Virtual Clinical Trials: Pathway to Attain Patient Centricity During the Current COVID 19 Pandemic

By

Shwetha T Thiraviam

Dissertation submitted for the partial fulfillment of the

MBA Pharmaceutical Management

Academic year, 2018-2020

The IIHMR University, Jaipur

1, Prabhu Dayal Marg, Sanganer, Airport
Jaipur 302029, Rajasthan
Ph: 0141 3924700, Fax: 3924738
Website: **www.iihmr.edu.in**

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Website: **www.iihmr.edu.in**

SALES + MARKETING

June 17, 2020

EXPERIENCE CERTIFICATE

This is to certify that Shwetha T (Employee ID – 23544) was interning in our organization from February 3, 2020 to May 29, 2020. At the time of leaving she was working in the capacity of Knowledge Management Associate – Intern based at the New Delhi office.

We wish you all the success in future endeavors.

For ZS Associates India Pvt Ltd

Mohit Sood
Office Managing Principal

THE IIHMR UNIVERSITY, JAIPUR

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled "**Virtual Clinical Trials: Pathway to Attain Patient Centricity During the Current COVID 19 Pandemic"** and submitted by SHWETHA. T, enrollment no. 0151 under the supervision of Dr. Rahul Sharma for award of MBA in Pharmaceutical Management carried out during the period from 03.02.2020 to 31.05.2020 embodies my original work and has not formed the basis for the award of any degree, diploma associateship, fellowship, titles in this or any other institute or other similar institution of higher learning.

Signature

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INTERNSHIP

During my tenure as a Knowledge Management Associate Intern at ZS Associates, Gurgaon, I had great exposure to understand about the organization as a whole and the team I was aligned to. In the orientation days, I had attended training sessions on various skills which were required by my position in the organization. As I am employed with the ZS Associates at the capacity of Knowledge Management Associate (Research and Development Expertise) so, I have taken the opportunity to prepare the dissertation titled **"Virtual Clinical Trials: Pathway to Attain Patient Centricity During the Current COVID 19 Pandemic"**

INTRODUCTION

Industry overview: Virtual clinical trials

Virtual clinical trials represent a new way of gathering data from the comfort of the patients from their homes by taking complete advantage of technologies like wearables, sensors to conduct each stage of the trial starting from recruitment, informed consent, patient counseling, to measuring clinical endpoints and adverse reactions. These patients facing digital technologies play a crucial role in the execution of virtual clinical trials as there is increasing demand for these technologies in the market as well. The following terms, decentralized trials, remote trials, site less trials, direct-to-patient trials, hybrid trials, patient-centric trials, and most commonly referred to virtual clinical trials. It means that there would be no physical site and no face to face interaction with PI (Principal Investigator).

Virtual trial is one among the emerging trends in the clinical trials space such as patient centricity, precision medicine, real-world evidence, big data analytics, virtual clinical trials, innovative trial designs and blockchain-based platforms.

Drug manufacturers spend around $2.6 billion to launch a new drug, according to a recent estimate from the Tufts Center for the Study of Drug Development. Projected returns on investment in pharma R&D have decreased to 1.8 per cent in 2019, since 2010 when it was 10.1 per cent - a decline of 8.3 percentage points. The past decade decline in IRR has stressed the importance of innovation to transform the R&D and executing the virtual trials. One key factor is the length of time in clinical trial cycle development which can be optimized by leveraging the use of digital technologies including AI to expedite the patient enrolment, improve protocol design, site selection, capture ePRO and digital biomarkers(Ten years on measuring the return from pharmaceutical innovation 2019, 2019).

The global Digital Clinical Trials market is estimated to reach 7.61 Billion by 2022, at a CAGR of 12.4% during the forecast period (2017-2022) as there is rise in the innovative practices like adoption of digital technologies to transform the traditional clinical trials setting. Some companies have started running pilot trials with digital technologies with the support of regulatory agencies like FDA and EMA. Mobile Health Technology has fascinated pharma industry to leverage them in clinical trial for optimizing the timeline and performances. A survey

of participantsfrom CROs, academia, and labs stated that the ~78 percent of them have been using mHealth in clinical trials for more than a year(Digital Trials Category Intelligence, 2020).

Traditional recruitment mechanisms have ended up with 86% failure rate in meeting their recruitment timelines and one third of phase 3 trials fail owing to enrollment issues. This ability to adapt to digital technologies will pave way for success in the future of clinical trials. Accomplishing a digital attitude is vital in order to thrive the transition in the clinical trials space as the market for AI is about to reach $20billion in next 5 years will drive the clinical trials through RWD(Ten years on measuring the return from pharmaceutical innovation 2019, 2019).

