

Decentralized Clinical Trials – Systematic Review of Methods, Awareness, and Inclusiveness in Clinical Research

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Abstract

"Decentralised" trials (also known as hybrid, remote, or virtual trials) are the trials that covers a wide range of services and solutions that can be mixed and matched based on the conditions, preferences, and needs of patients, clinical locations, and sponsors. The research on Decentralised Clinical Trials is carried out through a series of interviews to better understand the perspectives of stakeholders involved in the DCT and how the industry accelerates and fast tracks the digital transformation to strive for paperless and patient-centric outcomes. In the present study, the data Collection were performed through extensive survey with the detailed questionnaire on the awareness of DCT, applied DCT tools in their research project, benefits and challenges overcome during the trial and DCT applications during the list of study phases, timeframe for using the rapid adoption of DCT. The current study's findings give significant evidence that decentralised clinical trials offer a promising new strategy to clinical research, allowing for speedier, more efficient, and more flexible study designs. DCTs are set to become an increasingly essential element of the clinical research landscape as digital technologies evolve and improve, providing new opportunities to enhance healthcare outcomes for all. The use of DCT in clinical trials has the potential to overcome a number of important drug development difficulties. DCT solutions may improve easier data collection, patient adherence and overall retention rates in addition to improving patient access and convenience.

Keywords: Anticipated challenges, Clinical trials, COVID pandemic; Decentralized trials, Feasibility; Health care.

Introduction

Clinical trials are critical for the development of novel medicines, and excellent trial results considerably promote regulatory approval and the market launch of novel pharmaceuticals [1]. Each new drug and treatment began with volunteers taking part in clinical trials. The current high standards of medical care are purely based on the studies conducted under the supervision of the US Food and Drug Administration (FDA). Clinical trials, in addition to testing novel medications and equipment, provide a scientific foundation for guiding and treating patients. Even if

researchers do not get the expected findings, trial data can put scientists in the right direction [2].

Clinical trials are a fundamental tool used to evaluate the efficacy and safety of new drugs and medical devices and other health system interventions. The traditional clinical trials system acts as a quality funnel for the development and implementation of new drugs, devices and health system interventions. The concept of a "digital clinical trial" involves leveraging digital technology to improve participant access, engagement, trial-related measurements, and/or interventions, enable

concealed randomized intervention allocation, and have the potential to transform clinical trials and to lower their cost. They are the safest and quickest way to uncover new therapies and techniques to improve health when done correctly.

Given the pandemic's concerns, pharma industries are seeking for solutions to minimise disruptions to their research. The decentralisation of trials is one technique that is gaining attraction. Decentralised clinical trials (DCTs), in contrast to the standard clinical trial approach, are carried out through telemedicine and mobile/local healthcare providers [4]. DCTs have been quiet inactive to acquire attraction, accounting for only 0.5% of all trials, with 63% in North America and 23% in Europe [5]. Recognising the barriers to DCT adoption, a recent poll indicated that 78% of clinical trial professionals believed the pandemic was promoting DCT usage [6].

DCTs employ "virtual" techniques such as telemedicine, sensory-based technologies, wearable medical devices, home visits, patient-driven virtual health care interfaces, and home drug and material delivery [7]. Subject recruitment, study medication delivery and administration, and trial outcome data gathering all occur in a completely decentralised clinical trial, with no in-person contact between the study team and the patient/subjects[8].

The primary reason for selecting this research topic is to critically evaluate the Clinical Research Industries awareness on the emerging concept of Decentralised Clinical Trials and to comprehend how the application of DCT tools plays a significant role in patient retention and data quality from the study sponsors and Investigational Sites perspectives. Although the Global Pandemic hastened the adoption and popularity of DCTs, it has also caused pharmaceutical companies to consider this as a mainstream, there are several questions to be answered about whether DCTs were carried out with proper adoption and implementation, and whether this has improved

patient experience on safety usage of clinical trials.

Materials and Methods

The research on Decentralised Clinical Trials is carried out through a series of interviews to better understand the perspectives of stakeholders involved in the DCT and how the industry accelerates and fast tracks the digital transformation to strive for paperless and patient-centric outcomes. This research problem analysis is based on survey results from various clinical research stakeholders from drug companies, contract research professionals, and hospital research institutions who have experience conducting clinical trials and have participated in clinical research and trials during the COVID-19 Pandemic. To be consistent with the specified clinical trial, there is an express demand that digital technologies be used generally to permit more pragmatic, reduced Site travel in parallel.

Data Collection were performed through extensive survey with the detailed questionnaire on the awareness of DCT, applied DCT tools in their research project, benefits and challenges overcome during the trial and DCT applications during the list of study phases, time fame for using the rapid adoption of DCT.

