The Future of Clinical Trials is Digital.

Are You Ready?

TLGG CONSULTING

Contents

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Executive Summary

The traditional clinical research enterprise necessary for the development of new medical technologies is plagued by high costs, lengthy timelines and inefficient, and somewhat ineffective, processes. As a result, clinical trials too often fail—and frequently for reasons unrelated to the safety or efficacy of the investigational product. The cost of this inefficient system is astronomical. Clinical trials account for nearly 40% of the US pharma research budget, totaling approximately $7B per year[1] and significantly contributing to high product costs, which impair product access. Despite the large investments in clinical trials, only 1 in 10 drug candidates that enter Phase I trials will ultimately be approved by the FDA[2]. Some of the drivers of trial failures and, in turn, cost include:

- Difficulties in recruiting trial participants
- Drop-out of participants before completion of trials
- Inconsistent and/or inadequate patient data capture

Many of the pain points driving these failures relate to burdensome and unpleasant experiences for trial participants. Further, barriers to participating in clinical trials disproportionately impact already underserved demographics, including racial minorities and the elderly, rendering it more difficult to recruit and retain representative trial populations and to test technologies aimed at addressing health issues disproportionately present in such demographics. Improving trial participant experiences could lead to improved rates of recruitment and retention, more diverse study cohorts, more robust data and generalizable results, shorter timelines, reduced costs, and increased health equity.

Digital clinical trials (DCTs), simply defined as trials that use novel, digital technologies or processes to enable participation outside of conventional clinical settings, have the potential to address many of the inefficiencies of traditional trials, clearing a path to improved participant experiences and a wide range of benefits to other product developers and other clinical research stakeholders. The COVID-19 pandemic prompted forced innovation in the clinical research space, leading to increased adoption of DCT practices by product developers and associated new regulatory guidance, indicating a growing willingness for regulators to embrace DCT approaches. Potential impacts of DCT approaches include:

IMPROVED RECRUITMENT:

Digital tools can open paths to new and more diverse participant subpopulations, making it easier to fill trials with more representative cohorts, including trials with more strict exclusion criteria that have traditionally presented significant recruiting challenges.

INCREASED RETENTION OF TRIAL PARTICIPANTS:

Reduced participant burden in the form of fewer visits to trial sites, clearer explanations of trial process, improved communications between researcher and participants, and less arduous and more automated self-reporting are patient-centric innovations that reduce participant drop-out and lead to more trials being completed more quickly.

IMPROVED DATA COLLECTION AND ANALYSIS:

Adoption of digital tools and technologies, including automated monitoring and wearables lead to more regular, robust, and reliable capture of safety and efficacy monitoring and data collection, opportunities to collect real-world data previously difficult or impossible to collect, and reduced the burden for trial participants.

OPTIMIZED TRIAL METHODS AND DESIGNS:

Digital tools will enable advanced analysis of trial operations to help determine the most effective methods of participant engagement. In the longer term, artificial intelligence (AI) and machine learning could enable fully virtual trials, or trial arms, conducted in virtual human models. Such evolutions, and their associated cost-savings, could enable product developers to embrace new approaches to research and risk tolerance, as well as allow them to conduct a wider range of activities in-house.

The implications of the growing role of DCT in clinical research are diverse and will impact several stakeholder groups, prompting the need for new business models, new partnerships, new operational processes, and increased prioritization of innovations that focus on improving trial participant experiences. Those impacted will include:

- Product Developers: pharmaceutical companies
- Trial Centers: Hospitals, Universities, and Contract Research Organizations (CROs)
- Digital Experts, Service Providers, and Entrepreneurs

Current clinical research stakeholders should prepare for an increasingly digital trial ecosystem. In doing so, such groups are likely to benefit from guidance by experts in change by way of digitization and optimization of products, services, and systems to improve user experiences.

How the Traditional Clinical Trial Model Fails Product Developers & Burdens Trial Participants

Bringing a new medical technology to market is a lengthy and expensive process. The average pre-tax cost of a new drug is estimated at nearly $2.6 billion (including failures and capital costs)[3]. Developing a new medical technology requires a series of clinical trials, which increases in complexity as a product candidate progresses from Phase I to Phase III. The cost of clinical trials accounts for nearly 40% of the US pharma research budget, totaling approximately $7B per year[1].

It is not uncommon for the full clinical trial phase of a product's development to take a decade or longer. Yet, despite the tremendous resources invested in clinical trials, only 1 in 10 drug candidates that enter Phase I trials will ultimately be approved by the FDA[4].
In 2020, Genfit's elafibranor was unable to show improved patient outcomes in its phase 3 RESOLVE-IT study for non-alcoholic steatohepatitis (NASH). As a result, Genfit reduced its staff by 40% to conserve money[5]. The high failure rates of drug candidates are the leading driver of the costs to launch a new drug.[6]

Brick-and-Mortar Clinical Trial Patient Journey

Recruiting Trial Participants

- Antiquated communications channels.
- Hesitant to engage and unaware of studies

Screening Patients

- Paper pre-screening forms and evaluations
- Takes several weeks and multiple visits just to determine if patient is fit for study

Obtaining Consent of Trial Patients

- In-person signatures with a study team member
- In-office manual process

Retaining Trial Participants/ Enrollment

- Lenghty follow up periods to ensure no relapse or side effects
- Lengthy trials and travel to site is required

Collecting Trial Data

- Manual data entry on “paper”
- Patients burdened with maintanace and sending medical records