The virtual trials will benefit in patient convenience, patient centricity, improved compliance, reduced risk and strong regulatory support as there is a surge in patient engagement during the recent years. It will also tackle the patient recruitment challenges, enrich the process of remote monitoring of patients with real time data capture through virtual assistants and refine patient adherence approaches(Miseta, 2019).

Trials conducted virtually will also reduce the site burden financially as more amount is invested in setting up a site and managing it.

Physicians and researchers must deal with the wealth of data sets from different sources like mobile apps, social media, electronic health records, and wearable devices for clinical and patient reported outcomes. This RWD gathered from the above-mentioned sources will expand the source of evidence aimed at the safety and effectiveness of the medicinal product.

The virtual trial is an alternative approach during this COVID19 pandemic. As a result of this crisis there is decreased access to the physical sites and nearly 30 biopharmaceutical companies have reported disruption in recruitment and engagement. At times like this, conducting a virtual trial becomes essential by incorporating virtual elements telemedicine which in due course makes protocols less burdensome to all the stakeholders(Covid-19: Experts say clinical trials may be affected from enrolment to data analysis, 2020).

LITERATURE REVIEW

The challenges of visiting a physical site that is low participation rate leading to failed enrollment goals can be overcome by virtual trials. In the U.S, patients need to travel more than 50 miles for their site visit. Seventy percent of them live two hours away from the site(Miseta, 2019). In multi-site trials, less than 5% of patients are actively engaging in clinical research, with 49% drop out rate before their study ends(Peterson, 2018). The speed of recruitment was faster through Facebook and AdWords than through traditional mechanism and moreover it is cost effective when patients are identified through EHR and EMR data(Lucchini, 2018) . In order to accelerate the drug development process vast utilization of virtual trials should take center stage (Virtual trials take centre stage during COVID-19, 2020).

According Science 37, the firm's virtual trials have a 97 percent retention rate and speed is faster than traditional trials by 30%(The Benefits and Challenges of Virtual Clinical Trials, 2018). Traditionally, 80% of all trials experience delays due to recruitment challenges and show a 30% dropout rate in standard Phase III trials. The dropout rate decreases to only 5% in virtual trials(Clinical Research Sites, 2019)

The 21st Century Cures Act supports the implementation of RWD for RWE from the virtual trials as the main objective of this act is to bring the products in development stage quickly to the market(Virtual Trials and Real-World Evidence Data Collection: Identifying Core Needs and Defining "Virtual Trials", 2020). In addition, the FDA has announced a pilot pre-certification program with the aim to evaluate a firm's safety in product development so that each product would not require regulation(Johnson, 2020).

CTTI has worked to address the actual and perceived challenges to conducting decentralized clinical trials (DCTs) and Mobile Clinical Trials (MCTs) to engage patients and sites through telemedicine and mobile healthcare providers and created recommendations to help advance widespread use of mobile technologies in DCTs(Decentralized Clinical Trials, 2020).

CTTI has released a set of guidelines to adopt practices that will enhance the quality of the clinical trials by making it virtual through mobile technologies that are defined as mobile applications and other wearables, ingestible, implantable, and portable technologies containing sensors for the remote capture of outcomes data(CTTI Recommendations:, 2019).

Implementing a virtual trial setting will let the sponsors know about the complexity in adherence and compliance towards the medications as the need for evidence outside the

randomized clinical trial setting is in great demand regarding the safety and effectiveness of the drug(Real World Data and Evidence Revolutionize Clinical Research, 2020).

Both FDA and EMA have recognized the potential of RWE and looking for ways to leverage its application in drug development and innovating the clinical trials efficiently.

Wearables will reduce the patient burden by reducing the number of visits to the trial site and allows data to be collected over a wider timespan by continuously tracking the clinical trial participants which significantly contrasts with the traditional trial setting(Messmer, 2017).

The IoMTalso hasten the process of virtual clinical trials, allowing information to be shared between patients and other stakeholders involved in the trial(Medtech and the Internet, 2018). Several technology companies have entered this arena working with pharma to develop cutting edge solutions that allow digitallyenabled trials gather data from the comfort of the patient. In fact, projections for the global wearable healthcare device market suggest it will be worth $4.5 billion by 2020.