1. Detailed Survey is being designed and conducted with the clinical research professionals who are actively participated on clinical trials through SURVEY MONKEY.
2. Survey is being conducted to observe the methods, understanding and awareness on the Decentralized Clinical Trial approaches among various stakeholders.
3. In the electronic survey conducted, the link was sent to 50 participants of which 32 responses were received from different health care professionals. The current job role of clinical research professionals were 88% CRO Sponsor Personnel, 3% were Clinical Research Coordinators and 9% were Other Investigational site staffs.

4. The awareness survey on DCT by clinical research professionals was carried out globally. 12 professionals from India, 5 from Singapore and 5 from Australia, 1 from China, Croatia, Denmark, Georgia, Japan, Poland, Republic of Korea, Serbia, Spain, use and USA responded to the Questionnaire.
5. 75% of the respondents were involved in pharma sponsored trial, 3% were involved in Investigator initiated trial and the remaining 22% were involved in combination of both pharma sponsored and Investigator initiated trial.

IRB Approval

Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research.

The Ripon independent ethics committee reviewed, discussed and approved the Research Proposal (Application no: TEHTA00001) to conduct the Research entitled “Decentralized Clinical Trials—Systematic review of Methods, Awareness, and Inclusiveness in Clinical Research”.

Confidentiality of the Survey Participants was maintained, and the required consent was obtained prior to survey and all the research participants were informed about the study objective. Also the survey participants were being informed that the participation for the

study was a voluntary participation and analysis was taken for the research purpose.

The following questionnaire were framed and distributed to professionals

1. 75% of the respondents were involved in pharma sponsored trial, 3% were involved in Investigator initiated trial and the remaining 22% were involved in combination of both pharma sponsored and Investigator initiated trial.
2. The questionnaire contained the following.
 - a. Demographic responses.
 - b. Type of Clinical Trial Involved.
 - c. Number of clinical trials involved in past 3 years.
 - d. Awareness on usage of DCT.
 - e. Experience of Utilizing DCT methodology.
 - f. Feasibility of using DCT.
 - g. Promising future of DCT in Clinical trial.
 - h. Adoption of DCT during pandemic.
 - i. Reachability of DCT to clinical trial participants.
 - j. Readiness to adopt DCT methodologies.

Results and Discussion

In the electronic survey conducted 32 responses were received from different health care professionals. From the data obtained, among clinical research professionals. 88% were CRO Sponsor Personnel, 3% were Clinical Research Coordinators and 9% were Other Investigational site staffs. This study does not contain any inputs from site investigators.

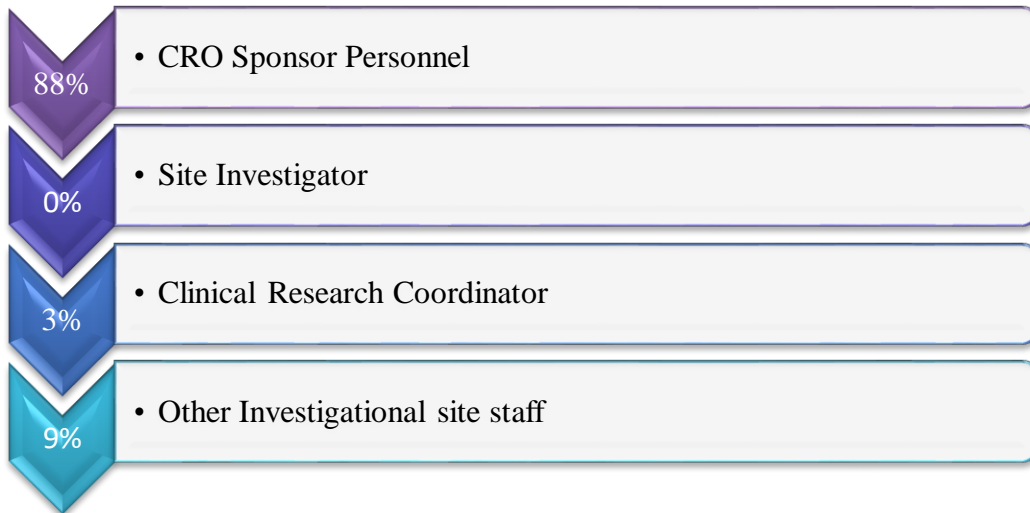


Figure 1. Current Job Role of Clinical Research Professionals

In the electronic survey conducted 32 responses were received from different health care professionals. Figure 1 represents the current job role of clinical research professionals. 88% were CRO Sponsor

Personnel, 3% were Clinical Research Coordinators and 9% were Other Investigational site staffs. This study does not contain any input from site investigators.

