THE FUTURE OF MEDICINE: EXPLORING THE ACCELERATION OF DRUG DEVELOPMENT WITH DECENTRALIZED CLINICAL TRIALS

CAPSTONE PROJECT REPORT

Presented to the Education Council of the

School of Biomedical Sciences

University of North Texas

Health Science Center at Fort Worth

in Partial Fulfillment of the Requirements

For the Degree of

MASTER OF SCIENCE

IN CLINICAL RESEARCH MANAGEMENT

By

Opemipo Ajape

Fort Worth, Texas

November 2023

Acknowledgement

I would like to express my heartfelt gratitude to Dr. Stephen Mathew, our esteemed Program Director, for his unwavering support and guidance throughout my academic journey. Dr. Mathew’s mentorship and dedication to our program have been instrumental in shaping my educational experience.

I would also like to extend my deepest appreciation to my major professor, Dr. Roxanne Zascavage, PhD. Dr. Zascavage's expertise, encouragement, and tireless commitment to my academic and research pursuits have been truly invaluable. To my amiable site mentor, Dr. Obinna Odoemena, your mentorship has been a source of inspiration and knowledge that has enriched my educational endeavors. I appreciate you.

I am profoundly grateful for the opportunities and knowledge that Dr. Mathew, Dr. Zascavage and Dr. Odoemena have provided, which have been instrumental in my academic and personal growth. Their support and guidance have been instrumental in shaping my academic journey, and for that, I am truly thankful.

Abstract

The present study explores the transformative potential of Decentralized Clinical Trials (DCT) within the field of medical research. The primary objective is to investigate how the adoption of DCT influences efficiency, patient engagement, and data quality in medical research. DCT offers the potential to streamline data collection, reduce administrative complexities, and overcome geographical constraints. This is achieved through real-time monitoring, electronic data capture, and remote data gathering techniques, making it particularly advantageous in complex scenarios like rare disease research. These efficiencies can expedite drug development, ensuring timely access to novel treatments; however, concerns about data security and privacy must be addressed to sustain these benefits.

Patient engagement is a significant advantage of DCT. It allows patients to participate in research remotely, removing geographical barriers and promoting inclusion. The patient-centric approach in DCT design enhances diversity, recruitment, and retention rates. Nonetheless, maintaining patient engagement may be challenging due to limited face-to-face interactions with healthcare professionals. Data quality in DCT depends on methodologies that generate substantial data, but this complexity requires advanced analytics.

DCT emphasizes a practical approach to clinical research, prioritizing patient care and valuable data collection. Ensuring the exclusion of ineligible or fraudulent participants, especially in cases involving financial incentives, is crucial. The implementation of Decentralized Clinical Trials holds the promise of fundamentally transforming medical research by enhancing efficiency, inclusivity, and data-centricity in trials. While challenges exist, current research suggests that the advantages of DCT outweigh the obstacles, paving the way for advancements in medical practices.

Table of Content

Introduction

Clinical trials are a fundamental pillar of medical research, providing a robust structure for assessing the safety and effectiveness of novel therapies and interventions. Historically, the execution of these studies has followed a centralized, site-based approach, necessitating patients to attend designated healthcare establishments for evaluations, interventions, and data gathering (de Jong et al., 2022). Although this methodology has shown to be fruitful in generating significant knowledge and facilitating breakthroughs that potentially save lives, it has inherent difficulties and obstacles.

Recently, there has been a notable change in clinical trials due to the advent and widespread acceptance of Decentralized Clinical Trials (DCT). The use of DCT signifies a deviation from the traditional framework, capitalizing on technological advancements to provide trials that prioritize patient needs, enhance efficiency, and rely on data analysis (Dorsey et al., 2020). The primary objective of DCT is to facilitate the accessibility of clinical trials for patients, therefore minimizing the inconvenience of travel and enabling participants to actively participate in research activities from the convenience of their residences or nearby healthcare facilities.

This study aims to investigate the effects of Decentralized Clinical Trials on three critical aspects of clinical research: efficiency, patient engagement, and data integrity. Efficiency is defined as the capacity of Decentralized Clinical Trials to optimize trial procedures, diminish operational expenditures, and accelerate the advancement of innovative medical therapies (Goodson et al., 2022). In contrast, patient involvement pertains to the degree to which Decentralized Clinical Trials may effectively include a broader and more inclusive range of participants, including those who may have faced past exclusion as a result of geographical, logistical, or economic obstacles (Zawada et al., 2023). Finally, data quality evaluation entails

assessing the soundness, precision, and dependability of data obtained through Decentralized Clinical Trials.

Using Decentralized Clinical Trials can significantly transform the landscape of medical research, presenting many advantageous outcomes (Khozin & Coravos, 2019). The benefits above include heightened availability of trials, expedited participant recruitment, improved data precision, and the possibility of expanding the applicability of trial findings (Ali et al., 2019). Nevertheless, the implementation of DCT poses a set of obstacles and concerns that need attention. These include issues about data security, regulatory compliance, and the requirement for robust digital infrastructure.