Communicating With Trial Participants

- Inconsistent trial summary
- Broken communication; test resullsts not alsways shared

Follow-up Visits

- Office visits for in-person followup required.
- Travel to site, and required to provide updates via manual diaries and memory

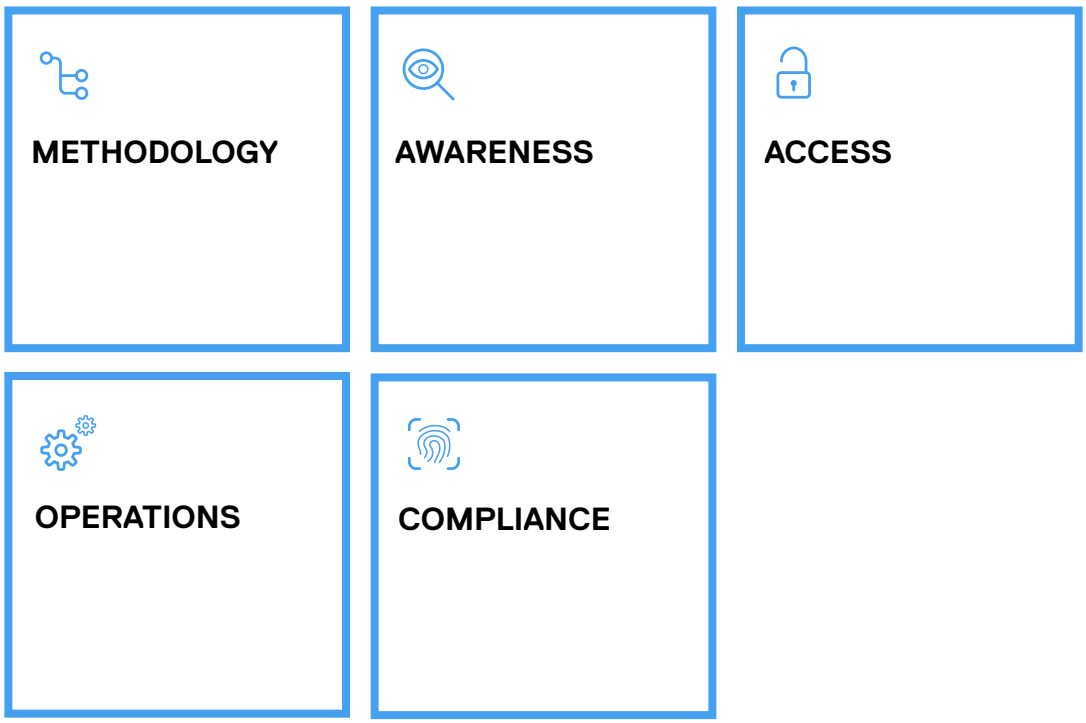
Current Process

Participant Pain point

Why Clinical Trials Fail

Clinical trials fail for a variety of reasons unrelated to the safety or efficacy of experimental technology. The reasons include failure to recruit enough participants, inability to retain participants, incomplete or inconsistent data, or inability to find or maintain trial sites. Several of these pain points point to the participant experience, as trials tend not to be participant friendly because they place significant time, physical, and even resource burdens on participants. Such pain points are present throughout all stages of designing, filling, and operating a clinical trial.

Successful Clinical Trials Hinge On:

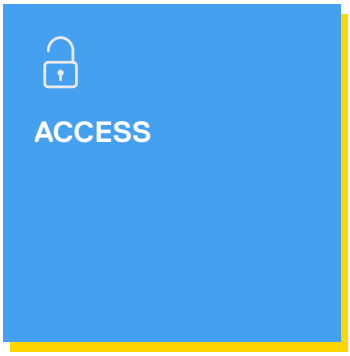


Difficulties in Recruiting Participants

Recruiting participants for clinical trials presents many challenges. In addition to the difficulty of convincing individuals to participate in the trial of an unapproved medical technology, several logistical challenges and research trends present barriers to enrollment as well.

At the most basic level, efforts to raise awareness of clinical trials are largely reliant on antiquated communications channels and tools, such as posters in hospitals and recruitment through the doctor-patient relationship. Thus, many potential trial participants remain unaware of potentially helpful studies for which they could volunteer.

Further, emerging health trends like personalized medicine have led to increasingly complex protocols, often requiring narrow patient populations and resulting in new challenges to recruitment and increased competition for trial sites. An August 2018 Tufts Center for the Study of Drug Development Impact Report found that the total number of endpoints in a protocol increased 86% between 2001-2005 and 2011-2015. [7]



A 2017 analysis noted more than 40,000 clinical studies actively recruiting patients in the U.S. alone. Each trial requires participants to meet specific criteria and some trials require thousands of participants. Considering these dynamics, the finding that 80% of clinical trials are delayed due to recruitment problems is unsurprising.[8] The cost of delays can be staggering, amounting to $600K - $8M USD for each day that a trial delays a product's development and launch.[9]

Many trials will fail to recruit the requisite number of patients and therefore fail without having a chance to test a potentially life-saving medical technology. 85% of all clinical trials fail to recruit enough patients[10] and up to 50% of sites enroll one or no patients in their studies![1]

Trial failures due to lack of enrollment are particularly tragic from both a health and financial

perspective when late-stage trials are unable to recruit participants. Roughly one-third of Phase III clinical studies are terminated because of enrollment difficulties.[11] By the time a candidate has reached Phase III trials, it has generated significant efficacy and safety evidence and has been heavily invested in by its sponsor. The failures of Phase III trials are both disappointing to those who could stand to benefit from the experimental technologies they are designed to test and financially disastrous for product developers.