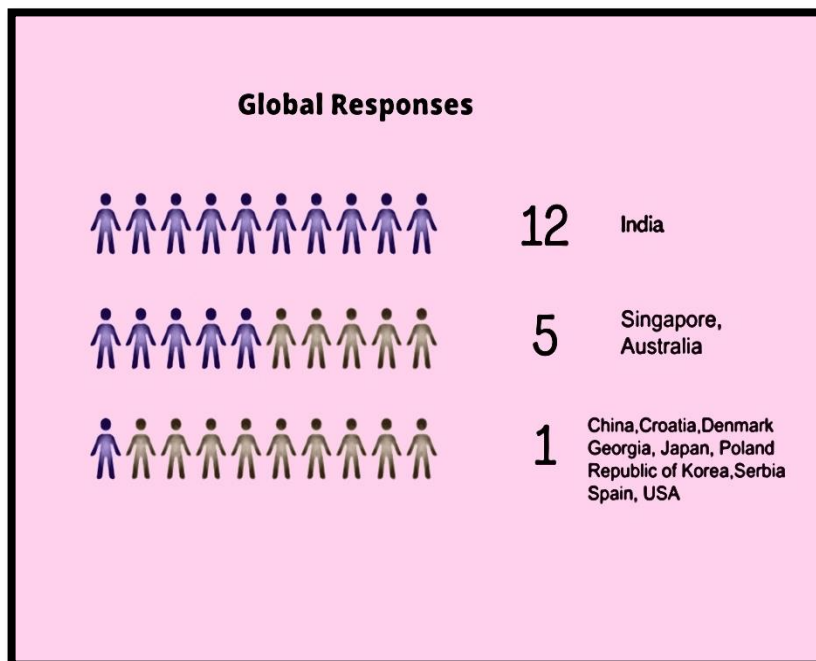


Figure 2. Demographic Responses

Figure 2 show the demographic responses. The awareness survey on DCT by clinical research professionals was carried out globally. 12 professionals from India, 5 from Singapore

and 5 from Australia, one from China, Croatia, Denmark, Georgia, Japan, Poland, Republic of Korea, Serbia, Spain, USA responded to the Questionnaire.

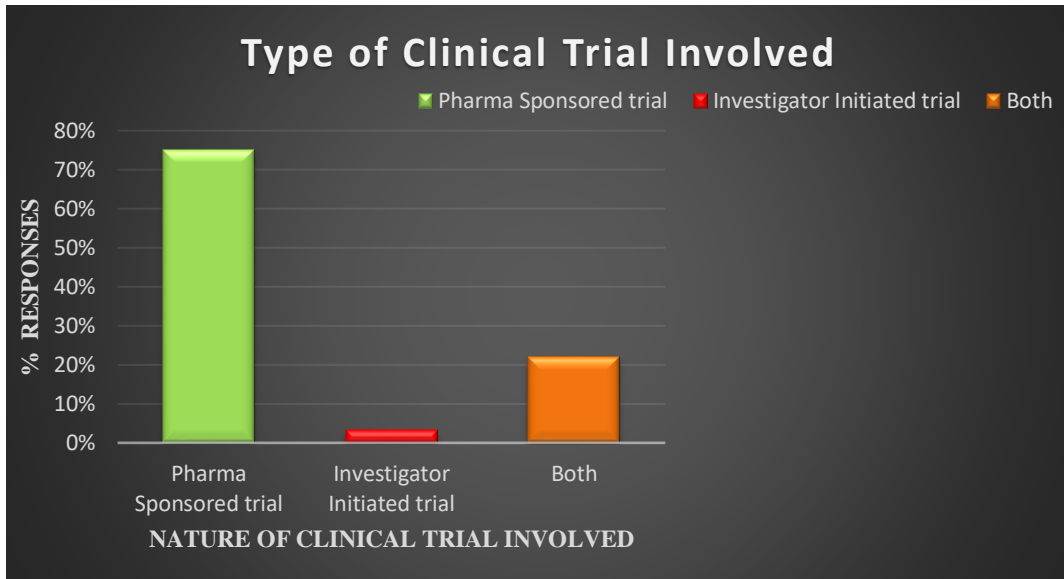


Figure 3. Type of Clinical Trial Involved

Figure 3 showcases the type of Clinical trial involved. 75% of the respondents were involved in pharma sponsored trial, 3% were involved in Investigator initiated trial and the remaining 22% were involved in combination of both pharma sponsored and Investigator initiated trial.

Clinical trials are not, and cannot be, designed to determine all the potential uses for a medication. IITs expand product knowledge,

including safety. The driving need for Investigator Initiated Trials is that the clinical trials cannot be intended to cover all of a drug's possible applications. IITs broaden consumer product understanding, encompassing safety.