This research aims to show how DCT is living up to its promise regarding efficiency, patient participation, and data quality (De Brouwer et al., 2021). By exploring these key dimensions, we can better understand how DCT shapes the medical research landscape, potentially accelerating the development of life-changing medical interventions.

Significance of Decentralized Clinical Trials in medical research.

Decentralized Clinical Trials in the context of medical research are of paramount importance due to the potential transformative impact of this innovative approach. Decentralized Clinical Trials are significant in medical research due to the following reasons:

i. Patient-Centric Revolution

The patient-centric revolution, driven by Decentralized Clinical Trials, transforms the traditional model, prioritizing patient needs (Sundquist et al., 2021). This shift alleviates physical and logistical challenges, enabling remote trial participation from homes or nearby healthcare facilities, enhancing patient satisfaction, retention, and trial experience understanding.

ii. Wider Accessibility

DCT dramatically improves accessibility, removing geographical, economic, and travel barriers, facilitating diverse patient participation, and providing more precise real-life treatment effectiveness insights.

iii. Enhanced Efficiency and Cost Savings

DCT uses digital tech and remote monitoring, which optimizes trial procedures, reduces costs, and expedites novel treatment delivery by enhancing efficiency and reducing reliance on physical infrastructure and staff.

iv. Data Quality and Integrity

DCT leverages real-time data acquisition, improving precision, consistency, and reliability while reducing errors (Banks, 2021). This strengthens safety and effectiveness assessments and advances individual treatments, scientific knowledge, and future investigations.

v. Adherence to Evolving Regulations

DCT's compliance with evolving regulations is crucial and acknowledged by regulatory agencies like the FDA. Researchers, pharmaceutical companies, and healthcare practitioners must understand the relationship between DCT and dynamic regulatory standards to ensure compliance.

vi. Global Health Impact

DCT's rapid advancement and authorization of novel therapies have profound global health implications. Timely access to effective treatments can prevent mortality, improve patient outcomes, and mitigate social and economic consequences, extending its impact beyond national boundaries.

vii. Ethical and Regulatory Considerations

DCT introduces ethical and regulatory challenges. These include data privacy, informed consent, and the potential marginalization of vulnerable populations. Examining DCT allows for addressing these issues, ensuring its ethical use and regulatory compliance for responsible decentralized trials.

The examination of Decentralized Clinical Trials has significant importance due to its potential to bring about a transformative impact on the field of clinical research, primarily by improving operational efficiency, promoting inclusiveness, and elevating the standard of data integrity (Petrini et al., 2022). Adopting this revolutionary strategy has the potential to result in improved patient outcomes, accelerated progress in the creation of medical therapies, and improvements in the field of medical science (DiMasi et al., 2023). By conducting in-depth research on the impact of DCT in these pivotal dimensions, researchers can contribute to the ongoing evolution of clinical trial practices and realize a more patient-centric, efficient, and data-driven approach to medical research.

Literature Review

Decentralized Clinical Trials play an important role in the evolving world of healthcare, patient-centered care, and technological advancements due to its profound impact on medical research. This literature review seeks to provide a comprehensive analysis of the existing research.

COVID-19 and Clinical Trials

Phase III trials, typically the last phase of a clinical trial before a new treatment gains approval, often involve large cohorts of hundreds to thousands of participants. The conventional manual recruitment of participants for these trials presents a significant financial, operational, and time burden for trial organizers and participants themselves (Kelsey et al., 2022). Moreover, participants are usually required to travel to a designated clinical site for treatment and follow-up, thereby imposing additional logistical and financial burdens, potentially excluding individuals who cannot travel due to geographic, economic, or health-related constraints. As a result, conventionally organized clinical trials frequently encounter challenges related to the recruitment and retention of participants (Burger et al., 2023). A comprehensive review of randomized control trials (RCTs) indicates that only 63% successfully achieved their target sample size, necessitating revisions to the original recruitment targets in 30% of the studies (Hu et al., 2022). The same review identifies a participant dropout rate of at least 10%.

Disruption of Ongoing Trials

The pandemic disrupted many ongoing clinical trials. Due to the pandemic, healthcare systems worldwide grappled with the sudden surge in COVID-19 cases, and healthcare facilities and research sites were repurposed to address the immediate needs of COVID-19 patients. This cascaded clinical trials across a spectrum of medical research areas (Sarraju et al., 2022). One of

the primary consequences was the interruption in trial data collection. The very infrastructure that supported clinical trials, from hospitals and clinics to research laboratories, was redirected to respond to the pandemic. This meant that the trial sites, which were originally dedicated to conducting research, were transformed into COVID-19 treatment centers and testing facilities. The clinical staff and resources, including specialized equipment and personnel, were diverted to address the pandemic's urgent demands (Ali et al., 2023). This sudden transformation posed several challenges for ongoing trials. Patients enrolled in these trials often faced uncertainty and disruption in their care; scheduled in-person visits and treatments were postponed or canceled, leading to concerns about the safety and well-being of trial participants (Izem et al., 2023). For many patients with chronic or life-threatening conditions, interrupting their trial participation added to their medical uncertainties and anxieties.