Failure to Retain Participants

Once trial participants are enrolled, ensuring they complete the trial presents additional challenges. Trials are often lengthy and require significant numbers of site visits, often including long periods of follow-up to ensure lack of relapse or emergence of longer-term side effects.

The logistical and time burdens of participating in a traditionally designed clinical trial can't be overstated. For example, 70% of potential participants in the United States live more than two hours away from the nearest study center[12]. In other cases, patients with conditions that impair their mobility may be unwilling to travel to trial sites. Participants may find themselves unwilling to continue to invest the time in repeatedly traveling for site visits and follow-ups. In some cases, participating in trials presents a financial burden to a participant, either in the forms of resources required to travel to sites or in opportunity cost due to the time spent participating in the trial that could otherwise be monetized. As a result, the average patient drop-out across all clinical trials is around 30%.[1]

By the time a participant drops out, the study sponsor has already invested substantially in that person in the form of recruiting, screening, and administering of treatment. 43% of clinical trial experts consider participant compliance with the trial a main challenge.[1] Discontinuing therapy mid-trial is also potentially dangerous to a participant, who may then go untreated. For example, incomplete treatment in the case of antibiotics is conducive to the development of drug resistance.

Insufficient Infrastructure & Communications with Participants

Despite the high costs and increasing complexity of clinical trial operations, many clinical trial activities have failed to evolve over past decades. Some of the areas plagued by antiquated methods and techniques include raising awareness of trials, data collection, storage, and interoperability, and communication with stakeholders, including participants. Often, the lack of modern operational infrastructure and tools negatively impacts the participant experience in a clinical trial.

For example, many clinical studies still use rudimentary data collection and verification methods, burdening trial participants with tasks such as maintaining and sending personal medical records (often via older technologies, like fax machine), keeping diaries to determine adherence to experimental treatment regimens, and keeping track of remaining treatment courses. Furthermore, researchers often rely on paper-based forms, meaning participants must fill them out on site, presenting challenges to storage and integration into databases.

A 2017 study by Center for Information and Study on Clinical Research Participation (CISCRP) on trial participant experiences found that only 18% of trials implemented text messaging and only 17% provided the Informed Consent Form (ICF) via tablet. Only 10% of studies utilized smartphone apps and 8% utilized wearable devices. While trial participants maintain that receiving a study summary after participation is very important, 53% never received a report or an update on the study results after trial completion; about a quarter of study participants reported never receiving any updates while they were enrolled.[13]

The reliance on analog tools and methods common to traditional clinical trials results in poor participant experiences for trial volunteers and fails to meet best practices for researchers to ensure complete, timely, secure, and accurate data collection.

Dynamics in Low- and Middle-Income Settings

While this analysis focuses on US-based clinical trials, it is important to note that many of the challenges and costs associated with carrying out clinical research are even more acute in low- and middle-income settings. Additional challenges to recruiting and retaining trial participants can emerge when working across cultures and navigating less robust and resilient local health systems and research environments.

When operating in low-resource settings, investment in building local capacity and infrastructure to conduct clinical research is often a prerequisite to launching studies and maintaining capacity post-trial is a challenge. Poverty also creates additional challenges to participant recruitment and retention. However, given the level of human and financial resources required to ramp up and conduct research in these settings, the inability to recruit and retain patients or complete studies can be serious setbacks for researchers and product developers looking to target interventions for these markets.

The Emergence of Digital Clinical Trials (DCTs)

Clearly, the clinical trial system is in need of modernization. The growth of digital tools and artificial intelligence may be the key to doing so. The 2007 Clinical Trials Transformation Initiative (CTTI)[14] was founded with the aim of generating novel ways to increase the quality and efficiency of clinical trials. However, for years since its launch, the adoption of innovative research strategies by product developers remained limited.

While elements of a decentralized clinical trial paradigm have been established, since the formation of CTTI and other stakeholder pushes to modernize the clinical research space, these elements have not been widely integrated. Trends like mobile and home healthcare as well as alternative care locations established infrastructure through which increasing decentralization of clinical trials was possible. In addition, advances in technology, including eConsent, electronic clinical outcome assessment (eCOA), data storage and privacy, connectivity, and communications devices and platforms enable digitizing and decentralizing of clinical trials.

Recently, the COVID-19 pandemic proved a major catalyst to changing the infrastructure of and approach to clinical trials. Perhaps the signature change has been the increased integration of digital tools and decentralized methodologies within clinical trials.

Going forward, DCTs have the potential to transform clinical trials, lower their cost, and speed new medical technologies to those who need them.

What is a Digital Clinical Trial (DCT)?

Simply stated, DCTs use novel digital technologies or processes to enable participation outside of conventional clinical settings. DCTs adhere to several key principles including:

Decentralization	Participant-Centricity	Efficiency	Interoperability
A digital trial will enable access for participants with less importance on where they live or work.	Digital trials aim to improve the participant experience, making it easier for a participant to join and complete a trial.	By digitizing and simplifying processes, digital trials aim to reduce the length and cost of trials and drive higher rates of trial completion.	Digital trials are enabled by a direct exchange of information between systems.

