Optimizing Decentralized Clinical Trial Strategy and Technologies

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Decentralized clinical trials (DCTs) enable patients to enroll and participate while minimizing or eliminating travel to a central investigator site, often by leveraging the use of technology. The elements comprising a DCT may look completely different from one individual or organization to the next, though, a deliberate design that makes DCTs adaptable to any sponsor's needs.

Rather than being completely remote or completely traditional, in the sense of all activities occurring at a central investigator site, many clinical trials now embrace a hybrid format. Starting with a more patient-centric trial protocol and study design, each trial is optimized by combining any number of DCT elements, which include both technologies and strategies (Fig. 1). However, ill-conceived implementation of these elements, particularly as it relates to technology, can increase burdens on the site, patients, and/or sponsors.

DCT Strategies	Technologies and Applications
• Telehealth • Home health visits to administer treatments, collect specimens, collect patient reported data • Visits to local labs • Direct-to-patient clinical supply shipping models	• Online recruitment and enrollment • Remote electronic health records access • Electronic patient reported outcomes (ePROs) • Tools and apps for primary and secondary data collection including web-based, wearables, handheld devices, medical devices

Fig. 1 — Potential DCT strategies and technology elements

Accordingly, careful consideration is required to determine which strategies and technologies can help a trial — simplify it, reduce patient burdens, or ensure more accurate data collection.

Understanding Typical DCT Challenges

Implementation of DCT technology and strategies can help sponsors to overcome difficulties that almost all clinical trials (traditional, decentralized, and hybrid) encounter. Modern clinical trial protocols are increasingly complex, involving more sites, patients, and data points than ever before. Typically, the more complex a protocol becomes, the greater the potential burdens on both patient and site. All the technology available can be thrown at perceived challenges, but sites and patients are likely to remain overburdened until simpler protocols can be devised. Other challenges generally fall into three broad categories: operational, patient-centric, and site-centric.

Patient-Centric Challenges — The inherent difficulty of recruiting and retaining clinical trial patients typically makes patient-centric concerns sponsors' principal hurdle to address. As competition between sponsors for trial participants becomes increasingly fierce (particularly in therapy areas like orphan disease or oncology), anything that can reduce overall patient burden provides trial recruiters an edge. And, the faster patients can be recruited, the faster the study kicks off and is completed. The second most-prominent obstacle is patient retention, since effective recruiting means little if attrition/patient dropouts are significant.

Operational Challenges — Operational concerns include reducing timelines and costs, minimizing burdens on clinical operations personnel, and optimizing the personnel necessary (i.e., doing more with fewer people). The most prominent operational concerns, though, surround how data is to be collected and secured, then delivered accurately and expeditiously back to the sponsor. Moreover, that data must be integrated and packaged in a manner conducive to regulatory submission.

Site-Centric Challenges — Site-centric concerns, meanwhile, are paradoxical in being both significant and often overlooked. Consider that, for the most part, everything related to the trial lands on the site coordinator's desk, from patient recruitment and retention to data collection. They usually work with multiple technology providers and multiple clinical research associates (CRAs), often across multiple studies with multiple sponsors. With so many moving, interrelated parts, reducing site burden is a complicated endeavor that often takes a backseat to patient-centric and operational concerns.

Why Challenges Still Exist with Implementing Technologies in DCTs

The above challenges exist for all sponsors and the aim of technological solutions is to overcome one or more of those difficulties, whether that entails reducing work volume and the full-time equivalents (FTEs) necessary to support that volume or achieving database lock faster. But the introduction of even cutting-edge technology does not inherently make a trial more efficient, simpler, or capable of producing higher-quality data.

DCT solutions must be considered through a holistic lens, peering at the benefits and drawbacks associated with their implementation and use. How might each available DCT technology — and each possible combination of those solutions — fit within the context of the patient's daily life, the site's daily operations, the trial protocol, and the therapy area? It's important to clearly identify and prioritize how efficiencies may be gained in one area while simultaneously generating complex issues in another.

Only a few technologies (e.g., "convenience" technologies like eConsent and virtual visits) offer the luxury of a margin for error. Interactive response technology (IRT) and electronic clinical outcome assessment (eCOA) systems do not fall under that category. From an IRT perspective, errors in randomization or blinding and unblinding can sabotage an entire trial. In eCOA, lost data relevant to primary and secondary endpoints can critically damage a trial.

While demand for such technologies spiked during the pandemic, they were not brand new: eConsent, televisits, digital patient recruitment, and wearables all have been utilized for years. Still, sponsor skepticism remains around several technologies for varying reasons.

- eConsent technologies may be avoided because some countries' health regulators still require a paper copy of consent forms on-file. Sponsors also may be skeptical of digital patient recruitment since recruitment is costly no matter the methodology or tools, and sponsors often require multiple patient recruitment partners to meet a study's needs.
- Many sites simply are used to using their own technology — something well-understood by personnel and established in their workflows — and have no interest in "reinventing the wheel" for a task they feel is adequately covered already.
- Sponsors and sites that have had negative experiences with certain technologies — often because of ill-considered implementation or ineffective training and use, rather than shortcomings in the technology's capability — may default to more traditional methodologies, even if it is not the most efficient or cost-effective way to proceed.

Technology + Expertise = Optimized DCTs

As the industry continues to adopt more DCT strategies and technologies, it becomes even more critical that modern protocol development incorporates an understanding of how technologies intersect with the patient visit and data collection. This requires specialized insight into each patient population, the scientific expertise to focus the protocol on the most important research questions that meet regulatory requirements, and data science experts who can optimize technology to drive better outcomes and deliver cleaner data. Ideally, protocol considerations and technology implementation begin in parallel.

Seek a technology provider that can deeply discuss options, outcomes, and concerns surrounding the protocol and potential technologies (like eCOA and IRT). The partner should be able to explain, clearly and honestly, how each technology may or may not fit based on the trial protocol, site setup, and patient population. They also should be able to talk on an ancillary basis about some other technologies that might be useful, as well as how those technologies fit within the trial's ecosystem.

The technology provider should offer a help desk capable of solving problems over the phone in minutes. Things inevitably go awry in clinical trials, related to numerous touchpoints, human interaction with technology, and the technology itself. Every call a sponsor has to make to solve an issue takes money out of their pocket and slows down the clinical trial process.

The sponsor must have individuals with the expertise to effectively participate in both initial discussions and continued collaboration. Large and some mid-size biopharmas tend to have infrastructure allowing more qualified personnel to assess technologies, enabling them (theoretically) to capably mitigate their risk. Small or emerging organizations often lack sufficient internal resources to effectively collaborate in this process and thus allocate the responsibility to CRO partners. But CROs usually are not technology driven companies; they are service oriented, so they often lack the resources to assess and stay up to date on DCT technologies.

In the sense of both risk aversion and not adding unnecessary burdens — to site, patient, or operations staff — less is more. An optimal approach sometimes leverages just two or three technologies because they are the simplest to implement, the least burdensome, and the most effective in the context of what they will provide versus the resources necessary to acquire, implement, and use them. Throwing every technology that seems like it might help at a trial ignores the necessity of understanding daily site operation or a day in the life of a study participant, within that trial's schedule of events, enduring burdens associated with that disease.

Final Thoughts

Many modern studies combine traditional tools and methodologies with DCT components. The most successful organizations and studies align protocol, patient type, and therapeutic area through a collaborative effort with partners, minimizing burdens and risk while maximizing the effectiveness of technologies applied.