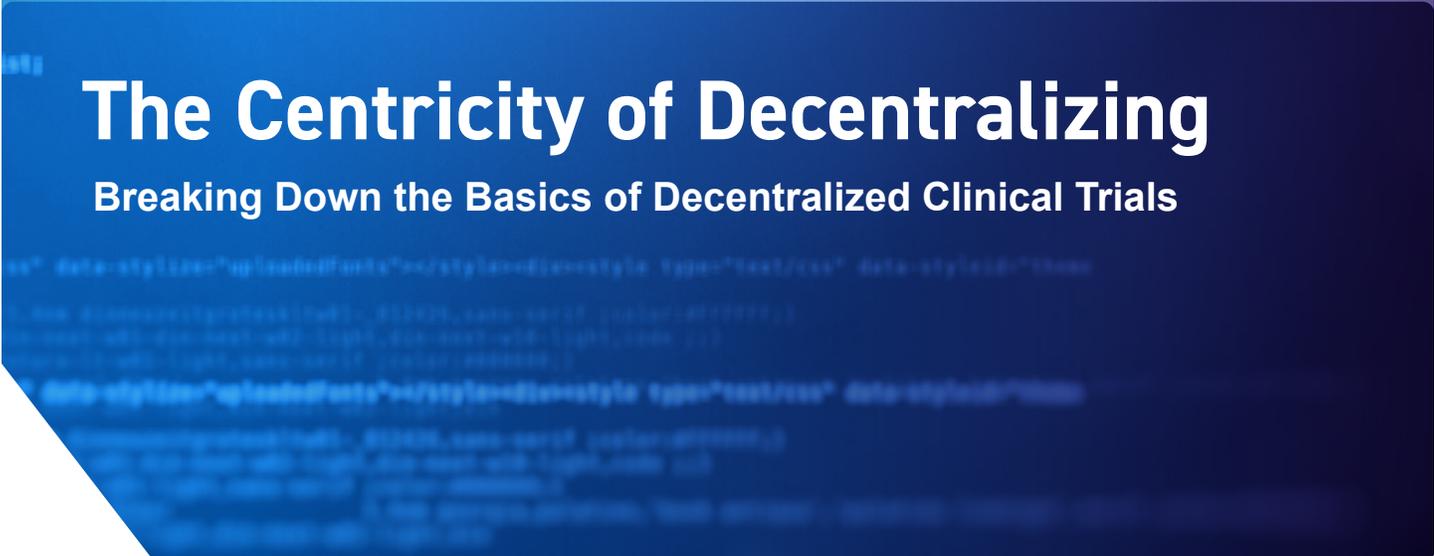




The Centricity of Decentralizing

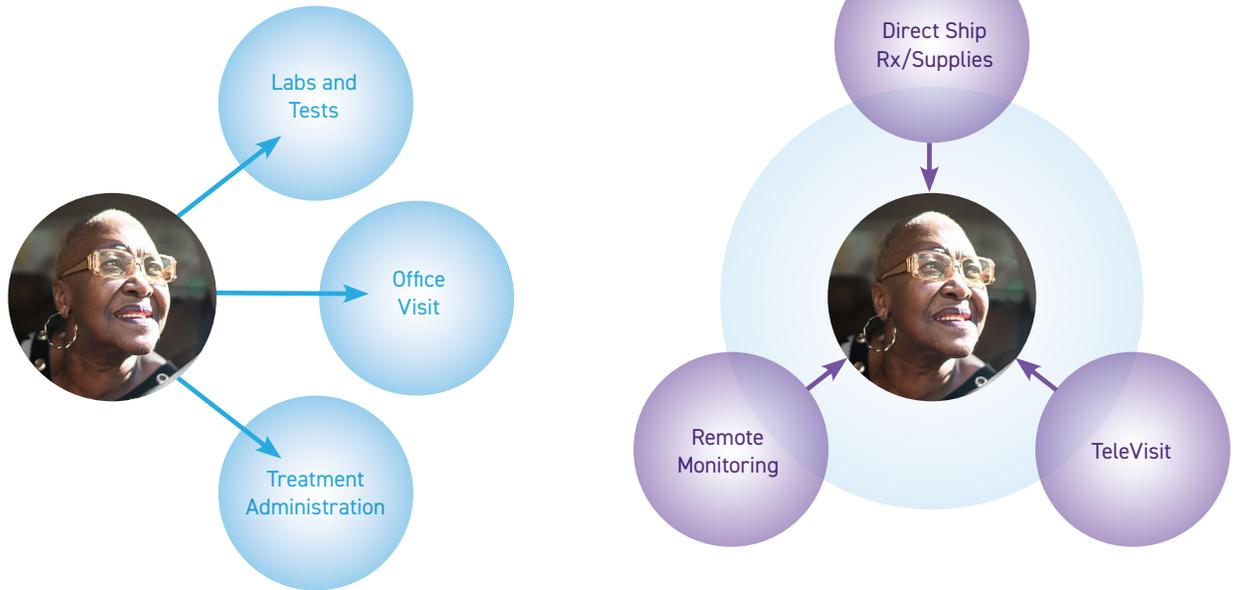
Breaking Down the Basics of Decentralized Clinical Trials





