statistics or data — they're people. Many potential trial participants will be managing health conditions while running businesses, working full-time jobs, and raising families. Where this is the case, requiring patients to attend site visits, which involve hours of travel and accumulated costs, isn't just difficult — it can be impossible.

In this way, the current clinical trial model prohibits participation from otherwise willing patients. This reduction in the available pool of participants not only has an impact on recruitment and retention, but it also impacts the integrity of the study by limiting diversity.

Fully decentralized or hybrid (a mix of site and home-based activities) clinical trials have huge potential to positively impact clinical trial development in numerous ways, including:

- Accelerating patient recruitment by making it easier to find potential participants (for example, in rural areas where travel to/from sites is difficult). More patients would be able and willing to take part if participation is easier, reducing the recruitment burden on CROs and sponsors.
- Increasing participant diversity by enabling patient recruitment from a much wider pool rather than limited to those within a reasonable distance of a participating site. This especially benefits rare disease research, where clinical trials are often "competing" for the same limited pool of participants.
- Patients become more knowledgeable, informed, and engaged as a result of autonomy enabled by technology. There is a wide body of evidence suggesting engaged patients complete tasks such as electronic diaries with more accuracy and honesty. Electronic records can also be automatically time-stamped and verified as required.
- Gathering more diverse and applicable data sets by monitoring patients remotely in real-time. Collecting data from a real-world setting is more likely to deliver insight free from the bias that results from undergoing assessments in a clinical setting.
- Improved reliability and accuracy of data; paper can be lost or damaged or forms can be inaccurately filled out. Collecting data using technology such as wearables, apps, and smartphones keep data organized and safe.
- Easier reporting and analysis of results as technologies enable data collection and sharing to be standardized.

Source: mdgroup

Kalali says. "We launched with just under 60 organizations and membership is rapidly approaching 100. We represent regulators, biopharma companies, service companies, tech companies, site networks, and patient groups — it's a broad range."

Even though the group is very diverse, there is broad agreement in terms of where the gaps lie, and where DTRA can have an impact. Both co-founders agree that collaboration is the only way to drive improvement across the ecosystem.

"The biggest competition in decentralized trials is not one company versus another, but a lack of market adoption," Mr. Lipset says. "If, and when, we get to a state of full adoption of decentralized clinical trials at scale, organizations may have less motivation to work together. Until then, everyone realizes that their true target is driving adoption in the market."

Many companies have not gone beyond pilots of decentralized trials, and some haven't even gone that far, which demonstrates the need for a forum where people can learn from one another.

"We want to make sure all biopharma companies have the tools they need to enable decentralized clinical trials because we believe this is best for patients," Dr. Kalali says. "Another benefit of being a neutral group is our ability to provide educational programs that are not just sponsored or that focus on one area, but knowledge that brings the whole ecosystem together."

Breaking Down Barriers

DTRA's members are largely focused on four initial priorities.

The first is breaking down the "Tower of Babel" — whether around archetypes for decentralized trials or key performance indicators — to ensure everyone is on the same page in terms of the discussion starting points. The second is to capture the learnings from each organization in the space and share best practices. The third is to build on those by improving education and awareness leveraging data and evidence to bring all parties along in support of evidence-based decentralization. The fourth priority is to address the remaining barriers for meaningful adoption, which may include challenges such as implementation across global regulatory bodies and even in the United States with regard to telemedicine and interstate licensing.

An example is e-consent barriers around scaled adoption due to some ambiguity with different regulators in certain geographies.

"There are data and learnings around adoption, retention, and other parameters that we can start to gather and then share the successes around e-consent in a vendor-agnostic way," Mr. Lipset says.

The drive toward DCTs does not suggest all trials would be been done remotely going forward, Dr. Kalali says. Rather, the idea is for patients to be able to choose for each visit whether they need to be in the clinic or not. "DCTs offer a broad range of possibilities, and this movement will continue to need the cooperation of everyone in the ecosystem," he says.

As the effects of the pandemic continue to rage and concerns for patient safety remain a priority, the impact on clinical trials remain severe. Indeed, there are estimates that the pandemic could set back non-pandemic clinical trials by several years with patients unable or reluctant to schedule visits with research centers.

"We have a responsibility to advance the health of people with unmet medical needs, and by convening stakeholders we can remove remaining barriers to adopting new policies and practices that can impact patients today," Mr. Lipset says. PV

EXECUTIVE VIEWPOINTS

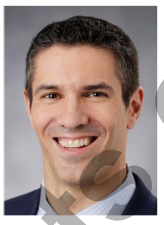
Julie Ross
President
Advanced Clinical

Planning an Upfront DCT Approach

A DCT/hybrid approach must be considered upfront during clinical trial planning so protocols are written to accommodate and maximize the use of a DCT environment. Barriers exist when DCT strategies are an afterthought following protocol development and trial funding. Hybrid or complete DCT trial execution requires a different approach to study management across all trial stakeholders and necessitates a different operating and cost structure with consideration to site capabilities, burden, and matching grant compensation.

