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The Centricity of Decentralization

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Browse your email, attend a conference, or read a journal and you are bound to see terms like "digital health," "virtual" and "decentralized clinical trials (DCTs)." Recruitment, retention, diversity, efficiency, safety and accuracy are all driving the need for radical innovation. This need is painfully apparent during the current COVID-19 pandemic. We can no longer do the same things and expect different results.

Fortunately, the clinical research industry is rapidly transforming its practices. As of May 20, 2020, one-third of sponsors were switching to virtual or decentralized models, according to the Tufts Center for the Study of Drug Development (CSDD).[1]

The Center for Information and Study on Clinical Research Participation's (CISCRP's) 2019 Patient Experience Report found that 75% of patients say that collecting all study data from their own home is appealing and 73% like the idea of a hybrid trial.[9]

Since two-thirds of investigative sites fail to meet enrollment requirements, according to the CSDD, reducing participant burden is particularly important, especially when considering time to market for a new drug.[1]

Key elements of decentralized clinical trials (DCTs)

DCTs leverage technology and decentralized services to treat study participants remotely and through hybrid models that include fewer than normal in-person visits. The use of specific digital technologies varies by study and can include eConsent, telemedicine, wearable devices, mobile applications, electronic clinical outcome assessments (eCOA), and electronic health (eHealth) records, to name some of the most important. Mobile technologies are often used as electronic diaries and to collect data from wearable sensor devices. Home nursing visits and devices shipped to study participants allow assessments and procedures, such as blood pressure readings, ECGs, blood draws and infusions within the participant's home and at nearby sites, such as pharmacies. This model improves patient centricity by reducing participant burden while leveraging technology to enable remote doctor/patient interactions.

Advancing the delivery of healthcare and clinical research with technology

Twenty years ago, the healthcare industry realized that to advance healthcare, improve efficiency and care coordination, and make it easier for health information to be shared between different care providers, electronic health records were needed. In early 2009, the Health Information Technology for Economic and Clinical Health Act (HITECH) was enacted.

Ten years later, many other types of healthcare technology have also expanded. Tools such as remote patient monitoring and telemedicine are becoming commonplace. In a 2019 report by *Fierce Healthcare*, a survey by American Well found that one in five physicians use telehealth and 61% of those not currently using telehealth indicated they are likely to start by 2022.[2] Among those using telehealth now, 93% said it improves access, 77% said it is more efficient for doctors and patients, and 60% said it enhances the doctor-patient relationship. Many healthcare providers have learned that delivering care digitally is a great way to accommodate patients who may find travel time-consuming, difficult because they cannot take time off from work or childcare, or simply inconvenient.

In an effort to be more patient-centric and efficient and to extend clinical research as a care option, the clinical research industry is quickly adopting new technology. Expanding clinical research to the 80% or more of patients who say they would participate in clinical studies requires companies to keep pace with the technology patients are already comfortable using.[3] The COVID-19 pandemic is accelerating the use of remote technologies and the public's comfort with these devices and systems.

Given that there will be no going back to the old days, the Innovative Medicines Initiative (IMI), a partnership between the European Union and the European pharmaceutical industry, established Trials@Home in January 2019 to examine the potential of digital technologies utilized in DCTs. The initiative aims to demonstrate that DCTs will improve participant recruitment and retention, while also increasing the number of patients from typically underrepresented groups, who are often find getting to doctors' offices a financial burden. In addition, since data collection will be more continuous, the results should be more reliable and representative of the real world.

Many fear that at least one demographic, seniors, will resist utilizing the technology required for DCTs. However, an American Association of Retired Persons (AARP) survey published in 2020 says otherwise.[4] Of the 77% of seniors who own a mobile device, almost a third use it to manage or receive healthcare. The percentage of seniors who own a wearable (17%) is comparable to the percentage in the 18-49 age group (20%), demonstrating that age may not be as significant a barrier to adopting new technologies in clinical research as perceived.[4]

How do we ensure standardization and regulatory compliance?

Scientific rigor remains a guiding principle of the clinical research industry, with guidance from governmental agencies and bodies like the Clinical Trials Transformation Initiative (CTTI), a public-private partnership co-founded by Duke University and the FDA. This initiative includes representatives from entities involved with providing healthcare and conducting clinical trials and academic research studies. CTTI is working to identify legal, regulatory and practical barriers to DCTs and then recommending adjustments to policies that affect their implementation. Their final recommendations have covered DCT approaches and protocol design, state-level telemedicine issues, drug supply chain, mobile healthcare providers, investigator delegation and oversight, and safety monitoring.