Medical researchers or physicians find novel application for currently used therapies by using the input of IITians and therefore non industry sources of data are always given more weight [9]

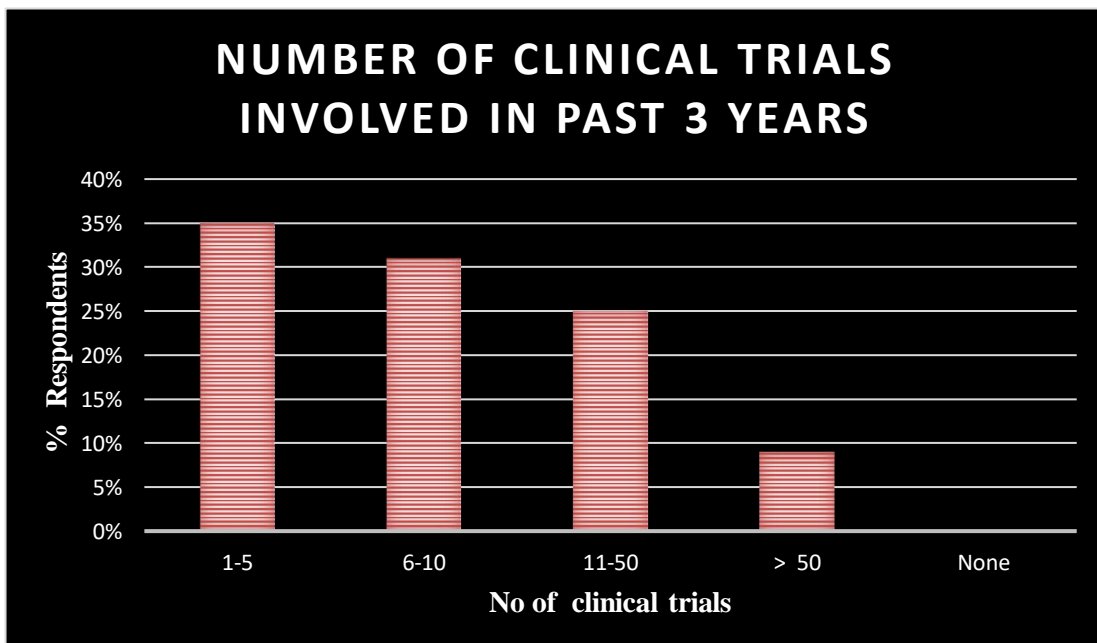


Figure 4. Number of Clinical Trials Involved in Past 3 Years

In the study conducted, it was found that 38% of the respondents reported being involved in around one to five clinical trials over the past 3 years. Out of the respondents surveyed, 31% reported having handled 6-10 clinical trials. 25% respondents have handled 11-50 clinical trials. 9% were involved in handling more than 50 clinical trials.

Clinical trials are very mandatory to strengthen the evidence of efficacy and safety of new therapies. The diversity of clinical trial participants is often required to ensure that the trial population is representative of the patients who will use the medicine or medicinal product

and ensure that the results are generalizable [10-11]. However, increasing clinical trial diversity in an effective, sustainable, and scalable manner remains a mutual challenge for the pharmaceutical industry, academic institutions, and clinical research overall. Health care professionals play a critical role in clinical trials, as they are directly involved in various aspects of the trial process. By participating in clinical trials, health care professionals contribute to advancing medical knowledge and improving patient care. They play a vital role in the development of new treatments and therapies.