Opening DCT Strategies Are Opening Doors

The hybrid approach is the biggest trend today as most Phase I to III trials require some on-site procedures. Jump started by COVID-19, remote monitoring and telemedicine became a must, and decentralized components such as eConsent and patient engagement applications are becoming mainstream. With enrollment delays remaining the biggest timeline/cost challenge, innovative approaches to efficiently enroll and engage patients continue. DCT strategies open doors to additional and diverse populations and also create new data repositories. Capitalizing on the data assets is an evolving trend.



Costa Panagos
President, Research and Development Operations
IQVIA

Designing Trials To Fit Patients' Lives

Patient centricity is at the core of decentralized and hybrid trial design. The idea is to design trials that fit into patients' lives seamlessly. This includes thoughtful integration of connected devices or designing protocols that eliminate unnecessary assessments, blood draws, or site visits. We want patients to feel great about their clinical trial experience. These trials may include trial concierges and nurse trialists who assist both the site and the patient through the study journey.

The Need for Diverse Data Integration

As patient-centric data capture and real-world data sources evolve quickly, there is increasing need for diverse data integration, master data management, and more complex technology infrastructure. As evidenced by the COVID-19 vaccine programs, diversity and inclusion must be integrated into all aspects of design and delivery to engage broader patient populations and ensure trials are balanced and representative. Lastly, decentralized trials necessitate specialized skill sets, including technical, data science, and diagnostic specialties (e.g. mobile nursing).

Alison Holland
Head of Decentralized Trials
Medable

Improving Accessibility

The decentralized model improves accessibility by removing the time and travel constraints of having to make regular journeys to sites, which are often a significant distance from a patient's home. DCTs also offer greater choice for patients so they are empowered to decide if they prefer to go to a site or have the study come to them at home. Decentralized trials increase accessibility to the physician/caregiving team, even as some may think the opposite. In contrast, the convenience of televisits, electronic support materials with on-demand training refreshers, reminders, updates, and newsletters all make regular contact with physicians easier,

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and therefore, more likely to happen more often.

Right now, the industry is still trying to tackle several important challenges, including a lack of connected systems. We still have too many disparate, siloed point solutions that only manage one part of the process and don't interface with other systems. Success requires data and systems to be unified and available in real time. Another misperceived barrier is a misconception commonly assumed that patients are not tech-savvy enough to participate seamlessly in a DCT. However, we've seen the opposite, with patient uptake and engagement very high across all age groups.

Enhancing Clinical Trial Monitoring

As we engage with more and more patients within their real-world settings, we start to collect data that reflects how they experience their symptoms in the environment that matters to them. For instance, the "white coat syndrome" that causes stress in some patients can spike blood pressure in the clinic versus at-home monitoring with a less obtrusive device. DCTs offer accessibility to more patients with the benefits of enhanced clinical trial monitoring without the burdens of travel to clinics, making those patients apprehensive to participate more likely to do so for the potential benefits of the investigational therapy.

Greg Licholai, M.D.
Chief Medical Information Officer
PRA Health Sciences

DCTs and Technology

Hybrid and fully decentralized clinical trials leverage technological advances in communication platforms, digital health technologies (DHTs, e.g., wearables and sensors), and integrated electronic medical records (EMRs) with the goals of increasing efficiencies of DCTs and enhancing convenience for trial participants. DCTs enhance data collection in real time and reduce geographic and travel barriers, leading to increased diversity and overall reduction of burden on trial participants, caregivers, and clinical sites. DCTs may lead to faster and cost-effective results.

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PRA Health Sciences

Research as a Care Option

PRA Health Sciences developed Clinical Research as a Care Option (CRAACO), a collaborative and holistic approach to leveraging standard healthcare and clinical research (e.g., DCTs). CRAACO offers data integration from patients in standard healthcare systems and from trial participants in DCTs, as well as effective coordination between all trial stakeholders. DCTs will increase convenience and optimize enrollment, which improves access, retention, and health outcomes, expedites medical product development, and boosts diversity. This leads to more efficient and faster DCTs in all therapeutic areas, including COVID-19 treatments and vaccines.

Maria Fotiu
Executive VP, Decentralized Solutions
Syneos Health

Overcoming Barriers

Like other "new" developments, we often find that sites, patients, biopharma, and service providers put up barriers to implementation. As scientists, we want data to show an approach is effective, and in the absence of case studies, we may resist implementing new approaches. Most barriers are therefore self-imposed — fear of the new and the unknown impact of change; however, we should not minimize the possible legal and regulatory barriers that may also delay new approaches.

Patients' Real-Time Access to Data

Before COVID-19, telehealth, home health options, and wearable trackers were transforming how healthcare is being delivered and how physicians interacted and tracked patients' health. By introducing these capabilities into clinical trials, we more closely mirror care options that patients are already becoming accustomed to, and trial participation may feel less burdensome. The use of DCT capabilities provides patients with real-time access to some of their data, affording them the same insights into their care as in the traditional medical care space. By bringing clinical trial activities closer to the home, we increase the type of care patients have access to; they are no longer constrained by geographic limitations on treatment options.