As 5G cellular network will be rising in near future, the content developers will find innovative ways to upgrade the interactions for engagement which means that patient experience in virtual clinical trials will become more impactful and engaging with the virtual clinicians and thus the CROs need to strategize the way they conduct trials to motivate the patients.

By 2025, there will be more than 75 billion connected devices, according to a recent Statista IoT forecasting report, thus with the help of virtual assistants, the amount of data collected, and information shared will be enhanced between the patients and doctors in trial settings(Weisman, 2019), (Rey, 2019).

Even if the trial is not completely virtual, it can be made hybrid by incorporating few changes in the way it is conducted where some site visits will be required for initial measurements, consent, or other elements of the trial and then patients will be able to produce or submit data or otherwise participate in a trial remotely(Myshko, 2019). With the emergence of wearable devices such as Fitbits and ResearchKit – Apple's mobile research framework. Each of these solutions has contributed to trial sponsors that can improve clinical trials(Davis, 2020).

U.S Food and Drug Administration (FDA), the National Institutes of Health (NIH), the European Medicines Agency (EMA), China's National Medical Products Administration and several other countries have issued guidelines concerned to the conduct of trials during the pandemic and are in full support of incorporating virtual services.

The alternative approaches to avoid delays in drug development process is to implement DTP/DFP and HHC services in ongoing clinical trials with real time updates in supply chain process to increase protocol compliance(Strien, 2020). FDA also recommends engaging with IRBs and IECs as early as possible since changes should be consistent with the trial protocol and remote monitoring programs should be considered. Conducting trials amid this pandemic is an extremely high degree of difficulty(Miseta, Clinical Trials And COVID-19: Don't Attempt To Do It Alone, 2020). And, as the pandemic and the lockdown drag on, the difficulty in conducting trials will only increasing. The demand for the digital technologies has never been so high as now during the COVID19 outbreak since they can constantly monitor a patient's vital signs and integrate that data alongside patient reported subjective, this powerful device will change the way the trials are being conducted. In a multiple site-based trial adherence is an issue, whereas in virtual trial, it is well above 90% even for covid19 trials, virtual approach seems to be a better option in avoiding exposure to the virus(Underwood, 2020). The ongoing pandemic has not only affected recruitment but also data collection and analysis and it is the phase 1 studies that is held up drastically since enrolment is an issue at such times. At times like this monitoring a patient becomes stressful and virtual study visits helps in overcoming such challenges.

BACKGROUND OF THE STUDY

Pharmaceutical industry is highly influenced by the patient centricity norms and that applies to clinical trials also wherein the completion of a trial is greatly dependent on the patients which can be determined by the recruitment rate and retention rate that determines the enrollment goals. Gradually the clinical trials have evolved from traditional setting through site less, remote monitoring, decentralized and lately stepping into virtual concept which promises to reduce the patient burden and eventually the enrollment goals are achieved as fixed by the other stakeholders.

In the current scenario of pandemic due to COVID 19, the industry needs to embrace virtual clinical trials like never before since the FDA also urges to take this path and has also released the guidelines on how to conduct visits remotely as to overcome the hurdles like interrupted supply chain and closure of sites along with research activities being temporarily ceased. The impact of this novel pandemic is quite severe in the pharmaceutical industry and will reform the way the clinical trials are being conducted now and virtual trials is the answer in order to reduce the rate of contraction of the virus to support flattening the curve. With the rise in demand for the wearables and other digital healthcare technologies coupled with site less concept, virtual clinical trials can be made possible.

Virtual clinical trials will also be the solution for the unmet needs that is existing in the traditional trial setup such as lack of diversity in patient population, patient burden in terms of transport facilities, increased time invested by patients, financial burden, etc. The stakeholders of this field need to strategize the ways to engage patients which can be executed digitally by leveraging the application of wearables, sensors, mobile technologies that collects the endpoints required for the study and enhances the data integrity. These wearables have also proved its worth when it comes to data collection virtually from the patients as it continuously tracks the patients over a wider timespan.

RATIONALE

This study aims at analyzing how the trends of clinical trials in the pharmaceutical industry are evolving with regards to virtual concept over time is proposed. It also aims to analyze the initiatives taken by the pharmaceutical companies to adapt to the shifting focus in the industry.

OBJECTIVES

General objective

To map the current scenario of virtual clinical trials in the pharmaceutical industry in the USA through scoping analysis

Specific objectives

- To analyze the evolutionary trends in clinical trials to achieve patient centricity
- To determine the reasons for the emerging needs to adopt virtual clinical trials concept

RESEARCH METHODOLOGY

Study design:Systematic review through qualitative secondary research

Data collection:Secondary resources using various combinations of relevant strings and keywords using search engine like Google

Duration of the study: 3rd Feb 2020 to 31st May 2020

Source of information: Research studies and publications

Method of analysis: Combination of content and narrative analysis.

