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The Signal

Key Technology Elements for Successful Hybrid Trials

As the industry continues to predict and debate what the "new normal" in clinical development will look like in an era of rapid change, there seems to be consensus that technology will be an essential ingredient. Technological innovation, alongside regulatory support, has transformed clinical trials – the traditional site-centric model which can be associated with high burden for patients has shifted to a flexible, patient-focused, paradigm in which patient settings are considered with the goal of reducing the need for regular in-clinic attendance. Some refer to this as a decentralized trial; however, the industry has not yet agreed on a single definition of decentralized clinical trials, evidenced by the many terms often used interchangeably such as "remote", "virtual", or "site-less" clinical trials. The Clinical Trials Transformation Initiative (CTTI) defines decentralized trials as, "… those executed through telemedicine and mobile/local healthcare providers (HCPs), using procedures that vary from the traditional clinical trial model…" This definition is more akin to a fully remote or site-less trial, but what we see in practice is a hybrid model – one that digitalizes certain parts of the process to simplify and streamline operations as well as make trial participation more accessible, convenient, and engaging. We consider this simply part of the increased digitalization that is necessary to enhance participant experience and improve data quality, accuracy, and availability.

What are the components of increased digitalization?

Evidence generation

Hybrid trials utilize smartphones, tablets, or computers to help researchers generate evidence through remote data capture, affording many benefits to participants, sites, and study teams. Electronic clinical outcome assessment and telemedicine applications, hosted on a participant- or vendor-provided device, improve the quality and integrity of PRO and ClinRO data. When ClinRO assessments are conducted virtually using telemedicine, this offers the opportunity to reduce in-clinic visits, making trial participation more convenient. It also facilitates access to larger, more diverse participant populations, which is especially advantageous when developing new treatments for rare diseases. Digital health technologies such as sensors and wearables can collect additional data about patient functioning, providing study teams with the ability to measure these elements more frequently than during clinic visits. They also provide deeper insights into the impact of a condition or its treatments without burdening patients.

Informed consent

Electronic informed consent, a frequently included element of hybrid clinical trials, helps participants review study information and determine their interest in participation. Enabling this component to be performed from home ensures potential participants can digest this information in an unhurried environment, share and discuss with family and friends as appropriate, and avoid unnecessary and time-consuming travel to clinic. Implementing electronic consent remotely does not diminish the importance of the physician-patient discussion which can be incorporated in the consenting workflow using a telemedicine appointment.

Telemedicine & Engagement

Reducing physical in-clinic appointments brings the risk of reduced patient engagement and oversight. A pillar of any hybrid trial, telemedicine and patient engagement applications keep patients closely connected to study teams, ensuring their ongoing engagement with the trial. Engagement solutions, as a component of the ePRO application, guide the patient through their study providing easy access to study information reference materials, schedules and reminders for upcoming visits, and detailed visit information to ensure patients know what to expect each time – whether in person or via video. Telemedicine enables regular, interactive follow up of patients in addition to remote assessments, ensuring patients continue to feel connected with site personnel and allowing investigators to collect more regular assessment of adverse events and concomitant treatments to enhance oversight and data accuracy.

Drug Supply Management

A vitally important but often overlooked aspect of hybrid trials, study supply management solutions that allow sites and depots to ship products directly to patients benefit all stakeholders. Patients do not need to embark on unnecessary travel to sites to receive their next medication pack, and this added convenience again means that sponsors can attract a broader and more diverse range of participants from a wider geographical radius for each study site. Sites are also less burdened with the storage and management of investigational product. Management of the supply chain for direct-to-patient solutions requires additional complexity that can be accommodated within a Randomization and Trial Supply Management (RTSM) system.

Virtual site monitoring and home health

Hybrid clinical trials offer opportunities to reduce site visits not only for patients but also for clinical research associates who play pivotal roles in the success of clinical trials. In the traditional model, CRAs travel extensively and complete two or three site visits and reports per week. The demands of their roles predictably lead to burnout and high turnover rates. Emerging solutions such as Signant's Virtual Site Monitoring enable CRAs to eliminate the need to travel to sites, ensuring they can complete far more monitoring activities in a reduced

timeframe. This technology has also been employed to provide study monitors access and oversight to home healthcare provider visits.

What are the gaps?

There is much to gain by digitalizing aspects of clinical research, but technology adoption can introduce new challenges. Measuring vital signs outside of the clinic can be accomplished and supervised using sensors and telemedicine, but what if lab samples are required? Are microsamples accurate enough to measure the items of interest? Outpatient sampling technologies are more patient-friendly but they present new operating and logistical complexities as well as regulatory challenges. In the case of home health visits, how can a study monitor or principal investigator demonstrate that they have appropriate oversight? When utilizing increased digitalization and remote collection, how can we efficiently aggregate data to ensure it can be reviewed easily and in a timely manner, and ultimately analyzed to derive clinical meaning? What are the learning curves for implementation and adoption?

When considering a hybrid trial, it is better to plan this study design from the start as this will impact the protocol's schedule of events in terms of the measurements needed to meet the study objectives, their frequency, and their setting – whether in the home or in-clinic.

As the industry moves towards greater digitalization and decentralization of clinical trials, sponsors should consider all aspects of their research process to determine how technology can improve data quality as well as increase participation, engagement, and compliance. Not all trials can or need to be decentralized. The best way to accommodate the needs of all stakeholders is to collaborate early in the planning process with the objective of building flexibility into a protocol before study launch. An experienced partner like Signant Health can provide the advanced technologies, scientific guidance, and operational expertise sponsors need to design and conduct hybrid, patient-centric trials.

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