Driving the speed of adoption with decentralized clinical trials

The evolution of clinical research throughout the pandemic, and beyond

merative™

Contents

Understand decentralized or digital clinical trials and how they are now part of the “new normal” for executing studies in light of events such as the COVID-19 pandemic.

Explore the necessary considerations and unique challenges of adopting and designing a decentralized or digital clinical trial at the time of protocol design and development.

Investigate the importance of a patient-centric approach and the role patient centricity plays in the design and execution of a decentralized clinical trial. Explore the ways patient and provider engagement need to be considered in a decentralized clinical trial.

Explore the use of established and new technology in decentralized clinical trials and its impact on protocol design, study start-up, patient and provider experience and quality study outcomes.

Introduction

While decentralized clinical trials are not new to life sciences, studies conducted with a hybrid approach or entirely virtual are becoming part of the industry norm.

For better or worse, the COVID-19 pandemic forced life sciences organizations around the globe to adapt at a scale unheard of in the history of today's industry. Biopharma companies and contract research organizations (CROs) adopted decentralized or digital clinical trials (DCTs) to reduce contact, improve the patient experience and keep studies on track during the pandemic. It's already clear that the virtual approach of DCTs are benefiting life science organizations. From improvements in clinical trial operations such as enhanced patient engagement and site experience to cost savings and better data integration, the clinical trial dynamic has shifted and supports DCTs as a legitimate way to execute studies.

However, challenges remain. This new clinical trial dynamic merges traditional clinical trial challenges with those created by the transition to digital solutions and decentralized designs. The burden is on biopharma companies and CROs to understand and name the problems when executing a decentralized clinical trial. Study success depends on the evaluation and adoption of intuitive solutions that can be quickly implemented and streamlined without adding unnecessary strain on providers and patients while maintaining security and regulatory standards.

A unique shared approach

No matter the approach, clinical development will face challenges. The key is to assess and apply flexible, scalable solutions and reduce clinical trial burdens overall.

Traditional clinical trials typically leverage “brick and mortar” study site(s), serving as the epicenter of clinical development within a region or geographic location. Required study visits, tests and evaluations are conducted in-person by a designated investigator team, with the ability to conduct tests at satellite facilities and/or direct from the patient in the case of patient reported outcomes.

By contrast, a decentralized clinical trial is driven by the study’s demands and patient experience. For example, in each hybrid clinical trial there can be patients visiting a physical site for an EKG or tumor biopsy, and others in another treatment arm participating virtually. In this scenario, and in others like it, patients use a mobile app or other electronic patient-reported outcome (ePRO) device in addition to electronic clinical outcome assessment (eCOA) tools to track their data.

In some cases, patients undergoing treatment cycles, traditionally requiring site visits, can request a patient kit or drug be shipped directly to their home. For example, clinical study investigators requiring blood or saliva samples (to test insulin or cortisol levels) ship sampling kits to patients. Participants then have access to a digital platform and virtual healthcare provider to conduct tests via telemedicine, discuss concerns and share data.

Though the benefits of reaching patients closer to/in their home are tangible, there are significant hurdles in execution. The coordination of home-based procedures where a skilled healthcare practitioner is required to administer/sample, is one of the greatest treatment challenges to overcome for a decentralized study. Especially if the clinical study includes a large population and/or is geographically diverse.

There has never been a more critical time to focus on the patient than now. While the decentralized clinical trial approach is both unique and essential, developing solutions that are scalable, flexible, and smarter is going to be essential for long-term success.