Delayed Recruitment

Lockdowns and restrictions limited access to healthcare facilities where clinical trial recruitment typically occurred. Many research sites were closed, operating with reduced staff or prioritizing COVID-19-related care. This made it difficult to carry out the initial recruitment processes (Anderson, 2021). The fear of exposure to the virus led to a significant hesitancy among potential participants to visit healthcare facilities. People were concerned about the risk of contracting COVID-19, especially in settings with infected individuals. This hesitancy extended to potential trial participants and the healthcare staff involved in the recruitment process. During the pandemic, there were significant logistical challenges that affected both participants and researchers. According to Banks et al. (2021), transportation restrictions, reduced public transportation options, and concerns about compliance with social distancing measures added to the complexity of attending trial-related appointments. Additionally, the healthcare workforce was

stretched thin due to the pandemic; there was a decreased availability of healthcare professionals who could dedicate their time to clinical trial recruitment. Some healthcare workers were reassigned to COVID-19-related roles, leaving fewer staff members to conduct recruitment activities.

Protocol Modifications

The COVID-19 pandemic necessitated significant modifications to clinical trial protocols. One of the most notable changes involved reducing the frequency of in-person visits and embracing remote monitoring and telehealth solutions to ensure the safety of trial participants and maintain the collection of essential data. Trials that traditionally required frequent in-person visits, often for procedures like lab tests and physical examinations, were adapted to minimize face-to-face interactions. This reduction helped protect participants from potential exposure to the virus and alleviated concerns about virus transmission within healthcare facilities. To maintain the collection of critical trial data, researchers turned to remote monitoring and data collection methods. Participants were equipped with devices and tools for self-assessment and data reporting from the comfort of their homes. This included wearable devices, smartphone apps, and telehealth consultations.

Rapid Vaccine Development

The urgency of the pandemic accelerated vaccine development. Clinical trials for COVID-19 vaccines were executed unprecedentedly, breaking historical records. Researchers and pharmaceutical companies adopted innovative trial designs that expedited the development process. Adaptive designs allowed real-time adjustments based on accumulating data, streamlining the evaluation of vaccine candidates. The pandemic prompted massive global collaborations, with

researchers, institutions, and governments working to fast-track vaccine development. Information and data were shared at an unprecedented scale, fostering a collaborative environment that transcended geographic and institutional boundaries. Regulatory agencies introduced flexible procedures for vaccine approval. Rolling submissions allowed pharmaceutical companies to submit data in real-time as it became available, expediting the review and approval process.

Data Collection Challenges

The pandemic underscored the challenges related to data collection and data quality in clinical trials. Researchers had to balance the need for data integrity with the embrace of remote methods for data collection. Data integrity became paramount as trials transitioned to remote data collection (Van Norman, 2021). Robust data security and privacy measures were implemented to safeguard the accuracy and reliability of the data. Innovations in remote data collection tools, including wearable devices and digital health platforms, emerged as essential components to maintain the quality and consistency of data collected outside traditional clinical settings.

Patient Safety Concerns

The pandemic highlighted the critical importance of patient safety within clinical trials. Ensuring that trial participants were not exposed to unnecessary risks in the context of a highly contagious virus became a top priority. Rigorous safety protocols were implemented within trials to minimize participant exposure to the virus. These measures included the provision of personal protective equipment (PPE) and stringent hygiene guidelines. The pandemic emphasized the value of patient-centric trials that prioritize participants' well-being. This recognition led to an evolving understanding of the need for more patient-friendly trial designs, fostering greater empathy and responsiveness to participant needs.

According to Van Norman (2021), the COVID-19 pandemic disrupted clinical trials, delaying therapeutic releases and spurring virtual physician-patient interactions amid social distancing. Technology advancements—better internet, electronic health records, real-time video, health apps, and remote monitoring—paved the way for DCT using virtual tools, data collection, patient-centric designs, and reduced reliance on research facilities. Van Norman (2021) notes that DCT improve accessibility, benefiting marginalized populations and enabling personalized treatment with biometric sensors. Fewer review boards, redundancies, and lower costs make protocol adjustments easier. However, shipping drugs to multiple sites ensuring stability, storage, access control, and temperature monitoring are challenges. Robust cybersecurity is vital for patient privacy. Support from organizations like the Decentralized Trials and Research Alliance (DTRA) and FDA guidance signal DCT adoption.