It is instructive to note that digital trial tools and approaches are correlated but not synonymous with decentralized trials. The trends to digitize and decentralize trials are synergistic. While the term "decentralized" generally refers to reducing the need of participants to visit the trial center(s), "digital" trials focus on the use of digital technologies to improve participant experiences and better answer research questions. Digital tools are often means of enabling the decentralization of a trial, but decentralization can be achieved in non-digital ways as well. For example, sending researchers to trial participants' homes to collect data as opposed to asking participants to visit trial centers would further the decentralization of clinical trials, though such a modification would not make a trial more digital. This analysis focuses mostly on digital trials and digital trial tools.

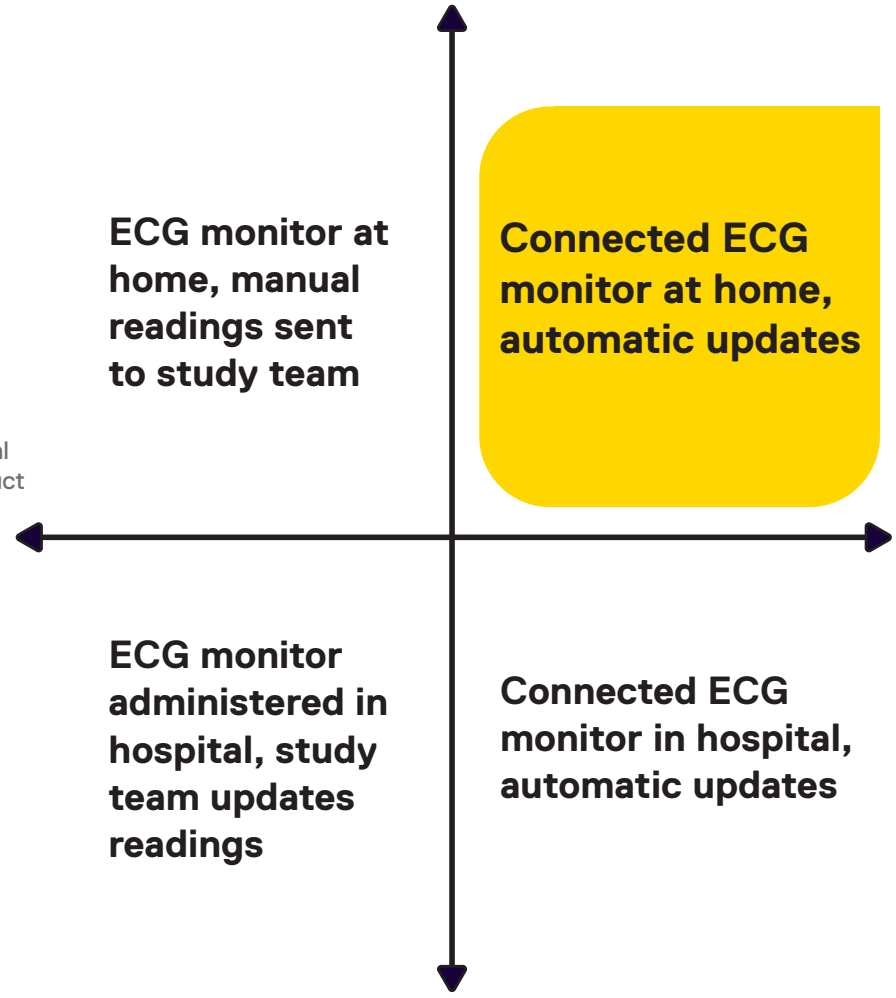
It is also important to note that clinical trials may incorporate some DCT elements while retaining elements of a traditionally designed trial. Elements of a trial that may be digitized include but are not limited to data collection and analysis, recruitment, retention, stakeholder communication, efficacy and safety monitoring and biomarkers, and cohort randomization. Trials currently making use of DCT approaches tend to be and are likely to remain in the short- to mid-term, hybrid trials.

In coming years, a greater proportion of overall trials and a greater proportion of activities within a given trial will utilize DCT approaches. However certain trials that involve serious illnesses, or complex or invasive procedures, such as advanced imaging and biopsies, or that pose significant risk to participants will continue to require close oversight by researchers and clinicians. Therefore, the opportunity and path for integration of DCT methods is not uniform across all trials.

Scenario: Measuring Participants' Heart Function

Remote

Clinical trial activities taking place outside of a traditional site, allowing the study to be conducted from afar



Analog

Using traditional, manual methodologies to conduct aspects, or all, of the clinical study

Digital

Leveraging technological capabilities to conduct aspects, or all, of the clinical study virtually

On Site

Clinical trial activities taking place at a traditional trial site, requiring participants to travel to a fixed location

The Transformative Potential of DCT

DCT approaches have the potential to revolutionize many aspects of clinical trials, including participant recruitment and retention, safety monitoring, data storage, stakeholder communications, and trial methods and design.

Recruiting Diverse Participants

Recruiting heterogenous participants is a longstanding challenge in clinical research. This issue is particularly relevant for medical conditions that disproportionately affect patients according to race, sex and economic background. Traditionally, trial enrollment rates may be reduced when enrolling a representative population is prioritized, thus hard-to-reach populations are often excluded from studies even when they represent the most appropriate participant groups.

To effectively develop therapies for all patient groups, enhance health equity, and ensure the validity of results across diverse populations, it is important to increase the diversity of trials. Digital tools could enable more tailored communications to reach and recruit specific subpopulations and modernized digital health and social media platforms to increase awareness of trials, while remote monitoring could increase participation for patients who require assistance to get to study sites, including many older patients.

