Decentralization of Clinical Trials: Taking Into Account All Stakeholder Perspectives

At first, the COVID-19 pandemic threatened clinical research, with patients struggling to get to sites, hospitals becoming overloaded, and screening criteria becoming increasingly muddled due to widely circulating symptoms.

However, the industry rallied to rapidly adapt and enable decentralization of clinical trials with community-based solutions, telehealth, and the assistance of connected devices capable of expanding data capture, precision, and flexibility at home. Leveraging this rapid evolution and adoption of technology, pharmaceutical sponsors, CROs, technology providers, and sites collaborated to start-up and deliver a study in 50% of the traditional timeline, culminating in the market approval of lifesaving vaccines.

The Patient Perspective

Matthew McCarty
Chief Strategy & Marketing Officer
ERT

Now, the accelerated timelines and integration of decentralized trial technologies are here to stay.

"What we've seen throughout this crisis is that a significant number of studies can indeed collect some clinical trial endpoints remotely," says Matthew McCarty, VP of integrated customer solutions.

A July 2020 survey of pharmaceutical, biotechnology, and medical device companies found that 82% of respondents had already adopted virtual trial technologies. McCarty says it is ERT's prediction that nearly 80% of studies will include a hybrid of on-site and decentralized activities over the next few years. "With the combination of experience, endpoint expertise, and humanized technology, solutions are emerging that enable the collection of robust data in the community," he says.

There is no question that decentralizing clinical trials will change a lot for patients, sites, and sponsors. There are certainly challenges to overcome, but there are as many, if not more, opportunities that technology is able to solve.

Now that we know the art of what is possible, how can the industry collectively work to best support hybrid and decentralized clinical trials moving forward at scale?

First, it must strive to better understand the broad spectrum of challenges ahead.

Topping the list of obstacles for decentralized clinical trials is the increased responsibility for enrolled patients.

"In a traditional clinical trial model, site staff control much of the study, including administration of assessments," McCarty says.

Previous challenges, therefore, included the time, availability, and cost of travel to and from the site, as well as inflexibility of appointments complicating work, childcare, and social lives.

Decentralized clinical trials can address all of those, but at home and in the community, patients must now be much more aware of and active in scheduled assessments for study success.

"They need to log on to telehealth visits, know how to use connected devices, and still be available for home visits from healthcare professionals if required," McCarty says. "This can potentially impact compliance and quality as we ask the patient to take the lead in managing much of that endpoint data collection."

For example, when staff take a patient's blood pressure on site, they are certain the patient has been resting.

"We now have smart devices that determine blood pressure, but what happens if the patient has been chasing their kids or pets or climbing stairs?" McCarty asks. "How can we know that the data we're collecting with smart technology is truly evaluable in order to build accurate evidence?"

Furthermore, what kind of support can a patient expect to receive at home?

"It's easy to turn to a receptionist or investigator on site, but if a patient is filling out an electronic patient reported outcome — ePRO — at 9 p.m., and they have a question, where can they turn to for help?" McCarty asks. "What happens if the battery dies in their connected device? Even in the case where telephone support is available, it can be confusing for a patient to have a different number to call for each component of the study. Patients need to be able to confidently manage these challenges."

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The Site Perspective

Elisa Cascade
Executive VP and Product Line Executive, eCOA
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While one might think that the shift toward decentralization and more activities in the patient's home or community would decrease site burden, in actuality the opposite can be true. Understanding how the site's role is changing is key to determining the competencies, tools, and support they need.

With the expansion of hybrid and decentralized trials, sites will need to shift their operating model from all activities being conducted at the site to one of ensuring patient safety. This includes safety across their own site and the patient's home through visiting nurse organizations and local providers with

the need for adapting to site and study-specific technologies as an added challenge.

"What makes this even more complicated is the role that the site is being asked to play will differ by sponsor, study, and potentially patient choice," says Elisa Cascade, executive VP, and product line executive for eCOA.