Data Quality and Integrity

Clinical trials provide evidence for the safety and efficacy of new treatments and interventions. The quality, accuracy, and reliability of data collected during these trials are paramount, as they underpin the integrity and validity of research outcomes. The welfare of participating patients is at the core of clinical trials (Omar et al., 2021). The research team must collect high-quality data by maintaining accuracy and reliability. This ensures that safety and efficacy assessments are based on dependable information, thereby reducing the risk of harm to participants. Clinical trial data serves as the foundation for decisions by regulatory authorities to approve new drugs and treatments. Inaccurate or unreliable data can lead to regulatory rejection, causing delays in patients' access to innovative therapies. The accuracy and reliability of clinical trial data are essential for advancing medical science (Taniguchi et al., 2023). Researchers rely on this data to build on existing knowledge and inform future investigations. Inaccuracies can lead to

misguided conclusions and hinder scientific progress. Additionally, data integrity is an ethical imperative because participants in clinical trials place their trust in researchers and the scientific process. Therefore, ensuring data accuracy and reliability is a scientific duty and an ethical responsibility.

Strategies for Ensuring Data Quality, Accuracy, and Reliability

- **Straightforward Protocol Design:** Clear guidelines for study objectives, methodologies, and data collection procedures help prevent errors and misinterpretations.
- **Robust Informed Consent:** A thorough and comprehensible informed consent process is fundamental, and participants must fully understand the trial's purpose, procedures, and potential risks.
- **Data Management Plan:** Create a comprehensive data management plan that should outline data entry and validation procedures and data cleaning and storage protocols.
- **Electronic Data Capture (EDC):** EDC systems offer numerous advantages, including reducing manual data entry and transcription errors and real-time data validation.
- **Training and Standardization**: Adequate training of research staff involved in data collection is crucial. Standardizing data collection processes and terminologies minimizes inconsistencies compromising data quality and accuracy.
- **Quality Assurance and Quality Control (QA/QC):** Implementing robust QA/QC measures ensures data collection and management processes meet established standards. Regular audits and reviews are necessary to maintain data quality.

- **Blinding and Randomization:** Blinding and randomization techniques help reduce the potential for bias and data inaccuracies. Researchers unaware of the treatment groups are less likely to introduce unconscious biases into data collection and interpretation.
- **Monitoring and Auditing:** Monitoring and auditing trial sites and data are essential for identifying errors and ensuring data quality and reliability. This proactive approach helps maintain data integrity.
- **Data Transparency and Sharing:** Promoting transparency and open data-sharing practices is a means of enhancing data reliability. Independent verification of results and scrutiny by the scientific community contribute to the robustness of the data.

Quality, Accuracy, and Reliability of Data in Decentralized Clinical Trials

Decentralized Clinical Trials are transforming the clinical research landscape by utilizing digital technologies to enable remote data collection, significantly reducing the need for in-person visits to research sites (Hang et al., 2022). While DCT offer numerous advantages, maintaining data quality, accuracy, and reliability is essential to ensure the credibility and validity of trial results.

DCT utilize electronic data capture (EDC) systems to minimize manual data entry errors and omissions, enhancing data quality. These systems are designed to ensure that data is accurately recorded during patient interactions, reducing errors in data collection (Burger et al., 2023). Additionally, real-time data capture and validation through digital tools increase data reliability as it can be checked for inconsistencies immediately. Remote monitoring and wearable devices provide continuous data collection, improving data quality by offering a comprehensive view of a patient's health over time. These devices are equipped with sensors that accurately measure

physiological parameters, such as heart rate and blood pressure, reducing the potential for human error in data collection (Huh et al., 2022). The continuous nature of data collection through wearables minimizes the chances of missing data points, thus ensuring reliable data and improving the accuracy of recorded measurements.

Electronic patient-reported outcomes (ePRO) platforms allow patients to report their health status, symptoms, and treatment adherence, thus contributing to data accuracy. Electronic patient-reported outcomes provide direct input from patients and are a reliable source of real-time information that accurately reflects the patient's experiences (Akechi et al., 2023). Other than real-time data collection, DCT often employ real-time data validation to ensure that the data collected meets predefined quality criteria. Real-time validation enhances data quality by preventing inaccurate or incomplete data from being recorded. This validation contributes to the accuracy and reliability of the data collected, as errors and inconsistencies are addressed as they occur.

Centralized data management systems used in DCT provide a unified data storage and analysis platform and reduce the likelihood of errors caused by disparate data sources. This approach is crucial for ensuring data quality, as it centrally integrates data collected from various sources (Saraju et al., 2022). Data discrepancies and inaccuracies are minimized through centralization, further enhancing the accuracy and reliability of data. Additionally, research involving DCT provides proper training and support for patients to use digital tools and devices. This training is essential for data quality, accuracy, and reliability because patients need to understand how to use technology effectively to ensure accurate data collection (Ali et al., 2023). Adequate training and support lead to reliable data collection by reducing the likelihood of errors caused by patient misunderstanding or misuse of digital tools.

Methodology

Research Design

This study employed a comprehensive literature review research design with a primary focus on Decentralized Clinical Trials. This research design was appropriate for this research topic due to its inherent capacity to synthesize existing knowledge, critically analyze published research, and identify emerging trends in the field of DCT. DCT is a rapidly evolving paradigm within clinical research, driven by technological advancements and a shifting healthcare landscape. To understand the current state of DCT, it is essential to synthesize the vast body of existing literature. A literature review offers an efficient means to assimilate and consolidate the existing knowledge, providing a holistic view. By adopting a literature review approach, this study can comprehensively assess the impact of DCT on efficiency, patient participation, and data quality in medical research. The research design also ensures that the study's findings are grounded in a broad spectrum of reliable sources and are poised to contribute valuable insights to the field of DCT and medical research.

