A Review of significance of Decentralized Clinical Trials in India and impact of Data Analytics in Clinical Data

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Abstract:

Clinical trials are essential for developing new treatments. As the traditional site-based trails are costly, time consuming, decentralized clinical trials (DCT) is need of the hour. DCTs employ a more patient centric approach reducing barriers of study participants by utilizing new technologies such as sensory, wearable devices and use telemedicine, home visits like approaches. DCT reduce time, cost, travel burden and also bring more data accuracy and real-time monitoring. This paper also explains significance of conducting Decentralized trials in India. Vast pool of patients, skilled medical & paramedical professionals and low cost has put India firmly on the global clinical trials map.

Key words: *Clinical trials, Decentralized Clinical trials, contract research organization, drug development, India, data analytics.*

Introduction:

A new era in clinical research began in 1948 with the famous trial of streptomycin for pulmonary tuberculosis1, the first contemporary randomized controlled experiment. Since then, clinical trials have astonishingly advanced in terms of their scientific and statistical foundations and influence on regulation. Over the past ten years, the Clinical Trials Transformation Initiative (CTTI) has addressed a wide range of operational and scientific trial-related difficulties and proposed solutions, which has significantly aided in this evolution. Clinical trials were conducted all over the world in a fragmented and segmented manner for the majority of the 20th century. This strategy has changed and evolved for with the success of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), 5. Many clinical trials conducted today have as their main objective supporting international drug marketing approval. Many clinical trials had to be expanded to include the entire world [1].

As Clinical Trials may term as ‘‘clinical trial’: any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy.’ [2]

Why CRO?

Over the past ten years, the contract research organization (CRO) market has experienced enormous expansion, and at the same time, pharmaceutical and biotechnology corporations have increased their outsourcing significantly. Although the pharmaceutical industry initially used CROs to solve such short-term needs as extra capacity, the major growth in outsourcing among CROs is being driven by those businesses that concentrate on offering creative solutions. These CROs have succeeded by realizing that it is their knowledge, not just their data or technology, that makes them indispensable allies throughout all stages of the drug development continuum. They comprehend the value of being a research partner to the pharmaceutical and biotechnology industries. Sponsors are also learning how to benefit from CROs' expertise.

There will undoubtedly be a greater dependence on CROs to perform these essential, knowledge-based outsourcing services in the face of mounting pressure to maintain pipelines full, control R&D costs, bring more medications to market, and increase shareholder value.

The choice to outsource should be supported by a long-term, strategic perspective that tackles and resolves any internal capability gaps. By limiting a pharmaceutical company's capital investments, such as lab equipment and real estate, and turning fixed costs into variable costs (since researchers are CRO workers, not the pharmaceutical company's), outsourcing can lower financial risk. By outsourcing, biotech firms can defer forming a partnership with a significant pharmaceutical company and retain a bigger share of the ownership of the first medicine.

The procedure of approving drugs will save a lot of time and money. A drug's anticipated revenue loss per day it takes to reach the market can reach $1 million or more. Sponsors are prepared to outsource studies to complete them more quickly, but they must pay extra to assure

accuracy and attention to detail due to the growing complexity of research. This raises concerns about both quality and speed.

Additionally, businesses are starting to use a "fail fast" strategy in an effort to speed up the drug development process. This strategy recognizes the value of rejecting compounds sooner, during preclinical or Phase I, once it has been confirmed that they would ultimately fail. Since unsuccessful compounds account for around 75% of the cost of developing a new medicine, there are more funds available to support promising candidates, increasing return on investment. Another chance for outsourcing exists here, as CROs could be able to finish research more quickly than sponsor businesses.

The development of genomics and proteomics, which is predicted to increase the number of therapeutic targets from the present 500 to as much as 5,000–10,000, complicates this procedure. The danger of compound failure will increase due to the rapid growth in new targets, many of which will have weak validation. In order to ensure that the right drugs are advanced, it will be crucial to make the right choice of CRO with excellent preclinical and early clinical skills.