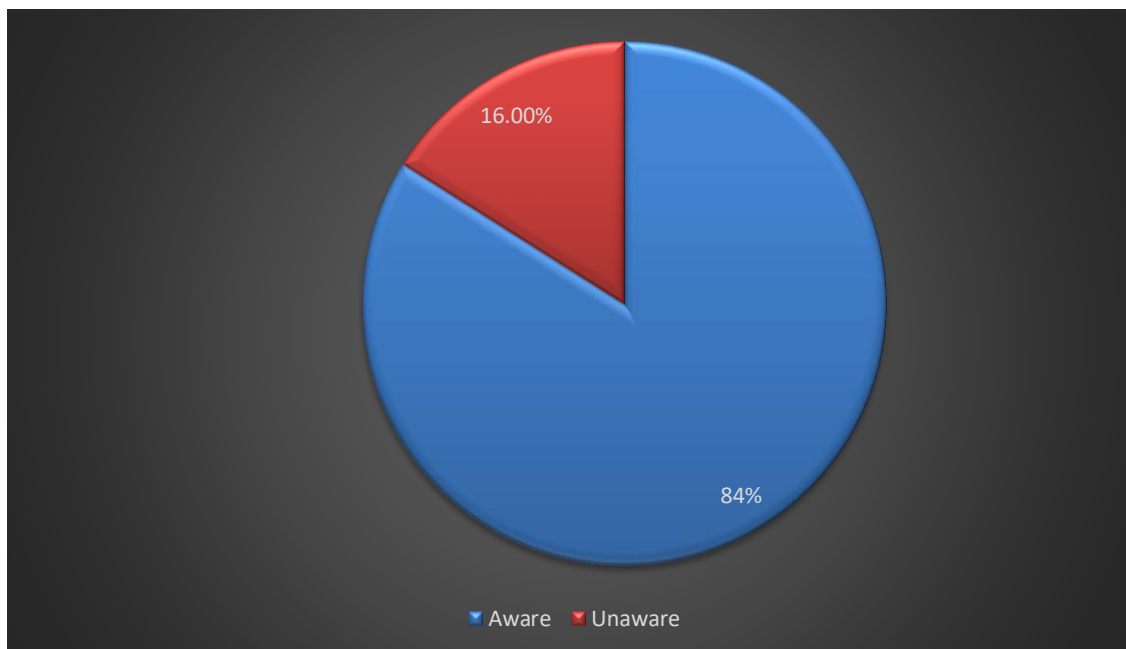


Figure 5. Awareness about DCT

Figure 5 depicts the awareness about the effective usage of DCT by clinical research professionals. 84% of the respondents were aware of the various DCT methods and 16% of Clinical research professionals were unaware of DCT.

Decentralised clinical trials (DCTs) use digital technologies and other means to allow patients access to clinical research, remote data collecting and monitoring, and communication between investigators and participants. Diabetes, neuro-rehabilitation, cardiovascular disorders, lung diseases, and, more recently,

COVID-19 are among of the therapeutic areas where DCTs are most readily relevant [12]

As DCT is patient centric approach, 84% respondents adopted well to DCT. As technologies continue to advance, the process of collecting, transferring, and storing electronic data becomes increasingly streamlined. Simultaneously, both patients and healthcare providers are rapidly enhancing their tech savviness and embracing telemedicine with greater comfort (FDA) and this study also confirms that the clinical research professionals have upgraded themselves to use DCT along with traditional onsite treatment [13] (FDA,

2023). DCTs eliminate waiting hours, contact with other patients' suffering, hospitalisation in some situations, and potential exposure to

microorganisms in hospital settings that might cause difficulties [14-17].