With only 15% of sites stating they have used decentralized study tools over the past two years, sites will need to evolve their competencies across a number of dimensions, including but not limited to:

- Technology: A growing number of systems, applications, and devices at both the site and study level with potential overlap in functionality
- Study set-up, training, and support: Preparing patients for at-home activities, including registration for healthcare services and devices, as well as diagnosing and triaging patient issues when they arise, often outside of normal business hours
- Telehealth: assessing the patient's condition remotely or via care coordination
- Care coordination: Expanding the number of roles involved in a study, such as visiting nurses, community diagnostics, or local primary care physicians
- Monitoring: Assess patient status via multiple systems with for-cause patient outreach coupled with a shift to risk-based and remote monitoring, shifting tasks to the sites that were historically supported via on-site CRAs

"While the industry has been advancing on this wave of patient-centricity, hybrid and decentralized trials will fail if we do not recognize and address the added burden to sites," Cascade says. "Ultimately, coordination between sponsors, CROs, sites, and third-party service and technology providers is needed to streamline activities to support both our patients and our sites."

The Sponsor Perspective

It becomes the sponsor's responsibility, then, to ensure proper support is made accessible to both patients and sites across the globe via on-demand video training, live chats, 24/7 telephone hotlines, and more.

Sponsors must also handle any data management and privacy issues.

"Taking a photo of an injection site reaction, for example, is not complex with smartphones these days, but sponsors will need an intuitive application and a streamlined process to then remove any patient identifiers and control the quality of images," McCarty says.

Matthew Johnson
VP, Wearables and Digital Biomarkers
ERT

It is therefore recommended that sponsors carefully consider how, when, and why connected devices be used in each study, says Matthew Johnson, VP for wearables and digital biomarkers at ERT.

"Meaningfulness and functionality are very important," Johnson says. "Which tests should be conducted on-site or supplemented by data collected at home? Different modalities can also produce different results."

Sponsors must determine whether technology is to be used synchronously with coordinators for oversight and performance monitoring, or asynchronously with patient self-administration.

Finally, sponsors must consider geographical barriers of the study.

"Sponsors need to consider international logistics, 24/7 customer support, localized training, and of course, international quality standards," Johnson says. "Are the technology versions controlled? What quality management systems are implemented? How will the privacy of cross-border data transfers be handled. Not all connected devices, even medical-grade connected devices, are ready for global clinical trials."

Technologies Designed to Rise Above

All of these challenges call for more intuitive technologies designed to rise above to meet the future. For patients, that means more personalized and intuitive connected devices that provide real-time notifications and instructions.

"We need to build solutions that not only fit effortlessly into patients' lives, but also support and educate patients to preserve data quality," McCarty says. "For example, a patient may receive an alert to measure their blood pressure, but then must also be given instruction and a built-in timer to rest for a prescribed number of minutes before the reading can even be taken."

For sites and sponsors, increased collaboration and coordination across technologies and systems will result in a more streamlined user experience, which in turn will result in higher quality and more real-time access to data.

"Not one of us can do this alone," Cascade says. "It really is going to take partnership across all of us to ensure users flow seamlessly from one tool or system to the next without duplicative and potentially contradicting information."

For example, there is real need for single sign-on capabilities across the entire industry.

"We need to integrate across providers and tools so that our customers don't need to sign into multiple systems." Cascade says. "From the site perspective, this has historically been substantial with CenterWatch reporting an average of 10 systems in 2016 before the addition of decentralized tools, such as connected devices.

To start, Cascade recommends looking to collaborative organizations, such as TransCelerate BioPharma, the Society for Clinical Research Sites, the Association of Clinical Research Professionals, and the newly formed Decentralized Trials and Research Alliance, for guidelines.

"We must work to create interoperability across technologies and systems so as to streamline data collection across all stakeholders - patients, sites, sponsors, and CROs," Cascade says. "By supporting these stakeholders, the industry will be supporting itself in improving our user satisfaction and study delivery timelines."

Finally, as decentralized trials evolve, more flexible options may become the norm.

"We foresee increased site and patient choice regarding virtual or in-person assessments, as each individual and circumstance is always different," Cascade says. "It simply becomes a matter of flagging where and how that assessment occurred."

To help determine the flow and virtual integration of future clinical trials, both Johnson and McCarty recommend more patient-focused research and workshops to support a user-friendly study design.

"By asking study participants what's meaningful to them before a study even begins, you can further personalize questions, and better monitor changes throughout the course of the clinical trial," Johnson says. PV

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To learn more about the many considerations in implementing decentralized clinical trials, contact ERT at info@ERT.com, or visit virtualtrials.ert.com.