The Need to Improve Equity in Cohorts

Black Americans represented less than 4% of all patients enrolled across multiple trials that supported the approval of immune checkpoint inhibitors for the treatment of lung cancer, despite previous studies indicating black Americans represented more than 10% of deaths from lung cancer[16] and that proportionate rates of lung cancer were higher among black Americans than white Americans.[17]

An estimated 40% of all cardiology clinical trials exclude older adults[18], despite older age being a well-established factor associated with cardiovascular risk.

Regulatory guidance has been issued on the use of new technologies in obtaining informed consent[19], but similar guidance for recruiting study participants has yet to be issued. However, progress is being made in this area despite this lack of clarity. For example, the SWOG Cancer Research Network proposes the incorporation of a social media toolkit for new clinical trials.[20]

Increasing Retention of Trial Participants

Challenges to retaining trial participants are various. Some challenges are largely material and logistical, such as length and schedule of clinic visits, time spent traveling to visits, and lack of renumeration or out-of-pocket cost of trial participation. Other reasons for participant drop out center on communication or trial literacy issues, such as randomization and assignment to a placebo arm, misinterpretations stemming from poorly executed informed consent processes, or myriad other confusions relating to the clinical processes. Decentralized trials offer the potential to help address each of these challenges, with digital tools at the heart of the opportunity.

Digital Tools Can Drive Retention of Trial Participants

- Digital tools to enable more trial activities to be completed at home or in local sites, reducing the need for site visits
- Digital tools, including video, to help improve informed consent
- Digital applications to enable easier, more frequent, and more efficient outreach to participants—including forums where participants can get answers to their questions about the trial and trial process.
- Digital provision of payments

Improving Data Collection and Analysis

One of the areas in which digital tools can have the greatest impact on the clinical trial process is in data collection. Digital tools can streamline the collection of data, collect more and diverse real-world data, and reduce the need for participants to visit trial centers. Additionally, the ability to share these data across interoperable networks would create new opportunities to inform and improve future research, interact with electronic medical records to proactively recruit participants and improve health outcomes, and recognize emerging data patterns in real time. The types of data collected digitally could encompass anything from clinical and demographic data, sensed physiological and activity data, patient-reported outcomes and images collected via a smart phone or tablet, electronic medical record data from a vendor API, or biological samples drawn at home or in a local lab[21]. Some examples of these data include:

Digital monitoring of biomarkers

A patient self-report that can be acquired using digital technology and "evaluated as an indicator of normal biologic processes, pathologic processes, or biological responses to therapeutic interventions" is known as a digital biomarker[22] [23]. Examples of digital tools enabling monitoring of biomarkers include wearable sweat sensing for glucose, lactate, and electrolytes[24], and cardiogenic chest wall vibrations to assess clinical status of patients with heart failure.[25]

Additionally, digital technologies can enable the collection of previously unobtainable data. Recently the Food and Drug Administration (FDA) approved digital approaches to detect rhythm abnormalities, such as atrial fibrillation, through sensors in the Apple Watch, including electrodes for electrocardiography and optical sensors for photoplethysmography[26] [27].

Safety monitoring in digital clinical trials

The ability of digital tools to continually collect data and transmit it to researchers can improve the likelihood of detecting infrequent events or events that are most likely to occur outside a traditional trial setting. Increasing the accuracy and speed of detecting adverse events, and expanding the scope of events likely to be identified could accelerate the completion of trials and make for safer and less burdensome experiences for trial volunteers. CTTI has published recommendations relating to data collection from mobile technologies[28].

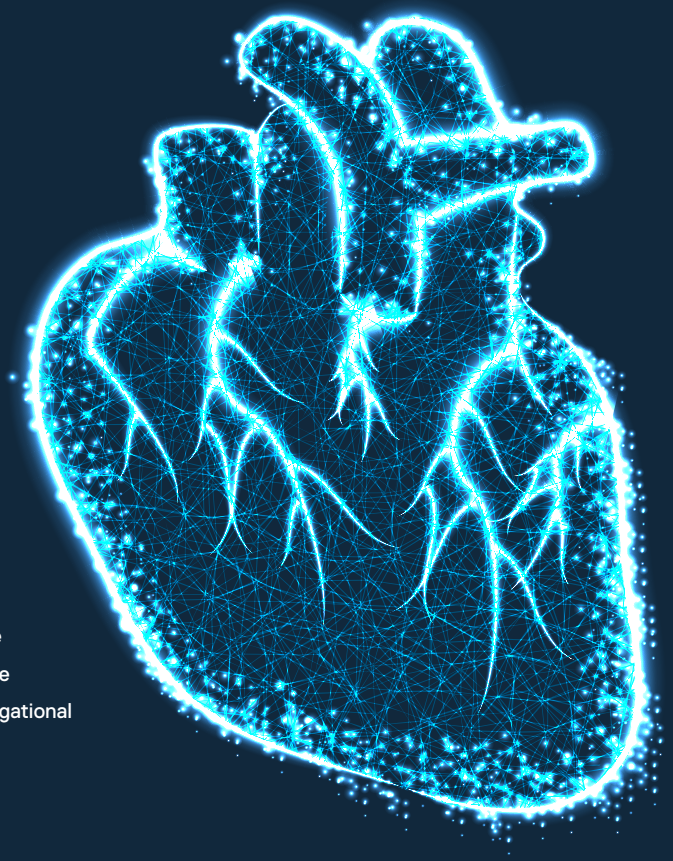
Some of the core principles include:

- Using evidence-based approaches
- Collecting appropriate data while maximizing privacy
- Developing plans to optimize data collection, including how to deal with missing data
- Having a plan for the analysis of all data captured
- Establishing common metrics, norms, standards around digital data collection

Recruiting Digital Twins

One technology that is beginning to find real world applications in transforming the data collection and analysis in clinical trials is “digital twins.” These are virtual representations of an object or system across its life cycle. In the case of clinical trials, there can be digital twins of individuals or even organs.