PROTOCOL DESIGN

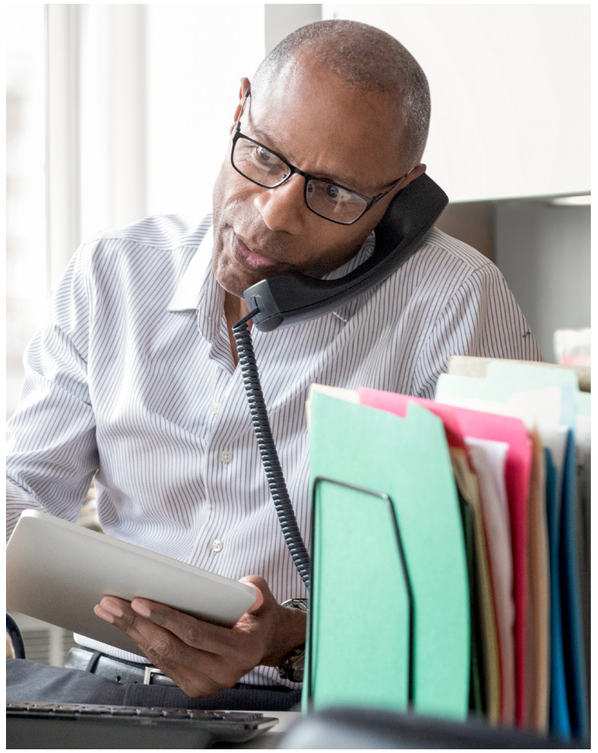
The challenges of protocol development and study design

The COVID-19 pandemic force the pivot to a decentralized clinical trial approach for some study areas. Protocol framework and study structure are now required to be robust, and include DCT solutions as an integrated option in any future study design.

Perhaps the greatest challenge in a clinical study is developing a robust and flexible protocol and study design. In late 2019 and early 2020, many organizations underwent a clinical study by fire. For many in-flight traditional clinical studies, the COVID-19 pandemic forced sponsors, CROs and tech companies to scramble for tools and capabilities that collected data remotely and reduced or eliminated the need for in-person visits.

When pivoting to a decentralized or digital study approach, both the protocol framework and study structure require a dynamic design characterized by the ability to withstand and react to clinical study changes and challenges regardless of physical location. Given the typical clinical study considerations of the patient visit schedule, methodology, and drug formulation/IND approvals needing to stay on track, there are additional necessities to execute a successful decentralized clinical trial. DCTs include the sustainability of remote/tele-visits, adherence to changing quality/regulatory standards (global and cultural) and ensuring clinical study safety regardless of setting. Clinical study procedures also have variation in how they are conducted which has the potential to influence the clinical results. These differences can introduce variability into critical study endpoints which ultimately must be considered in the sample-size calculations, analysis plans and monitoring plans.

From start-up to the last patient interaction, all parts of the study must remain on target to ensure accurate patient results and reported outcomes. The key for moving forward, despite challenges, is to become more agile and efficient, reduce administrative burdens, and promote patient centricity without compromising clinical study quality or data integrity.



Here are a few ways you can maximize successful clinical study outcomes:

01

Incorporate logical digital/ decentralized approaches as part of standard study design and include them in the initial protocol.

Bring DCT and digital solutions into study design where it makes sense and is a logical way to collect the required data. There is no need to require a study to be fully digital or fully traditional. A hybrid approach that optimizes the study execution will position the study for success. Account for remote/telemedicine study visits and digital data collection, including any relevant and appropriate technology (virtual connectivity tools, AI, etc.), or adaptive processes that may be required during the trial to maximize the efficiency of gathering data from patients.

This will help avoid delays with U.S. institutional review board (IRB) and/or EU independent ethics committee (IEC) approvals and protocol amendments. It also streamlines resubmission of regulatory or other essential documentation that may be necessary as changes are made.

02

Clinical study sponsors should write a protocol and study design with data-informed inclusion/exclusion criteria.

Reaching the patients where they are is key and is considered the new normal. Leverage digital solutions to create a positive Screening and eConsent experience. Inclusion/exclusion criteria should be designed to allow for reaching the patient in the most efficient and optimized manner and reducing site burden. This helps create optimal patient recruitment and ensures accurate results for patient enrollment.

Excessive screen failure rates are discouraging for site staff and participants, in addition to delaying study completion and delivery of new medicines. Thus, it is important that sponsors and clinical study sites assess the feasibility of the inclusion/exclusion criteria using various technologies to assure that patients are not inundated with a burdensome level of complexity related to the technology solutions.