A crucial research technique for improving patient care and medical understanding is clinical trials. Only when doctors are unsure of a novel approach's efficacy and safety, as well as whether therapies or approaches are most effective for a certain ailment or population, do they do clinical research. Clinical trials are crucial for identifying novel disease treatments as well as innovative methods of disease detection, diagnosis, and risk reduction. Researchers can learn things about what works and doesn't work in humans through clinical trials that cannot be discovered through laboratory or animal testing. Clinical trials also assist medical professionals in determining whether a novel treatment's adverse effects are tolerable in comparison to its potential benefits. The outcomes of clinical trials are unknown to researchers. A patient may find it challenging to determine whether or not to take part in a clinical trial due to this ambiguity. Millions of people have been benefitted because others before them volunteered to participate in a study that led to the development of a new, more effective treatment, even though in rare instances, patient volunteers have been harmed by the treatment or procedure on a clinical trial.

Key findings

- According to IQVIA Global Trends Report, a record 84 novel active substances (NASs) were initially launched globally in 2021, double the number of five years ago.
- The total number of products that are in active development in human trials globally exceeds 6,000, up 68% over the 2016 level, as life sciences companies continue to invest and advance innovative therapeutics and vaccines across a wide range of disease areas, despite the disruptions caused by the COVID-19 pandemic.
- In 2021, 5,500 new planned clinical trial starts were reported, up 14% over 2020 and 19% higher than 2019.
- Currently, more than 3,200 companies and more than 200 academic or research groups around the world are involved in the R&D pipeline. [5].
- The global CRO services market is projected to grow from $73.38 billion in 2022 to $163.48 billion by 2029, at a CAGR of 12.1% in forecast period, 2022-2029.

- In 2021, total 25 new drugs have been approved and as of May 2022, 15 new drugs are approved, serving patients globally.

Methods: The selected keywords were grouped into sets based on the criteria. Where possible, the synonyms of the keywords were considered and comprised of the following search terms: “clinical trial”, “Decentralized Clinical trials”, “contract research organization”, “data analytics”, “India”.

Decentralized Clinical Trials

Innovative technologies and participant-centered design are combined in decentralised clinical trials. Decentralized clinical trials (DCT) can be conducted entirely remotely or using a hybrid technique that still requires some physical site attendance. They are accomplished through the use of direct-to-patient drug delivery, home health professionals, neighborhood labs, digital consent data gathering, and remote monitoring and diagnostics. These studies aim to minimise or do away with the necessity of face-to-face interactions between researchers and participants [6].

DCTs, also known as "direct-to-participant trials" or "virtual" investigations, differ from conventional research studies in that they rely less on specialised intermediates or typical research facilities to gather data. DCTs make use of "virtual" techniques like telemedicine, sensory-based technology, wearable medical devices, home visits, patient-driven virtual health care interfaces, and direct drug and material delivery to patients' homes for study purposes. In a fully decentralised clinical trial, subject enrollment, medicine delivery and administration, and data collection on trial outcomes all take place without the patient or subject having direct interaction with the study staff. DCTs frequently incorporate traditional design with decentralised patient/subject interactions, and clinical trials for medication approval frequently already involve decentralised components [7].

Advantages of Decentralized clinical trials

DCTs may facilitate the logistics of running a clinical trial by enhancing subject acquisition and retention [1]. Because remote monitoring and data collection reduce barriers to participation, such as logistical challenges in accessing the trial location—for example, travel costs, non-acceptance of job absences for study activities, and mobility challenges posed by medical comorbidities—patients who would otherwise face daunting challenges from centralised study trials may be able or willing to enrol in DCTs. The enhancement of trial access for participant demographics that are presently most underrepresented in traditional trials, such as the elderly, the poor, those residing in distant areas, and many ethnic minorities, is a spillover consequence. Both recruitment timelines and results generalizability to various demographics are probably going to get better.

DCTs decrease expenses and site-specific inconsistencies by having fewer central research sites, fewer institutional review boards, and fewer repetitive applications. Fewer sites also improve flexibility and the capacity to pivot and make broad protocol alterations to match changing study parameters. Fewer sites also imply fewer resubmissions to several institutional review boards to implement changes. Remote monitoring results in fewer individual

evaluations, decreased reporting variability, and maybe smaller studies. In order to improve compliance and perhaps increase both short- and long-term research safety, remote patient/subject interactions can take place more frequently and at times and places that are more convenient for the subject.