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 (DCT)'. What is all the buzz?

Traditional Clinical Trials → *Decentralized Clinical Trials*



DCTs use technology to enable interactions, which often lead to increasing the quality of the interaction.

Recruitment, retention, diversity, efficiency, safety and accuracy are all factors driving the need for radical innovation. This need is painfully apparent during the current COVID-19 pandemic. We can no longer 'do the same thing and expect a different result'; it is time to take some giant steps forward.

How do Decentralized Clinical Trials (DCTs) work?

There are many interpretations of the term but there is a generally accepted framework of how they are operationalized. Let us start with what it is not. A DCT does not mean a trial without any sites or principal investigators. It is an approach to research that leverages digital technology to treat patients remotely and through hybrid models that often include minimal in-person visits. Inclusion of digital technologies varies by study but can include eConsent, telemedicine, wearable devices, electronic clinical outcome assessments (eCOA), and electronic health (eHealth) records, to name a few. Mobile technologies are often used as electronic diaries and to collect data from wearable sensor devices.

Home health nursing or devices shipped to patients allow the performance of assessments such as blood pressure, ECG and phlebotomy services within the patient's home. These technologies and approaches improve patient centricity of studies by reducing their burden. Patient-centric does not mean we isolate the patient from the investigator. Patients need interaction with trial physicians and staff for reassurance and support. DCTs use technology to enable interactions, which often lead to increasing the quality of the interaction. No patient wants to feel segregated or alone. Patients will continue to want access to the experts conducting the trial.

Technology: Advancing the delivery of healthcare and clinical research

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.



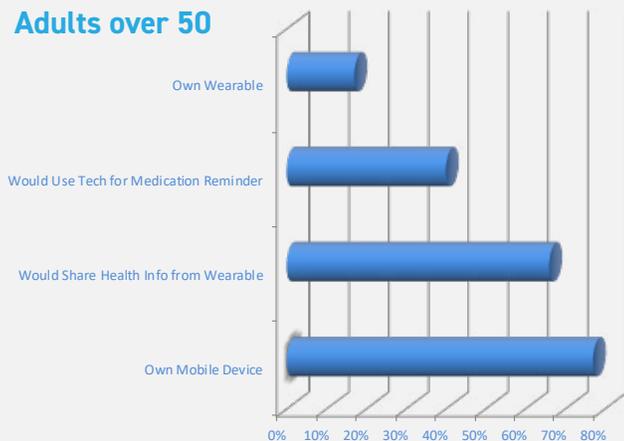
Since the onset of COVID-19, the industry has realized that DCTs are no longer optional. The FDA quickly provided guidelines that not only govern DCTs but also encourage them.