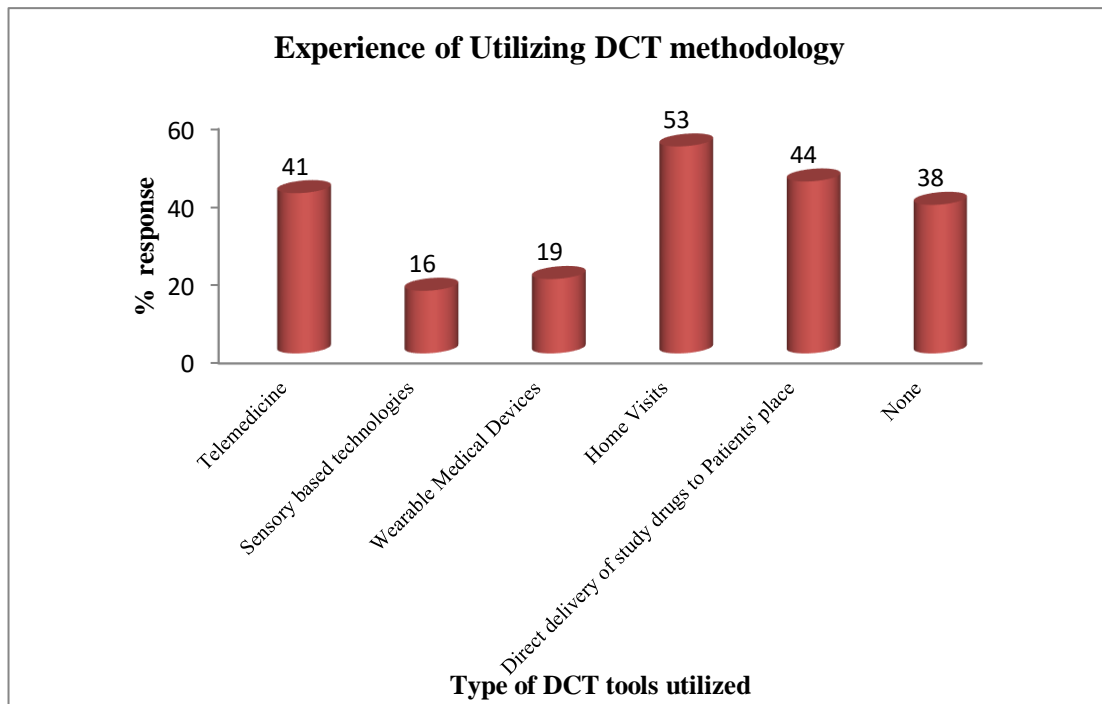


Figure 6. Experience of Utilizing DCT Methodology

The different DCT methodologies utilized by clinical research professionals is depicted in Figure 6. 41% CRP's has used telemedicine for treating their patients and 19% has experimented DCT by making usage of wearable medical devices. 16% has opted for sensory based technologies. More than half the respondents (53%) preferred home visits and 44% supplied the drugs directly to the participants. This study shows that the Clinical research professionals have experience in decentralised clinical trials. Digital health technologies (DHTs), which are systems that directly collect patient health information for clinical trials, are frequently used in DCTs. Numerous DHTS are portable devices, including spirometers (measuring devices for lung function), glucose monitors, blood

pressure monitors, and activity trackers. These sensors can be ingested, implanted, or worn. DHTs also have interactive mobile applications that let users rate their level of happiness, level of pain or depressive symptoms, level of everyday functioning, or take tests of functional abilities including cognition, coordination, and vision. DHTs can capture data much more frequently than scheduled trial visits, sometimes even constantly, in addition to being more convenient. Additionally, these technologies record participant routines in order to gather data on the treatment's efficacy and security in "real life." Practically speaking, DCTs can decrease or eliminate the requirement for the resources associated with a traditional site, which can ultimately save time and money [18]

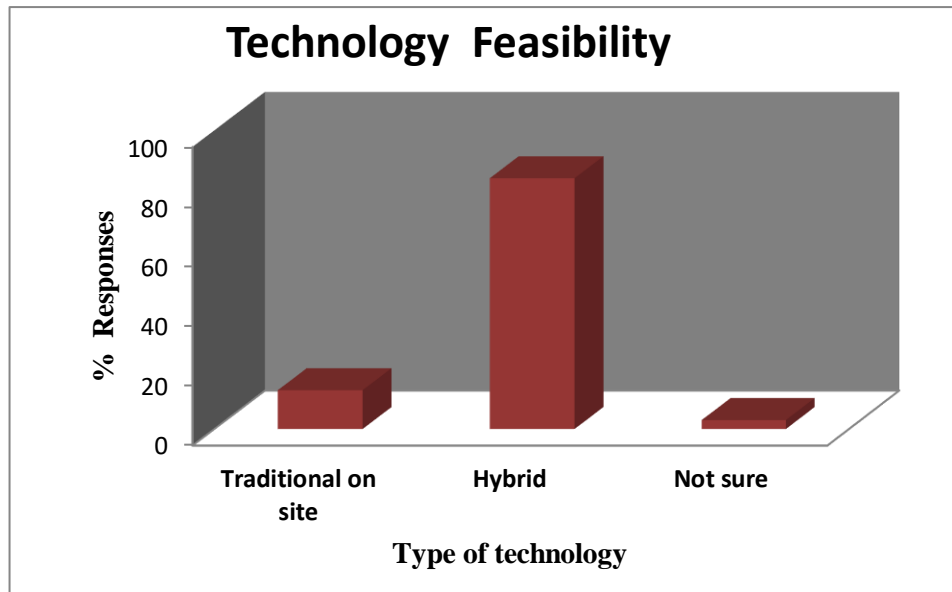


Figure 7. Feasibility of Using DCT

Figure 7 exhibits the feasibility of using clinical trials technologies. 13% respondents feels that traditional onsite treatment is feasible and 84% respondents thinks that hybrid mode of clinical trial i.e traditional and DCT is more feasible. 3% were not sure which technology is

feasible. Physical examinations must be conducted on-site during visits to ensure effective safety monitoring. Engaging digitally illiterate patients (eg, the elderly) in DCT can be a challenge [19].

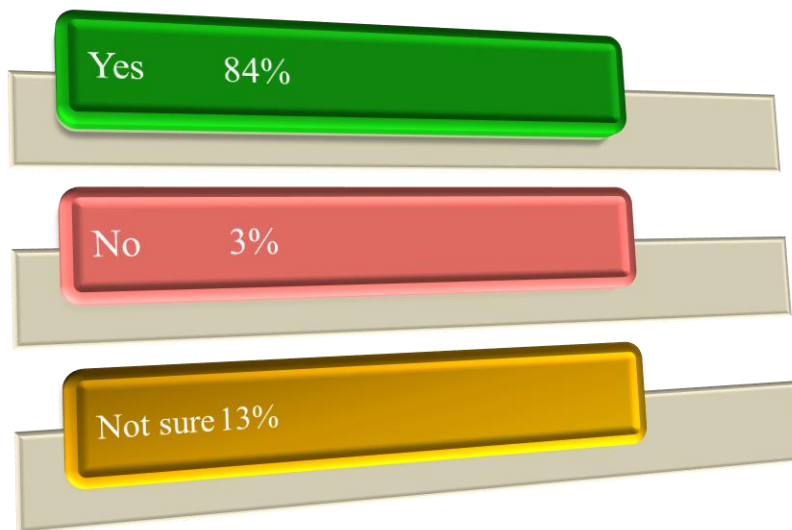


Figure 8. Promising Future of DCT in Clinical Trial

According to the survey results, 84% of the respondents expressed their acceptance that DCT has a promising future. The advantages of