Research Objectives

The research objectives of this study are:

i. To assess the impact of Decentralized Clinical Trials on efficiency in medical research.

ii. To evaluate the role of Decentralized Clinical Trials in enhancing patient participation in clinical trials.

iii. To determine the challenges and concerns associated with Decentralized Clinical Trials.

Literature Search

The literature search process for this research involved a systematic approach to identify and collect relevant articles addressing the impact of Decentralized Clinical Trials. The literature search process involved finding articles on databases and academic repositories. The primary sources used in this research included PubMed, Scopus, Web of Science, and Google Scholar. These databases are known for extensively covering biomedical and clinical research articles. This study took steps to ensure the inclusion of recent and up-to-date research; the literature search focused on articles published within the last five years. This time frame was chosen to encompass the most current research and developments related to DCT. The selected period aimed to strike a balance between capturing recent trends and allowing for accumulating a substantial body of relevant literature.

The search strategy involved a set of keywords and search terms designed to identify articles directly related to DCT. Some of the key terms and phrases used in the search strategy included: “Decentralized Clinical Trials,” “Remote Clinical Trials” and “Digital Clinical Trials.” The keywords and search terms were used in various combinations to maximize the retrieval of relevant articles. Using specific terminology related to DCT and its impact on clinical trials ensured that the search results were tailored to the research objectives.

Data Analysis and Synthesis

The initial search yielded 18 articles that were eligible for inclusion. After further research, this number was reduced to 10 articles. The selected articles were organized into thematic categories based on the research objectives, highlighting the impact of Decentralized Clinical Trials on efficiency, patient participation, and data quality in medical research.

Findings

This section synthesizes the key findings across the identified themes related to the impact of Decentralized Clinical Trials on the future of medicine regarding efficiency, patient participation, and data quality, drawing on the selected articles.

Efficiency in Clinical Trials

The literature consistently highlights the potential for DCT to streamline data collection and reduce administrative burdens. This is achieved through electronic data capture, real-time monitoring, and remote data collection methods. According to Ghadessi et al. (2023), DCT offer a hybrid approach that allows remote participation, thereby reducing the burden on participants. DCT are particularly beneficial for rare diseases, where patient populations are scattered and may need help to visit traditional trial sites easily. DCT reduce local sites' responsibilities and limitations, allowing for a more extensive trial network and serving more participants (Petrini et al., 2022). This can enhance the efficiency of patient recruitment and data collection. Goodson et al. (2022) suggest that DCT can enhance the efficiency of clinical trials by overcoming geographical constraints and reducing wait times at trial sites.

Mahoney and Sridhar (2023) found that DCT can offer more flexibility with scheduling and reduce accessibility concerns, such as mobility issues, transportation costs, and psychological stress associated with commuting to the cancer center. Additionally, DCT allow remote sampling, data collection, and health technologies to support remote monitoring. This reflects a patient-centric approach that can streamline the clinical trial process. According to Pennestrì et al. (2023), Decentralized Clinical Trials can enhance efficiency by streamlining data collection and reducing the need for physical visits to labs or trial sites. Dorsey, Kluger, and Lipset (2020) emphasized that

Decentralized Clinical Trials can increase the efficiency of clinical trials by reducing the burden on participants and enabling broader access to a diverse patient population. Singh et al. (2023) notes that DCT have the potential to streamline the trial process, resulting in greater efficiency.

Although Decentralized Clinical Trials have massive potential for improving efficiency, the literature notes challenges such as robust data security and privacy measures to protect sensitive patient information in remote settings (Goodson et al., 2022). The suitability of DCT design gives due consideration to the safety, target population, investigational medicinal product (IMP), and data quality (Singh et al., 2023). Therefore, DCT can improve the efficiency of drug development for compounds with an existing safety profile and approved formulation.

Ensuring data integrity while maintaining efficiency remains a concern. DCT has the potential to significantly enhance the efficiency of clinical trials by simplifying data collection processes, reducing patient travel and associated costs, and enabling real-time data validation. These trends suggest that DCT can expedite drug development, bringing innovative therapies to patients more swiftly.

The Future of Medicine

The study findings indicate that DCT can accelerate the future of medicine by addressing current pitfalls. Goodson et al. (2022) note that DCT may not entirely overcome structural issues related to trial participation, such as structural racism and industry trends that increase trial burden. Also, the "digital divide" poses a significant barrier, as not all participants have access to the required technology. DCT must address potential disparities in access to telemedicine services, such as issues related to race, socioeconomic status, and living in rural areas.