Ten years later, many other avenues 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 1 in 5 physicians use telehealth and by 2022, 61% of those not currently using telehealth indicated they are likely to start. 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. Healthcare providers have learned that delivering care digitally is a great way to put patients at the center of care.

In an effort to be more patient-centric, efficient, and to extend research as a care option, the clinical research industry is quickly adopting a technology-focused strategy. If we are to expand

research to the 80%+ of patients that report they would participate, we must keep pace with the technology they are using and through which their day-to-day healthcare is delivered. The COVID-19 pandemic is further strengthening the use of remote technologies and the public's comfort with it—there will be no going back to 'the old days'. To that end, the Innovative Medicines Initiative (IMI), a partnership between the European Union and the European pharmaceutical industry established Trials@Home to examine the potential of digital technologies utilized in DCTs. The initiative launched in January 2019 and aims to demonstrate that DCTs will improve participant recruitment and retention while also increasing the number of patients from typically under-represented groups. In addition, since data collection will be more continuous the results should be more reliable and representative of the real world.

Adults over 50



Many fear that seniors will resist utilizing the technology required for DCTs. However, an American Association of Retired Persons (AARP) survey published in 2020 says otherwise (Figure 1). Of the 77% that own a mobile device, almost a third use it to manage or receive healthcare. The percentage that own a wearable (17%) may not seem high, but it is comparable to the 18-49 age group (20%), demonstrating that age may not be as significant a barrier to adopting new technologies in research as some perceive it to be.

How do we ensure standardization and regulatory compliance?

Scientific rigor remains the guiding principle of the industry and to that end, a leading authority has been established. The Clinical Trials Transformation Initiative (CTTI) is a public-private partnership co-founded by Duke University and the U.S. Food and Drug Administration (FDA). The initiative includes representatives from

entities involved with providing healthcare and conducting clinical trials and research studies. CTTI works to identify perceived and actual legal, regulatory, and practical barriers to DCTs and clarify and inform policies that affect their implementation. Their final recommendations cover DCT approaches and protocol design, state-level telemedicine issues, drug supply chain, mobile healthcare providers, investigator delegation and oversight, and safety monitoring.



"I think large pharma companies should be thinking about building digital therapeutics groups that will use patient-reported outcomes (PRO) in novel ways to monitor patients' symptoms. This will better allow us to integrate PRO into clinical care with new or existing drugs to catch problems early."

— Dr. Ethan Basch,
Director of the Cancer Outcomes
Research Program, UNC
Lineberger Cancer Center,
in an interview
with Clinical Leader

Transformative value for investigator sites

Investigator 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 physically transitioning patients through in-person visits means that investigators and site staff can be leveraged in more meaningful ways. These activities include providing clinical guidance and support directly to patients, expanding access to potential participants per trial and increasing the capacity for additional studies.

Increased capacity for additional studies

The total number of endpoints in a single clinical trial rose 86% from 2008–2018, according to Tufts Center for the Study of Drug Development, making the burden on sites almost unbearable. Digitizing study processes with tools such as eConsent, TrialFit, eCOA and 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. TrialFit from Medable, for example, is a proprietary telemedicine solution that provides secure, HIPAA-compliant video consultations with clinical study participants in an integrated eCOA solution.

This enables better clinical care and high quality data. The efficiencies and resources gained can be used to expand the number of trials that can be simultaneously conducted.

Expanded trial access and diversity of participants

Distance, travel and participant diversity have long been challenges in recruitment and in developing therapeutics that are generalizable to the population. DCTs allow patients to participate in clinical research from where they are, removing the traditional barriers of travel and geography to accelerate enrollment and increase diversity. In a 2018 study conducted in Switzerland and published by National Center for Biotechnology Information (NCBI), a traditional

model was compared to a decentralized model. The decentralized model recruited three times as many patients as the traditional model and did so three times faster. The patients in the decentralized model also better represented urban and rural areas, whereas the traditional model only consisted of those living near to an existing clinical trial site. These potential benefits apply to trials across all disease states, but are particularly important for rare diseases, as 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 day-to-day life as much as possible without the burden of frequent site visits.