DCT are it removes the need for travel, which can make participation more difficult.

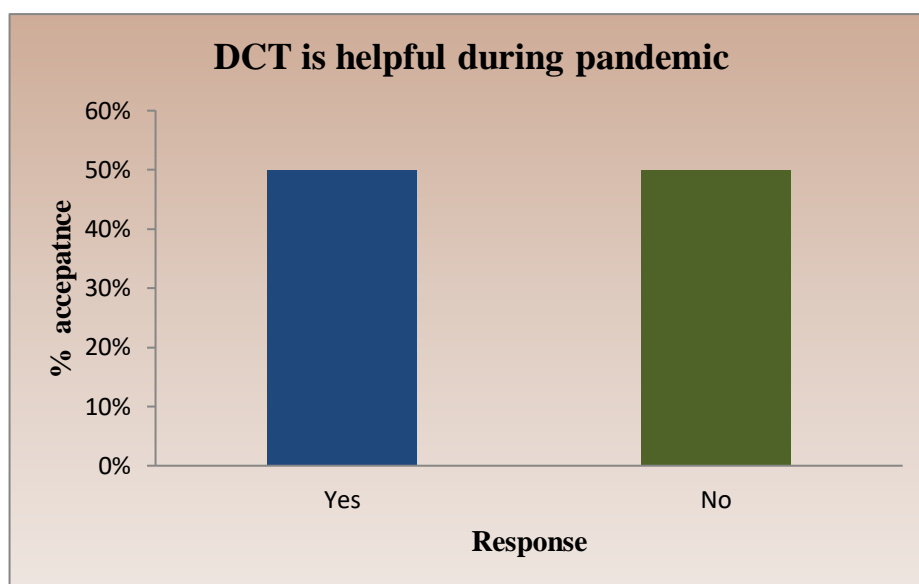


Figure 9. Adoption of DCT During Pandemic

The adoption of DCT before and during pandemic is depicted in Figure 10. In the conducted survey, half of the respondents (50%) answered yes, while the other half (50%) answered no. The pandemic has significantly accelerated the adoption of decentralized clinical trials, leading to a notable rise in remote trial activities conducted directly at participants' homes. Although certain aspects of decentralized trials were present before the pandemic, they were not widely utilized. The global health crisis has expedited the virtualization of both trial and consumer settings [20]. The pandemic of COVID-19 has a tremendous impact on the clinical research model. Patients who had previously participated in clinical trials were unable to access hospital

trial sites for treatment and/or follow-up visits due to government travel restrictions or because they did not wish to attend for fear of infection.

During the pandemic, flexible DCT models are largely relied on to preserve patient continuity and to conduct studies for COVID-19 therapies and vaccinations. Pharmaceutical and biotechnology businesses are increasingly transitioning to flexible, digitally enabled trial methods, industry organisations are advocating for their usage, and regulators around the world look ready to investigating the potential benefits of digital technologies in clinical research. Following the pandemic, several RAs have expressed a desire to expand DCT techniques [21].