Unlearn.AI, a startup building digital twins for clinical research, “administers” a placebo to cohorts of digital twins to compare an intervention with a patient baseline. Whereas Dassault Systèmes has built a digital twin of the heart to evaluate artificial heart valves. These tools could potentially reduce the size of human control groups needed to conduct trials, improve data capture, and boost enrollment by offering the investigational product to all participants.



Leveraging EHRs, wearables, and digital tools to improve real-world data collection

By implementing digital technologies within clinical trials, researchers will be able to plug into additional participant data collected and housed in their electronic health records (EHRs). With the expanding role of EHRs in healthcare, the potential for researchers,

clinical providers, and trial participants to connect apps and various points of the health system through EHR platforms is growing. Data from sensors and mobile devices, patient-generated data and patient-reported outcomes all could become more routine in trial markers and endpoints as researchers harness this capability.[29]

Enabling advanced analytics through AI and machine learning

Machine learning and artificial intelligence can power advanced analytic methods to aid clinical trial design and operations. For example, algorithms can automatically infer sub-types, increasing the personalization and accuracy of detection methods.
Similarly, learning methods can be developed to support adaptive trial design. Advanced analytic methods can be used to better match participants to studies, improve data-based decision-making, and enhance researchers' abilities to interpret trial results.

Optimizing Trial Methods and Design

The adoption and implementation of digital tools can impact the way clinical trials are designed and the methods used within the trial to communicate with stakeholders and ensure their compliance. Digital tools can be used to analyze and optimize the delivery of digital trials tools, and ultimately power entirely virtual trials and experiments using virtual human models.

Optimizing trial methods and digital trial technologies

Digital approaches can dramatically impact the administration of trials, often leading to increased personalization in trials, which aligns with the overall trend toward more personalized medicine. For example, methods such as micro-randomization. can be used to optimize and personalize the delivery of digital trial tools such as reminders and engagement strategies for recruiting, enrolling, and retaining trail participants. Trial coordination and operations will move away from roles like "site coordinator" in favor of "trial community managers," who oversee engagement with increasingly decentralized trial participants.

In silico clinical trials

In the long term, digital tools can unlock the path to full in silico trials—an individualized computer simulation that can aid in the development or regulatory review of a new medical technology. In such a trial, virtual treatments would be administered to virtual patients and observed through advanced computer simulations to determine whether the intervention is safe and effective. In silico trials could reduce the size and cost of clinical trials while improving the predictive value of trials by:

- Enabling greater specificity in medical or demographic characteristics of participants
- Increasing the ability of trials to reach participants with rare diseases, characteristics, or conditions that make participation in traditional trials especially difficult
- Enabling the observation and prediction of longer-term effects of an intervention through simulations
- Offering greater insight as to why a product fails, increasing the likelihood experimental products that experience failure could be refined as opposed to abandoned[30]
- Improving safety through use of virtual human models
- Reducing cost and increasing predictivity of early-stage research through use of virtual human models that can be used indefinitely and scaled infinitely

Regulatory and Institutional Embrace of DCTs

The rise in DCTs has prompted regulators to be more accepting of DCT data. For example, the FDA recommendations for Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency includes guidance for implementing decentralized data collection tactics.[31] Additionally, the NIH has made pragmatic trials, which include the use of digital technologies, a priority[32] and urged trialists to responsibly adopt digital technologies and other pragmatic features[33] that disrupt and create efficiencies while maintaining the strength of the randomized clinical trials enterprise.[34]

Implications of Expansion of DCT: How Various Stakeholders Can Prepare

The implications of the expansion of DCTs will be both broad and deep, impacting many different stakeholders across the clinical research ecosystem, all in various ways. Stakeholders impacted will include:

- Product developers
- Current trial sites (including hospitals and universities)
- Contract Research Organizations (CROs)
- Digital Experts and Digital Service providers
- Entrepreneurs

The facets in which the expansion of DCT will impact these stakeholders can be grouped into three main categories:

- Needs for new partnerships, collaborations, and acquisitions
- Opportunities to evolve or create new operating models, organizational structures, and skillsets
- Increased focus on trial participant experience

Proactively embracing DCT and preparing for its impacts will be critical for players across the clinical research ecosystem to expand and maintain their roles and to properly organize and outfit their organizations to thrive in a digital research environment. This means there is also an important role for futurists and organizations, like TLGG, which specialize in identifying change by way of digitalization and helping organizations prepare for it, and thus to assist clinical research stakeholders navigate the transition to DCT.

Clinical Trial Ecosystem

*Illustrative

Investing in New Partnerships

As DCT expands, proficiencies relating to digital tools and environments become higher priority. While organizations will likely seek to build some of this capacity in-house, many of these needs will need to be met through new partnerships, collaborations, or acquisitions. This creates opportunities both for product developers and service providers. Some of the areas of elevated importance are likely to be:

- Creating seamless workflow across remote sites and wider partner networks
- Streamlining of trial processes, including sample collection, participant monitoring, obtaining consent
- Improving data sharing and security; building interoperable systems
- Developing digital tools to improve participant experience
- Training researchers and trial participants in best practices for use of digital tools
- Forming DCT advisory boards to address best practices and ethical considerations

Who is Impacted?