03

Protocol development should require the seamless deployment of eCOA, eConsent and telemedicine visits.

When this occurs, investigators and coordinators can execute their functions with the same level of quality despite the absence of a physical patient visit. Likewise, the clinical study protocol needs to explore the flexibility of how certain services are provisioned to permit remote lab assessments, imaging, etc.

Additionally, using integrated digital technology for virtual pre-screening and e-consent reduces screen failure rates and expedites study start-up.

One benefit of the DCT experience during COVID was the reduction in unnecessary data collection during the clinical study. Incorporating research best practices that eliminate unnecessary visits and/or data (those not connected to primary or key secondary endpoints) will benefit all studies and procedures in the research portfolio, not just decentralized clinical trials.

For years, site feasibility has been considered somewhat of a broken process. However, having technology for virtual pre-screening and eConsent should reduce screen failure rates and expedite study start-up. eConsent solutions are now readily available on the market, are seamlessly integrated with core clinical study systems and have a proven ability to improve the overall patient onboarding experience.

The importance of an integrated econsent solution (optimally, interoperable with both eCOA and EDC clinical study platforms) is now a necessity and should be considered the standard solution for the post-pandemic clinical study blueprint.

REIMAGINING PATIENT AND PROVIDER EXPERIENCE

Patient engagement and retention

Decentralized clinical trials have made impressive improvements when it comes to patient engagement and patient retention. Yet, it is still a factor that must be calculated into overall clinical study design and comes with challenges.

Many variables impact patient visits and the quality of their data reporting. Often these variables are burdensome on the patient and lead to increased patient drop-out rates which, in turn, cause clinical study delays and inaccurate results. Most of the time, these issues are mitigated by identifying sites with higher patient retention performance scores in addition to understanding the patient enablement process implemented in a decentralized clinical trial approach.

Patient retention is a constant concern of the protocol-writing equation in decentralized / digital clinical trials despite the completely virtual, and often effective, approach of a decentralized clinical trial. Often, decentralized clinical trials achieve quality results without the typical site-specific challenges that impact study participants, sponsors and investigators during the traditional approach. Patients complete online surveys, e-Feasibility questionnaires, econsent, patient diary forms and other awareness protocol-related documents from the comfort of their own device with minimal person-to-person interaction. Collectively, this data can then be e-sourced and verified in real-time by clinicians using a virtual technology platform. Nonetheless, a study's purpose and design complexity should be taken into account when considering patient burden and the feasibility of collecting patient data remotely.

Biopharma companies and large CROs need to work with an ecosystem of technology solutions to bolster patient convenience and comfort — using digital technology and unified solutions. For example, a decentralized clinical trial may work with patients in several geographical areas, tracing these “sites” through the use of geofencing technologies that automate some reporting based on location data provided by patient devices such as cell phones with an app relevant to the study. Thus, investigators can record the time, date, location and type of medical interaction automatically, provided the patients are within an area that supports the system’s geofencing.

Additionally, predictive analytics based on previous studies can help anticipate the behaviors of patients and help influence improved data collection and patient retention. Remote patient monitoring tracks these trends, allowing investigators to identify anomalies, often before they happen. For example, a study site is expected to have a 30 percent risk rate of adverse events. The rate currently sits at 15 percent, but it is trending to exceed 30 percent. Leveraging predictive analytics and AI, a sponsor could work with investigators and patients to introduce mitigation actions before that occurs.

Still, it must be acknowledged that some patient groups may experience increased difficulty participating in a remote environment. These challenges will differ depending on the study, but examples might include teenagers disinclined to report promptly, elderly participants unfamiliar with their digital devices, or patients whose illness or disability makes using a digital platform (or its user interface) challenging. Ideally, these potential problems are identified and addressed during protocol development and selection of e-solutions for the study. An ecosystem approach should leverage technology that meets the patient where they are and improve the overall likelihood a study participant will adhere to reporting requirements.

Patient engagement, retention and care is a large factor of study success. While decentralized clinical trials often increase patient enablement, there are still considerations and challenges to overcome regarding patient retention and patient engagement. It is necessary to include patient burden in study design, protocol-writing, and technology selection to support the study.