Challenges related to data security, patient engagement, and regulatory considerations must be addressed to realize the potential benefits of DCT fully. Shifting to DCT models requires significant investment in health technology, resources, education, and training, and navigating legal and regulatory parameters (Mahoney & Sridhar, 2023). Singh et al. (2023) noted the need for regulatory updates and addressing issues related to informed consent, privacy, and data security. Decentralized Clinical Trials present a challenge of safety assessment in the remote setting, can be a potential pitfall, and highlight the need for adequate safety monitoring and communication. There are risks related to data collection in less controlled settings, reliability of clinical measurements, potential impact on patient safety, data protection, data breaches, and a potential weakening of the physician-patient relationship in DCT (Petrini et al., 2022).

Ghadessi et al. (2023) emphasize that DCT should not replicate traditional clinical trials but provide a real-world perspective on clinical research, focusing on quality care and meaningful data collection. It is also essential to prevent ineligible or fraudulent participants from signing up for studies, especially when financial incentives are involved (Ali et al., 2020). Decentralized Clinical Trials can transform the medical research landscape by making trials more efficient, inclusive, and data driven. While challenges exist, the literature suggests that the benefits far outweigh the hurdles, offering a promising path for the future of medicine.

Challenges and Considerations of Decentralized Clinical Trials

Addressing the challenges and considerations surrounding DCT sheds light on the critical issues that researchers, sponsors, and healthcare professionals must address when transitioning to this innovative clinical research model. One of the foremost concerns in DCT is data security and privacy. The decentralized nature of these trials introduces new risks of data breaches and unauthorized access, potentially compromising participants' sensitive information. Robust security measures are paramount to address this challenge. This includes secure and encrypted data transmission, secure storage, and strict access controls. Additionally, adherence to data privacy regulations and compliance standards, such as the Health Insurance Portability and Accountability Act (HIPAA) in the United States, is non-negotiable. Maintaining trust and protecting participants' confidentiality and integrity are fundamental to the success of DCT.

DCT require a meticulous approach to trial design. As highlighted by Singh et al. (2023), factors such as the safety of the investigational medicinal product (IMP), the target population, and data quality must be carefully considered. Not all trials are equally suitable for the DCT model, and assessing the risk-benefit profile of each trial is essential. Safety concerns may vary depending on the specific drug or intervention being tested, and researchers must evaluate whether the remote model can adequately ensure participants' well-being and the trial's integrity.

Maintaining data integrity in DCT is paramount. As Petrini et al. (2022) rightly point out, data collection's decentralized and remote nature can introduce challenges related to data accuracy, reliability, and adherence to regulatory standards. Stringent monitoring and validation processes are crucial. Where possible, employing redundancy in data collection methods can safeguard

against inaccuracies. Moreover, the capacity to detect and correct data discrepancies promptly is essential to ensure the credibility and validity of trial results.

While DCT offer numerous advantages for patient participation, including reduced travel and flexible participation, there are challenges in maintaining participant motivation and retention. As noted by Anderson (2021), reduced direct contact with clinical staff can make it more challenging to keep participants engaged. Innovative strategies for remote participant engagement and support must be developed to address this. Telehealth options, virtual support groups, and regular communication can bridge the gap and provide participants with the necessary motivation to stay committed to the trial.

As mentioned by Ali, Zibert, and Thomsen (2020), the issue of digital literacy and technology access is of critical consideration. Ensuring that patients have access to the required technology and are digitally literate is vital to the success of DCT. Researchers and sponsors need to develop strategies to address these barriers and support participants in navigating the digital aspects of remote trials. This may involve providing technology, training, or assistance to participants who require it. Additionally, considering a diverse patient population is essential to ensure equitable access to DCT.

Impact of Decentralized Clinical Trials on the Future of Medicine

DCT has the potential to accelerate the progress of medical research significantly. DCT promises to make trials more efficient, inclusive, and data-driven, which is essential for advancing medical research. DCT can overcome geographical and logistical barriers that often limit patient participation in traditional trials by allowing participants to engage from their homes or local healthcare providers. To fully realize this potential, addressing issues such as the digital divide,

data security, regulatory considerations, and safety monitoring is imperative while ensuring that DCT focuses on quality care and meaningful data collection. The future of medicine is likely to be significantly influenced by the continued development and implementation of DCT, with the potential to advance healthcare for diverse populations and improve the overall quality of clinical research.

Reference

Adams, D. V., Long, S., & Fleury, M. E. (2022). Association of remote technology use and other decentralization tools with patient likelihood to enroll in cancer clinical trials. *JAMA Network Open*, *5*(7), e2220053-e2220053. doi:10.1001/jamanetworkopen.2022.20053

Akechi, T., Yamaguchi, T., Uchida, M., Imai, F., Momino, K., Katsuki, F., ... & Iwata, H. (2023). Smartphone psychotherapy reduces fear of cancer recurrence among breast cancer survivors: a fully decentralized randomized controlled clinical trial (J-SUPPORT 1703 study). *Journal of Clinical Oncology*, *41*(5), 1069-1078. https://doi.org/10.1200/JCO.22.00699