For data collection and compilation, traditional clinical trials rely significantly on trained study team members, such as study coordinators, research assistants, and nursing and medical professionals. This function is partially or entirely virtualized by DCTs. A partially virtual intermediary is one that still needs some direct patient engagement, but isn't always an investigator. For example, a partially virtual intermediary can ask patients to enter daily information about drug side effects in a portal of the research platform. A wearable continuous glucose monitoring device that automatically transmits data to the research platform at specified intervals while requiring neither the patient nor a research intermediary to intervene is an example of a fully virtual data collection system [1]. Studies that rely on such virtual technologies and automation may need fewer investigation teams and decrease sponsorship expenses for full-time professionals as well as for training. Lessening the hassles caused to patients/subjects as a result of virtual data gathering may raise their willingness and capacity to engage in a study, leading to outcomes that more accurately depict the study drug's safety and efficacy behavior in a "real world" setting. [7].

According to Precision Reports, the global decentralized clinical trials (DCTs) market size is projected to reach $1.63 billion by 2027.

Advantages of conducting Decentralized Clinical Trials in India

In India in the early 2000s, the future of clinical research—particularly the delivery of market-driven international clinical trials (CTs), including global bioequivalence studies—began as a nice dream. Many think tanks and experts predicted that India would become a world centre of excellence for clinical research.

Let’s look at how India’s advantages can be helpful becoming hub for Global Clinical Trials.

- India provides a sizable and varied genetic pool of a population that is treatment-naive for clinical trials, and this patient pool's diversity holds good financial potential. According to PwC, India will surpass China as the world's most populated nation by 2050, when its population is expected to reach 1.6 billion from its current level of over 1.2 billion. India is in a good position given the difficulties of finding people for clinical trials in affluent nations and the idea of expanding the patient pool in developing nations, which is coupled with cost savings [9].
- Healthcare market in India is expected to reach US $372 billion by 2022, driven by rising income, USD $11.28 billion was allocated to Ministry of Health and Family welfare [10].
- As a testimony to the fast growing healthcare sector in India, two vaccines Covaxin and Covishield were instrumental in medically safeguarding Indian population against Covid-19 outbreak.
- India is second largest English speaking county after US and availability of highest numbers of English speaking physicians.
- Presence of well-equipped and state-of-the-art healthcare institutions across the country.

- For patients who have restricted access to healthcare due to geographic distance, transportation challenges, or other impediments to visiting a healthcare institution in person, India has the huge information technology capabilities that aid in conducting trials and adopting revolutionary technology platforms.
- India has low cost of drug development are cost-effective human resource, low recruitment cost, and lower rate of compensation for any injury sustained or death during the research process [11]. According to an analysis, conducting clinical trials in India can cost up to 60% less than US.
- The government has made great efforts to put new regulations into place to support clinical research. For instance, the processing time for applications has been lowered to a maximum of 90 days. The application will be handled within 30 days in the case of an investigational new drug that is subject to discovery, research, and manufacture in India. Additionally, there would be no application fees for orphan medication studies in India. These new regulations seek to promote more homegrown research and development (R&D) for rare diseases impacting patients in India by expediting the clinical trial application procedure [12]. Improved regulatory environment [Notification of amended Schedule Y, publication of revised national guidelines for biomedical research, changes in rules doing away with .phase lag. in clinical trials and introduction of a new patent regime in pharmaceuticals respecting product patents (instead of just process patents)] [18].
- Home care and Teleconsultation are essential part of the Decentralized Clinical trials. India has achieved robust improvement in implementation of these during Covid-19. In March 2022, India made an important landmark in its digital health journey by completing 170,000 teleconsultations in a single day through its nationwide telemedicine service.
- For use in clinical trials, a number of digital and sensor technologies have been created that enable the collection of high-quality, reproducible data and offer realists instantaneous insights [13]. Following the US and China, India is the third-largest market for wearable medical technology. Analytics for the study experiment can be determined using the data from these devices.
- Clinical research benefits greatly from mobile technologies, including shorter study times, more precise data, and more. Organizations are integrating technology at a faster rate as they start to realise the potential mHealth has to influence clinical trials in a good way [14]. Considering that India has over 700 million internet users. This benefit will be very helpful for gathering data from mobile app for clinical trial study.