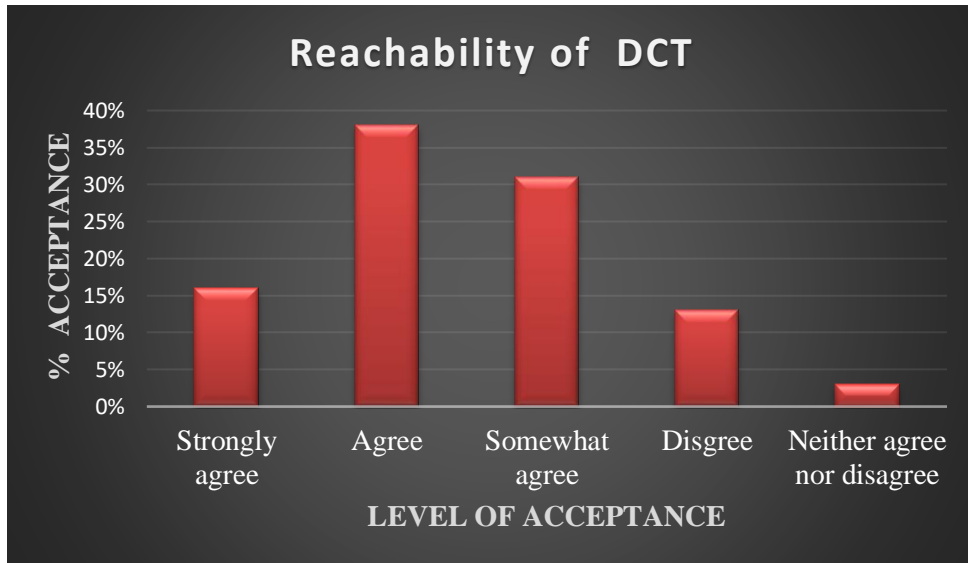


Figure 10. Reachability of DCT to Clinical Trial Participants

The view of respondents in reachability of DCT to clinical trial participants in short time is presented in Figure 10. In the survey conducted 38% respondents agreed that Clinical trial recruitment period is likely to improve as DCT is more reachable to Clinical trial Participant in a short time. 15% strongly agreed that DCT is more reachable to clinical trial participants in short time. 31% somewhat agreed the question and 13% neither agree or disagree the view.

Based on Global Data's Clinical Trial Database, the count of decentralized clinical

trials (DCT) has shown a consistent rise, from 250 trials in 2012 to 1,291 trials in the previous year. As of this year, there have been 950 trials conducted, and it is projected to reach approximately 1,425 trials by year-end. Notably, from 2012 to 2016, both industry and non-industry sponsors demonstrated comparable DCT usage. This survey also confirms that DCT has reached clinical trial participants in short time through the responses from clinical research professionals.

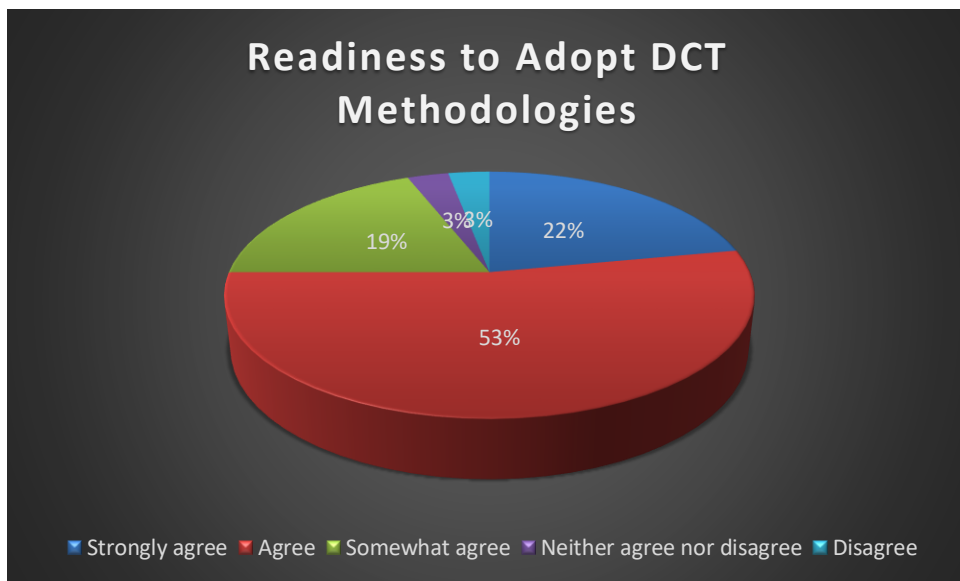


Figure 11. Readiness to Adopt DCT Methodologies

The percentage readiness to adopt DCT methodologies is depicted in figure 11. Around 3/4 th of the respondents are ready to adopt and use DCT methodologies. 22% somewhat agree, as respondents may want to try hybrid mode of clinical trial. 3% neither agree nor disagree and 3% disagree the statement. The survey results show that a significant proportion of participants are ready and open to adopting DCT methodologies. This positive response indicates a willingness to explore the potential benefits of DCT and suggests that the adoption of these methodologies may be well-received within the surveyed population. **Conclusion**

The current study's findings give significant evidence that decentralised clinical trials offer a promising new strategy to clinical research, allowing for speedier, more efficient, and more

flexible study designs. Their execution, on the other hand, necessitates careful consideration of data security, technology infrastructure, regulatory compliance, and participant involvement. DCTs are set to become an increasingly essential element of the clinical research landscape as digital technologies evolve and improve, providing new opportunities to enhance healthcare outcomes for all.

Conflict of Interest

The authors declare no conflict of Interest.

Acknowledgement

The authors acknowledge the clinical research professionals who participated in the survey.

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