Ali, Z., Valk, T. J., Bjerre-Christensen, T., Brandt, S., Isberg, A. P., Jensen, M. L., ... & Robert Zibert, J. (2023). Exploring decentralized glucose and behaviometric monitoring of persons with type 2 diabetes in the setting of a clinical trial. *Journal of diabetes science and technology*, *17*(1), 117-124. https://doi.org/10.1177/19322968211045656

Ali, Z., Zibert, J. R., & Thomsen, S. F. (2020). Virtual clinical trials: perspectives in dermatology. Dermatology, 236(4), 375-382. https://doi.org/10.1159/000506418

Anderson, M. (2021). How the COVID-19 pandemic is changing clinical trial conduct and driving innovation in bioanalysis. *Bioanalysis*, *13*(15), 1195-1203. https://doi.org/10.4155/bio-2021-0107

Banks, M. A. (2021). In the wake of COVID-19, Decentralized Clinical Trials move to center stage. *Proceedings of the National Academy of Sciences*, *118*(47), e2119097118. https://doi.org/10.1073/pnas.2119097118

Berwanger, O., & Machline-Carrion, M. J. (2022). Digital Health–Enabled Clinical Trials in Stroke: Ready for Prime Time? *Stroke*, *53*(9), 2967-2975. https://doi.org/10.1161/STROKEAHA.122.037378

Burger, H. U., Van de Casteele, T., Rantell, K. R., Corey-Lisle, P., Sfikas, N., Abt, M., & Working group on Decentralized Trials as part of the European Scientific Interest Group (ESIG) in Neuroscience. (2023). Opportunities and challenges with decentralized trials in Neuroscience. *Biometrical Journal*, 2200370. https://doi.org/10.1002/bimj.202200370

De Brouwer, W., Patel, C. J., Manrai, A. K., Rodriguez-Chavez, I. R., & Shah, N. R. (2021). Empowering clinical research in a decentralized world. *NPJ Digital Medicine*, *4*(1), 102. https://doi.org/10.1038/s41746-021-00473-w

de Jong, A. J., van Rijssel, T. I., Zuidgeest, M. G., van Thiel, G. J., Askin, S., Fons-Martínez, J., ... & Trials@ Home Consortium. (2022). Opportunities and challenges for Decentralized Clinical Trials: european regulators' perspective. *Clinical Pharmacology & Therapeutics*, *112*(2), 344-352. https://doi.org/10.1002/cpt.2628

de Las Heras, B., Daehnke, A., Saini, K. S., Harris, M., Morrison, K., Aguilo, A., ... & Marcus, R. (2022). Role of Decentralized Clinical Trials in cancer drug development: Results from a survey of oncologists and patients. Digital Health, 8, 20552076221099997. https://doi.org/10.1177/20552076221099997

DiMasi, J. A., Smith, Z., Oakley-Girvan, I., Mackinnon, A., Costello, M., Tenaerts, P., & Getz, K. A. (2023). Assessing the Financial Value of Decentralized Clinical Trials. *Therapeutic Innovation & Regulatory Science*, *57*(2), 209-219. https://doi.org/10.1007/s43441-022-00454-5

Dorsey, E. R., Kluger, B., & Lipset, C. H. (2020). The new normal in clinical trials: decentralized studies. Annals of Neurology, 88(5), 863-866. https://doi.org/10.1002/ana.25892

Ghadessi, M., Di, J., Wang, C., Toyoizumi, K., Shao, N., Mei, C., ... & Beckman, R. A. (2023). Decentralized Clinical Trials and rare diseases: a Drug Information Association Innovative Design Scientific Working Group (DIA-IDSWG) perspective. Orphanet Journal of Rare Diseases, 18(1), 79. https://doi.org/10.1186/s13023-023-02693-7

Goodson, N., Wicks, P., Morgan, J., Hashem, L., Callinan, S., & Reites, J. (2022). Opportunities and counterintuitive challenges for Decentralized Clinical Trials to broaden participant inclusion. *NPJ Digital Medicine*, *5*(1), 58. https://doi.org/10.1038/s41746-022-00603-y

Hang, L., Chen, C., Zhang, L., & Yang, J. (2022). Blockchain for applications of clinical trials: Taxonomy, challenges, and future directions. *IET Communications*, *16*(20), 2371-2393. https://doi.org/10.1049/cmu2.12488

Huh, K. Y., Moon, S. J., Jeong, S. U., Kim, M. J., Yang, W., Jeong, M., ... & Lee, S. (2022). Evaluation of a blockchain-based dynamic consent platform (METORY) in a decentralized and multicenter clinical trial using virtual drugs. *Clinical and Translational Science*, *15*(5), 1257-1268. https://doi.org/10.1111/cts.13246

Kelsey, M. D., Patrick-Lake, B., Abdulai, R., Broedl, U. C., Brown, A., Cohn, E., ... & Bloomfield, G. S. (2022). Inclusion and diversity in clinical trials: actionable steps to drive lasting change. Contemporary Clinical Trials, 116, 106740. https://doi.org/10.1016/j.cct.2022.106740

Khozin, S., & Coravos, A. (2019). Decentralized trials in the age of real-world evidence and inclusivity in clinical investigations. Clin Pharmacol Ther, 106(1), 25-27.