Product Developers:

Product developers will need to determine which capabilities to build in-house and which to fill through partnerships, joint-ventures, or acquisitions. Cost-savings enabled by DCT approaches could allow product developers to embrace bold, new approaches to research and alter organizational approaches to risk tolerance, while advances in AI and machine learning may also allow pharmaceutical companies to conduct a wider range of activities in-house, thereby reducing their reliance on traditional CROs. Operationally, R&D Leadership Teams will be in the best position to identify needs and advise on services to adopt or acquire, while C-Level Executives will determine strategic visions and organizational approaches to partnership.

Hospitals, Universities, and CROs:

Capabilities of trial centers to work seamlessly with increasingly remote trial participants will be key, as physical trial centers will play a reduced but still important role in trials. This may enable sites well-equipped for remote operation to participate in more trials. Trial centers with strong infrastructure to enable reduced participant visits and staff well trained in the required technologies and ethical considerations central to DCT will be best positioned to thrive in the transition.

Digital Experts, Service Providers, and Entrepreneurs:

Organizations and individuals with expertise in fields such as data security, building

user-friendly digital tools and communication platforms, digital ethics, or those with visions for new digital health technologies will be presented with new opportunities to be further engaged in clinical research and medical technology development.

How Stakeholders Can Begin Preparing Now

Stakeholders should prepare for change by:

- Analyzing industry trends and best practices
- Developing strategic visions for new approaches to partnerships
- Identifying industry-leading partners that can enhance digital capabilities of product developers
- Engaging experts for guidance on capabilities and infrastructure to be developed to position organizations as attractive partners for other players in the DCT space.

Optimizing Operating Models for DCT Engagement

Successfully scaling DCT approaches within organizations will rely on making proactive and appropriate pivots internally to identify and empower the best people, processes, and tools to thrive in the DCT space.

Who is Impacted?

Product Developers:

Product developers will need to recruit new employees with new skills sets and knowledge relating to conducting remote trials and/or train existing employees in new areas, including digital ethics, digital tool proficiency, digital-based communications, online marketing (recruiting), trial community management, and outpatient-based care and oversight. This may result in shifts in the way research teams are organized and how trials are managed. Additionally, as the use of digital clinical trial platforms grows, organizations that control such platforms and underlying technologies, such as operating systems or algorithms, and scale them across the industry will be positioned for new growth areas, as well as for increased influence on trial operations and access to participant data, such as electronic medical records. Pharmaceutical companies looking to capture this lucrative and influential standing will likely not only have to compete with other pharma companies, but also traditional platform developers like Amazon and Google.

Hospitals, Universities, and CROs:

As the roles of trial centers evolve, their value propositions do as well, thereby opening new operating model opportunities. Trial centers will have to determine which types of DCT studies are most appropriate in which to pursue participation and tailor staff and technologies accordingly. This may lead to changes in the composition of trial teams. Trial centers that distinguish themselves as leaders will potentially be able to develop training programs for DCT preparation and compliance and other similar new business models. In some cases, trial centers may even seek to develop and validate their own proprietary models or tools to support DCT activities.

How Stakeholders Can Begin Preparing Now

Stakeholders should prepare for change by:

- Developing change management plans for new team structures and governance models to support growth of DCT capabilities, the development of policies, SOPs, and training of employees [methodology, awareness, access, compliance, operations]
- Piloting, pressure testing, and validating potential new digital processes, partners, and tools [methodology, awareness, access, compliance, operations]
- Identifying new potential DCT-specific obstacles to participant recruitment and retention, and developing plans to proactively address concerns [access, compliance, operations]
- Strengthening internal capacity to build digital platforms

Real World Case Study

From Managing Sites to Managing Communities

The role of trial site coordinators is likely to evolve into trial community managers, as trial participants will be less defined by their interaction with site centers. These new roles will be defined by utilizing digital tools to oversee and optimize participant engagement and compliance across a wider range of trial activities among a more decentralized and diverse participant community.

Increased Focus on Participant Experience

The chief benefits of DCT approaches for product developers are faster, cheaper, and more generalizable trial results, but these benefits are only possible if potential participants volunteer for and complete trials. Increased rates of participation and compliance will be driven most significantly by offering participants an improved experience.

Who is Impacted?

Product Developers

Product developers will need to determine how and how much to digitize trials. In addition to considering regulatory guidance, when considering which digital tools to implement or trial processes to decentralize, a leading criterion should be which modifications most improve the participant experience.

Hospitals, Universities, and CROs

Trial centers with proficiency in telehealth, remote capabilities and support for trial participants, and demonstrated commitment to DCT and participant-first strategies and tools will emerge as the partners of choice for product developers looking to expand DCT approaches.

Real World Case Study

Bringing Seamless Workflows to Trial Participants' Homes

UPS Healthcare's clinical trial logistics unit, Marken, recently announced a partnership with THREAD, an innovative DCT tech provider, to deliver a decentralized clinical trial solution into patients' homes. It creates a seamless workflow for clients and patients, enabling patients to coordinate all aspects of a trial, from consent to sample analysis, with a single entity[35].

Digital Experts, Service Providers, and Entrepreneurs

Individuals and organizations that specialize in improving user experience will be of utmost value to facilitating an effective transition to DCT. Entrepreneurs looking to develop interfaces, APIs, devices, and systems that improve user experience and are compliant with DCT principals and regulatory guidance will be presented with an expanding market for their products.