Process of research work: Keywords selected to search relevant articles – Virtual clinical trials, remote monitoring, decentralized clinical trials, site less monitoring, pragmatic trials, hybrid trials and direct to patient trials. From the vast list of around 100 articles in the search engine only relevant articles of about 4 that are applicable for the study such as use cases were taken for analysis and rest of about 20 articles were used for literature review.

FINDINGS

Case studies of virtual clinical trials:

Company Name	Trial Name	Year	Details
Pfizer	REMOTE trial	2011	The REMOTE trial is the first "virtual" clinical trial under an IND application that used digital technologies like to step into patient recruitment, enrollment, and collection of study data without requiring patients to visit a physical study site. The clinical trial was designed to assess the safety and efficacy of Detrol LA (tolterodine tartrate), a treatment for overactive bladder. But the trial failed to advance from pilot study since the patient population included mostly the elderly and they had very little acquaintance with the mobile phones facilities as compared to younger adults.
Sanofi	VERRKO	2015	This study was used to test online platform, wireless glucose meter. VERKKO.All the patients were recruited through Facebook. Before signing the electronic informed consent form the patients were selected and reviewed properly. The selected patients could review the electronic consent form before reviewing and study materials and other training materials were delivered to patients through Clinpal account established by eClinical health Ltd.
Janssen	Canagliflozin: (CHIEF-HF)	2020	Janssen Pharmaceuticals and PRA Health Sciences recently designed the first completely decentralized clinical trial, to assess the effectiveness of INVOKANA in adults with heart failure. The recruitment process will start recruiting in early

			2020 and relies on PRA's patient facing mobile platform to remotely monitor and analyze patient healthcare data and patient – reported outcomes via smartphones and wearable devices. This study setup will allow patients to engage well from their homes in the study as their routine physical activities will be recorded in the wearables and have facilities to connect with their healthcare stakeholders online. These integrated networks of technology will allow researchers to gather patient data in real time.
LabCorp	LabCorp's virtual trial	**2020**	Laboratory Corporation of America Holdings (LabCorp) is partnering with software provider Medable to accelerate the acceptance of virtual clinical trials to reduce the dropout rate of study participants from clinical trials during the ongoing COVID 19 pandemic. Labcorp's drug development unit Covance will expand its decentralized trials ecosystem by teaming up with Medable, a modular software platform to facilitate engagement between clinical research investigators and patients. This approach will help the organization to maintain the proposed timelines.

Other initiatives:SCIENCE 37 partnerships with big players – Big pharma companies like Sanofi, Novartis, UCB, Boehringer Ingelheim and Eli Lilly have teamed up with Science 37 to conduct decentralized and virtual clinical trials. Science37 NORA (Network Oriented Research Assistant) is capable of leveraging telehealth platforms and mobile technologies and integrate them to collect data in a streamlined manner. Thus, it reduces the burden of travel and frequent visits for the patients and as such NORA's platform is a patient centric one than the conventional site centric trials. In March 2018, Novartis announced that it has broadened its agreement with Science 37 to conduct site less trials. And to note that Novartis had made an early investment in NORA to execute virtual clinical trials. Through this recent expansion of the alliance, Novartis has

announced that it will conduct a minimum of 10 virtual clinical trials through this partnership. Boehringer Ingelheim has also announced to scale up this partnership by expanding the virtual trial capabilities in collaboration with Science 37's NORA or Science 37's remote clinical trial model site, Metasite internationally.

CONCLUSION

The COVID 19 pandemic is continuing to disrupt the traditional clinical trials. The international bodies directly influencing the healthcare ecosystem are focusing on system efficiencies to deliver the healthcare services in a cost efficient and innovative way during this ongoing COVID 19 pandemic. And virtual trial is a promising solution which can be adopted by the pharmaceutical industry not only in this current pandemic but also to make it sustainable in future. Though the shift of clinical research from a controlled environment to a dynamic space like patient's home will be a challenge, the parallel explosion of digital technologies like wearables and other mobile based technologies will offer many more possibilities. The ongoing pandemic has well demonstrated the benefits of virtual trails and made the stakeholders of clinical trials space to realize that its worthy enough to invest time and efforts in virtual clinical trials.