How Data Analytics helps Clinical Trials

Big Data has revolutionized how we collect, analyze, and use data in various industries. Healthcare is a notable area where the use of data science and analytics can have a significant impact. Currently, there are numerous innovations in the field of clinical trials.

Data analytics opens up new opportunities in pharmaceutical research and development, which coincides with the rise of artificial intelligence (AI) and machine learning (ML) technologies during the past five years. Massive datasets can be combed through quickly and accurately by AI/ML algorithms, yielding insightful conclusions that would take countless hours to complete by people.

Below are some key benefits that data analytics can bring to the drug development process:

- **More accurate clinical trials**

  Millions of datasets may be present in thousands of active clinical trials at a large pharmaceutical business. With so many data points, there is a greater need than ever for efficient data management and data analysis. Data management errors can be expensive, wasteful, and time-consuming for staff members, or even worse, endanger the entire clinical experiment.

  Despite these options, a lot of clinical studies still use conventional data collecting and verification techniques, like manually counting unused pills in bottles, faxing patient records, and tracking patients' paper diaries to gauge medication adherence. These responsibilities frequently fall on the patient, who is more prone to forget things or make mistakes.

  Researchers will be able to recognise critical patterns and probable trial difficulties in real time by combining digital data collection and applying cutting-edge technologies like data analytics.

- **Safer production of drugs**

  A new pharmaceutical drug's creation has traditionally been a protracted, laborious procedure that relies on manual data processing and collection. However, recent uses of statistical and machine learning methods have produced more efficient processes that can even aid in forecasting the results of randomised clinical trials for novel medications. As a result, estimations of the risks and benefits are more precise and timely for all parties concerned, including researchers, regulators, and the patients themselves.

  Scientists can imitate the effects of medications on the human body using body proteins, a variety of cells, and settings in addition to speeding data collecting. The medicine developed from that clinical study is much more likely to treat a wide range of patient profiles and receive FDA approval.

  Researchers can create better clinical trials that avoid expensive delays in a market launch by using more precise estimates of the risk associated with drug development. The selection criteria for patients can be expanded with the use of data science and analytics. Researchers can more effectively target individuals who meet the inclusion and exclusion criteria by having the ability to swiftly and reliably sort through variables such patient characteristics, disease state, and genetics.

- **More efficient trials**

  Data analytics can increase the effectiveness of research and clinical trials in addition to helping decision-makers along the drug development process make more knowledgeable choices. In order to find new possible candidate compounds that can be effectively turned into medications with a high degree of confidence, predictive modelling of drugs and biological processes will become essential.

Pharmaceutical businesses can react instantly to new clinical data insights by utilising big data and automation tools. They can also execute smaller tests with similar power or shorter trials to increase trial efficiency. These tiny improvements add up quickly to shorten the trial period by months or even years [15].

Results: India is favorable destination to conduct Decentralization Clinical Trials as having many advantages including vast genetic pool population, cost effectiveness, well-equipped and state-of-the-art healthcare institutions, large internet users etc. More improvised policy-regulations on trials with strong push from the government and more advanced data analytical approach, India has the potential to become hub for the Decentralized Clinical trials.

Conclusion

Asian nations are being chosen by international pharmaceutical companies as a means of overcoming numerous obstacles in medication discovery and development. It is commonly known that phase I, II, and III drug trials typically cost $20, $50, and $100 million, respectively, in the United States, whereas they cost between 50 and 60 percent less and take 75 percent less time to complete in India. A further advantage of conducting international clinical trials in India as opposed to other Asian nations is that English is the predominant language of commerce and medicine [16]. From 2022 to 2030, the Indian clinical trials market is anticipated to expand at a compound yearly growth rate of 8.2%, reaching USD 3.88 billion. However, the market for Decentralized Clinical Trials is quite small. The Indian government has strengthened the sector throughout time by implementing supportive policies as well as extensive, long-lasting structural reforms. Since subject safety and data integrity are the main goals, regulations norms and standards are getting more stringent and thorough. Clinical trial conduct is being improved by the quick advancement of technology and improvised methods and gadgets [17].

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