Benefits to investigative sites

Investigative sites continue to play key roles in clinical trials. In fact, there are many advantages to DCTs for investigators and site staff. The reduction in time spent documenting outcomes, collecting data, and managing and conducting in-person participant visits means that investigators and site staff can use their time in more productive ways.

The total number of endpoints in a single clinical trial rose 86% from 2008 to 2018, according to the CSDD, making the burden on sites almost unbearable.[5] Digitizing study processes with tools such as eConsent, electronic clinical outcome assessment (eCOA), and electronic patient-reported outcomes (ePRO) allows patients to complete study tasks at home that would typically be performed at the site and frees investigators and staff from redundant data entry. The result is better clinical care, higher quality data, and more capacity for expanding study enrollment and adding new studies. In addition, DCTs drive down costs for sites as far less manual inputting of data is required.

The Society for Clinical Research Sites' (SCRS's) most recent Site Landscape Survey revealed that 68% of sites that had been approached about conducting a hybrid or virtual

trial had said "yes."[6] The survey also reported that more than half of respondents would do "whatever is required" to conduct a virtual trial.

Expanded trial access and diversity of participants

Distance, travel and participant diversity have long been challenges in patient recruitment and in developing therapeutics that are generalizable to a broad population. DCTs address these issues. For instance, while those who live in major cities may have relatively easy access to study sites, one contract research organization (CRO), Parexel, estimated that 70% of potential clinical trial participants live more than two hours away from a study center.[7]

In a 2018 Swiss study published by National Center for Biotechnology Information (NCBI), a traditional model was compared to a decentralized model.[8] The decentralized arm of the study recruited three times as many patients as the traditional arm and in one-third the time. Further, participants in the decentralized arm better represented both urban and rural areas, while the traditional arm consisted only of those living near an existing study site. These potential benefits apply to studies across many disease states, but are particularly important for rare diseases, as the scarce potential participants may be spread across wide geographic areas. Patients are often willing to travel for an initial assessment and final visit — the bookends of their trial experience — but want to maintain their daily life as much as possible without the burden of frequent site visits.

More and higher-quality data and improved accuracy

The apps, wearables and other portable devices deployed in DCTs collect data on compliance and symptoms, providing better oversight of adherence and enhanced safety monitoring. These tools allow data collection to be frequent, continuous and accurate. They also do not rely on patients to fill out forms or remember scheduled visits. DCTs can deliver data directly from the source, eliminating second-hand data sources and reducing the need for data verification. In the NCBI study referenced earlier, 50% of the participants in the decentralized arm of the trial reported that the activity patch helped improve protocol adherence, whereas no patients in the traditional arm did so.

DCTs can also provide insights on how study interventions affect normal life, generating useful real-world data (RWD). For example, perhaps a medication is suspected of causing an immediate but minor and short-term side effect. If participants can self-administer the study drug during their regular daily activity, a wearable can detect the side effect as a drop-in activity, change in heart rate or respirations, or other data points. The participant can then quickly use a telehealth visit to rule out or address an adverse event and be reassured, thus preventing a study dropout.

Study protocols that enhance patient engagement and retention

Before a study even starts, the sponsor can use DCT technology to facilitate the collection of lifestyle and other data to design protocols that best fit patients' lives.

DCTs decrease participant burden (e.g., travel costs, time off work, or time away from family), which makes study participation more attractive to patients and anyone helping them through their disease experience. Reducing visits is especially helpful for patients with limited mobility and for their caregivers.

In the previously referenced NCBI study[8], the retention rate was 89% for the decentralized arm and only 60% for the traditional arm.

DCTs enable investigators to engage with remote patients, providing participants with assurances and investigators with confidence that participants are safe. While patients appreciate face-to-face interactions with heathcare providers, they also appreciate the convenience and greater availability of remote interactions.

Expedited patient identification

Patient identification and outreach have always been significant drivers of the costs and inefficiencies of clinical research. DCTs can alleviate this burden on sites, study sponsors, and patients.

A recent longitudinal study targeting a rare genetic variant of dry age-related macular degeneration (AMD), which affects just 2% of the AMD population, had to screen more than 8,000 patients.[10] Traditional methods would have limited the pool to those living near specific sites or alienated potential participants altogether who, due to their illness, have visual impairments that make driving impossible. The biotech sponsor and CRO therefore designed a digital workflow that allowed patients to be pre-screened at home, opening access to underrepresented populations and decreasing the time needed to recruit patients by 80%. The faster recruitment time also reduced total study costs by $20 million.

Conclusion

Clinical research, wherever it occurs, will always require the expertise and experience of qualified investigators and study personnel. Decentralizing clinical trials to prioritize patient needs ensures a higher-quality, more representative participant population and a more efficient study for all stakeholders so that breakthrough medicines get to patients who need them faster.

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