And as there are lot of virtual trials services organizations blooming, it clearly shows there is a spike in the demand for site less clinical trials.Virtual clinical trials symbolize a new way of collecting safety and efficacy data throughout the execution process by strengthening the data gathered from mobile apps, other social media platforms thereby the process from recruitment till analyzing the clinical endpoints are streamlined. While it is well understood that virtual concept in clinical trials space would require sites to support in house staff, the remote concept proves to be more cost effective than the traditional setup.

RECOMMENDATIONS

In the current dynamic situation that has evolved due to this COVID-19 pandemic, the need for proactive approach is highly appreciated by the regulatory bodies as well.

On the same lines virtual trials are in high demand which can be implemented by the pharmaceutical industry since it resonates with the social distancing measures to a greater extent.

For the same reason as mentioned above, a collaborative planning is required in order to mitigate the impact of COVID-19 on patient centricity.

Virtual clinical trials should include telemedicine, real world data and evidence by leveraging digital technologies.

The protocol for virtual clinical trials should be carried out electronically and must be compliant with HIPPA (The Health Insurance Portability and Accountability Act) guidelines.

LIMITATIONS

Not enough research articles are published around the scope of virtual clinical trials. The reasons could be lack of awareness amongst the stakeholders in the past and lack of understanding of the unmet needs of the participants. Thus, I could not deep dive to gather enormous data since the current articles are majorly focused on the scope of virtual concept and not the use cases of the same.

REFERENCES

1. *Clinical Research Sites.* (2019). Retrieved from virtrial: https://virtrial.com/wp-content/uploads/2020/02/virtrial-whitepaper-hi-quality.pdf
2. *CTTI Recommendations:*. (2019, febraury). Retrieved from https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/ctti_recommendations_-_mct_engaging_patients_and_sites_final.pdf
3. Davis, T. (2020). *Getting the Most out of Wearable.* Retrieved from ert.com: https://www.ert.com/wp-content/uploads/2018/02/ERT_JCS_Getting_Most_out_of_Wearables_Feb_2018.pdf
4. *Decentralized Clinical Trials.* (2020). Retrieved from ctti-clinicaltrials.org: https://www.ctti-clinicaltrials.org/projects/decentralized-clinical-trials
5. Johnson, T. (2020). *The life of a virtual clinical trial participant*. Retrieved from Hallorancg: http://www.hallorancg.com/blog/virtual-clinical-trials
6. Lucchini, C. (2018, june). Industry embraces the virtual trial platforms.
7. *Medtech and the Internet.* (2018, july). Retrieved from deloitte: https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-medtech-iomt-brochure.pdf
8. Messmer, K. (2017, november). *Wearable Devices and Mobile Technology in.* Retrieved from evidera: https://www.evidera.com/wp-content/uploads/2017/11/Wearable-Devices-and-Mobile-Technology-in-Clinical-Trials.pdf
9. Miseta, E. (2019, november 4). Will Virtual Trials Mean The End Of CROs? Retrieved from Clinical leader: https://www.clinicalleader.com/doc/will-virtual-trials-mean-the-end-of-cros-0001
10. Miseta, E. (2020, march). Clinical Trials And COVID-19: Don't Attempt To Do It Alone.
11. Myshko, D. (2019, march). Wearables In Clinical Trials.
12. Peterson, M. (2018, october). How full virtual clinical trials can become reality in the next 10 years.
13. *Real World Data and Evidence Revolutionize Clinical Research.* (2020). Retrieved from obviohealth: https://www.obviohealth.com/2020/01/20/real-world-data/
14. Rey, C. M. (2019, march). Wearable Data Revolution.
15. Strien, A. v. (2020, june). COVID-19: Keeping Clinical Trials Moving.
16. *The Benefits and Challenges of Virtual Clinical Trials*. (2018, november). Retrieved from https://www.anjusoftware.com/about/all-news/insights/virtual-clinical-trials
17. Underwood, G. (2020, april). Virtual trials take centre stage during COVID-19.

18. *Virtual Trials and Real-World Evidence Data Collection: Identifying Core Needs and Defining "Virtual Trials"*. (2020). Retrieved from evidera: https://www.evidera.com/virtual-trials-and-real-world-evidence-data-collection-identifying-core-needs-and-defining-virtual-trials/

19. Weisman, N. (2019, january). *The Clinical Research Transformation has Begun… Are You Ready?* Retrieved from continuumclinical: https://continuumclinical.com/blog/the-clinical-research-transformation-has-begun-are-you-ready