SMARTER TECHNOLOGY

Identifying and using smarter technology

Smarter technology is the key to a direct, patient-centric home healthcare model that effectively serves the interests and goals of sponsors, study participants, and investigators.

Clinical studies are not without disruption. The pandemic has caused additional previously unforeseen burdens. Emerging as a path to overcome decentralized clinical trial challenges are digital health solutions and unified platforms enabled with smarter technology. Technology such as AI and advanced analytics, virtual study capabilities, and diverse interoperability are considered better solutions for organizations conducting clinical studies. The result is often the acceleration of studies, improved data integrity, and faster adoption among the patient and site participants.

Site and patient portals are critical to improve data quality, site/patient engagement, and relationships with the sponsor, especially for online survey/e-Feasibility, and econsent completions. And, despite some shortcomings, clinical study start-up management solutions can help accelerate site selection and patient recruitment.

Additional solutions empowering sponsors and CROs to recognize more value from the data they collect, improve the patient experience, and create valuable evidence during the clinical studies program (versus post-market) include:

- **Real-World Data** (**RWD**) Integration and unification with diverse solutions that leverage EHR/EMR data and patient endpoints inform quality decision-making relevant to progress of the study and the therapy.
- **Digital Therapeutics Across All Digital Health Platforms** Pre-developed intelligent algorithms assist in optimal site selection to accelerate the study start-up processes.
- **mHealth Solutions** in this arena include wearables, mobile apps/sensors, voice recognition technology, video capability, and virtual/augmented reality (VR/AR).
- **Unify eClinical & CDMS Solution Landscapes** deliver a single-source solution for the user community to leverage results with AI/analytics.
- **Risk-Based Detection Solutions with Risk Assessment Models** detect the frequency of data changes and reported outcomes.

The sum of these parts is a direct, patient-centric home healthcare model that effectively serves the interests and goals of sponsors, study participants, and investigators. Digital therapeutics and digital health platforms integrate the telehealth and telemedicine aspects of a remote study in one place: the video capability, the gamification capability, the built-in VR/AR, etc. For example, decentralized clinical trials include a virtual nurse or a virtual coordinator and the capacity to use voice recognition.

Interest in using health technology to enable decentralized clinical trials and support the effectiveness of traditional clinical studies has exploded since the pandemic began, driving innovation in the space. Sponsors are discovering a more patient-centric approach improves study efficacy by applying technology to provide better care, being more responsive to patient needs, and reducing site and participant burden.

Using smarter technology, site teams and investigators can devote more time and attention to patient consultation and wellbeing, even before the patient is recruited. To that end, in recent years, patient engagement has been bolstered by community websites for studies that allow patients to log in and request clinical study information ahead of time, so they can decide if they want to enroll.

Patients can provide econsent and complete any other documentation virtually, without travel. They can even communicate questions or concerns at that time, establishing a relationship with the investigator before the clinical study has kicked off. Clinicians reviewing those questions have discovered the answers of patients participating remotely are much more consistent, leading to improved reporting quality.

While smarter technology has numerous advantages, it is always necessary to take into account the study's purpose and design complexity. It is essential to consider and discuss various technologies' appropriateness and effectiveness for study success.

The “new” industry standard

Decentralized clinical trials are not an anomaly attributable to the current pandemic. Fueled by health technology that can help with everything from protocol development and clinical study design to patient recruitment and clinical study management, studies conducted in part or entirely virtual are the new industry standard. They reduce sponsor, investigator, and patient burdens while contributing to improved data integrity and more efficient studies (in terms of both time investment and cost). Digital clinical study solutions also offer scalability. Users can start with something basic and add components as their clinical operations and ambitions grow.

Most important, digitally-enabled clinical studies offer the versatility to adjust and pivot as circumstances demand, as well as ease theregulatory documentation and logistical challenges associated with such changes, all while staying laser-focused on a positive patient experience and overall patient wellbeing.

Explore life sciences technology