Improved data robustness and accuracy

The apps, wearables and other technologies deployed in DCTs directly track things such as compliance and symptoms, providing more oversight of adherence and enhanced safety monitoring. These tools allow data collection to be frequent, continuous and accurate because we do not rely on patients to remember or even document scheduled visits. This also means DCTs can deliver data from the source, eliminating second-hand data sources and reducing the need for verification. In the NCBI study, 50% of the patients in the decentralized study reported in a survey that the activity patch motivated them to be more active, whereas no patients in the traditional model responded affirmatively.

DCTs can also provide us with insights about how the interventions affect normal life, real-world data (RWD) if you will. For example, perhaps a medication is suspected of causing an immediate but short-term side effect. If the patient is able to self-administer during their regular daily activity, a wearable can record a drop in activity, change in heart rate, respirations or other data points. The patient can use telemedicine to rule out an adverse event and be reassured—thus preventing a dropout.



Improved patient engagement and retention

DCTs decrease participant burden (e.g., travel costs, time off work or away from family), which makes study participation more attractive to patients and anyone helping them through the disease experience. Fewer visits are especially helpful for patients with limited mobility and their caregivers. Since two-thirds of investigator sites fail to meet patient enrollment requirements, according to the Tufts Center for the Study of Drug Development, this is particularly important, especially when considering time to market for a new drug.

Mitigating the fundamental issue of patient convenience, bringing the site to the patient, can not only accelerate study start-up times but also minimize dropouts. This was demonstrated in the NCBI study, where the retention rates were 89% for the decentralized model and only 60% for the traditional model. Enhanced retention is augmented by the technology-driven connection that patients have with their investigator and site staff. Decentralized trials offer choices and facilitate connections. They are enabling remote physicians to engage with remote patients, providing the patient with assurances and the physician with confidence that the patient is safe. The technology serves as an extension of the investigator team, especially through telemedicine.

Expedited patient identification and cost reduction

Patient identification and outreach have always been significant drivers of the costs and inefficiencies of research. Medable has demonstrated that deploying technology remotely can alleviate the burden for sites, sponsors and patients. In a recent longitudinal study targeting a rare genetic variant of dry age-related macular degeneration (AMD) that affects just 2% of the population, 11,000 participants

needed to be identified, pre-consented and screened. Traditional methods would have limited the pool to those living nearby specific sites and required patients to travel, making it difficult to recruit an adequate number of qualified patients in a reasonable timeframe. Through Medable technology, patients were contacted and pre-screened at home, enabling the ability to reach underrepresented populations, reducing valuable time of site staff and improving participant data capture via a mobile app. Genetic tests were also shipped to and picked up from patient homes. **Medable's model resulted in decreased participant burden of time by 5X and reduced study costs by \$20M.**

Decentralized trials, while previously considered a challenging transformation, are beneficial to all stakeholders, and sites are welcoming innovation. In fact, a recent Site Landscape Survey by the Society for Clinical Research Sites (SCRS) revealed that 68% of sites that had been approached about conducting a hybrid virtual trial said 'yes'. The survey also reported that more than half of them would do "whatever is required" to conduct a virtual trial. This is important because according to the Center for Information and Study on Clinical Research Participation (CISCRP) 2019 Patient Experience Report, 75% of patients say that collecting all study data from their own home is appealing and 73% like the idea of a hybrid trial.

Clinical research, wherever it occurs, will always require the expertise and experience of qualified investigators. Our 'patient first' approach is utilized to inform study design, long before the first patient visit. By employing our technology to conduct pre-recruitment assessment data collection, we can understand how people live so that protocols can be customized, essentially delivering precision medicine in research. As with any transformation, collaboration is key and we look forward to enhancing clinical trials with our investigational site partners.

For more information on Decentralized Trials, visit [Medable.com](https://www.medable.com).





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