Real World Case Study

Specialized Advisory Boards Provide Key Insights to Improving DCTs

Syneos Health's Decentralized Clinical Trial capabilities include a dedicated Decentralized Clinical Trials Site Advocacy Group designed to engage with sites and community stakeholders, including patients and advocacy groups. The goal of the Site Advocacy Group is to move clinical trials closer to patients by adopting new and innovative mobile, digital and telemedicine capabilities that better inform decentralized protocol design, data capture, and patient retention strategies[36].

How Stakeholders Can Begin Preparing Now

Product developers should analyze which aspects of the patient experience most drive participation and completion in trials and identify opportunities to effectively and efficiently implement participant-first approaches, tools, and trial designs.

Hospitals, universities and CROs should move to adopt patient-first tools, and implement patient-first approaches in clinical operations, both to improve participant experience and to position themselves as partners of choice for product developers using DCT approaches.

Digital experts and service providers should identify opportunities for partnerships with researchers and trial centers.

Entrepreneurs should study the markets, target product profiles and ethical and regulatory concerns of their target customers to enable them to continue to create valuable new tools and services to aid the transition to DCT.

TLGG Predicts

By 2028, the global virtual clinical trials market size is expected to reach $11.5 billion with a CAGR of 5.7% from 2021 to 2028.[37] The lingering COVID-19 pandemic is projected to continue impacting clinical research operations, meaning the trends of forced innovation toward DCT tools and methodologies are poised to continue. The disruption of the traditional clinical research ecosystem will continue and lead to a reorganization of roles and operating models for players in the space.

- Pharmaceutical developers who lean into this shift can be rewarded with cost-savings, growth opportunities, and expanded roles in clinical development, as the shifts to DCT present potential to bring more trial activities in-house.

- CROs, hospitals and other trial centers have the potential to establish themselves as early-adopters and DCT leaders, positioning themselves for growth through additional workstreams and development of proprietary tools and processes. However, these same stakeholders face a potential overall reduction of roles in the clinical research process. Therefore, it is likely the players within this sector experience more extreme stratification between winners who capture new opportunities and losers who fail to adequately protect their current roles.

- The need for new digital and participant-first tools creates opportunities for experts and entrepreneurs to enter the space and earn influence through control of key products, services, and platforms. With both money and power on the line, this race will attract traditional industry players, start-ups and other disruptors, as well as established tech giants.

TLGG specializes in identifying change by way of digitalization and helping organizations prepare for it and would be excited to work with clinical research stakeholders intent on expanding their DCT capabilities and seeking assistance in ensuring a smooth and effective path to do so.

Table:

Digital Trial Tools and Their Potential to Relieve Pain Points in the Clinical Trial Process

	Benefits to Trial Participants	Benefits to Product Developers
Recruiting Trial Participants	Increased awareness of planned and ongoing trials allows for increased participation	• Increased pace and scale of recruitment leads to more trials meeting enrollment targets and schedules • Enhanced ability to reach traditionally unrepresented participant groups can overcome diversity gaps in trials, leading increasing validity and generalizability of trial results
Obtaining Consent of Trial Participants	Easier, more seamless and personalized consent process improves comprehension of materials and reduces burden on participants	• Easier to administer, collect, translate, and store Informed Consent forms. • Improved comprehension of consent forms decreases likelihood of subsequent dropout from trial
Retaining Trial Participants	Reduced number of visits to trial centers enabled by digital tools address common reasons for default, such as length of commute and schedule or trial	• Reducing burden on trial participants increases likelihood of completing trials, doing so more quickly, and reduces sunk cost of investments in recruiting and enrolling participants who fail to complete trial
Collecting Trial Data	Digital monitoring devices relieve burden from trial participants by automatically reporting data and eliminating or reducing need for self-reporting and visits to study centers	• Automatically collected, objective data makes data collection more robust, regular, and reliable • Application of new tools enable the collection of real-world data that was previously difficult or impossible collect, as well as the collection of data in real-life settings
Safety Monitoring	Improved safety monitoring reduces risk for participants and mitigates hesitance to enroll in or complete studies	• Enhanced safety monitoring technologies enable the faster and more accurate identification of side effects and adverse events, improving safety for trial participants, generating more robust data, and leading to quicker and better-informed go/no-go decisions
Communicating with Trial Participants	Additional pathways for communication keep trial participants better informed of trial questions, status, and results, and offer tools and forums to have their questions and concerns addressed	• Digital communications platforms enable continuous communication with participants, driving compliance and trial completion. • Digital tools offer new technologies to implement trial tools such as reminders and engagement activities

Table (cont.):

	Benefits to Trial Participants	Benefits to Product Developers
Analyzing Trial Results	Clear and rapid interpretation of trial results enhances value proposition of trial participation and improves participant experience through increased engagement	• Digital tools, machine learning, and AI enable new, complex analyses of data capable of identifying new relationships data across systems and more clearly answering research questions or identifying future research needs.
Trial Design	Digital tools enable the development of patient-centric trials that reduce participant burden	• Digital tools enable shorter, quicker, and more adaptive trials that more effectively and efficiently investigate research questions
Financial Implication	• Reduced participant burden minimizes costs and opportunity costs associated with participation in trial. • Participants can receive compensation electronically	• Cost savings enable more research and reduce prices of new products
Speed of Trials	Faster trials reduce participant burden.	• Faster completion of trials lowers cost and speeds research process, which enables new products to reach those in need faster.

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