Mahoney, M. E., & Sridhar, S. S. (2023). Clinical trial reform in the post-COVID era. Therapeutic Advances in Medical Oncology, 15, 17588359231183676. https://doi.org/10.1177/17588359231183676

McCarthy, M. W., Naggie, S., Boulware, D. R., Lindsell, C. J., Stewart, T. G., Felker, G. M., ... & Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)-6 Study Group. (2022). Fluvoxamine for outpatient treatment of COVID-19: a decentralized, placebo-controlled, randomized, platform clinical trial. *medRxiv*, 2022-10. doi: https://doi.org/10.1101/2022.10.17.22281178

Moore, J., Goodson, N., Wicks, P., & Reites, J. (2022). What role can decentralized trial designs play to improve rare disease studies? *Orphanet Journal of Rare Diseases*, *17*(1), 240. https://doi.org/10.1186/s13023-022-02388-5

Omar, I. A., Jayaraman, R., Salah, K., Yaqoob, I., & Ellahham, S. (2021). Applications of blockchain technology in clinical trials: review and open challenges. *Arabian Journal for Science and Engineering*, *46*, 3001-3015. https://doi.org/10.1007/s13369-020-04989-3

Pennestrì, F., Banfi, G., & Tomaiuolo, R. (2023). Remote Decentralized Clinical Trials: A new opportunity for laboratory medicine. Clinical Chemistry and Laboratory Medicine (CCLM), (0). https://doi.org/10.1515/cclm-2022-1184

Petrini, C., Mannelli, C., Riva, L., Gainotti, S., & Gussoni, G. (2022). Decentralized Clinical Trials (DCT): A few ethical considerations. Frontiers in Public Health, 10, 1081150. https://doi.org/10.3389/fpubh.2022.1081150

Sarraju, A., Seninger, C., Parameswaran, V., Petlura, C., Bazouzi, T., Josan, K., ... & Dash, R. (2022). Pandemic-proof recruitment and engagement in a fully decentralized trial in atrial

fibrillation patients (DeTAP). *NPJ Digital Medicine*, *5*(1), 80. https://doi.org/10.1038/s41746-022-00622-9

Sehrawat, O., Noseworthy, P. A., Siontis, K. C., Haddad, T. C., Halamka, J. D., & Liu, H. (2023, September). Data-Driven and Technology-Enabled Trial Innovations Toward Decentralization of Clinical Trials: Opportunities and Considerations. In Mayo Clinic Proceedings (Vol. 98, No. 9, pp. 1404-1421). Elsevier. https://doi.org/10.1016/j.mayocp.2023.02.003

Singh, P., Burden, A. M., Natanegara, F., & Beckman, R. A. (2023). Design and Execution of Sustainable Decentralized Clinical Trials. Clinical Pharmacology & Therapeutics. https://doi.org/10.1002/cpt.3009

Sommer, C., Zuccolin, D., Arnera, V., Schmitz, N., Adolfsson, P., Colombo, N., ... & McDowell, B. (2018). Building clinical trials around patients: evaluation and comparison of decentralized and conventional site models in patients with low back pain. *Contemporary clinical trials communications*, *11*, 120-126. https://doi.org/10.1016/j.conctc.2018.06.008

Sundquist, S., Batist, G., Brodeur-Robb, K., Dyck, K., Eigl, B. J., Lee, D. K., ... & Dancey, J. E. (2021). CRAFT—a proposed framework for Decentralized Clinical Trials participation in Canada. *Current Oncology*, *28*(5), 3857-3865. https://doi.org/10.3390/curroncol28050329

Taniguchi, H., Masuishi, T., Ogata, T., Ando, M., Mizuno, N., & Muro, K. (2023). First experience of a fully decentralized clinical trial: The dawn of a new era in oncology. *Cancer Science*, *114*(7), 3050. https://doi.org/10.1111%2Fcas.15792

Van Norman, G. A. (2021). Decentralized Clinical Trials: the future of medical product development? Basic to Translational Science, 6(4), 384-387. https://doi.org/10.1016/j.jacbts.2021.01.011

van Rijssel, T. I., de Jong, A. J., Santa-Ana-Tellez, Y., Boeckhout, M., Zuidgeest, M. G., van Thiel, G. J., & Trials@ Home Consortium. (2022). Ethics review of Decentralized Clinical Trials (DCT): results of a mock ethics review. *Drug Discovery Today*, *27*(10), 103326. https://doi.org/10.1016/j.drudis.2022.07.011

Zawada, S. J., Ruff, K. C., Sklar, T., & Demaerschalk, B. M. (2023). Towards a conceptual framework for addressing state-level barriers to Decentralized Clinical Trials in the US. *Journal of Clinical and Translational Science*, *7*(1), e162. https://doi.org/10.1017/cts.2023.584